Aarhus University
Aarhus Graduate School of Health Sciences

PHD DAY
13 JANUARY 2012

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Welcome

It is our pleasure to welcome students, faculty and guests to the PhD Day 2012. A special welcome to all PhD students and their supervisors as this year's theme is 'Successful supervision – a two-way process'. Good supervision is essential for a successful degree programme. It is our belief that a positive and productive collaboration between supervisor and PhD student is one of the most important aspects of research education. As a pioneer in research education Health has more than 30 years of experience, and central to the consistent quality of the education offered here at Health are our supervisors. These are researchers employed at Health or Aarhus University Hospital recognized internationally for their results and academic knowledge. Similarly, the importance of dedicated and ambitious PhD students prepared to take the initiative in the collaboration can not be underestimated.

To speak on 'Successful supervision – a two-way process' we have invited Professor Emeritus Gunnar Handal from Oslo University and Associate Professor Gitte Wichmann from the Centre for Teaching Development and Digital Media here at Aarhus University. Gunnar Handal is behind several publications on supervision in research education as is Gitte Wichmann, who is also a former PhD study counsellor at Health. Moderator will be Professor Berit Eika, vice-dean of education at Health.

Skou lecturer will be the esteemed Professor Sir Andrew McMichael, an expert on the immune system response to viruses such as HIV, and Director of the Weatherall Institute of Molecular Medicine at Oxford University. As a PhD in immunology from 1974 and a knight from 2008 for his contribution to medical science, he has been invited to speak of supervision, describing also his own career.

As is evident from the abstracts presented in this programme book the Graduate School of Health, Aarhus University provides a vibrant scientific environment ready to meet new challenges and offering many opportunities. The PhD projects are an important part of the research activities at Health, and we hereby acknowledge the contribution of the PhD students to the high quality research done here.

Last but not least, we warmly thank all those who have taken the time to participate and help make this PhD Day a leading event.

Professor Kimmo Jensen
Chairman of the Organizing Committee
Health, Aarhus University

Professor MSO Lise Wogensen Bach
Vice-dean and Head of Graduate School
Health, Aarhus University

Professor Allan Flyvbjerg
Dean
Health, Aarhus University

Practical Information

Practical information:

- Lunch will be held in the Lake Auditorium Building.
- Posters will be shown in the Lake Auditorium Building, the Bartholin Building
- Posters should be hung between 4.30pm and 8pm on January 12th or between 7.30am and 8am on January 13th. All posters must be taken down immediately after the closing of the conference.
- Oral presenters for sessions O1-O5 must meet in the auditorium concerned between 7.30am and 8am on January 14th to save their presentation onto the auditorium hard disk.

Organizing committee:

- Claus Gravholt, Department of Endocrinology, Institute of Clinical Medicine
- Grethe Elholm, PhD student, Department of Environmental and Occupational Medicine, School of Public Health
- Martin Skøtt, PhD student, Institute of Biomedicine
- Kristina Laut, PhD student, Institute of Clinical Medicine
- Kimmo Jensen, Department of Physiology and Biophysics
- Søren Gregersen, Department of Endocrinology and Metabolism, Institute of Clinical Medicine
- Thomas Vorup-Jensen, Department of Medical Microbiology and Immunology
- Lene Birkegaard Pedersen, PhD Administration
- Tanja Hansen, PhD Administration

Programme

08.15 Welcome by Allan Flyvbjerg, Dean of Aarhus Faculty of Health Sciences (Lake Auditorium)

08.20 Welcome by Anna Sellmer Sørensen, Chairman of the PhD Association (Lake Auditorium)

08.25 Welcome by Kimmo Jensen, Chairman of the Organizing Committee (Lake Auditorium)

08.30 Invited speakers on "Successful supervision – a two way process" (Lake Auditorium)
Moderated by Berit Eika, Vice-dean for education, Aarhus Faculty of Health Sciences

Gunnar Handal, Professor Emeritus, Oslo University
Gitte Wichman, Associate Professor, PhD, Aarhus University

09.45 Poster session part 1 and oral presentations (Lake Auditorium & Bartholin Building)

Poster session part 1
P01, P03, P05, P07, P09, P11, P13: Lake Auditorium
P15, P17, P19, P21, P23, P25, P27: Bartholin Building

Oral presentations
Session O1: Auditorium 1 Per Kirkeby, Lake Auditorium
Session O2: Auditorium 2 Merete Barker, Lake Auditorium
Session O3: Auditorium 3 Jeppe Vontillius, Lake Auditorium
Session O4: Auditorium 4 Eduard Biermann, Lake Auditorium
Session O5: Auditorium 101 Samfundsmedicinsk, Bartholin Building

11.15 Lunch

11.45 Poster sessions part 2 and coffee

Poster session part 2
P02, P04, P06, P08, P10, P12: Lake Auditorium
P14, P16, P18, P20, P22, P24, P26, P28: Bartholin Building

13.15 Skou Lecture by Professor Sir Andrew McMichael
Chaired by Allan Flyvbjerg, Dean of Aarhus Faculty of Health Sciences

14.15 Fogh Nielsen Prize Competition
Chaired by Søren Kragh Moestrup, Chairman of the Fogh Nielsen board, and Anna Sellmer Sørensen, Chairman of the PhD Association

15.00 Hanstedgaard Fund Prize and Misses Anna and Dagny Hjerrild scholarship for the elimination of animal testing in scientific research
Chaired by Allan Flyvbjerg, Dean of Aarhus Faculty of Health Sciences

15.30 Closing remarks by Lise Wogensen Bach, Head of Graduate School

18.00 Dinner and presentation of prizes in 'Stakladen'.

22.00 Band and dance

The Skou lecture

Sir Andrew McMichael qualified in Medicine from Cambridge and St Mary's Hospital Medical School in 1968 and obtained a PhD in Immunology at NIMR supervised by Ita Askonas and Alan Williamson in 1974. He first showed that virus specific CD8 T cells were HLA restricted and, later, Alain Townsend in his group demonstrated that influenza virus derived peptides were presented to T cells by MHC class I molecules.

In recent years he has studied the T cell response to both influenza virus and HIV, with a particular interest in HIV escape from T cell recognition during acute infection. He has also focussed on HIV vaccines and pandemic influenza. His group has also been involved in developing novel methods for measuring T cell responses, such as HLA tetramer staining.

He is Director of the Weatherall Institute of Molecular Medicine in Oxford University and founded the Medical Research Council Human Immunology Unit. He was knighted in 2008 for services to medical sciences and is a Fellow of both the Royal Society and the Academy of Medical Sciences.

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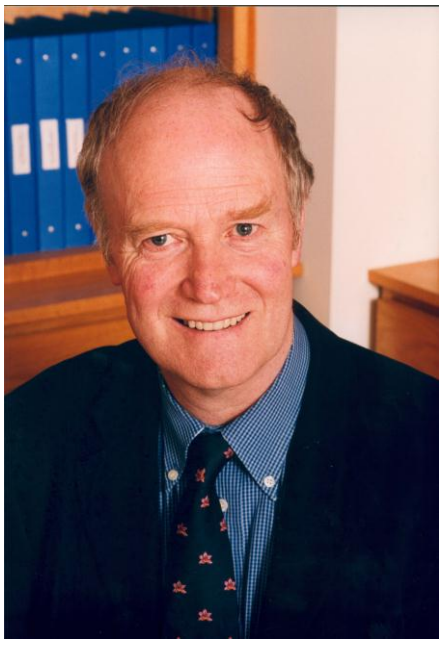

Aarhus Graduate School of Health Sciences

Aarhus Faculty of Health Sciences is one of the four main academic areas at Aarhus University and comprises a number of pre-clinical departments within biomedicine and public health, a department of odontology, and a department of clinical medicine located at the Aarhus University Hospital – a collaboration between the Faculty of Health Sciences and the health care region of central Denmark. The Aarhus Graduate School of Health Sciences was established in 1996, and was based on a tradition of providing quality postgraduate courses started in the 1970s. The Aarhus Graduate School of Health Sciences is headed by the Vice-dean of Talent Development in close collaboration with the PhD committee and the graduate programme leaders. The school has about 600 PhD students shared between the 12 graduate programmes and 100 research year students.

Research training at both pre- and postgraduate level at the Faculty falls under the Aarhus Graduate School of Health Sciences – a multidisciplinary graduate school with long-standing traditions for recruiting students from the entire health science area. The graduate school aims to give the individual students broad knowledge of scientific theories, methodologies and tools required for health science research, and to develop their ability to independently address scientific issues.

Across departmental boundaries 12 graduate programmes help ensure that all PhD students at the faculty are part of a relevant and challenging environment: Membrane Transporters and Receptors, Molecular Metabolism and Endocrinology, Public Health, Haematology, Inflammation and Infection, Cardiovascular, Laboratory Medicine, Neuroscience, Oncology, Translational Molecular Medicine, Odontology, Orthopaedics and Rheumatology, and Clinical Medicine. A unified approach at graduate school level ensures a consistent level of quality of the PhD education, while thematic and cross-disciplinary graduate programmes guarantees the availability of cross-disciplinary resources.

The graduate school offers three-year PhD programmes as well as four-year and five-year integrated MD/PhD programmes. In addition, the school offers PhD programmes for combination with clinical work or a specialist training position. The research year is another offer to undergraduate medical students, who wish to take a year off to complete a research project under supervision. Four times a year a general call for grant applications is announced. Depending on external funding the general call is supplemented by specialized calls.

All PhD students at HEALTH are members

including you!

We work on improving your PhD education at HEALTH.

Main activities include

- **Collaboration with the Graduate School of Health to**
  - improve PhD courses
  - facilitate studying abroad
  - influence the structure of our PhD education

- **Organizing ”after-work meetings”**
  - 3 meetings each term with interesting speakers

- **Co-organizer of the PhD day.**

The PhD association has a board of 11 PhD students. If you are interested in joining our work or just have good ideas please contact us at kontakt@phdforeningen.dk

We look forward to seeing you!

Studenterforskning.dk

Selskab for Medicinsk Studenterforskning

Society for Medical Student Research

(Selskab for Medicinsk Studenterforskning)

Society for Medical Student Research (SMS) is an independent organization of medical students with interest in medical research.

The object of the society is to disseminate and facilitate pregraduate medical research.

SMS organizes courses in experimental surgery (pigs and rodents) and information events where medical students can meet potential supervisors for a future research year.

SMS manages a web-site (www.studenterforskning.dk) that coordinates research year projects and distributes contact between supervisors and potential prospective research year students.

SMS hosts in March 2012 the fourth national Danish conference for pregraduate medical research, where medical students nationwide are invited to present their research and network with other students. Find more information on www.studenterkongres.dk.

Studenterforskning.dk

Selskab for Medicinsk Studenterforskning

Student counsellor for PhD students

Surviving you dissertation

From time to time it is more than a book title.

In the knowledge that studying for a PhD can be an overwhelming challenge, the Aarhus Faculty of Health Science has established a student counsellor for PhD students. What would you answer if I asked:

Is it difficult to plan your daily work?

Are things not working?

Is it hard to collaborate with your supervisor?

Do you find your situation as a PhD student difficult or unsatisfactory?

I am always an interested listener. As PhD student counsellor I am a professional interlocutor. Conversations with me are confidential and anonymity is promised. It is not an alternative to the professional research supervision. By means of conversations, the counsellor can help students become aware of what they perceive as difficult and why. This is done in close collaboration with the Secretary of The Graduate School of Health Sciences if the process related issues have administrative elements. The intention is to help PhD students gain clarity, come to terms with their situation. It is also to help them to see other opportunities, if they experience personal problems or other difficulties related to the process of working and studying as a PhD student. The counsellor can also assist students to make competent decisions.

You are always welcome to contact the PhD student counsellor!

Sometimes sooner is better than latter - no problem is too small for a talk.

Personal contact: Sanne Angel

phdstudievejleder@sun.au.dk

Phone: 8942 4452

International Helpdesk and the Staff Mobility Unit at International Centre

In close collaboration with AU Human Resources, the Staff Mobility Unit helps foreign researchers (including PhD students) and their families overcome the practical challenges tied to their life in Denmark. As part of this, the unit operates a service desk and an extensive portal for international and Danish PhD students admitted to AU.

The Staff Mobility Unit assists international staff and PhDs through social and cultural events, counseling AU researchers planning a period abroad, counseling about issues of relevance for the family, including job for spouse, international schools and kindergarten etc.

The Staff Mobility Unit furthermore assists international staff and PhD students through guidance with paperwork and practical challenges during their stay in Denmark, including health insurance, extension of residence and work permits etc.

Lastly, the unit organizes social activities for staff and their families through the University International Club (UIC) and in cooperation with the PhD Activities Group.

For further information about the Staff Mobility Unit and the service helpdesk, see au.dk/IC

The PhD-House and PhD Café at Dale's Café

The PhD House is located in the Dale T. Mortensen Building (Høegh-Guldbergs Gade 4). The PhD-House offers a combination of administrative services, lecture rooms for PhD courses on transversal skills and a café for young researchers at Aarhus University. Furthermore, the PhD associations have the possibility to use the PhD House's facilities to hold events.

The PhD House is thus a focal point for national and international PhD students, where they can meet both professionally and socially.

The PhD House contains:

- Dales Café, which offers quality coffee, sandwiches and a wide selection of beers
- Conference facilities for PhD courses
- IC Dormitory for international PhD students
- Office facility for AU PhD associations
- A service desk for PhD students at the International Centre
- AU housing department at the International Centre dealing with housing matters for international PhD students

Every Thursday there is a PhD-Café from 4pm to 6pm, where all PhD's are very welcome to visit Dale's Café. This is an opportunity to meet both Danish and international PhD-students in a relaxing atmosphere.

For further information about the PhD-house and Dale's Café, see phd.au.dk

Det Sundhedsvidenskabelige Bibliotek – Library of Health Sciences

Your library!

www.statsbiblioteket.dk

The library provides help and guidance on information and literature search

- Fast and easy finding of and access to relevant literature
- E-alerts with table of contents from your favourite journals
- E-alerts matching the keywords of your project
- Individual instruction and help for literature search designed for your specific project
- PhD course '*Literature search in medical databases*'

Just contact us…

Library of Health Sciences
Aarhus University / The State and University Library
The Victor Albeck Building, Vennelyst Boulevard 4, 8000 Århus C

Phone: 8946 2362
E-mail: svb@statsbiblioteket.dk

Session Chairmen

Fogh Nielsen prize competition	Søren Kragh Moestrup, Anna Selmer Sørensen
O1	Thomas G Jensen, Randi Groslier Bjælde & Martin Gottliebsen
O2	Christian Aalkjær, Annette Langager Høgh & Esben Laugesen
O3	Bodil Hammer Bech, Jakob Jakobsen, Maiken Kudahl Larsen & Matias Grynderup
O4	Jens O.L. Jørgensen & Dariusz Orlowski
O5	Marina Romero-Ramos, Niels Fristrup & Anders Kirch Dige
P1	Mai Marie Holm, Muhammad Umar Cheema, Sabina Jelen & Carina Henriksen
P2	Britt Elmedal Laursen & Louise Wamberg
P3	Jesper Hjortdal, Xiaoping Chen & Carina Agerbo Rosenberg
P4	Karin Birkenkamp-Demtröder, Chris Bath Søndergaard & Anders P. Søndergaard
P5	Ole Bækgaard, Dorte Guldbrand Nielsen & Regina Gonzalez Dosal
P6	Annelli Sandbæk, Peter Hjorth & Anne Sophie Ågård
P7	Jør Olsen, Connie Berthelsen & Marie Louise Svendsen
P8	Kim Overvad, Berit Hvass Christensen & Sofie Gry Pristed
P9	Svend Sabroe, Anette Werner
P10	Vivi Schlünssen, Anne-Birgitte Vogelsang & Lisa Gregersen Østergaard
P11	Kari Tanderup, Christina Malmose Stapelfeldt & Tue Fryland
P12	Michael Borre & Stefan W. Harders
P13	Lise Lotte Hansen & Peter Sandegaard Skyt
P14	Helle H. Damkier & Anette Luther Christensen
P15	Jacob Fog Bentzon & Christian Alcaraz Frederiksen
P16	Vladimir Matchkov, Lars Jakobsen & Niels Ramsing Holm
P17	Jan Blaakær, Kari Konstantin Nissen & Stephen Austin
P18	Jens Randel Nyengaard, Karina Bendixen & Kathrine Just Andersen
P19	Morten Nielsen & Louise Buur Lund

P20	Helle Prætorius, Jan Danz & Marie Bagger Bohn
P21	Marianne Hokland, Thomas Damgaard Sandahl & Asger Granfeldt
P22	Eskild Petersen, Rikke Olesen & Anne-Cathrine Bareid Østby
P23	Søren Paludan, Louise Hauge Matzen & Christina Bisgaard
P24	Bente Jespersen, Jens Christian Jensen, Anders Jensen & Mai-britt Guldin
P25	Bent Deleuran, Søren Beck Jensen & Annett Andersen
P26	Erling Bjerregaard Pedersen, Jeppe Barckman & Dan Østergaard Pradsgaard
P27	Niels Gregersen & Kirstine Kjær Kirkegaard
P28	Jesper Vuust Møller, Torsten Bloch Rasmussen & Christel Krøigaard

Session Overview

Fogh Nielsen prize competition

Emma Tina Bisgaard Olesen. VASOPRESSIN-INDEPENDENT TARGETING OF AQUAPORIN-2 BY SELECTIVE E-PROSTANOID RECEPTOR AGONISTS ALLEVIATES NEPHROGENIC DIABETES INSIPIDUS

Yonglun Luo. DEVELOPMENT OF BRCA1 KNOCKOUT PIGS AND TRANSCRIPTOME STUDIES OF DISEASE PROGRESSION

Morten Søndergaard Jensen. CRYPTORCHIDISM IN DENMARK: STUDIES OF REGISTRY VALIDITY, DISEASE ETIOLOGY, AND TIMING OF CORRECTIVE SURGERY

Oral session 1 : GP1: Membrane Transporters and Receptors, GP7: Laboratory Medicine, GP11: Tooth, bone and joint diseases .

Chairmen: Thomas G Jensen, Randi Groslier Bjælde (PhD student) & Martin Gottliebsen (PhD student)

O01.01 Ole Halfdan Larsen. COMBINATION OF RECOMBINANT FACTOR VIIA AND FIBRINOGEN CORRECTS THE COAGULOPATHY OF PRIMARY IMMUNE THROMBOCYTOPENIA AT VERY LOW PLATELET COUNTS

O01.02 Jennifer Heather Christensen. THERMOGRAPHY AS A QUANTATIVE METHOD FOR ASSESSING POSTOPERATIVE INFLAMMATION

O01.03 Mette Sørensen. ZOLEDRONATE-IMPREGNATED ALLOGRAFT IMPROVES THE FIXATION OF ORTHOPAEDIC REVISION IMPLANTS

O01.04 Britta Weber. NEW METHODS FOR IDENTIFYING RESPONDERS AMONG PATIENTS WITH NON-CELL LUNG CANCER TREATED WITH ERLOTINIB

O01.05 Rita Marques. THE AVP-STIMULATED NACL ABSORPTION IN MOUSE MEDULLARY THICK ASCENDING LIMB IS ABOLISHED BY THE V2 RECEPTOR ANTAGONIST SATAVAPTAN

O01.06 Mette Laursen. STRUCTURAL INSIGHT INTO THE HIGH AFFINITY BINDING OF CARDIOTONIC STEROIDS TO THE NA^+,K^+-ATPASE

Oral session 2 : GP2: Molecular Metabolism and Endocrinology, GP6: Cardiovascular.

Chairmen: Christian Aalkjær, Annette Langager Høgh (PhD student) & Esben Laugesen (PhD student)

O02.01 Thomas Svava Nielsen. FASTING, BUT NOT EXERCISE, INCREASES ADIPOSE TRIGLYCERIDE LIPASE (ATGL) AND REDUCES G(0)/G(1) SWITCH GENE 2 (GOS2) PROTEIN AND MRNA CONTENT IN HUMAN ADIPOSE TISSUE

O02.02 Jakob Østergaard. MANNAN-BINDING LECTIN IN TYPE 1 DIABETES -

PRODUCTION AND TURNOVER

O02.03 Anna Sellmer Sørensen. URINE OSMOLALITY AS PREDICTOR OF OPEN DUCTUS ARTERIOSUS IN NEONATES LESS THAN 32 WEEKS OF GESTATION

O02.04 Mikkel Vendelbo. METABOLIC ADAPTATIONS TO FASTING IN HUMAN SKELETAL MUSCLE

O02.05 Rebekka Thomsen. REMOTE ISCHEMIC PRECONDITIONING RELEASES A CIRCULATING CARDIOPROTECTIVE FACTOR BUT TARGET TISSUE RESPONSE IS ATTENUATED DUE TO AN INTRINSIC CARDIOPROTECTIVE ACTIVATION IN DIABETIC PATIENTS

O02.06 Runa Hyldgaard Poulsen. ^{99M}SESTAMIBI A POTENTIAL MARKER OF AREA AT RISK AFTER REVASCULARISATION IN AN ISCHEMIC-REPERFUSION PORCINE MODEL.

Oral session 3 : GP3: Public Health, GP10: Translational Molecular Medicine.

Chairmen: Bodil Hammer Bech, Jakob Jakobsen (PhD student), Maiken Kudahl Larsen (PhD student) & Matias Grynderup (PhD student)

O03.01 Dorthe Sørensen. PATIENT EXPERIENCES WITH NON-INVASIVE VENTILATION: A GROUNDED THEORY STUDY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

O03.02 Charlotte Uggerhøj Andersen. PULMONARY HYPERTENSION IN INTERSTITIAL LUNG DISEASE AND CHRONIC OBSTRUCTIVE LUNG DISEASE – NT-PROBNP AND IMPACT ON FUNCTIONAL CAPACITY

O03.03 Grethe Elholm. FARMING EXPOSURES PROTECT AGAINST NEW ONSET OF POLLEN SENSITIZATION IN YOUNG ADULTS

O03.04 Christian Wulff. A RANDOMISED CONTROLLED TRIAL OF HOSPITAL-BASED CASE MANAGEMENT TO IMPROVE CANCER PATIENTS' SELF-RATED QUALITY OF LIFE

O03.05 Elise Røge Nielsen. INVOLVEMENT OF KCNQ K^+ CHANNELS IN HYPOXIC VASODILATATION IN PORCINE CORONARY ARTERIES

O03.06 Raffaella Magnoni. HETEROZYGOUS HSP60 KNOCK-OUT MICE REPRESENT A MODEL OF HEREDITARY SPASTIC PARAPLEGIA TYPE 13

Oral session 4 : GP8: Neuroscience, GP12: Clinical Medicine.

Chairmen: Jens O.L. Jørgensen & Dariusz Orlowski (PhD student)

O04.01 Michael Eriksen Benros. AUTOIMMUNE DISEASES AND SEVERE INFECTIONS AS RISK FACTORS FOR DEPRESSION

O04.02 Yu Wang. SELECTION OF LOWEST INSTRUMENTED VERTEBRA IN DIFFERENT TYPES OF ADOLESCENT IDIOPATHIC SCOLIOSIS

O04.03 Emilia Horjales. INFLUENCE OF EMOTIONALLY-LOADED VISUAL AND GUSTATORY STIMULI ON EXPERIMENTAL JAW-MUSCLE PAIN.

O04.04 Morten Charles. THE IMPACT OF INTENSIVE TREATMENT VERSUS ROUTINE CARE ON CARDIAC AUTONOMIC NEUROPATHY. THE ADDTION-DENMARK STUDY

O04.05 Rune Erichsen. PROGNOSIS OF INTERVAL AND SPORADIC COLORECTAL CANCER IN DANISH PATIENTS: A NATIONWIDE COHORT STUDY.

O04.06 Mette Richner. SORTILINS IN NEUROPATHIC PAIN

Oral session 5 GP5: Inflammation og Infection, GP9: Oncology

Chairmen: Marina Romero-Ramos, Niels Fristrup (PhD student) & Anders Kirch Dige (PhD student)

O05.01 Christine Lodberg Hvas. BRAIN DEATH CAUSES HYPERCOAGULATION - AN EXPERIMENTAL PIG STUDY

O05.02 Martin Skøtt. ACUTE KIDNEY INJURY (AKI) IN RATS WITH PRE-EXISTING CHRONIC KIDNEY DISEASE (CKD) INDUCES A MAJOR INCREASE IN PRO-INFLAMMATORY CYTOKINES (IL-1[BETA], IL-6) AND CHEMOKINES (RANTES, MCP-1) IN KIDNEY AND LUNG

O05.03 Charlotte Rotbøl Bøje. COMORBIDITY IS A STRONG PREDICTOR OF OVERALL SURVIVAL IN HEAD AND NECK CANCER: RESULTS FROM A POPULATION BASED STUDY ON 11,056 RADIOTHERAPY-TREATED HEAD AND NECK CANCER PATIENTS

O05.04 Thomas Reinert. TUMOR-SPECIFIC METHYLATION IN URINE: A PROMISING BIOMARKER FOR EARLY DETECTION OF BLADDER TUMOR RECURRENCE

O05.05 Simon Lønbro. RESISTANCE TRAINING AND DIETARY SUPPLEMENTS AS INTERVENTION FOR REGAINING MUSCLE MASS FOLLOWING RADIOTHERAPY IN HEAD AND NECK CANCER PATIENTS

O05.06 Malene Bek-Thomsen. EVOLUTION OF STREPTOCOCCUS PNEUMONIAE INTO GENETICALLY DISTINCT SUBPOPULATIONS

Poster session 1 GP1: Membrane Transporters and Receptors.

Chairmen: Mai Marie Holm, Muhammad Umar Cheema (PhD student), Sabina Jelen (PhD student) & Carina Henriksen (PhD student)

P01.01 Tine Kjærgaard. INVESTIGATION OF MEGALIN, CUBILIN AND AMNIONLESS IN HUMAN PLACENTA AND THEIR STRUCTURAL, FUNCTIONAL AND MECHANISTIC ROLE IN MATERNAL/FETAL TRANSPORT

P01.02 Lena Lindtoft Rosenbæk. REGULATION OF A NOVEL PHOSPHORYLATION SITE OF NCC AT SERINE 124 BY VASOPRESSIN

P01.03 Gitte Qvist Kristiansen. TARGETING CYTOSTATICS TO CD163-EXPRESSING HISTIOSARCOMA CELLS IN XENOGRAFTED IMMUNODEFICIENT MICE

P01.04 Francesco Trepiccione. ACUTE LITHIUM ADMINISTRATION INCREASES WATER EXCRETION THROUGH ACTIVATION OF MAP KINASES.

P01.05 Sascha Eichendorff. PH-REGULATED INTRACELLULAR DELIVERY OF BIOACTIVE SUBSTANCES TARGETED TO CD163 IN MACROPHAGES

P01.06 Mie Rostved Rasmussen. GENERATION OF A ZEBRAFISH KNOCKDOWN MODEL FOR STUDIES OF ABCC6 AS A POTENTIAL TRANSPORTER FOR CELLULAR EXPORT OF VITAMIN B_{12}

P01.07 Rikke Holm Jensen. NA^+,K^+-ATPASE AMINO ACIDS INVOLVED IN TRANSPORT OF THE 3RD SODIUM ION

P01.08 Kaspar Renÿ Nielsen. POLYMORPHISMS IN INFLAMMATORY MEDIATORS - RELATION TO DISEASE ACTIVITY IN B-CELL DISEASES

P01.09 Søren Brandt Poulsen. ISOLATION OF KIDNEY CONNECTING TUBULE CELLS USING FLUORESCENT-ACTIVATED CELL SORTING

P01.10 Pernille Munk Frandsen. ACTIVATION AND RECEPTOR STUDIES OF HUMAN MAST CELLS IN HEALTHY INDIVIDUALS AND PATIENTS WITH ASTHMA AND ALLERGY

P01.11 Kristian Stødkilde-Jørgensen. STRUCTURAL AND FUNCTIONAL STUDIES OF THE HAPTOGLOBIN-HEMOGLOBIN RECEPTOR

P01.12 Pauline de Bruijn. P2 RECEPTOR EXPRESSION PROFILE IN MOUSE THICK ASCENDING LIMB

Poster session 2 GP2: Molecular Metabolism and Endocrinology.

Chairmen: Britt Elmedal Laursen & Louise Wamberg (PhD student)

P02.01 Jesper Sand Sørensen. RESIDUAL &BETA;-CELL FUNCTION IN CHILDREN AFTER 3-6 YEARS OF DIABETES MELLITUS.

P02.02 Lars Rolighed. CLINICAL AND BIOCHEMICAL VARIABLES DETERMINING BMD IN PRIMARY HYPERPARATHYROIDISM

P02.03 Morten Møller Poulsen. POTENTIAL BENEFICIAL EFFECTS OF RESVERATROL ON OBESITY, METABOLIC SYNDROME AND INFLAMMATION.

P02.04 Marie Juul Ørnstrup. INVESTIGATIONS OF THE EFFECTS OF RESVERATROL ON BONE

P02.05 Jurgita Janukonyte. PHARMACOKINETIC PROFILES OF GROWTH HORMONE (GH) ADMINISTERED AS A BOLUS INJECTION VERSUS A CONTINUOUS INFUSION AND WITH AND WITHOUT EXERCISE IN ADULTS WITH GH DEFICIENCY (AGHD)

P02.06 Ravikiran Mahadevappa. THE ROLE OF MEGALIN IN CISPLATIN INDUCED ACUTE KIDNEY INJURY

P02.07 Mark Reinhard. EFFECT OF INSULIN INFUSION ON LIVER PROTEIN SYNTHESIS DURING HEMODIALYSIS

P02.08 Thomas Nordstrøm Kjær. INVESTIGATIONS OF THE ANTI-INFLAMMATORY EFFECTS OF RESVERATROL STUDIED IN VIVO AND IN VITRO

P02.09 Sara Heebøll. RESVERATROL IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (LIRMOI 3)

P02.10 Zhulin Ma. EFFECT OF NPH INSULIN, INSULIN DETEMIR AND INSULIN GLARGINE ON IGF-1 AND IGFBP PRODUCTION IN PATIENTS WITH TYPE 1 DIABETES: AN OPEN-LABEL, RANDOMISED, TRIPLE CROSS-OVER TRIAL

P02.11 Christian Selmer Buhl. EFFECTS OF 3-4 MONTHS OF SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI)-TREATMENT ON METABOLISM AND HYPOTHALAMIC-PITUITARY-ADRENAL (HPA)-AXIS IN YOUNG MEN BORN WITH LOW BIRTH WEIGHT (LBW)

P02.12 Lærke Egefjord. EFFECTS OF LIRAGLUTIDE ON INTRACEREBRAL AMYLOID DEPOSITION IN ALZHEIMER'S DISEASE

Poster session 3 GP2: Molecular Metabolism and Endocrinology.

Chairmen: Jesper Hjortdal, Xiaoping Chen (PhD student) & Carina Agerbo Rosenberg (PhD student)

P03.01 Anne Kirstine Fisker Pedersen. SAPHENOUS NERVE BLOCKADE: SINGLE SHOT VERSUS CONTINUOUS INFUSION TO SUPPLEMENT A CONTINUOUS SCIATIC NERVE BLOCK AFTER MAJOR ANKLE SURGERY

P03.02 Birgitte Nellemann Sørensen. MECHANISTIC PATHWAYS IN LIPID INDUCED INSULIN RESISTANCE IN SKELETAL MUSCLE

P03.03 Jennie Maria Christin Strid. INCIDENCE, INTENSIVE CARE TREATMENT, AND PROGNOSIS OF PATIENTS WITH STATUS ASTHMATICUS IN DENMARK: A NATIONWIDE COHORT STUDY

P03.04 Susani Rothmann Larsen. CONGENITAL HEART DEFECTS: QUALITY OF LIFE ASSESSMENT - CHILDREN VERSUS PARENTS

P03.05 Marianne Kjær Poulsen. LIPID TURNOVER IN NON-ALCOHOLIC FATTY LIVER DISEASE: EFFECTS OF THE DIET SUPPLEMENTATION RESVERATROL ON LIVER FAT CONTENT, BASAL AND INSULIN STIMULATED FFA AND VLDL-TRIGLYCERIDE METABOLISM IN OBESE

P03.06 Niklas Blach Rossen. NIGHTTIME DOSING OF ANTIHYPERTENSIVE DRUGS IN TYPE 2 DIABETES

P03.07 Anne Cathrine Søndersgaard Thorup . INVESTIGATING THE HEALTH PROMOTING EFFECTS OF VEGETABLES ON PEOPLE WITH TYPE 2 DIABETES AND THE METABOLIC SYNDROME

P03.08 Ermina Bosnjak. CYTOKINE TNF-α INDUCES PROTEIN LOSS AND IMPROVES INSULIN SENSITIVITY IN HUMAN LEG

P03.09 Berthil Frederik Forrest Clasen. GROWTH HORMONE AND LONGEVITY: A SEARCH FOR THE MECHANISM.

P03.10 Jeppe Skov. SHORT-TERM IMPACT OF GLUCAGON-LIKE PEPTIDE-1 ON KIDNEY FUNCTION IN HEALTHY MEN

P03.11 Poul Vestergaard Nielsen. GH SIGNALING I MUSCLE AND FAT AS A FUNCTION OF AGE: A COMPARATIVE STUDY OF STAT, MAPK, SOCS MRNA PI3K, MTOR CONCENTRATION IN YOUNG AND ELDER.

P03.12 Ulrick Espelund. SURVIVAL AFTER BREAST CANCER SURGERY PREDICTED BY INSULIN-LIKE GROWTH FACTOR MEASUREMENTS.

Poster session 4 GP7: Laboratory Medicine, GP3: Public Health

Chairmen: Karin Birkenkamp-Demtrøder, Chris Bath Søndergaard (PhD student) & Anders P. Søndergaard (PhD student)

P04.01 Charlotte Green. EXPERIENCE WITH USE OF A PIG MODEL IN GROIN HERNIA OPERATION TRAINING IN SURGICAL EDUCATION

P04.02 Mie Hessellund Samson. DO ASSAYS FOR THE SAME COMPONENTS GIVE COMPARABLE RESULTS? A COMPARISON BETWEEN COMMERCIAL AND IN-HOUSE ASSAYS FOR TREFOIL PEPTIDES.

P04.03 Alice Østergaard. CHARACTERISATION OF FUNCTIONAL INACTIVE ANTITHROMBIN VARIANTS CAUSING THROMBOSIS - A SUB STUDY OF "NEW TECHNOLOGIES FOR INTERVENTION WITH CONFORMATIONAL DISEASE"

P04.04 Henriette Vind Thaysen. VALIDATION OF THE DANISH VERSION OF THE DISEASE SPECIFIC INSTRUMENT EORTC QLQ-CR38 TO ASSESS HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH COLORECTAL CANCER

P04.05 Kristina Grønborg Laut. "HEALTH TECHNOLOGY DIFFUSION: ACCESS TO PRIMARY ANGIOPLASTY IN THE EU15 COUNTRIES"

P04.06 Anette Tarp Hansen. IN VITRO FERTILIZATION DOES NOT INCREASE THE RISK OF THROMBOSIS: A DANISH NATIONAL COHORT STUDY

P04.07 Helen Nordahl Madsen. IS ANTI MüLLERIAN HORMONE (AMH) RESPONSIBLE FOR THE IMPAIRED FOLLICLE MATURATION IN PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME?

P04.08 Solveig Klok Matthesen. EFFECT OF POTASSIUM SUPPLEMENTATION ON RENAL TUBULAR FUNCTION, AMBULATORY BLOOD PRESSURE AND PULSE WAVE VELOCITY IN HEALTHY MAN

P04.09 Eva Greibe. BIOAVAILABILITY OF VITAMIN B12 IN FISH EGGS; FINDINGS OF AN INDIGESTIBLE B12-BINDER IN RAINBOW TROUT EGGS

P04.10 Therese Koops Grønborg. THE RECURRENCE OF AUTISM IN DANISH FAMILIES

P04.11 Jacob Mørup Schlütter. THE NUMBER OF FETAL CELLS IN MATERNAL BLOOD INCREASES OVERNIGHT AND AFTER EXERCISE

P04.12 Johan Frederik Berg Arendt. CLINICAL AND BIOCHEMICAL ASSESSMENT OF HIGH SERUM VITAMIN B12 LEVELS

Poster session 5 GP6: Cardiovascular, GP9: Oncology.

Chairmen: Ole Bækgaard, Dorte Guldbrand Nielsen (PhD student) & Regina Gonzalez Dosal (PhD student)

P05.01 Martin Bødtker Mortensen. HYPERTENSION AND ATHEROSCLEROSIS - THE MISSING LINK

P05.02 Lotte Abildgaard. MINIMAL RESIDUAL DISEASE MARKERS IN CHILDHOOD ACUTE MYELOID LEUKAEMIA

P05.03 Anja Pagh. THE VALUE OF ROUTINE FOLLOW-UP AFTER TREATMENT FOR HEAD AND NECK CANCER

P05.04 Janus Adler Hyldebrandt. EVALUATION OF THE EFFECT OF THREE DIFFERENT INOTROPIC SUPPORT STRATEGIES IN THE NORMAL AND STUNNED NEWBORN PIGLET HEART ON HEMODYNAMICS AND MYOCARDIAL METABOLISM.

P05.05 Stine Elleberg Petersen. ANO-RECTAL FUNCTION IN PATIENTS WITH PROSTATE CANCER FOLLOWING RADIOTHERAPY OR RADICAL PORSTATECTOMY

P05.06 Søren Haack. DIFFUSION WEIGHTED MRI (DWI) FOR BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER – DETERMINING THE DEGREE OF DISTORTION AT 1.5T AND 3T MRI

P05.07 Xue Lin. GENOME-WIDE TAG-BASED PROFILING FOR MEASUREMENT OF DNA METHYLATION, COPY NUMBER VARIATION AND GENE EXPRESSION

P05.08 Christina Gade. THE INFLUENCE OF CARDIOVASCULAR MORBIDITY ON THE PROGNOSIS OF PROSTATE CANCER. EXPERIENCE FROM A 12-YEAR NATIONWIDE DANISH POPULATION-BASED COHORT STUDY.

P05.09 Sandy Mohamed Ismail Mohamed. FEASIBILITY OF APPLYING ONE TREATMENT PLAN FOR SUCCEEDING FRACTIONS IN IMAGE GUIDED BRACHYTHERAPY IN CERVIX CANCER

P05.10 Søren Ravn Laustsen. DETERMINATION OF BRAIN TOXICITY AFTER RADIOTHERAPY USING ADVANCED 3T MRI.

P05.11 Thomas Larsen. VITAMIN D3 SUPPLEMENTATION IN THE WINTER LOWERS DIASTOLIC BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION AND VITAMIN D DEFICIENCY

Poster session 6 GP3: Public Health.

Chairmen: Annelli Sandbæk, Peter Hjorth (PhD student) & Anne Sophie Ågård (PhD student)

P06.01 Pia Viuf Ørby. CAPE: CO-EXPOSURE OF AIR POLLUTION AND ALLERGENIC POLLEN

P06.02 Trine Allerslev Horsbøl. FACTORS ASSOCIATED WITH WORK OUTCOME FOR SURVIVORS FROM HEMATOLOGICAL MALIGNANCIES – A SYSTEMATIC LITERATURE REVIEW

P06.03 Stina Lou Fleron. SCREENING FOR DOWNS SYNDROME AND THE SOCIAL CONSTRUCTION OF 'INCREASED RISK'

P06.04 Seija Ylijoki-Sørensen. PRESENTATION OF A PH.D. PROJECT: MEDICO-LEGAL AUTOPSY AS A TOOL TO IMPROVE MORTALITY STATISTICS AND HEALTHCARE: COMPARING PRACTICES IN DENMARK AND IN FINLAND.

P06.05 Malene Krogsgaard Bording. CLINICAL DECISION MAKING IN OUTPATIENT MENTAL HEALTH CARE

P06.06 Rasmus Foldbjerg. MECHANISMS OF NANOSILVER TOXICITY

P06.07 Trine Nøhr Winding. PARENTAL SOCIOECONOMIC STATUS AND CHOICE OF EDUCATION AMONG DANISH ADOLESCENTS -THE INFLUENCE OF PERSONAL AND FAMILY CHILDHOOD CONDITIONS.

P06.08 Lene Søndergård Larsen. AN AMBIGUOUS RELATIONSHIP – A QUALITATIVE META-SYNTHESIS OF HOSPITALIZED PATIENTS' EXPERIENCE OF INTERACTION WITH FELLOW PATIENTS.

P06.09 Lene Nyboe. PHYSICAL ACTIVITY IN PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA

P06.10 Mette Vinther Skriver. HBA_{1C} AS PREDICTOR OF MORBIDITY AND ALL-CAUSE MORTALITY IN PEOPLE WITH TYPE 2 DIABETES. A DANISH POPULATION-BASED OBSERVATIONAL STUDY

P06.11 Lena Hohwü. MATERNAL STRESS BY LIFE EVENTS DURING PREGNANCY AND RISK OF OVERWEIGHT OFFSPRING AT THE AGE OF 9-11 YEARS OLD

P06.12 Marianne Johansson Jørgensen. IDENTIFYING KEY TOPICS FOR A DESCRIPTION OF SEXUAL BEHAVIOR AMONG DANISH ADOLESCENTS: A QUALITATIVE STUDY

Poster session 7 GP3: Public Health.

Chairmen: Jør Olsen, Connie Berthelsen (PhD student) & Marie Louise Svendsen (PhD student)

P07.01 Ioanna Milidou. BIRTH WEIGHT (BW), GESTATIONAL AGE (GA), AND INFANTILE COLIC (IC) - THE DANISH NATIONAL BIRTH COHORT

P07.02 Annesofie Lunde Jensen. OSTEOPOROSIS GROUP-EDUCATION: A WAY TO HEALTH MAINTENANCE

P07.03 Anne Sofie Bjerrum. DOES DYAD TRAINING COMPETES WITH INDIVIDUAL TRAINING? A RANDOMIZED, CONTROLLED BRONCHOSCOPY-SIMULATION-STUDY.

P07.04 Kirsten Hansen. CONCERNING CHILDREN OF PARENTS WITH DEPRESSION

P07.05 Charlotte Olesen. GENERIC SUBSTITUTION OF ORAL TABLETS IN ELDERLY IN DENMARK

P07.06 Jette Pedersen. THE EFFECT OF FOLLOW-UP ON NUTRITION INTERVENTION AFTER DISCHARGE IN UNDERNOURISHED GERIATRIC PATIENTS

P07.07 Anne Vested. EFFECTS OF IN UTERO EXPOSURE TO PFOA AND PFOS ON HUMAN SEMEN QUALITY AND HORMONE PROFILE

P07.08 Charlotte Hyldgaard. A RETROSPECTIVE COHORT STUDY OF DANISH PATIENTS WITH INTERSTITIAL LUNG DISEASE: BURDEN, SEVERITY, TREATMENT AND SURVIVAL.

P07.09 Camilla Plambeck Hansen. INTAKE OF RUMINANT FATTY ACIDS AND CHANGES IN WEIGHT AND WAIST CIRCUMFERENCE

P07.10 Bjørn Bay. ASSISTED REPRODUCTION AND CHILD NEURODEVELOPMENT

P07.11 David Høyrup Christiansen. PHYSIOTHERAPY AFTER SUBACROMIAL DECOMPRESSION SURGERY: A SYSTEMATIC REVIEW AND DEVELOPMENT OF A GRADED EXERCISE REHABILITATION PROTOCOL

Poster session 8 GP3: Public Health.

Chairmen: Kim Overvad, Berit Hvass Christensen (PhD student) & Sofie Gry Pristed (PhD student)

P08.01 Connie Timmermann. HOSPITALISED PATIENTS AND AESTHETIC SENSORY IMPRESSIONS

P08.02 Dorthe Hasfeldt-Hansen. NOISE IN THE OPERATING ROOM - A LITERATURE REVIEW

P08.03 Anette Hvenegaard Kjeldgaard. INCIDENT CANCER PATIENTS' USE OF GENERAL PRACTICE

P08.04 Susanne Lemcke. THE EARLY SIGNS OF ADHD IN TODDLERS: A FOLLOW-UP STUDY IN THE DANISH NATIONAL BIRTH COHORT.

P08.05 Else-Marie Dalsgaard. SOCIOECONOMIC FACTORS, PSYCHOSOCIAL FACTORS AND HBA_{1C} LEVEL AMONG PERSONS AT HIGH RISK FOR TYPE 2 DIABETES

P08.06 Ditte Lammers Vernal. A REGISTER- BASED STUDY OF THE OUTCOME OF EARLY ONSET SCHIZOPHRENIA COMPARED TO ADULT ONSET SCHIZOPHRENIA

P08.07 Hanne Mainz. THE RELATIONSHIP BETWEEN NURSE STAFFING AND PATIENT OUTCOME

P08.08 Noora Ronkainen. 'THAT IS WHY I GAVE IN TO AGE MY COMPETITIVE ABILITY BUT NOT MY SOUL!' - THE SEARCH FOR MEANING IN ATHLETIC CAREER AND RETIREMENT

P08.09 Tue Kjølhede. MULTIPLE SCLEROSIS – INFLAMMATORY, NEUROLOGICAL AND MUSCULAR ADAPTATIONS TO HEAVY RESISTANCE TRAINING

P08.10 Rasmus Beedholm Laursen. DANISH FOOTBALL FAN CULTURE – THE DANISH ULTRAS

P08.11 Joe Larner. THE EFFECT OF ECCENTRIC EXERCISE ON CARBOHYDRATE METABOLISM IN ISOLATED SOLEUS AND EDL RAT MUSCLES

P08.12 Jean Farup. THE ROLE OF PROTEIN SIGNALLING AND STEM CELLS IN MUSCLE PROTEIN SYNTHESIS AND RECOVERY RATE AFTER EXCENTRIC EXERCISE

Poster session 9 GP3: Public Health.

Chairmen: Svend Sabroe, Anette Werner (PhD student)

P09.01 Pia Løvschal-Nielsen. SOCIAL RELATIONS OF CHILDREN WITH CANCER DURING TREATMENT AND REHABILITATION AT HOSPITAL

P09.02 Simon Grandjean Bamberger. DERIVED EFFECTS OF GLOBALIZATION ON PSYCHOSOCIAL WORK ENVIRONMENT - A MULTILEVEL LATENT CLASS ANALYSIS STUDY

P09.03 Heidi Cueto. SOCIO-DEMOGRAPHIC AND LIFESTYLE PREDICTORS OF FOLIC ACID AND MULTIVITAMIN SUPPLEMENTATION IN DANISH PREGNANCY PLANNERS

P09.04 Mads Lind Ingeman. THE NON-ORGAN-SPECIFIC CANCER FAST TRACK

P09.05 Kasper Grosen. PREDICTION OF ACUTE AND PERSISTENT POSTSURGICAL PAIN IN PATIENTS UNDERGOING MINIMALLY INVASIVE REPAIR OF PECTUS EXCAVATUM

P09.06 Louise Pape Larsen. LIFE AFTER STROKE

P09.07 Palle Larsen. GUIDELINES FOR NON-PHARMACOLOGICAL REHABILITATION FOR HEART FAILURE PATIENTS AND THE BASIC EVIDENCE - IS THERE A LINK?

P09.08 Malene Outzen. PROSTATE CANCER INCIDENCE AND MORTALITY IN DENMARK 1978-2009

P09.09 Karen Kjær Larsen. SCREENING FOR DEPRESSION IN PATIENTS WITH MYOCARDIAL INFARCTION BY GENERAL PRACTITIONERS

P09.10 Rikke Jørgensen. MEANINGFUL CHANGE WITH THE METHOD GUIDED SELF-DETERMINATION – A RANDOMISED CONTROLLED STUDY FOR PATIENTS DIAGNOSED WITH SCHIZOPHRENIA

P09.11 Nils Bjerregaard. TRANSVERSUS ABDOMINAL PLANE (TAP) KATETER ANLÆGGELSE TIL COLONRESEKTION: ET METODESTUDIE.

P09.12 Michael Smærup Brandt. PERCENTAGE OF VESTIBULAR DYSFUNCTION IN 361 ELDERLY CITIZENS RESPONDING TO A NEWSPAPER ADVERTISEMENT.

Poster session 10 GP3: Public Health.

Chairmen: Vivi Schlünssen, Anne-Birgitte Vogelsang (PhD student) & Lisa Gregersen Østergaard (PhD student)

P10.01 Katja Glejsted Ingstrup. BEREAVEMENT AND CONGENITAL ANOMALIES

P10.02 Vita Ligaya Ponce Dalgaard. EVALUATING A COGNITIVE TREAMENT PROGRAM FOR PATIENTS ON SICK LEAVE DUE TO WORK RELATED STRESS: A RANDOMISED CONTROLLED STUDY

P10.03 Philip Finn Rising Nielsen. ASSOCIATION BETWEEN PARENTAL HOSPITAL-TREATED INFECTION AND THE RISK OF SCHIZOPHRENIA IN ADOLESCENCE AND EARLY ADULTHOOD

P10.04 Rasmus Østergaard Nielsen. DEMOGRAPHIC CHARACTERISTICS FOR 931 PARTICIPANTS INCLUDED IN THE DANO-RUN STUDY: A 1-YEAR OBSERVATIONAL FOLLOW UP STUDY ON RUNNING RELATED INJURIES.

P10.05 Therese Juul. INTERNATIONAL VALIDATION OF THE LOW ANTERIOR RESECTION SYNDROME SCORE (LARS SCORE)

P10.06 Mona Lisa Idriss Kise. ASSOCIATION BETWEEN SOCIOECONOMIC POSITION AND TIME TO DIAGNOSIS OF CANCER

P10.07 Mette Trøllund Rask. TOWARDS A CLINICAL USEFUL DIAGNOSIS FOR MODERATE MEDICALLY UNEXPLAINED SYMPTOMS IN PRIMARY CARE

P10.08 Anna Budtz-Lilly. BODILY DISTRESS SYNDROME: A NEW DIAGNOSIS FOR FUNCTIONAL DISORDERS.

P10.09 Stine Yde Nielsen. Q FEVER SEROLOGY AND PREGNANCY OUTCOME IN WOMEN EXPOSED TO LIVESTOCK ANIMALS

P10.10 Birgitte Blicher Pedersen. POSTSTROKE FATIGUE - DEVELOPING AND TESTING A PROGRAM TO REDUCE AND COPE WITH FATIGUE

P10.11 Kirsten Krabek Frantzen. CARING FOR THE CAREGIVER - A MIXED METHOD STUDY OF PARENTAL TREATMENT PREFERENCES IN AUTISTIC CHILDREN

P10.12 Lone Flarup. USE OF DANISH PRIMARY CARE OUT-OF-HOURS SERVICES BY PATIENTS WITH CHRONIC DISEASES

Poster session 11 GP4: Haematology, GP9: Oncology.

Chairmen: Kari Tanderup, Christina Malmose Stapelfeldt (PhD student) & Tue Fryland (PhD student)

P11.01 Sara Thörnqvist. ROBUST OPTIMIZATION TO ACCOUNT FOR GEOMETRICAL UNCERTAINTIES CAUSED BY INDEPENDENTLY MOVING TARGETS

P11.02 Maria Bach Laursen. THE ROLE OF MIRNA AND AID IN B-CELL MALIGNANCIES

P11.03 Niels Frost Andersen. HEPARANASE AND MULTIPLE MYELOMA – IMPACT OF SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN THE HEPARANASE GENE ON SURVIVAL AND BONE MARROW ANGIOGENESIS

P11.04 Jens Reumert Laurberg. PROGNOSTIC AND PREDICTIVE SIGNIFICANCE OF CELL CYCLE, APOPTOSIS AND DNA DAMAGE RESPONSE REGULATORS IN LOCALLY ADVANCED LYMPH NODE NEGATIVE BLADDER CANCER

P11.05 Christina Daugaard Lyngholm. BREAST CONSERVING THERAPY:

P11.06 Mette Marcussen. CANCER THERAPY INDUCED MUCOSITIS: CELLULAR AND HUMORAL FACTORS INFLUENCE PRESENCE AND HEALING IN CONSECUTIVE MUCOSA BIOPSIES AND BLOOD SAMPLES BY MICROARRAY AND FLOWCYMETRY.

P11.07 Andreas Carus. PREOPERATIVE LEUCOCYTOSIS IS AN INDEPENDENT RISK FACTOR ONLY IN EARLY STAGE NON-SMALL CELL LUNG CANCER (NSCLC)

P11.08 Jesper Thygesen. QUANTITATIVE CT-IMAGING BASED ON CONTRAST MATERIAL ENHANCEMENT

P11.09 Kim Steve Bergkvist. STUDIES OF SMALL DISCRETE POPULATIONS OF B CELLS BY MICROARRAY TECHNOLOGY

P11.10 Eduardo Vázquez Garza. CHARACTERIZATION OF NK-, NKT- AND T-CELLS IN HCMV REACTIVATION OF IMMUNOCOMPROMISED PATIENTS, FOCUSING ON CD94/NKG2A,C,D AND CD56-NEGATIVE NK CELLS

P11.11 Maria Cathrine Corneliussen Vestergaard Schmidt. HYPODONTIA AND OVARIAN CANCER - THE CONNECTION BETWEEN DENTAL AGENESIA AND EPITHELIAL CANCERS, ESPECIALLY OVARIAN CANCER.

P11.12 Martin Bjerregård Pedersen. PERIPHERAL T-CELL LYMPHOMAS – A STUDY TO IDENTIFY CLINICAL, PATHOLOGICAL AND BIOLOGICAL PARAMETERS TO IMPROVE CLASSIFICATION, PROGNOSTIC ASSESSMENT AND TREATMENT STRATEGY

Poster session 12 GP9: Oncology.

Chairmen: Michael Borre & Stefan W. Harders (PhD student)

P12.01 Johanne Lade Keller. CELL ADHESION MOLECULES IN 404 CUTANEOUS MELANOMAS: A TISSUE MICROARRAY STUDY

P12.02 Peter Bondeven Frederiksen. LENGTH OF DISTAL RESECTION MARGIN AFTER PARTIAL MESORECTAL EXCISION FOR UPPER RECTAL CANCER ESTIMATED BY MAGNETIC RESONANCE IMAGING

P12.03 Marie-Louise Feddern. CHRONIC PAIN AFTER RECTAL CANCER TREATMENT

P12.04 Louise Tram Henriksen. PEG-ASPARAGINASE TREATMENT IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA, ALL, IN THE NORDIC COUNTRIES

P12.05 Bente Thoft Jensen. PRE-OPERATIVE NUTRITIONAL RISK IMPACTS SIGNIFICANTLY ON ONE YEAR SURVIVAL FOLLOWING RADICAL CYSTECTOMY

P12.06 Patricia Nielsen. MELANOMA KI67 EXPRESSION BY AUTOMATED IMAGE ANALYSIS: A SIGNIFICANT PROGNOSTIC MARKER

P12.07 Thomas Lyhne Ravkilde. GEOMETRIC ACCURACY OF DMLC TRACKING WITH AN IMPLANTABLE WIRED ELECTROMAGNETIC TRANSPONDER

P12.08 Trine Tramm. PROGNOSTIC FACTORS AND RESPONSE TO RADIOTHERAPY IN HIGH RISK BREAST CANCER: A STUDY OF GENE EXPRESSION IN THE DBCG82BC COHORT

P12.09 Sidse Bregendahl. BOWEL DYSFUNCTION AFTER PREOPERATIVE RADIOTHERAPY AND LOW ANTERIOR RESECTION FOR RECTAL CANCER

P12.10 Martin Skovmos Nielsen. NITI STENT AS A MARKER FOR LUNG TUMOR IN RADIOTHERAPY: PRECISION IN MARKER DETECTION DURING TREATMENT PREPARATION AND DELIVERY

P12.11 Tinne Laurberg. LOCO-REGIONAL RECURRENCE OF BREAST CANCER - A GENETIC STUDY OF AGE-RELATED PROGNOSTIC BIOMARKERS

P12.12 Mohamed Ahmed Hassan. PRELIMINARY RESULTS, QUALITY ASSURANCE & MOLECULAR BIOLOGICAL STUDIES OF PATIENTS WITH HEAD AND NECK CARCINOMA UNDERGOING ACCELERATED RADIOTHERAPY WITH OR WITHOUT NIMORAZOLE IN A RANDOMIZED MULTICENTER TRIAL

Poster session 13 GP9: Oncology.

Chairmen: Lise Lotte Hansen & Peter Sandegaard Skyt (PhD student)

P13.01 Esben Schjødt Worm. ON-LINE USE OF 3D MARKER TRAJECTORY ESTIMATION FROM CONE-BEAM CT (CBCT) PROJECTIONS FOR PRECISE SETUP IN RADIOTHERAPY FOR TARGETS WITH RESPIRATORY MOTION

P13.02 Julie Damgaard Sandahl. HYPERDIPLOIDY IN CHILDHOOD AML ASSOCIATED WITH YOUNG AGE AND AML-M7- A NOPHO-AML STUDY AND LITERATURE REVIEW

P13.03 Lotte Sander. REMOVABLE MR COMPATIBLE PROSTATE MARKER FOR HIGH DOSE RADIOTHERAPY OF PROSTATE CANCER – 3 YEARS RESULTS COMPARED TO STANDARD GOLD MARKERS.

P13.04 Lars Mikael Stensman. ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (ALICCS) - LATE RENAL AND GASTROINTESTINAL EFFECTS AND THEIR PREVENTION IN CHILDHOOD CANCER SURVIVORS

P13.05 Maria Thor. INVESTIGATING THE ASSOCIATIONS BETWEEN LATE RECTAL MORBIDITY AND SIMULATED RECTAL MOTION

P13.06 Katja Maretty Nielsen. TREATMENT RESULTS AND PROGNOSTIC FACTORS IN SOFT TISSUE SARCOMA PATIENTS AT AARHUS SARCOMA CENTER, 30 YEARS EXPERIENCE

P13.07 Hanna Rahbek Mortensen. RISK OF FATAL ASPIRATION PNEUMONIA IN PATIENTS TREATED WITH CURATIVE RADIOTHERAPY FOR HEAD AND NECK CANCER

P13.08 Lotte Bonde Bertelsen. ENDOTHELIAL OUTGROWTH CELLS - HOMING PATTERN AND ASPECTS OF IMMUNO-INCOMPATIBILITY

P13.09 Kasper Jarlhelt Andersen. THE NATURAL HISTORY OF LIVER REGENERATION IN RATS : DEVELOPMENT OF AN ANIMAL MODEL FOR LIVER REGENERATION STUDIES.

P13.10 Trine Grantzau. SECOND PRIMARY CANCER AMONG DANISH WOMEN WITH EARLY BREAST CANCER TREATED WITH POSTOPERATIVE RADIOTHERAPY.

P13.11 Peter Niekerk. DELINEATION OF STEM CELLS IN CHRONIC MYELOID LEUKEMIA; A TOOL FOR IMPROVED MINIMAL RESIDUAL DISEASE MONITORING

P13.12 Jesper Kallehauge. PRELIMINARY RESULTS OF COMPARISON OF DCE-CT AND DCE-MR FOR ADVANCED CERVICAL CANCER

Poster session 14 GP6: Cardiovascular.

Chairmen: Helle H. Damkier & Anette Luther Christensen (PhD student)

P14.01 Christoffer Laustsen. NON-INVASIVE DIABETIC NEPHROPATHIC ASSESSMENT WITH HYPERPOLARISED ^{13}C PYRUVATE

P14.02 Johan Heiberg. POSTOPERATIVE RIGHT BUNDLE BRANCH BLOCKS LONG-TERM EFFECT ON THE HEARTS RIGHT VENTRICLE IN CHILDREN OPERATED FOR VENTRICULAR SEPTAL DEFECT

P14.03 Michael René Skjelbo Nielsen. GENETIC POLYMORPHISMS IN THE LIPOXYGENASE PATHWAY AND THE RISK OF MYOCARDIAL INFARCTION

P14.04 Henrik Vadmann. ATRIAL FIBRILLATION: ABLATION OR SURGICAL TREATMENT II: FAST II. A RANDOMIZED STUDY COMPARING NON-PHARMACOLOGIC THERAPY IN PATIENTS WITH DRUG-REFRACTORY ATRIAL FIBRILLATION REFERRED FOR A FIRST TIME INVASIVE TREATMENT.

P14.05 Asger Andersen. RIGHT VENTRICULAR HYPERTROPHY AND FAILURE ABOLISH CARDIOPROTECTION BY ISCHEMIC PRECONDITIONING

P14.06 Rikke Esberg Kirkfeldt. RISK FACTORS FOR LEAD COMPLICATIONS IN CARDIAC PACING. A POPULATION-BASED COHORT STUDY OF 28,860 DANISH PATIENTS

P14.07 Karl Erik Tilly. THE DIAGNOSTIC VALUE OF ADENOSINE CONTRAST STRESS ECHOCARDIOGRAPHY IN PATIENTS WITH CHEST PAIN OF UNKNOWN CAUSE

P14.08 Anne Sophie Pinholt Kancir. EFFECT OF HYDROXYETHYL STARCH ON RENAL HANDLING OF SODIUM AND WATER, VASOACTIVE HORMONES, BIOMARKERS AND CIRCULATION IN PATIENTS UNDERGOING LAPAROSCOPIC NEPHRECTOMY, RADICAL PROSTATECTOMY OR HIP REPLACEMENT

P14.09 Peter Juhl-Olsen. SYSTOLIC HEART FUNCTION REMAINS DEPRESSED FOR AT LEAST ONE MONTH AFTER ON-PUMP CARDIAC SURGERY

P14.10 Frank Holden Christensen. NO ACTIVITY DURING STATIN TREATMENT IN HEALTHY HUMANS

P14.11 Dirk Troitzsch. PREISCHEMIC HIGH-DOSE CYCLOSPORINE A TREATMENT PROTECTS THE LATISSIMUS DORSI MYOCUTANEOUS FLAP FROM ISCHEMIA-REPERFUSION INJURY: EFFECTS ON TISSUE OXYGENATION AND MITOCHONDRIAL OXIDATION

Poster session 15 GP6: Cardiovascular.

Chairmen: Jacob Fog Bentzon & Christian Alcaraz Frederiksen (PhD student)

P15.01 Sisse Anette Thomassen. SHOULD BLOOD FLOW DURING CARDIOPULMONARY BYPASS BE INDIVIDUALIZED MORE THAN TO BODY SURFACE AREA?

P15.02 Troels Fogh Pedersen. THE EFFECT OF PRECONDITIONING FOR PREVENTION OF PERIOPERATIVE MYOCARDIAL ISCHEMIA IN ABDOMINAL AORTIC ANEURYSMS.

P15.03 Karen Axelgaard Lorentzen. MECHANISMS OF HYALURONIC ACID INDUCED DEVELOPMENT OF VASCULAR PATHOLOGY

P15.04 Dinah Sherzad Khatir. THE ROLE OF RENAL AND PERIPHERAL VASCULAR RESISTANCE IN THE PROGRESSION OF CHRONIC KIDNEY DISEASE (CKD)

P15.05 Carsten Stengaard. THE ROLE OF BIOMARKER ANALYSIS IN THE PRE-HOSPITAL DIAGNOSIS AND TRIAGE OF HEART ATTACK PATIENTS (THE PRE-HAP STUDY)

P15.06 Anne Dorte Blankholm. MR ANGIOGRAPHY WITHOUT GADOLINIUM CONTRAST AGENTS COMPARED TO CT AND ULTRASOUND IN PATIENTS UNDERGOING KIDNEY TRANSPLANTATION. PRELIMINARY RESULTS.

P15.07 Lau Brix. REAL-TIME MOVIE DISPLAY OF GASTRIC VENTRICLE MOVEMENT WITH MRI

P15.08 Janni Majgaard Jensen. URINARY BIOMARKERS FOR MEASUREMENT OF SODIUM- AND WATER CHANNEL ACTIVITY IN THE NEPHRON IN HEALTHY PERSONS AND PATIENTS WITH CHRONIC KIDNEY DISEASE. AN INTERVENTION STUDY WITH ISOTONIC AND HYPERTONIC NACL, THIAZIDE AND AMILORIDE.

P15.09 Olga Kudryavtseva. THE ROLE OF L-TYPE VOLTAGE-DEPENDENT CALCIUM CHANNELS IN THE PHENOTYPIC EXPRESSION OF VASCULAR SMOOTH MUSCLE CELLS

P15.10 Morten Würtz. DOES THE ANTIPLATELET EFFECT OF ASPIRIN DECREASE DURING THE 24-HOUR DOSING INTERVAL?

Poster session 16 GP6: Cardiovascular.

Chairmen: Vladimir Matchkov, Lars Jakobsen (PhD student) & Niels Ramsing Holm (PhD student)

P16.01 Michael Kanstrup Dahl. AMPLIFICATION OF RESPIRATORY INDUCED ARTERIAL PRESSURE VARIATIONS DURING SPONTANEOUS BREATHING – A METHOD TO ASSESS FLUID RESPONSIVENESS?

P16.02 Sanne Bøjet Larsen. THE ASPIRIN PARADOX - ANTIPLATELET EFFECT OF ASPIRIN IS REDUCED IN PRIOR ASPIRIN USERS

P16.03 Bent Roni Ranghøj Nielsen. SHORT TERM MANIPULATION OF INTRACELLULAR MYOCARDIAL LIPID CONTENT: EFFECT ON LEFT VENTRICULAR FUNCTION, CONTRACTILITY, EXERCISE CAPACITY AND OXYGEN CONSUMPTION IN HEART FAILURE PATIENTS WITH TYPE 2 DIABETES.

P16.04 Nikolaj Grøndal. THE CARDIAC CYCLE IS A MAJOR CONTRIBUTOR TO VARIABILITY IN SIZE MEASUREMENTS OF ABDOMINAL AORTIC ANEURYSMS BY ULTRASOUND

P16.05 Anders Sommer Knudsen. EMPIRIC VERSUS IMAGING GUIDED LEFT VENTRICULAR LEAD PLACEMENT IN CARDIAC RESYNCHRONIZATION THERAPY: STUDY PROTOCOL SYNOPSIS

P16.06 June Anita Ejlersen. 2D STRAIN ANALYSIS IN PATIENTS WITH REDUCED IMAGE QUALITY ON ECHOCARDIOGRAMS: EFFECT OF MICROBUBBLE CONTRAST (MBC) ON SEGMENTAL TRACKING

P16.07 Anders Jorsal. CARDIAC AND METABOLIC EFFECTS OF GLP-1 TREATMENT IN PATIENTS WITH CHRONIC HEART FAILURE

P16.08 Jo Bønding Andreasen. EX-VIVO RESPONSE TO BLOOD PRODUCTS AND HAEMOSTATIC AGENTS IN WHOLE BLOOD COAGULATION AFTER CARDIAC SURGERY IN CHILDREN

P16.09 Thomas Andersen Rix. VALIDITY OF THE DIAGNOSES ATRIAL FIBRILLATION AND ATRIAL FLUTTER IN THE DANISH NATIONAL PATIENT REGISTRY

P16.10 Morten Engholm Pedersen. VASOACTIVE EFFECTS OF CYSTAMINE

P16.11 Jonas Agerlund Povlsen. ISCHAEMIC CARDIOPROTECTION: PATHOGENIC MECHANISM IN TYPE 2 DIABETES MELLITUS?

P16.12 Rozh Husain Al-Mashhadi. ADVANCED ATHEROSCLEROSIS IN TRANSGENIC HYPERCHOLESTEROLEMIC YUCATAN MINIPIGS

Poster session 17 GP8: Neuroscience.

Chairmen: Jan Blaakjær, Kari Konstantin Nissen (PhD student) & Stephen Austin (PhD student)

P17.01 Sanne Kjær Vandborg. MEMORY AND EXECUTIVE FUNCTIONS IN PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER ARE NOT ASSOCIATED WITH OUTCOME OF COGNITIVE BEHAVIORAL THERAPY

P17.02 Ditte Olsen. SORLA REGULATES GDNF SIGNALLING THROUGH RETROGRADE SORTING OF GDNF AND GFR1

P17.03 Line Bie Mertz. ANGELMAN SYNDROME: GENOTYPE COMPARED WITH PHENOTYPE.

P17.04 Marie Louise Schmitz. LONG-TERM OUTCOME IN ISCHEMIC STROKE PATIENTS TREATED WITH TROMBOLYSIS IN DENMARK: A NATIONWIDE FOLLOW-UP STUDY

P17.05 Lise Neerup-Jensen. NEUROPATHY AND PAIN FOLLOWING DOCETAXEL AND OXALIPLATIN

P17.06 Søren Dinesen Østergaard. THE VALIDITY OF THE SEVERITY-PSYCHOSIS HYPOTHESIS IN DEPRESSION

P17.07 Nicolai Ladegaard. SOCIAL COGNITIVE DEFICITS IN DEPRESSION

P17.08 Eugenio Gutierrez Jimenez. BRAIN BLOOD FLOW PATTERNS IN ALZHEIMER'S DISEASE

P17.09 Zita Dósa. EFFECT OF PRENATAL CORTICOSTEROID EXPOSURE ON THE GABAERGIC INHIBITION IN RAT HIPPOCAMPUS

P17.10 Karen Lund. PLACEBO RESPONSE IN ANALGESIC TREATMENT: EXPERIMENTAL AND CLINICAL

Poster session 18 GP8: Neuroscience.

Chairmen: Jens Randel Nyengaard, Karina Bendixen (PhD student) & Kathrine Just Andersen (PhD student)

P18.01 René Ernst Nielsen. NEUROLEPTIC MALIGNANT SYNDROME – AN ELEVEN YEAR LONGITUDINAL CASE-CONTROL STUDY

P18.02 Eva Hauge. TOPICAL VALRUBICIN APPLICATION REDUCES TPA-INDUCED SKIN INFLAMMATION IN A MURINE MODEL

P18.03 Sarah Holmboe. ACUTE INOTROPIC EFFECTS OF ILOPROST IN THE PRESSURE OVERLOADED, HYPERTROPHIC AND FAILING RIGHT HEART

P18.04 Konstantin Kazankov. SOLUBLE CD163, A MARKER OF ACTIVATED MACROPHAGES, AS A PROGNOSTIC MARKER IN NON-ALCOHOLIC FATTY LIVER DISEASE

P18.05 Kasper Pryds. CHRONIC REMOTE ISCHEMIC PRECONDITIONING

P18.06 Mohit Kothari. MOTIVATIONAL FACTORS: INFLUENCES MOTOR BEHAVIORAL LEARNING

P18.07 Jesper Jeppesen. DETECTION OF EPILEPTIC SEIZURES BY MEANS OF POWER SPECTRUM ANALYSIS OF HEART RATE VARIABILITY: A PILOT STUDY

P18.08 Nicoletta Nava. ULTRASTRUCTURAL STUDY OF THE STRESSED GLUTAMATERGIC-SYNAPSE

P18.09 Kartheeban Nagenthiraja. ACCURATE AND FAST PERFUSION LESION SEGMENTATION TOOL FOR CLINICAL SETTINGS

P18.10 Henriette Bjerregaard. DICYSTEINE CROSSLINKING IN THE HUMAN SEROTONIN TRANSPORTER

P18.11 Anne Virring Sørensen. SLEEP IN CHILDREN WITH ADHD BEFORE AND AFTER TREATMENT WITH METHYLPHENIDATE

Poster session 19 GP8: Neuroscience.

Chairmen: Morten Nielsen & Louise Buur Lund (PhD student)

P19.01 Pernille Lühdorf. FISH, MARINE N-3 POLYUNSATURATED FATTY ACIDS AND STROKE.

P19.02 Adjmal Nahimi. A COMMON NORADRENERGIC MECHANISM OF DEPRESSION AND L-DOPA INDUCED DYSKINESIA IN PARKINSON&ACUTE;S DISEASE IN VIVO?

P19.03 Jafar Hyder Ali Shaik. DJ-1 PROTECTS AGAINST P25 INDUCED ALPHA-SYNUCLEIN CYTOTOXICITY

P19.04 Louise Ørum Olesen. SEROTONERGIC MODULATION OF ALZHEIMER-LIKE DISEASE IN MICE

P19.05 Jeanette Springer. CHRONIC PAIN AND ALTERED SENSATION AFTER THORACOTOMY: IS INTRAOPERATIVE NERVE IMPAIRMENT A RISK?

P19.06 Anne Hansen. POST-STROKE HEADACHE: A 3-YEAR FOLLOW-UP STUDY

P19.07 Jin Zheng. P25 INDUCED ALPHA-SYNUCELIN DEPENDENT TOXICITY IN PRIMARY CULTURED HIPPOCAMPAL NEURONS

P19.08 Signe Rode Andreasen. NEUROPHYSIOLOGICAL IMPACT OF NORMAL AND MUTATED SODIUM-POTASSIUM PUMP IN THE MOUSE BRAIN

P19.09 Morten Jønsson. INFLUENCE OF DOPAMIN ON GAMMA SYNCHRONIZATION - A MEG STUDY

P19.10 Justyna Zareba. STUDY OF THE ROLE OF CALCIUM IN THE ALPHA-SYNUCLEIN INDUCED NEUROPATHOPHYSIOLOGY

P19.11 Kim Henningsen. HIPPOCAMPAL BIOMARKERS OF SUSCEPTIBILITY AND RESILIENCE TO STRESS IN A RAT MODEL OF DEPRESSION

P19.12 Annemette Bondo Lind. LONGING FOR EXISTENTIAL RECOGNITION: A QUALITATITVE STUDY OF EVERYDAY CONCERNS FOR PEOPLE WITH SEVERE SOMATOFORM DISORDERS

Poster session 20 Research year .

Chairmen: Helle Prætorius, Jan Danz (PhD student) & Marie Bagger Bohn (PhD student)

P20.01 Stine Karlsen. GASTROINSTESTINAL TRANSIT TIMES IN PATIENTS WITH LIVER CIRRHOSIS AND PORTAL HYPERTENSION

P20.02 Lise Haubjerg Nielsen. HOSPITALIZATION FOR PNEUMONIA AMONG INDIVIDUALS WITH AND WITHOUT END STAGE RENAL DISEASE: A DANISH NATIONWIDE, POPULATION-BASED COHORT STUDY

P20.03 Lærke Valsøe Munk-Petersen. ANTIGEN SPECIFIC POLYFUNCTIONAL T-CELL POPULATIONS IN HIV-1 INFECTED PATIENTS BEFORE AND AFTER TLR9-ADJUVANTED PNEUMOCOCCAL VACCINATION

P20.04 Nis Brix Lauridsen. PREDICTING FAILURE TO EXTUBATE AFTER INSURE IN NEWBORNS BORN BEFORE 32 WEEKS GESTATION

P20.05 Michelle Heidner. DISCREPANCY IN GESTATIONAL AGE BASED ON DATE OF LAST MENSTRUAL PERIOD AND ULTRASOUND AND NEWBORN DISEASE

P20.06 Christina Mikkelsen. HUMAN MANNAN-BINDING LECTIN AND FICOLINS: INTERACTIONS WITH VIRUSES

P20.07 Sidsel Hyldgaard Støy. THE TH17-CELL PATHWAY IN THE COURSE OF ACUTE ALCOHOLIC HEPATITIS.

P20.08 Morten Bue Svendsen. THE RELATION BETWEEN PERIPHERAL VASCULAR RESISTANCE AND PULSE WAVE VELOCITY

P20.09 Niels Johansen. BRAIN SWELLING DURING DIALYSIS (BRASE). ACUTE BRAIN VOLUME CHANGES IN HAEMODIALYSIS: COMPARISON OF LOW FLUX HAEMODIALYSIS WITH PRE-DILUTION HAEMODIAFILTRATION

P20.10 Marie Maagaard Sørensen. CARDIOVASCULAR FUNCTION FOLLOWING THE NUSS PROCEDURE FOR PECTUS EXCAVATUM - 3 YEARS FOLLOW-UP. A PROSPECTIVE, CONTROLLED STUDY.

P20.11 Peter Hjertholm. DIAGNOSTIC VARIABILITY IN DANISH GENERAL PRACTICE AND PROGNOSIS OF CANCER PATIENTS

P20.12 Caroline Emma Hedsund. A GASTROINTESTINAL TRANSIT TIME STUDY: HEALTHY CHILDREN INVESTIGATED WITH MOTILITY TRACKING SYSTEM

Poster session 21 GP5: Inflammation og Infection.

Chairmen: Marianne Hokland, Thomas Damgaard Sandahl (PhD student) & Asger Granfeldt (PhD student)

P21.01 Randi Berg. GENOMIC HIV RNA INDUCES INNATE IMMUNE RESPONSES THROUGH RIG-I-LIKE-RECEPTOR-DEPENDENT SENSING OF SECONDARY STRUCTURED RNA

P21.02 Anders Jul Kjærgaard. DO SOLUBLE LEVELS OF ENDOTHELIAL ADHESION MOLECULES REFLECT ENDOTHELIAL EXPRESSION?

P21.03 Mariane Høgsbjerg Schleimann. THE DIRECT REPEAT 6 PROTEIN FROM HUMAN HERPES VIRUS-6B ACCUMULATES IN VIRAL REPLICATION COMPARTMENTS

P21.04 Srikanth Chiliveru. IFI16 AND ACTIVATION OF INFLAMMATION IN PSORIASIS

P21.05 Steffen Bank. CAN GENETIC MARKERS PREDICT THE RESPONSE OF TNF INHIBITOR THERAPY?

P21.06 Winnie Ridderberg. MARKED INCREASE IN INCIDENCE OF INFECTIONS CAUSED BY SPORADIC ACQUISITION FROM THE ENVIRONMENT

P21.07 Babak Jalilian. THE COORDINATED ROLES OF CD18 INTEGRINS AND MATRIX METALOPROTEINASE-9 IN RHEUMATOID ARTHRITIS

P21.08 Sanne Jespersen. VACCINATION SCARS IN HIV INFECTED PATIENTS - DOES VACCINIA VACCINATION CONFER PROTECTION AGAINST AIDS?

P21.09 Caroline Winther Tørring. SPONTANEOUS LYMPHOCYTE TRANSFORMATION IN MULTIPLE SCLEROSIS

P21.10 Stine Maria Andersen. VALRUBICIN TARGETS AND ACTIVATES PROTEIN KINASE C A IN KERATINOCYTES.

P21.11 Johannes Martin Schmid. IN SUBJECTS ALLERGIC TO GRASS POLLEN, BASOPHIL SENSITIVITY DECREASES DURING SUBCUTANEOUS IMMUNOTHERAPY DUE TO BOTH HUMORAL FACTORS AND CELLULAR DESENSITIZATION

P21.12 Søren Behrndtz Brandsborg. ILEO POUCH-ANAL ANASTOMOSIS IN PATIENTS WITH ULCERATIVE COLITIS: POUCH FUNCTION, QUALITY OF LIFE AND RISK OF CANCER

Poster session 22 GP5: Inflammation og Infection.

Chairmen: Eskild Petersen, Rikke Olesen (PhD student) & Anne-Cathrine Bareid Østby (PhD student)

P22.01 Anne Brosbøl-Ravnborg. CONTROL OF DENDRITIC-CELL FUNCTION BY VITAMIN D_3

P22.02 Rie Io Glerup. SUBCLINICAL BACTERAEMIA AND MORTALITY AMONG HAEMODIALYSIS PATIENTS - HD-BACT

P22.03 Hanne Vinter. IMIQUIMOD INDUCED SKIN INFLAMMATION: A HUMAN MODEL OF PSORIASIS

P22.04 René Østgård. INTESTINAL INFLAMMATION IN ANKYLOSING SPONDYLITIS ASSESSED BY FECAL CALPROTECTIN, CAPSULE ENDOSCOPY, AND COLONOSCOPY AND THE EFFECT OF ADALIMUMAB ON MUCOSLA HEALING

P22.05 Julie Prahl. PREVALENCE OF, RISK FACTORS FOR AND CONSEQUENCES OF LOW PLASMA CONCENTRATIONS OF FIRST-LINE TB DRUGS

P22.06 Nis Pedersen Jørgensen. BIOFILM FORMATION BY (SA) ON ORTHOPEDIC IMPLANTS IN A NOVEL MURINE INFECTION MODEL MIMICKING A CHRONIC, IMPLANT ASSOCIATED OSTEOMYELITIS (OM)

P22.07 Thomas Aagaard Rasmussen. COMPARISON OF HISTONE DEACETYLASE (HDAC) INHIBITORS IN CLINICAL USE: POTENTIAL FOR DISRUPTING HIV-LATENCY AND EFFECT ON T-CELL ACTIVATION

P22.08 Lone Schmidt Sørensen. RAPID INCORPORATION OF OMEGA-3 FATTY ACIDS INTO PATIENTS COLONIC TISSUE AFTER ORAL SUPPLEMENTATION

P22.09 Lise Tornvig Erikstrup. DISK DIFFUSION ANTIMICROBIAL SUSCEPTIBILITY TESTING OF CLOSTRIDIUM DIFFICILE

P22.10 Morten Leif Munding Stilund. SOLUBLE CD163 AS A DIAGNOSTIC MARKER IN MULTIPLE SCLEROSIS.

P22.11 Kresten Krarup Keller. INCREASING OSTEOCLASTIC BONE LOSS INSPITE OF FEWER OSTEOCLAST PRECURSORS DURING CHRONIC AUTOIMMUNE SKG-ARTHRTITIS EVALUATED BY 3D STEREOLOGICAL ESTIMATORS

P22.12 Kristian Kjær Andersen. IS ENDOVASCULAR COOLING LESS STRESSFUL THAN SURFACE COOLING? STRESS, CEREBRAL, AND METABOLIC RESPONSES IN A PORCINE MODEL OF MILD HYPOTHERMIA.

Poster session 23 Research year.

Chairmen: Søren Paludan, Louise Hauge Matzen (PhD student) & Christina Bisgaard (PhD student)

P23.01 Christina Kjærgaard Rasmussen. 2- AND 3-DIMENSIONAL ULTRASOUND IN DIAGNOSING ADENOMYOSIS &NDASH; DIAGNOSTIC ACCURACY AND OBSERVER VARIATION

P23.02 Anni Assing Winckelmann. CLINICAL USE OF TOLL-LIKE RECEPTOR 9 AGONIST CPG: EFFECT ON IMMUNE ACTIVATION AND PROVIRAL RESERVOIR IN HAART-TREATED HIV-INFECTED PATIENTS.

P23.03 Laura Laine Larsen. HMICL - A NOVEL MARKER FOR IDENTIFYING MPN PATIENTS AT RISK OF LEUKEMIC TRANSFORMATION?

P23.04 Kira Schreiner Simonsen. HAPTOCORRIN - A NEW BIOMARKER FOR PRIMARY LIVER CANCER?

P23.05 Lise Brehm Høj. CLINICAL DATABASE FOR PATIENTS WITH NEUROENDOCRINE TUMOURS

P23.06 Heidi Buvarp Dyrop. EFFECTS OF A LAW BASED TIME SCHEDULE FOR DIAGNOSTICS AND TREATMENT IN SUSPECTED SARCOMA PATIENTS

P23.07 Cecilie Ejerskov Pedersen. BOWEL FUNCTION IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1

P23.08 Jonas Franck Olesen. LOCAL EFFECTS OF AMINO ACIDS, ANDIN THE BILATERALLY PERFUSED HUMAN LEG

P23.09 Steen Kåre Fagerberg. α-HAEMOLYSIN FROM INDUCES SHRINKAGE AND PHAGOCYTOSIS OF ERYTHROCYTES BY THP-1 MONOCYTES

P23.10 Eva Mikkelsen. ELECTROMYOGRAPHIC CHARACTERIZATION OF LABOR

P23.11 Katrine Pedersen. THYMIC OUTPUT AND PROGRESSION OF HIV IN CHILDREN

P23.12 Line Mouritsen Underbjerg. HYPOPARATHYROIDISM, AUTOSOMALT DOMINANT HYPOCALCAMIA AND PSEUDOHYPOPARATHYROIDISM IN DENMARK - EPIDEMIOLOGY, CAUSES, SYMPTOMS AND PROGNOSIS

Poster session 24 GP12: Clinical Medicine.

Chairmen: Bente Jespersen, Jens Christian Jensen (PhD student), Anders Jensen (PhD student) & Mai-britt Guldin (PhD student)

P24.01 Lone Winther Lietzen. USE OF GLUCOCORTICOIDS AND RISK OF BREAST CANCER RECURRENCE

P24.02 Kristoffer Koch. IMPACT OF SOCIOECONOMIC POSITION ON ONE-YEAR MORTALITY AFTER BACTEREMIA. A POPULATION-BASED COHORT STUDY

P24.03 Ane Birgitte Telén Andersen. MATERNAL USE OF GASTRIC ACID-SUPPRESSIVE DRUGS DURING PREGNANCY AND RISK OF ASTHMA IN OFFSPRING: A POPULATION-BASED DANISH COHORT STUDY.

P24.04 Palle Bager. FATIGUE PREVALENCE IN IBD OUTPATIENTS IN SCANDINAVIA

P24.05 Karin Biering. WHEN IS RETURN TO WORK SAFE RETURN TO WORK? COMPARING MEASURES OF RETURN TO WORK IN A COHORT OF PATIENTS FOLLOWING PERCUTANEOUS CORONARY INTERVENTION

P24.06 Charlotte K. Lautrup. FAMILIAL RISK OF COLORECTAL CANCER - METHODS FOR TRACING FIRST DEGREE RELATIVES IN DENMARK

P24.07 Shallu Sharma. PREVELANCE OF COMPLICATIONS IN NEUROMUSCULAR SCOLIOSIS SURGERY: WHAT DOES THE LITERATURE TELL US?

P24.08 Nicoline Valentina Krogstrup. IMPROVED GFR AND RENAL BLOOD PERFUSION FOLLOWING REMOTE ISCHEMIC CONDITIONING IN A PORCINE KIDNEY TRANSPLANTATION MODEL

P24.09 Anne Gulbech Ording. THE CHARLSON COMORBIDITY INDEX SCORE AND BREAST CANCER INCIDENCE: A DANISH NATIONWIDE CASE-CONTROL STUDY

P24.10 Louise Hjort Nielsen. REDUCTION OF VIOLENCE AMONG MENTALLY ILL OFFENDERS IN DENMARK USING STRUCTURED RISK ASSESSMENT SCHEMES

P24.11 Jonathan Montomoli. LIVER DISEASE AND POST-OPERATIVE MORTALITY IN PATIENTS WITH COLORECTAL CANCER: A DANISH NATIONWIDE COHORT STUDY

Poster session 25 GP12: Clinical Medicine.

Chairmen: Bent Deleuran, Søren Beck Jensen (PhD student) & Annett Andersen (PhD student)

P25.01 Mikkel Andreas Strømgaard Andersen. CRITERIA-BASED EMERGENCY MEDICAL DISPATCH OF AMBULANCES - FIRST EXPERIENCES IN DENMARK

P25.02 Eva Bjerre Ostenfeld. USE OF GLUCOCORTICOIDS AND COLORECTAL CANCER RISK; A POPULATION-BASED CASE-CONTROL STUDY IN NORTHERN DENMARK, 1991-2010

P25.03 Michael Dalager-Pedersen. MYOCARDIAL INFARCTION AND STROKE AFTER INCIDENT COMMUNITY-ACQUIRED BACTEREMIA: A 15-YEAR COHORT AND CASE SERIES STUDY

P25.04 Efe Levent Aras. PEDICLE SCREW FIXATION FOR UNSTABLE THORACIC SPINE FRACTURES: CLINICAL AND RADIOLOGICAL EVALUATION OF 120 CASES.

P25.05 Anne Fia Grann. MELANOMA: THE INFLUENCE OF COMORBIDITY ON SURVIVAL

P25.06 Anne Nakano Jensen. QUALITY OF HOSPITAL CARE AND CLINICAL OUTCOME AMONG PATIENTS WITH INCIDENT HEART FAILURE IN DENMARK: A NATIONWIDE STUDY

P25.07 Gija Rackauskaite. WEB BASED QUESTIONAIRE FOR GROSS MOTOR FUNCTION AND TREATMENT OF CEREBRAL PALSY

P25.08 Eva Sædder. DEVELOPMENT OF AN ALGORITHM FOR DIFFERENTIATED INTERVENTION AGAINST MEDICATION ERRORS IN ACUTE HOSPITAL ADMISSIONS ON THE BASIS OF INDIVIDUALIZED RISK STRATIFICATION

P25.09 Dorthe Krogsgaard Bonnerup. PHYSICIANS' ATTITUDES TOWARDS DRUG COUNSELLING FROM EXTERNAL HEALTH PROFESSIONALS

P25.10 Henrik Gammelager. ONE-YEAR MORTALITY AMONG DANISH INTENSIVE CARE PATIENTS WITH ACUTE KIDNEY INJURY: A COHORT STUDY

P25.11 Malene Schou Nielsson. MORTALITY IN ELDERLY PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT: A DANISH ONE YEAR COHORT STUDY

Poster session 26 GP11: Tooth, bone and joint diseases.

Chairmen: Erling Bjerregaard Pedersen, Jeppe Barckman (PhD student) & Dan Østergaard Pradsgaard (PhD student)

P26.01 Lene Rahr Wagner. IMPACT OF DIFFERENT GRAFT TYPES AFTER ACL RECONSTRUCTION: RESULTS FROM THE DANISH REGISTRY OF KNEE LIGAMENT RECONSTRUCTION

P26.02 Charlotte Hartig Andreasen. FACTORS PREDICTING FAILURE FOLLOWING PERIACETABULAR OSTEOTOMY: A 2-12 YEARS FOLLOW-UP STUDY OF 406 PERIACETABULAR OSTEOTOMIES

P26.03 Michael Skovdal Rathleff. PREVALENCE OF TRAUMATIC AND NON-TRAUMATIC ANTERIOR KNEE PAIN AMONG ADOLESCENTS.

P26.04 Jannie Dahl Hald OSTEOGENESIS IMPERFECTA - GENETICS, PHENOTYPE AND QUALITY OF LIFE

P26.05 Anette Liljensøe. OBESITY INFLUENCES THE CLINICAL OUTCOME AND THE QUALITY OF LIFE FOLLOWING PRIMARY TOTAL KNEE ARTHROPLASTY.

P26.06 Jan Rölfing. EPO DOES NEITHER STIMULATE PROLIFERATION NOR OSTEOGENIC DIFFERENTIATION OF HMSC-TERT CELLS

P26.07 Karen Toftdahl Bjørnholdt. ACUTE AND CHRONIC PAIN AFTER SHOULDER SURGERY: TREATMENT AND EPIDEMIOLOGY

P26.08 Morten Christian Bay Grauballe. THE ROLE OF TNF-α AND AGES IN RATMODEL WITH DIABETES AND PERIODONTITIS

P26.09 Pernille Endrup Jacobsen. DENTAL ABNORMALITIES IN CHILDREN EXPOSED TO ANTICONVULSANTS PRENATALLY

P26.10 Lars Bo Petersen. POSTOPERATIVE COMPLICATIONS AFTER MANDIBULAR THIRD MOLAR REMOVAL BASED ON PANORAMIC RADIOGRAPHY OR CONE BEAM CT-SCANNING: A RANDOMISED CONTROLLED CLINICAL STUDY

Poster session 27 GP10: Translational Molecular Medicine.

Chairmen: Niels Gregersen & Kirstine Kjær Kirkegaard (PhD student)

P27.01 Steffen Jensen. EVALUATION OF TWO COMMERCIAL GLOBAL MIRNA EXPRESSION PROFILING PLATFORMS FOR DETECTION OF LESS ABUNDANT MIRNAS

P27.02 Lea Hougaard Pedersen. TREATMENT OF CHRONIC KIDNEY DISEASE WITH SIRNA NANOPARTICLES TARGETING MMP-2, MT1-MMP, AND TIMP-2

P27.03 Dennis Kjølhede Jeppesen. IDENTIFICATION AND CHARACTERIZATION OF CIRCULATING EXOSOMES IN BLADDER CANCER

P27.04 Juan Manuel Shiguetomi Medina. EPIPHYSIODESIS MADE WITH RADIOFREQUENCY ABLATION: FIRST RESULTS FROM A PILOT STUDY

P27.05 Anne Louise Askou. REDUCTION OF CHOROIDAL NEOVASCULARIZATION IN MICE BY AAV-DELIVERED ANTI-VEGF SHRNA

P27.06 Anne Skakkebæk Jensen. NEUROCOGNITIVE OUTCOME AND PSYCHOPATHOLOGY IN MEN WITH KLINEFELTER SYNDROME

P27.07 Maja Ludvigsen. TRANSLATIONAL RESEARCH IDENTIFIES PROGNOSTIC MARKERS INCLUDING GALECTIN-1 IN THE TUMOR MICROENVIRONMENT OF CHL PREDICTIVE FOR RELAPSED /REFRACTORY DISEASE

P27.08 Yujia Cai. TRANSPOSON-BASED LENTIVIRAL VECTOR TECHNOLOGY FOR GENE DELIVERY AND PERSISTENT TRANSGENE EXPRESSION

P27.09 Terese K. Jeppesen. ABSENCE OF A GENERAL BENEFICIAL EFFECT OF RENAL SMAD3 BLOCKAGE

P27.10 Ulla Munksgaard Stahlschmidt. FUNCTIONALIZED BI-PHASIC OSTEOCHONDRAL PLUG FOR CARTILAGE REPAIR

P27.11 Shivani Shivprasad Joshi. NOVEL MUTATION CAUSING CNDI IN SWEDISH PATIENT.

Poster session 28 GP10: Translational Molecular Medicine.

Chairmen: Jesper Vuust Møller, Torsten Bloch Rasmussen (PhD student) & Christel Krøigaard (PhD student)

P28.01 Anto Praveen Rajkumar Rajamani. T(9;17) (Q33.2;Q25.3) TRANSLOCATION REVEALS THE ASSOCIATION BETWEEN BIPOLAR DISORDER AND AS WELL AS GENES

P28.02 Aida Solhøj Hansen. SIGNIFICANCE OF CD46 ISOFORMS ON THE REGULATION OF CELLULAR RESPONSES

P28.03 Siri Strand. LONG NON-CODING RNAS IN PROSTATE CANCER: REGULATION, FUNCTION AND BIOMARKER POTENTIAL

P28.04 Ming Sun. NANOMEDICINE IN BREAST CANCER BONE METASTASIS: TARGETING CANCER STEM CELL

P28.05 Miao Wang. NEUROLOGICAL FUNCTION AND SURVIVAL OUTCOME OF AARHUS ALGORITHM IN PATIENTS WITH SPINAL SOLITARY PLASMACYTOMA OR MULTIPLE MYELOMA

P28.06 Anders Britze Hansen. THE CHOLESTEATOMA PROTEOME

P28.07 Kim Blauenfeldt Gosmer. CHEMICAL PROFILING OF ILLEGAL DRUGS AS A FORENSIC TOOL

P28.08 Inge Gram Carlsen. REGULATION OF HSP27 IN UNILATERAL OBSTRUCTED KIDNEY AND IN RMIC SUBJECTED TO MECHANICAL AND INFLAMMATORY STRESS.

P28.09 Paula Fernandez Fernandez Guerra. ANALYSIS OF MITOCHONDRIAL RESPONSE TO INDUCED OXIDATIVE STRESS IN NORMAL HUMAN DERMAL FIBROBLASTS USING NUCLEOCOUNTER NC-3000

P28.10 Helle Kristensen. EPIGENETIC SILENCING AND BIOMARKER POTENTIAL OF , AND THEIR HOST GENE IN PROSTATE CANCER

PhD Student Chairmen.

CH.01 Martin Gottliebsen. LONG BONE GROWTH CONTROL CAN BE ACHIEVED WITH TOTALEPIPHYSIODESIS USING 8-PLATES

CH.02 Randi Groslier Bjælde. AGONISTS THAT INCREASE $[CA^{2+}]_I$ HALT THE MOVEMENT OF ACIDIC CYTOPLASMATIC VESICLES IN MDCK CELLS

CH.03 Esben Laugesen. INCREASED ARTERIAL STIFFNESS IS INDEPENDENTLY ASSOCIATED WITH RISK OF ISCHEMIC CEREBRAL DISEASE IN PATIENTS WITH TYPE 2 DIABETES DESPITE GOOD BLOOD PRESSURE AND LIPID CONTROL

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Abstracts

Emma Tina Bisgaard Olesen

VASOPRESSIN-INDEPENDENT TARGETING OF AQUAPORIN-2 BY SELECTIVE E-PROSTANOID RECEPTOR AGONISTS ALLEVIATES NEPHROGENIC DIABETES INSIPIDUS

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The kidney collecting duct water channel aquaporin-2 (AQP2) is regulated by vasopressin (VP) by phosphorylation at three sites (pS256, pS264 and pS269) leading to apical membrane accumulation (AMA). The present aim was to identify VP independent pathways for AQP2 regulation with focus on prostaglandin E2 (PGE2) receptors EP2 and EP4. AMA was assessed by cell surface biotinylation in cells and immunohistochemistry in tissue, and phosphorylation was assessed by immunoblotting with phosphospecific antibodies. In vitro, Madine-Darby canine kidney (MDCK) cells stably transfected with AQP2 were stimulated with selective agonists for either EP2 (butaprost, 10^{-9}M-10^{-6}M) (BU) or EP4 (CAY10580, 10^{-8}M-10^{-5}M) (CAY). Both agonists induced AQP2 AMA and pS264-AQP2. BU, but not CAY, increased pS269-AQP2 and second messenger cAMP. Ex vivo, both agonists increased pS256-AQP2 in tubule suspensions from kidney cortex of normal wistar rats (NWR) and BU induced AQP2 AMA in kidney slices from NWR. In vivo, nephrogenic diabetes insipidus (NDI) was mimicked in 12 NWR by VP receptor antagonist OPC-31260 (10mg/day). Rats were additionally treated with BU (6mg/kg/day) or solvent control for two days (n=6). BU increased urine osmolality (265±27 vs 192±18 mosm/kg H2O on day1; 455±47 vs 285±34 on day2) and reduced urine flow rate to 59% on day 1 and 51% on day 2 with no decline in creatinine clearance (605±84 vs 536±45 µl/min/100g). Conclusion: EP2 and EP4 increase AQP2 AMA in cells and in native tissue with differential intracellular signaling mechanisms, and BU alleviates polyuria in rats. This indicates that PGE2 is involved in body water homeostasis and may provide a new treatment strategy for NDI.

Yonglun Luo

DEVELOPMENT OF BRCA1 KNOCKOUT PIGS AND TRANSCRIPTOME STUDIES OF DISEASE PROGRESSION

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[Background] Inherited breast cancer is commonly caused by mutations in breast cancer susceptibility genes, such as BRCA1 or BRCA2. Pigs are crucial preclinical animal models of breast cancer due to the genetic and physiological similarities between pigs and human. [Methods] Using recombinant adeno-associated virus-mediated gene targeting and SCNT by handmade cloning, we aimed at generating a pig model with a 55 bp deletion in exon 11 of BRCA1 and using transcriptomics to study disease progression. [Results and discussion] In one study, we transferred 347 cloned embryos to 3 recipient sows and generated 7 BRCA1 knockout ($BRCA1^{+/-}$) piglets. However, all $BRCA1^{+/-}$ pigs died within 18 days after birth. We then used a re-cloning strategy, in which 291 cloned embryos were transferred to 3 recipient sows and generated 8 $BRCA1^{+/-}$ piglets. Only one piglet survived

and is now growing to maturity. In a third cloning effort, in which a mix of BRCA1$^{+/-}$ cell clones were used as nuclear donor cells, 15 Yucatan BRCA1$^{+/-}$ piglets were born and 14 of these are still alive. We are also working on generating BRCA1$^{+/-}$ Göttingen minipigs. Microarray-based transcriptome analyses conducted on the BRCA1$^{+/-}$ and wildtype (WT) cells showed that gene expression in BRCA1$^{+/-}$ cells is distinctly different to WT cells. Several of the differently expressed genes are involved in cancer and genetic disorder regulation. [Conclusions] This study has generated the first BRCA1 KO pig model and this may be used as preclinical animal model for studying the pathogenesis of breast cancer.

Morten Søndergaard Jensen

CRYPTORCHIDISM IN DENMARK: STUDIES OF REGISTRY VALIDITY, DISEASE ETIOLOGY, AND TIMING OF CORRECTIVE SURGERY

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Early delivery and low birth weight are strong predictors of the two urogenital anomalies cryptorchidism (undescended testis) and hypospadias. Understanding these associations may lead to important etiologic clues, and we therefore revisited the prevailing hypotheses regarding fetal growth restriction as a risk factor for urogenital anomalies. We studied a population of 934,538 Danish boys born alive from 1 January 1980 to 31 December 2008. Cryptorchidism and hypospadias were inversely associated with weight for gestational age. The higher risk among boys born light-for-gestational age, an indicator of fetal growth restriction, was strongly aggravated by early delivery. A low birth weight compared with singleton or twin brothers' birth weight was associated with a higher risk of urogenital anomalies, suggesting an effect of relative fetal growth restriction within families. Contrary to previous reports, newborns' body dimensions assessed independently of birth weight were not associated with urogenital anomalies. The hypothesis, that shared factors cause both fetal growth restriction and urogenital anomalies, was supported by comparison of urogenital anomaly risks in singletons and twins, and by patterns of cryptorchidism and hypospadias co-occurring in individuals. These novel insights might also extend to other male reproductive conditions with prenatal etiology, including testicular cancer and poor semen quality.

O01.01 Ole Halfdan Larsen

COMBINATION OF RECOMBINANT FACTOR VIIA AND FIBRINOGEN CORRECTS THE COAGULOPATHY OF PRIMARY IMMUNE THROMBOCYTOPENIA AT VERY LOW PLATELET COUNTS

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Haemostatic treatment modalities alternative to platelet transfusion are desirable if they enable control of serious acute bleeds in primary immune thrombocytopenia (ITP). This study challenged the hypothesis that recombinant factor VIIa (rFVIIa, NovoSeven®) combined with fibrinogen concentrate (Haemocomplettan®) may correct whole blood (WB) clot formation in ITP. Blood from ITP patients (n=12) was drawn into tubes containing 3.2% citrate and corn trypsin inhibitor 18.3 μg/ml (final concentration). The WB (mean platelet count 22 × 10^9/L (range 0-42)) was spiked in vitro with buffer, donor platelets (+40×10^9/L), rFVIIa (1 or 4μg/mL), fibrinogen (1 or 3mg/mL), or combinations of rFVIIa and fibrinogen. Coagulation profiles were recorded by tissue factor (0.03pM) activated ROTEM® Thromboelastometry. Coagulation in ITP was characterised by a prolonged clotting time (CT, 1490s (mean)), a low maximum velocity (MaxVel, 3.4mm×100/s) and maximum clot firmness (MCF, 38.2mm). Fibrinogen showed no haemostatic effect, whereas rFVIIa reduced the CT and increased the MaxVel. The combination of fibrinogen and rFVIIa revealed a significant synergistic effect improving all parameters (CT 794s, MaxVel 7.9mm×100/s, MCF 50.7mm) even at very low platelet counts. Data suggest that rFVIIa combined with fibrinogen corrects the coagulopathy of ITP even at very low platelet counts, and may represent an alternative to platelet transfusion.

O01.02 Jennifer Heather Christensen

THERMOGRAPHY AS A QUANTATIVE METHOD FOR ASSESSING POSTOPERATIVE INFLAMMATION

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Introduction: Thermography is an imaging method to assess heat emission from a surface. Inflamed tissue is characterised by liberation of heat, and therefore assessment of surface temperature may be a useful surrogate of inflammation. If thermography can be used to quantify inflammation, it could be a useful imaging tool in many clinical studies.

Objectives: To assess differences in skin temperature between left and right side of the face after unilateral third molar surgery using thermography.

Materials and methods: 127 patients had one mandibular third molar removed. Before surgery, standardised thermographic images were taken of both sides of the patient's face in profile. The imaging procedure was repeated 2 and 7 days after surgery. A ROI was marked on each image. A mean temperature within each ROI was calculated. Paired t-tests were used to assess differences between sides and over time.

Results: No significant difference was found between the operated side and the control side neither before surgery nor 7 days after surgery ($p>0.1$). The temperature of the operated side was significantly higher than that of the control side 2 days after surgery ($\Delta 0.33$ degrees, $p<0.001$). No significant difference was found over time between the preoperative and the 7 days

postoperative temperature of both sides (p>0.35). After 2 days, the operated side was not significantly different from the temperature preoperatively (p=0.12). The control side had a significantly lower temperature after 2 days (0.57 degrees, p<0.001).
 Conclusions and discussion: Thermography seems useful for a quantitative assessment of temperature differences between ROIs, i.e. intervention side and control side.

O01.03 Mette Sørensen

ZOLEDRONATE-IMPREGNATED ALLOGRAFT IMPROVES THE FIXATION OF ORTHOPAEDIC REVISION IMPLANTS

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Introduction

Loss of bone stock is a major problem in revision surgery often compensated by use of bone allograft impacted around the implant. Resorption of the allograft may reduce early implant fixation.

The overall purpose of this research was to improve early fixation of bone-grafted joint replacement implants. We hypothized that bisphosphonate-soaked morcelized bone allograft would improve the fixation of orthopaedic revision implants.

Materials and methods

Twenty-four micromotion implants were inserted bilaterally into the knees of 12 dogs according to our revision protocol producing a standardized revision cavity. After eight weeks revision surgery was performed removing the fibrous capsule and reaming of the endosteal neocortex. This left a 1.1 mm gap around the non-motioning, plasma-sprayed titanium revision-implant. The gap was impacted with morcelized allograft. On the intervention side the allograft was soaked in zoledronate (0.005mg/ml) for 3 minutes and rinsed while the allograft for the control side was soaked in saline following the same procedure. Observation after revision was 4 weeks.

Data was evaluated by paired t-test. P-values <0.05 were considered statistically significant.

Results

On the Zolendronate-treated side the revision implants had improved fixation by at least 50% in all biomechanical parameters (shear stiffness, p=0.002; shear strength, p=0.02; energy absorption, p=0.01).

Discussion

When allograft bone is used in revisions, topical Zolendronate may improve initial biomechanical fixation of the revision implant. Previous experiments have shown that bisphosphonates can be easily overdosed, and protocolled clinical trials are needed.

O01.04 Britta Weber NEW METHODS FOR IDENTIFYING RESPONDERS AMONG PATIENTS WITH NON-CELL LUNG CANCER TREATED WITH ERLOTINIB

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Introduction: Most patients with Non-Small Cell Lung Cancer (NSCLC) are diagnosed with advanced or metastatic disease and their prognosis is poor, even with cytotoxic chemotherapy. Survival can be improved in a small subgroup of patients with mutations in the EGF receptor by treatment with the tyrosine kinase inhibitor, erlotinib, targeting the EGF receptor. To identify erlotinib responders, we collected blood and tumour tissue samples from 300 NSCLC patients treated with erlotinib. We studied the concordance between the biopsies and the blood samples as well as the correlation with response and survival.

Methods: DNA was extracted from blood samples and the diagnostic biopsy. Mutations in the EGF receptor gene was analyzed with massive parallel picoliter reactpr sequencing.

Results: We developed a massive parallel picoliter reactor sequencing technique. This method uses amplification of specific amplicons from the EGFR gene. Individual DNA molecules from the tumor or blood are sequenced and a DNA sequence is obtained from approximately 1000 DNA molecules in each sample. This makes it possible to identify mutations even when only 1% of the DNA is mutated. We identified mutations in both biopsies and blood samples but as the study is still ongoing, the entire data is not yet available.

Conclusions: We have shown that mutations can be detected both in tissue samples and in blood samples. Future studies will show if it is feasible to analyse only a blood sample and if the presence of mutations in the blood can predict treatment response.

O01.05 Rita Marques THE AVP-STIMULATED NACL ABSORPTION IN MOUSE MEDULLARY THICK ASCENDING LIMB IS ABOLISHED BY THE V2 RECEPTOR ANTAGONIST SATAVAPTAN

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Arginin-vasopressin (AVP) activates water and electrolyte absorption in the collecting duct as well as electrolyte absorption in the thick ascending limb (TAL). In these renal segments, the hormone causes increases of cAMP and intracellular Ca^{2+}. The V2 receptor is critical for most renal tubular actions of AVP. However, other AVP receptors (V1) are known to be expressed in TAL of certain mammalian species. Objective: Investigate the effect of the highly specific V2 receptor antagonist satavaptan on AVP-stimulated NaCl transport in mouse thick ascending limb. Methods: Transepithelial NaCl transport was studied in isolated, perfused mouse mTALs using the electrical measurement of equivalent short circuit current (I_{sc}). Results: Non-

stimulated mTALs showed a lumen-positive transepithelial voltage (V_{te}) of +6.26±1.02 mV and a transepithelial resistance (R_{te}) of 3.05±0.45 Ω cm² and an equivalent short circuit current (I_{sc}) of 2196±356 μA/cm² (n=5). Within 5-10 minutes basolateral AVP (10nM) triggered a pronounced and ongoing activation of transport as seen by an increase of V_{te} to +11±0.71 mV and I_{sc} to 3460±475 μA/cm². R_{te} remained unaltered. In paired experiments satavaptan (1μM) completely abolished the AVP-induced increase in V_{te} and I_{sc} (n=5). Satavaptan did not influence baseline mTAL transport.
Conclusion: These are the first functional data in isolated perfused mTAL to quantify the effect of specific V2 antagonists on NaCl transport. V2 receptor blockage is sufficient to suppress the AVP-activated NaCl absorption in mouse mTAL. Other AVP receptors appear not to be involved. Thus, the critical role of the V2 receptor for AVP-mediated transport activation is confirmed.

O01.06 Mette Laursen STRUCTURAL INSIGHT INTO THE HIGH AFFINITY BINDING OF CARDIOTONIC STEROIDS TO THE NA^+,K^+-ATPASE

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The Na^+,K^+-ATPase is the specific target for cardiotonic steroids (CTS), a family of naturally derived compounds used in the medical treatment of congestive heart failure and arrhythmia, i.e. digoxin (digitalis). CTS inhibit the pump activity by binding to an extracellular site of the catalytic α-subunit and have the highest affinity to the Na^+,K^+-ATPase in its phosphorylated E2P conformational state. Moreover, endogenous CTS binding have been associated with the regulation of several intracellular processes, such as gene activation, mortality, cell-proliferation and apoptosis [1].

We have determined the crystal structure of the pig kidney Na^+,K^+-ATPase phosphoenzyme in its E2P form, stabilized by high affinity bound ouabain to a resolution of 3.8 Å. The structure differs from previously reported low affinity ouabain-soaked complex [2]. Most importantly, the actuator domain is rotated towards the phosphorylation domain in response to phosphorylation and the transmembrane segments αM1 and αM2 undergo a downward movement and lateral shift towards αM3 and αM4, forming a high affinity binding pocket for the CTS. Additional electron density, clearly visible in between the transmembrane segments αM1– αM6, enables us to place ouabain in the high affinity binding pocket, where it plugs the ion pathway from the extracellular side [3]. Structural and biochemical data will be presented with the emphasis on interactions between the cations and the CTS.

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O02.01 Thomas Svava Nielsen

FASTING, BUT NOT EXERCISE, INCREASES ADIPOSE TRIGLYCERIDE LIPASE (ATGL) AND REDUCES G(0)/G(1) SWITCH GENE 2 (G0S2) PROTEIN AND MRNA CONTENT IN HUMAN ADIPOSE TISSUE

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Introduction: Fasting and exercise are characterized by increased lipolysis, but the underlying mechanisms are not fully understood. Here, we investigated whether fasting or exercise induced changes in human adipose tissue (AT) levels of Adipose Triglyceride Lipase (ATGL) and its inhibitor G(0)/G(1) Switch Gene 2 (G0S2).

Methods: We studied 8 healthy men (25.5±4.3 yr) for 6 h (240 min basal and a 120 min clamp period) on 3 occasions: (i) in the basal state and after (ii) 72-h fast and (iii) 1-h ergometer cycling (65% VO2-max). AT biopsies were taken at t=30 and 270 min. Messenger-RNA was analyzed by RT-PCR, and proteins were analyzed by western blotting.

Results: Circulating FFA levels and whole-body lipid oxidation were increased to similar levels (approximately 2-fold and 75% respectively, compared to control) by both fasting and exercise. Insulin suppressed lipid oxidation in control, but not in fasting or exercise conditions. Furthermore, during fasting insulin failed to suppress FFA levels, suggesting AT insulin resistance. ATGL protein was increased by 44% ($P<0.001$) and G0S2 mRNA and protein were decreased by 56% ($P=0.016$) and 55% respectively after fasting but was not affected by exercise. Protein and mRNA of Hormone Sensitive Lipase (HSL) and the ATGL coactivator Comparative Gene Identification-58 (CGI-58) were unaffected.

Conclusion: We found increased AT content of ATGL and decreased content of the ATGL inhibitor G0S2, suggesting increased ATGL activity during fasting in humans. These results are the first human data to support the recent finding that G0S2 is an important long-term regulator of lipolysis.

O02.02 Jakob Østergaard

MANNAN-BINDING LECTIN IN TYPE 1 DIABETES - PRODUCTION AND TURNOVER

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Background: Type 1 diabetic patients have increased blood-level of mannan-binding lectin (MBL). This is not explained by MBL-genotype differences. High levels of MBL are associated with later signs of diabetic kidney disease. We have found that mice lacking MBL are protected from important diabetic

kidney changes.

Methods: In a type 1 diabetes model (multiple low-dose STZ in female C57BL/6 mice), murine MBL isoforms A and C were measured before and after diabetes. Production and half-life of MBL was estimated to explain changes in MBL level. Complement activation was measured in plasma and in the kidney.

Results: Both isoforms of MBL increased in diabetic animals compared with controls. The increase was most pronounced for MBL-C that increased 3.6-fold (2.9;4.5) in diabetic animals (P<0.001) compared with 0% (-7;9) in controls (P=0.93). The change in MBL-C was significantly different in the two groups, P<0.001. Likewise, change in MBL-A was significantly different between diabetic and control animals (P=0.02). However, in separate analyses, MBL-A did not change in diabetic animals (P=0.12) or in controls (P=0.12). We then compared MBL half-life in diabetes compared with control animals. Half-life of recombinant human MBL was significantly prolonged in mice with diabetes (P=0.017). The half-life of MBL was estimated to 14.3 hours (11.3;19.4) in diabetic animals compared with only 11.8 hours (11.0;12.9) in non-diabetic controls.

Conclusion: Our study supports the clinical observations and furthermore show that MBL increases as result of diabetes. This change may be explained by alternations in MBL turnover.

O02.03 Anna Sellmer Sørensen

URINE OSMOLALITY AS PREDICTOR OF OPEN DUCTUS ARTERIOSUS IN NEONATES LESS THAN 32 WEEKS OF GESTATION

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Background: Delayed closure of the ductus arteriosus (DA) is associated with major complications in extremely preterm babies.
Aims: To investigate 1) median urine osmolality on day four in neonates with and without open DA on day seven 2) the association of urine osmolality measured on day four with the risk of having an open DA on day seven.
Methods: Newborns with gestational age (GA) <32 weeks were consecutively recruited from our department (February 2010 - April 2011). Echocardiography was performed on day seven. Urine osmolality was analysed in intended 24-hour urinary samples collected on day four.
Results: Ninety-one newborns were included. Their median GA was 28 (interquartile range (IQR): 26-30) weeks. Their median birth weight was 1066 (IQR: 840-1280) g. DA was open on day seven in 35 children (38%). Urine osmolality was increased in children with an open DA compared to children with a closed DA (277 (IQR): 224-401) vs. 215 (IQR: 154-295) mOsm/kg, p< 0.01. Logistic regression showed that urine osmolality above 200 mOsm/kg carried a six times higher risk of an open DA on day seven compared with values equal to or below 200 mOsm/kg (OR 6.3 (96% CI 1.9-20)). When adjusted for GA, the risk was 4.5-fold increased (OR 4.6 (95% CI 1.3-16)).
Conclusions: Urine osmolality was found to be higher in children with an open DA than in children with a closed DA. Urine osmolality above 200

mOsm/kg was associated with an increased risk of an open DA. Further analyses are required to determine if water retention or changes in sodium reabsorption can explain these findings.

O02.04 Mikkel Vendelbo

METABOLIC ADAPTATIONS TO FASTING IN HUMAN SKELETAL MUSCLE

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During human evolution, adaptation to famine has been pivotal. Metabolic flexibility, where skeletal muscle shifts to lipid oxidation, is a distinguished inherent ability that enables survival during fasting. This physiological condition is associated with insulin resistance and mimics aspects of the pathology behind type 2 diabetes.

To understand the mechanisms that regulate metabolic flexibility, we investigated the response to 72 hours of fasting in 8 healthy men. Glucose uptake was assessed by hyperinsulinemic-euglycemic clamp and protein metabolism was assessed using amino acid tracers. In addition, myocellular signaling, substrate oxidation, muscle lipid content and regulation of glycogen synthesis were assessed.

Results: Peripheral insulin sensitivity was reduced and substrate oxidation shifted toward lipid oxidation during fasting. This was associated with lipid and glycogen accumulation in skeletal muscle, and net protein breakdown was increased. In muscle, insulin signaling protein synthesis and glucose transport was impaired at the level of mTOR and AS160, regulators of protein synthesis and glucose uptake respectively. However, upstream kinases and regulation to protein breakdown was unaffected.

This work defines physiological adaptations to fasting. The findings suggest that net protein breakdown is due to reduced mTOR mediated protein synthesis. Furthermore, insulin resistance may be induced by regulation of AS160, indicating that AS160 is a key regulator of metabolic flexibility. This leads to improved understanding of insulin action under physiological conditions, and may lead to new insight into pathological conditions as type 2 diabetes and sarcopenia.

O02.05 Rebekka Thomsen

REMOTE ISCHEMIC PRECONDITIONING RELEASES A CIRCULATING CARDIOPROTECTIVE FACTOR BUT TARGET TISSUE RESPONSE IS ATTENUATED DUE TO AN INTRINSIC CARDIOPROTECTIVE ACTIVATION IN DIABETIC PATIENTS

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Introduction: The mechanism behind an elevated threshold for ischemic preconditioning in diabetic patients may be impaired release of a mediating humoral factor or reduced response of the target tissue.

Objective: To investigate the release and effect of a circulating

cardioprotective factor in type 2 DM patients.

Methods: The cardioprotective effect of plasma dialysates from 9 type 2 DM patients and 10 non-DM patients before (control) and after remote ischemic preconditioning (rIPC) was tested in two perfusion models: a Langendorff-model with non-DM rabbit hearts and a model of human atrial trabeculae from DM and non-DM patients.

Results: In the non-DM rabbit hearts rIPC dialysates from both non-DM and DM patients reduced infarct size and improved hemodynamic recovery compared their respective control dialysates (P<0. 05 for both comparisons; n≥9/group). There was no difference in infarct size between control dialysates from DM and non-DM (p=0.16). In human atrial tissue, hemodynamic recovery was enhanced with control dialysate from DM patients compared to non-DM patients. rIPC dialysate from non-DM patients improved hemodynamic recovery compared to control dialysate whereas no further protection was acquired by rIPC dialysate from DM patients. Diabetic atrial trabeculae also had improved recovery when perfused with control dialysate and no additional protection was acquired by rIPC in diabetic trabeculae.

Conclusion: rIPC induced release of a circulating cardioprotective factor is preserved in type 2 diabetic patients. Type 2 DM is associated with an endogenous species specific activation of cardioprotective mechanisms, which attenuate further protection by rIPC.

O02.06 Runa Hyldgaard Poulsen

^{99M}SESTAMIBI A POTENTIAL MARKER OF AREA AT RISK AFTER REVASCULARISATION IN AN ISCHEMIC-REPERFUSION PORCINE MODEL.

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^{99m}Tc-Sestamibi (MIBI) is a reliable tracer of myocardial perfusion in chronic ischemic hearts. MIBIs myocardial binding is less evaluated in the acute ischemic myocardium. The binding is known to be influenced by mitochondrial changing seen in the reperfusion phase.

We hypothesized that MIBI administered to the post ischemic heart after revascularization would overestimate myocardial perfusion defect and equalled Area at Risk (AAR).

In 12 pigs left anterior descending coronary artery was occluded in 45 min. Two hours after reperfusion MIBI was injected in a central vein, and 15µm ^{153}Gd-Microspheres (MS) in the left atrium for arterial distribution. AAR and final infarct size (IS) were determined by histochemical staining (TTC), MIBI and MS uptake by planar imaging on gamma camera.

We found that MIBI defect (21% of left ventricle (LV)) was not significantly differed from AAR (25% of LV) (p=0.30) but larger than perfusion defect studied by MS (7.3% of LV) (p=0.0001).

CONCLUSION: In a porcine model of myocardial infarction, MIBI administered 120 minutes after reperfusion delineates AAR and

overestimates myocardial perfusion defect.

These results suggest that MIBI distribution in post ischemic myocardium is influenced by other factors than myocardial perfusion. In vitro studies have shown that MIBIs binding capacity to cardiomyocytes decrease when the mitochondrial calcium concentration increases, and when the mitochondrial membrane depolarises. These physiological changes are known to mediate reperfusion injury. Thus, the MIBI defects could in part be due to the mitochondrial dysfunction seen in reperfusion injury.

O03.01 Dorthe Sørensen

PATIENT EXPERIENCES WITH NON-INVASIVE VENTILATION: A GROUNDED THEORY STUDY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim and objectives: This paper gives a theoretical account of chronic obstructive pulmonary patients' significant patterns of behaviour and strategies during treatment with non-invasive ventilation at the hospital.

Background: Strong evidence exists of the effect of non-invasive ventilation but treatment success remains a huge challenge. Little attention has been given to patient intolerance as a cause of treatment failure. A better understanding of how patients manage non invasive ventilation may contribute to improvement.

Design: A constant comparative classic-grounded theory study

Method: The data collection comprised sessions of qualitive participant observation during treatment with 21 patients in non-invasive ventilation and semi structured interviews with 11 patients after treatment completion.

Findings: Patient behaviour spanned a continuum of three behavioural approaches: the accepter, the doubter and the avoider. In spite of these different approaches all participants managed their fear of escalating discomfort by striving towards comfort and wellbeing. This process involved two separate strategies forming a dynamic whole and being integral to the process 1) Personalizing through participation using knowledge and using habits 2) Controlling discomfort through perseverance and self-comforting behaviour.

Conclusions: This study offers a robust account of patients' persistent striving towards comfort and well-being throughout non-invasive ventilation and their deploying of strategies to manage.

O03.02 Charlotte Uggerhøj Andersen

PULMONARY HYPERTENSION IN INTERSTITIAL LUNG DISEASE AND CHRONIC OBSTRUCTIVE LUNG DISEASE – NT-PROBNP AND IMPACT ON FUNCTIONAL CAPACITY

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Pulmonary hypertension (PH) worsens the prognosis in interstitial lung disease (ILD) and chronic obstructive lung disease (COPD). The aim of this study was to investigate NT-proBNP as a diagnostic marker for PH, and to assess the impact on functional capacity of PH in ILD and COPD.

Based on echocardiographic screening, and right heart catheterization if possible, the presence of PH was established. ROC analysis of NT-proBNP to detect PH was performed in out-patients with ILD, and the result was tested in new ILD patients and patients with COPD. The impact of PH on 6 minute walk test (6MWT) corrected for lung function, age sex and BMI was assessed.

Results (mean±SEM): In out-patients with ILD (n=143), the optimum NT-proBNP cut-off for exclusion of PH was 95 ng/l. Applying this finding in new ILD (n=65) and COPD patients (n=116), NT-proBNP values below 95 ng/l ruled out PH with a negative predictive value of 100%. 42±6 % and 31± 4% of new ILD- and COPD patients, had values below 95 ng/l, respectively.

In patients with ILD (n=208), the presence of PH (n=30) reduced the 6MWT by 53±21 m (P=0.017) per se. In COPD patients (n=116), the presence of PH (n=15) did not significantly reduce the 6mwt (difference = 55±42 m (P=0.2)) when corrected for the other variables.

Conclusion: a value of NT-proBNP below 95 ng/l excludes the presence of PH in ILD and COPD patients, and PH independently reduces the functional capacity in ILD.

O03.03 Grethe Elholm FARMING EXPOSURES PROTECT AGAINST NEW ONSET OF POLLEN SENSITIZATION IN YOUNG ADULTS

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Objectives

Farmers are exposed to a wide range of allergens and supposedly run the risk of developing allergies. However, the prevalence of atopic sensitisation has been reported to be low in farmers.

Aim

We aim to describe the relation between farm-related exposures and changes in atopic sensitisation over time in young adults in The Danish Farming Cohort (SUS).

Methods

The SUS cohort (n=1166) were examined twice with a 15 year follow-up

period. Specific IgEs against cat, birch, grass, HDM and storage mite allergens were determined (ADVIA Centaur, ALK Abellò ®). Sensitisation was defined as sIgE≥0.35 kU/L, and atopy was defined as sensitisation to one or more of the 5 allergens tested for. Personal average yearly exposure to endotoxin during the follow-up period was estimated from more than 500 personal inhalable dust measurements and a farm-specific internal job exposure matrix.

Results

New onset pollen sensitisation was negatively associated with current farming status, exposure to animals, dust and endotoxin in a dose dependent manner (Table 1). The Farming exposures showed a significant and strong protective effect against new onset of pollen sensitisation.

Conclusion

These analyses suggest exposures in the farming environment to have a significant protective effect against new onset of pollen sensitization in young adults.

O03.04 Christian Wulff

A RANDOMISED CONTROLLED TRIAL OF HOSPITAL-BASED CASE MANAGEMENT TO IMPROVE CANCER PATIENTS' SELF-RATED QUALITY OF LIFE

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Introduction:Case management (CM) is increasingly used to improve both system and patient aspects of cancer care. CM is conducted by a nurse, the case manager, whose task is to function as a consistent, pro-active, and cross-disciplinary member of the health care team. However, evidence of CM effectiveness is vaguely established. We tested the hypothesis that CM could improve cancer patients' self-rated quality of life.

Methods: Randomised controlled trial. Bowel cancer patients at Surgical Department P, Aarhus University Hospital, were randomised 1:1 to either the CM intervention or the control group.

The CM intervention followed detailed protocol describing the pro-active patient contacts and when to pass on information to other health professionals etc. Control group patients had usual support from health professionals including statutory contact persons.

The EORTC QLQ-C30 was used to assess quality of life at baseline, at eight and 30 weeks after randomisation. The primary endpoint was global quality of life. Secondary endpoints were the five functioning subscales. Estimated sample size was 280 patients. Analysis of covariance was used to compare the two groups at each follow-up.

Results: 140 patients were randomised to each group. Follow-up was 88% at eight weeks and 79% at 30 weeks. Drop-out, non-response and missing

scales were equal in the two groups.

We found no statistical significant group difference on any subscale at eight or 30 weeks.

Discussion: An explanation for the negative findings could be that frustrations caused by insufficient information and support have lower impact on quality of life compared with adverse treatment effects and survival concerns.

O03.05 Elise Røge Nielsen

INVOLVEMENT OF KCNQ K^+ CHANNELS IN HYPOXIC VASODILATATION IN PORCINE CORONARY ARTERIES

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Purpose: The aim was to investigate the mechanisms behind the vasodilation seen in response to acute hypoxia in porcine arteries. We hypothesized that hypoxia results in K^+ channel opening in porcine large coronary arteries thereby leading to vasorelaxation.

Experimental approach: Porcine left anterior descendent coronary artery segments without endothelium were mounted in myographs for isometric tension recording. Functional studies examining the influence of K^+ channels were performed and the presence of K^+ channels was examined by PCR and immunoblotting.

Key results: In prostaglandin $F_{2\alpha}$ ($PGF_2\alpha$)-contracted artery relaxations induced by gradually reducing oxygen from 95% to 1% were more pronounced than in 30 mM K^+-contracted arteries. The hypoxic relaxation in $PGF_{2\alpha}$-contracted arteries were inhibited by: TEA, a non-specific potassium channel blocker; by iberiotoxin, a blocker of large-conductance calcium-activated K^+ channels; by 4-aminopyridine, a blocker of voltage-dependent K^+ channels; by glibenclamide, a blocker of ATP-sensitive K^+ channels; but the largest effect was seen by XE991 and linopirdine, blockers of the KCNQ1-5 channels, while no effect was seen by chromanol 293B, a blocker of KCNQ1. KCNQ1, KCNQ4, KCNQ5 and the large-conductance calcium-activated BK_{Ca} channels were expressed in porcine coronary arteries.

Conclusion: Our findings suggest that hypoxia induces K^+ channel opening in isolated porcine coronary arteries. The effect is mainly mediated through KCNQ channels, which for the first time has been identified in porcine coronary arteries.

O03.06 Raffaella Magnoni

HETEROZYGOUS HSP60 KNOCK-OUT MICE REPRESENT A MODEL OF HEREDITARY SPASTIC PARAPLEGIA TYPE 13

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Mitochondria are the primary energy-generating system in the cell and they are involved in many catabolic and anabolic metabolisms. In particular, neuronal health relies strongly on mitochondrial functionality and integrity. Molecular chaperones and proteases form an efficient protein quality control system that maintains the activity of mitochondria. Among those proteins Hsp60 exerts a crucial role in folding and maintenance of mitochondrial proteins and its role is necessary for cell survival in yeast and mice. Mutations in Hspd1, the gene encoding for HSP60, are associated with a dominantly inherited form of spastic paraplegia. Hspd1 heterozygous mice show motor impairment and neurodegeneration that become evident at 12 months of age at the rotarod test, and this is associated with abnormal extension reflex of the hindlimbs and a clasping tendency that correlates with myelin abnormalities in both central and peripheral nervous systems and an increase of carbonylated proteins in mitochondria. Lack of functional Hsp60 has a deep effect on mitochondrial morphology and metabolism. Big mitochondria with abnormal cristae are detected in axons in the spinal cord and sciatic nerve, indicating a crucial role in neurons. In addition, Sod2 protein levels are decreased and its activity reduced in neuronal tissues. These findings point out that oxidative stress may play a key a role in the disease pathogenesis and that myelin could be a primary target of damage. However, decreased abundance of other substrate proteins of Hsp60 may interfere with various mitochondrial metabolic pathways, leading to mitochondria dysfunctions specifically in neurons.

O04.01 Michael Eriksen Benros

AUTOIMMUNE DISEASES AND SEVERE INFECTIONS AS RISK FACTORS FOR DEPRESSION

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Objective: Depression is a frequent co-morbidity in many chronic diseases and the development of depressive symptoms has been linked to inflammation. Inflammation and infections can increase the permeability of the blood-brain barrier opening the possibility that immune components may affect the brain. We therefore investigated whether autoimmune diseases and severe infections can increase the risk of depression.

Method: Nationwide population-based registers were linked and data were analyzed as a cohort study using survival analysis techniques. All analyses were adjusted for calendar year, age and sex. We used incidence rate ratios (IRRs) and accompanying 95% confidence intervals (CIs) as measures of relative risk.

Results: A prior autoimmune disease increased the risk of depression by 45% (IRR=1.45; 95% CI=1.39-1.52). Any history of hospitalization with infection increased the risk of depression by 64% (IRR=1.64; 95% CI=1.61-1.66). The risk of depression was increased in a dose-response relationship, where five or more infections were associated with an IRR of 4.80 (95% CI=3.81-6.04). The risk of depression was highest with the proximity of the last infection but remained significantly elevated if the last infection had

occurred more than fifteen years before. Hospital contact with an autoimmune disease had occurred in 5% of cases and hospital contact with infection had occurred in 32% of cases before the depression diagnosis.

Conclusions: Autoimmune disease and the number of infections requiring hospitalization are risk factors for depression. The increased risk is compatible with an immunological hypothesis for subgroups of patients with depression.

O04.02 Yu Wang

SELECTION OF LOWEST INSTRUMENTED VERTEBRA IN DIFFERENT TYPES OF ADOLESCENT IDIOPATHIC SCOLIOSIS

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Background. Fusion extent selection is crucial for scoliosis surgeries because it is highly correlated with postoperative outcomes. Inappropriate selections can result in decreased lumbar mobility, correction loss or spinal imbalance.

Methods. We performed a series of studies based on a 2-year radiographic follow-up of 278 AIS patients. We investigated how the deformities responded to the surgeries and discussed how to improve the surgical outcomes by carefully selecting fusion extent.

Results and Conclusions.

1. In Lenke 1A type scoliosis, the selection of LIV is highly correlated with the presence of distal adding-on; choosing DV as LIV may provide the best outcome as it not only prevents adding-on but also conserves more lumbar motion.

2. Selective thoracic fusion is prone to cause leftward spinal imbalance in Lenke 1C scoliosis patients. Postoperative spinal alignment remodeling can enable some patients to regain spinal balance. Both LIV selection and ratio of MT: TL/L curve were found to be highly correlated with the onset of postoperative trunk shift in Lenke 1C scoliosis. When the ratio of MT: TL/L Cobb angle ≥ 1.3 and Pre-op LIV-CSVL distance≥0, postoperative trunk shift is unlikely to occur.

3. In Lenke 3C and 6C scoliosis, post-op lumbar curve behaviour differs due to different choices of LIV with reference to LAV. Although the greatest correction occurs when the LIV is below the LAV, choosing LAV as LIV can still be the optimal option in certain cases.

O04.03 Emilia Horjales

INFLUENCE OF EMOTIONALLY-LOADED VISUAL AND GUSTATORY STIMULI ON EXPERIMENTAL JAW-MUSCLE PAIN.

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Previous studies have focused on the effect of negative emotions generated by music, pictures or odours on pain perception. This study tested whether

emotionally-loaded visual and gustatory stimuli could influence experimental tonic jaw muscle pain in healthy subjects. To this 32 healthy subjects (16 men, 16 women; 18-39 years old) participated. In two sessions experimental jaw muscle pain was evoked by injection of 0.2 ml hypertonic saline into the masseter muscle. In the first session with each injection an emotion (positive, negative or neutral) was generated by visual stimuli. In the second session, emotions were generated by gustatory stimuli. The participants continuously rated pain intensity (electronic visual analogue scale - VAS) as well as mood and unpleasantness/pleasantness of the conditioning stimuli (visual/gustatory).

Hypertonic saline evoked moderate levels of pain in all subjects (mean peak VAS = 5.2 +/- 2.4). During conditioning with negatively-loaded pictures VAS pain scores were increased (19.3%) compared with neutral (p=0.03) and positive emotions (p=0.001). There was a linear relation between negative emotions and VAS pain scores (r=0.40, p=0.02). Although there was a tendency, no significant effect was observed during positive pictures in comparison with neutrals (p=0.1). Surprisingly no effect on VAS pain scores was observed during neither negative (p=0.1) nor positive (p=0.2) gustatory stimuli. This may be due to failure of the gustatory stimuli to generate a change in emotions. These results suggest that not all conditioning stimuli are potent modifiers of emotions, which seem to be a prerequisite for effects on pain perception.

O04.04 Morten Charles

THE IMPACT OF INTENSIVE TREATMENT VERSUS ROUTINE CARE ON CARDIAC AUTONOMIC NEUROPATHY. THE ADDTION-DENMARK STUDY

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Objectives: It is unknown whether Cardiac Autonomic Neuropathy (CAN) can be prevented among patients with screen detected type 2 diabetes. We studied the impact of multifactorial treatment in general practice on CAN in a population with screen detected diabetes.

Methodology: In 190 general practices 1533 patients were identified with type 2 diabetes through a stepwise screening program. Before initiation of the screening programme practices were randomized to apply either intensive target driven multifactorial treatment (IT) or to give routine care (RC) according to national guidelines. At follow-up 701 patients in 3 centres were tested for CAN according to a standardized protocol. Presence of one abnormal test out of three was defined as early CAN. Logistic regression, accounting for the cluster design, was used to calculate the odds ratio for early CAN by treatment group.

Findings: The prevalence of early CAN in the RC group was 27.3% (CI95%: 22.1; 32.5) compared to 24.8% (20.6; 29.0) in the IT group. The odds ratio for early CAN in the IT group compared to the RC group was 0.88 (0.61; 1.27).

Conclusion: We did not find that intensive multi-factorial treatment versus routine care in general practice led to a statistically significant difference in the prevalence of CAN. The prevalence of early CAN in a population with screen detected diabetes was high, indicating that this complication deserves clinical attention also among those with a recent diagnosis of type 2 diabetes.

O04.05 Rune Erichsen PROGNOSIS OF INTERVAL AND SPORADIC COLORECTAL CANCER IN DANISH PATIENTS: A NATIONWIDE COHORT STUDY.

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Introduction: Almost all colorectal cancers (CRCs) develop from normal mucosa through adenomatous polyps within an estimated 10 year period. Polyp resection can arrest this development. Even so, some CRCs arise within 5 years of colonoscopy (interval CRCs). These cancers could represent missed lesions at colonoscopy or arise from insufficiently resected polyps, but may also represent highly aggressive and rapidly growing tumors with a poor prognosis.

Methods: We conducted a population-based nationwide cohort study (2000-2006) using Danish registries to investigate the prognosis after interval CRC – CRCs diagnosed 1-5 years after colonoscopy. Sporadic CRCs were defined as those with no colonoscopy (except for the diagnostic) prior to diagnosis. We estimated survival using the Kaplan Meier method and used Cox regression to compute mortality rate ratios (MRR) and associated 95% confidence intervals (95%CI) comparing interval with sporadic CRC, adjusting for age, gender, cancer site, stage, and comorbidities.

Results: We identified 587 interval CRCs and 24,446 sporadic CRCs. Interval CRC patients were older (74 vs. 72 years); more likely to be female (52% vs. 48%), to have comorbidities (58% vs. 44%), and right-sided lesions (36% vs. 22%); but were less likely to be metastatic at diagnosis (16% vs. 21%). One year survival was 69% in interval CRC patients and 70% in sporadic CRC patients corresponding to an adjusted 1 year MRR of 0.88 (95% CI 0.76, 1.0). After 5 years survival was 40% and 42%, respectively, corresponding to an adjusted MRR of 1.1 (95%CI 0.95, 1.3).

Conclusion: Our results do not indicate that interval CRCs have a markedly poorer prognosis than sporadic CRCs.

O04.06 Mette Richner SORTILINS IN NEUROPATHIC PAIN

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The molecular mechanisms underlying neuropathic pain are still incompletely understood. Upon peripheral neuronal injury, activated microglia release brain-derived neurotrophic factor (BDNF) in the spinal cord stimulating neuronal TrkB, which through unknown signalling pathways leads to reduced neuronal potassium-chloride co-transporter 2 (KCC2) levels.

Sortilin is known to regulate neuronal Trk receptor trafficking and signalling. We therefore speculated whether Sortilin deficiency might influence neuropathic pain development. Wild-type (wt), Sortilin knockout mice (Sort1$^{-/-}$) and knockout mice of the Sortilin related receptor SorCS2 (SorCS2$^{-/-}$) were examined in the spared nerve injury (SNI) model. Whereas wt mice developed profound hypersensitivity towards tactile stimulation (mechanical allodynia), Sort1$^{-/-}$ and SorCS2$^{-/-}$ mice were partially and fully protected, respectively. In addition, intrathecal injection of antibodies raised against Sortilin or SorCS2 at the time of SNI surgery inhibited development of mechanical allodynia in wt mice for 2-3 days and was furthermore able to rescue wt mice from mechanical allodynia to a level identical to the knockout animals when injected one week after SNI surgery. Finally, intrathecal injection of BDNF induced mechanical allodynia in wt mice, whereas Sort1$^{-/-}$ and SorCS2$^{-/-}$ mice were resistant.

As we found no changes in microglia activation or BDNF levels in Sort1$^{-/-}$ and SorCS2$^{-/-}$ spinal cord compared to wt upon SNI, we hypothesize that Sortilin and SorCS2 are involved in neuropathic pain development by regulating TrkB targeting or downstream signalling in spinal cord sensory neurons.

O05.01 Christine Lodberg Hvas

BRAIN DEATH CAUSES HYPERCOAGULATION - AN EXPERIMENTAL PIG STUDY

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Background: Coagulopathy associated with brain injury represents a serious complication, and severe increased intracranial pressure has been linked to hypercoagulation. There is a high prevalence of pulmonary thrombi in lungs rejected for transplantation, suggesting hypercoagulation and thrombosis as the pathogenesis.

Hypothesis: Brain death causes hypercoagulation and microvascular thrombosis.

Methods: Twenty animals were randomized to either brain death or control, and observed for 8 hours after brain death. Outcome variables: Thrombelastometry (ROTEM), thrombin generation (CAT), plasma clotting time and standard coagulation parameters (APTT, Prothrombin time, Protein C, Antithrombin, D-dimer). The kidneys were examined for microvascular thromboses.

Results: Brain death induced maximum hypercoagulation following 60 mins as demonstrated by ROTEM (reduced clotting time, increased maximum velocity), CAT (reduced lag time, increased peak thrombin), as well as reduced plasma clotting time. All functional coagulation parameters returned to baseline levels 180 minutes after brain death. No thromboses were found in the kidneys. Hypercoagulation was associated with reduced levels of Protein C.

Conclusion: Brain death causes sudden but temporary hypercoagulation, but leaves no microvascular thromboses in the kidneys. The change in the

levels of Protein C suggests that the Protein C pathway is linked to this hypercoagulation.

O05.02 Martin Skøtt

ACUTE KIDNEY INJURY (AKI) IN RATS WITH PRE-EXISTING CHRONIC KIDNEY DISEASE (CKD) INDUCES A MAJOR INCREASE IN PRO-INFLAMMATORY CYTOKINES (IL-1[BETA], IL-6) AND CHEMOKINES (RANTES, MCP-1) IN KIDNEY AND LUNG

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AKI in patients with pre-existing CKD have increased co-morbidity and mortality. Although it is well established that AKI is associated with a major increase in pro-inflammatory cytokines and chemokines, it is unknown to which extent AKI in pre-existing CKD leads to changes in the expression of pro-inflammatory cytokines/chemokines. The aim of this study was to assess the changes in the expression of pro-inflammatory cytokines and chemokines in kidney and lung in response to AKI in rats with pre-existing CKD.

CKD was induced by 5/6 nephrectomy (5/6 Nx) for 6 weeks. AKI was induced by intestinal ischemia for 45 min followed by reperfusion for 90 min (II/R): 1) Nx+II/R; 2) Sham Nx+II/R; 3) Nx+Sham II/R; 4) Sham Nx+Sham II/R, 5) controls. Cytokines/chemokines were measured in homogenized whole kidney and lung preparations with LuminexTM 100.

S-Cr increased significantly in response to II/R:from 66.2[plusmn]7.3 to 88.9[plusmn]8.3 in Nx rats, resp., and from 32.0[plusmn]0.7 to 54.7[plusmn]2.9 in Sham Nx rats. The levels of IL-1[beta], IL-6, RANTES, and MCP-1 in lung and kidney, were significantly higher in rats undergoing II/R compared to sham II/R. Important also is that the 5/6 Nx rats II/R induced a significant increase in IL-1[beta], IL-6, RANTES, and MCP-1 expression in kidney and lung compared to sham 5/6 Nx. Morever, the response was even more pronounced in the 5/6 Nx compared to the response in sham 5/6 Nx rats.

The results demonstrate a significant increase in pro-inflammatory cytokines and chemokines in response to AKI in rats with pre-existing CKD.

O05.03 Charlotte Rotbøl Bøje

COMORBIDITY IS A STRONG PREDICTOR OF OVERALL SURVIVAL IN HEAD AND NECK CANCER: RESULTS FROM A POPULATION BASED STUDY ON 11,056 RADIOTHERAPY-TREATED HEAD AND NECK CANCER PATIENTS

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Background: Head and neck cancer (HNC) patients may suffer from comorbidity due to smoking habits and high age. Comorbidity may impact treatment decisions and outcome and consequently prognosis. The purpose

of this study was to 1) describe the prevalence and type of comorbidity in a large cohort of HNC patients and 2) to investigate the prognostic impact of comorbidity on survival for HNC patients treated with primary radiotherapy (RT).

Materials and methods: The DAHANCA database contains information on all HNC-patients in DK and we included all patients treated with primary RT from 1992 to 2007, a total of 11,056 patients. Data on comorbidity was obtained from the National Patient Registry and adapted to Charlson Comorbidity Index (CCI).

Results: Median age was 62 years, 73% were males and 43% had comorbidity at time of diagnosis. The prevalence of the most common comorbidities was: other prior cancers (16%), cardiovascular diseases (10%), cerebrovascular diseases (10%), and chronic pulmonary diseases (9%). Increasing age was significantly associated with increasing CCI score. In multivariate analysis comorbidity was statistically associated with overall survival with a HR 1.55 [95% CI 1.42; 1.69] for patients with CCI score 2+. Only a prior cancer, liver- and ulcer-disease was individually significantly associated with poorer OS.

Conclusions: Comorbidity is common among HNC-patients. Comorbidity is a strong predictor of OS and the impact is comparable to the impact of tumor-size and nodular metastasis. Comorbidity will be of increasing importance as the population becomes older and should therefore be considered and incorporated in prognostic staging of patients with HNC.

O05.04 Thomas Reinert

TUMOR-SPECIFIC METHYLATION IN URINE: A PROMISING BIOMARKER FOR EARLY DETECTION OF BLADDER TUMOR RECURRENCE

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Purpose: Non muscle invasive bladder cancer (NMIBC) has the highest recurrence rate of any malignancy. As many as 70% of patients experience relapse. Aberrant DNA methylation is present in all bladder tumors and can be detected in urine specimens. In a previous study we identified a number of DNA methylation markers that showed significant diagnostic value. Here we evaluated the significance of the biomarkers for early detection of recurrence.

Experimental Design: The methylation levels of VIM, TWIST1, ZNF154, POU4F2, HOXA9, and EOMES in urine specimens were measured by MethyLight. We analyzed 665 urine specimens from 240 patients with NMIBC (192 incident cancer and 384 control visits) and 45 control-matched individuals with no bladder malignancies. Recurrence was diagnosed by cystoscopy and biopsies performed during cystoscopy.

Results: We searched for significant differences in methylation levels of VIM, TWIST1, ZNF154, POU4F2, HOXA9, and EOMES in urine specimens from patients with bladder tumor recurrences compared to patients with no recurrences. Data is being generated now and sensitivity and specificity

values of the markers will be presented at the meeting.

Conclusions: Based on previous studies, gene methylation of VIM, TWIST1, ZNF154, POU4F2, HOXA9, and EOMES in urine specimens is expected to be promising biomarkers for bladder cancer recurrence with higher sensitivity than cytology. We expect the methylation profiles to be similar in primary tumors and recurrences and combination of markers to be able to predict subsequent tumor recurrences with a high sensitivity.

O05.05 Simon Lønbro

RESISTANCE TRAINING AND DIETARY SUPPLEMENTS AS INTERVENTION FOR REGAINING MUSCLE MASS FOLLOWING RADIOTHERAPY IN HEAD AND NECK CANCER PATIENTS

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Background: Post treatment, head and neck cancer (HNC) patients (pts) often experience a large loss of body mass (around 10%) - mainly muscle mass. This is an independent mortality predictor and lowers muscle strength and functional capacity (FC). Progressive Resistance Training (PRT) is most effective in regaining these parameters. Protein (P) and Creatine (Cr) can enhance the positive effects.

Aims: 1) Do HNS pts tolerate PRT ± P and Cr, 2) what are the effects on lean body mass (LBM), muscle strength and FC.

Methods: 30 HNC patients are randomly assigned into two groups. During week one Group 1 completes an oral Cr loading regime. Group 2 ingests placebo. In the following 12 weeks, Group 1 completes a PRT protocol + P and Cr suppl., and Group 2 completes the same PRT + placebo suppl. Treatment induced loss of body weight is recorded. At baseline and pre and post the 12 weeks of PRT, LBM, muscle strength and FC are evaluated. Preliminary results: At abstract deadline 17 pts have completed the protocol, 4 pts are ongoing, 9 pts have dropped out (7 before training with causes unrelated to intervention). To uphold the blinding process, the two groups are pooled in the preliminary analyses. We report a treatment induced mean loss of body weight of 11% (9.5 kg). This remains unchanged following intervention, but LBM increases 5% (2.7 kg), muscle strength increases 30% (49N-m) and 32% (27N-m), respectively. 30 s sit-to-stand and 30 s arm curl capacity increase by 26% (5 reps) and 23% (5 reps), respectively. Conclusion: We report only two drop outs related to intervention. Thus, HNC pts do tolerate PRT ± P and Cr and it has a positive effect on LBM, muscle strength and FC.

O05.06 Malene Bek-Thomsen

EVOLUTION OF STREPTOCOCCUS PNEUMONIAE INTO GENETICALLY DISTINCT SUBPOPULATIONS

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Streptococcus pneumoniae is a leading cause of invasive disease and respiratory-tract infections in children, elderly and immunocompromised

individuals. S. pneumoniae is an opportunistic pathogen that normally colonizes the nasopharynx asymptomatically in young children. Differences in virulence and disease potential between pneumococcal strains are poorly understood. In general, S. pneumoniae is characterized by extensive recombination resulting in blurring of distinct evolutionary lineages. Nevertheless, preliminary analyses based on all known multilocus sequence types (STs) of this species demonstrate the existence of distinct evolutionary clades. The present study investigates the existence of functionally and genetically distinct evolutionary lineages within S. pneumoniae with differences in virulence and disease potential. 109 clinical S. pneumoniae strains, representing various genetic backgrounds and serotypes were examined by multilocus sequence analyses (MLSA) and characterized by Comparative Genome Hybridization (CGH) by use of a "pan-genome" micro-array designed from public available genome sequences of S. pneumoniae, S. mitis and S. oralis. Based on preliminary results all strains were separated into two distinct clades by hierarchical clustering of our CGH data. The pathogenicity island harboring the pneumococcal serine rich protein (psrp) was exclusively associated with clade I. We do not find any correlation between major linages of MLSA trees and hierarchical clustering based on CGH data. In conclusion CGH based analyses will help to identify genetic features of S. pneumoniae relevant to virulence and disease. New vaccine candidates may be revealed.

P01.01 Tine Kjærgaard

INVESTIGATION OF MEGALIN, CUBILIN AND AMNIONLESS IN HUMAN PLACENTA AND THEIR STRUCTURAL, FUNCTIONAL AND MECHANISTIC ROLE IN MATERNAL/FETAL TRANSPORT

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During the human pregnancy, the placenta, a highly specialized organ, has a verity of important functions supporting normal growth, development and protection of the fetus. Little is known about the specific cellular mechanisms involved in the transport and catabolism of the macromolecules transported across the placenta. The three proteins, megalin, cubilin and amnionless (AMN), are known for their function in the kidney, where they re-absorb a panel of different ligands via receptor-mediated endocytosis. Other expression sites have been mentioned for megalin, cubilin and AMN, e.g. placenta. However, their function and structural characteristics in the human placenta are unknown. Studies of cubilin and megalin in rodents indicate that they both play an important role in embryonic development, a least in rodents. However, rodent and human pregnancies are basically very different. Therefore, the aim of this study is to characterize the structure, function and mechanistic role of megalin, cubilin and AMN in human placenta.

Preliminary results indicate the presence of megalin and cubilin mRNA and protein in human term placenta. So far, only the presence of AMN mRNA has been detected in term human placenta. Initial immunohistochemical studies show megalin and cubilin in term human placenta in syncytiotrophoblastic cells. The cellular localization needs to be further investigated e.g. by electron microscopy. Functional studies of megalin,

cubilin and AMN in different placental cell lines will hopefully provide insight to their involvement in endocytosis in this organ and their potentially important role during human pregnancy.

P01.02 Lena Lindtoft Rosenbæk

REGULATION OF A NOVEL PHOSPHORYLATION SITE OF NCC AT SERINE 124 BY VASOPRESSIN

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Using large-scale LC-MS/MS-based phosphoproteomic profiling of biochemically isolated membranes from the rat renal cortex, a novel phosphorylation site in NCC was identified (Feric et al 2011). Bioinformatic studies suggested the neighbouring S127 site as also highly likely to be phosphorylated. Immunoblotting with a novel pS124-NCC antibody demonstrated a band of ~160 kDa in the kidney cortex, but not medulla, which was preabsorbed by a corresponding phosphorylated peptide. Confocal microscopy with segment-specific markers localized pS124-NCC to all DCT cells, with greater abundance in the early DCT. Double immunogold electron microscopy with total NCC revealed that pS124-NCC was associated predominantly with the apical plasma membrane of DCT cells, although some labelling was associated with intracellular vesicles. Acute, but not long-term, vasopressin treatment significantly increased pS124-NCC abundance at the plasma membrane. Similar observations were apparent after rats were fed a low salt diet. Kinase profiling assays using a synthetic peptide corresponding to the region surrounding S124 against 24 protein kinases, chosen based upon their potential to phosphorylate this region, showed either weak or no significant activity. Immunoblotting and ^{36}Cl uptake studies of various NCC mutants in oocytes showed decreased activity of NCC at the plasma membrane when replacing serine124 with alanine, thus preventing phosphorylation at this site.

Feric, M., B. Zhao, J.D. Hoffert, T. Pisitkun & M.A. Knepper. (2011). Large-scale phosphoproteomic analysis of membrane proteins in renal proximal and distal tubule. American Journal of Physiology.Cell Physiology 300, C755-70.

P01.03 Gitte Qvist Kristiansen

TARGETING CYTOSTATICS TO CD163-EXPRESSING HISTIOSARCOMA CELLS IN XENOGRAFTED IMMUNODEFICIENT MICE

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CD163 is the macrophage scavenger receptor for uptake of haptoglobin and hemoglobin. In addition to being expressed in monocytes/macrophages, minor amounts of soluble CD163 circulates in plasma.

In the present study we have studied the effect of the cytotoxic drug doxorubicin encapsulated in liposomes targeting CD163 in order to increase

efficacy and decrease side effects of the drug (increase therapeutic index). A human CD163$^+$ cell line, SU-DHL-1 was xenografted subcutaneously into immunosuppressed NOD/scid mice and solid tumors were established in 82% of the mice. A two week treatment study with doxorubicin-liposomes with anti-human CD163-antibodies linked to the liposomes showed regression of the tumors but the effect was not significantly different from non-targeting doxorubicin-liposomes not targeting CD163. It is our hypothesis that vascularisation in the tumor areas is too inadequate to obtain an optimal tumor targeting in this xenograft model. Hence we are now trying to establish a modified model where the tumor is grafted to the peritoneal cavity in order to improve tumor cell accessibility of the liposomes.

Instead of the physical measure of tumor growth as an endpoint, we, due to expected improved exchange with the circulation, expect to be able to monitor tumor growth biochemically by measuring the content of soluble CD163 in plasma.

P01.04 Francesco Trepiccione

ACUTE LITHIUM ADMINISTRATION INCREASES WATER EXCRETION THROUGH ACTIVATION OF MAP KINASES.

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Acute lithium (Li^+) treatment impairs the water permeability of the kidney collecting duct.

Here we used a phosphoproteomic approach to detect the early molecular targets of Li^+ in inner medullary collecting duct (IMCD).

Rats were treated with a gavage of either LiCl or NaCl (2.4 mmol/Kg of BW). After 4 or 9 hours rats were killed and IMCD suspensions were prepared. Phosphopeptides from IMCD isolated after 9 hours of Li^+-treatment were enriched by immobilized-metal affinity chromatography (IMAC) and then analysed on a LTQ-Orbitrap LC-MS/MS system.

Nine hours after LiCl gavage, rats showed a significantly increased urine volume and decreased urine osmolality ($p<0.01$ $n=8$). A total of 1222 unique phosphopeptides were identified in 578 proteins. DAVID analysis of the obtained phosphopeptide database highlighted a MAPK cluster of proteins. In addition, phosphopeptides in the Li^+-treated group with ≥ 1.5 fold increased abundance shared a common “proline-directed” kinase motif as determined by Motif-X analysis, further evidence that MAP kinases may be regulated by acute Li^+. The phosphopeptides in this group included AQP2 phosphorylated at S261, a potential MAPK target.

Western blot analysis of IMCD isolated 4 hours after LiCl gavage showed increased phosphorylation of p38 and ERK1/2. No changes were observed in pS261-AQP2 and pJNK1/2 at 4 hours. After 9 hours of LiCl gavage pS261-AQP2 and pS256-261-AQP2 were significantly increased, while no changes in pS256-AQP2 or phosphorylated MAPKs were observed.

We conclude that MAPK pathways are an early target of Li^+ action in IMCD and the Li^+-related polyuric effect may involve the associated increase in pS261-AQP2.

P01.05 Sascha Eichendorff

PH-REGULATED INTRACELLULAR DELIVERY OF BIOACTIVE SUBSTANCES TARGETED TO CD163 IN MACROPHAGES

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CD163 is a scavenger receptor exclusively expressed in monocyte/macrophage lineage. Monocyte maturation into macrophages leads to a highly increased surface expression of CD163 and inflammation induces a further increase in CD163 expression. This makes the receptor an interesting target for intracellular drug delivery and for this purpose we have constructed liposomes targeting CD163 via an anti-CD163 antibody linked to the liposome surface.

In an ongoing study we use different CD163-targeting liposomal formulations in order to find the optimal conditions for intracellular drug release in the endosomal/lysosomal pathway. By combining membrane-forming lipids (DOPE, CHEMS, HSPC, cholesterol) with different pH-dependent net-charges, we have established a panel of formulations with different response to pH changes. Confocal microscopy analysis of the intracelluar uptake and transport combined with a fluorometric assay are currently carried out to evaluate the formulations in respect of their stability and pH-dependent release of dye encapsulated in the liposomes.

P01.06 Mie Rostved Rasmussen

GENERATION OF A ZEBRAFISH KNOCKDOWN MODEL FOR STUDIES OF ABCC6 AS A POTENTIAL TRANSPORTER FOR CELLULAR EXPORT OF VITAMIN B_{12}

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Vitamin B_{12} (B_{12}) deficiency or abnormal B_{12} homeostasis in humans is a common cause of hematological and neurological disorders. The intercellular transport of the vitamin is essential for homeostasis. However, in contrast to well-characterized receptor-mediated import of B_{12}, it has so far been uncertain how the vitamin is exported from the cell.

We are currently searching among the ATP-binding cassette (ABC) transporter family for proteins responsible for such export. So far, screening of a panel of candidate transporters by cellular gene silencing has revealed that the ABC transporter, ABCC1, alias multidrug resistance protein 1 (MRP1), plays a role in cellular B_{12} efflux. ABCC1 is present in the basolateral membrane of intestinal epithelium and in other cells. Data from this study suggests, however, that there may be alternative B_{12} exporters, because B_{12} efflux from cells from ABCC1 knockout mice was not completely abolished. Furthermore, B_{12} export is evident in locations in which ABCC1 is not expressed.

The present study focuses on another ABC transporter, ABCC6, which is

interesting in terms of B_{12} export owing to its expression in the kidney from which export of this vitamin is unascertained. To study transporter function, the abcc6a and abcc6b genes were knocked down in zebrafish embryos by means of morpholino oligonucleotide antisense technology. Knockdown of the abcc6a gene induced a detectable phenotype. This indicates that the ABCC6a protein may be important in zebrafish embryo development. This animal model will be studied in detail in future experiments in order to investigate ABCC6 substrates and to elucidate whether B_{12} is transported by this protein.

P01.07 Rikke Holm Jensen

NA⁺,K⁺-ATPASE AMINO ACIDS INVOLVED IN TRANSPORT OF THE 3RD SODIUM ION

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Available evidence indicates that two of the three Na^+ ions bound in the E1 form occupy approximately the same positions as the K^+ ions in E2, but the location of the third Na^+ ion is unsolved. We have previously found a marked decrease in Na^+ affinity for activation of phosphorylation in the human α3 mutant D923N, which is associated with RDP (Einholm AP et al. (2010)). D923 is located in the cytoplasmic half of transmembrane helix M8 in a putative transport channel between M5, M7, M8 and M10. The external K^+ sites behaved wild type (wt)-like in the mutant, suggesting that D923 is associated with the third Na^+ ion. I have mutated several residues of the rat α1 isoform related to the channel structure and have characterized the effects on Na^+ and K^+ affinities and the E2-E1 and E1P-E2P conformational transitions of the pump cycle. Mutation D928N of rat α1, equivalent to D923N of human α3, shows a conspicuous reduction of apparent Na^+ affinity without effect on external K^+ affinity. D928L shows a large reduction of apparent Na^+ affinity, even though the E2-E1 conformational equilibrium is shifted strongly in favor of the Na^+ binding E1 form. Located deeper in the channel than D923/928 is Q856. Mutants Q856A and Q856E exhibit >10- and ~5-fold reduction of Na^+ affinity, respectively, relative to wt, and the Q856 mutants display wt-like interaction with K^+ at the E2P sites, thus supporting the hypothesis that the channel containing D923/928 and Q856 is a transport pathway for the third Na^+ ion. I mutated C932 close to the proposed channel inlet. C932F reduced Na^+ affinity ~90-fold. This fits into a model, where the bulky phenylalanine prevents Na^+ from entering the channel.

P01.08 Kaspar Renÿ Nielsen

POLYMORPHISMS IN INFLAMMATORY MEDIATORS - RELATION TO DISEASE ACTIVITY IN B-CELL DISEASES

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Background and present status:

B-cells are regulated by a complex network of growth factors and inflammatory mediators. Dysregulation of B-cell differentiation can result in a broad spectrum of B-cell malignancies and autoimmune diseases. Genetic polymorphisms in inflammatory response genes affect gene expression and

function, which can affect both immune regulation and tumor/host interaction, facilitating proliferation of malignantly transformed B-cell clones.

Hypothesis and aims:

We hypothesize, that genetic polymorphisms in selected inflammatory and immune modulating mediators can influence the inflammatory response. The altered inflammatory host response may result in a micro environment that facilitate the growth of malignantly transformed B-lymphocytes and stimulates autoimmune diseases. The objective is to investigate the relationship between 28 polymorphisms in inflammatory genes with overall survival in B-cell-non-Hodgkin's lymphoma (B-NHL), Hodgkin's disease and Multiple Myeloma and with disease activity in Rheumatoid Arthritis.

Material and methods:

A pilot study including 60 B-NHL patients were used to validate genotyping methods. The present study includes 273 B-NHL patients, and 330 Myeloma patients, 308 RA patients and 605 healthy controls. DNA is extracted from whole blood or archival formalin-fixed, paraffin wax-embedded tissue taken at biopsy. 28 SNP's in selected inflammatory mediators are tested using TaqMan genotyping assays. Single-gene, haplotype and genetic load data will be used in multivariate survival analysis.

Deliverables: The main goal is to investigate genetic polymorphism in the inflammatory system as prognostic biomarkers in B-cell diseases.

P01.09 Søren Brandt Poulsen ISOLATION OF KIDNEY CONNECTING TUBULE CELLS USING FLUORESCENT-ACTIVATED CELL SORTING

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Background: In the kidney, the final salt reabsorption takes place in the distal nephron [the distal convoluted tubule 2 (DCT2) and connecting tubule (CNT)] and in the collecting duct. The CNT cells are crucial for the sodium and potassium homeostasis. A population of CNT cells has, yet to date, not been successfully isolated from whole kidneys.

Aim: Using mice, we want to isolate a cell population consisting mainly of CNT cells. The mice will be subjected to long-term aldosterone administration to study the regulation of transcripts in the CNT cells.

Methods: We use a transgenic mouse model expressing enhanced green fluorescent protein (EGFP) in the DCT2, CNT, and initial cortical collecting duct (iCCD). A single-cell suspension is produced by subjecting whole kidneys to enzymatic digestion. The EGFP-positive cells are isolated using fluorescent activated cell sorting (FACS). During the sorting, the green fluorescent cells from the DCT2 and iCCD will be excluded, because they have a different granularity and size compared to the CNT cells.

Results: The concentration of CNT cells in the whole kidney cell suspension is ~2 %. After FACS sorting, we have increased the CNT cell concentration to ~90%.

Summary: Using transgenic mice, we have the tools to produce a cell population consisting predominantly of CNT cells (~90%.). The transgenic mice will be subjected to long-term aldosterone administration. Aldosterone-regulated transcripts in the CNT cells will be identified by RNA sequencing.

P01.10 Pernille Munk Frandsen

ACTIVATION AND RECEPTOR STUDIES OF HUMAN MAST CELLS IN HEALTHY INDIVIDUALS AND PATIENTS WITH ASTHMA AND ALLERGY

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Introduction: The human mast cell is a central effector cell in the innate immune response and plays a key role in the allergic inflammatory process. Present studies are limited as mature mast cells are difficult to isolate from human tissue in sufficient quantities.

Objectives: he aim of this study is to characterize some of the properties of the mast cells. These include description of the reaction upon activation of the FcεRI receptor. We want to analyze the release of inflammatory mediators.

Another objective is to characterize the profile of expressed miRNA in mast cells from healthy individuals and patients with type-1 allergy. This will be done by use of microarrays.

Methods: $CD133^+$ cells are purified from buffy coats and cultured for 7 weeks under defined conditions giving a homogenous culture of mature mast cells.

The last ten days of the maturation period, the mast cells are cultured with different concentrations of IgE before activation. The release of histamine and PGD_2 is measured by commercial kits.

For characterization of miRNA profile, the mast cells are activated for 24 hours before purification of miRNA.

Results: The release of histamine from human mast cells is related to the concentrations of IgE in the culture in a dose-dependent manner from 50 ng/ml – 5 µg/ml IgE. The total content of histamine in the mast cell is not affected by the IgE concentration in the culture. The release of PGD_2 is not affected by IgE in concentrations above 50 ng/ml. The amount of IgE receptors (FcεRI) on the surface of the mast cell were measured by flow cytometry and the amount of receptor increased with increasing concentrations of IgE.

P01.11 Kristian Stødkilde-Jørgensen

STRUCTURAL AND FUNCTIONAL STUDIES OF THE HAPTOGLOBIN-HEMOGLOBIN RECEPTOR

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Human African trypanosomiasis is a tropical disease endemic in Southern

Africa. It is caused by protozoan parasites of the genus Trypanosoma and it is fatal if untreated. Humans and other primates have evolved innate immunity to all but two of these parasite subtypes. This immunity arises as the parasites are tricked into taking up a lethal compound via the Trypanosoma brucei haptoglobin-hemoglobin receptor (TbHpHbR).

TbHpHbR displays no sequence homology with proteins of known function, thus leaving no clues as to its overall structure or how it binds its ligand - the haptoglobin-hemoglobin complex. Using x-ray crystallography and mutational studies, the present project seeks to elucidate the interaction between TbHpHbR and the haptoglobin-hemoglobin complex.

The paper will describe the expression and purification of TbHpHbR together with the purification of haptoglobin-hemoglobin from both ascites and blood plasma. Finally, the purification of TbHpHbR in complex with haptoglobin-hemoglobin will be presented.

P01.12 Pauline de Bruijn

P2 RECEPTOR EXPRESSION PROFILE IN MOUSE THICK ASCENDING LIMB

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Extracellular ATP acts as an auto- and paracrine signaling molecule, which stimulates different cellular functions. Its effect is mediated by the family of purinergic receptors (P2) that are subdivided into metabotropic P2Y and ionotropic P2X receptors. In the mouse genome 14 P2 receptors are identified. P2 receptors are ubiquitously expressed in all renal epithelia and commonly several P2 receptors are found in a single nephron segment. In the mouse medullary thick ascending limb (mTAL) functional data suggests the presence of several P2 receptors. In this project we performed a comprehensive survey of all 14 mouse P2 receptors (7 P2Y and 7 P2X) in mTAL. Methods: RT-PCR. For all P2 receptors, positive controls were established from reference mouse tissues. As the mTAL segment comprises ~90% of the tissue mass in the inner stripe of the outer medulla (ISOM), we used ISOM tissue to screen for the expression of P2 receptors in mTAL. We found the following P2Y receptors: $P2Y_2$, $P2Y_6$, $P2Y_{12}$, $P2Y_{13}$ and $P2Y_{14}$. Furthermore, we identified the following P2X receptors in ISOM: $P2X_1$, $P2X_2$, $P2X_3$, $P2X_4$, $P2X_5$ and $P2X_7$. In the next step we micro-dissected single mTAL tubules and repeated this analysis. An average of 5.5 mm of mTAL length was sufficient to perform RNA extraction. The following receptor mRNAs were identified in isolated mTALs: $P2Y_2$, $P2Y_6$, $P2X_1$, $P2X_4$ and $P2X_5$. These results provide a comprehensive view of all P2 receptors expressed in mouse mTAL. Previous and new functional data suggests a physiological role of the $P2Y_2$ and the $P2X_4$ receptor. These data thus complement the functional studies that investigate the role of purinergic signaling in intact renal epithelium.

P02.01 Jesper Sand Sørensen

RESIDUAL &BETA;-CELL FUNCTION IN CHILDREN AFTER 3-6 YEARS OF DIABETES MELLITUS.

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Background: The phenotype of diabetes mellitus (DM) in children is not well-characterized. Generally, it is believed that β-cell function is exhausted after 1-2 years of Type1 DM. However, after 3 years with diabetes, some children have well-controlled and easy regulated diabetes, which may partly be due to residual β-cell function.

Objective: To determine prevalence of residual β-cell function(RBF) in children after 3-6 years of DM. Furthermore to determine the association between RBF and glycaemic control(HbA1c) and incidence of severe hypoglycaemia.

Methods: Three hundred and forty two children (173 boys), aged 4–18 years with DM for 3-6 years were included. Residual β-cell function was assessed by testing meal-stimulated C-peptide (MCP). Information on current HbA1c and incidence of severe hypoglycaemia within the last year was retrieved.

Results: Of the 342 children 26.9% had a MCP of more than 0.04 nmol/l, and 7.9% even had a MCP of more than 0.2nmol/l. Comparing the children with and without RBF(MCP of more or less than 0.04 nmol/l respectively), the group with RBF had a significantly lower HbA1c (mean ± SD) 7.9% ±1.2 vs. 8.5% ±1.3 (p<0.001) and a significantly lower incidence of severe hypoglycaemia 7.6% vs. 17.6% (p<0.02).
 Conclusions: The study showed a considerable phenotypical diversity with respect to RBF in children after 3-6 years of DM. Children with RBF were found to have a significantly better diabetes regulation and a lower risk of hypoglycaemia compared to children without RBF.

Future studies will investigate other possible effects(metabolic, longterm etc.) of and factors (immunological, genetic etc.) possibly associated with residual β-cell function.

P02.02 Lars Rolighed CLINICAL AND BIOCHEMICAL VARIABLES DETERMINING BMD IN PRIMARY HYPERPARATHYROIDISM

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Purpose: To analyze the association between different clinical and biochemical variables and BMD in a large series of PHPT patients.

Methods: We identified all 1391 consecutive patients undergoing parathyroid surgery at Aarhus University Hospital in a 15 year period. We retrieved preoperative biochemical data and preoperative DXA measurements. A complete set of biochemical data were available on 785 patients.

Results: Median age was 62 years (range 13-91) and 638 (81%) patients were women. PTH (median [min-max]) was 12.1 [5-330] pmol/l and 25OHD was 51 [5-238] nmol/l. Women had slightly lower Ca^{2+} (1.50 ± 0.09 mmol/l) than men (1.53 ± 0.12 mmol/l, P<0.001) and also lower plasma creatinine (P<0.001). Insufficient plasma 25OHD levels (< 50 nmol/l) were found in 365 (46%) patients. Associations with BMD were calculated in a multiple regression model. BMD of the spine, hip and forearm were negatively

associated with age (P<0.001). PTH was inversely associated with BMD of forearm (P<0.001) but not associated with total hip or spine BMD (NS). In men, but not in women, PTH was inversely associated with BMD and hip (P=0.05) and spine (p=0.02). BMD of the spine, hip and forearm were not associated with 25OHD levels (NS).

Conclusions: In PHPT DXA of the forearm is recommended due to the negative association between PTH and BMD of the forearm and the higher prevalence of subnormal values. PTH seems to have a stronger association with the forearm than spine and hip BMD, perhaps explaning the higher bone loss in the forearm observed in patients with PHPT. Although most patients are women, the detrimental effect of high PTH levels on BMD seems to be more pronounced in men than in woman.

P02.03 Morten Møller Poulsen

POTENTIAL BENEFICIAL EFFECTS OF RESVERATROL ON OBESITY, METABOLIC SYNDROME AND INFLAMMATION.

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OBJECTIVE: Obesity is associated with a markedly increased risk of metabolic disease including type II diabetes, cardiovascular disease and non-alcoholic fatty liver disease (NAFLD). In animal studies the polyphenol resveratrol, which orginates from natural sources and is found in e.g. various berries, peanuts and red wine, has shown promising tendencies in ameliorating the development of metabolic disease, improving health and overall mortality. However, so far no human trials on efficacy outcomes have been conducted.

AIM: In a human context, we investigate the physiological and molecular biological properties of resveratrol, hypothesizing that resveratrol holds the potential to improve the dysmetabolic profile associated with obesity.

DESIGN: Randomized, placebocontrolled, double-blinded trial. 24 obese but otherwise healthy men are randomly assigned to resveratrol or placebo treatment, 500 mg*3 for 5 weeks. Before and after the treatment period the participants will undergo extensive metabolic examination.

METHODS: Include hyperinsulinemic euglycemic clamp, MR spectroscopy, DEXA-scan, indirect calorimetry, 24 h blood pressure, muscle and fat biopsy (Real time RT-PCR, ELISA), various metabolic serum markers.

RESULTS: Recruitment was initiated in November 2010, and the last participant is expected to complete the trial primo December 2011. Hopefully we will be able to present the first preliminary results at the PhD day 2012.

P02.04 Marie Juul Ørnstrup

INVESTIGATIONS OF THE EFFECTS OF RESVERATROL ON BONE

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Background and hypothesis

Obesity and metabolic syndrome are associated with insulin resistance, shortened life expectancy and, in some studies, development of osteoporosis and increased risk of fractures. Recently, low-grade inflammation has been hypothesized to be the causative link. The polyphenol Resveratrol, which is found in red wine, has anti-inflammatory effects, and has shown promising effects in rodent studies on inflammation and bone mineral content. Resveratrol inhibits NFκB, which is of special interest as the new anti-osteoporosis drug Denosumab, also inhibits NFκB. Cell culture studies indicate that resveratrol can influence osteoclasts and osteoblasts directly.

Aim

The aim of this PhD project is to investigate the effects of resveratrol on human bone metabolism though a large clinical trial and cell culture investigations.

Methods

Double-blinded, randomized, placebo-controlled study with 80 obese volunteers with metabolic syndrome. Treatment is either resveratrol or placebo for one year. DXA, CT-scan, biochemical markers and bone marrow examination will be done to follow the effects on bone turnover, BMD, BMC and bone structure. Cell culture study (cells from healthy donors) will reveal effects on proliferation, differentiation and expression of the Wnt pathway genes of human osteoblasts, and formation and activity of human osteoclasts in vitro.

Perspective

The present investigation will increase our knowledge on the association between obesity, low-grade inflammation and bone metabolism, and may increase our understanding of the pathogenesis underlying the simultaneous increase in the prevalence of osteoporosis and obesity.

P02.05 Jurgita Janukonyte

PHARMACOKINETIC PROFILES OF GROWTH HORMONE (GH) ADMINISTERED AS A BOLUS INJECTION VERSUS A CONTINUOUS INFUSION AND WITH AND WITHOUT EXERCISE IN ADULTS WITH GH DEFICIENCY (AGHD)

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Background

GH replacement therapy has proved beneficial in AGHD patients due to its metabolic actions. GH may be administered by different routes, and subcutaneous (sc) therapy is the most commonly used. Only a few studies have investigated the systemic bioavailability of GH after sc injection. GH is absorbed lymphatically, and factors influencing lymph flow, e.g. physical activity may play a role for systemic bioavailability of GH. A study by Hvas E. et al. has demonstrated a higher clearance rate of radioactively labelled

albumin from the lymphatic flow during physical exercise compared to the rest. Up to date, this issue has not been addressed in AGHD patients.

Aims

To compare the pharmacokinetic profiles of GH administered sc as a bolus or as an infusion in AGHD patients during interval exercise or in supine rest. To compare the response of insulin and glucose after intake of a carbohydrate rich breakfast in the bolus as well in the infusion group.

Methods

7 subjects with AGHD have finished the study and 1 is ongoing. 4 treatment regiments were carried out in random order after a screening visit. In the bolus group (B with exercise and A without exercise sessions) the subjects were treated with a single 3mg/day dose of GH for two consecutive days. In the infusion group (D with exercise and C without exercise sessions) the subjects were treated with a sc infusion of 3 mg/day of GH over 60 hours. Blood samples for serum GH, GH binding proteins, insulin-like growth factor 1 (IGF-1); IGF-1 bioactivity, insulin and plasma glucose profiles were taken for 48 hours under B and A sessions and for 60 hours under sessions D and C.

Results

No results are available at the moment.

P02.06 Ravikiran Mahadevappa

THE ROLE OF MEGALIN IN CISPLATIN INDUCED ACUTE KIDNEY INJURY

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Cisplatin (cis-diamminedichloroplatinum; CDDP), a widely used chemotherapeutic drug used for treating cancer, is known to be nephrotoxic inducing acute kidney injury (AKI). Megalin, an endocytic receptor, expressed on luminal cell membrane of proximal tubular epithelial cells, is involved in the nephrotoxic effect of substances such as aminoglycosides and myoglobin, by mediating the tubular uptake of these substances. CDDP has been shown to affect proximal tubule endocytic function and genetic polymorphisms in megalin are associated with increased sensitivity to the CDDP ototoxicity. So far, a role for megalin in development of CDDP induced AKI has not been demonstrated and the potential mechanism remains unresolved. We injected megalin knockout mice (MKO) and wild type(WT) mice with 15mg/kg of CDDP, and collected blood, urine, and tissue samples after 4 days. Renal functional markers such as p-creatinine, KIM-1, and NGAL were analysed by HPLC and ELISA. Apoptosis were assessed by TUNEL staining. Inflammatory markers like interleukin, MCP1, TGFβ, NF–kB and the amount of CDDP in renal tissues will be investigated. CDDP induced AKI were confirmed by creatinine analysis. Hematoxylin and eosin stained kidney sections revealed more areas of tubular necrosis and brush border shedding in CDDP treated WT mice compared to CDDP treated MKO

mice which was supported by increased apoptosis. AKI urinary markers, KIM-1 and NGAL, increased in CDDP treated WT and MKO mice; however, they were higher at baseline in MKO, suggesting decreased tubular absorption of these. In conclusion, mice lacking megalin revealed less renal tissue damage following CDDP treatment than the WT.

P02.07 Mark Reinhard

EFFECT OF INSULIN INFUSION ON LIVER PROTEIN SYNTHESIS DURING HEMODIALYSIS

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Introduction: Hemodialysis (HD) is a catabolic procedure that may contribute to the high frequency of protein-energy wasting among patients on maintenance HD. The aim was to investigate the effect of insulin infusion on liver protein synthesis during HD.

Methods: In a randomized cross-over study 11 non-diabetic HD patients (M/F:8/3, median age 57 years, range 33-79) received 1) no treatment (NT), 2) glucose infusion (G) (10% glucose, 2.5 mL/kg/h), and 3) glucose-insulin infusion (GI) (10% glucose added 30 units of NovoRapid® per liter, 2.5 mL/kg/h) during a standardized 4 h HD session. During infusions blood glucose levels were maintained at 8.0-10.0 mmol/L by additional glucose infusion. Glucose and glucose-insulin infusions were commenced 2 h prior to HD and continued throughout the HD session. Fasting blood samples were collected before infusions were started (baseline) and followed by a meal.

Results: Data presented as mean±SD. There was an overall increase in serum fibrinogen from HD start to 2 h post-HD (12.1±1.8 to 12.8±1.8 μmol/L, $p<0.0001$) but no difference between groups ($p=0.28$). Serum albumin showed no overall change (39.9±2.4 to 40.4±2.6 g/L, $p=0.14$), and no difference between groups ($p=0.13$). There was a marked overall decrease in serum IGF-binding protein 1 (IGFBP-1) 4 h after baseline (from 267±147 to 143±89 μg/L, $p=0.0001$) but no difference between groups ($p=0.40$). However, 4 h after baseline serum IGFBP-1 concentrations increased in the NT group but remained suppressed in the infusion groups ($p=0.003$).

Conclusion: Neither glucose nor glucose-insulin infusion appear to add to the anabolic effects of a meal on liver protein synthesis during HD.

P02.08 Thomas Nordstrøm Kjær

INVESTIGATIONS OF THE ANTI-INFLAMMATORY EFFECTS OF RESVERATROL STUDIED IN VIVO AND IN VITRO

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Background: Low-grade inflammation due to macrophage infiltration and hypoxia in adipose tissue is thought to be the link between obesity and the metabolic syndrome (MS). Resveratrol (RV), a natural anti-inflammatory compound, reduces inflammation and normalizes both insulin sensitivity and lifespan of diet induced obese rodents. RV also inhibits proliferation of

vascular smooth muscle cells that play a role in developing cardiovascular disease.

Sirt1 enzymes, thought to mediate the RV-effects in rodents, are present in human fatty tissue (HFT). In vitro, RV stimulates HFT to increase lipolysis, reduce secretion of the macrophage-attracting MCP1 and reduce inflammation. Furthermore, hypoxia induced inflammation in HFT is completely normalized when exposed to RV.

Aim: To investigate the anti-inflammatory effects of RV in vivo and in vitro to clarify its potential in preventing or treating MS.

Method:

In vivo: 80 men with the MS are treated with RV 500mg x 3 daily or placebo for 1 year. Before and after treatment, biopsies from skeletal muscle, adipose tissues are obtained. MR/DEXA-scan is used to quantify body fat amount and body composition respectively. Every other month blood tests are taken to follow inflammation, lipid profile, liver function, insulin sensitivity (HOMA), RV and RV-metabolites.

In vitro: 3T3 adipocyte, skeletal muscle and THP macrophage cell lines are inflamed and exposed to RV. Substance secretion is then characterized using ELISA. Selected genes and gene-expression is followed by rt-PCR. Specific RV-effects on protein production, cell signalling and post-translational modification is studied by SILAC.

P02.09 Sara Heebøll RESVERATROL IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (LIRMOI 3)

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Background

Non-alcoholic fatty liver disease (NAFLD) is strongly associated with the obesity epidemic and now the most common liver disease in the western world. Indeed, NAFLD is the hepatic expression of the metabolic syndrome. NAFLD covers a wide range of conditions, from simple steatosis to non-alcoholic steatohepatitis (NASH) with inflammation and fibrosis, which may progress to cirrhosis. NASH increases mortality and the risk of end-stage liver disease, cardiovascular disease, and diabetes. Yet, knowledge regarding treatment of NAFLD is scarse.

Resveratrol (RES) is an antioxidant compound, abundant in grapes, and registered as a nutritional supplement. Growing evidence show that RES is anti-inflammatory with decreased expression of cyto- and adipokines. Moreover, RES mimics the effect of calorie restriction by activating sirtuin and AMPK pathways, thereby offering protection against obesity-related disorders.

Clinical trial

We plan a randomized, double-blind study, including 50 NAFLD/NASH patients. Participants will be treated with either placebo or RES 500 mg

three times daily for six months. Participants are male, overweight with at least one sign of the metabolic syndrome and with elevated ALT >70. Exclusion criteria are diabetes or cancer.

We also wish to study RES in in vitro and in an animal NASH model.

Aim

We expect that RES: reduces ALT levels reduces hepatic fat content, assessed by MR spectroscopy; reduces hepatic inflammation, assessed histologically; and it inhibits the expression of proteins in the inflammatory pathways, assessed by gene expression studies. Thereby, we expect to show that RES is a promising new treatment for NAFLD/NASH patients.

P02.10 Zhulin Ma

EFFECT OF NPH INSULIN, INSULIN DETEMIR AND INSULIN GLARGINE ON IGF-1 AND IGFBP PRODUCTION IN PATIENTS WITH TYPE 1 DIABETES: AN OPEN-LABEL, RANDOMISED, TRIPLE CROSS-OVER TRIAL

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Background: Type 1 diabetes mellitus is characterized not only by a primary deficiency of insulin, but also by an equally important secondary disruption of growth hormone—insulin-like growth factor— insulin-like growth factor binding protein (GH-IGF-IGFBP) axis. It is possible that some of the new insulin analogues due to their altered pharmacokinetic profiles and receptor affinity may have the eventual differential impact on the GH-IGF-IGFBP axis in type 1 diabetic patients.

Aim: To investigate whether the serum insulin profile obtained by once-daily injection of long-acting insulin analogue, insulin detemir or insulin glargine, has a different impact on IGFBPs production and IGF-I concentrations (total IGF-I, free IGF-I, bioactivity IGF-I and tissue-available IGF-I) than that seen during treatment with long-acting human insulin, NPH insulin.

Methods: At least 16 type 1 diabetes patients will receive individually identical doses of three different insulin on 3 separate visits in this randomized crossover study. Having achieved stable blood glucose control by intravenous infusions of insulin and isotonic glucose, one of the trial insulin will be injected subcutaneously at 18:00 h. Blood samples will be taken for endpoints measurement and safety monitoring in the following 16 hours.

Perspective: The results may bring new knowledge on improving insulin sensitivity and the safety assurance of insulin analogues.

P02.11 Christian Selmer Buhl

EFFECTS OF 3-4 MONTHS OF SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI)-TREATMENT ON METABOLISM AND HYPOTHALAMIC-PITUITARY-ADRENAL (HPA)-AXIS IN YOUNG MEN BORN WITH LOW BIRTH WEIGHT (LBW)

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Background: LBW (<2.5kg) leads to an increased risk of type 2 diabetes (T2DM), hypertension and depression. Disturbances in the HPA-axis play a major pathophysiological role. We have previously shown that SSRI-treatment of LBW animals for 5-6 weeks can normalize HPA-axis function and insulin sensitivity.

Aims: Examine metabolic differences between young men born with LBW and NBW (3.5-4.5kg) and evaluate the potential benefit of SSRI-treatment for 3-4 months.

Design: Double-blinded, randomized and placebo-controlled trial. LBW (n=40) and NBW (n=20) groups were matched by age, BMI and physical activity.

Methods: Insulin sensitivity (OGTT, hyperinsulinemic euglycemic clamp), blood samples (cholesterol, ALAT, SR, CRP), HPA-axis activity (24-hour urine and plasma profile, DXM-suppression test), total body fat (DXA-scan), fat content in liver and skeletal muscle (MRI-spectroscopy), physical activity (questionnaire, pedometrics), blood pressure (24 hour profile), psychiatric profile (MDI, SCL-92).

Preliminary results: LBW is associated with insulin resistance (Rd clamp ↓ 13,8 to 20,4%), higher cholesterol levels (2,8 vs 2,3mM), higher total body fat (18,0 vs. 14,7%), higher fat content in liver (↑ 130%) and muscle (↑ 48%), higher MDI-score (7,65 vs. 4,25), reduced hypothalamic sensitivity (ACTH suppression 49% vs. 79%) and higher diastolic blood pressure during day (76,5 vs. 70,7 mmHg). (All p<0.05.)
Conclusion: The results clearly indicate that LBW is associated with disturbances in the metabolic profile which could increase the risk of developing T2DM, hypertension and depression. The potential benefit from the SSRI-treatment can be evaluated when the analyses are completed.

P02.12 Lærke Egefjord

EFFECTS OF LIRAGLUTIDE ON INTRACEREBRAL AMYLOID DEPOSITION IN ALZHEIMER'S DISEASE

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Background:

Premature cell degeneration develops in both type 2 diabetes (DM-2) and Alzheimer's Disease (AD). DM-2 is characterized by a loss of beta-cell function, whereas AD shows a loss of neuronal function and cell death. Glucagon-like-peptide-1 (GLP-1) exerts glucose-dependent stimulation of insulin secretion. In cell and animal experiments beta-cell neogenesis, growth and differentiation are stimulated by GLP-1, and inhibition of beta-cell apoptosis has been shown in vitro. GLP-1 receptors have also been located in the CNS. GLP-1R stimulation in the hippocampus induces learning ability and memory and leads to neurite outgrowth and protects against nerve cell apoptosis in the CNS.

AD is characterized by an increased level of beta-amyloid. A reduced memory, also a characteristic of AD, has been shown in GLP-1 receptor KO mice. We have recently shown that GLP-1 has a neuroprotective function in patients with DM-2.

The insulin-producing beta-cells are also characterized by accumulation of amyloid in DM-2 models. There are no registered drugs which change the deposition of amyloid and there are no drugs with convincing effect on the progression of the disease in AD patients. Moreover, the marketed drugs for AD treatment today have disadvantageous side effect profiles.

Hypothesis:

6-month treatment with the GLP-1 receptor agonist Victoza® will reduce amyloid deposition in the CNS of patients with AD.

Design:

Controlled, randomized, double-blinded intervention study.

Methods:

The primary endpoint is to determine amyloid accumulation in the CNS using PET scanning.

The secondary endpoint is to evaluate cognitive functions by means of validated tests.

P03.01 Anne Kirstine Fisker Pedersen

A.K. Pedersen

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Background: The most effective pain management after major ankle surgery is infusion of local analgesics via a catheter close to the sciatic nerve. The saphenous nerve also carries sensation from the ankle leading to moderate to severe postoperative pain typically the first two postoperative days despite a continuous sciatic nerve block.

Aim: To test whether continuous saphenous nerve block via a catheter provides better pain control compared to single injection saphenous nerve block.

Hypothesis: Continuous saphenous nerve block as a supplement to continuous sciatic nerve block reduces opioid consumption.

Methods: Fifty patients will be included in this randomized, double-blinded,

controlled study. Before major ankle surgery a sciatic catheter and a saphenous catheter are inserted in addition to two single injections of Ropivacaine around both nerves with ultrasound-guidance. After surgery a continuous infusion of 0.2% Ropivacaine 10 mL/h is started in the sciatic catheter in all patients. Patients are randomized into two groups. The experimental group receives continuous infusion of Ropivacaine 0.2% 5 mL/h for 48 hours in the saphenous catheter. The control group receives continuous infusion of isotone saline 5 mL/h for 48 hours. The primary outcome measure is consumption of opioid the first 48 postoperative hours. Secondary outcomes are success rates of saphenous nerve sensory block, clinical analgesia of foot and ankle the first 48 hours, and cost-effectiveness of single shot versus continuous saphenous nerve blockade. These are measured by Numeric Rank Scale for pain, tactile sense tests of the toes and time recording.

Results: This is an ongoing study.

P03.02 Birgitte Nellemann Sørensen

MECHANISTIC PATHWAYS IN LIPID INDUCED INSULIN RESISTANCE IN SKELETAL MUSCLE

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Background: During fasting, insulin resistance in skeletal muscle is essential to preserve glucose for brain metabolism, and insulin resistance is a component of the pandemic increase in obesity related diseases. Elevated free fatty acid (FFA) levels are presumably one explanation behind reduced insulin sensitivity in these situations. Two pathways are ongoing in the debate: 1) defects in insulin signalling pathways, and 2) regulation of key enzymes in glycolysis.

Aim: To elucidate mechanistic pathways of insulin resistance in skeletal muscles during an induced insulin resistant state.

Methods: 8 healthy young men were investigated in a randomised, placebo-controlled, cross-over study on four occasions: 1) 12h fast+placebo infusion (control day), 2) 12h fast+GH infusion, 3) 36h fast+placebo infusion, and 4) 36h fast+GH infusion. Blood samples, indirect calorimetry, hyperinsulinemic euglycemic clamp, and muscle biopsies were applied to determine circulating FFA levels, substrate oxidation, glucose uptake, myocellular signalling and enzyme activity.

Results: Circulating FFA and lipid oxidation increased on the three intervention days. This was associated with reduced insulin sensitivity and pyruvate dehydrogenase activity. Further, insulin signalling to glucose uptake was unaffected.

Conclusion: Our data shows that glycolytic activity is impaired in human skeletal muscle during hyperinsulinemia in the insulin resistant states. Also, insulin signalling to glucose uptake was unaffected by the interventions. These findings suggest that reduced insulin sensitivity is due to decreased glycolytic activity. This leads to improved understanding of mechanisms behind type 2 diabetes.

P03.03 Jennie Maria Christin Strid

INCIDENCE, INTENSIVE CARE TREATMENT, AND PROGNOSIS OF PATIENTS WITH STATUS ASTHMATICUS IN DENMARK: A NATIONWIDE COHORT STUDY

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INTRO.

Status asthmaticus (SA) is a medical emergency. Studies on incidence and prognosis reported contradictory results, but data included readmissions or were restricted to specific age groups or hospitals. A nationwide study is needed to better understand the SA epidemiology.

OBJECTIVE

Examine the SA hospitalization rate in Denmark, describe the characteristics of SA patients, and estimate their prognosis.

METHOD

We identified all patients with an incident SA diagnosis from 2005-09. Those previously diagnosed with chronic obstructive pulmonary disease were excluded to avoid misclassification. We obtained data on hospitalizations, comorbidity, and demographics from registries. We calculated hospitalization rates, ventilatory support frequencies, and mortality by the Kaplan-Meier method.

RESULT

After exclusion of 179 COPD patients, 1,437 patients were analyzed. Mean hospitalization rate was 52.7 per 1,000,000 person-years, being remarkably higher for young (370.9 for age 0-1 year;139.5 for age 2-14) and slightly higher for males than females (55.9 vs 49.4). The 119(8.3%) patients admitted to intensive care units (ICU) were primarily

P03.04 Susani Rothmann Larsen

CONGENITAL HEART DEFECTS: QUALITY OF LIFE ASSESSMENT - CHILDREN VERSUS PARENTS

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Objective: To compare children's self-reported Quality of Life (QoL) following congenital heart defect (CHD) surgery with parental report and examine the influence of socioeconomic factors on the difference.

Methods: We did a population based study from 2007 to 2008 on 236 children who underwent CHD surgery during 1996-2002. QoL was measured by the Child Health Questionnaire-child report version 87 for the child and by the Child Health Questionnaire parent form 50 for the parent. We converted these into 14 main domains regarding health, physics,

emotions, behavior and family, of which 12 enabled child versus parent comparison. We obtained socioeconomic data from Statistics Denmark and divided data into four socioeconomic classes. A paired t-test and Intraclass Correlation Coefficient(ICC) were used to compare QoL from child and parent reports. ICC in each socioeconomic class was calculated and regression analysis used to evaluate the influence of socioeconomic factors.

Results: Children reported higher QoL after CHD surgery than their parents in Physical Functioning (mean 96-94 $p<0.05$), Behavior (83-78 $p<0.001$), Self Esteem (87-80 $p<0.001$), General Health Perception (77-70 $p<0.001$) and Family Cohesion (81-78 $p<0.05$), while parents reported higher scores in the domain Bodily Pain/Discomfort (90-87 $p<0.01$). However, agreement was fair to good in all domains with ICC values from 0.3-0.8. Socioeconomic class had no statistical significant influence on the QoL difference.

Conclusion: Children's QoL following CHD surgery is higher in several domains when assessed by the children. However, agreement was acceptable and socioeconomic factors did not affect the difference.

P03.05 Marianne Kjær Poulsen

LIPID TURNOVER IN NON-ALCOHOLIC FATTY LIVER DISEASE: EFFECTS OF THE DIET SUPPLEMENTATION RESVERATROL ON LIVER FAT CONTENT, BASAL AND INSULIN STIMULATED FFA AND VLDL-TRIGLYCERIDE METABOLISM IN OBESE

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Obesity is characterized by insulin resistance, dyslipidemia, abnormal free fatty acid turnover and abnormal liver fat content. The last, known as non-alcoholic fatty liver disease (NAFLD), ranges form pure steatosis to a state with inflammation and fibrosis called steatohepatitis (NASH), with an increased risk of liver cirrhosis, primary liver cancer, diabetes and cardiovascular disease. Steatosis is seen in 50-90 % of obese persons.

Former studies of obeseity have shown increased insulin resistance in both the liver and adipose tissue. Until now studies on animals treated with Resveratrol have shown positive results on liver fat content, glucose turnover and insulin sensitivity. The underlying mechanisms are not exactly clarified, but one hypothesis is that Resveratrol activates the enzyme SIRT1, thereby imitating the beneficial effects of caloric restriction.

The study is a double-blind placebo-controlled trial of 16 obese healthy men with NAFLD treated with either Resveratrol or placebo for 6 months and compared at baseline with 8 obese healthy men without NAFLD. All participants in the intervention group are examined at baseline and after 6 month with MR-scan and DEXA-scan to determine changes in subcutaneous and visceral fat distribution, with MR-spectroscopy to determine changes in liver fat content, and a Study Day using different radioactive tracers to determine changes in FFA turnover, VLDL-TG turnover and insulin sensitivity before and after treatment and during basal and clamp period. All examinations are repeated to enlighten long-term effects of Resveratrol treatment, especially on fat metabolism.

P03.06 Niklas Blach Rossen

NIGHTTIME DOSING OF ANTIHYPERTENSIVE DRUGS IN TYPE 2 DIABETES

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BACKGROUND

Hypertension and diabetes are well-established risk factors for the development of atherosclerosis. With the increasing use of ambulatory blood pressure monitoring (ABPM), extensive data on nighttime blood pressure (BP) has been obtained. Several studies suggest that increased nighttime BP is an independent risk factor for atherosclerosis and cardiovascular disease. Therefore, new strategies to treat increased nighttime BP are warranted. One possibility is simply to change the time of administration of antihypertensive drugs from morning to nighttime.

AIM

In a population of type 2 diabetic patients with increased nighttime BP, we want to investigate if it is possible to reduce nighttime BP by changing the time of administration of antihypertensive drugs from morning to nighttime. This reduction should of course be achieved without increase in daytime BP.

METHODS

Cross-over study of 40 type 2 diabetic patients with increased nighttime BP (>120 mmHg) despite stable antihypertensive treatment. Patients will be randomized to 8 weeks of treatment with morning or nighttime dosing of once daily antihypertensive drugs followed by 8 weeks of treatment with the opposite time of administration. At baseline and after each of the two 8 week periods, patients will undergo ABPM, measurements of arterial stiffness and blood and urine samples.

PERSPECTIVES

If nighttime dosing of antihypertensive drugs can reduce increased nighttime BP without increasing daytime BP, this simple intervention might contribute to a reduced number of cardiovascular events in type 2 diabetic patients.

P03.07 Anne Cathrine Søndersgaard Thorup

INVESTIGATING THE HEALTH PROMOTING EFFECTS OF VEGETABLES ON PEOPLE WITH TYPE 2 DIABETES AND THE METABOLIC SYNDROME

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Background: Vegetables are an important part of human diet and a major source of biologically active substances called phytochemicals. Phytochemicals contribute to the nutritional quality of food giving a bitter

and strong taste, but more importantly they have health promoting effects.

Aim: to determine if a high dietary intake of bitter and strong tasting vegetables has a beneficial impact on insulin resistance related to the metabolic syndrome (MS) and type 2 diabetes (T2D), when compared to an equivalent intake of mild and sweet tasting vegetables.

Method: The study is carried out as a 3-month randomized controlled parallel intervention study involving 60 participants aged 30-65 years with MS and T2D. The participants are randomized into 3 different diets respectively; 1) consisting of 500 g daily bitter and strong tasting vegetables, 2) consisting of 500g sweet and mild tasting vegetables, 3) normal diet (control). The participants visit the clinic for a screening, and afterwards once a week in the following 12 weeks. At the three major visits (0, 6, 12 week) the participants collect urine samples, complete a 3-days food diary and undergo a thorough clinical examination incl. 24-h blood pressure, body composition and collection of fasting blood samples (glucose, insulin, glucagon, HbA1c, GLP-1, lipids, cytokines, adipokines, parathyroid hormone and vitamin D). At week 0 and 12 an oral glucose tolerance test is performed. Furthermore, compliance is measured in week 4 and 8.

Perspective: The study is ongoing and is expected to contribute to the understanding of how a high vegetable diet with either high or low levels of phytochemicals effects subjects with MS and T2D.

P03.08 Ermina Bosnjak

CYTOKINE TNF-α INDUCES PROTEIN LOSS AND IMPROVES INSULIN SENSITIVITY IN HUMAN LEG

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BACKGROUND:

Tumor Necrosis Factor Alpha (TNF-α) is an inflammatory cytokine. Systemic TNF-α administration has widespread metabolic actions and generates stress hormone response with activation of the hypothalamo-pituitary axis.

Our study was designed to test the hypothesis that local leg perfusion with TNF-α directly induces protein loss and affects glucose metabolism.

METHODS:

Acute metabolic effects of TNF-α were studied in eight healthy subjects. Catheters were inserted into the femoral vein and femoral artery in each leg. TNF-α vs. placebo were perfused into the femoral artery of the leg. Furthermore, catheters were inserted into the antebrachial veins for infusion of isotope-labeled tracers. Femoral vein sampling allowed assessment of local metabolic events in leg. Each study comprised a 3 h basal period and a 3 hour glucose clamp. Muscle biopsies were performed in order to

investigate intracellular signalling.

RESULTS:

TNF-α perfusion significantly increases protein degradation in the perfused leg during the clamp (measured by ^{15}N-phenylalanine tracer), and improves glucose uptake in the muscles in the perfused leg during the clamp (measured by raw arterio-venous differences).

There is no effect of TNF-α perfusion on lipolysis and lactate release.

PERSPECTIVES:

In order to investigate systemic metabolic effects of TNF-α and bacterial Endotoxin via stress hormone response placebo, Endotoxin and TNF-α were given systemically in the antebrachial vein in eight patients with hypopituitarism (to block stress hormone release) and in eight healthy subjects, all studied thrice. Every study comprised a 4 h basal period and a 2 h glucose clamp. Muscle and fat biopsies were performed.

P03.09 Berthil Frederik Forrest Clasen

GROWTH HORMONE AND LONGEVITY: A SEARCH FOR THE MECHANISM.

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Caloric restriction (CR) has been shown to increase longevity and decrease the risk of developing a number of metabolic diseases in a broad range of organisms. The underlying mechanisms has not been elucidates, but numerous studies indicate that the deacetylase SIRT1 is central in the observed effects of CR. Furthermore, growth hormone (GH) has also been shown to have profound impact on longevity and metabolic diseases. GH has two distinct effects: At high energy levels GH induces IGF-1 transcription which ultimately has anabolic effects on the organism and this will reduce longevity. At low energy levels, GH increases lipolysis which increases longevity. Disregarding the final outcome of GH stimulation, binding of GH to its receptor leads to phosphorylation of STAT5. A STAT5 homologue, STAT3, has in a recent study been shown to be regulated by acetylation and deacetylation, the latter mediated by SIRT1. In a pilot study performed in our laboratory, STAT5 has been shown to be acetylated. This leads to a hypothesis which proposes that the effect of GH switches between IGF-1 transcription and lipolysis in muscle- and adipose tissue via reversible STAT5 acetylation, and this effect involves interaction with SIRT1.

The project is composed of three connected studies:

1) Identification of the global gene expression in human muscle tissue after GH stimulation.

2) A closer in vitro study of the degree, location and effect of STAT5 acetylation.

3) A study on the GH signaling in human muscle and adipose tissue after resveratrol mediated SIRT1 activation.

P03.10 Jeppe Skov

SHORT-TERM IMPACT OF GLUCAGON-LIKE PEPTIDE-1 ON KIDNEY FUNCTION IN HEALTHY MEN

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Type 2 diabetes mellitus (T2DM) is reaching epidemic proportions and diabetic nephropathy (DN) is now the principal cause of end-stage renal failure in the western world. DN is a progressing disease characterized by different phases - initial hyperfiltration and hyperperfusion, a silent period and then microalbuminuria followed by overt proteinuria and renal failure. Glycemic regulation and systemic blood pressure control are crucial in the prevention, but local kidney factors are of great importance as well.

GLP-1 is a gut hormone that stimulates insulin secretion subsequent to food intake. Due to its antihyperglycemic properties and an advantageous side effect profile, GLP-1 analogs are becoming increasingly popular in the treatment of T2DM.

Recently, GLP-1 mimetics have revealed evidence of kidney protective properties in diabetic mice by preventing hyperfiltration and decreasing albumin excretion. In man, native GLP-1 is found to increase natriuresis; however, the effect on kidney haemodynamics remains unrevealed.

To elucidate the immediate physiological impact of native GLP-1 on the human kidney function we perform a randomized, double blind, cross-over study involving 12 healthy young men.

Glomerular filtration rate is assessed by steady state 51Cr-EDTA clearance and renal plasma flow by steady state 123I-hippuran clearance. Lithium clearance will estimate proximal tubular sodium reabsorption, and various electrolyte clearances along with urine albumin excretion will be measured. Also GLP-1 impact on the renin-angiotensin-aldosterone system and insulin-like growth factors binding proteins will be investigated.

Studies are ongoing. Results will be presented.

P03.11 Poul Vestergaard Nielsen

GH SIGNALING I MUSCLE AND FAT AS A FUNCTION OF AGE: A COMPARATIVE STUDY OF STAT, MAPK, SOCS MRNA PI3K, MTOR CONCENTRATION IN YOUNG AND ELDER.

P.F. Ves

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Introduction

Growth Hormone (GH) is the primary anabolic hormone during calorie restriction. GH is secreted in short bursts during night, and secreted at the onset of physical activity. GH induces include hepatic IGF-I and IGF-II

production, whole body protein synthesis, collagen synthesis and.

The objective of this study is based on 2 earlier studies. First study: there is a correlation between the age related reduction in GH secretion, and the reduction in Lean body mass (LBM), this reduction in LBM can be reduced with supplementation of GH. The mechanism behind this has to our knowledge not been investigated, but could be explained with changes in GH effects on muscle signalling. Second study: Females has a reduced hepatic IGF-I stimulated GH response compared to men. It could be speculated that this phenomenon, reduced GH sensitivity, would be present in fat and muscle cells as well. Neither of the assumptions above have been investigated and we find it therefore interesting to design a study where we investigate GH's effect on signalling mechanisms response in muscle and fat as a function of age and sex.

Objective

The purpose of this study is to compare the GH induced response in signalling mechanism between sexes and different ages.

Methods

20 persons will be include in this controlled randomized blinded intervention study, the persons will be divided in 4 groups– 1) young Males <30 years, 2) young females < 30 years, 3) elderly males > 60 years, 4) elderly females > 60 years. The intervention consist of 2 days, one day the participants will be given a bolus of GH, the other a bolus of salin, post 30 and 120 min we will do muscle and fat biopsies.

P03.12 Ulrick Espelund

SURVIVAL AFTER BREAST CANCER SURGERY PREDICTED BY INSULIN-LIKE GROWTH FACTOR MEASUREMENTS.

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Context: The Insulin-like Growth Factors (IGF) IGF-I and IGF-II have potent growth promoting and anti-apoptotic effects in cancer cells. Large prospective studies have demonstrated increased risk of breast cancer with increasing levels of serum IGF-I. Our group have previously found marked changes in the IGF system in women breast cancer in spite of minimal extent of disease.

Objective: Firstly to perform a thorough comparison of the IGF-system between women with breast cancer and healthy, age-matched controls, and secondly to investigate the predictive value of IGF measurements in serum for survival.

Design: 400 patients from the county of Funen were enrolled around the time of primary breast cancer surgery or biopsy (from 1993 to 1998). Treatment was given independently of study participation. 600 age-matched controls from the same geographical region were recruited. All participants underwent a structured interview and physical examination. Blood was drawn, and serum was stored at -80^0 until time of assay in 2011. Information on surgery, pathology, adjuvant treatment follow-up schedule

as well as vital status was obtained from Danish Breast Cancer Cooperative Group.

Main outcome measure: Primary outcomes are survival rates for patients with high vs. intermediate vs. low serum IGF concentrations and IGF bioactivity (determined in vitro by specific IGF-I receptor activation assay). Secondary outcome is a baseline comparison of bioactive IGF-I, IGF and IGF binding protein (IGFBP) levels between patients and controls.

Results: Analyses should be complete by the time of the Ph.D day 2012.

P04.01 Charlotte Green

EXPERIENCE WITH USE OF A PIG MODEL IN GROIN HERNIA OPERATION TRAINING IN SURGICAL EDUCATION

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Background: In the Danish surgical specialist education programme there has been no formal skills training in groin hernia (Lichtenstein). As part of a PhD we have designed a formal training course in this field involving theory and hand-on training in plastic phantoms as well as in anaestesized pigs.

Methods: We designed a course for doctors in their first year of specialty training in general surgery. In the programme we included training in pigs with congenital hernias in the inguinal region (usually male pigs). This gave us the possibility of supervising and training dissection techniques in real tissue.

Results: Fifteen first year specialty trainees have been enrolled in the course so far. All have been very content with the curriculum and especially the ability to practice in real tissue and the supervised feedback.

Conclusion: By using an animal model with congenital hernia in the inguinal region we have been able to design a new and relevant course for doctors in specialty training. This course offers the possibility of training in a model that imitates a human groin with relevant dissection of a “real” hernia witch gives a good base for a clinical training programme.

P04.02 Mie Hessellund Samson

DO ASSAYS FOR THE SAME COMPONENTS GIVE COMPARABLE RESULTS? A COMPARISON BETWEEN COMMERCIAL AND IN-HOUSE ASSAYS FOR TREFOIL PEPTIDES.

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Background:

Trefoil peptides (TFF1, TFF2 and TFF3) are 7-12 kDa molecules, secreted by mucin-producing epithelial cells. Increased serum concentrations have been reported in a number of pathological conditions, which warrants the need for validated commercially available assays.

Methods:

We validated commercial assays for TFF1-3 and compared results obtained

with our in-house assays, using serum from blood donors.

Results:

Level of detection was: ≤0.008 nmol/L. Measuring ranges were: 0.032-0.51 (TFF1), 0.038-0.76 (TFF2) and 0.019-0.15 (TFF3) nmol/L. Imprecision (CV), judged from measurement of serum pools in two levels, was below 9% (TFF2 and TFF3) but up to 18% (mean 0.41 nmol/L) for TFF1. No cross reactivity between the TFFs (concentrations >100 nmol/L) was observed. The 95% nonparametric reference intervals were: <0.0032-0.53 (TFF1), 0.099-1.4 (TFF2) and 0.086-0.87 (TFF3) nmol/L. Comparing commercial to in-house assays (n=132), showed biases explained by differences in the calibrators (TFF1 and TFF2). A number of samples showed markedly different results.

Conclusions:

The commercial assays for TFF2 and TFF3 are acceptable for use on serum samples, while the TFF1 assay revealed a poor imprecision and a too narrow measuring range. Results obtained with the commercial and the in-house assays differed, partly because of differences in the calibrators employed.

P04.03 Alice Østergaard

CHARACTERISATION OF FUNCTIONAL INACTIVE ANTITHROMBIN VARIANTS CAUSING THROMBOSIS - A SUB STUDY OF "NEW TECHNOLOGIES FOR INTERVENTION WITH CONFORMATIONAL DISEASE"

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Conformational diseases are a newly recognized group of heterogeneous disorders resulting from conformational instability of proteins including serpins. Antithrombin (AT) is a member of the serpin super family and is considered as the most important endogenous anticoagulant. It modulates blood coagulation by inhibition of coagulation factors including FIIa and FXa. Mutations in the AT gene can result in conformational diseases where changes in molecule structure hinders AT in performing the inhibition of coagulation factors and the risk of patients suffering from thrombosis increases.

The overall aim of this study is to characterize and elucidate the kinetic and biophysical properties of various AT mutants causing conformational diseases, in order to describe func-tion and thrombogenicity.

AT protein will be purified from both recombinant protein production and from plasma of patients suffering type II AT deficiency, by chromatography purification. The kinetics and biophysical properties of AT will be elucidated by both established and novel characterisation techniques.

This project is a part of a larger project with the pur-pose of developing new technologies for stabilisation of functionally in-active serpins, with new treatments as its main purpose.

Only a few therapies are available for treatment and prevention of venous thrombosis for patients with AT deficiency, and heparin therapy may not

always be sufficient. The characteristic analysis in this project may serve as an important brick in the development and isolation of specific nucleic acid aptamers against AT mutational variants to preserve the functional and active conformation and inhibitory mechanism of AT.

P04.04 Henriette Vind Thaysen

VALIDATION OF THE DANISH VERSION OF THE DISEASE SPECIFIC INSTRUMENT EORTC QLQ-CR38 TO ASSESS HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH COLORECTAL CANCER

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Introduction

EORTC QLQ-CR38 is a disease specific instrument developed by the European Organization for Research and Treatment of Cancer (EORTC) in 1990. A validation of the questionnaire has never been undertaken in Danish or any other Scandinavian language. The aim of this study was to examine the psychometric properties of the Danish version of EORTC QLQ-CR38.

Methods and material

Patients with colorectal cancer from two Danish Hospitals answered EORTC QLQ-CR38 one month after their operation. A psychometric evaluation of the questionnaire's structure, reliability, convergence, divergence and known group validity was performed.

Results

Data from 164 (86.3%) patients were available for analysis. The criterion of Cronbach´s alpha coefficient >0.70 was fulfilled in five out of nine scales. For convergent validity the criterion of a correlation >0.40 was fulfilled for all items in three of the scales: Body image, sexual activity and male sexual problems. None of the items in the chemotherapy side effects scale meet the criterion. Seventeen (60.0%) out of 30 comparisons distinguished between subgroups of patients, with respect to clinical and demographic variables.

Conclusion

The lack of specificity in some of the scales should be taken into account in the evaluation of results from Danish studies including EORTC QLQ-CR38. The update of EORTC QLQ-CR38, EORTC QLQ-CR29, seems relevant and the results from this study indicate that it might be a valid instrument in Danish settings.

P04.05 Kristina Grønborg Laut

HEALTH TECHNOLOGY DIFFUSION: ACCESS TO PRIMARY ANGIOPLASTY IN THE EU15 COUNTRIES

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Background: Despite irrefutable scientific evidence that early revascularization with primary percutaneous coronary intervention (PPCI) in patients with ST-elevation myocardial infarction (STEMI) is life saving, many patients remain untreated. Access to and the use of PPCI varies substantially across Europe. This study seeks to identify important predictors of diffusion of PPCI in the EU15 countries.

Methods: An ecological study using aggregated data from 135 regions in 11 European countries. Main outcome measure was PPCI usage.

Information about regional characteristics — such as number of physicians per 100,000 population — were collected in all of the regions. These characteristics were used as covariates in a linear regression model with PPCI usage as the outcome variable.

Results: Linear regression analyses revealed significant correlations with usage of PPCI: type of health care system (Beta (B) -215.4 to 3.3), number of general hospital beds per 100,000 population (B -5.5 to 196.4), number of physicians per 100,000 population (B -2.9 to 272.8), number of nurses per 100,000 population (B -140.4 to 65.0) and population density (B -71.2 to 126.5), and educational level (ISCED index 0-6) (B 23.3 to124.4). Although the estimates were individually imprecise, the final model explained 50% of the variation in PPCI usage.

Conclusion: Diffusion of PPCI is influenced by characteristics of the region and of the healthcare system. The analyses explained half of regional variation in usage of PPCI. Additional factors, such as organisational structure and management of regional STEMI treatment, are hypothesized to influence PPCI usage, and will also be examined in this project.

P04.06 Anette Tarp Hansen

IN VITRO FERTILIZATION DOES NOT INCREASE THE RISK OF THROMBOSIS: A DANISH NATIONAL COHORT STUDY

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Background: Case reports have reported venous and arterial thrombosis in women undergoing assisted reproduction. No large systematic studies on the risk of thrombosis have been published.

Aim: To investigate the risk of venous and arterial thrombosis in women undergoing in vitro fertilization (IVF) with or without Intra Cytoplasmic Sperm Injection (ICSI).

Methods: A national register-based cohort study. Data was obtained from The National Patient Registry and the IVF-Registry. Thrombosis occurring within the first 6 and 12 months after assisted reproduction was considered potentially related to the treatment.

Thrombosis during pregnancy was excluded. The incidence rates of venous and arterial thrombosis were compared to previously published estimates of the risk of thrombosis among young Danish women.

Results: We analyzed 30,884 Danish women undergoing 75,141 treatments from 1994 to 2005. The mean age of the women at first treatment was 32.3 years. The incidence rate ratio, with 95% confidence interval, of venous thrombosis within 6 months was 0.95 (0.38-1.95). The incidence rate ratio of arterial thrombosis within 6 months was 0.36 (0.04-1.30).

Conclusion: Our study showed no evidence that IVF increases the risk of thrombosis.

P04.07 Helen Nordahl Madsen

IS ANTI MüLLERIAN HORMONE (AMH) RESPONSIBLE FOR THE IMPAIRED FOLLICLE MATURATION IN PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME?

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Background: Polycystic ovary syndrome (PCOS) is a syndrome of ovarian dysfunction. The prevalence of PCOS is approximately 5-8% in the western world, making PCOS among the most common endocrine disorder affecting women in the reproductive age.

In PCOS the ovary is characterized by highly increased number of immature follicles and the arrest of follicular maturation despite normal FSH concentration.

We hypothesize that the follicular development of patients with PCOS is altered because of factors that impair the FSH dependent follicular maturation, and that Anti-Müllerian Hormone (AMH) which is secreted in the granulosa cells of developing follicles is a candidate factor for this.

Objective:

1) Mapping of the gene expression profile in follicles from patients with PCOS and controls.

2) To elucidate the regulation of AMH in patients with PCOS and controls.

Methods: We will obtain ovary tissue from PCOS and control patients undergoing laparoscopic surgery or oophorectomy. Firstly, by gene expression profiling of developing follicles ranging from early primordial follicles, over primary and preantral follicles; we will map the basic differences between the gene expression in controls and in patients with PCOS, respectively. Secondly, we will establish primary granulosa and theca cell cultures and cultures of intact follicles from eight patients with PCOS and eight controls, in order to screen for factors affecting AMH regulation and gene/ protein expression, including factors known to be altered in PCOS like androgen and pituitary hormones.

The perspective behind this basic research project is to identify causative factors of PCOS.

P04.08 Solveig Klok Matthesen

EFFECT OF POTASSIUM SUPPLEMENTATION ON RENAL TUBULAR FUNCTION, AMBULATORY BLOOD PRESSURE AND PULSE WAVE VELOCITY IN HEALTHY MAN

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Background

Potassium is the main intracellular cation, which contributes to keeping the intracellular membrane potential slightly negative. A change in potassium intake modifies both cardiovascular and renal tubular function.

The purpose of the trial was to investigate the effect of dietary potassium supplementation, 100 mmol daily in a randomized, placebo-controlled, crossover trial of healthy participants during two periods of 28 days duration. The participants (n=21) received a standardized diet.

Methods

24-hour ambulatory blood pressure (ABP) and applanation tonometry were used to assess blood pressure, pulse wave velocity (PWV), augmentation index (AIx) and central blood pressure (CBP). Immunoassays were used for measurements of plasma concentrations of vasoactive hormones: renin (PRC), angiotensin II (Ang II), aldosterone (Aldo), atrial natriuretic peptide (ANP), vasopressin (AVP), pro-brain natriuretic peptide (pro-BNP), endothelin (Endo), urinary excretions of aquaporin 2 (AQP2), cyclic AMP (cAMP), and the β-fraction of the epithelial sodium channel ($ENaC_{ß}$).

Results

AQP2 excretion increased during potassium supplementation, and free water clearance fell. The changes in urinary potassium excretion and urinary AQP2 excretion were significantly and positively correlated. Aldo increased. GFR, u-ENaC- β, PRC, Ang II, ANP, BNP, Endo, blood pressure and AI were not significantly changed by potassium supplementation, whereas PWV increased slightly.

Conclusions

Potassium supplementation changed renal tubular function and increased water absorption in the distal part of the nephron. In spite of an increase in aldosterone in plasma, blood pressure remained unchanged.

P04.09 Eva Greibe

BIOAVAILABILITY OF VITAMIN B12 IN FISH EGGS; FINDINGS OF AN INDIGESTIBLE B12-BINDER IN RAINBOW TROUT EGGS

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Intro: Foods of animal origin have high Vitamin B12 (B12) content and are the usual dietary sources of B12. In food items, B12 is bound to a protein matrix that is degraded in the intestine by digestive enzymes and low pH, liberating the B12 molecule for absorption. We have characterized the B12-

binding protein in rainbow trout eggs and examined its sensitivity towards intestinal degradation. B12-absorption - when bound to the trout protein – was investigated in rat model.

Methods: Homogenized trout eggs were incubated with 57Co-labelled B12 (57Co-B12) and characterized with regard to B12 binding capacity, affinity and glycosylation. The protein was purified from egg fluid by affinity chromatography on B12-coupled sepharose. Protein stability at low pH and against treatment with increasing conc. of chymotrypsin and trypsin was investigated. Finally, 57Co-B12 - either free or protein-bound - was given orally to rats and 57Co-B12 in the feces was measured.

Results: Characterization of the B12-binder from trout eggs suggested a protein with high resemblance to human HC. In accord with the features for HC, the protein was stable at pH 2, but in contrast to HC it showed no degradation by chymotrypsin or trypsin. Absorption studies in rats showed that 63%, 27% and 26% of the orally administered 57Co-B12 ended up in feces when bound to trout B12-binder, human rec. HC or unbound, respectively. This indicates that B12 is poorly liberated from the trout binder and therefore less assessable for absorption.

Conclusions: The findings suggest that the B12 binder in trout eggs is partly indigestible and that the bioavailability of B12 in fish eggs may be lower than currently expected.

P04.10 Therese Koops Grønborg

THE RECURRENCE OF AUTISM IN DANISH FAMILIES

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BACKGROUND: Autism spectrum disorders (ASDs) are neurodevelopmental disorders with a strong genetic component. Monozygotic twins have a higher recurrence risk than dizygotic twins, and siblings of an affected child have a higher risk of ASD than the background population. The prevalence of ASD has increased for the last two decades to a current average of 70 per 10,000. The aim of the study is to estimate recurrence risk of ASD in Denmark and investigate whether the recurrence risk of ASD has changed over time. We will also compare full siblings with half siblings.

METHODS: We consider all families where the firstborn and second-born children are born in Denmark from 1 January 1980 through 31 December 2004, identified in the Danish Medical Birth Registry. A family is defined as children with the same mother. We compare families where the firstborn is diagnosed with ASD with families where the firstborn is not diagnosed with ASD. We estimate the relative recurrence risk of ASD for the second-born child. For further analyses, we stratify on the biological status between the two siblings and on birth year. Diagnoses of ASDs are found in the Danish Psychiatric Central Register using ICD-8 and ICD-10 diagnoses.

RESULTS: We find a relative recurrence risk of ASD of 6.6 (5.5 ; 7.7). The relative recurrence risk for full siblings is 7.5 (6.3 ; 9.0), and for half siblings (same mother, different father) the relative recurrence risk is 2.4 (1.4 ; 4.2).

More results will be ready for presentation at the PhD day 2012.

P04.11 Jacob Mørup Schlütter

THE NUMBER OF FETAL CELLS IN MATERNAL BLOOD INCREASES OVERNIGHT AND AFTER EXERCISE

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Introduction: We have established a robust method to identify and isolate a subgroup of placental-derived fetal cells in maternal blood (fcmbs). These cells may be used as a source of genetic information to identify Down syndrome and other genetic disorders. A major challenge for the implementation is that we need at least six cells for effective prenatal screening, a number we have not achieved for all pregnant women. We conducted a study to identify if exercise affects the number of fcmbs and if there is a change in the number of fcmbs overnight.

Methods: Ten pregnant women carrying a male fetus at weeks 11-14 were included. Fetal gender was obtained through analyses of free fetal DNA. Participants stayed overnight at the hospital and performed strenuous exercise (cycling at a pulse of 150 beats per minute for 30 minutes) early the next morning. The number of fcmbs was assessed in 30 ml blood at 8:00 pm, 7:00 am and immediately after exercise at 7:45am.The blood samples were processed immediately by initial isolation of fcmbs by magnetic cell sorting followed by staining with a cocktail of fetal cell-specific antibodies, identification and counting.

Results: A significant higher number of fcmbs were found in the morning compared to the evening (median: 1.5 vs. 3.5; p=0.03). Exercise resulted in a further increase in the number of fcmbs when compared to samples taken immediately prior to exercise (median: 3.5 vs. 6; p=0.06).

Conclusion: The number of fcmbs is significantly increased overnight as well as after exercise. This should be taken into account when planning the collection of fetal cells in connection with prenatal diagnosis.

P04.12 Johan Frederik Berg Arendt

CLINICAL AND BIOCHEMICAL ASSESSMENT OF HIGH SERUM VITAMIN B12 LEVELS

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Introduction: Measurement of serum cobalamin (Cbl, Vitamin B12) is routinely used to diagnose or rule out a suspected deficiency state. Surprisingly, around 15% of all samples analysed for serum Cbl show values above the reference interval of 200-600 pmol/L.

Aim: We hypothesized that an increased level of Cbl is caused by alterations in the circulating Cbl binding proteins haptocorrin (HC) and/or transcobalamin (TC), and that such changes may be of clinical importance.

Materials and methods: We collected 834 blood samples from patients with serum Cbl levels: <200, 200-600, 601-1000 and >1000 pmol/L. We

excluded non-hospital treated patients, and patients in Cbl supplementation therapy were not included in analyses of diagnoses. In-house ELISAs were used for measurement of HC and TC. Data on diagnoses of chronic and acute diseases and medication was obtained from the electronic patient medical chart in the Region of Central Denmark and the Aarhus University Prescription Database.

Results: In 38 % of patients, high Cbl levels could be associated to Cbl supplementation. Among non-treated patients we found that high median levels of HC were associated with high levels of Cbl, while median TC levels stayed within reference range for all levels of Cbl. In non-treated patients with high HC levels, significantly higher proportions were found for diagnoses of alcoholism, liver disease, cancer and non-malignant bronchopulmonary disease in patients with concurrent high Cbl levels than in patients with normal or low Cbl levels.

Conclusion: Unexplained high Cbl levels are mostly due to high HC levels and can be associated to several diseases, most significantly alcoholism and cancer.

P05.01 Martin Bødtker Mortensen

HYPERTENSION AND ATHEROSCLEROSIS - THE MISSING LINK

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Atherosclerosis is the leading cause of mortality and morbidity in the Western world. It is the cause of coronary artery disease (CAD) leading to heart attack, and also underlying a significant part of ischemic strokes. Atherosclerosis is initiated early in life and usually develops over decades before giving rise to clinical manifestations. In addition to the level of hypercholesterolemia, the rate of progression is strongly influenced by other risk factors, including hypertension. Although hypertension is known to be one of the most important risk factors for the development of atherosclerosis, its pathophysiological contribution to atherogenesis is not clear.

We hypothesize that hypertension mediate its atherosclerosis-promoting effect through changes to the extracellular matrix. In order to test this hypothesis, we will transplant the common carotid artery (CCA) from hypertensive and normotensive mice into normotensive gene-modified hypercholesterolemic mice that over-express PCSK9 (knock-in) and are heterozygos for a disrupted apoE allele. These PCSK9/apoE mice are able to accept blood vessels from wildtype mice without immunological rejection. Atherosclerosis in the transplanted CCA is induced by applying a constrictive collar around the distal part of the vessels. After 6 weeks, the mice are terminated and the degree of atherosclerosis in the transplanted vessel are then measured by histological evaluation. Any difference between the normotensive and hypertensive group is caused by atherosclerosis-promoting changes to the vessel wall. This study may provide insight into the mechanism by which hypertension accelerates atherosclerosis.

P05.02 Lotte Abildgaard

MINIMAL RESIDUAL DISEASE MARKERS IN CHILDHOOD ACUTE MYELOID LEUKAEMIA

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Background

Despite survival rates of about 65% with high-dose chemotherapy regimens, many children with acute myeloid leukaemia (AML) still suffers from relapse. Minimal residual disease monitoring can be used for long term follow-up of patients in order to detect a molecular relapse before the patient develops a haematological relapse thereby broadening the window of opportunity in order to find donors for stem-cell transplantation or start pre-emptive therapy.

Methods

Using real-time quantitative polymerase chain reaction (RQ-PCR) the normal expression of six potential MRD markers (WT1, PRAME, SPAG6, ST18, GAGED2 and MSLN) will be quantified and any possible influence of infections or chemotherapeutic treatment on these levels will be examined.

Results

Ten samples from children with fever have been analysed. Five patients had CRP levels above 50 mg/L (four above 100 mg/L). No patients showed WT1 expression within the detection range of the assays. MSLN were the most expressed gene with a mean expression level of 1.21E-01, (range from 3.66E-03 to 7.63E-01). PRAME and SPAG6 were the second most expressed genes with expression levels of 1.61E-02 (range 7.43E-06 to 1.08E-01) and 1.50E-02, (range 4.70E-03 to 4.43E-02). The ten patients expressed GAGED2 at a level of 1.68E-04 (range 6.89E-06 to 4.65E-04). Only eight patients expressed ST18 with a mean level of 5.40E-04 (range 2.26E-04 to 1.18E-03). No correlation between CRP and gene-expression levels was found.

Conclusion

The number of analysed samples are small but several of the genes are highly expressed in febrile patients which could reduce these genes applicability as MRD markers.

P05.03 Anja Pagh

THE VALUE OF ROUTINE FOLLOW-UP AFTER TREATMENT FOR HEAD AND NECK CANCER

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Background:

The post treatment surveillance is well integrated in the oncologic care tradition. Regarding, in particular, the tumor of the head and neck, regular follow-up is thought of as being indispensable. This idea has evolved because

patients are at risk of developing both a recurrence and a new primary cancer.

Aims:

To review the failure pattern (local, regional and distant) and prevalence of significant morbididity after treatment for head and neck cancer in Denmark 2000-2008.

To assess the activity and effectiveness of the system practice in a single institution focusing on the clinical path after primary treatment and through the follow-up system to termination, recurrence or death.

To assess the outcome of the follow-up activity and effectiveness in a 6 weeks period in all Danish head and neck oncology clinics.

Hypothesis:

Salvage treatment is helpful.

The prevalence of severe morbidity after primary curative intended treatment is negligible.

The majority of recurrences are patient-detected.

The expenses for the 5 year follow-up might be too high compared to the gain of it.

No significant improvement in disease free or overall survival in the physician-detected versus the patient-detected recurrences.

Project 1: A retrospective population based DAHANCA register study of 7000 patients treated for head and neck cancer in the period 2000-2008

Project2: A medical chart review of patients treated with curative intention at Aarhus University Hospital during a three month time period in 2007 (N=50).

Project 3: A prospective cross section cohort of patients seen in the follow-up clinic after treatment for SCC during a 6 weeks period will be included (N=850).

P05.04 Janus Adler Hyldebrandt

EVALUATION OF THE EFFECT OF THREE DIFFERENT INOTROPIC SUPPORT STRATEGIES IN THE NORMAL AND STUNNED NEWBORN PIGLET HEART ON HEMODYNAMICS AND MYOCARDIAL METABOLISM.

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Objectives:Evaluation of the effect of three inotropic strategies on hemodynamics and metabolism in a neonatal piglet model with normal or stunned right ventricular myocardium. Methods: Piglets (2-4 days) had pressure-volume catheters inserted in both ventricles. Microdialysis catheters were inserted in the myocardium and metabolites were measured

in the dialysate. In half of the animals stunning of the right ventricle was induced by 10 cycles of 3 minutes of ischemia induced by a tourniquet around the right coronary artery, followed by a 3 minutes of reperfusion. Animals were infused for three hours with either: Dobutamin (DO), milrinone and adrenalin (MA) or dopamine and milrinone (MD) or isotonic saline.Results: In the normal functioning hearts, heart rate increased significantly in all intervention groups, but no significant change was observed in CO. Contractility was increased by MA only, but diastolic function was significantly improved by DO and MA. Lactate concentration increased significantly in RV and LV microdialysate samples, myocardial biopsies and plasma in the MA treated animals. In the stunned right ventricle lactate increased after ischemia-reperfusion. Results from microdialisys and pre and afterload independent measurements of contractility are pending analysis. Conclusions: In the normal myocardium the three inotropic strategies were comparable with respect to effect on hemodynamics. MA had the most pronounced effect on contractility. Results from the stunned right ventricle are pending analysis.

P05.05 Stine Elleberg Petersen

ANO-RECTAL FUNCTION IN PATIENTS WITH PROSTATE CANCER FOLLOWING RADIOTHERAPY OR RADICAL PORSTATECTOMY

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Background: Patients receiving radiotherapy (RT) for prostate cancer (PC) may suffer from bowel dysfunction due to irradiation of the rectum. We evaluated the ano-rectal function using a novel scoring system for evaluation of bowel dysfunction.

Materials and methods: We conducted a cross-sectional study based on a patient administrated questionnaire. The questionnaire consisted of questions formed at The Department of Surgery, Aarhus University Hospital. A condensed ano-rectal dysfunction score (ARD) consisting of 5 items (fecal frequency, urgency and incontinence, clustering of stools and soiling) is extracted from the questionnaire. The study included 372 PC patients treated with RT from 1999-2007 and 249 patients treated with radical prostatectomy (RP) from 2005-2007 at Aarhus University Hospital with at least 3 years follow-up time.

Results: A total of 90% (564 patients) returned the questionnaire. 42% (135/323) of the patients treated with RT and 20% (42/214) of the patients treated with RP reported minor or moderate ARD (OR=2.95 (95% CI: 1.97-4.42; p<0.001)). Rectal bleeding (OR=4.81 (95% CI: 2.95-7.83; P<0.0001)), fecal urgency (OR=3.96 (95% CI: 2.66-5.90 P<0.0001)) and fecal incontinence (OR=3.16 (95% CI: 2.05-4.88; P<0.001)) were more frequent in the RT group compared to the RP group. A ROC-analysis revealed that the ARD score correlated significantly with QL (sensitivity 68%; specificity 79%).

Conclusion: The risk of rectal bleeding, urgency, and fecal incontinence was significantly higher in RT patients compared to RP patients and a condensed score covering 5 items on ano-rectal dysfunction correlated significantly

with patients QL in RT patients.

P05.06 Søren Haack

DIFFUSION WEIGHTED MRI (DWI) FOR BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER – DETERMINING THE DEGREE OF DISTORTION AT 1.5T AND 3T MRI

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Diffusion Weighted MRI (DWI) enables identification of tissue with high cellular density such as tumors. This makes DWI a potentially valuable tool in oncology imaging for both diagnostic imaging and monitoring of treatment. Locally advanced cervical cancer is usually treated with brachytherapy using an intracavitary applicator. MRI guided brachytherapy can be performed by imaging with the applicator in place prior to dose planning and treatment. This study evaluates the amount of distortion in DW images in vivo at both 1.5T and 3T MRI. DWI was performed in six patients at 1.5T MR and in four patients at 3T MRI. All MRI examinations were performed with the plastic applicator for brachytherapy in place. The cervix and lower uterus was manually contoured on T2 weighted images (T2W) and on DW images with b-value = 0 s/mm2. The contours were compared by calculating the Jaccard similarity coefficient (the common area compared to the union area). The center of the applicator tandem was identified and marked on T2W and DW images and the difference was calculated. The Jaccard coefficient (mean ± std.dev.) was 73.6 ± 8.3 (1.5T) and 67.6 ± 12.7 (3T). The difference between the location of the tandem center was (mean ± std.dev.) 2.2 ± 1.2 mm (1.5T) and 1.6 ± 0.93 mm (3T). If DW images should be used dose planning of brachytherapy the shift and distortion should be corrected to match the morphological images

P05.07 Xue Lin

GENOME-WIDE TAG-BASED PROFILING FOR MEASUREMENT OF DNA METHYLATION, COPY NUMBER VARIATION AND GENE EXPRESSION

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Better understanding of the gene regulation mechanism depends on precise characterization of the effects of DNA methylation and copy number variation (CNV) on gene expression. We describe a tag-based technical platform combined with massively parallel DNA sequencing platform. This platform consists of three types of tag-profiling methods: 1. modified DNA methylation-specific digital karyotyping (MMSDK), 2. digital karyotyping (DK) and 3. digital gene expression (DGE), allowing low-cost, ultra-deep and genome-wide mapping of DNA methylation, CNV and transcriptome, respectively.

The first step in the three types of tag-profiling is to sample genomic loci. In MMSDK, we first select loci by the digestion with a methylation-sensitive

restriction enzyme; In DK, they are selected by digestion with a DNA methylation-insensitive enzyme; In DGE, mRNA is converted to cDNA. Thus the resulting DNA and cDNA from the first step in the three types of tag methods is cleaved with NlaIII. Short fragment tags (20~21 nucleotides) are obtained by a tagging enzyme (MmeI). The tags are amplified by PCR with adaptor-specific primer, followed by direct, massively parallel sequencing. Additionally, an index system has been developed for the tag-profiling method to allow multiplexed sequencing.

A series of breast cancer cell lines, which have developed resistance to endocrine therapy during different forms of selection, are now under investigation. With the tag-based platform, we can simultaneously obtain genomic, epigenomic and transcriptomic profiles for these samples, thus gaining knowledge about genome wide cis-regulation and dysregulation as well as the mechanisms leading to drug resitance.

P05.08 Christina Gade THE INFLUENCE OF CARDIOVASCULAR MORBIDITY ON THE PROGNOSIS OF PROSTATE CANCER. EXPERIENCE FROM A 12-YEAR NATIONWIDE DANISH POPULATION-BASED COHORT STUDY.

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Background

To determine the impact of pre-existing ischemic heart disease (IHD) and stroke on overall survival in prostate cancer patients.

Methods

We conducted a cohort study of patients with incident prostate cancer registered in the Danish Cancer Registry from 1997 through 2008. We identified patients diagnosed with IHD or stroke prior to the date of prostate cancer diagnosis in the Danish National Patient Registry. We constructed Kaplan-Meier curves to analyze time to death and Cox regression was used to estimate 1- and 5-year mortality rate ratios (MRRs) to compare mortality rates by pre-existing IHD or stroke status, adjusting for age, stage, comorbidity, and calendar period.

Results

Of 30,721 prostate cancer patients, 4,276 (14%) had a history of IHD and 1,331 (4%) a history of stroke. Crude 1- and 5-year survival rates were 85% and 44% in men without preexisting IHD or stroke, 81% and 36% in men with preexisting IHD, and 78% and 27% in men with pre-existing stroke. Adjusted 1- and 5-year MRRs were 1.03 (95% confidence interval (CI) 0.95–1.12) and 1.05 (95% CI 1.00–1.10) for patients with IHD and 1.12 (95% CI 1.00–1.27) and 1.20 (95% CI 1.12–1.30) for patients with stroke compared with patients without pre-existing IHD or stroke.

Conclusions

A history of IHD had minimal impact on mortality in prostate cancer patients, whereas 5-year mortality was 20% higher in prostate cancer patients with pre-existing stroke compared to those without IHD or stroke.

These results highlight the importance of differentiating between various comorbidities.

P05.09 Sandy Mohamed Ismail Mohamed

FEASIBILITY OF APPLYING ONE TREATMENT PLAN FOR SUCCEEDING FRACTIONS IN IMAGE GUIDED BRACHYTHERAPY IN CERVIX CANCER

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Aim: Optimal image guidance requires imaging and planning for each brachytherapy (BT) fraction. This study explores the feasibility of limiting dose optimisation to the first fraction (BT1) and applying the same plan for the second fraction (BT2).

Material & Methods: 71 patients (pts) with cervical cancer were reviewed. Pulsed dose rate BT was initiated after about 4 weeks of external beam radiotherapy, with an intracavitary (IC) tandem-ring applicator alone or combined with interstitial needles (IC/IS). The target volumes and organs at risk (OAR) were delineated according to GEC ESTRO guidelines. For patients with the same applicator geometry the optimised BT1 plan was copied to BT2 with no further optimisation (single plan scenario). Dose volume histogram (DVH) parameters for full optimisation were compared to those of the single plan scenario.

Results: 31/41 IC and 4/30 IC/IS pts had the same applicator geometry in both fractions. For the 31 IC pts, mean DVH parameters were comparable between full optimisation and single plan scenario. Only D100 and V100 for the high risk clinical target volume (HR CTV) were significantly different. 2/31 pts would receive HR CTV dose marginally less than 85 Gy (84 Gy) for single plan scenario. OAR planning aims were fulfilled for all with a single plan, although 5/31 pts would receive between 3 Gy and 10 Gy extra to the D2cc (bladder, rectum).

Conclusion: For IC BT, comparable mean DVH parameters with the single plan, although individual benefit of full optimisation was still observed for some pts. Individual optimisation for each brachytherapy fraction is recommended for high precision brachytherapy when interstitial needles are used.

P05.10 Søren Ravn Laustsen

DETERMINATION OF BRAIN TOXICITY AFTER RADIOTHERAPY USING ADVANCED 3T MRI.

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Background:

Approximately 1000 new cases of primary brain tumours are diagnosed in Denmark each year. The main treatment objective is to remove/destroy as much tumour tissue as possible, using surgery and/or radiation and chemo

therapy, without damaging healthy tissue.

Today there is very little knowledge regarding dose-limits in radiation therapy (RT) towards the different functional areas of the brain, mainly because conventional MRI doesn't allow us to visualize these areas. As a consequence we treat all normal appearing tissue as being equally important for the patients´ wellbeing.

Objective:

To investigate if a correlation can be identified between brain toxicity after RT to healthy tissue and changes in tissue characteristics measured with advanced MRI.

Material and Methods:

53 patients who have received RT directed towards the brain more than 1 year ago at Aalborg Hospital are invited to participate. Patients with any contraindication to MRI examination with contrast will be excluded.

Each MRI-exam consists of: 1 anatomical 3D sequence, 3 functional Magnetic Resonance Imaging (fMRI) sequences (1 sequence for each paradigm - language, right and left hand), 1 Diffusion Tensor Imaging (DTI) sequence (for visualization of the arcuate fasciculus and the pyramidal tracts), 1 Diffusion Weighted Imaging (DWI) sequence and 1 Perfussion Weighted Imaging (PWI) sequence.

The functional areas delineated with fMRI and DTI will be investigated with DWI and PWI and the RT dose received by each area will be compared with the DWI, DTI and PWI measurements.

Results:

Preliminary results on the first 6 patients will be presented.

P05.11 Thomas Larsen

VITAMIN D3 SUPPLEMENTATION IN THE WINTER LOWERS DIASTOLIC BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION AND VITAMIN D DEFICIENCY

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Purpose

In the northern hemisphere vitamin D deficiency is highly prevalent during winter months, and observational studies have associated hypertension with poor vitamin D status. We tested the hypothesis that vitamin D supplementation in the winter lowers 24-hr ambulatory blood pressure (ABP) in patients with hypertension.

Methods

A daily oral dose of 75 mcg cholecalciferol was investigated in a randomized, placebo-controlled, double-blinded study in patients with hypertension. Before and after 20 weeks of treatment (fall and spring, resp.), ABP measurement and applanation tonometry (SphygmoCor®) were performed,

and blood was drawn for biochemical analysis.

Results

112 patients (mean age 61±10) with a baseline p-25-OHD of 57±26 nmol/l completed the study. Compared with placebo, cholecalciferol caused a significant increase in p-25(OH)D (62 nmol/l, $p<0.001$) and p-Ca^{++} (0.01 mmol/l, $p<0.05$), and a significant suppression of p-PTH (0.97 pmol/l, $p<0.001$). Central systolic and diastolic BP was reduced 6.8 mmHg ($p=0.007$) and 1.7 mmHg ($p=0.15$), resp. However, no significant differences were observed in overall ABP. In patients with p-25(OH)D

P06.01 Pia Viuf Ørby CAPE: CO-EXPOSURE OF AIR POLLUTION AND ALLERGENIC POLLEN

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10% of the population in Denmark is suffering from a pollen allergy, and yet this is a neglected research area. Research related to pollen allergies is often cross disciplinary, and the aim of this project is to increase knowledge about pollen allergies by combining two main research fields at Aarhus University; Public Health and Atmospheric Environment.

The research in the area of public health involves human exposure studies of dose-response relationships for grass and birch allergens. The study is performed before, and at the end of the pollen season, to evaluate the priming effect.

Previous studies have shown that components in air pollution can increase allergic response. To examine this effect co-exposure studies with allergens and ozone will be performed.

All exposure studies are carried out in a climate chamber.

The research within the atmospheric environment area involves analysis of the local variation of pollen levels. Results from 3 pollen traps in Aarhus show that the local pollen counts on days with clinically relevant pollen levels are not correlated to the counts measured in Viborg. This suggests that high grass pollen levels are a local phenomenon. This must be taken into account in clinical assessments.

A clinical relevant description of local grass pollen levels require precise information on the location of the sources, and how the pollen from these sources disperse in the atmosphere. This project will therefore also produce pollen source maps for the city of Aarhus.

The results from this project will get us one step further towards an improved individualised pollen exposure system for research and daily warnings to the public.

P06.02 Trine Allerslev Horsbøl

FACTORS ASSOCIATED WITH WORK OUTCOME FOR SURVIVORS FROM HEMATOLOGICAL MALIGNANCIES – A SYSTEMATIC LITERATURE REVIEW

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Introduction Recent years have seen a growing number of survivors from hematological malignancies. Previous studies have suggested that this patient group may be facing an increased risk of delayed return to work, unemployment, reduced work ability, and early retirement. To enable early assessment and intervention to prevent survivors from losing their connection to labour marked, factors associated with work outcome must be identified. This systematic review was performed to provide an overview of these factors.

Methods A systematic search of literature on work outcome and hematological malignancies was conducted. All potentially relevant studies were reviewed and nine relevant studies were critically appraised.

Results Eight studies met the inclusion criteria and 21 different factors were evaluated for their association with work outcome. The reviewed studies differed in terms of design and study characteristics and the reported results differed between prospective studies and cross-sectional studies. No general trends could be discerned from the review and we found no consistency between reported results.

Discussion/conclusion It is difficult to draw conclusions on the association of single factors with work outcome. However, this review pinpointed a number of factors that may inform future studies. Such future studies should preferably be designed as prospective studies that also include cancer-free individuals. Work outcomes must be well-defined and recorded with valid methods, e.g. social registers, if possible.

P06.03 Stina Lou Fleron

SCREENING FOR DOWNS SYNDROME AND THE SOCIAL CONSTRUCTION OF 'INCREASED RISK'

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Background

In Denmark, all pregnant women are offered a risk assessment for Downs Syndrome and every year, approx. 3,000 pregnant women receive a message that their fetus is at increased risk for Downs syndrome or other chromosomal abnormalities. These pregnant women are offered a chorionic villus sample, which gives a conclusive answer but also involves a 1% risk of abortion by miscarriage.

An increased risk for Downs Syndrome leaves pregnant women in an unexpected and complex situation, with few definite answers. It is the start of a stepwise clarification of the fetus' health. We lack knowledge of how health professionals and pregnant women perceive and handle these

complex processes where both medical, ethical and personal perspectives are at stake. What are the concerns and needs of pregnant women in this situation, and what are the professional, medical practices and perspectives?

Aim

An anthropological analysis of the social construction of increased risk for Downs Syndrome and processes following this.

Materials and methods

The study's exploratory perspective calls for a qualitative, anthropological research strategy and methodology. One year of anthropological fieldwork will be carried out at an ultrasound clinic. Data collection oscillates between participant observation, qualitative interviews and tentative analysis in order to generate a dynamic exchange between data material and theoretical perspectives.

Perspectives

To generate knowledge that will contribute to the continued development of medical practice in order to minimize pregnant womens' worries, concerns and insecurities during and after an increased risk for Downs Syndrome.

P06.04 Seija Ylijoki-Sørensen

PRESENTATION OF A PH.D. PROJECT: MEDICO-LEGAL AUTOPSY AS A TOOL TO IMPROVE MORTALITY STATISTICS AND HEALTHCARE: COMPARING PRACTICES IN DENMARK AND IN FINLAND.

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Background: The medico-legal practices differ much in Finland and Denmark. The average medico-legal autopsy rate in Finland is around 24% of all deaths, while in Denmark it is around 3%, meaning Denmark has the lowest frequency of medico-legal autopsies in the Nordic countries, while Finland has the highest.

Hypothesis: The low medico-legal autopsy rate in Denmark could possibly mean that mortality statistics are not correct in Denmark. As a consequence, important knowledge of diseases is not obtained, which can cause a sub-optimal diagnosis and treatment of these diseases. On the contrary, the high medico-legal autopsy rate in Finland is likely to give a higher degree of certainty regarding the description of death.

Aim: 1) To describe the history of medico-legal legislation and compare mortality statistics in Denmark and Finland in the period 1995-2005, 2) to compare causes and manners of medico-legal deaths with or without autopsy, in a one year prospective period, at the Forensic Institute of Aarhus University, Denmark and the Forensic Institute of Helsinki University, Finland, and to analyze any discrepancies between them.

Conclusion: Currently the value of medico-legal autopsies has not been investigated in any great detail with regard to sudden unexplained death.

This study will examine the contribution of such procedures.

P06.05 Malene Krogsgaard Bording

CLINICAL DECISION MAKING IN OUTPATIENT MENTAL HEALTH CARE

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Clinical Decision Making in Outpatient Mental Health Care

Introduction: The major reason for lack of knowledge on outpatient treatment in mental health is that research on clinical decision making in health care has primarily focused upon well-defined situations in physical conditions, while there has not been research in clinical decision making in people with schizophrenia with its high demands on treatment adherence and therapeutic relationships.

Objective: This study is about clinical decision making in outpatient mental health care with specific focus on patients diagnosed with schizophrenia.

Aims of the study: To identify the style of decision making between patient and therapist (paternalistic, shared and informed). Investigate the patient's understanding of the decision making and identification of factors leading to this understanding. Furthermore the study will include an analysis of style of decision making as a possible predictor of adherence to treatment.

Methods: The study is an open, explorative study using a combination of both qualitative and quantitative methods. The study population consists of severe mentally ill outpatients diagnosed with schizophrenia. Data consist of questionnaires, field observation and patient interviews.

Expected results: Specifications of primary areas for further improvement in CDM is an expected result of the study. Recommendations will be extracted and formulated from the study data to implement elements of best practice in CDM in the routine care for people with schizophrenia in particular and severe mental illness in general. The explicit focus will contribute to strengthening of the patient perspective.

P06.06 Rasmus Foldbjerg

MECHANISMS OF NANOSILVER TOXICITY

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The rapid development of nanotechnologies has been accompanied by an increased concern for the safety of nanomaterials and consequently the number of publications on nanotoxicology has increased rapidly. However, inadequate characterization of the investigated nanomaterials has obscured risk assessment. Today, nanosilver is used in more manufacturer-identified consumer products than any other nanomaterial. A major concern is the possibility that these materials possess novel physico-chemical properties compared to the bulk counterparts. Our in vitro data in cultured human cells

suggest that the toxicity of nanosilver is comparable to that of silver ions. From a mechanistic perspective, ROS generation and oxidative stress, demonstrated by the hierarchical oxidative stress paradigm, is a generally accepted model to explain the toxic effects of various types of nanoparticles. We have previously reported that both silver ions and silver nanoparticles induce ROS, apoptosis and necrosis in A549 and THP-1 cells. This increase was found to correlate with increased gene expression of stress-related genes (e.g. HO-2 and HSP70). Thus, to further compare the effect of silver ions and nanosilver on gene expression, global gene arrays were conducted and the results revealed very similar profiles of the two compounds at EC20 doses after 24 h. These findings indicate the importance of evaluating the toxic contribution of nanoparticle dissolution. Furthermore, preliminary data suggest that NP mediated toxicity is higher in murine cell lines compared to their human counterparts. This information could be of importance when risk assessment is based upon animal experimentation.

P06.07 Trine Nøhr Winding

PARENTAL SOCIOECONOMIC STATUS AND CHOICE OF EDUCATION AMONG DANISH ADOLESCENTS -THE INFLUENCE OF PERSONAL AND FAMILY CHILDHOOD CONDITIONS.

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Background: Socioeconomic status is strongly linked to educational attainment. One of the most consistent predictors of children's level of educational attainment is their parents' level of educational attainment.

It has previously been shown that personal determinants as well as family determinants are connected to educational attainment among adolescents, but it is unclear to what degree it is maintained in a Danish youth population and to what degree personal and family determinants can explain a possible association between parental socioeconomic status and choice of education after public school.

The primary aim of this study is to examine the association between parental socioeconomic status measured as parental educational level and income and educational attainment after public school among Danish adolescents. The secondary aim is to investigate to what degree this association is influenced by parental disability pension, whether a child was brought up by one or two adults, and intellectual performance when finishing public school.

Methods: Study participants are all adolescents born in 1989 (n=3687) living in Ringkøbing County, Denmark. Information will be collected through linkage between different national registers (Danmarks Statistik and DREAM - a register of all public transfer payments). The primary outcome is choice of education after public school.

Data will be analysed with use of appropriate regression methods.

P06.08 Lene Søndergård Larsen

AN AMBIGUOUS RELATIONSHIP – A QUALITATIVE META-SYNTHESIS OF HOSPITALIZED PATIENTS' EXPERIENCE OF INTERACTION WITH FELLOW PATIENTS.

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Background: The significance of social interaction is commonly discussed and intensively studied as a substantial concept in the nursing profession. Interaction is inherent to nursing care and acknowledged as such. The patient-patient relationship has been studied in psychiatric settings since the early 1960s; but interestingly, social research conducted in hospital settings has prioritised examination of interaction between patients and doctors, patients and nurses, and patients and relatives over patient-patient interaction.

Aim: To provide an understanding of patients' significance to fellow patients during hospitalisation.

Methods: We conducted a qualitative meta-syntheses of literature that described empirical investigations of patients interaction with fellow patients during hospitalization. We searched the online databases: Bibliotek.dk, CINAHL, PubMed (Medline), CSA and Psychinfo, using the search terms "fellow patients", "social interaction", "interpersonal relationship", "camaraderie", and "patients' experience". Six qualitative studies were included.

Findings: Available empirical evidence pointed to fellow patients' experiences as an enforced hospitalization condition, as a care provider, as a provider of humoristic breaks, as an expert on disease and hospital life and as a carrier of hope. The interaction was mainly experienced as positive but negative experiences with fellow patients were present.

Conclusion: The relatively sparse literature pertaining to patients' interaction to fellow patients, largely indicated patients to care for each other. Furthermore, the relationship seemed ambiguous and with both positive and negative experiences.

P06.09 Lene Nyboe

PHYSICAL ACTIVITY IN PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA

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Introduction:

The metabolic syndrome (MetS) is a cluster of factors significantly increasing the risk of cardiovascular disease and type 2 diabetes and MetS is highly prevalent in patients with schizophrenia. Besides the metabolic side effects of antipsychotic medication physical inactivity might also increase the risk of developing MetS.

One aim of the study "Metabolic syndrome in patients with first-episode schizophrenia" is to investigate the independent risk of physical inactivity in

developing MetS.

Methods and material:

All patients consecutively assigned to The OPUS project and in-patients in The Region of Midtjylland (Denmark) having an ICD-10 diagnosis of first – episode schizophrenia (18-40 years) is the population of interest. In comparison in-patients with ICD-10 diagnosed depression and healthy controls matched on age, gender and level of education are also included.

Assessments are made at inclusion and 1 year follow-up.

Among other assessments the level of physical activity as well as physical fitness is assessed using The Physical Activity Scale (PAS): respectively, Aastrands physical fitness-test.

Results:

The study´s preliminary results on physical activity-levels in 55 patients with first-episode schizophrenia and 27 patients with depression will be presented and discussed. Furthermore findings from follow-up will be presented.

P06.10 Mette Vinther Skriver

HBA_{1C} AS PREDICTOR OF MORBIDITY AND ALL-CAUSE MORTALITY IN PEOPLE WITH TYPE 2 DIABETES. A DANISH POPULATION-BASED OBSERVATIONAL STUDY

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BACKGROUND

The evidence for recommending individuals with type 2 diabetes to strive toward a HbA_{1c} level below a certain value is growing. However, information from population-based studies are sparse. Since 2003 the National Board of Health, Denmark have recommended intensive antiglycaemic treament aimed at reducing HbA_{1c} to less than 7% to all individuals with type 2 diabetes.

AIM

In a population-based setting, with inclusion of all individuals with type 2 diabetes, to investigate whether people with a HbA_{1c} level below 7% have lower diabetes related morbidity and/or all-cause mortality than those with a HbA_{1c} level above 7%.

MATERIALS AND METHODS

Individuals with type 2 diabetes were identified with a dedicated validated algorithm, from public data files in Aarhus county, Denmark. In total 17,760 individuals with type 2 diabetes who had at least one HbA_{1c} mesurement and who were identified in the years 2001-2003 were included in this study. HbA_{1c} level was defined as the average for each individual of all HbA_{1c} measurements in the year of the first registered HbA_{1c} measurement. Information of morbidity, death, emigration and prescriptions was obtained by record linkage with Danish Registers. Survival was estimated by the Kaplan-Meier method and possible excess morbidity and/or mortality for

those with a HbA1c above 7% compared to those with a HbAc below 7% were estimated using Cox proportional hazard models.

RESULTS AND CONCLUSION

After adjustment for age, sex, comorbidity and non-awareness, a HbA_{1c} level above 7% increased mortality and diabetes related morbidity. The impact of HbA_{1c} level on mortality depend on whether individuals recieve glucose lowering therapies or not.

P06.11 Lena Hohwü

MATERNAL STRESS BY LIFE EVENTS DURING PREGNANCY AND RISK OF OVERWEIGHT OFFSPRING AT THE AGE OF 9-11 YEARS OLD

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Introduction: Today, every fifth child in Denmark is overweight caring an increased risk of developing diabetes and cardio vascular diseases later in life. We have recently found that severe stress from bereavement around gestation was associated with a higher risk of overweight during school age. We aim to test the association between more common stress by life events during pregnancy and overweight in the offspring.

Material & Methods: We followed a cohort of children (n=3899) born 1990-92 at the Dept. of Obstetrics, Aarhus University Hospital from 16th gestational age until the age of 9-11 years. Twice during pregnancy the mothers were asked to report stressful life events using the Newton Life Events questionnaire. Height and weight of the child were collected at birth and in 2001. We considered children with a BMI>20 kg/m^2 as being overweight. We present data for the association using logistic regression.

Results: We found a dose response association between number of stressful life events and the risk of overweight. Children born of women, who experienced stress of three life events or more, had a higher risk of overweight (Odds ratio 1.69 [95% CI: 1.04 – 2.72], controlled for gender).

Conclusion: Maternal stress during pregnancy was associated with higher risk of overweight in the offspring. Further analyses are needed to rule out potential confounding.

P06.12 Marianne Johansson Jørgensen

IDENTIFYING KEY TOPICS FOR A DESCRIPTION OF SEXUAL BEHAVIOR AMONG DANISH ADOLESCENTS: A QUALITATIVE STUDY

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Background: Surveying sexual behavior in the general population serves to identify critical points, monitor the effects, and interpret changes in the spread of sexually transmitted infection.

Aim: The aim of this qualitative study was to identify points of particular importance to adolescents' sexual behavior in order to initiate and design a behavior surveillance programme in Denmark.

Methods: We conducted four semi-structured focus group interviews with a total of 19 sexually experienced adolescents aged 18 to 23. Boys and girls were interviewed separately. Each group contained pupils from one Danish Folk High School, but with different social and educational backgrounds. The interview guide was developed from literature reviews and hypotheses based on years of experience with sexually transmitted infections. Data were transcribed verbatim and analyzed using qualitative description.

Results: Four major categories of risk behavior were identified: alcohol consumption is associated with "no condom use"; nights on the town and meetings in foreign countries or at festivals are associated with one night stands and often lead to unsafe sex; low self-esteem increases the risk of pushing one's personal boundaries, thus resulting in promiscuous sexual behavior; and increased sexual experience is associated with a lack of condom use.

Conclusion: Danish adolescents identified four key elements that could lead to unsafe sex. These results differed slightly from our expectations and will be included in a sexual behavior questionnaire to describe important elements influencing the sexual behavior of adolescents.

P07.01 Ioanna Milidou

BIRTH WEIGHT (BW), GESTATIONAL AGE (GA), AND INFANTILE COLIC (IC) - THE DANISH NATIONAL BIRTH COHORT

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Background

IC is a condition of unknown origin characterized by paroxysms of crying during the first months of life. A few studies have identified low BW as a risk factor among infants born at term, while the association between GA and IC has not been studied.

Aim

We aimed to investigate the association between BW, GA, and IC.

Methods

We studied 62,785 singletons enrolled in the Danish National Birth Cohort. Information on IC symptoms and possible confounders was collected by computer-assisted telephone interviews of the mother during pregnancy and post partum.

Adjusted odds ratios (OR) with 95% confidence intervals are presented. IC was defined as crying for more than three hours per day and for more than

three days per week.

Results

A total of 4,944 infants (8%) fulfilled the IC criteria. The risk of IC increased with lower BW. The highest risk was observed among infants weighing < 2,000 grams (OR= 1.7 [1.3-2.1]) compared with infants weighing 3,500-4,000 grams.

The risk for IC increased with lower GA. Infants with GASmall for GA infants, defined as infants with BW<10th percentile, had higher risk of IC compared with normal for GA infants in gestational weeks 32-40. Finally, after adjusting for GA, low BW was associated with IC only in infants born at term (gestational weeks 37-41), but not in pre- or post-term infants.

Conclusion

The results indicate that low BW and preterm birth are independently associated with IC. After adjusting for gestational age, low birth weight increased the risk of infantile colic in children born at term (gestational weeks 37-41).

P07.02 Annesofie Lunde Jensen

OSTEOPOROSIS GROUP-EDUCATION: A WAY TO HEALTH MAINTENANCE

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Background

Osteoporosis is a disorder in which bone mass is progressively lost leading to an increased risk of bone fracture. Patients are well-informed about the general aspects of osteoporosis but lack knowledge on how to reduce the risk of complications and how to maintain the quality of life. Studies have reported that group-education increases the patients' awareness of osteoporosis, intake of medicine, and may have a preventive effect but the evidence is limited. The current knowledge on how patients with osteoporosis receive group-education and use and integrate the health care information leaves several unsolved questions, e.g. the impact of disease duration, disease intensity, sex, age, social status and educational level on the patients' benefit and involvement in group-education.

Aim

To describe how patients with osteoporosis use and integrate group-based osteoporosis education.

Methods

An interpretive description study. Data consist of women and men with osteoporosis. Two groups of patients are followed:

(A) 20 patients starting training sessions. Participant observation during classes and in patients' everyday life. Patients are interviewed before training

starts and 6 months after.

(B) 20 patients who attended the Osteoporosis School in 2007 are interviewed.

Perspectives

To develop an integrative description of osteoporosis group-education which can contribute to the disease-specific education. This includes pedagogical and organisational actions. Further, to describe how participants interact with the health care professionals and use and integrate their health education in everyday life.

P07.03 Anne Sofie Bjerrum

DOES DYAD TRAINING COMPETES WITH INDIVIDUAL TRAINING? A RANDOMIZED, CONTROLLED BRONCHOSCOPY-SIMULATION-STUDY.

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Background:

Extant knowledge on motor skills learning derives from studies of simple motor skills and may therefore not be applicable to more complex motor skills learning, like bronchoscopy simulation training. The current paucity of studies exploring the curriculum of medical simulation training is surprising: especially in light of the costly and instructor-dependent nature of simulation training and its significant cost-effective savings potential. The present paper compares the relative effectiveness of dyad and individual training.

Summary of work:

A randomized, controlled study featuring 36 medical students randomized to dyad training or individual training . In the dyad training group, participants alternate between physical and observational practice, and thus perform only half as many bronchoscopy simulation cases as those who train alone. The two groups are tested with pre-tests, post-tests and retention-tests using simulator metrics.

Summary of results:

Data was analysed with Univariate Repeated Measurements Anova. Both groups showed statistically significant improvement in bronchoscopy score from pre to post- and retention-tests. ($p< 0.001$). No statistically significant difference in the bronchoscopy score between the two training groups at pre-, post- and retention-tests were found ($p=0.38$).

Conclusions:

Dyad training in medical simulation is effective and efficient. Combining physical- and observational-practice, and encouraging dialog between participants enhances learning. As simulation training is costly and instructor-dependent, dyad training has great cost-effective potential.

P07.04 Kirsten Hansen

CONCERNING CHILDREN OF PARENTS WITH DEPRESSION

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Background:

The prevalence of depression has been increasing for many years.

Numerous international studies have documented that a parent's depression increases the risk that the child experiences psycho-social or cognitive impairment and psychiatric or somatic disease during childhood or as an adult.

Protecting factors for the child will be of relevant information and knowledge as well as contact to other caring adults.

In Denmark, it is an open question if, and eventually which, support is given to children of parents with depression.

Investigation questions:

In Denmark, what support is given to 2-14-year-old children of parents with depression?

How does the actual support match the children's needs?

Methods:

Phase one:

Qualitative interviews in 4-5 specific municipalities

This phase will give detailed and specific information of a number of families having a parent listed with depression.

Phase two:

A national questionnaire investigation, distributed among parents listed with depression, general practitioners and municipalities.

Results from the investigations will be analysed in comparison with results from literature studies.

Results:

Examples of preliminary results from interviews and from the survey among general practitioners will be presented.

Perspectives:

The combination of an increasing prevalence of depression and the consequences that parental depression may cause to a child indicates an increasing problem – individually and socio-economically.

The results of the actual investigation will give evidence to the eventual

development of feasible methods to provide cross-sectional support to children of parents with depression in Denmark.

P07.05 Charlotte Olesen

GENERIC SUBSTITUTION OF ORAL TABLETS IN ELDERLY IN DENMARK

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Introduction

Generic substitution in Denmark means that pharmacies must provide the cheapest medicine. Every time you buy a drug, the drug name or brand-name may have changed. Consequently tablet or packaging appearance has changed. Substitutions therefore make many patients uneasy.

Our aim is to describe the number of substitutions of oral tablets used by the elderly.

Method

Substitutions were counted in the medicine used by 183 persons aged 65 years or older living in Aarhus, Denmark. The elderly were selected consecutively from a control group in a Danish compliance study, Methods for Improving Compliance with Medicine Intake. Substitutions were counted manually in the prescription database for one year in 2008-2009. Only substitutions for oral tablets were included.

Results

In one year 183 elderly bought 837 drug (4.6 (1-9) per elderly). Purchase per elderly was 20.3 (3-64). Purchase per drug was 4.4 (1.5-11.0).

The number of substitutions of drug name or brand-name was 837.

Substitutions per drug in one year were 1.0 (0-14). Substitutions per purchase in one year were 0.2 (0-0.9).

Each elderly was exposed to 0-4 substitution per drug or 0-0.6 substitution per purchase.

The name was changed in 48% of the drugs.

Conclusion

Nearly half of the drugs used by an elderly population in Denmark changed drug name and/or brand name during one year. This may be a substantial problem for the elderly. The impact of substitution in drug name or brand-name will be further investigated in relation to compliance.

P07.06 Jette Pedersen

THE EFFECT OF FOLLOW-UP ON NUTRITION INTERVENTION AFTER DISCHARGE IN UNDERNOURISHED GERIATRIC PATIENTS

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The effect of follow-up on nutritional intervention after discharge in undernourished geriatric patients

Background:

Undernutrition in geriatric patients is a recurrent and well documented problem. Up to 55% of the elderly admitted to hospital are undernourished. Undernutrition and acute illness are associated with loss of muscle mass and physical ability and with complications, dependency, morbidity and mortality. Elderly who live alone are more exposed to nutritional problems than those who live together with another person or in a nursing home.

Aim:

The purpose of this study is to test two programmes of nutritional intervention with follow up after discharge.

Methods:

Geriatric patients aged 75 years or older, living alone and admitted to the geriatric ward at Aarhus University Hospital due to acute somatic disorders, are included in the study. Patients who suffer from mental disorders or active cancer are excluded as well as patients living together with another person or staying in a nursing home. Randomization is computerised. The patients are allocated to a "home visit" group, a "telephone consultation" group or a "control group". Patients in the home visit group and patients in the telephone consultation group, as well as their home care helper, get dietary advice after discharge by a dietician at week one, two, and four. The control group is not contacted after discharge. The primary outcome is functional ability at follow-up 8 weeks after discharge. Secondary outcomes are quality of life, re-admission and mortality at 30 and 90 days after discharge.

Results: Till now 25 patients are included.

Conclusions: Data collection is ongoing.

P07.07 Anne Vested EFFECTS OF IN UTERO EXPOSURE TO PFOA AND PFOS ON HUMAN SEMEN QUALITY AND HORMONE PROFILE

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Introduction. Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) are man-made compounds found globally in humans. They are suspected to act as endocrine disrupters, and since they are able to cross the placental barrier, in utero exposure is inevitable. The aim of the current study was to investigate the hypothesis, that in utero exposure to PFOA and

PFOS is negatively associated with semen quality and hormone profile.

Material and methods. We recruited 169 sons who were offspring from a Danish pregnancy cohort. The sons' semen samples were analysed for sperm concentration, total count, motility, volume, and morphology, and blood samples were assessed for reproductive hormone profile. As a proxy of in utero exposure, maternal blood samples from pregnancy week 30 were analysed for levels of PFOA and PFOS. Based on tertiles of exposure, the sons were grouped into three groups (low, medium, and high) according to maternal PFOA and PFOS serum levels, and multiple regression analysis was used to evaluate possible associations.

Results. Higher in utero exposure to PFOA was significantly associated with lower sperm concentration and total count, and higher levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH). Sons in the medium PFOA group had 11% (95% CI: 2%-19%) lower percentage progressive spermatozoa than the sons in the low PFOA exposure group, but the trend was not significant (p=0.22). There were no associations between in utero exposure to PFOS and any of the traditional semen parameters, or the reproductive hormones.

Conclusions. The results indicate that in utero exposure to PFOA negatively affects semen quality and hormone profile.

P07.08 Charlotte Hyldgaard

A RETROSPECTIVE COHORT STUDY OF DANISH PATIENTS WITH INTERSTITIAL LUNG DISEASE: BURDEN, SEVERITY, TREATMENT AND SURVIVAL.

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Interstitial lung diseases (ILD) are an inhomogeneous group of rare diseases in the connective tissue of the lung with inflammation and in many cases irreversible fibrosis. Some of these diseases are amenable to treatment and have a good prognosis, whereas others have a very serious course with respiratory insufficiency and death. The most common subtype of ILD is idiopathic pulmonary fibrosis, which is important to distinguish from other ILDs because of its poor prognosis.

The objectives of this study are to describe the incidence of interstitial lung disease in Western Denmark, to assess morbidity and mortality from ILD, and to evaluate factors of importance for the prognosis of interstitial lung disease with emphasis on lung function and comorbidity.

The study is based on 431 incident patients with ILD diagnosed at the Department of Respiratory Diseases, Aarhus University Hospital, between April 2003 and April 2009. All diagnoses have been re-evaluated according to current diagnostic criteria. The study database contains information on referral pattern, diagnostics, comorbidity, lung function, treatment, side effects and outcome.

Special focus in this study will be on patients diagnosed with "unclassified" or "end stage" pulmonary fibrosis, where clinical, radiological and histological examinations have excluded well defined subtypes of ILD. The clinical characteristics and disease course for these conditions will be

studied, and compared to other subgroups of ILD.

P07.09 Camilla Plambeck Hansen

INTAKE OF RUMINANT FATTY ACIDS AND CHANGES IN WEIGHT AND WAIST CIRCUMFERENCE

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Background: Studies have suggested that total intake of trans fatty acids (TFA) and intake of industrially produced TFA is a risk factor for weight and waist gain. This leaves the question of what the effect of the ruminant trans fatty acids (R-TFA) from dairy and ruminant meat products is.

Objective: Our objective was to investigate the associations between intake of R-TFA and subsequent changes in weight and waist circumference (WC). Furthermore, potential effect modification by sex, age, body mass index (BMI) and WC at baseline was investigated.

Design: A Danish cohort of 30,851 women and men aged 50-64 y for whom information on weight, WC, habitual diet and lifestyle was collected at baseline. Follow-up information on weight and WC was collected 5 y after enrolment. The associations between intake of R-TFA and average annual change in weight and WC were studied using multiple linear regression with cubic spline modelling.

Results: Intake of R-TFA, both absolute and energy-adjusted intake, was statistically significantly associated with weight change. An inverse association was observed at lower intakes with a levelling-off at intakes above 1.2 g/day and 0.4 E%. Only absolute intake of R-TFA was statistically significant associated with WC change; an inverse association was observed at lower intakes with a levelling-off at intakes above 1.2 g/day. Sex modified the association between energy-adjusted intake of R-TFA and WC change. Age did not modify any of the associations, whereas there was indication of effect modification by baseline BMI and WC in women.

Conclusion: The present study suggests that intake of R-TFA is weakly inversely associated with changes in weight and WC.

P07.10 Bjørn Bay

ASSISTED REPRODUCTION AND CHILD NEURODEVELOPMENT

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BACKGROUND:

Infertility affects 10-20% of couples in industrialized countries, and an increasing number seek medical treatment. In developed countries, assisted reproduction techniques (ART) contribute to more than 1% of births – in some countries (e.g. Denmark) up to 9%. Over the last few years, several studies have been published on potentially adverse pregnancy outcomes,

however few studies have been performed on the neuropsychological development of these children. The infertility of the parents, the higher prevalence of chromosomal abnormalities in subfertile men and the possible increased risks of genomic imprinting disorders are among the biologically plausible reasons for increased vigilance.

OBJECTIVES:

1. To investigate the effect of ART on child IQ, attention, behavior and executive functions at age 5.

2. To investigate the effect of ART on the child risk of mental retardation.

METHODS:

Ad 1) A study of 1,628 mother and child pairs who participated in the Lifestyle During Pregnancy Study and who completed a neuropsychological test battery including validated tests of child IQ and attention, and self-administered tests of behavior and executive function. Exposure information is obtained from the Danish National Birth Cohort along with information on a set of potentially confounding factors.

Ad 2) A study of 33,139 children conceived after ART and 555,828 children born after natural conception. The risk of light, moderate and severe mental retardation is compared between the two groups. Exposure information is obtained from the Danish IVF registry and the Danish drug prescription registry and outcomes from the Danish National Patient Registry.

P07.11 David Høyrup Christiansen

PHYSIOTHERAPY AFTER SUBACROMIAL DECOMPRESSION SURGERY: A SYSTEMATIC REVIEW AND DEVELOPMENT OF A GRADED EXERCISE REHABILITATION PROTOCOL

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Introduction: Most patients with subacromial pain can be treated conservatively, but decompression surgery is a common option in patients with more persistent symptoms. Although high success rates have been reported for this surgical procedure, a small percentage experience difficulties returning to normal activity. In clinical practice, further treatment (e.g. physiotherapy with exercises) is generally recommended. However, little is known about optimal contents of such interventions. Objective: To develop an evidence-based postoperative rehabilitation protocol. Methods: The literature was systematically reviewed and components of previous exercise programs were extracted. A series of workshops were organized with clinical physiotherapists specializing in shoulders. A rehabilitation protocol was synthesized and implemented in two municipality rehabilitation units. Four pilot patients were recruited to test the protocol. Results: A total of seven studies were identified. The methodological quality was low and description of interventions sparse.

During workshops consensus were reached for clinical examination, exercises, treatment techniques and progression. Three out of four pilot patients experienced clinically important changes in pain and function at three months measured by the Oxford Shoulder Score. Conclusion: A rehabilitation protocol based on empirical evidence and clinical expertise was developed. The protocol was found feasible for clinical practice reducing pain and promoting function in surgical shoulder patients. The effectiveness of the rehabilitation protocol will be further evaluated in The Shoulder Intervention Project; a randomized controlled trial.

P08.01 Connie Timmermann

HOSPITALISED PATIENTS AND AESTHETIC SENSORY IMPRESSIONS

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Aim: The study explores and describes how hospitalised patients with a life-threatening illness experience sensory impressions from the care settings in the hospital environment such as architecture, interior and decoration. Sensory impressions related to the communication between patients and healthcare professionals will also be explored.

Method: Ethnographic fieldwork consisting of participant observation and both informal and formal qualitative interviews have been chosen for data generation. The analysis of data will be guided by the hermeneutical-phenomenological theory of interpretation as presented by the French philosopher Paul Ricouer.

Background: Existing research literature shows that positive sensory impressions such as a view to nature, sunlight through a window and art presenting natural scenes affect patients positively regarding anxiety, blood pressure, pain and stress. Some studies also suggests that experiencing welcoming in the environment, being in a familiar and calm environment and being able to maintain social relations in the environment are experienced as important by hospitalised patients. However, research exploring the experiences of hospitalised patients with a life threatening illness regarding the meaning of aesthetic sensory impressions is few.

Implications: The knowledge generated by this project can help to improve the quality of nurses' caring practice by providing research-based knowledge about the meaning of positive sensory impressions in the hospital environment as experienced by patients. Likewise, the project could contribute knowledge relevant to architecture, interior design and decoration of current and future hospitals.

P08.02 Dorthe Hasfeldt-Hansen

NOISE IN THE OPERATING ROOM - A LITERATURE REVIEW

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Background & Aim:

Noise is a general stressor, and out of consideration for both patients and

staff, noise in the operating room should be avoided as much as possible. This study was conducted with the aim of identifying the current knowledge about noise in the operating room upon which new research can be built.

Methods:

A systematic literature search for primary research articles written in English was performed in the Medline, Cinahl and Cochrane databases using the search terms: noise, operating room, operating theatre. Abstracts were searched for suitable articles and reference lists were examined for additional sources.

Each study was assessed according to the strength of the evidence and the quality of the study including the following quality indicators: aim, inclusion, data collection, end points. The studies were rated from A (well-designed study) to D (study with major flaws).

Results:

Eighteen relevant articles were identified and categorized as follows:

Noise levels; Noise sources; Staff performances; Patient's perceptions of noise.

All studies had nonexperimental study designs and the level of evidence was found to be no higher than 3. In general the quality of the studies was high. 60% was rated A and the rest was rated B and C.

Conclusions:

Noise levels in the operating room in general exceed recommended levels. Noise sources are related to equipment and staff behavior. The main effect of noise on staff performances is related to impaired communication, resulting in a negative effect on patient safety. There is a lack of literature on patient's perception of noise in the operating room. Further research using experimental designs is needed.

P08.03 Anette Hvenegaard Kjeldgaard

INCIDENT CANCER PATIENTS' USE OF GENERAL PRACTICE

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Introduction: The role of general practice is becoming increasingly important through all phases of the cancer pathway. However, we lack knowledge about how cancer patients use general practice before diagnosis of cancer, and how this is affected by the transition between primary and secondary care investigation and treatment. The Danish health and disease registries give a unique opportunity on a population-based scale to assess the attendance patterns to general practice and link this information to date of cancer diagnosis.

Aim: To describe incident cancer patients' attendance patterns to general practice before and after the date of diagnosis compared with the attendance patterns for a sample of population based controls.

Methods: A population-based case control study of all incident cancer patients in the Danish Cancer Register from 1 January 2004 to 31 December 2009 (approx. 130,000 patients) matched to 5 controls by incidence density sampling on age and gender. Use of general practice is assessed as number of visits per month in the year preceding the cancer diagnosis and two years after the diagnosis using data from the Danish Health Service Register stratified on age and gender.

Results: Data processing and analyses are ongoing, and preliminary results will be presented.

Discussion/Conclusions: This study will illuminate how cancer patients use general practice before and after their diagnosis of cancer, and hereby contribute important new knowledge, that may be able to improve the diagnostic, supportive and coordinating role of general practice in cancer care.

P08.04 Susanne Lemcke

THE EARLY SIGNS OF ADHD IN TODDLERS: A FOLLOW-UP STUDY IN THE DANISH NATIONAL BIRTH COHORT.

S. Lemcke

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Background: The prevalence of Attention Deficit Hyperactivity Disorder (ADHD) in children is estimated to be 3-7% and the average age of diagnosis is 8-10 years. Early treatment of the disorder has been shown to improve prognosis for the children but studies on early detection are still sparse.

Aim: To study whether prospectively collected information from mothers on distinctions in development and behaviour during the first two years of life can predict the risk of the child later being diagnosed with ADHD.

Methods: In the Danish National Birth Cohort (DNBC) mothers were interviewed about their child's development, behaviour and growth when the child was 6 and 18 months of age. Children diagnosed with ADHD at child and adolescent psychiatric hospitals are registered in the Danish National Patient Register; thus, it is possible to identify children with ADHD in the cohort. Analyses of the information in DNBC about children later diagnosed with ADHD will provide us with information about signs of ADHD before the age of two years.

Results: At the end of follow-up, the study cohort consisted of 76,441 children, out of which 681 children were diagnosed with ADHD, corresponding to a prevalence of 0.9%. Only few signs reported early by the parents were found to be associated with the risk of the child subsequently being diagnosed with ADHD.

Conclusions: In the preliminary analysis only a few signs can be associated with the risk of a child being diagnosed with ADHD; but the prevalence of ADHD in the study population is too low, and the next step is to include more outcome data from the Register of Medicinal Product Statistics in order to make the ADHD population more complete.

P08.05 Else-Marie Dalsgaard

SOCIOECONOMIC FACTORS, PSYCHOSOCIAL FACTORS AND HBA_{1C} LEVEL AMONG PERSONS AT HIGH RISK FOR TYPE 2 DIABETES

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Background:

Glycemic control is important to reduce the risk of microvascular complications in persons with diabetes. Studies have found higher Hba1c level among persons with type 2 diabetes who were deprived, had a low sense of coherence or had low self-rated health, but it is unknown whether this association applies to persons at a high risk for diabetes. We aimed at examining the relationship between socioeconomic factors, psychosocial factors and Hba_{1c} level in a population at high risk for diabetes attending screening.

Methods:

A total of 163,185 persons were invited to participate in screening for type 2 diabetes, 2001-2006. Among these, 28,031 persons who were categorised as being at a high risk for diabetes on the basis of a self-administrated risk score attended a further screening test in general practice. A total of 1,533 persons were diagnosed with type 2 diabetes. Data on socioeconomic factors (education, occupation, income and cohabiting status) were obtained from Statistics Denmark, data on psychosocial factors (self-rated health, sense of coherence and anxiety) were obtained from questionnaires filled in by persons diagnosed with type 2 diabetes. Hba_{1c} was measured in EDTA blood from a venous sample. Relationship between socioeconomic factors and psychosocial factors and Hba_{1c} level will be examined by multivariate analyses taking into account both confounding, collinearity and interaction.

Results:

Data is available and analyses will be conducted this autumn. Results will be presented at the Phd Day.

P08.06 Ditte Lammers Vernal

A REGISTER- BASED STUDY OF THE OUTCOME OF EARLY ONSET SCHIZOPHRENIA COMPARED TO ADULT ONSET SCHIZOPHRENIA

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The aim of the Ph.D. project is to study the outcome of early onset schizophrenia (EOS) by use of national register data. EOS is defined as patients diagnosed with schizophrenia before age 18. Studies of EOS are limited because the frequency of the disorder is low and often based on small samples or short follow-up periods. The findings from previous studies on outcome of EOS are inconclusive but most point to a poor prognosis.

With the Danish Psychiatric Central Register we have the means to investigate the outcome of EOS in a large sample that will be representative for Denmark. Only cases from the ICD-10 period will be considered, thus

patients diagnosed after 1994 will be included in the study. The inclusion of patients in the cohort will last until 2005 since this will allow for a sufficient follow-up period in the registers. The sample with EOS will be compared to adult patients diagnosed with schizophrenia in the same period.

Outcome will be assessed using both psychiatric course and psychosocial functioning measures. Psychiatric course of illness will be studied in terms of number of admissions, number of days spent in psychiatric hospital, number of out-patient contacts, and whether the diagnosis changed over time. Social registers will be used to gather information on social support such as premature pension, institutionalization, and working ability. Data from the Cause of Death register will be used to test whether EOS has a higher mortality and suicide rate than AOS. Among demographic variables, sex and age will be considered in the analysis.

The findings should be contributing to a more realistic understanding of the long-term needs of patients with EOS.

P08.07 Hanne Mainz THE RELATIONSHIP BETWEEN NURSE STAFFING AND PATIENT OUTCOME

H. Mainz

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Background

Many studies especially from the US show a strong effect of increased nurse staffing on patient safety with less hospital-related mortality, failure to rescue, hospital-acquired infections and other adverse events. However the results are not consistent, presumably caused by different measurement tools, study designs and healthcare systems. There is no international consensus on an appropriate method for measuring nurse staffing containing the elements: nursing resources (number and skills), nurse intensity (workload), and contextual factors (work environment). In Denmark no method has been validated and tested to assess nurse staffing in a Danish context. The object of the first study is to test a method for assessing nurse staffing in Danish somatic wards. Subsequently the relationship between nurse staffing and outcome for patients with hip fractures will be evaluated.

Methods

Nurse staffing was measured in four Danish somatic hospital wards in May and June 2011. Nurse intensity of 2388 patients was estimated thee times a day and surveys about work environment and nurse's skills were collected. The number of nursing hours per patient day (NHPPD) was estimated for a total of 112 days. The nurses assessed staffing level and quality of patient care during every shift. The relationship between intensity, skills, environment, NHPPD and the nurse's assessment of staffing and quality will be analyzed.

Expected results

If the method is a suitable tool for measuring nurse staffing, it will be used in a multicenter study in ten specialized orthopaedic surgical wards to

analyze the relationship between nurse staffing and patient outcomes

P08.08 Noora Ronkainen

'THAT IS WHY I GAVE IN TO AGE MY COMPETITIVE ABILITY BUT NOT MY SOUL!' - THE SEARCH FOR MEANING IN ATHLETIC CAREER AND RETIREMENT

N. Ronkainen

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In this research, we explore the spiritual dimensions of running. We draw on theological and existential perspectives, athletic career research as well as postmodern cultural critique to construct a multi-voiced representation of the spiritual meanings of endurance running current in Scandinavian running cultures. Our theoretical framework is existential psychology, where spirituality is understood as a broad concept encompassing both religious and humanistic worldviews. In the first section of the dissertation, we conducted a critical discourse analysis of the Finnish runner's magazine, Juoksija. The research results suggest that spiritual aspects of running underlie, but are rarely given voice to, the dominant performance discourse of Finnish (competitive) running culture. The spiritual and/or existential dimensions become especially meaningful, however, when transitioning from elite level sports. We suggest that finding spiritual dimensions from running can be a protective element in athletic retirement, enabling runners to sustain their runner identity as a central life-narrative even after the transition from competitive sports.From here, I will proceed to interview runners to gain insight and depth to these findings. Adopting the life narrative perspective, I will conduct a series of interviews with retiring or already retired Scandinavian runners.

P08.09 Tue Kjølhede

MULTIPLE SCLEROSIS – INFLAMMATORY, NEUROLOGICAL AND MUSCULAR ADAPTATIONS TO HEAVY RESISTANCE TRAINING

T. Kjølhede

Section of Sport Science, Department of Public Health

Exercise in general, and resistance training (RT) in particular, is regarded as an important tool in the rehabilitation of people with multiple sclerosis (MS).

Previous studies have reported positive effects of 8-12 weeks of RT on muscle strength, function (walking speed etc.) and quality of life (QoL). Also, a possible disease modifying effect has been proposed. However, the underlying physiological mechanisms that might explain these beneficial effects and the possible effects on disease progression are unresolved. Furthermore, none of the previous studies have given attention to the possible impact of MS progression type, gender and medication.

Using gender stratification in a randomized, controlled, cross-over study design, the purpose of this study is to investigate the effects of 24 weeks of RT on underlying mechanisms potentially explaining improvements in strength, function and QoL. Endpoints include (1) neuro-muscular measurements such as EMG, rate of force development and voluntary muscle activation ratio closely associated with strength and function, (2) structural measurements of the brain obtained with MRI such as rate of

atrophy and plaque incidence, (3) cytokine levels in blood that is linked to disease progression (the latter aspect especially examined with respect to gender).

The study will include 40 men and 40 women suffering from the most prevalent MS disease course, named relapsing-remitting. Participants must have an EDSS-score of 2.0-5.5 and be medicated with beta-interferon 1a or 1b. Subjects will be randomized into two groups that will perform either RT or continue their habitual lifestyle. After 24 weeks interventions will switch between groups.

P08.10 Rasmus Beedholm Laursen

DANISH FOOTBALL FAN CULTURE – THE DANISH ULTRAS

R.B. Laursen

institute of Sport Sciences

Purpose:This PhD project explores the Danish football fan culture concerning the fan group categorized and named ultras. Though ultras are defined as non-violent fan groups they in one way or another tend to contribute to conflicts between football fans and the police. The aim of this project is to provide in-debt knowledge of this particular segment of the football culture in Denmark and thus lay the foundation for development of adequate crowd management, which can lead to a reduction of football riots.Background and methodological triangulation:

Although Ultras and hooligans from time to time collaborate, they are not the same. Contrary to hooligans ultras reject the use of violence. However their forward style and fanatical behaviour often contribute to or cause conflicts with the police and stadium inspectors. A consequence of an undifferentiated police (and stadium inspector) effort toward football fans can lead to a radicalization process, where football fans begin to identify with and seek support from declared hooligans. In order to pursue the hypotheses below the project will use a methodological triangulation. There will be conducted semi-structured interviews with ultras from AGF, OB and Brøndby IF. Alongside the semi-structured interviews there will be performed participant observations among various ultras. The advantage of this methodological approach is that the additional interviews may help to validate the observations conducted along the way.

P08.11 Joe Larner

THE EFFECT OF ECCENTRIC EXERCISE ON CARBOHYDRATE METABOLISM IN ISOLATED SOLEUS AND EDL RAT MUSCLES

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It has been well documented that eccentric exercise causes a reduction in muscle performance which could be termed as long lasting fatigue or muscle damage (1). Symptoms include, but are not limited to, compromised contractile function (2,3), especially at low frequency stimulation (low-frequency fatigue) (4,5), muscle pain and tenderness (6), and changes to carbohydrate metabolism including reduced glucose uptake rate, leading to low glycogen stores, decreased energy status in the cells, and therefore

increased recovery time (7). These changes are of greater magnitude and longer lasting when compared to concentric exercise of similar intensity and duration (8). These factors altogether result in decreased ability to carry out everyday tasks or perform elite sports following eccentric actions.

This study aims to further elucidate the time course and fibre type dependence of the muscle's impaired carbohydrate uptake and storage following eccentric exercise. Glucose uptake rates will be monitored in isolated rat soleus and EDL muscles following eccentric work and content of glycogen and glycogen synthase will be investigated. The muscles will be exposed to conditions both with and without insulin following the eccentric work to examine the insulin-mediated regulation of glucose uptake and glycogen synthase. As the effect of eccentric activity on contractile performance is also of interest, the ability of the muscles to develop force before, during and after an eccentric protocol will also be measured and analysed.

P08.12 Jean Farup

THE ROLE OF PROTEIN SIGNALLING AND STEM CELLS IN MUSCLE PROTEIN SYNTHESIS AND RECOVERY RATE AFTER EXCENTRIC EXERCISE

J. Farup

Section of Sport Science, Institute of Public Health

Exercise stress (metabolic and/or mechanical) and energy status (amino acid and carbohydrate availiability) of the muscle cell is known to initiate muscle hypertrophy signaling and protein synthesis. Eccentric muscle contractions has previously been shown to be superior in inducing muscle hypertrophy compaired to concentric contractions. Little is known about the underlying explanatory cellular mechanisms, but mechanotransduction (i.e. cell membrane proteins able to sense mechanical strain) muscle stem cells (satellite cells and mesenchymal stem cells) may likely be involved. Also, little is known on the effect of protein supplementation after eccentric exercise.

The overall purpose of this phd project is ; 1) to investigate the acute reponse of cell mechanotransducing membrane proteins (e.g. integrins and adhesion kinases) and hypertrophy signalling proteins to eccentric versus concentric exercise; 2) Determine the membrane protein and stem cell reponse to longterm eccentric versus concentric exercise; 3) Investigate the muscle stem cell responses in regeneration from muscle damaging eccentric exercise. Furthermore, all exercise interventions are investigated under conditions of administration of either protein or placebo

The methodological approches comprise; 1) Western blotting to quantify mechanotransducing and hypertrophy signalling protein; 2) Immuno-histochemisty to localize and quantify stem cells; 3) Flow cytometri to determine to quantify mesenchymal stem cells in plasma.

P09.01 Pia Løvschal-Nielsen

SOCIAL RELATIONS OF CHILDREN WITH CANCER DURING TREATMENT AND REHABILITATION AT HOSPITAL

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BACKGROUND: 3 of 4 children fortunately survive cancer. But child survivors face various obstacles compared to peers, such as bullying and stigmatizing. Little is known about how children and their relations navigate through the social consequences of cancer, such as the social isolation required by the treatment, and what they experience and learn from the process. As it is well known that positive social relations and strong networks are central to health and well-being, it is important to know how to benefit from their experiences, for creating rehabilitation interventions that may improve the community participation of cancer survivors. AIM: To gain insight into how social relations and networks work and are made to work in the 'social borderland' of children with cancer, from the time of identification of the disease, as a means to improve their health and prospects of community participation. METHODS: Multiple methods are used, such as participant observation, extended case method, and qualitative interviews, creating data 'on location'. SETTING: Department of Child Oncology, Aarhus University Hospital, Skejby & homes and vicinity of children with cancer, who are in treatment at the department. PARTICIPANTS: A smaller sample of children between the age of 4 and 15, their various associations, and staff at the hospital. DESIGN: Ethnographic fieldwork at the isolation ward of the hospital for 1 year, following the everyday life of children commuting between hospital and home and how they navigate socially in this 'social borderland'. Data is analyzed through anthropological and sociological theories of child & childhood, child agency, and social capital.

P09.02 Simon Grandjean Bamberger

DERIVED EFFECTS OF GLOBALIZATION ON PSYCHOSOCIAL WORK ENVIRONMENT - A MULTILEVEL LATENT CLASS ANALYSIS STUDY

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Background: In the context of globalization and technological innovation the competition pressure on companies is rapidly escalating in effect, instigating an unstable and unpredictable psychosocial work environment. Factors in the psychosocial work environment have been consistently linked with both negative physical and psychological outcomes adding to the importance of studying this matter.

Aim: The primary objectives are to determine 1) if there is a direct negative effect of globalization on the employees' appraisal of the psychosocial work environment and 2) if the negative effect of globalization will be positively modified by work organization.

Design: A multilevel study combining longitudinal exposure data and cross-sectional employee survey data. We compare different levels of competition pressure to employee appraisal of the psychosocial work environment, and use the company work organization as a moderating variable.

Materials: 601 companies and 3,651 randomly selected employees participated in the survey. Data was obtained by web questionnaires;

company data in 2006 and 2010, and employee data in 2010.

Analysis: Exposure is characterised by company experienced competition pressure over time. Outcome is measured using the Copenhagen Psychosocial Questionnaire and the Effort Reward Imbalance model. The exposure variable and the moderating variable work organisation are created using latent class analysis. Multilevel regression analysis is applied to analyse the associations.

Results: Preliminary results will be presented at the conference.

P09.03 Heidi Cueto

SOCIO-DEMOGRAPHIC AND LIFESTYLE PREDICTORS OF FOLIC ACID AND MULTIVITAMIN SUPPLEMENTATION IN DANISH PREGNANCY PLANNERS

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Introduction: Danish pregnancy planners are advised to take a daily supplement of 400 µg folic acid. Knowledge about possible predictors of folic acid and multivitamin supplementation in the preconceptional period is scarce.

Aim: To examine the relation between socio-demographic and lifestyle factors and folic acid and multivitamin supplementation, respectively, among Danish pregnancy planners.

Methods: Using data from 5291 participants from the 'Snart-Gravid' Study, we conducted multivariable log-binomial regression controlling for covariates to estimate prevalence ratios (PR) and 95% confidence intervals (CI) for the relation between selected predictors and folic acid and multivitamin supplementation, respectively. Dietary supplementation and covariates were self-reported at baseline.

Results: Overall, 56% used multivitamins and 43% used folic acid supplements. Smoking was inversely associated with folic acid supplementation (PRs: 0.99 (95% CI=0.92, 1.07), 0.91 (95% CI=0.81, 1.02), and 0.79 (95% CI=0.68, 0.91) for <5, 5-9, and ≥10 pack-years, respectively, vs. none). Alcohol intake was inversely associated with folic acid supplementation (PRs: 0.89 (95% CI=0.83, 0.95), 0.80 (95% CI=0.73, 0.88), 0.82 (95% CI=0.71, 0.94), and 0.57 (95% CI=0.39, 0.82) for 1-3, 4-7, 8-14, and ≥15 drinks per week, respectively, vs. none). Similar results were found for multivitamin supplementation.

Conclusion: These results suggest that pregnancy planners who follow other preconceptional guidelines are more likely to comply with the folic acid recommendations.

P09.04 Mads Lind Ingeman

THE NON-ORGAN-SPECIFIC CANCER FAST TRACK

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Denmark has a high cancer morbidity and mortality compared to the rest of Western Europe - a longer diagnostic delay in Danish cancer patients probably plays an important role in these findings. As a result, fast tracks for patients with classic organ-specific alarm symptoms are currently in use, but only 50% of cancer patients had alarm symptoms at their first visit to their General Practitioner. In the light of these results, several new initiatives concerning the examination of patients with uncharacteristic or atypical symptoms are on their way. Central Denmark Region has selected Silkeborg Regional Hospital to establish a fast track for patients with suspected occult cancer or other serious disease without organ-specific symptoms – a non-organ-specific fast track.

There is no scientific evidence of the effect of a non-organ-specific fast track and to our knowledge, no similar projects have been set up internationally. Furthermore, we do not know how the GPs will use this fast track in their diagnostic strategy and which factors will influence this.

This project is a population-based, prospective questionnaire and registry-based study and the aim is to examine GPs' need for and use of the non-organ-specific fast track as well as to examine who is referred and why. Additionally, the results of the fast track will be examined.

P09.05 Kasper Grosen

PREDICTION OF ACUTE AND PERSISTENT POSTSURGICAL PAIN IN PATIENTS UNDERGOING MINIMALLY INVASIVE REPAIR OF PECTUS EXCAVATUM

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Postsurgical pain remains inadequately managed and the transition from acute postsurgical pain to a chronic pain state is now increasingly being recognized as a frequent adverse effect of surgery. The aim of the present study is to explore whether conditioned pain modulation efficiency and psychological factors measured preoperatively predict intensity of acute postsurgical pain and unpleasantness, analgesic requirements and development of persistent postsurgical pain. Six patients undergoing minimally invasive repair of pectus excavatum are currently enrolled in this ongoing study. Surgical procedure, anesthesia and analgesia are standardized. When assessing conditioned pain modulation preoperatively, pressure pain thresholds measured on the quadricep muscle serves as the 'test' stimulus and the cold pressor test as the 'conditioning' stimulus. The difference in pressure pain thresholds before and after cold pressor test indicates the effect of conditioned pain modulation. In addition, questionnaires on pain catastrophizing, depression, anxiety, personality,

positive and negative affect, self-esteem, health-related quality of life, and pain are administered on the day before scheduled surgery; following preoperative psychophysical assessments; at 72 hours, six weeks, and six months postoperatively. Moreover, quantitative sensory testing is performed prior to the experimental induction and assessment of conditioned pain modulation and at six weeks postoperatively. Finally, intensity of clinical postsurgical pain and unpleasantness and analgesic consumption are assessed by means of a study specific pain diary for up to six weeks postoperatively.

P09.06 Louise Pape Larsen

LIFE AFTER STROKE

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Introduction
Stroke is one of the most common causes of death and disability with an annually incidence of 12-13,000 in Denmark. Neurological handicaps and loss of functional independence are common after stroke, and are often associated with symptoms as pain, fatigue, depression, anxiety, and various cognitive deficits.
30-40% of stroke patients depend on different kinds of care after one year as a result of reduced functional ability. Several studies finds that large groups of patients have highly affected functional ability and health related quality of life (HRQL) several years after stroke.
The aims of the present PhD-study are:
To describe the prognosis of stroke in terms of patient reported outcomes (PRO)
To describe the frequency and time trends for Return to Work (RTW) and identify predictors of RTW
Investigating the association between compliance of clinical guidelines and RTW.
Testing the hypothesis that compliance of clinical guidelines causes improved long time prognosis of PRO
Identify predictors of new cerebrovascular event
Identify determinants for use of health services.

Methods
The project is a longitudinal observational study in a cohort of consecutive patients admitted with first time apoplexy at a hospital in the Central Denmark Region.
All patients younger than 80 years and discharged to their own home are included in the study.
They are asked to participate in a long-term follow-up survey with six questionnaires distributed over 2,5 years from the onset of their stroke.
Furthermore, a register based follow-up of all patients will be implemented.
About 3500 patients are expected to participate with a total follow-up time at 8750 person years.

P09.07 Palle Larsen

GUIDELINES FOR NON-PHARMACOLOGICAL REHABILITATION FOR HEART FAILURE PATIENTS AND THE BASIC EVIDENCE - IS THERE A LINK?

P. Larsen

Background

Cardiovascular diseases are the most common cause of morbidity and mortality in the western world [1]. In clinical practice, awareness of the importance of reducing risk factors is increasing, so focus is on rehabilitation to cardiac patients, which allows a better understanding of their own situation and the increased action possibilities [3-4].

Focus on behavioral changes is an essential part of the individual self-care-based component of health behavior. This is a basic circumstance when living with heart failure [5]. During the last 15 years, there have been focus on the rehabilitative efforts in cardiovascular diseases and the ESC non pharmacological recommendations. These are transformed in to a 12 point measurement scale by T. Jaarsma, which measures self care behavior.

Method

Systematic literature search at: Cochrane, Pub Med, Cinahl, embase Search terms rehabilitation, heart failure, daily weighing, fluid intake, dietary salt intake, exercise, dyspnoe, ankle edema, daily rest, fatigue, flu vaccination in several combinations: AND; OR; NOT.

Results

5 articles covering daily weighing, dietary salt intake, fluid restriction and regular exercise.

Discussion

The limited amount of coverage and therefore evidence in relation to the recommendations is a challenge in terms of motivating heart failure patients to be more self-care reliant. Therefore, the existing knowledge is essential to use in caring for patients with heart failure when they are discharged to phase III rehabilitation in their own municipality. It is important to develop a systematic review of the materials that are available within each area, although the number of items is quite limited.

P09.08 Malene Outzen PROSTATE CANCER INCIDENCE AND MORTALITY IN DENMARK 1978-2009

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Background: The incidence of prostate cancer (PC) has increased during the last 15 years in Denmark, while the mortality has remained largely unchanged. This study aimed to investigate the trends in PC incidence and mortality in Denmark between 1978 and 2009 with a special focus on the recent decade.

Methods: In this population-based register study, all cases of PC in Denmark during 1978-2009 were obtained from the Danish Cancer Registry. Age-standardised (World Standard Population 2000) incidence and mortality rates (The Danish Registers of Causes of Death) for five-year calendar periods (1978-2007) and a two-year calendar period (2008-2009)

were calculated. Trends in rates were estimated for specific age groups, birth cohorts, and clinical stage.

Results: Age-standardised incidence rates of PC increased from 29.2 per 100,000 person-years (1978-1982) to 76.2 per 100,000 person-years (2008-2009). The increasing trend was almost exclusively observed from the mid-1990s. Mortality rates of PC remained largely unchanged during the entire study period; from 15.8 to 17.9 per 100,000 person-years. The increasing incidence rates were most pronounced in PC patients aged 60+ years. A clear pattern was seen for the age-specific PC incidence rates for selected birth cohorts. Increasing trends were especially seen in PC patients aged 60+ years and born 1943-1947 or 1933-1937. The distribution of stage changed from 1998-2002, with an increasing proportion of PC patients with localised disease.

Conclusions: Trends in PC incidence rates increased steadily from 1993-1997 to 2008-2009, whereas the mortality rates remained stable during the entire study period.

P09.09 Karen Kjær Larsen

SCREENING FOR DEPRESSION IN PATIENTS WITH MYOCARDIAL INFARCTION BY GENERAL PRACTITIONERS

K.K. Larsen

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BACKGROUND Depression in patients with myocardial infarction (MI) is highly prevalent and associated with increased morbidity and mortality. Routine screening for post-MI depression is recommended. We studied general practitioners' (GP) practice of screening for post-MI depression, and analysed whether screening rate varied among subgroups of MI patients with a particularly high risk of depression.

DESIGN Population-based cohort study in the Central Denmark Region.

METHODS All patients with a first-time MI in 2009 received a questionnaire three months after discharge from hospital. The questionnaire included information on anxiety, depression, severity of the disease, and smoking habits. The responders' general practitioners received a questionnaire one year after the patient had been discharged from hospital. This questionnaire provided information on screening for depression, co-morbidity, and previous mental illness of the patient. Nationwide registers supplied the patients' socio-demographic status the year before the MI.

RESULTS Response-rates were 70.5% (908) among patients, and 64.9% (589) among GPs. According to the GPs, 27.3% (95% CI 23.7%-30.9%) MI patients were screened for depression. The screening rate was higher among patients with a history of mental illness (50.0%, $p<0.001$), and among patients with anxiety (37.0%, $p=0.002$) or depression (37.5%, $p=0.007$) as compared with those without these conditions.

CONCLUSION Screening for depression was not complete among MI patients, not even among subgroups of MI patients with a particularly high risk of depression. More detailed guidelines may help to optimise general practitioners' screening for post-MI depression.

P09.10 Rikke Jørgensen

MEANINGFUL CHANGE WITH THE METHOD GUIDED SELF-DETERMINATION – A RANDOMISED CONTROLLED STUDY FOR PATIENTS DIAGNOSED WITH SCHIZOPHRENIA

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Rehospitalisation and discontinued treatment is common among patients with schizophrenia and is often associated with lack of insight into the illness. Improving patients' insight has been attempted but without any considerable change. The method Guided Self-Determination (GSD), a shared decision-making and problem solving method developed from qualitative research, has shown a positive influence on patients' insight into the illness in a qualitative evaluation.

The aim of this study is to evaluate the effects of the method GSD in the care of patients with schizophrenia compared to treatment as usual.

The study design is a randomized controlled trial that investigates if the method GSD has effect on the outcomes clinical and cognitive insight, self-esteem, recovery, psychopathology and social functioning when applied in psychiatric care in 3 Assertive Outreach Teams and 3 Psychosis Teams. All participants are diagnosed with schizophrenia or schizoaffective disorder, are between 18 and 70 years old and 50 are randomly assigned to immediate receipt of individual training with the method GSD (intervention group) and 50 to a control group. All participants complete four self-rating questionnaires (Insight Scale, Beck Cognitive Insight Scale, Recovery Assessment Scale and Rosenberg Self-Esteem Scale), a demographic data sheet with questions on pharmacological treatment, compliance and alcohol and drug abuse, an interview concerning psychopathology (Positive and Negative Syndrome Scale) and an assessment of social functioning (Global Assessment of Functioning) at baseline, and after 3, 6, and 12 monthx.

Only baseline results will be presented as the study is ongoing.

P09.11 Nils Bjerregaard

TRANSVERSUS ABDOMINAL PLANE (TAP) KATETER ANLÆGGELSE TIL COLONRESEKTION: ET METODESTUDIE.

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Background and Objectives:

Transversus abdominis plain block have shown effect on postoperative pain after abdominal surgery[i]. Only limited data exists on TAP-catheter and extended analgesic effect through bolus injection or infusion[ii]. This study demonstrates the use of TAP-catheters for open colon surgery.

Methods:

15 patients scheduled for open colon resection were prospectively included. Bilateral ultrasound guided TAP-catheters were placed preoperatively using the posterior approach and a bolus of 20 mL bupivacaine ¼ % with

epinephrine 5 µg/ml was given after placement and every 12 hours. A total of 4 boluses were given. We recorded NRS and opioid consumption.

Results:

Bilateral TAP-catheters with the posterior approach prior to surgery and administration of bupivacaine boluses is feasible, showed no complications and gave sufficient analgesia and low opioid requirements. Total opioid requirement for the 48 hours was 35 mg iv morphine-equivalent. The median NRS was 3 at rest and 5 while coughing.

Conclusion:

TAP catheter, as part of a multimodal analgesic regime, seems to be a good alternative for postoperative pain management after major abdominal surgery. However the technique is best suited for non-extensive surgery where the pain derives primarily from the surgical incision.

[i] McDonnell JG, et al The analgesic efficacy of transversus abdominis plane block after abdominal surgery: a prospective randomized controlled trial. Anesth Analg 2007; 104: 193–7.

[ii] Heil JW, et al. Ultrasound-guided transversus abdominis plane catheters and ambulatory perineural infusions for outpatient inguinal hernia repair. Reg Anesth Pain Med. 2010 Nov;35(6):556-8.

P09.12 Michael Smærup Brandt

PERCENTAGE OF VESTIBULAR DYSFUNCTION IN 361 ELDERLY CITIZENS RESPONDING TO A NEWSPAPER ADVERTISEMENT.

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Introduction

Elderly patients with vestibular dysfunction have an eight-fold increased risk of falling compared to other fall patients. The aim of this study was to identify the percentage of vestibular dysfunction among elderly citizens with complaints of dizziness.

Method

To recruit elderly citizens with dizziness we advertised in a local newspaper. A telephone interview with the respondents was done by a physiotherapist (PT). If the PT concluded that the reason for the dizziness could be vestibular dysfunction the citizen was invited for further examination. The citizen was tested by the PT and a nurse in the Fall Clinic, Department of Geriatrics, Aarhus University Hospital. If the patient was still under suspicion of vestibular dysfunction he/she was examined by a geriatrician and eventually by a specially trained otoneurologist on the ENT Department,

Aarhus University Hospital.

Results

361 elderly citizens responded to the advertisement. 124 patients were suspected of vestibular dysfunction and further tested in the Fall Clinic. 71 of these patients have been seen until now and in 37 (52%) vestibular dysfunction were diagnosed. BPPV was diagnosed in 21 (30%) of the patients having vestibular dysfunction. Of 37 patients having vestibular dysfunction, 16 needed further testing in the ENT Department. BPPV was diagnosed in further 4 patients.

Conclusions

Vestibular dysfunction among the elderly is an overlooked problem and may be relatively simply diagnosed by vestibular bedside tests. In this study, surprisingly many citizens had BPPV, which can be diagnosed by the Epley maneuver or the Roll test.

P10.01 Katja Glejsted Ingstrup

BEREAVEMENT AND CONGENITAL ANOMALIES

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Background: Congenital anomalies (CA) such as neural tube defects are often serious and lethal to the fetus and the etiology is largely unknown. The prevalence of CA is about 5-8% in most affluent countries. The theory of developmental origins of health and disease suggests that fetal environment plays an important role for the child's future disease susceptibility. Stress exposures in animal studies have shown an association with CA. Emotional stress in humans during the perinatal period has previously been associated with CA related to the neural cranial crest, but numbers were too small to study specific CA's and the possibility of chance findings could not be excluded. Objective: To investigate the associations between maternal stress measured as bereavement due to loss of a close relative in the perinatal period and CA of the neural tube, cleft lip/ palate, hypospadias and cryptorchidism. Methods: The project is part of a European Research Council / FP7 starting grant. It is designed as a follow-up study based on 20 national registries in Denmark, Sweden and Finland. The total study population is approximately 6.7 million children. Bereavement is defined by a single life event - the death of a close relative - and approximately 163,000 are exposed. Follow-up starts at birth and continues until diagnosis of CA or the child's first birthday. The registers allow for adjustment of a number of covariates/potential confounders, such as demographic variables, birth characteristics, socioeconomic conditions and history of maternal diseases. We believe that our studies will probably provide worthy epidemiological evidence to the theory of prenatal stress exposure and CA.

P10.02 Vita Ligaya Ponce Dalgaard

EVALUATING A COGNITIVE TREAMENT PROGRAM FOR PATIENTS ON SICK LEAVE DUE TO WORK RELATED STRESS: A RANDOMISED CONTROLLED STUDY

L. Dalgaard

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Abstract

Background: Clinics of occupational medicine have experienced a rise in patients with work related stress reactions. Many of these patients are also on sick leave. Work related stress symptoms may have many individual and socio-economical consequences. Still, only few well-documented treatment interventions seem to be available. Research indicates that cognitive interventions are more effective than other treatments in reducing stress symptoms. The aim of this study is to evaluate the effect of a cognitive treatment intervention in reducing stress symptoms and length of sickness absence.

Methods: A randomized controlled trial is being carried out with 60 patients in the treatment group and 60 patients in the control group (treatment as usual). People on long term sick leave (4-8 weeks) are referred to the regional Clinic of Occupational Medicine from three municipalities. All patients receive a psychological interview and a medical examination. Only patients who are diagnosed with adjustment disorder related to work are included in the trial. The intervention is designed to help patients identify stressors at work and develop useful cognitive and behavioral coping strategies. The program comprises of 6 individual sessions. Questionnaires are answered at baseline, after 4 months and after 10 months. Main outcomes are perceived stress and length of sick leave; other outcomes are general health, cognitive symptoms, sleep, and coping style.

Hypothesis: It is hypothesised that the intervention will be more effective than care-as-usual in decreasing the level of perceived stress as well as reducing sickness absence duration.

P10.03 Philip Finn Rising Nielsen

ASSOCIATION BETWEEN PARENTAL HOSPITAL-TREATED INFECTION AND THE RISK OF SCHIZOPHRENIA IN ADOLESCENCE AND EARLY ADULTHOOD

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It has been suggested that infection during perinatal life may lie at the etiological root of schizophrenia. It has thus been hypothesized that the origin of schizophrenia may lie either in direct fetal infection and/or in a generally increased familial susceptibility to infections, some of which may occur during pregnancy. We explored these two hypotheses by assessing maternal infection during pregnancy and maternal as well as paternal infection in general as predictors of schizophrenia in their offspring. We found a slightly increased risk to be associated with prenatal infection exposure. However, the effect of prenatal infection exposure was not statistically significantly different from the effect of infection exposure in general. Parental infection appeared to be associated with development of schizophrenia in adolescence and early adulthood. Our study does not exclude a specific effect of infection during fetal life; yet, it does suggest that schizophrenia is associated with an increased familial liability to develop severe infection.

P10.04 Rasmus Østergaard Nielsen

DEMOGRAPHIC CHARACTERISTICS FOR 931 PARTICIPANTS INCLUDED IN THE DANO-RUN STUDY: A 1-YEAR OBSERVATIONAL FOLLOW UP STUDY ON RUNNING RELATED INJURIES.

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Background

Previously, body mass index (BMI) and previous injuries have been identified as risk factors for Running Related Injuries (RRIs). The aim of this abstract is to present the demographic characteristics of healthy individuals included in a 1-year prospective follow up study investigating the mechanisms leading to RRIs.

Methods

Recruitment was assisted by advertisements in the local media, hospitals, and at Aarhus University. Healthy participants between 18 and 65 years of age, who had no injury of the lower extremity in the three months prior to inclusion and who have not been running on a regular basis in the previous twelve months were eligible for inclusion in the study. During summer 2011 a total of 1532 persons requested to participate by completing a online questionnaire; of these 970 persons were tested at baseline. Information on age, BMI, and previous injuries were obtained from the questionnaire. The assumption of normality for each numerical variable was checked by histograms and Q-Q plots. Descriptive analysis was made for the following variables: age, BMI, previous injuries for both genders.

Results

A total of 931 participants were included in the study. Mean age and BMI were 37.2 ± 10.3 SD and 26.0 ± 4.1, respectively. A total of 21.7% have had an injury in the lower extremity. Among women the mean age and BMI were 36.8 ± 10.0 and 25.4 ± 4.2, while age and BMI for males were 37.6 ± 10.6 and 26.6 ± 3.8, respectively.

Conclusion

It was possible to include a cohort of 931 persons to a study which investigates the link between training characteristics and RRI. This study may be the first study to adequately measure running patterns reliably in a large sample.

P10.05 Therese Juul

INTERNATIONAL VALIDATION OF THE LOW ANTERIOR RESECTION SYNDROME SCORE (LARS SCORE)

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Hospital

Background: Rectal cancer patients undergoing Low Anterior Resection (LAR) often experience impairment of their bowel function. The complex of bowel symptoms is described as “Low Anterior Resection Syndrome” (LARS). Comparison of results has been limited by the lack of a common outcome measure. The LARS score is a five-item questionnaire recently developed in order to provide a common “quick and easy” tool for scoring the severity of LARS. The score needs an international validation in order to facilitate its usage internationally.

Aim: To investigate the test-retest reliability of the LARS score and to investigate the validity of the LARS score by means of analysing the association between LARS score and the impact of LARS on quality of life.

Methods: The original Danish LARS score was translated to English, Swedish, German and Spanish according to current recommendations. Eight centres in 5 European countries participate in the validation of the LARS score and each country contributes with 250 former LAR patients. All patients receive by mail a quality of life questionnaire (EORTC QLQ C30) and the LARS score combined with a single anchor question concerning the impact of symptoms on quality of life. A subgroup of 75 patients from each country will receive the LARS score questionnaire twice to test the test-retest reliability.

Current status: The data collection is completed in Sweden and Denmark, while the Spanish and German centres are expected to complete data collection in October 2011. The English centres have not yet initiated the study, but will start within a month. The data analysis will be initiated in January 2012 and an article will be submitted in March 2012.

P10.06 Mona Lisa Idriss Kise

ASSOCIATION BETWEEN SOCIOECONOMIC POSITION AND TIME TO DIAGNOSIS OF CANCER

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Aim: It is well-documented that lower socioeconomic position (SEP) is associated with a lower relative cancer survival. The social gradient in survival is not explained by the social gradient in incidence of cancer. Therefore, other explanations must be sought. We aimed to examine the association between cancer patients’ SEP and the length of time intervals in cancer diagnosis.

Design/method: We conducted a cross-sectional study combining questionnaire data with registry data. The study included approx. 15,000 patients who received a first-time diagnosis of cancer during 2004-2005 and 2007-2008. All types of cancers, except non-melanoma skin cancer, were included. A detailed questionnaire on the diagnostic pathway was filled out by the patients' general practitioners. The patients' demographic and socioeconomic characteristics were obtained from Statistics Denmark. Associations between socioeconomic and demographic variables and the time intervals in the diagnosis of cancer were calculated as odd ratios with the length of the time interval as the outcome variable. Analyses were

adjusted for comorbidity and presenting symptoms.

Results: Analyses are ongoing. Preliminary results suggest that a social gradient in the diagnostic interval exist. The final results will be presented for all cancers combined as well as specific for the most frequent cancers.

Conclusion: An association between lower SEP and longer time intervals in cancer diagnosis might contribute to explain some of the social inequality in cancer survival. Our results will indicate where in the diagnostic pathway to intervene.

P10.07 Mette Trøllund Rask

TOWARDS A CLINICAL USEFUL DIAGNOSIS FOR MODERATE MEDICALLY UNEXPLAINED SYMPTOMS IN PRIMARY CARE

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Introduction: Medically unexplained symptoms (MUS) represent a spectrum of disorders ranging from mild symptoms to serious and persisting disorders. However, current diagnostic classifications of MUS only include single symptoms or chronic cases of somatoform disorders.

Aim: To investigate general practitioners' (GPs) application of a suggested new diagnostic category 'multiple symptoms' for moderate MUS and their views on its clinical usefulness.

Methods: A mixed methods approach was used. For two weeks 20 GPs classified symptoms presented in consecutive consultations according to the International Classification of Primary Care (ICPC) supplemented by 'multiple symptoms'. Subsequently the GPs participated in semi-structured focus group interviews. Analysis of interview data followed ethnographic principles.

Results: A minority of consultations concerned 'multiple symptoms' though a substantial variation was seen in between GPs. 'Multiple symptoms' was described as a tool for improved communication about and raised awareness of patients with MUS hindering them from a futile odyssey in the health care system. We identified three main themes influencing the clinical usefulness of 'multiple symptoms': while (1) relational continuity was seen as an essential pre-requisite, (2) lack of consensus on categorization and (3) complexity of patient cases hampered the use of this new category.

Conclusion: 'Multiple symptoms' as a category for moderate MUS may serve more clinical purposes. However, underlying values, attitudes, and structures in general practice have to be addressed in the continuing development of diagnostic classifications of MUS if these are to be clinical useful.

P10.08 Anna Budtz-Lilly

BODILY DISTRESS SYNDROME: A NEW DIAGNOSIS FOR FUNCTIONAL DISORDERS.

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Aim: Medically unexplained or functional symptoms and disorders are common in primary care. Empirical research has proposed specific criteria for a new unifying diagnosis for functional disorders and syndromes: Bodily Distress Syndrome (BDS). This new diagnosis is expected to be integrated into upcoming versions of classification systems. The objective of this study is to estimate the prevalence and describe the characteristics of patients with BDS in primary care.

Method: We recruited a cohort of 4870 patients of 18+ years from the Central Denmark Region from December 2008 until December 2009 as part of a study on reasons for encounter and disease patterns in general practice (Kontakt- og Sygdomsmønster i almen praksis – KOS). A total of 404 general practitioners (GPs) included all patients consecutively for one day. At inclusion, the GPs reported: reason for encounter, diagnoses, and their interpretation of the content of the contact.

Patients in the cohort were assessed with a number of measures in addition to the BDS scale; self evaluated health, mental health, health anxiety, smoking habits, alcohol dependency and social network.

Results: We will present data on the prevalence of BDS in a primary care population as well as the characteristics of patients with BDS.

Conclusion: Results from this study will make precise and clinically relevant contributions to the development of diagnostic classification for primary care patients who are poorly described in the present classification systems. Results from this study will help GPs diagnose patients with functional disorders and thereby provide the opportunity for improved management.

P10.09 Stine Yde Nielsen

Q FEVER SEROLOGY AND PREGNANCY OUTCOME IN WOMEN EXPOSED TO LIVESTOCK ANIMALS

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Q-fever is a bacterial zoonosis caused by Coxiella burnetii. Cows, goats, and sheep are primary reservoirs and human infection occurs by inhalation of aerosols from animal birth products.

Pregnant women may, when infected, experience adverse pregnancy outcomes.

The Danish National Birth Cohort collected blood samples and interview data from 100,418 pregnant women between 1996-2002. This study sampled 200 pregnant women with occupational exposure to domestic animals

(veterinarians and female farmers), 200 women with domestic exposure (women living on farms with dairy cattle and/or sheep) and a random sample of 500 controls. All samples were screened for antibodies against C. burnetii in a commercial enzyme-linked immunosorbent assay (ELISA). Samples positive either for IgG or IgM antibodies in the ELISA were confirmed with an immunofluorescence (IFA) test.

Reporting the IFA results, the proportion of women with serologic evidence of Q fever was significantly higher in the group with occupational exposure to livestock (19.1%, OR: 39.0; 95%CI : 11.9-128.4) as well as in the group with domestic exposure to livestock (11.0%, OR: 20.5; 95%CI: 6.1-69.2) when compared to pregnant women from the reference group (0.6% IFA positive). However, the risk of spontaneous abortion was not higher among women with occupational exposure (0.52%, OR: 0.13; 95%CI: 0.02-1.05) nor among women domestically exposed (1.5%, OR: 0.41; 95%CI: 0.12-1.34).

These findings suggest that veterinarians, farmers and other people exposed to livestock animals experience greater risk of C.Burnetii infection, but this study did not find any association between exposure and spontaneous abortion.

P10.10 Birgitte Blicher Pedersen

POSTSTROKE FATIGUE - DEVELOPING AND TESTING A PROGRAM TO REDUCE AND COPE WITH FATIGUE

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Background

Fatigue is a common complaint after stroke, reported by 39-72% of patients. It has been shown that poststroke fatigue may be related to poor neurological recovery, low level of activities of daily living and decreased quality of life. However, little is known about strategies to address poststroke fatigue and the effectiveness of such strategies. A theory and evidence based program has been developed addressing the needs of patients suffering from poststroke fatigue.

Material and Methods

The overall approach is Intervention Mapping, and the program is developed by 1) conducting a literature review for a Needs Assessment, 2) creating matrices of change objectives based on determinants of behaviour and environmental conditions, 3) selecting theory-based intervention methods and practical strategies, and 4) translating methods and strategies into an organized program.

Results

The program is based on “partnership”, involving both patient and spouse/family members as active participants. The theoretical approach is social cognitive theory, focusing on self-efficay. Furthermore motivational interviewing and the stage of change model is applied. The program consists of two main topics, a coping-oriented communicative part and a part

focusing on increasing physical activity. The main strategy is a workbook aimed at supporting patient and spouse/family members reflect on poststroke fatigue, strategies to reduce and cope with poststroke fatigue, and goal setting. Practical strategies are for example the use of a pedometer and a step diary. These strategies serve both as a motivational strategy for the patient and as objective measures for evaluating physical activity.

P10.11 Kirsten Krabek Frantzen

CARING FOR THE CAREGIVER - A MIXED METHOD STUDY OF PARENTAL TREATMENT PREFERENCES IN AUTISTIC CHILDREN

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Background

In a Danish population where treatment of children with autism is compulsory it is unclear how parents' sense of competence, locus of control and parenting style influence treatment preferences.

Children with autism suffer impairments in communication, social interaction and stereotyped repetitive behaviours and the condition has pervasive impact on their families. Parental and family aspects influence the parents' reasons for treatment choice and thereby also the outcome for the affected child. In this sparsely investigated research area it is important to study the parental and family aspects to optimize the conditions for intervention and development.

Aim

This study explores if parental indicators may be identified and if they do exist how such aspects determine which elements of treatment parents deem to be important.

Method

An extensive Mixed Methods design is applied to gain varied insight and information about parameters important for parents in evaluating different treatment choices. A convergent parallel design is chosen where the qualitative semi-structured interviews are combined with quantitative psychological test. Merging the results from both data sources and combining them with child characteristics such as a severity score provides us with an opportunity to analyze a complex and unclarified question regarding parental treatment preferences.

The study is conducted at Aarhus University Hospital and includes 12 couple of parents whose children have received different types of intervention in both normal and specialised settings.

The perspective is to gain information that can be studied further in larger populations of parents.

P10.12 Lone Flarup

USE OF DANISH PRIMARY CARE OUT-OF-HOURS SERVICES BY PATIENTS WITH CHRONIC DISEASES

L. Flarup

Forskningsenheden for Almen Praksis, Aarhus Universitet

Background

In recent years, focus has increasingly been on treatment of patients with chronic diseases. These patients are in need of increased medical efforts, thus demanding a significant amount of resources.

Although GPs are supposed to take sufficient care of patients with chronic diseases in daytime we do not know the reason for their contacts to the out-of-hours services (OOH) and why they are in acute need of medical help out of hours. Due to a lack of research in this area, we do not know if the need is caused by the chronic disease.

Aim

The aim of this study is to describe the OOH utilisation by people with chronic diseases compared with a matched group without such diseases. For a subgroup we will furthermore describe the reason for encounter, the GP's diagnosis and the severity of the disease as estimated by both the GP and the patient.

Methods

The study is based on national data and data collected in LV-KOS2010.

The study population: All persons with personal identification numbers in DK. Cases: Persons aged 18+ with chronic diseases identified via pretested algorithms. Controls: Persons aged 18+ without chronic diseases. Data from the National Health Insurance Service Registry was used for analysing the use of OOH and other health care services for the two groups.

To analyse patient characteristics, reason for encounter and patient and GP experience with the contacts we use both register data and data from LV-KOS2010 including information from patient and GP questionnaires. Study period: One year from 18 June 2010.

Data will be statistically analysed using multivariate analysing and other relevant models.

Results

Results are not ready for publication.

P11.01 Sara Thörnqvist

ROBUST OPTIMIZATION TO ACCOUNT FOR GEOMETRICAL UNCERTAINTIES CAUSED BY INDEPENDENTLY MOVING TARGETS

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Aim

To account for independent movement of multiple targets in pelvic radiotherapy, margins and image-guidance is used. Margins are usually based on population-data and may lead to unnecessary irradiation of normal tissue. Our previous study on prostate RT revealed difficulties in target coverage of the seminal vesicles (SV) still when the dose to rectum was just within our planning criteria. This was due to movement and deformation of the SV, hence seen independent of image guidance strategy. We are now aiming to calculate margins that are robust for deformations but still having high specificity and sensitivity.

Material and Methods

The study includes image data of 20 patients with 8-9 repeat CT scans, all with manual delineations of lymph nodes, prostate, SV, rectum, bladder and the bowel cavity. The repeat CTs are co-registered to the planning CT rigidly by intra-prostatic fiducials and by deformable image registration. A principal component analysis (PCA) is made on the deformation fields and the results used for simulating probable deformations. The simulations will be used as evaluation of the number of scans needed for the coverage probability maps (CPM). Calculation of the CPMs is based on the rigid co-registration of the contours from the repeat CTs. A dosimetric comparison of the CPM planning versus the conventional population based planning will then be performed.

Perspectives

An accurate description of geometric uncertainties e.g. deformations and movement is paramount for dose escalation in RT of prostate cancer. With high dose thresholds, motion during treatment will degrade high dose gradients if not accounted and this will be addressed in future studies.

P11.02 Maria Bach Laursen

THE ROLE OF MIRNA AND AID IN B-CELL MALIGNANCIES

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miRNAs are small non-coding RNA molecules that binds to specific mRNAs (their targets), and thereby inhibits protein translation. Deregulated miRNA expression is often associated with cancer, and is considered to play a profound role in both cancer initiation and progression. Deregulation of mature miRNA may take place at the level of biogenesis as a result of mutations in the miRNA transcripts. In B-cell cancers, such mutations could be caused by AID (Activation Induced cytidine Deaminase), a mutagenic factor which is involved in cutting double stranded DNA during antibody diversification in normal B-cell differentiation. Aberrantly high AID expression, in Diffuse Large B-Cell Lymphoma (DLBCL) patients, is correlated with aggressive tumor growth and poor disease prognosis.

Our hypothesis is that over-expressed AID leads to mutations in miRNA transcripts, resulting in deregulation of mature miRNA and potentially

lymphomagenesis.

We observed, using miRNA array analysis of tissue from 50 DLBCL patients, that high or low AID expression levels was correlated with distinct miRNA expression signatures. This indicates that AID might affect the miRNA expression pattern in patients. The specific impact of AID on miRNA expression will further be investigated by mutational screening of miRNA transcripts in patient samples with high AID expression. In addition, the consequence of AID over-expression in B cell lines with inherent low AID will be studied, allowing for in depth evaluation of AID effect on miRNA mutation rate and expression patterns.

A part of the scientific programme CHEPRE supported by The Danish Agency for Science, Technology and Innovation.

P11.03 Niels Frost Andersen

HEPARANASE AND MULTIPLE MYELOMA – IMPACT OF SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN THE HEPARANASE GENE ON SURVIVAL AND BONE MARROW ANGIOGENESIS

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Multiple myeloma is a plasma cell neoplasm characterized by proliferation of clonal plasma cells in the bone marrow, presence of a monoclonal protein in serum and/or urine, osteolytic bone lesions, renal insufficiency, anaemia and hypercalcaemia.

Heparanase promotes angiogenesis by releasing heparin-binding angiogenic growth factors as fibroblastic growth factor 2 (FGF-2) and vascular endothelial growth factor (VEGF) that is trapped in the extracellular matrix. Active heparanase is present in bone marrow plasma from myeloma patients as well as high heparanase activity is associated with high microvessel density an estimate of angiogenesis. Recent studies have shown that heparanase promotes expression and shedding of syndecan-1, thereby stimulating endothelial invasion and angiogenesis. Furthermore, heparanase enhances osteoclastogenesis through syndecan-1 and may influence bone resorption. Different single nucleotide polymorphisms (SNPs) in the heparanase gene have been described and some are associated with increased heparanase expression. Recent studies have examined the potential association between specific SNPs in the heparanase gene and malignancies and a possible correlation with acute leukaemia, multiple myeloma and ovarian cancer has been demonstrated.

In this study we examine different SNPs in the heparanase gene in 350 multiple myeloma patients and describe the relation with estimated bone marrow angiogenesis, efficacy of angiogenesis inhibitor treatment, osteolytic bone disease and survival. The results will be presented at the PhD-day.

P11.04 Jens Reumert Laurberg

PROGNOSTIC AND PREDICTIVE SIGNIFICANCE OF CELL CYCLE, APOPTOSIS AND DNA DAMAGE RESPONSE REGULATORS IN LOCALLY ADVANCED LYMPH NODE NEGATIVE BLADDER CANCER

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ABSTRACT:

Background: Treatment options for invasive bladder cancer include cystectomy and radiotherapy, but guidelines differ between countries. Biomarkers may aid in personalized, and hence optimal, treatment decisions for each patient. Yet, no such biomarkers are currently applied in the clinical setting. Some of the main problems are lack of validation of significant results, and a scarcity of studies evaluating biomarkers in suitable cystectomy and radiotherapy cohorts. Here, we report the association between the markers Tip60, p16, MRE11, pATM, pRB, ki67, and p53 and clinical outcome.

Methods: Protein expression was studied by immunohistochemistry in pre-treatment tumor specimens from two independent cohorts of bladder cancer patients treated with cystectomy (n = 162 and 276) and one cohort of patients receiving radiotherapy (n = 148).

Results: P16 was significantly correlated with survival in all three cohorts. Tip60 was significantly correlated with survival in the cystectomized cohorts but not in the cohort receiving radiotherapy. In contrast, MRE11 was significantly correlated with survival in the cohort receiving radiotherapy but not in the cystectomized cohort.

Conclusion: In this immunohistochemistry study, Tip60 protein expression was demonstrated as a predictive factor associated with survival following cystectomy. MRE11 was demonstrated to be a predictor of radiotherapy response for bladder cancer patients. Our study demonstrated the novel marker Tip60 to be the strongest prognostic factor in multivariate analysis in cystectomized patients, justifying its potential inclusion in further validation studies and subsequent trial designs.

P11.05 Christina Daugaard Lyngholm

BREAST CONSERVING THERAPY:

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Background: DBCG introduced BCT as a standard treatment in Denmark in 1990. No evaluations have been performed since to ensure good cosmetic outcome and low levels of adverse reactions. The aim of our study was to evaluate these issues. Material and Methods: 214 patients treated with BCT participated in a single follow-up visit. Patients were divided into 3 treatment-groups: no adjuvant treatment, chemotherapy and anti-hormone therapy. Results: With a mean follow-up time of 12.3 years, Moderate/Severe fibrosis was found in 49 patients. Fibrosis was more common if patients were receiving CEF-chemotherapy (OR 2.8 p = 0.028),

were current smokers (OR 2.4, p=0.02) or had large breasts (bra cup size ≥C; OR 3.2, p=0.001). Assessed by a clinician 50% of patients scored Good/Excellent on cosmetic outcome compared to 88 % when reported by the patients themselves. Patients more likely to be satisfied were young (< 50 years; OR 3.2 p=0.03), had no postoperative complications (OR 3.7, p=0.01) and no fibrosis (OR 6.4, p<0.0005). Patients with a satisfactory cosmetic outcome when assessed by a clinician had small tumors (≤2 cm; OR 3.2, p=0.003), bra cup size < C (OR 1.9 p=0.02) and no adverse reactions to radiotherapy (excluding fibrosis; OR 4.4, p=0.02). Conclusions: our study showed satisfying levels of cosmetic outcome with an uncomplicated course of disease being decisive of the patients evaluation while cosmetic outcome from the clinician's point of view seemed to be associated more with variables representing less surgical procedures or less irradiation. The level of Moderate/Severe fibrosis was acceptable and most importantly associated with patients receiving CEF.

P11.06 Mette Marcussen

CANCER THERAPY INDUCED MUCOSITIS: CELLULAR AND HUMORAL FACTORS INFLUENCE PRESENCE AND HEALING IN CONSECUTIVE MUCOSA BIOPSIES AND BLOOD SAMPLES BY MICROARRAY AND FLOWCYMETRY.

M. Marcussen

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Clinical research project, running 3 years from September 2010.

OMFS specialist Mette Marcussen, PhD student enrolled into the Haematology programme, Graduate School of Health Sciences Aarhus University, Aalborg Hospital (Supervisor Proff HE Johnsen).

Object: Mucositis, a complication to chemo- or radiotherapy, is characterized by inflammation/ ulceration through oro-pharynx and gastrointestinal canal. As a consequence diarrhoea, dysphagia, secondary infection, febrile episodes and septicaemia are side effects with impact on treatment doses and therapeutic outcome. In highly select groups of patients undergoing HDT/ASCT, 75 % will suffer from mucositis. There is no effective evidence-based preventive strategies and only palliation is implemented.

Hypothesis: Circulating humoral and cellular factors may be important for pathogenesis and healing of mucositis – which can be evaluated by paired analysis of human mucosa biopsies and peripheral blood by global gene and protein expression analysis and multiparametric flow cytometry.

Materials and methods: Consecutive biopsies and blood samples from 10 HDT/ASCT, 10 AML in chemotherapy, 10 tonsil cancer patients and 10 healthy controls will be sampled and stored in the Biobank. Analysis will be performed by standard multiparametric flow cytometry and microarray technologies and data modulated to identify tissue and blood changes correlated to clinical data registration of oral mucositis by the WHO method.

Perspectives: It is expected that this study will identify new pathogenetic biomarkers with potential for drug design and preventive intervention.

P11.07 Andreas Carus

PREOPERATIVE LEUCOCYTOSIS IS AN INDEPENDENT RISK FACTOR ONLY IN EARLY STAGE NON-SMALL CELL LUNG CANCER (NSCLC)

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Background

Non-small cell lung cancer is the most common cause of cancer-related death worldwide. Preoperative leucocytosis has previously been associated with impaired survival in smaller cohorts of resectable NSCLC. We reviewed baseline prognostic factors in patients with surgically resectable NSCLC with focus on inflammatory markers.

Patient and Methods

The clinical database of NSCLC patients at the Dept. of Thoracic Surgery at Skejby from 2000 through mid 2008 was reviewed retrospectively and 906 patients with complete data were identified. 234, 292, 197 and 183 had cancer stage IA, IB, II and III, respectively.

Results

Elevated White blood cell count (WBC) and CRP were more frequent in higher tumour stages and in non-adenocarcinoma histologies.

Multivariate analysis of all patients showed pathologic tumour stage to be the strongest prognostic factor for overall survival (OS). Moreover, elevated WBC, hyponatremia, anaemia, male sex, higher Charlson index, microscopic irradicality and adjuvant treatment were also negative prognostic factors.

Multivariate analysis stratified for tumour stage revealed elevated WBC as a significant prognostic factor for recurrence-free survival (RFS) (hazard ratio[HR] 2.0; 95% CI 1.5 to 2.7; P<0.0001), cancer specific survival(CSS) (hazard ratio[HR] 2.0; 95% CI 1.4 to 2.8; P<0.0001) and OS (hazard ratio[HR] 1.5; 95% CI 1.1 to 1.9; P<0.004) in stage I cancer, but not in stage II and III.

Conclusion

Elevated white blood cell count has negative prognostic value for recurrence free survival, cancer specific survival, and overall survival in stage I NSCLC, but not in stage II and III.

Further research in inflammatory markers in NSCLC is warranted.

P11.08 Jesper Thygesen

QUANTITATIVE CT-IMAGING BASED ON CONTRAST MATERIAL ENHANCEMENT

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Background

In X-ray CT we have seen a tremendous development of both technical performance, the number of scanners installed and in the number of examinations carried out.

The improved volume coverage, spatial (submilimeter) and temporal resolution is raising the interest in expanding the morphological CT gathered information to include functional information of the tissue of interest.

With Functional CT imaging we measure the transport by blood flow of an intravenously administered iodinated contrast agent to the tumor and exchange by diffusion of these contrast molecules between the intravascular space and the extravascular interstitial space. With the current fast CT scanners, both tissue and vascular contrast concentrations can be measured and traced over short intervals to allow detailed modelling of the distribution of contrast agent in tissue. The functional parameters can be quantified and tracked in time as a marker of response to therapy.

Hypothesis

1. It is possible to develop a iodine calibration scheme that tracks the intra- and intervariability of the scanners iodine signal response.

2. We can test important acquisition and CM policy parameters in an animal model, in order to test the reproducibility of the functional parameter results. These optimized parameters can be transferred to clinical problem settings.

3. We can improve our measurement reproducibility in a clinical setting so the variations in our functional parameters can be related to changes in pathology.

P11.09 Kim Steve Bergkvist

STUDIES OF SMALL DISCRETE POPULATIONS OF B CELLS BY MICROARRAY TECHNOLOGY

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Multiple myeloma (MM) is an incurable B-cell malignancy characterised by the accumulation of malignant plasma cells in the bone marrow. It is at present unclear whether the malignant transformation occurs solely in the end stage differentiated plasma cell or in some instances can be traced back to an earlier B-cell maturation stage like the memory B-cell or plasmablasts. The hypothesis is that dysregulated and aberrantly spliced genes in B-cell subpopulations can provide clues to the cellular origin of the disease and that subpopulation specific gene expression in patients is correlated to disease outcome.

The aim of the project is to establish a protocol for handling small number of cells and performing global gene expression on B-cell subpopulations from blood and bone marrow of MM patients and healthy donors.

Results: By combining an optimized panel of CD markers for flow sorting and mRNA purification with magnetic beads, successfully amplification has

been performed on 5000 memory B-cells and 2800 plasmablasts from healthy individuals for the Affymetrix Exon array 1.0. An important observation is that the mRNA content from different B subpopulations varies from a fixed number of cells. Preliminary data shows that the oncogene WHSC1 is expressed at the same levels, but with with marked differences in splice pattern between naive, memory and plasmablasts in the blood from healthy donors and a MM patient. The goal is to identify population-specific splice variants in patient samples which could provide novel clues to the understanding of the cellular origin of MM.

P11.10 Eduardo Vázquez Garza

CHARACTERIZATION OF NK-, NKT- AND T-CELLS IN HCMV REACTIVATION OF IMMUNOCOMPROMISED PATIENTS, FOCUSING ON CD94/NKG2A,C,D AND CD56-NEGATIVE NK CELLS

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Background

Approximately 60-85% of the population worldwide is seropositive for human cytomegalovirus (HCMV). HCMV infection in immunocompromised patients cause increased morbidity and mortality. Natural killer cells (NK) are crucial in controlling these infections. Groups with increased risk of HCMV disease include patients after hematopoietic stem cell transplant (HSCT), and untreated/treated patients with chronic lymphocytic leukemia (CLL).

Hypothesis

HCMV positive leukemic and HSCT treated patients show changes in the NK-, NKT- and T-cell peripheral blood subpopulations.

Purpose

To characterize NK-, NKT- and T-cell populations in patients with malignant hematological diseases in the course of cytoreductive treatment, and comparing it to normal gender-and age-matched controls. Analyze the expression of CD56-negative NK cells in this group since they are related to chronic viral diseases.

Materials and Methods

Use of an in-vitro system co-culturing HCMV (strain AD169) with mononuclear cells from 45 mL peripheral blood samples from patients and donors, infection will be assessed by viral antigenemia at Aarhus University Hospital. To characterize the effect of HCMV induced proliferation of NK, NKT- and T-cells and expression of NKG2A, NKG2D and NKG2C by multi-color flow cytometry, proliferation by Cell Trace Violet staining, viability with PI as well as production of key cytokines.

Perspective

To improve the characterization and understanding of the immune system response focusing on NK-, NKT- and T-cell surface marker changes against HCMV, being of importance for future infectious diseases diagnosis and

treatment.

Status

Starting sample collection October 2011.

P11.11 Maria Cathrine Corneliussen Vestergaard Schmidt

HYPODONTIA AND OVARIAN CANCER - THE CONNECTION BETWEEN DENTAL AGENESIA AND EPITHELIAL CANCERS, ESPECIALLY OVARIAN CANCER.

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AIM: To examine possible genetic factors that cause a predisposition to developing epithelial cancers thereby being able to identify high-risk families and offer them diagnostic examinations as a means of screening and thus diminish their risk of developing cancer.

INTRODUCTION: Ovarian Cancer is known as the silent killer. A tumor can reach a substantial size before causing any symptoms, which is one of the reasons why ovarian cancer is often diagnosed too late with considerable negative effect on the prognosis. A small American study showed a surprising connection between hypodontia and ovarian cancer. A similar connection has been shown to colon cancer. Our hypothesis is that this is caused by genetic mutations.

MATERIALS AND METHODS: To confirm the connection between hypodontia and ovarian cancer, all women referred to the Departments of Obstetrics and Gynecology in Aarhus and Copenhagen, who are given the diagnosis of ovarian cancer, will be asked to fill in a validated questionnaire regarding their dental status, as will a matched control group. We will distribute the same questionnaire to already known families with genetic predisposition to cancer (HBOC and HNPCC) to see if this confirms a connection. A sample of blood and tissue from high-risk families (suffering from ovarian cancer and hypodontia) will be reserved for later genetic analysis. This will be screened for relevant target genes based on the current literature.

P11.12 Martin Bjerregård Pedersen

PERIPHERAL T-CELL LYMPHOMAS – A STUDY TO IDENTIFY CLINICAL, PATHOLOGICAL AND BIOLOGICAL PARAMETERS TO IMPROVE CLASSIFICATION, PROGNOSTIC ASSESSMENT AND TREATMENT STRATEGY

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Peripheral T-cell lymphomas (PTCLs) are a rare heterogeneous group of clinically aggressive lymphomas accounting for 10% of all non-Hodgkin's

lymphomas. The diseases are often disseminated at the time of diagnosis and associated with poor outcome. The aim of the project is to contribute to the understanding of disease biology and pathogenesis, which is lacking but internationally demanded, with a perspective of developing more effective outcome predictors and eventually management strategies in the field of PTCL.

A total of 244 patients diagnosed with PTCL at Aarhus University Hospital within the period 1983 through 2010 were identified from the Danish Lymphoma Registry LYFO and clinical, para-clinical and laboratory data were integrated into a project specific database. Additional data was collected from clinical medical records and entered into the study database. Archival paraffin-embedded pre-therapeutic tissue biopsies were identified and collected from the archives of the department of pathology participating in the study. Tissue slides from each PTCL case will be reviewed by an experienced hemato-pathologist and updated according to the criteria of the 2008 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Within each tissue block representative tumor areas will be identified and cores will be extracted and transferred into a tissue-micro array platform for further immunohistochemical study. Cases (n=17), where frozen tissue material is available, will be investigated by means of a mass spectrometry-based proteomic assay aiming at identifying differentially expressed proteins related either to specific histological subtypes or to outcome.

P12.01 Johanne Lade Keller

CELL ADHESION MOLECULES IN 404 CUTANEOUS MELANOMAS: A TISSUE MICROARRAY STUDY

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Several cell adhesion molecules have been proposed as prognostic and diagnostic markers of cutaneous melanoma. An accepted hypothesis explains how loss of E-cadherin and up-regulation of N-cadherin and/or Melanoma Cell Adhesion Molecule (MCAM) promote melanoma cells to detach from epidermis, invade dermis and intravasate blood- and lymph systems. Our objective was to examine the expression of E-cadherin, N-cadherin, and MCAM, and their individual and combined effects on survival in a large melanoma cohort.

The immunohistochemical expression of E-cadherin, N-cadherin, and MCAM in 404 melanomas was examined using tissue microarrays, and the frequency of positively stained cells was estimated semiquantitatively.

Low E-cadherin expression significantly predicted distant-metastases-free survival in combination with a high N-cadherin expression (HR, 2.0, 95% CI, 1.0-4.0, p=0.043), overall survival in combination with a high MCAM expression (HR, 1.6, 95% CI, 1.0-2.7, p=0.045) and melanoma-specific survival in combination with high expression of both N-cadherin and MCAM (HR, 2.4, 95% CI, 1.1-5.3, p=0.029), all when adjusted for primary tumor thickness and ulceration.

Low E-cadherin and high N-cadherin expression was significantly associated with increasing primary tumor thickness both individually (p=0.0013 and p=0.0005 respectively) and combined (p=0.004).

In conclusion, melanoma cell adhesion molecule profiles are significant and independent predictors of recurrence and death and show significant association with primary tumor thickness.

P12.02 Peter Bondeven Frederiksen

LENGTH OF DISTAL RESECTION MARGIN AFTER PARTIAL MESORECTAL EXCISION FOR UPPER RECTAL CANCER ESTIMATED BY MAGNETIC RESONANCE IMAGING

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BACKGROUND: Rectal cancer requires surgery for cure. Partial mesorectal excision (PME) is suggested for tumours in the upper rectum and implies transection of the mesorectum perpendicular to the bowel a minimum of 5 cm below the tumour. The rationale is that PME is associated with fewer post-operative complications, the functional outcome after surgery is better and it is as oncologically safe as total mesorectal excision (TME). Reports have shown distal mesorectal tumour spread of up to 5 cm from the primary tumour; therefore, guidelines for cancer of the upper rectum recommend PME with a distal resection margin (DRM) of at least 5 cm or TME. Studies at our department have shown inadequate DRM in 75% of patients estimated by post-operative MRI of the pelvis and on the histopathological specimen. Consequently, PME exerts a hazard of removing less than 5 cm - leaving microscopic tumour cells that have spread in the mesorectum.

AIM: To estimate the length of the DRM by MRI of the surgical specimen from patients operated for rectal cancer with PME.

METHODS: Rectal PME-specimens will undergo MRI immediately after surgery (fresh specimen) and once more after pathological fixation (fixed specimen). Normal procedures for handling, pathological examination and reporting are completed according to international guidelines. Length of DRM measured on MR-imaging and by pathological examination will be compared.

PERSPECTIVE: PME for cancer of the upper rectum may be associated with suboptimal surgery. Knowledge of the exact morphometrics in the mesorectal- and tumour surrounding tissues after surgery and fixation will help to improve the surgical quality of PME for rectal cancer.

P12.03 Marie-Louise Feddern

CHRONIC PAIN AFTER RECTAL CANCER TREATMENT

M. Feddern

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Background: The survival rate of rectal cancer has been increasing over the past decades. With improved prognosis functional outcome is of growing

importance. Chronic pain as an outcome is seldom mentioned in rectal cancer studies. Nevertheless a recent study of rectal cancer patients, whom have undergone extended abdominoperineal resection, found that only 47% of their patients were pain free and 21% had difficulty sitting for 10 minutes, at a mean of 26 months postoperatively.

Aim: To study the incidence and extent of chronic pain after rectal cancer treatment.

Methods: We have developed a pain questionnaire and approximately 2,200 patients have been invited to participate. The patients have undergone curatively intended surgery for their rectal cancer in the period of May 2001 to September 2010. In our study cohort approximately two-thirds of the patients have undergone low anterior resection and one-third has undergone abdominoperineal resection. As a control-group, we will invite a group of right-sided colon cancer patients to participate in the study of chronic pain. They will provide us with an exceptionally fine control-group, since they have equality to our study cohort, in terms of a cancer illness and abdominal surgery. They will be matched according to age, sex, adjuvant therapy and time of surgery.

Results: Results are not yet available. At present approximately 80% of the invited patients have chosen to participate in our chronic pain study.

P12.04 Louise Tram Henriksen

PEG-ASPARAGINASE TREATMENT IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA, ALL, IN THE NORDIC COUNTRIES

L.T. Henriksen

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Asparaginase is an important drug in the treatment of childhood ALL. The enzyme induces asparagine depletion leading to impaired protein synthesis and apoptosis in lymphoblasts. The Nordic Society of Paediatric Haematology and Oncology (NOPHO) coordinate the treatment of childhood ALL in the Nordic countries and have included a randomized study with PEG-asparaginase in the current NOPHO ALL-2008 protocol. Non-HR-patients are randomized to receive PEG-asparaginase either every 2nd or every 6th week for 6 months.

This PhD study is an add-on study to the randomized PEG-asparaginase study. Focus is on asparaginase associated side effects, mainly allergy and development of antibodies.

Primary hypothesis:

The presence of allergic reactions is related to the development of IgE antibodies

Aims:

To investigate:

Frequency of IgE asparaginase antibodies in relation to allergic reactions, enzyme activity and asparagine depletion.

Frequency of neutralizing IgG antibodies.

Presence of IgG and IgE in the same patients.

Frequency of side effects.

Asparagine depletion in cerebrospinal fluid related to serum asparaginase activity and serum asparagine depletion

Patients:

200 patients aged 1-18 years

Methods:

Antibodies: IgG; ELISA. IgE, and IgG-subclasses; Biacore T100, SPR

Asparaginase enzyme activity: Spectrophotometric method

Asparagine depletion in blood and spinal fluid: HPLC

Allergic reactions: Registered in the NOPHO database

Perspective:

This study provides new knowledge about PEG-asparaginase treatment regarding pharmacokinetics, pharmacodynamics, asparaginase associated allergy and antibodies. Thus it may enable NOPHO to improve future asparaginase therapy with respect to dose, toxicity and effect.

P12.05 Bente Thoft Jensen

PRE-OPERATIVE NUTRITIONAL RISK IMPACTS SIGNIFICANTLY ON ONE YEAR SURVIVAL FOLLOWING RADICAL CYSTECTOMY

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Background

Malnutrition has been recognized as an important prognostic factor in cancer patients. Patients referred to Radical Cystectomy (RC) because of invasive bladder cancer (IBC) are more likely to harbour substantial comorbidity because of advanced age at diagnosis. However, evidence is sparse concerning pre-operative nutritional risk (NRS) and risk of comorbidity before radical cystectomy (RC), specifically concerning survival.

Aim

To define the impact of pre-operative NRS and Charlson's Comorbidity Index Score concerning one year survival following RC.

Material & Methods

The design was a historical combined registry study. Comorbidity and survival were indentified by linking the unique Danish Civil Registration Number with the National Patient Registry. NRS was calculated using the NRS-2002 and Charlson's Comorbidity Index Score to calculate comorbid

factors.

Statistics

Regression analysis was performed with one year survival as the dependent variable, fitting the cox proportional hazard ratio for NRS and comobidity. Log-rank test was performed to test for equality of survivor functions between variables. Statistical significance was defined as $p \leq 0.05$

Results

Log-rank test showed a significant difference in survivor function in those at severe nutritional risk compared to low risk HR=4.8 (95% CI: 1.1, 20), $p<0.02$. Women showed significantly reduced survival compared to men, HR=5.7 (95% CI:1.3, 24), $p<0.01$. No significant difference was found concerning comorbidity.

Conclusion

Identification of modifiable risk factors like nutritional risk and comorbidity before RC is of clinical importance. Early detection of nutritional risk might contribute to increased survival.

P12.06 Patricia Nielsen

MELANOMA KI67 EXPRESSION BY AUTOMATED IMAGE ANALYSIS: A SIGNIFICANT PROGNOSTIC MARKER

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Even though the Ki67 proliferation rate has been widely studied and correlation with clinical outcome has been demonstrated in melanoma, improvements may be gained by combining Ki67 with the melanocytic marker MART1. Hence, Ki67-positive melanocytic cells can be accurately distinguished from proliferating lymphocytes, stromal, and epithelial cells. Yet, manual Ki67 quantification is time-consuming and cumbersome. Instead, automated image analysis (AIA) enables rapid and novel quantification methods for entire tumor sections.

Our objective was to investigate the prognostic value of Ki67 expression in Ki67/MART1 double stained melanomas and to compare corresponding manual and automated rates.

Whole slide images were captured from 153 Ki67/MART1 double stained melanomas. Proliferation rates were established by manual counting in a counting frame and AIA with different output equations based on number or area.

Automated rates were significantly higher than the corresponding manual rates ($P<.001$); however, their abilities to predict clinical outcome were comparable. In all rates, high Ki67 was strongly associated with reduced progression-free and melanoma-specific survival. Yet, prediction was only independent of tumor thickness using the automated rate based on the proportion between the area of Ki67-positive and Ki67-negative melanocytic nuclei. The adjusted hazard ratio of this rate was 2.32 (95% CI, 1.05 to 5.09; $P=.036$) for recurrent disease and 2.33 (95% CI, 1.02 to 5.36; $P=.046$) for

melanoma-specific death.

In conclusion, the automated Ki67 rate based on nuclear area is a significant prognostic marker; however, subsequent studies are needed to validate these findings.

P12.07 Thomas Lyhne Ravkilde

GEOMETRIC ACCURACY OF DMLC TRACKING WITH AN IMPLANTABLE WIRED ELECTROMAGNETIC TRANSPONDER

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Purpose: About half of all cancer patients are treated with radiotherapy (RT). Tumor motion during RT treatment delivery can substantially deteriorate the target dose distribution. A promising method to overcome this problem is dynamic multi-leaf collimator (DMLC) tracking. The purpose of this phantom study was to integrate a wired electromagnetic transponder localization system with DMLC tracking and to investigate the geometric accuracy of the integrated system.

Materials and methods: DMLC tracking experiments were performed on a Trilogy accelerator (Varian Medical Systems, CA, USA) with a prototype DMLC tracking system. A wired implantable electromagnetic transponder (RayPilot, Micropos Medical AB, Sweden) was mounted on a motion stage and used to generate a 3D transponder position signal for DMLC aperture adaption. The tracking system latency was determined and the geometric accuracy of the tracking system was measured by programming the phantom to reproduce eight representative patient-measured trajectories (prostate and lung tumors). For each trajectory, three treatments of 72 seconds duration were delivered: (1) a 358° arc field, (2) a vertical static field, and (3) a horizontal static field.

Results: The tracking system latency was 140 ms. The mean rms of the 2D beam-target error was 0.7mm (prostate) and 1.0mm (lung tumors) with tracking and 3.4mm (prostate) and 4.9mm (lung tumors) without tracking.

Conclusions: DMLC tracking was integrated with a novel electromagnetic transponder localization system and investigated for arc and static field delivery. The system provides sub-1mm geometrical errors for most trajectories.

P12.08 Trine Tramm

PROGNOSTIC FACTORS AND RESPONSE TO RADIOTHERAPY IN HIGH RISK BREAST CANCER: A STUDY OF GENE EXPRESSION IN THE DBCG82BC COHORT

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Background: Recommendations for postmastectomy radiotherapy (PMRT) is well established in patients estimated to have a high risk of local regional recurrence (LRR) (e.g. tumor size > 5 cm, or ≤ 4 positive lymph nodes).

Large randomized trials have also shown a substantial overall survival benefit in patients with low risk of LRR (e.g. 1-3 positive nodes), and shown that the largest translation of LRR into reduction of breast cancer mortality occurs within the most favorable prognosis group. The positive effect of PMRT is heterogeneous, and establishing a more refined partitioning of patients likely to benefit from RT would be desirable. Hypothesis: Genes interacting with PMRT to reduce the hazard of LRR can 1) be identified and 2) can predict benefit of PMRT. Material: 200 fresh frozen tumor (FFT) samples and corresponding formalin fixed, paraffin embedded tissue (FFPE) from the DBCG82bc cohort of high-risk patients, randomized to +/- RT, constitutes the material in the hypothesis generating part. FFPE from additional 800 DBCG82bc pts. will constitute the validation part. Microarray analysis and quantitative RT-PCR will be used. Results: 7 genes, whose expression level interacts with the effect of PMRT in influencing risk of LRR has been identified, and their combined expression levels reduces the risk of LRR. Two of these genes in the group of women with 1-3 pos. lymph nodes, and 1 gene in the 4+ nodal group, were also associated with distant metastasis(DM). Conclusion: The identified genes can predict which patients will have the largest benefit from PMRT, but contributes little in preventing DM in women, who already have disseminated disease at the time of debut.

P12.09 Sidse Bregendahl

BOWEL DYSFUNCTION AFTER PREOPERATIVE RADIOTHERAPY AND LOW ANTERIOR RESECTION FOR RECTAL CANCER

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Background:Bowel dysfunction (low anterior resection syndrome, LARS) following preoperative radiotherapy (PRT) and low anterior resection (LAR) for rectal cancer is well-described in terms of fecal incontinence and increased bowel frequency. This study was designed to describe symptom frequency and severity following LAR with or without PRT taking all aspects of LARS into consideration.

Methods: We identified all patients who underwent curative LAR for non-disseminated rectal cancer in Denmark between 2001 and 2007. A detailed questionnaire on bowel function (The Low Anterior Resection Score) was administered to live, recurrence-free patients. We retrieved disease- and treatment-related information from the national colorectal cancer registry.

Results: Median time since surgery was 54 months. Among 986 respondents (90%) major low anterior resection syndrome (LARS-score ≥ 30) was observed in 121 (65%) irradiated patients compared to 264 (35%) patients who underwent surgery alone ($p < 0.001$). A higher proportion of irradiated patients compared to non-irradiated patients suffered daily from more than 7 bowel movements (16% vs. 5%), incontinence for flatus (48% vs. 32%) and liquid stools (10% vs. 2%), clustering (29% vs. 14%) and urgency (21% vs. 9%) (all $p < 0.001$). Irradiated patients as opposed to non-irradiated patients reported of a higher impact of bowel dysfunction on their quality of life (55% vs. 34%, $p < 0.001$).

Conclusion: Severe bowel dysfunction is a frequent and distressing long-term condition present in 2/3 of irradiated patients and 1/3 of non-

irradiated patients after low anterior resection for rectal cancer.

P12.10 Martin Skovmos Nielsen

NITI STENT AS A MARKER FOR LUNG TUMOR IN RADIOTHERAPY: PRECISION IN MARKER DETECTION DURING TREATMENT PREPARATION AND DELIVERY

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Respiratory correlated CT (4D-CT) can be used to define organ motion for the period of respiration and to select a desirable respiration phase for treatment. Several studies have shown that tumor position still has to be monitored throughout treatment delivery due to changes in tumor movement path and baseline shifts.

Baseline shift, shift in tumor position relative to fixed patient points (bony structure) and different internal motion pattern can lead to lack of precision. Image guided RadioTherapy (IGRT) must be considered but low contrast in CT/kV images might limit precision at treatment site.

Animal studies have shown that a fiducial marker (NiTi stent) can be inserted into lung tissue by using a bronchoscope. This makes the marker suitable for IGRT and potential reduction in treatment volume which might limit toxicity following radiotherapy.

This study will describe the uncertainty in marker definition on treatment planning 4D-CT and detection at treatment site using stereoscopic X-ray images.

Marker definition achieved by precision in centre of mass detection on 4D-CT scan for different markers of length 5mm, 10mm and 15mm and marker rotation relative to gold markers and motion path.

Precision at treatment site is verified by fast stereoscopic images (100 mS) for marker detection using BrainLAB ExacTrac gating for IGRT at predefined CT phases (inhale, exhale and mid-ventilation) for treatment.

P12.11 Tinne Laurberg

LOCO-REGIONAL RECURRENCE OF BREAST CANCER - A GENETIC STUDY OF AGE-RELATED PROGNOSTIC BIOMARKERS

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One thousand women below the age of fifty are being diagnosed with breast cancer in Denmark every year. Compared to older women, the young ones have a higher incidence of recurrences and an elevated mortality.

Today all patients below the age of 50 are recommended medical treatment in addition to local treatment because we lack the knowledge to sub classify the young patients in proportion to their prognosis.

The aim of my study is to find prognostic biological markers which correlate with loco-regional recurrence and low mortality.

Gene expression analysis is in the center of this search for prognostic biomarkers. T Sørlie et al in 2001 provided evidence for a connection

between five distinct molecular portraits and clinical outcomes. The tumors were allocated among others by the level of gene expression of Estrogen, Progesterone and HER2. In this project we want to test if they also are prognostic among the group of young patients. Furthermore, we are studying eight specific genes, which are represented in both a Dutch and a Danish gene signature (Mammaprint and HUMAC32). Finally we want to test a new gene signature level at radiation sensitivity.

The study will be based on paraffin embedded breast carcinoma specimen from 850 patients receiving local treatment in the period from 1989-1998. Clinical information and follow-up data is available from the Danish Breast Cancer Cooperative Group. From a 7 µm thick full size tumor section, RNA extraction will be made from every specimen, and a number of genes will be tested by using quantitative real-time PCR.

The results of this project will be linked to the clinical data, and hopefully we find prognostic biomarkers.

P12.12 Mohamed Ahmed Hassan

PRELIMINARY RESULTS, QUALITY ASSURANCE & MOLECULAR BIOLOGICAL STUDIES OF PATIENTS WITH HEAD AND NECK CARCINOMA UNDERGOING ACCELERATED RADIOTHERAPY WITH OR WITHOUT NIMORAZOLE IN A RANDOMIZED MULTICENTER TRIAL

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Objective:

The objective of the study is to suggest a new rational of improving the radiotherapy effect in HNSCC on a worldwide scale & identify a category of patients most likely to benefit from hypoxia modification.

Background:

Significant improvement in loco-regional control & disease specific survival by radiotherapy for patients with head & neck cancer could be achieved by reducing the overall treatment time and modification of hypoxia by Nimorazole. So, it is expected that the optimal treatment option is reducing the overall treatment time with concomitant use of Nimorazole. Quality assurance should be an integrated part of any study particularly if it is international study involved multicenters in different countries. A recent study could identify a robust hypoxia profile consisting of 15 genes. These genes may be able to distinguish hypoxic tumors from non hypoxic tumors in vivo.

Material and methods:

- A stratified, randomized phase III study of patients with HNSCC randomizes to accelerated radiotherapy ± Nimorazole. The QA procedures are applied to ensure consistency and validity of the data. Biological materials are collected from the participating centers for RNA extraction from samples & quantitative PCR analysis will be done as well as immunohistochemistry for p16 expression.

Results:

-The trial is in the initial stages now. The last modified treatment protocol, the radiotherapy quality assurance (RTQA) protocol and the clinical research forms (CRFs) have been developed and uploaded on the website developed specifically for the trial. The dummy run procedure is ongoing now in collaboration with the participating centers.

P13.01 Esben Schjødt Worm

ON-LINE USE OF 3D MARKER TRAJECTORY ESTIMATION FROM CONE-BEAM CT (CBCT) PROJECTIONS FOR PRECISE SETUP IN RADIOTHERAPY FOR TARGETS WITH RESPIRATORY MOTION

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Purpose:

To develop accurate on-line patient setup based on a novel technique where 3D marker trajectories were estimated from 2D CBCT projections.

Methods and Materials:

Seven patients received stereotactic body radiation therapy (SBRT) for liver tumors in 21 fractions in total. Each patient had 2-3 gold markers implanted close to the tumor(s). Before treatment, a CBCT scan with approximately 675 2D projections was acquired during a full gantry rotation. An in-house made software program segmented the marker positions in each projection and 3D marker trajectories were estimated using a probability based method. The required couch shifts for patient setup were calculated from the mean marker positions along the trajectories. A motion phantom moving with known tumor trajectories was used to examine accuracy of the method. Trajectory-based setup was used off-line for the first 15 treatment fractions and on-line for the last 6 fractions. Automatic marker segmentation was compared with manual segmentation. The trajectory-based setup was compared with setup based on conventional volumetric CBCT-guidance.

Results:

Phantom measurements showed that trajectory-based setup was accurate within 0.5mm. Automatic marker segmentation agreed with manual segmentation within 0.36 ± 0.50 pixels (mean ± SD, pixel size = 0.26mm). The accuracy of conventional volumetric CBCT guidance was compromised by motion smearing (max 20mm) that induced a 3D setup error of 1.6 ± 0.9mm (max = 3.2mm).

Conclusions:

The first on-line clinical use of trajectory estimation from CBCT projections for precise setup in SBRT was demonstrated. The new method eliminated uncertainties in the conventional setup procedure.

P13.02 Julie Damgaard Sandahl

HYPERDIPLOIDY IN CHILDHOOD AML ASSOCIATED WITH YOUNG AGE AND AML-M7- A NOPHO-AML STUDY AND LITERATURE REVIEW

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Introduction: High hyperdiploidy (HeH)(50+) in childhood acute myeloid leukemia (AML) is a rare cytogenetic finding. It is often categorized as a complex karyotype, associated with an unfavorable outcome. Knowledge on this field is based on small adult series or case reports. In this study we describe the clinical and cytogenetic features in childhood HeH AML.

Material and method: We identified 29 HeH-AML children, age 0-18 years, in the Nordic NOPHO-AML database. They were compared to non-HeH NOPHO AML children. In addition, we searched for HeH childhood AML cases in literature. The 105 cases from this literature study were compared to the HeH NOPHO-AML cases. The total cohort of 134 hyperdiploid cases were used to characterize HeH AML in children.

Results: Clinical: The 29 HeH NOPHO-AML children constituted 5% of all Nordic childhood AML cases. Compared to non-HeH NOPHO-AML children, the HeH children were younger, median age 3 years, had a lower WBC, median WBC 9.5, and an excess of Fab M7 (28%) ($p<0.01$). Survival was similar; 5-year EFS in both groups 50%, OS 59% vs. 67%. The literature study showed similar age, WBC and FAB M7 pattern as the NOPHO patients.

Cytogenetics: The most frequently gained chromosomes were 8(78%), 19(67%), 6(63%), and 21(58%). Gain of chromosome 8 indicated favorable outcome ($p= 0.09$), whereas gain of chromosome 21 was unfavorable ($p <0.001$).
 Conclusion: HeH(50+) is found in 5% of childhood AML and is associated with young age, low WBC, and AML M7. OS seems similar to non-HeH. Most frequently gained chromosomes were 6, 8,19, and 21. Extra chromosome 8 was associated with favorable outcome and extra 21 was associated with an inferior outcome.

P13.03 Lotte Sander

REMOVABLE MR COMPATIBLE PROSTATE MARKER FOR HIGH DOSE RADIOTHERAPY OF PROSTATE CANCER – 3 YEARS RESULTS COMPARED TO STANDARD GOLD MARKERS.

L. Sander

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Introduction:

This study evaluates late toxicity and Quality of Life (QoL) 3 years after high dose radiotherapy for prostate cancer using a removable prostate stent (MemocoreTM) as fiducial marker comparing the results obtained with standard gold markers.

Materials & Methods:

This ongoing study includes 200 patients with locally or locally advanced prostate cancer (T1-T3N0M0) treated with radiotherapy at the Department Oncology, Aalborg Hospital between 2007 and 2009. 100 had standard gold markers as fiducial, another 100 the prostate stent. The groups are comparable according to age, Gleason score, T-stadium, co-morbidity. All patients received high dose (78Gy/39 fractions) imaged-guided radiotherapy (IGRT). The group of gold markers had no MR co-registration; CTV was outlined on planning CT only. 3 years after radiotherapy the patients are interviewed and have toxicity (CTC-AE) and Quality of life (EORTC q30 and PR25) registred.

Results:

Preliminary results from 32 patients in the stent group and 9 in the gold marker group are comparable regarding toxicity and QoL. We expect to present 3 years results of toxicity and QoL of about 50 patients from each group at the meeting.

Conclusions:

Late side effects after radiotherapy are dose-limiting. Accuracy in radiotherapy is therefore extremely important, and can be improved with suitable prostate markers visible on MR. The Memocore prostate stent could be such one depending on the long term results. Perspectives reducing morbidity could be dose escalation with better tumour control as a result.

P13.04 Lars Mikael Stensman

ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (ALICCS) - LATE RENAL AND GASTROINTESTINAL EFFECTS AND THEIR PREVENTION IN CHILDHOOD CANCER SURVIVORS

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Introduction

With the remarkable improved survival of childhood cancer, morbidities become more apparent. The life-long risk of late complications related to the cancer and its treatment, however, remain to be fully explored.

Aims

To investigate possible late renal and gastrointestinal complications after childhood cancer treatment in a large population-based setting, using the unique resources for conducting research in the Nordic countries.

Methods

The cohort will include around 55,000 children diagnosed with cancer before the age of 20 from the beginning of cancer registrations in the 1940s through 2008. A population comparison cohort, reflecting morbidity in the background population, will be randomly selected from the Central Population Registries and matched 1:5 by gender, country and age. Study subjects will be followed up for selected outcomes in the National Patient, Prescription and Cause of Death Registries in the Nordic countries. Information on treatment exposure will be retrieved from medical records and dose-response analyses will be performed. Cox proportional hazard models will be used to estimate the relative risks of the late effects in cancer survivors in comparison with population cohort members.

Results

In the next coming years, a variety of outcomes of renal and gastrointestinal diseases will be investigated. Characteristics of the cohort and the first preliminary results will be presented at the meeting.

Conclusion

The ultimate goals are to ameliorate treatment protocols, with fewer late effects and to improve long-term follow-up for survivors of childhood cancer.

P13.05 Maria Thor

INVESTIGATING THE ASSOCIATIONS BETWEEN LATE RECTAL MORBIDITY AND SIMULATED RECTAL MOTION

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Aim: To investigate the performance of a developed organ motion model by associating the obtained 'motion-inclusive' dose distributions to post-radiotherapy (RT) toxicity using the rectum and late rectal morbidity as examples.

Materials and methods: Rectal organ motion was simulated as random, systematic or combined random and systematic shifts over the 35 treatment fractions of 232 prostate cancer patients previously treated with RT to 70 Gy. Both isotropic and anisotropic motion patterns were investigated. The motion-inclusive delivered dose-volume histograms (dDVHs), and the planned DVH (pDVH) obtained from the static rectum were explored in relation to late rectal morbidity using Spearman's rank correlation coefficient (Rs).

Results: Different associations with rectal morbidity were seen with the dDVHs relative to the pDVHs. These tendencies were most pronounced in the mid-dose region (40-60 Gy). The associations were dependent on the applied motion design, with the strongest associations obtained by applying random shifts. Comparing the simulations of the isotropic motion to the anisotropic motion the latter followed the pDVH curve to a larger extent for

low doses.

Conclusions: A model simulating organ motion has been developed and investigated relative to post-radiotherapy toxicity using rectum and late rectal morbidity as examples. The associations with morbidity were different between the motion-inclusive DVHs and the pDVHs. At intermediate doses, the differences became the most evident. The model is currently being validated in other patient cohorts and on other more specific toxicity end-points.

P13.06 Katja Maretty Nielsen

TREATMENT RESULTS AND PROGNOSTIC FACTORS IN SOFT TISSUE SARCOMA PATIENTS AT AARHUS SARCOMA CENTER, 30 YEARS EXPERIENCE

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INTRODUCTION: Soft tissue sarcoma (STS) is a serious disease with approximately 200 cases annually in Denmark. The rarity makes it difficult to perform RCT; instead information can be obtained from clinical databases. The few existing STS databases are not population based and have not been systematically validated. Aarhus Sarcoma Registry (ASR) consists of validated population based data, which can be used to investigate treatment results and prognostic factors. The data value may be greater than comparable registers' data because of the unique possibility for individually linking to other population based data sources.

AIMS: 1) Examine patient registration completeness in ASR and trend in incidence. 2) Study prognostic factors for recurrence rate and survival. 3) Study comorbidity prevalence and influence on survival. 4) Compare survival of patients with lung metastases treated radically or palliatively.

MATERIALS AND METHODS: The study population (approximately 1300 patients) consists of all STS patients treated at Aarhus Sarcoma Center in 1979-2008. The validation of the ASR included 1) a revision of the registered variables and the standardized registration forms, and 2) systematic reviewing of all medical files.

Data from ASR will be assessed by linking to CPR, LPR and the Cancer Registry. Cox-regression analysis with both unadjusted and adjusted Hazard Ratios will be used as well as Kaplan-Meier survival curves.

PREELIMINARY RESULTS: 97.6% of the patients in the ASR have been validated. The completeness was > 99% in 11/18 registered variables. The 5 year local recurrence and metastasis rate was 14.2 and 15.2%, respectively. The 5 years overall survival was 79.5%.

P13.07 Hanna Rahbek Mortensen

RISK OF FATAL ASPIRATION PNEUMONIA IN PATIENTS TREATED WITH CURATIVE RADIOTHERAPY FOR HEAD AND NECK CANCER

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Background: Severe dysphagia leading to penetration of food to the larynx and manifest aspiration is a common side effect after radiotherapy (RT) for head and neck cancer (HNC). The aim of this study was to investigate the incidence and mortality of aspiration pneumonia in HNC patients treated with curative RT.

Materials and methods: Patients treated with curative RT for HNC in Aarhus from Jan. 1st 2006 to Dec. 31st 2008 were included. Data on patient, tumour and treatment characteristics were obtained from the DAHANCA database. Data on hospital admissions with infectious diseases, airway infections, pneumonia, other diseases in the airway and dysphagia were obtained from the National Patient Registry and data from the National Registry of Causes of Death were obtained on all deaths and causes of death.

Results: A total of 335 patients were included; median age was 62.9 years, 78% were men and most patients had Stage IV disease. 51 patients received chemotherapy as a part of the curative treatment. In the first year after RT there were 68 hospital admissions in 46 (14%) patients; 50 patients (15%) died.

Of the 120 patients who died, 76 had uncontrolled head-and-neck cancer. The remaining 44 deaths were unrelated to aspiration and pneumonia in 32 cases. In 12 cases aspiration and/or aspiration pneumonia could not be ruled out as contributing cause of death: 7 pneumonia, 4 unexplained causes and 1 with treatment complications.

Conclusions: Dysphagia-related aspiration and pneumonia are serious and potentially fatal treatment sequelae. More than one quarter of all deaths in relapse-free patients after radical RT may be associated with aspiration pneumonia.

P13.08 Lotte Bonde Bertelsen

ENDOTHELIAL OUTGROWTH CELLS - HOMING PATTERN AND ASPECTS OF IMMUNO-INCOMPATIBILITY

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Purpose: The Homing pattern and aspects of immuno-incompatibility of xenotransplanted ^{111}in-tropolone radio labelled Endothelial Outgrowth Cells (EOC) were to be evaluated in two mice models with implanted C3H tumors.

Materials and Methods: Experiments were performed on Human umbilical cord blood derived EOCs that were labelled with ^{111}Indium. EOCs were incubated with ^{111}Indium-tropolon equal to 0.37 Mbq pr $3x10^6$ cells for 15 minutes, washed with PBS, adjusted to a concentration of $3x10^6$ cells/200 µl and administered into either CDF1 or nude mice, carrying a C3H mammary

carcinoma implanted on their right rear foot. Following euthanasia (24 hours after cell injection) the mice were dissected and the ^{111}Indium activity in the individual organs were quantified by gamma counting.

Results: Cellular retention of incorporated ^{111}In-tropolone was 87% (93-83) decreasing to 46% (72-33) after 24 hours. The cellular viability was always more than 80%. Accumulation of Indium was seen in the liver, spleen and kidney and approximately 5% ID/g tissue were observed in the tumor after injection into the animals.

Conclusions: Cellular incorporation of Indium is possible in EOCs and a high percentage of the Indium was found in the liver, spleen and kidneys. However sites presenting ongoing angiogenesis such as tumor tissue were also positive for ^{111}Indium labelled EOCs.

P13.09 Kasper Jarlhelt Andersen

THE NATURAL HISTORY OF LIVER REGENERATION IN RATS & NDASH: DEVELOPMENT OF AN ANIMAL MODEL FOR LIVER REGENERATION STUDIES.

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Background: The aim of the present study was to evaluate the natural history of liver regeneration in healthy rats. The study was meant as a precursor for further interventional studies in healthy and cirrhotic animals.

Material and Methods: Partial hepatectomy (PHx) of 70% was performed on 64 rats. After PHx the animals were randomised into 8 groups for evaluation. The animals in each group were evaluated on same postoperative day (POD) from POD 1 to 8.

Results: At PHx the animals had a mean body weight of 238.4 g (211.4; 286.5). Liver weight analysis showed an ascending curve, with max slope POD 1-3, reaching a steady state of app 9 g on day 5-8. When correlated to body weight, through regeneration rate, a similar pattern was seen, with a RR of 100% reached day 5-8.

Interleukin-6 (Il-6) peaked POD 1 and was falling to undetectable levels day 4. Alfa-2-Macroglobulin (a-2-M) levels were high POD 1-3 before falling to low levels. Tumor-necrosis-factor-alpha (Tnf-a) was undetectable throughout the period.

At the moment functional capacity of the regenerating liver, is analysed by the enzymatic method BTR (Ratio of Branched-Chain Amino Acids to Tyrosine).

Stereological aspects are looked into regarding KI-67 analysis, as are more serological markers (Alanin-amino-transferase, Bilirubin, Alkaline-phosfatase and Hepatocyte-growth-factor).

Conclusion: Liver regeneration, regarding size and weight, were at top speed day 1-3. Full liver regeneration reached a plateau after 5-8 days, and

should after this point be considered practically at end.

Liver regeneration should in further studies be evaluated on postoperative day 2, 4 and 8.

P13.10 Trine Grantzau

SECOND PRIMARY CANCER AMONG DANISH WOMEN WITH EARLY BREAST CANCER TREATED WITH POSTOPERATIVE RADIOTHERAPY.

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OBJECTIVE: To analyze the long-term risk of second primary solid non-breast cancer in a population-based cohort of breast cancer patients treated with, or without, megavoltage postoperative radiotherapy.

METHODS: In 46,176 1+year survivors of early breast cancer treated in the period 1982-2007, the long-term risk of second primary solid non-breast cancer was estimated. The second cancers were grouped into sites associated to radiotherapy (oesophagus, lung, pleura, bones and connective tissue) and other sites. Risk was estimated by the standardised incidence ratio (SIR) and multivariate COX regression was used to estimate the adjust hazard ratio (HR) of second cancers in women treated with postoperative radiotherapy compared to no radiotherapy.

RESULTS: After a median follow-up of 6 years a total of 928 second cancers occurred among the irradiated women SIR=1.18 (95% CI 1.11-1.26) and 1430 second cancer SIR=1.06 (95% CI 1.01-1.12) among the non-irradiated women. The adjusted HR for radiotherapy-associated sites was 1.32 (95% CI 1.10-1.59). There was no increased risk for all other second cancers sites combined HR=1.05 (95% CI 0.94-1.16). The risk for radiotherapy-associated sites increased with time since diagnoses and became evident 10 or more years after diagnosis. There was no increased risk over time for the other sites combined.

CONCLUSIONS: Breast cancer patients treated with current treatment techniques have a small but significant increased risk of developing second primary cancers 10 or more years after treatment.

P13.11 Peter Niekerk

DELINEATION OF STEM CELLS IN CHRONIC MYELOID LEUKEMIA &NDASH; A TOOL FOR IMPROVED MINIMAL RESIDUAL DISEASE MONITORING

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BACKGROUND: Targeted therapy with Tyrosine Kinase Inhibitors (TKI) has revolutionized the treatment of Chronic Myeloid Leukemia (CML), and an increasing number of patients enter Complete Molecular Remission (CMR),

i.e. a phase of undetectable minimal residual disease (MRD), even when assessed by qPCR for BCR-ABL fusions transcript. Despite this, approximately 60% of patients in CMR will relapse when taken off therapy. Consequently, these patients remain on a costly therapy, which - for some - is accompanied by severe side effects.

We hypothesized that by specifically targeting cell-populations enriched for potential leukemic stem cells, the sensitivity of the current MRD assessment can be improved. We did this focusing upon the role of hMICL, a promising stem-cell marker in acute myeloid leukaemia in our hands.

METHODS: Fresh bone marrow aspirates is being obtained from CML patients in CMR and non-CMR. Based on surface antigen expression, stem cell subsets are enriched for employing both magnetic bead and fluorescence-activated cell sorting, and then analysed by qPCR for BCR-ABL, FISH for t (9:22) and CFU in vitro assays.

RESULTS SO FAR: Enriched populations had a purity of 98.2% (92.4%-100%) (median (range)) and viability of 99.8% (98,1%-100%). Total CD34+ cell fraction was 1.2% (0.8% - 3.0%), and seemed influenced by type of TKI treatment. In contrast to AML, hMICL was almost completely absent on CD34+/CD38- stem cells, but expressed on 47.4% (35.9%-62.7%) of CD34+/CD38+ progenitors.

CONCLUSIONS: This constitutes a promising approach to further studies of stem cell biology, and may enable identification of CML patients in which therapy can be safely terminated.

P13.12 Jesper Kallehauge

PRELIMINARY RESULTS OF COMPARISON OF DCE-CT AND DCE-MR FOR ADVANCED CERVICAL CANCER

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Introduction
The study of perfusion in advanced cervical cancer has the possibility to be an early indicator of treatment response in combined External Beam Radiotherapy (EBRT) with chemotherapy. Dynamic Contrast Enhanced Magnetic Resonance (DCE-MR) is the technique of choice because it has better soft tissue contrast and the fact it does not rely on ionizing radiation for image acquisition. However, there are inherent problems with signal-to-contrast conversion and geometrical stability in MRI. This study tries to compare the two techniques ability to estimate perfusion parameters as blood flow and permeability (K_{trans}), plasma volume fraction (v_{plasma}) and the extracellular-extravascular volume fraction (v_e).
Results
The change in volume during EBRT for Patient 1 and Patient 2 can be quantified as Tumor Regression Rate (TRR) and was estimated to be -0.03 CI = [-0.10, 0.03] and -0.08 CI= [-0.31, 0.16], respectively. This means that for Patient 1 and 2 the tumors regressed 3%/day and 8%/day, respectively during the 4 weeks of EBRT. Using a student t-test and an alpha level of 0.05 the two modalities (CT and MR) were tested if they, at different timepoints for different patients, resulted in significantly different mean value estimates for K_{trans}, v_{plasma} and v_e. All comparisons of the mean values revealed p-values <0.05.
Conclusion
The preliminary data shows that the two modalities DCE-CT and DCE-MR under these conditions does not give similar results. With $p<0.05$ we have to

reject the hypothesis that the mean values are the same. The reasons for this can be perhaps found in motion of the vowel during scanning or the need for a better start input for the model.

P14.01 Christoffer Laustsen

NON-INVASIVE DIABETIC NEPHROPATHIC ASSESSMENT WITH HYPERPOLARISED ^{13}C PYRUVATE

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Introduction: Diabetic nephropathy is the leading cause of chronic kidney failure and end-stage kidney disease. Early diagnosis is critical for early intervention. We introduce a novel non-invasive MRI methodology; in-vivo measurement of hyperpolarized of ^{13}C-labeled pyruvate, to investigate metabolic and anatomical changes associated with diabetics. The aim is to define a new non-invasive imaging methodology for real time monitoring of the progression of kidney function reduction and acute kidney failure in diabetic patients.

Materials and Methods: Type-1 STZ diabetic and control rats (n = 5, n = 6), were placed in a metabolic cage for 72 hours. Urine and faeces were sampled during the last 24 hours. The rats were anesthetized and a tail vein catheter was inserted for injection of hyperpolarized ^{13}C-labelled pyruvate. Temperature and respiration were monitored throughout the experiment. A baseline MRI was performed together with injection of 2 mL hyperpolarized ^{13}C pyruvate over 10 s. After a 1 hour waiting period another MRI/injection was performed. In both cases a dynamic slice selective sequence was used. The MRI spectroscopy data were analyzed by integration of the respectively metabolite signals. The blood glucose level was measured pre and post scanning.

Results: The initial study suggests a clear trend in reduced kidney function, via the reduced metabolic activity in the kidneys, in the diabetic rats compared with the controls. In conclusion, our encouraging results indicated a potential usefulness of hyperpolarized ^{13}C-labelled pyruvate MRI for evaluation of metabolic disorders, such as the nephropatic conditions associated with diabetics.

P14.02 Johan Heiberg

POSTOPERATIVE RIGHT BUNDLE BRANCH BLOCKS LONG-TERM EFFECT ON THE HEARTS RIGHT VENTRICLE IN CHILDREN OPERATED FOR VENTRICULAR SEPTAL DEFECT

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Right bundle branch block is an exceedingly frequent complication in heart surgery, and especially in patients whom undergone surgical closure of a ventricular septal defect which is the most common congenital heart disease. How this bundle branch block effects the right ventricle of the heart on a long-term basis for this group of patients is still unknown.

As a part of a PhD-study I therefore will try to illustrate this by echocardiography, MRI, exercise testing and other investigations 15 to 20 years after the surgical procedure. The study population thus consists of three different groups: 1. Patients whom undergo surgical closure of ventricular septal defect without postoperative right bundle branch block, 2. VSD-operated patients with right bundle branch block and 3. Healthy controls with no significant medical issues matched on age and sex. By carrying out the tests mentioned the right ventricles systolic function, diastolic function, the patients maximal exercise capacity and a lot of other parameters will be evaluated in the three groups of patients and compared amongst each other. The perspective therefore is the ability to point out a specific group of patients with an inferior outcome and with a possible further need of intervention. An additional perspective is to increase the awareness of protecting the bundle branch during the operation.

P14.03 Michael René Skjelbo Nielsen

GENETIC POLYMORPHISMS IN THE LIPOXYGENASE PATHWAY AND THE RISK OF MYOCARDIAL INFARCTION

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Background: Atherosclerosis is widely accepted as an inflammatory disease. Previous studies have suggested that inflammatory mediators from the lipoxygenase pathway may be causal factors in cardiovascular disease.

Aim: To investigate the association between single nucleotide polymorphisms (SNPs) in candidate lipoxygenase pathway genes and the risk of myocardial infarction (MI).

Methods: The Prospective Diet, Cancer and Health (DCH) study was initiated in 1993-1995 when 57,053 Danish born residents, aged 50 to 64 years, participated in a clinical examination, sampling of biological tissue and a detailed lifestyle survey. The primary outcome was incident MI and by linkage of the National Patient Register and the National Cause of Death Register combined with a review of medical records we identified 2,104 cases with incident MI. We used a case-cohort study design and for the creation of a case cohort sample, 1800 participants (“controls”) were randomly selected from the entire DCH cohort.

For genotyping, 28 SNPs previously described as either associated with CVD events or surrogate markers of CVD were selected. DNA from blood samples

collected at baseline will be used for the genotyping.

Statistics: Hazard ratios and 95% confidence intervals for the association between each of the SNPs and time to MI will be estimated using Cox proportional hazards regression with age as the underlying time-axis.

Perspectives: This study will contribute to answer the question, whether the lipoxygenase pathway plays a causal role in CVD or not. Such knowledge is important in the development of new drugs for the treatment and prevention of CVD.

P14.04 Henrik Vadmann

ATRIAL FIBRILLATION: ABLATION OR SURGICAL TREATMENT II: FAST II. A RANDOMIZED STUDY COMPARING NON-PHARMACOLOGIC THERAPY IN PATIENTS WITH DRUG-REFRACTORY ATRIAL FIBRILLATION REFERRED FOR A FIRST TIME INVASIVE TREATMENT.

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Introduction: The current understanding of the pathophysiology of atrial fibrillation (AF) implies that “triggers” foci located in the pulmonary veins (PV) can initiate AF.

New non-pharmacological interventions have evolved over the last decade and the main focus has been on percutaneous radiofrequency (RF) catheter ablation (P-RFA) and various forms of surgical maze ablation, especially mini invasive thoracoscopic RF ablation (S-RFA). Both approaches aim at minimizing the impact of “triggers” from PV by electrical isolation of the veins.

The rationale for eliminating AF includes improvement in quality of life, decreased stroke risk and improved survival.

Purpose: The purpose of this study is to compare P-RFA and S-RFA in patients referred for a first time invasive treatment of AF.

Hypothesis: S-RFA is more effective compared to P-RFA in patients with symptomatic paroxysmal AF refractory or intolerant to at least one antiarrhythmic drug (AAD).

Materials and methods: This study is a prospective randomized study and is conducted at Aalborg Hospital, Aarhus University Hospital Denmark and St Antonius Hospital, Nieuwegein, The Netherlands.

A total of 180 patients will be enrolled in the study. There is a 12 month follow-up period, with four visits. Each visit consists of Quality of Life questionnaires, ECG and interviews. Before ablation and at 6 and 12 month follow-up the patients are equipped with a 7 days Holter monitor.

Endpoints: The primary endpoint is the prevalence of AF at 6 and 12 months with or without AAD. Secondary endpoints consist of Quality of Life measures and health economy

P14.05 Asger Andersen

RIGHT VENTRICULAR HYPERTROPHY AND FAILURE ABOLISH CARDIOPROTECTION BY ISCHEMIC PRECONDITIONING

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Purpose: To investigate whether IPC protects the hypertrophic and failing right ventricle (RV) of isolated perfused hearts taken from rats operated by pulmonary artery banding (PTB).

Materials and Methods: Male Wistar rats were subjected to PTB or SHAM operation (n=30). Four weeks after the operation, hearts were isolated and perfused a.m. Langendorff with Krebs-Henseleit buffer. They were randomised to either IPC (2 x 5 min of global ischemia) or no preceding ischemia (CON) before 40 minutes of global ischemia and 120 minutes of reperfusion. The effect of IPC on the right ventricle was evaluated by measurement of the infarct size/area-at-risk ratio (IS/AAR) and post-ischemic RV function studied by RV pressures recorded through a fluid filled balloon catheter inserted into the RV.

Results: The PTB procedure caused RV hypertrophy and failure compared with SHAM operated animals seen by a decrease in cardiac output (PTB 116±36 vs. SHAM 148±40, $p<0.05$), an increase in RV mass correlated to tibia length (PTB 15.1±2.0 vs. SHAM 5.1±0.9, $p<0.0001$) and tricuspid regurgitation (PTB 80% vs. SHAM 0%, $p<0.0001$). In hearts from SHAM animals, IPC induced a marked decrease in IS/AAR (CON 35.64 vs. IPC 17.43 $p<0.001$) and improved hemodynamic recovery of RV contractile function. In hearts from PTB animals, IPC failed to reduce right ventricular IS/AAR (CON 59.34 vs. IPC 59.34, $p>0.05$) or improve post-ischemic RV contractile function.

Conclusion: In the isolated rat heart, right ventricular hypertrophy and failure abolish cardioprotection by ischemic preconditioning in the right ventricular myocardium.

P14.06 Rikke Esberg Kirkfeldt

RISK FACTORS FOR LEAD COMPLICATIONS IN CARDIAC PACING. A POPULATION-BASED COHORT STUDY OF 28,860 DANISH PATIENTS

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BACKGROUND: Lead complications are the main reason for reoperation after implantation of pacemakers (PM) or cardiac resynchronization therapy (CRT-P) devices, causing excess morbidity and increasing cost.

AIM: To describe the incidence of lead complications causing reoperation after device implantation and to identify risk factors for lead complications.

METHODS: A population-based historic cohort study was performed based on data from the Danish Pacemaker Register (DPR) which include all Danish patients who received their first permanent PM or CRT-P device from 1997

to 2008 (n=29,846). Multiple logistic regression was used to estimate adjusted odds ratios (aOR) for the association between risk factors and lead complications causing reoperations. Follow-up was three months.

RESULTS: The study population consisted of 28,860 patients. The incidence of any lead complication was 3.6%, encompassing right atrial (RA; 2.3%), right ventricular (2.2%) and left ventricular (4.3%) lead complications. Multivariate analysis identified the following significant risk factors: chronic heart failure as indication (aOR 3.0; 95% CI 2.1-4.3), implantation in a non-university center (aOR 1.4; 95% CI 1.2-1.6), inexperienced operator with less than 25 implantations (aOR 1.6; 95% CI 1.3-2.0), single lead RA device (aOR 1.4; 95% CI 1.1-1.8), dual-chamber pacing device (aOR 1.6; 95% CI 1.4-1.9), CRT-P device (aOR 3.3; 95% CI 2.4-4.4) and passive-fixation RA lead (aOR 2.2; 95% CI 1.7-2.9).

CONCLUSIONS: Lead complications causing reoperation remain a clinically important problem in device therapy. Mainly procedure-related factors were identified as independent risk factors for lead complications.

P14.07 Karl Erik Tilly

THE DIAGNOSTIC VALUE OF ADENOSINE CONTRAST STRESS ECHOCARDIOGRAPHY IN PATIENTS WITH CHEST PAIN OF UNKNOWN CAUSE

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Background: Since 2005, it has been possible to measure absolute myocardial blood flow (MBF ml/min/g) by myocardial contrast echocardiography (MCE). However, the clinical usefulness of MCE is not yet fully evaluated.

Purpose: In patients with chest pain of unknown cause and without previously known coronary artery disease (CAD), using quantitative coronary angiography (QCA) as reference.

To estimate the diagnostic value of MBF reserve at myocardial segmental level by adenosine stress MCE with respect to detect significant stenoses in the coronary artery supplying the segment.

To evaluate whether the diagnostic value of exercise test, in which known clinical variables such as hypertension, diabetes, smoking, etc. are included, is enhanced by adding the result of adenosine stress MCE.

Compare the diagnostic value of adenosine stress MCE to myocardial perfusion imaging (MPI).

Study design: It is an observational blinded study. 200 patients will be included.

Methods: The MCE is performed at rest and during medicamental stress with Adenosine. An ultrasound contrast agent (UCA) is infused for both examinations. The contrast filled myocardium is examined using low power ultrasound (low mechanical index, MI). After UCA destruction by a burst of high MI ultrasound, MBF refill curves are created. The MBF reserve is then

calculated as the ratio of MBF at stress divided by MBF at rest.

Results: The project is ongoing at Region Hospital Herning.

Perspective: If this study corroborates the diagnostic value of MCE, the method might in the future be used to confirm or rule out CAD noninvasively.

P14.08 Anne Sophie Pinholt Kancir

EFFECT OF HYDROXYETHYL STARCH ON RENAL HANDLING OF SODIUM AND WATER, VASOACTIVE HORMONES, BIOMARKERS AND CIRCULATION IN PATIENTS UNDERGOING LAPAROSCOPIC NEPHRECTOMY, RADICAL PROSTATECTOMY OR HIP REPLACEMENT

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Background: Hydroxyethyl starch (HES) is widely used in hospitals to maintain circulation in critically ill patients. In recent years studies have raised suspicion that HES is nephrotoxic. So far acute kidney injury has been diagnosed based on creatinine measurements, but new technology allows for earlier diagnosis using measurements of biomarkers in urine. The purpose of this project is to investigate HES's potential toxicity and effects on the circulation and kidneys using measurements of biomarkers specific for toxicity and for the sodium/water balance in the urine and by measurements of vasoactive hormones in the blood after administration of HES 130/0.4.

Design: The hypothesis will be investigated in three different randomised, double blinded, placebo-controlled studies with patients undergoing laparoscopic nephrectomy, radical prostatectomy or hip replacement.

Methods: Patients are randomized to receive either Voluven (HES 130/0.4) or sodiumchloride 9 mg/ml i.v during surgery. The patients will receive 7.5 ml/kg projectfluid the first hour and 5 ml/kg in subsequent hours. u-NGAL, u-Kim1, u-LFABP will be measured for nephrotoxic damage, u-AQP2, u-ENaCβ, u-NCC, u-NK2CC to investigate the effect on sodium/water balance, while the PRC, p-AngII, p-Aldo, p-AVP, p-ANP and p-Endot will be measured in the blood to assess the effect on circulation. Blood pressure, pulse and endtidal CO2 will be recorded continuously throughout the operation.

Perspectives: Results are expected to contribute new knowledge about HES's effect on the kidneys and circulation and may have implications for future clinical practice concerning fluid therapy in surgery.

P14.09 Peter Juhl-Olsen

SYSTOLIC HEART FUNCTION REMAINS DEPRESSED FOR AT LEAST ONE MONTH AFTER ON-PUMP CARDIAC SURGERY

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Introduction: Cardiac surgery remains a source of considerable morbidity and mortality. Impaired postoperative heart function is thought to be a main cause of this. The objective of this study was to quantify the duration of

cardiac dysfunction after on-pump cardiac surgery.

Methods: 59 patients scheduled for on-pump cardiac surgery were included. Echocardiography was performed at 1) the day before operation, 2) the 1st postoperative day, 3) the 4th postoperative day, 4) one month postoperatively and 5) 6 months postoperatively. Systolic function was quantified by ejection fraction (EF), global strain (GS) and tissue tracking score (TT). Diastolic function was evaluated as E/E' and E'/A'.

Results: All measures of systolic function changed over time (all P-values < 0.025). As compared with baseline data, values for EF, GS and TT were depressed on the 1st and 4th postoperative day (P-values < 0.047). 1 month after surgery, EF and TT were still decreased (P-values < 0.038), and GS was insignificantly decreased. 6 months after surgery, all measures of systolic function had returned to baseline values. Indices of diastolic function did not change significantly over time.

Discussion: This study showed that patients undergoing on-pump cardiac surgery had impaired systolic function for at least one month postoperatively as evaluated by echocardiographic methods. This finding may be explained by the ischemia and reperfusion injury induced by intraoperative cardioplegia and extra-corporal circulation.

Conclusion: Measures of systolic function remained depressed for at least 1 month after on-pump cardiac surgery. Indices of diastolic function did not change significantly.

P14.10 Frank Holden Christensen

NO ACTIVITY DURING STATIN TREATMENT IN HEALTHY HUMANS

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Purpose: We investigated the effects of short term atorvastatin treatment on blood pressure (BP) and kidney function during inhibition of nitric oxide synthase (NOS).

Methods: Twenty-six healthy men and women were included in a randomised, placebo-controlled, double-blinded, cross-over study. All subjects attended 2 study days and were given either Atorvastatin 80 mg per day or placebo 4 days prior to each examination day. The nitric oxide (NO) synthase inhibitor, L-NMMA, was administered as a 4.5mg/kg bolus injection followed by 3.0 mg/kg/hour IV infusion for one hour. BP, heart rate (HR) were repeatedly measured and urine and blood samples were collected every 30 min during the study day. Statistics were performed with t-test and paired t-test.

Results: Baseline levels of BP, HR, GFR and fractional excretion of sodium (FE-Na) were not different between groups. IV infusion of L-NMMA increased BP and decreased HR ($p<0.001$). There were no differences in change in SBP (4±3 vs. 4±3 mmHg), DBP (8±3 vs. 8±2 mmHg) and HR (-6±3 vs. -7±3/min) between groups.

GFR decreased during L-NMMA infusion ($p<0.001$), but there were no differences between groups (-8±6 vs. -10±7%). FE-Na decreased during L-NMMA infusion ($p<0.001$) and these decreases was significantly higher during Atorvastatin treatment (-34 vs. -44%, $p=0.007$). There were no

differences in 24 hour urine Na-excretion (p=0.32).

Conclusions: Short term Atorvastatin treatment significantly increased the reduction in FE-Na during NOS inhibition. Our results suggest that atorvastatin increases the bioavailability of renal NO and might be an explanation of the pleiotropic effects of statins.

P14.11 Dirk Troitzsch PREISCHEMIC HIGH-DOSE CYCLOSPORINE A TREATMENT PROTECTS THE LATISSIMUS DORSI MYOCUTANEOUS FLAP FROM ISCHEMIA-REPERFUSION INJURY: EFFECTS ON TISSUE OXYGENATION AND MITOCHONDRIAL OXIDATION

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Background:

We hypothesized that pretreatment with high-dose CsA may provide a protective effect against ischemia-reperfusion injury and improve tissue oxygenation and mitochondrial redox state (CytOx) after ischemia and reperfusion in the latissimus dorsi muscle.

Material/Methods:

The Latissimus dorsi muscle was prepared and mobilized in 20 New Zealand rabbits (n=20, 2.5±0.5 kg). Warm ischemia was induced by occlusion of the thoracodorsal artery and vein for 4 hours, followed by 2 hours of reperfusion. The animals were randomized to receive a 60 mg/kg intravenous bolus of cyclosporine (CsA-group, n=10) or saline (control, n=10) 10 mins before ischemia onset. Tissue $ptiO_2$ and mitochondrial redox state (CytOx)measured by near-infrared (NIR) spectroscopy were stored on-line during ischemia and reperfusion simultaneously. Histologic evaluation with score was used to quantitatively evaluate morphological changes between groups.

Results:

Regional tissue ptiO2 in the CsA group (31.5±4.6 mmHg, $p<0.05$ vs. control) was significantly higher compared with control group (13.9±3.1 mmHg). Mitochondrial redox state (CytOx) was also improved in the CsA group (+0.2±0.04 µmol/L, $p<0.01$) compared with the control group (-1.7±0.08 µmol/L). Histological results confirmed better morphological preservation in the CsA group and correlated with tissue ptiO2 (r=0.85) and mitochondrial CytOx (r=0.92).

Conclusion:

This study results support our hypothesis that high-dose CsA pretreatment preserves ischemic latissimus dorsi muscle from ischemia-reperfusion injury and the protective mechanism involves improved tissue oxygenation and cellular mitochondrial oxidation.

P15.01 Sisse Anette Thomassen

SHOULD BLOOD FLOW DURING CARDIOPULMONARY BYPASS BE INDIVIDUALIZED MORE THAN TO BODY SURFACE AREA?

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Blood flow during normothermic cardiopulmonary bypass (CPB) is calculated and based on the patient's body surface area (BSA). Increasing comorbidity, age and weight of today's cardiac patients questions this calculation as it may not reflect individual metabolic requirement. The hypothesis of the present study was that a measured cardiac output (CO) prior to CPB is a better estimate of an optimal blood flow during CPB.

A cross-over study with random allocation to CPB blood flow for 20 minutes based on either a calculation (2.4 L/min/m^2) or on CO with switch to the opposite flow for another 20 minutes was performed. Twenty-two elective adult cardiac surgery patients with left ventricular ejection fraction >50 %, no history of cerebral insult or headtrauma, or verified carotid artery stenosis, were included. Effect parameters were cerebral oxygenation measured by near infrared spectroscopy, mixed venous saturation, base excess and lactate concentration.

The calculated CPB blood flow was kept at 2.4 L/min, while the blood flow based on the measured cardiac index varied from 1.9 to 3.1 L/min (median 2.4 L/min). No differences were seen in the effect parameters; cerebral oxygenation ($p = 0.26$), mixed venous saturation ($p = 0.57$), base excess ($p = 0.26$), and lactate ($p = 0.73$).

In conclusion, a CPB blood flow based on individual estimate did not improve cerebral and systemic oxygenation compared to a blood flow based on BSA.

P15.02 Troels Fogh Pedersen

THE EFFECT OF PRECONDITIONING FOR PREVENTION OF PERIOPERATIVE MYOCARDIAL ISCHEMIA IN ABDOMINAL AORTIC ANEURYSMS.

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Purpose:

Primarily to investigate whether peripheral preconditioning can reduce the incidence of perioperative myocardial ischemia in patients operated electively for infrarenal aortic aneurysm. And secondly, to investigate the impact of perioperative inflammatory response, and whether preconditioning can protect against perioperative myocardial infarction and reduced cardiac function.

Methods:

The study is conducted as a prospective, randomized, single blinded study including 200 patients with abdominal aortic aneurysm hospitalized for elective surgery. Patients are randomized to 1) either preconditioning on an arm starting at the beginning of the operation and usual surgery or 2) no preconditioning and usual surgery.

The preconditioning is performed by a conventional blood pressure cuff attached to the arm and inflated for 4 x 5 minutes with a 5 minutes break in between. This will be performed by anesthesia staff, and will be blinded to the operators. There will be no further differences in treatment between the two groups.

Monitoring and investigations:

Patients will as a result of usual clinical practice be monitored during surgery for signs of cardiac ischemia and then have taken daily ECG. In addition, blood samples consisting of: troponin T, CKMB, LDH, hemoglobin, creatinine, urea, sodium, potassium, leukocyte count and CRP are collected after the surgery and the following five days. At all blood sampling, a sample (5 ml) will be centrifuged and plasma stored for analysis of inflammatory markers.

There will be performed an Echocardiography, preoperatively, before discharge from the hospital and after 3 months.

Events in the first 30 days postoperative will be registered.

P15.03 Karen Axelgaard Lorentzen

MECHANISMS OF HYALURONIC ACID INDUCED DEVELOPMENT OF VASCULAR PATHOLOGY

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Diabetic macroangiopathy is characterised by vessel wall thickening arising from extracellular matrix accumulation, in particular Hyaluronic Acid (HA). To explore the pathophysiological role of disseminated HA accumulation in the arterial wall in vivo we previously created a transgenic mouse model with HA overexpression in the smooth muscle cells. The model showed increased vessel stiffness and strength. Additionally we observed accelerated atherosclerosis development when crossed with atherogenesis prone (ApoE-/-) mice. Together with results suggesting that vessel wall stiffening causes susceptibility to atheromatosis, we propose that the HA accumulation has a definitive influence on the development of diabetic macroangiopathy.

In this study we examine whether HA itself attributes to the increase in mechanical stiffness and how the HA crosslinking is affected when HA is present in excessive amounts. We focus on the Bikunin protein family: Heavy Chains from the Bikunin proteins are transferred onto HA stabilising

the extracellular matrix.

We show that increased vessel stiffness persists after HA is removed by hyaluronidase treatment ($p \leq 0.005$) (Tg: n=5, WT: n=6). However when investigating the crosslinking pattern we see that excessive production of HA (n=8) leads to a 229% increase in Heavy Chain crosslinking compared to wild type littermates (n=8) ($p=0.001$). When the vessel wall undergoes atherosclerotic changes in ApoE-/- mice: the crosslinking increases by 403% ($p<0.001$) (n=8 per group). Based on these findings we suggest that the alteration in HA crosslinking is crucial to the enhanced mechanical stiffness and thus to the increase in atherosclerotic susceptibility.

P15.04 Dinah Sherzad Khatir

THE ROLE OF RENAL AND PERIPHERAL VASCULAR RESISTANCE IN THE PROGRESSION OF CHRONIC KIDNEY DISEASE (CKD)

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Chronic kidney disease (CKD) is often complicated by high blood pressure (BP). This condition is associated by structural remodeling of small resistance arteries in the entire body including the kidneys themselves in terms of reduced lumen diameter and increased wall thickness. BP reduction is very important for slowing the progression of CKD. While beta-blockers (BB) lower BP through reduction in cardiac output, calcium channel blockers (CCB) and angiotensin-converting enzyme-inhibitors (ACEi) reduce BP through vasodilatation and reduction of peripheral vascular resistance. In essential hypertension only the latter approach seems able to normalize structure of the resistance vessels. However, it remains unknown whether this also applies to hypertension due to renal disease.

The purpose of our study is therefore to compare antihypertensive treatment with a greater degree of vasodilation to a treatment regimen with less vasodilatation and investigate the effect on kidney function and various parameters of vascular function.

We aim to recruit 80 CKD patients (eGFR 15-60 ml/min and hypertension). Baseline examinations consist of 24 hour ambulatory BP measurement, ^{51}Cr-EDTA clearance, magnetic resonance imaging of the kidneys to evaluate size, blood flow and oxygen content and determination of resistance artery structure using forearm venous occlusion plethysmography. The patients are randomized to treatment with BB or CCB with both groups receiving ACEi and diuretics as needed. After 18 months the examinations will be repeated.

The primary endpoint is change in GFR, while secondary endpoints are changes in renal blood flow and resistance together with vascular parameters.

P15.05 Carsten Stengaard

THE ROLE OF BIOMARKER ANALYSIS IN THE PRE-HOSPITAL DIAGNOSIS AND TRIAGE OF HEART ATTACK PATIENTS (THE PRE-HAP STUDY)

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Introduction: In ST Elevation Myocardial Infarction, pre-hospital ECG diagnosis enables direct admission to Primary percutaneous intervention (P-PCI). This saves important time with improved outcome. However, if ST elevation is not present the AMI diagnosis is difficult to establish in the pre-hosptial setting. Current guidelines instruct that AMI patients without ST elevation (NSTEMI) must be admitted to a department of cardiology for diagnosis and planning of treatment. Yet some of these patients are high risk patients and may benefit from direct transfer for P-PCI. We are still awaiting the first randomised study evaluating acute P-PCI treatment for patients without ST elevation. One potential modality for pre-hospital identification of NSTEMI patients is pre-hospital biomarker analysis. In this study we hypothesise that pre-hospital Troponin T (TnT) analysis will identify the majority of AMI patients.

Methods: 1118 patients transported by ambulance suspected of AMI were included. A pre-hospital TnT analysis was performed. The blood sample was saved in a pre-hospital biobank. The AMI diagnosis will be determined by an endpoint committee. Data of mortality is obtained from the Danish Cause of death registry. Timing of pre-hospital and in-hospital TnT analysis is compared.

Evaluation: Diagnostic accuracy of the pre-hospital TnT analysis is evaluated by ROC curve analysis. Mortality stratified by quartiles of pre-hospital TnT is evaluated by Kaplan-Meier curves.

Results: 12.5% of the patients had a positive pre-hospital TnT analysis. This corresponds to the expected fraction. Endpoint evaluation is in process and needed for further analysis of the data.

P15.06 Anne Dorte Blankholm

MR ANGIOGRAPHY WITHOUT GADOLINIUM CONTRAST AGENTS COMPARED TO CT AND ULTRASOUND IN PATIENTS UNDERGOING KIDNEY TRANSPLANTATION. PRELIMINARY RESULTS.

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Purpose: To establish whether ultrasound (US), Computed Tomography (CT) or Magnetic Resonance Angiography (MRA) without contrast agents, or a combination of two of these methods, is sufficient in examinations prior to kidney transplantation.

Methods: Prior to kidney transplantation MRA examinations are evaluated versus US and CT all without contrast agents in examination prior to kidney transplantation. The agreement of the scanning methods is evaluated and

compared to surgery results. The latter are considered the golden standard.

Results: Forty patients were scanned. Only four have undergone transplantation and hence the golden standard is not yet part of the result. In 28 cases (70%) there was agreement between all the examination modalities, and in 12 cases (30%) there was disagreement. US was considered insufficient in 8 cases (20%). In 4 cases (10%) US was insufficient where occlusion or severe atherosclerosis was present on MRA or CT. Kappa values for US vs. CT: 0.60; absolute agreement 89%, Kappa for US vs. MR: 1; absolute agreement 100%; Kappa for CT vs. MR 0.73; absolute agreement 90%. In cases where US were insufficient, the Kappa for CT vs. MR was 0.78; absolute agreement: 88%.

Preliminary results show that none of the examination modalities alone were sufficient. US needed supplementary examination methods in 20% of cases. In CT calcifications were nicely visualized but stenoses were not. In MR stenoses can be identified but not calcifications.

Conclusions: The preliminary results indicate that a combination of CT and MR without contrast agents is sufficient for visualizing vessel anatomy before kidney transplantation. US was diagnostically weaker.

P15.07 Lau Brix

REAL-TIME MOVIE DISPLAY OF GASTRIC VENTRICLE MOVEMENT WITH MRI

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Background: Information of gastrointestinal motor function can be assessed in a variety of ways including gastric emptying scintigraphy, gastric barostat, barium based radiography and intraluminal manometry. This palette of techniques are either regarded as invasive, uncomfortable for the patient or utilize ionizing radiation. We have developed an MRI system that can visualize gastric emptying in real-time. The aim of the project was to test the MRI system in a group of healthy volunteers at satisfactory frame rates in absence of degrading image artifacts.

Methods: Ten healthy volunteers (two women and eight men; age 34±8 (24-47) years) drank approximately one liter of cold tap water to enhance image contrast of the gastric ventricle.

A Philips Achieva 1.5T MRI system was used and the images were acquired using the Golden Ratio method. The raw data stream was reconstructed on a graphics card and visualized in real-time on an external workstation. Furthermore, all raw data was saved for off-line image evaluation.

Results: Our real-time system acquired MRI movies of gastric ventricle movement at flicker free frame rates of up to 11 frames per second. The acquired movies had a better temporal and in-plane image resolution compared to standard vendor protocols.

Conclusion: Real-time acquisition and reconstruction using our system increases the temporal and in-plane resolution in gastric ventricle movies without compromising image quality in healthy volunteers. This study is a step toward using MRI for imaging of other moving organs (e.g. fetuses and intestines) and hereby overcoming some of the inherent problems with MRI being a time-consuming imaging modality.

P15.08 Janni Majgaard Jensen

URINARY BIOMARKERS FOR MEASUREMENT OF SODIUM- AND WATER CHANNEL ACTIVITY IN THE NEPHRON IN HEALTHY PERSONS AND PATIENTS WITH CHRONIC KIDNEY DISEASE. AN INTERVENTION STUDY WITH ISOTONIC AND HYPERTONIC NACL, THIAZIDE AND AMILORIDE.

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Background: Patients with chronic kidney disease (CKD) have a diminished capacity to excrete a sodium load. Biomarkers are now developed to measure the activity of transport channels reabsorbing water and sodium.

The purpose of this study is to measure renal biomarkers and gain knowledge of the renal mechanisms controlling sodium and water transport.

Design: Substudies 1 and 2 are randomised placebo-controlled, crossover studies of healthy subjects.

Substudy 3 is a case-controlled study of patients with CKD and healthy subjects.

Methods: In Substudy 1, subjects attend three examination days. On the examination day subjects receive an IV infusion with isotonic or hypertonic NaCl or glucose 5%. In Substudy 2, subjects attend three examination days. Five days prior to the examination day subjects receive treatment with 1.25 mg bendroflumethiazid, 5 mg amiloride or placebo, and on the examination day, they receive an IV infusion with hypertonic NaCl. In Substudy 3, subjects attend one examination day, and on the examination day they receive an IV infusion with hypertonic NaCl.

In all three subprojects the participants are on a standardised diet for four days prior to the examination.

Renal function and vasoactive hormones are measured prior, during and after infusion using renal clearance of ^{51}Cr-EDTA and radioimmunoassays, respectively. Urinary excretions of NCC, NKCC and ENaC$_\beta$ concentration will be measured to evaluate channel activity in the nephron.

Perspectives: This study is expected to contribute to increase the knowledge regarding pathophysiological mechanisms participating in the development and progression of diseases with abnormal water- and sodium balance

P15.09 Olga Kudryavtseva

THE ROLE OF L-TYPE VOLTAGE-DEPENDENT CALCIUM CHANNELS IN THE PHENOTYPIC EXPRESSION OF VASCULAR SMOOTH MUSCLE CELLS

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Intracellular Ca^{2+} plays dual roles in vascular smooth muscle cells (VSMCs). It mediates excitation-transcription coupling and activates transcriptional factors, such as CREB and NFAT. These transcription factors can affect the expression of contractile protein genes. Disturbance in contractile protein expression can lead to switch of VSMCs from a healthy contractile phenotype to a synthetic phenotype. Phenotypic switch is a hallmark of such pathological conditions, as atherosclerosis and pulmonary hypertension.

LTCCs are downregulated after phenotypic switch, but whether it is a cause or consequence of the process remains to be elucidated.

To address this question, we used a rat model in which the channels of interest were knocked down with siRNA in small mesenteric resistance arteries. The data indicated that VSMCs that lacked LTCCs underwent phenotypic switch. Firstly, the resting intracellular calcium level increased by 36% after LTCCs downregulation. Noteworthy, this increase in Ca^{2+} was not because of over expression of T and P/Q voltage-dependent calcium channels. Secondly, agonist and depolarization-induced force development were significantly decreased, while intracellular calcium reached the same level, as in control vessels. Thirdly, reduction in contractile-phenotype marker gene expression was observed. This suggests that LTCCs downregulation is a cause, rather than a consequence of phenotypic switch.

Next, I will investigate if increased store-operated calcium entry is responsible for the increase in intracellular Ca^{2+}. I will also immunohistochemically quantify transcriptional factors CREB and NFAT, which are affected by Ca^{2+} homeostasis.

P15.10 Morten Würtz

DOES THE ANTIPLATELET EFFECT OF ASPIRIN DECREASE DURING THE 24-HOUR DOSING INTERVAL?

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Introduction: Cardiovascular disease is the number one cause of death worldwide. Low-dose aspirin is given once daily to prevent cardiovascular events. We have previously shown, however, that some patients have an inadequate platelet response to aspirin, in particular patients with an increased platelet turnover. A higher frequency of acute coronary syndromes has been reported during the early hours of the day. Likewise, platelet reactivity is increased during these hours. Since most patients take their aspirin in the morning, these observations may reflect that the antiplatelet effect of aspirin decreases towards the end of the 24-hour dosing interval.

Hypothesis: The antiplatelet effect of aspirin is reduced at the end of the 24-hour dosing interval, in particular in individuals with an increased platelet

turnover.

Methods: A total of 210 individuals are included: 110 patients with stable coronary artery disease, 50 patients with previous definite stent thrombosis, and 50 healthy volunteers. All participants on aspirin mono-therapy (75 mg daily) for at least 7 days prior to blood sampling. Blood sampling is performed twice; 1 hour and 24 hours after aspirin ingestion. The antiplatelet effect of aspirin is evaluated by modern whole blood aggregometry using two different instruments (VerifyNow® and Multiplate®). Platelet turnover is evaluated by the immature platelet fraction and the immature platelet count assessed by flow cytometry. Compliance is evaluated by face-to-face interviews, pill-counting and serum thromboxane B_2 measurements.

P16.01 Michael Kanstrup Dahl

AMPLIFICATION OF RESPIRATORY INDUCED ARTERIAL PRESSURE VARIATIONS DURING SPONTANEOUS BREATHING – A METHOD TO ASSESS FLUID RESPONSIVENESS?

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INTRODUCTION: Assessment of hypovolemia and fluid responsiveness is often demanding. During controlled ventilation, increased arterial pressure variations have been shown to indicate fluid responsiveness. During spontaneous breathing these variations are minor and difficult to detect. We hypothesized that an inspiratory/expiratory resistor would amplify the intrathoracic pressure changes and the arterial pressure variations during spontaneous breathing.

METHODS: In eight, tracheotomized, anesthetized and spontaneously breathing pigs 30% of the blood volume was removed. They were breathing either through an inspiratory and/or an expiratory resistor (7.5 cmH_2O) or only through the tracheal tube. Hemodynamic and respiratory measurements were performed at hypo-, normo-, 20% hyper- and 40% hypervolemia. Normo- and hypervolemia was restored by a HES solution.

Statistics: Non-parametric tests and linear regression. Significance level: $p< 0.05$.

RESULTS: Stroke volume was significantly lower during hypovolemia. Values for systolic pressure variation (SPV) with expiratory resistor were 11 (9.12)% (median and interquartile range) during hypovolemia, 4 (2.5)% during normovolemia and 4 (2.5)% and 3 (2.4)% during 20% and 40% hypervolemia respectively. SPV without resistor were 5 (3.7)%, 2 (2.3)%, 2 (2.2)%, and 2 (1.3)%. There were statistical significant differences between the breathing modes at hypo- and 20% hypervolemia, and within the breathing modes between hypo- and normovolemia.

CONCLUSION: Arterial pressure variations were amplified during spontaneous breathing by use of an expiratory resistor, and were significantly increased during hypovolemia compares to normo- and hypervolemia.

P16.02 Sanne Bøjet Larsen

THE ASPIRIN PARADOX - ANTIPLATELET EFFECT OF ASPIRIN IS REDUCED IN PRIOR ASPIRIN USERS

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Introduction: Aspirin remainsthe firstchoice antiplatelet drug for coronary artery disease. Recent studies report that among patients with acute coronary syndromes, those already taking prophylactic aspirin had worse long-term outcomes. It remains unknown whether aspirin use before myocardial infarction (MI) is associated with a reduced antiplatelet effect of aspirin.

Aim: To investigate if the antiplatelet effect of aspirin differed between patients with previous MI with and without prior aspirin use at the time of acute MI.

Methods: We included 116 patients on chronic aspirin therapy who all had a history of previous MI: 59 with prior use of aspirin at the time of acute MI and 57 without prior use. Antiplatelet effect was assessed using turbidimetric optical detection (VerifyNow® Aspirin) and impedance aggregometry (Multiplate®) with arachidonic acid 1.0 mM and collagen 1.0 µg/mL as agonists. Compliance to aspirin was evaluated by serum thromboxane B_2.

Results: Platelet aggregation levels were higher among prior aspirin users than among prior non-users. This suggests a reduced antiplatelet effect among prior users. This finding was statistically significant when evaluated with VerifyNow® ($p<0.0001$) and with Multiplate®/collagen ($p=0.02$), but it could not be confirmed with arachidonic acid. Optimal compliance in the study population was confirmed by low serum thromboxane B_2levels.

Conclusions: Prior aspirin use at the time of acute MI was associated with higher aggregation levels among prior users compared with prior non-users. This indicates a reduced antiplatelet effect of aspirin in the acute phase of MI among patients already taking aspirin.

P16.03 Bent Roni Ranghøj Nielsen

SHORT TERM MANIPULATION OF INTRACELLULAR MYOCARDIAL LIPID CONTENT: EFFECT ON LEFT VENTRICULAR FUNCTION, CONTRACTILITY, EXERCISE CAPACITY AND OXYGEN CONSUMPTION IN HEART FAILURE PATIENTS WITH TYPE 2 DIABETES.

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Background: Increased levels of intracellular myocardial lipid is associated with reduced left ventricular (LV) function. We investigated whether short-term changes in circulating free fatty acids (FFA) and intracellular myocardial lipid affected LV contractility and cardiopulmonary exercise

capacity.

Methods: 20 heart failure patients (HF) (ejection fraction (EF)≤45%) NYHA class 2 or 3 with type 2 diabetes were studied in a randomized cross-over designed trial during 8 hours of high vs suppressed circulating FFA on two different occasions 1-6 weeks apart. Advanced echocardiography, cardiopulmonary exercise testing, MR Imaging (MRI) and MR proton-spectroscopy (MR-H1-S) were applied.

Results: 18 patients completed the protocol. Circulating FFA differed between the "suppressed" and "high FFA" arms (0.049±0.064 mmol/L vs 1.042±0.069 mmol/L; p<0.001). Intracellular myocardial lipid/water fraction determined by MR-H1-S increased from 0.78%±0.19 to 1.31%±0.25. No effect was found on ejection fraction, global strain, exercise capacity or peak oxygen consumption. However, resting double product and longitudinal mitral plane peak velocity S'max was higher during "High FFA" (7501±402 mmhg/min vs 8207±411 mmhg/min and 3.617±0.169 m/sec vs 3.846±0.198 m/sec respectively).

Conclusion: Short-term elevation of circulating FFA levels and intracellular myocardial lipid content does not depress left ventricular function, exercise capacity or peak oxygen consumption. Our findings argue against an acute myocardial lipotoxic effect in HF patients with DM-2.

P16.04 Nikolaj Grøndal

THE CARDIAC CYCLE IS A MAJOR CONTRIBUTOR TO VARIABILITY IN SIZE MEASUREMENTS OF ABDOMINAL AORTIC ANEURYSMS BY ULTRASOUND

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Abstract

Aim: To evaluate the impact of the cardiac cycle on ultrasound measurements of abdominal aortic aneurysm (AAA) diameters.

Methods: In total, 603 AAAs detected by screening were investigated with respect to the maximal systolic- and diastolic anterior-posterior aortic diameters during the cardiac cycle using recorded ultrasound video sequences.

Results: On average, the systolic AAA diameter was 41.60 mm, and the diastolic AAA diameter was 39.63 mm with a paired mean difference at 1.94 mm (p<0.0001). No association between aneurysmal size or the difference in systolic and diastolic size was noted.

The mean difference and variability between two observers, one measuring during peak-systole and the other measuring during end-diastole, was 2.65 mm and 2.21 mm, respectively, as compared to 0.86 mm and 1.52, respectively, when both were measured during the peak of systole. The intraobserver variability was 0.94 mm during systole, 1.18 mm during diastole and 1.94 mm when systole and diastole measurements were combined.

Conclusion: The lack of a standardised measurement of the AAA diameter

during the cardiac cycle is a potential major contributor to the variability in ultrasonography measurements.

P16.05 Anders Sommer Knudsen

EMPIRIC VERSUS IMAGING GUIDED LEFT VENTRICULAR LEAD PLACEMENT IN CARDIAC RESYNCHRONIZATION THERAPY: STUDY PROTOCOL SYNOPSIS

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Background

Cardiac resynchronization therapy (CRT) is an established therapy for selected heart failure patients. However, approximately 40% of patients do not respond clinically from the treatment. Retrospective studies have documented an improved response rate to CRT when the left ventricular (LV) lead is placed in the latest activated myocardial segment and in myocardial regions without scar tissue. Echocardiography, SPECT, and cardiac CT can visualize the latest activated LV segment, scar tissue, and cardiac venous anatomy. By integrating these cardiac imaging modalities prior to CRT implantation it is possible to perform LV lead placement targeted to the site of latest myocardial activation without scar tissue.

Aim and Hypothesis

We aim to investigate if LV lead placement guided by echocardiography, SPECT, and cardiac CT improves response rate to CRT. We hypothesize that this approach can increase the response rate to 80%

Methods

A total of 190 consecutive patients meeting the criteria for CRT are included in a prospective, double-blinded, randomized trial to LV lead positioning either guided by cardiac imaging or using standard clinical routine placing the LV lead in the posterior-lateral region.

Patients are followed-up in six months. The primary endpoint is response to CRT defined as a combination of survival, free of hospitalization for heart failure, and improved functional status. Secondary endpoints include changes of LV function and complications.

Perspective

No prospective randomized trials have previously investigated the effect of imaging guided LV lead positioning on the response rate to CRT. This study has the potential to increase response rate to CRT.

P16.06 June Anita Ejlersen

2D STRAIN ANALYSIS IN PATIENTS WITH REDUCED IMAGE QUALITY ON ECHOCARDIOGRAMS: EFFECT OF MICROBUBBLE CONTRAST (MBC) ON SEGMENTAL TRACKING

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2Dstrain based on speckle tracking is used for quantification of left ventricle deformation. We have previously shown that speckle tracking is impaired in patients with acceptable image quality when MBC is present in the circulation. Our purpose was to assess how MBC affects 2Dstrain analysis in patients with reduced image quality.

Methods

At baseline, during, 3, and 7 minutes after MBC infusion, the 3 standard apical loops were recorded and analysed (EchoPac, GE) twice on different days. All analyses were performed blind to each other. Tracking quality (TQ) was defined as the percentage of successfully tracked segments. Changes over time were analysed as repeated measurements by univariate ANOVA. Reproducibility of peak systolic segmental strain was assessed by the Bland Altman method, expressed as the coefficient of reproducibility (COR) and compared with F-tests.

Results

Twenty nine consecutive patients with stable angina and normal echocardiograms were included and divided in two groups: Baseline TQ<80% (10 patients) and baseline TQ≥80% (19 patients). TQ in the following is expressed as group mean (sd) at baseline, during, 3, and 7 minutes after MBC infusion. TQ<80% group: 59% (15%), 66% (13%), 72% (16%) and 75% (14%), p=0.002. TQ≥80% group: 92% (6%), 86% (12%), 93% (9%) and 93% (7%), p=0.008. Baseline strain was similar in the two groups (p=0.77). For the TQ<80% group, strain COR was 3.9%, 9.9%*, 8.7%* and 5.7%* at the 4 time points. For the TQ>80% group, COR was 4.4%, 6.1%*, 4.1% and 4.1% (*p<0.01 compared to group baseline value).

Conclusion

MBC seems to improve TQ in patients with reduced image quality but the reproducibility of segmental strain is compromised.

P16.07 Anders Jorsal CARDIAC AND METABOLIC EFFECTS OF GLP-1 TREATMENT IN PATIENTS WITH CHRONIC HEART FAILURE

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Background

Glucagon-like peptide 1 (GLP-1) is a naturally existing hormone, which is secreted from the incretine system. A beneficial effect of GLP-1 on cardiac function has recently been suggested in small, non-randomised clinical studies, demonstrating improved left ventricular ejection fraction (LVEF) in both diabetic and non-diabetic patients with chronic heart failure. Liraglutide (Victoza®) is a GLP-1-analogue developed for the treatment of type 2 diabetes (T2D). However, the impact of Liraglutide on cardiac function has not previously been investigated.

Hypothesis

Liraglutide will improve the left ventricular systolic and diastolic function in CHF patients with and without T2D.

Design and methods

An investigator initiated, multi-centre, randomised, double-blind, parallel, placebo controlled intervention trial.

A total of 240 patients with systolic CHF (50% with T2D) will be randomised to either subcutaneous injection of Liraglutide 1.8 mg once daily or matching placebo for 24 weeks. The effect of Liraglutide on left ventricular systolic and diastolic function will be evaluated by advanced echocardiography using 2D, 3D, and tissue Doppler imaging.

Perspectives

Potentially Liraglutide can improve heart function substantially, thus changing the prognosis of CHF patients worldwide.

P16.08 Jo Bønding Andreasen

EX-VIVO RESPONSE TO BLOOD PRODUCTS AND HAEMOSTATIC AGENTS IN WHOLE BLOOD COAGULATION AFTER CARDIAC SURGERY IN CHILDREN

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Introduction: Bleeding complications after cardiac surgery are of particular importance among children because they are more prone to volume overload. To optimize haemostatic intervention, the coagulopathy needs to be characterized, and knowledge about the effect of blood products and haemostatic agents is needed. The aim was to investigate the effect after ex vivo addition of blood products and haemostatic agents.

Methods: Coagulation profiles were evaluated by thromboelastometry (ROTEM®) in 54 children before and immediately after heart surgery. The haemostatic potential of various factor concentrates (fibrinogen concentrate, recombinant factor VIIa, and factor XIII), fresh frozen plasma, pooled platelets, and tranexamic acid was investigated.

Results: After surgery, the coagulation profiles revealed significantly prolonged clotting time (CT) (P=0.008), reduced clot propagation (MaxVel) (P < 0.01) and reduced whole blood clot stability (MCF) (P < 0.001). Addition of pooled platelets fully reversed the coagulopathy (CT; MaxVel, p< 0,001; MCF, p<0.05), which was also seen after addition of recombinant factor VIIa, although less pronounced. Addition of fibrinogen concentrate, fresh frozen plasma, and tranexamic acid improved clot stability significantly (MCF, p< 0.01).

Conclusions: Whole blood coagulation was significantly impaired after cardiac surgery in children. Ex vivo studies showed a total reversal of the coagulopathy after addition of pooled platelets and significantly improved clot stability after addition of fibrinogen concentrate, fresh frozen plasma,

and tranexamic acid.

P16.09 Thomas Andersen Rix

VALIDITY OF THE DIAGNOSES ATRIAL FIBRILLATION AND ATRIAL FLUTTER IN THE DANISH NATIONAL PATIENT REGISTRY

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Objectives: To assess the validity of the diagnoses atrial fibrillation (AF) and atrial flutter (AFL) for men and women recorded in the Danish National Patient Registry, and to assess the relative distribution of AF and AFL in the cohort.

Design: Review of medical records for incident cases of AF and/or AFL in the Diet, Cancer and Health cohort study.

Results: The positive predictive value of the combined diagnosis AF and/or AFL was 92.6% (95% CI 88.8%; 95.2%) with no significant difference between sexes (men 93.7%, women 90.9%). The proportion of AFL either alone or in combination with AF was significantly higher in men compared to in women (13.5% vs. 5.5%, p=0.03).

Conclusions: This study confirms earlier reports that the validity of the diagnosis AF and/or AFL is high and may be used for registry-based studies. A specified diagnosis of AFL was rarely used and was not reliable to distinguish between cases of AF and AFL.

P16.10 Morten Engholm Pedersen

VASOACTIVE EFFECTS OF CYSTAMINE

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Essential hypertension (EH) is associated with inward eutrophic remodelling of resistance arteries. Alterations are observed in small artery structure with a narrowing of the lumen diameter and increase in media: lumen ratio. The ubiquitous enzyme tissue-Transglutaminase (tTG) has been shown to play a part in this process. Cystamine (CYS), an organic disulfide and competitive inhibitor of tTG, has been demonstrated to inhibit small artery remodelling in rats. In this study we investigate the vasoactive effects of cystamine in rats. Small mesenteric arteries were mounted in wire-myographs for simultaneous measurements of $[Ca^{2+}]_i$ and force. Concentration response relationships were performed with or without presence of CYS. CYS reduced the response to phenylephrine (Phe), 5-HT and U46619 in a concentration dependent manner. No significant effect was observed on K^+PSS dose response curves with CYS in concentrations up to 10^{-4} M. CYS 10-3 M caused complete inhibition of all agonist induced responses. In Phe precontracted vessels CYS 10-4 M caused a transient fall (max at 11 ± 1.8 min) in $[Ca^{2+}]_i$ and active tension, followed by a rise in Ca^{2+}-influx and tension. In vessels precontracted with K^+PSS CYS 10^{-4} M caused a significant reduction in active tension without altering $[Ca2+]_i$ indicating a Ca^{2+}-desensitization effect of cystamine.
We conclude that the vasoactive effects of CYS involve concentration-dependent inhibition of agonist induced contractions, through a specific mechanism rather than non-specific blocking of Ca^{2+}-channels. We speculate that this may involve Ca^{2+}-desensitization. The possible role of these

findings in remodelling remains to be established.

P16.11 Jonas Agerlund Povlsen

ISCHAEMIC CARDIOPROTECTION: PATHOGENIC MECHANISM IN TYPE 2 DIABETES MELLITUS?

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HYPOTHESIS

Diabetes induces partial resistance to ischaemic cardioprotection. Inhibition of the malate-aspartate shuttle (MAS) during ischaemia mediates cardioprotection similar to local preconditioning and downregulates myocardial glucose oxidation. We hypothesized that ischaemic conditioning with inhibition of MAS operates as a stress response at onset of diabetes, and makes the heart insensitive to additional protection. Cardioprotection (infarct size (IS), hemodynamic recovery) was examined in relation to development of hyperglycemia in type 2 diabetic (T2DM) rats.

METHODS

Hearts of Zucker diabetic fatty rats (fa/fa) and matched heterozygote controls (fa/+) were studied at prediabetic state (6 wks of age), at onset of T2DM (12 wks) and in late T2DM (24 wks). Isolated perfused hearts (Langendorff) were exposed to 40min ischaemia/120min reperfusion. Myocardial metabolism was assessed by glucose tracer kinetics and myocardial microdialysis. MAS activity was elucidated by gene/protein expression of carrier proteins (citrin,aralar), enzymes (ASAT) and glutamate transporters (EAAT1).

RESULTS

The homozygote diabetic phenotype was associated with a non-significant increase in IS at prediabetic state, reduced IS at onset of T2DM and increased IS in long lasting T2DM. Metabolic/genomic/proteomic findings suggest a regulatory role of MAS on cardioprotection in diabetic hearts.

CONCLUSION

The stress-response at onset of diabetes includes activated ischaemic cardioprotection. Regulation of metabolic flux of MAS may be an underlying mechanism. Our findings explain previous conflicting results on ischemia reperfusion injury in T2DM.

P16.12 Rozh Husain Al-Mashhadi

ADVANCED ATHEROSCLEROSIS IN TRANSGENIC HYPERCHOLESTEROLEMIC YUCATAN MINIPIGS

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Institute of Clinical Medicine

Background: The pursue of animal models of atherosclerosis has spawned the creation of several mammalian models in mice, rats and pigs. In contrast to rodents, pigs develop human- like atherosclerotic lesions, bear close

resemblance to humans in terms of cardiovascular anatomy and physiology and have an adult size comparable to that of man.

Our research group has recently created a transgenic Yucatan minipig model exhibiting liver specific expression of the human proprotein convertase subtilisin kexin type 9 (PCSK9) gain-of-function mutant, D374Y-PCSK9. The transgene inactives the low density lipoprotein (LDL) receptors and thus increases plasma LDL cholesterol.

We aim to test the hypothesis that dietary cholesterol challenge increases plasma cholesterol and augmentes atherosclerosis in D374Y-PCSK9 transgenic minipigs compared to their wildtype siblings. We further hypothesize that diabetes mellitus and hypertension exacerbate the development of atherosclerosis in this transgenic model.

Methods: Eight wildtype (WT) and 24 transgenic minipigs will be fed a 20% saturated fat and 2% cholesterol diet for 45 weeks. The transgenic minipigs will be divided into 3 groups: a control group (C) a diabetes group (D) and a hypertension group (H). Diabetes will be induced by injection of the pancreatic b-cell toxin streptozotocin. Hypertension will be induced by aortic coarctation as described by Fossum et al, 2003. At the end of the study, the extent of atherosclerosis will be examined by positron emission tomography (PET), magnetic resonance imaging (MRI) and optical coherence tomography (OCT). Finally the major vessels will be explanted for detailed histological examination.

P17.01 Sanne Kjær Vandborg

MEMORY AND EXECUTIVE FUNCTIONS IN PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER ARE NOT ASSOCIATED WITH OUTCOME OF COGNITIVE BEHAVIORAL THERAPY

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Obsessive Compulsive Disorder (OCD) is a debilitating neuropsychiatric disorder characterized by intrusive, recurrent and distressful thoughts (obsessions) and repetitive behaviors (compulsions). Guideline recommendations for treatment are Cognitive Behavioral Therapy (CBT) and/or treatment with Serotonin Reuptake Inhibitors (SRI). However, up to 50% of OCD-patients do not have a clinically significant outcome of the current treatment approaches. Previous studies have found that some OCD-patients have cognitive dysfunctions compared to healthy controls, primarily poorer visuo-spatial memory and poorer executive functions, such as mental set shifting, mental inhibition and planning. Theoretically it seems plausible that poor memory and poor executive functions could limit patients' ability to comprehend and remember things discussed in psychotherapy. A main object of this PhD project is to investigate whether OCD-patients with poor outcome of CBT (non-responders) have poorer baseline memory and poorer executive functions than OCD-patients with good treatment outcome (responders). 42 adult OCD-patients have been assessed before and after 16 weekly CBT-sessions at Clinic for OCD and Anxiety Disorders, Aarhus

University Hospital Risskov. Patients were, among other things, assessed with neuropsychological tests of memory and executive functions, and with a semi-structured interview to establish symptom severity and treatment outcome. Results show that non-responders do not have poorer memory or poorer executive functions than responders. Based on these results, one may conclude that OCD-patients should be offered CBT regardless of their baseline memory and executive functions

P17.02 Ditte Olsen SORLA REGULATES GDNF SIGNALLING THROUGH RETROGRADE SORTING OF GDNF AND GFR&ALPHA;1

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To remain alive, neurons require constant survival signals from neighboring cells. Glial cell line-derived neurotrophic factor (GDNF) is a potent survival factor for a number of cell types, notably dopaminergic neurons. GDNF signalling is mediated via its interaction with two receptors. The GDNF dimer first binds its primary receptor GFRα1, which serves to concentrate the ligand on the cell membrane, and the resulting 2:2 complex subsequently interact with the receptor tyrosine kinase Ret to form a signalling complex. We have found that SorLA selectively binds GDNF but not other GDNF family ligands. In addition, SorLA forms a complex with the GDNF-GFRα1, resulting in retrograde sorting of both GDNF and GFRα1 from the cell surface. Through this mechanism, SorLA negatively modulates differentiation, proliferation, and survival of neuroblastoma cells and of primary dopaminergic neurons. Furthermore, SorLA knockout mice display hyperactivity, and altered response to amphetamine, strongly suggesting that SorLA is critical for dopaminergic functionality in vivo.

P17.03 Line Bie Mertz ANGELMAN SYNDROME: GENOTYPE COMPARED WITH PHENOTYPE.

L.G.B. Mertz

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Angelman syndrome:

Angelman syndrome (AS) is due to an abnormality on chromosome 15.

Characteristics of AS include severe intellectual disability and developmental delay, lack of speech, happy behaviour, ataxia, craniofacial dysmorphia, autistic behaviour, and epileptic seizures.

The incidence of AS is estimated to be between 1 in 10,000 and 1 in 20,000.

Genetic cause of Angelman syndrome:

·A maternal deletion of chromosome 15q11-13

·UBE3A mutations (5-10%)

·Uniparental disomy (UPD) (5%)

·Imprinting defects (5%)

·Unknown cause (10%)

AS is a classic example of genetic imprinting: If this happens on the paternally inherited chromosome 15 in exactly the same place a completely different syndrome occurs: Prader Willi syndrome, which is characterised by hypotonia, insatiable appetite, obesity, and hypogonadism.

Methods:

Genotype:

A blood sample from each participant will be examined by the oligoarrayCGH-(comparative genomic hybridization) technique.

Phenotype:

The severity of epileptic seizures is assessed by a questionaire answered by the parents and by information from the medical journal.

The severity of autism in each child is examined by ADOS (autism diagnostic observation schedule) and the general developmental stage by Mullen test.

Anthropometrical measures are collected from the paediatric department, the family doctors and the health visitors.

Specific aims:

The specific aim of this study is to look at the association between genotype and phenotype in Angelman syndrome. We will look especially at deletion size and location and how they correlate with the severity of epileptic seizures, autistic behaviour, and growth impairment.

P17.04 Marie Louise Schmitz

LONG-TERM OUTCOME IN ISCHEMIC STROKE PATIENTS TREATED WITH TROMBOLYSIS IN DENMARK: A NATIONWIDE FOLLOW-UP STUDY

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Background: Ischemic stroke is a major cause of death and disability world-wide. Acute treatment with intravenous trombolysis has been widely used during the last decade and reduces the risk of disabilities in ischemic stroke patients. However, patients with ischemic stroke have an increased risk of new cardiovascular events and death. Accurate data on long-term outcome in patients treated with trombolysis are important. To date, however, studies with follow-up for longer than three months are scarce.

Aim: To examine the long-term outcome (i.e. more than one year), including mortality and risk of myocardial infarction and recurrent stroke in patients treated with trombolysis. To compare the results with long-term outcome in

ischemic stroke patients not treated with trombolysis and the general population.

Methods: We are currently conducting a nationwide population-based follow-up study among all Danish patients treated with trombolysis due to first time ischemic stroke in the period 2004-2010, approximately 2000 patients. Data on outcomes are obtained from the Danish National Indicator Project, the Danish Civil Registration System and the National Registry of Patients. Comparisons with matched non-trombolysis treated ischemic stroke patients and matched persons from the general population, respectively, will be done using multivariable Cox's proportional hazards regression.

Results: Our results are pending.

P17.05 Lise Neerup-Jensen NEUROPATHY AND PAIN FOLLOWING DOCETAXEL AND OXALIPLATIN

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Background: Several patients develop peripheral neuropathy and pain after adjuvant chemotherapy due to neurotoxicity. Chemotherapeutics known to be neurotoxic include docetaxel, which is used in the treatment of high-risk breast cancer, and oxaliplatin, which used in the treatment of high-risk colorectal cancer. This neurotoxicity is a dose-limiting side effect. This is a major problem because chemotherapy increases recovery and survival. Unknown aspects of chemotherapy-induced neuropathies: Epidemiological aspects, risk factors for neuropathy, mechanisms of neuropathy and neuropathic pain, impact on quality of life and treatment.

Methods: Study 1: A prospective self-administered questionnaire study of 400 patients. Patients will be asked to fill out a detailed questionnaire about symptoms of neuropathy and pain, dysaesthesia, paraesthesia and quality of life at baseline, twice during treatment and 12 months after treatment. Study 2: A clinical prospective study examining patients with acute neuropathy and cold allodynia. Study 3: A clinical study with thorough clinical examinations of 20 patients in each chemotherapy group with persisting pain >6 months after adjuvant chemotherapy treatment. This will include a detailed medical history, a neurological examination, QST, questionnaires, thermal grill illusion, skin biopsies, nerve conduction velocity and examination with laser evoked potential.

Conclusion: This PhD project aims to determine the frequency, risk factors, prognosis, characteristics and mechanisms of neuropathy and neuropathic pain after chemotherapy. Furthermore, the aim is to describe the somatosensory profile and understand the mechanisms of cold allodynia

P17.06 Søren Dinesen Østergaard THE VALIDITY OF THE SEVERITY-PSYCHOSIS HYPOTHESIS IN DEPRESSION

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Background: The severity-psychosis hypothesis in depression assumes that psychosis will develop if a depression becomes sufficiently severe. Accordingly, psychotic depression is classified as a sybtype of severe depression in the current diagnostic classification systems. The aim of this study was to detect potential differences in the symptom profile of psychotic- (PD) and non-psychotic depression (non-PD) and to determine whether the severity of depression and psychosis correlate in accordance with the severity-psychosis hypothesis.

Methods: Quantitative analysis of Health of the Nation Outcome Scales (HoNOS) scores from all patients admitted to a Danish general psychiatric hospital between 2000 and 2010 with a diagnosis of severe depressive episode.

Results: A total of 357 patients with severe depression, of which 125 (35%) were of the psychotic subtype, formed the study sample. Mean HoNOS scores at admission differed significantly between patients with non-PD and PD on the items hallucinations and delusions (non-PD=0.33 vs. PD=1.37, $p<0.001$), aggression (non-PD=0.20 vs. PD=0.36, $p=0.044$) and on the total score (non-PD=10.55 vs. PD=11.87, $p=0.024$). The HoNOS scores on the two items “depression” and “hallucinations and delusions” were very weakly correlated (Spearman coefficient=0.12).

Conclusions: The results suggest that the severity of depression is not to the key determinant for the development of psychosis and offers further support to the hypothesis that the psychotic- and non-psychotic subtypes of depression may in fact be different clinical syndromes. This should be considered in the upcoming revisions of the diagnostic classification systems.

P17.07 Nicolai Ladegaard

SOCIAL COGNITIVE DEFICITS IN DEPRESSION

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Depressive disorders are frequently associated with significant and pervasive impairments in social functioning. Consequently, examining the social-cognitive grounds for social functioning has considerable potential to improve our understanding of depression. By social cognition we refer to the implicit and explicit act of interpreting the actions of oneself and others on the basis of perceptual cues and intentional mental states.

Three groups will participate:

A. Patients with chronic major depressive disorder. B. Patients experiencing their first major depressive episode. C. Healthy controls.

The investigation is comprised of two studies:

Study I: A comparative study encompassing the two patient-groups. The study will investigate the significance of multiple episodes along with symptom severity and chronicity in relation to individual social-cognitive capacity.

Study II: A controlled follow-up study assessing first time depressed patients prior to enrolment in a structured treatment program over a period of 6 months. Patients reaching full remission will be re-tested 6 months after remission. Through this design we wish to investigate whether social cognition is remediated through full remission from depression. Healthy subjects will tested twice with a 6 month gab to serve as controls for the test group.

Finally, we wish to investigate any associations between social cognitive measures and a basic neurocognitive assessment (attention, memory, learning, planning).

Primary measures: Metacognitive Assessment Scale (MAS), The Awareness of Social Inference Test (TASIT), Triangle Animation Task and Cambridge Neuropsychological Test Automated Battery (CANTAB).

P17.08 Eugenio Gutierrez Jimenez

BRAIN BLOOD FLOW PATTERNS IN ALZHEIMER'S DISEASE

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Introduction: The vascular hypothesis of Alzheimer's disease suggests that microvascular pathology and cerebral hypoperfusion may trigger cognitive and degenerative changes. Capillary transit time heterogeneity (CTTH) is crucial in oxygen extraction at the neurovascular unit. It is suggested that pericytes contract and dilate capillaries, therefore having a crucial role in the regulation of capillary transit time dynamics and extraction of oxygen. Loss of pericytes around brain microvessels impair brain perfusion, disturbs vasoreactivity, and induces pathological blood brain barrier (BBB) leakiness. The microvascular failure (i.e. increase CTTH) triggers an estate of high oxidative stress, up-regulation of secretases as well as a failure in the homeostasis of beta-amyloid by the BBB.

Objective: To describe the pericyte role in neurovascular and capillary flow regulation and the effect of the microvascular failure (increased CTTH) in the development and evolution of Alzheimer's disease.

Material and Methods: Adult β-actin-GFP transgenic mice will be used. Pericytes will be identified by morphology and localization. Linear scans, using two-photon microscopy will be performed at several capillaries to get blood flow measurements. Using two-photon phosphorescence lifetime microscopy and an oxygen probe, PO2 will be measured to detect eythrocite-associated transients in oxygen and evaluate the patterns before and after stimulus (heterogenity/homogeneity). To evaluate the role of different flow patterns in AD, the same approach described above will be performed, comparing wild type mice with the animal model APP(swe)/PS1DE9 for Alzheimer's disease at different ages.

P17.09 Zita Dósa

EFFECT OF PRENATAL CORTICOSTEROID EXPOSURE ON THE GABAERGIC INHIBITION IN RAT HIPPOCAMPUS

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Prenatal stress is believed to lead to the development of mental illnesses in humans, including major depression. Animal studies show cognitive, behavioral, and psychological abnormalities in different prenatal stress animal models. Exposure to restraint stress during pregnancy leads to elevated maternal plasma glucocorticoids (GC) in rats, which may influence the developing brain in offspring. The hippocampus, part of the limbic system, is particularly sensitive to the early stress–induced elevation in endogenous GCs.

In this study, we examined the electrophysiological properties of the GABAergic inhibition in the hippocampus using young or adult offspring of rat dams (Sprague Dawley) exposed to dexamethasone (DEX), a synthetic GC, during the last week of gestation (150 μg/kg/day). These rats show depressive-like behavior, and the GABAergic system is proposed to be involved in the pathophysiology of depression. Whole-cell patch-clamp recordings were performed from dentate granule cells of brain slices, to examine the spontaneous and evoked $GABA_A$ receptor mediated phasic inhibition. In 4-week-old rats there was a significant decrease in the frequency and rise time of the spontaneous inhibitory postsynaptic current (IPSC), while the action potential independent miniature IPSCs were unchanged. We also recorded evoked IPSCs by extracellular paired-pulse stimulation. In DEX rats, we observed a significantly higher paired-pulse ratio compared to controls. Our results demonstrate that there is a dysfunction in the limbic GABAergic inhibitory system in rats exposed to prenatal dexamethasone, which may contribute to the pathophysiology of depressive-like behavior in adulthood.

P17.10 Karen Lund

PLACEBO RESPONSE IN ANALGESIC TREATMENT: EXPERIMENTAL AND CLINICAL

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Background:

Medical treatment of neuropathic pain remains difficult, although anticonvulsants, antidepressants and opioids have been shown to have some effect. In recent years, however, large clinical trials have failed to demonstrate effectiveness of analgesics on neuropathic pain, and one explanation could be very large placebo responses. The effect size of a treatment consists of an active component and a placebo component, and

the two components are considered to be additive. Recent studies suggest that this might not be true.

Methods:

In a randomized, double-blind, placebo-controlled, crossover study with oxcarbazepine of patients with peripheral neuropathic pain, we will test two hypotheses: 1) High pain intensity and pain variability in the baseline period and few prior analgesic treatments and side effects are associated with a larger placebo response. 2) High expectations and positive emotions and low levels of anxiety, depressive thoughts, catastrophizing and the personality trait neuroticism will produce a larger placebo response.

In an experimental study of healthy volunteers with experimental pain in the masseter muscle induced by injections of hypertonic saline, two hypotheses are also put forward: 1) The effect of an active treatment and a placebo treatment is not additive. 2) High levels of suggestibility, absorption and expectations of pain reduction will generate a large placebo effect. In this study an open/hidden design will be used.

Purpose:

The aim of this PhD project is to find predictors of placebo responses in patients with peripheral neuropathic pain and to estimate the size and predictors of a placebo effect in healthy subjects.

P18.01 René Ernst Nielsen

NEUROLEPTIC MALIGNANT SYNDROME – AN ELEVEN YEAR LONGITUDINAL CASE-CONTROL STUDY

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Neuroleptic malignant syndrome (NMS) is a rare and potentially fatal disorder, with a not fully explained biological mechanism of action. NMS is characterized by fever, parkinsonism, autonomic instability, mental status alterations, leukocytosis and increased creatinine phosphokinase. To investigate factors associated with NMS, we did a longitudinal register linkage case-control study in Danish health care registers covering the period 1996 – 2007 and identified among 224,372 patients diagnosed with organic, psychotic, affective or neurotic diagnosis 83 cases of NMS, equivalent to an occurrence of 0.04%. Second generation antipsychotics treatment in the three months preceding admission increased NMS risk (OR 4.66 95%-CI: 1.96-11.10) as well as first generation (FGA) high potency (OR 23.41 95%-CI: 5.29-103.61), FGA mid potency (OR 4.81 95%-CI: 1.96-11.79), and depot antipsychotic drugs (OR 4.53 95%-CI: 1.60-12.80). Benzodiazepines (OR 3.43 95%-CI: 1.68-12.80) also increased the risk of NMS. NMS was associated with an increased mortality HR 1.88 (1.19-2.98) in cases compared with sex, age and diagnosis matched controls, but no significant difference in mortality between cases and controls was observed after the initial 30 days (p =0.266). The occurrence of NMS is low, and the prediction of NMS is difficult. Previous treatment with FGAs, SGAs and benzodiazepines were identified as risk factors for developing NMS. NMS increased mortality within 30 days after NMS.

P18.02 Eva Hauge

TOPICAL VALRUBICIN APPLICATION REDUCES TPA-INDUCED SKIN INFLAMMATION IN A MURINE MODEL

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Valrubicin belongs to a family of cytostatic anthracyclines, where it excels by its lack of toxicity by contact. Currently, it is approved solely for the treatment of bladder cancer. The availability of a cream formulation has provided the possibility for topical treatment of hyperproliferative skin diseases. Previously, we have demonstrated that valrubicin treats psoriasis in a xenograft transplantation model, and inhibits tumor development in a skin carcinogenesis model. Psoriasis and non-melanoma skin cancer are characterized by both keratinocyte hyperproliferation and inflammation. We have demonstrated that valrubicin explicates its effect by decreasing proliferation of keratinocytes; however, its effect on inflammation is still unknown. The aim of the present study was to investigate the effects of valrubicin on skin inflammation in vivo. For this purpose we employed the 12-O-tetradecanoylphorbol 13-acetate (TPA) induced irritant contact dermatitis model, where valrubicin treatment was applied topically 30 min post challenge. The inflammatory response was determined by ear thickness, myeloperoxidase activity, and histology; mRNA and protein expression of interleukin (IL)-1β and IL-6 was determined by qRT-PCR and ELISA. Valrubicin significantly reduced the inflammatory response, as seen by reduced ear edema and reduced number of infiltrating neutrophils. This was paralleled by a decrease in expression of the inflammatory cytokines IL-1β and IL-6. The present data prove an anti-inflammatory effect of valrubicin, and may suggest an interesting new role for valrubicin in other debilitating inflammatory skin diseases.

P18.03 Sarah Holmboe

ACUTE INOTROPIC EFFECTS OF ILOPROST IN THE PRESSURE OVERLOADED, HYPERTROPHIC AND FAILING RIGHT HEART

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Background: Right heart failure is the ultimate cause of death in patients suffering from pulmonary artery hypertension (PAH). Prostacyclin is a vasodilator known to improve right ventricular (RV) function in patients with PAH. Whether this effect is secondary to its pulmonary vasodilatory actions or a direct effect on the RV is still to be investigated.

Aim: We want to investigate the acute and direct effects of the prostacyclin analogue iloprost in the pressure overloaded, hypertrophic and failing right heart.

Methods: A dose-response experiment was carried out on rats in vivo and in the isolated perfused heart to determine relevant treatment doses. Rats are currently randomised to monocrotaline injection (60 mg/kg) (n=8), to induce pulmonary endothelial growth and PAH, pulmonary trunk banding (n=8), to induce isolated RV hypertrophy and –failure, or sham operation

(n=8). After RV hypertrophy and failure have been established, they are treated intravenously with vehicle, iloprost 10 ng/kg/min or iloprost 100 ng/kg/min. The acute effects on the RV will be evaluated by MRI measuring cardiac output and ejection fraction, pressure catheter measuring blood pressure and RV pressure, and echocardiography measuring TAPSE as an estimate of RV function.

Preliminary results: Dose-response studies showed no effect of iloprost on TAPSE or RV pressures. There was an increase in coronary artery flow (baseline vs $iloprost_{2000\ pg/mL}$,13.95 ±2.948 vs 15.70 ±2.898, mL/min, $p<0.001$) in the isolated perfused heart.

Perspectives: This study will investigate if the prostacyclin analogue iloprost exerts direct functional/hemodynamic effects on the hypertrophic and failing right rat heart.

P18.04 Konstantin Kazankov

SOLUBLE CD163, A MARKER OF ACTIVATED MACROPHAGES, AS A PROGNOSTIC MARKER IN NON-ALCOHOLIC FATTY LIVER DISEASE

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Obesity is associated with non-alcoholic fatty liver disease (NAFLD) and steatohepatitis (NASH) and liver macrophages are activated in obesity and may play a central role in the development of NAFLD/ NASH. There is a need to develop and validate simple, reproducible, non-invasive tests that accurately distinguish NASH from NAFLD and determine disease stage and grade, as at this point it can only be done by liver biopsy. An important question is whether these biomarkers can be used to evaluate the effect of intervention in the individual. If the macrophage marker sCD163 follows the disease course and responds to effective treatment or life-style intervention, sCD163 can be used to individually tailor the most efficient intervention.

We wish to study sCD163 levels in different Danish and international cohorts of children and adults with NAFLD/NASH and examine associations with parameters of the metabolic syndrome. Further, we want to study sCD163 during treatment of obesity and NAFLD/NASH (life-style intervention, bariatric surgery etc.).

We expect to prove that sCD163 may be used as a biomarker in NAFDL/NASH associated with more progressive diseases. Further, we expect sCD163 to be a prognostic marker during intervention of NAFLD/NASH and obesity.

P18.05 Kasper Pryds

CHRONIC REMOTE ISCHEMIC PRECONDITIONING

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Background: Remote ischemic preconditioning (rIPC) is a well-described and powerful method to achieve myocardial protection against ischemia-reperfusion (I/R) injury. rIPC has a biphasic protective effect: the acute protection wanes after several hours but protective effects return 24-72 h later.

Objective: Our primary objective is to assess whether repeated episodes of rIPC induces a distinct and durable protection against I/R injury and compare this with first and second window preconditioning effects.

Methods: The study is a randomised, single blinded parallel group study. 20 healthy volunteers are randomised to either a single episode of rIPC or daily rIPC for 14 days. The changes in forearm endothelial function before and after 20 min ischemia and 15 min reperfusion will be assessed on two occasions by venous occlusion plethysmography.

The statistical analysis will be performed using student's t-test, one-way ANOVA and two-way repeated measurement (two-way ANOVA) with post hoc multiple comparison test.

Conclusion: It is our intention to explore the various effects of these later windows of rIPC in vivo.

Prospective: As ischemic episodes, i.e. AMI are unpredictable, daily rIPC, should it be effective, would provide an attractive prophylactic strategy to mitigate the harm from these acute conditions.

P18.06 Mohit Kothari MOTIVATIONAL FACTORS: INFLUENCES MOTOR BEHAVIORAL LEARNING

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Objectives: The role of motivation in learning has not been systematically examined in the tongue motor learning literature. We investigated the influence of motivational factors and gender on the degree of improvement of training success during complex tongue training paradigm using Tongue Drive System (TDS). We also compared subject-based reports of fun, pain, fatigue and motivation between groups.

Methods: 48 healthy subjects were randomized into three groups (16 subjects in each group). Each subject was asked to use a complex tongue training paradigm (TDS) for 1 h. In 2/3 groups, a motivational factor was introduced (monetary reward vs. self-practice) and the third group served as a control. With TDS, the subjects were instructed to play a computer game having control of the computer cursor through a magnet attached to the tongue. Degree of motor learning (number of game points) was compared between groups. Data were analyzed with ANOVAs.

Results: Performance improved during training in all groups from baseline ($P<0.001$) with a significant difference between groups ($P<0.008$) and between genders ($P=0.002$). The monetary reward group tended towards a significantly higher success than in the control group ($P=0.075$) and the self-practice group was significantly better than controls ($P=0.039$). There was

no significant difference between different groups in the subject-based report of fun (P=0.772), pain (P=0.471), fatigue (P=0.962) and level of motivation (P=0.437).

Conclusion: Introduction of motivational factors influenced behavioral aspects of tongue motor learning. The influence of these paradigms on tongue motor cortical plasticity needs further study.

P18.07 Jesper Jeppesen

DETECTION OF EPILEPTIC SEIZURES BY MEANS OF POWER SPECTRUM ANALYSIS OF HEART RATE VARIABILITY: A PILOT STUDY

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Objective: To investigate whether epileptic seizures could be predicted or detected by means of spectral analysis of heart rate variability (HRV).

Methods: Six patients with temporal lobe epilepsy (4 females, 2 males) participated in the prospective pilot study while enrolled for video/EEG monitoring (24 h/day, 2–4 days). ECG was continuously recorded and 30 min seizure-sessions (25–30 min pre-seizure to 30 sec-5 min post-seizure onset) and 30 min non-seizure-sessions (day- and night sessions for each patient, as control) were chosen for further HRV-analysis. Low frequency (LF) (0.04–0.15 Hz), High frequencies (HF) (0.15–0.40 Hz), LF/HF, LF/(LF+HF) and reciprocal HF-power was determined using continuous FFT-spectral analysis of 64 R-R interval windowing with maximum overlapping.

Results: Six seizures were recorded and analyzed from three patients (2 females, 1 male). All of the analyzed EEG-correlated seizures showed reciprocal HF-power peaks between 10 sec pre seizure-onset and 24 sec post seizure-onset with peak amplitudes 2.96–93.63 times higher than control maximum peak. For the other parameters we could not find significant difference between seizure and nonseizure sessions.

Conclusion: Specifically high reciprocal HF-power peaks suggest suppressed parasympathetic activity just around seizure-onset time. Seizure detection using HRV-analysis seems to be a promising method for non-invasive seizure detection in the early phase of the clinical event (even preceding the onset).

Keywords: Heart rate variability, seizure onset detection, temporal lope epilepsy, FFT-spectral analysis, reciprocal HF-power.

P18.08 Nicoletta Nava

ULTRASTRUCTURAL STUDY OF THE STRESSED GLUTAMATERGIC-SYNAPSE

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Abnormal function of the glutamatergic system has been implicated in the pathophysiology of many stress-related disorders, such as depression, schizophrenia and anxiety. Nevertheless, the mechanisms whereby behavioral stress affects glutamatergic trasmission are only starting to be elucidated. In a previous study, acute footshock (FS)-stress was found to induce a marked increase of glutamate trasmission from prefrontal/frontal cortex (P/FC) synaptosomes, which was completely prevented by chronic antidepressants (ADs). Moreover, FS-stress induced increase of glutamate release was found dependent on the activation of the glucocorticoid receptor. At the molecular level, FS-stress induced accumulation of SNARE complexes in presynaptic membranes. Patch-clamp recordings of P/FC pyramidal neurons revealed that FS-stress induced an increase in glutamate release, completely prevented by chronic desipramine (DMI) [1]. The aim of the present study was to evaluate if FS-stress induced increase in glutamate release is correlated with an increase in the number of vesicles anchored to the presynaptic membrane, thus affecting the distribution of vesicles among different presynaptic pools. Therefore, through the use of stereological methods, we performed the following experiment: (1) Analysis of the ultrastructure of asymmetric synapses and of the number of vesicles docked to the presynaptic membranes with electron microscopy, in medial PFC (mPFC); (2) Evaluation of the volumetric modifications with light microscopy in mPFC.

[1] Musazzi et al., PLoS One. 2010 Jan 5;5(1): e8566

P18.09 Kartheeban Nagenthiraja

ACCURATE AND FAST PERFUSION LESION SEGMENTATION TOOL FOR CLINICAL SETTINGS

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CFIN

Background: The mismatch between perfusion-weighted imaging (PWI) and diffusion-weighted imaging (DWI) is used as selection criteria for thrombolytic therapy. The DWI lesion represents the ischemic core while PWI lesion represents the region of hypo-perfused voxels but still viable if perfusion is restored timely. In this paper (part I) we present a novel algorithm for automatic PWI lesion segmentation on time-to-peak maps (TTP).

Methods: PWI lesions on TTP maps can have indistinguishable boundaries and the lesion can appear scattered due to inherent noise, hence we sought for initial coherent PWI lesions by threshold (> 4 seconds) and adjusted the lesion boundaries to be smooth, closed curve minimizing mean squared errors between image TTP values and the respective mean values in the hypo- and normoperfused regions. Automatically generated lesion masks were compared with manual delineations provided by four experts in 168 acute stroke patients. Results: For the novel algorithm the overall volumetric correlation was 0.92, the DC was 0.72 (0.46-0.80), the sensitivity was 76% (61-85%) and the specificity was 97 (93-99%). Median processing time was

3.4 seconds (1.9-4.9) per patient.

Conclusions: We present a time efficient algorithm for automatically delineating perfusion lesions in TTP maps. We demonstrate good agreement between this algorithm and expert consensus lesion volumes. We speculate that extending this methodology to automatic DWI segmentation will provide a clinically useful framework for rapid and reproducible quantification of the volume of salvageable tissue in acute stroke.

P18.10 Henriette Bjerregaard

DICYSTEINE CROSSLINKING IN THE HUMAN SEROTONIN TRANSPORTER

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The human serotonin transporter (hSERT) actively regulates the concentration of serotonin in the synaptic cleft by mediating reuptake of serotonin. hSERT is a molecular target for drugs used to treat affective disorders such as depression.

Conformational changes of hSERT occur during substrate and ligand binding and during translocation of serotonin. During the transport cycle, hSERT shifts from an outward facing conformation to an occluded state ending in an inward facing conformation.

A bound ligand induces a given conformation on hSERT and vice versa; the conformation of hSERT has profound implications on ligand characteristics.

The interplay between ligand binding, transport, and hSERT conformation is not fully understood. This interplay can be studied by analyzing the reactivity of introduced cysteines directed by the structure of LeuT and our homology model of hSERT. Furthermore, the effect of locked conformations established by cysteine crosslinking on ligand binding kinetics can reveal important aspects about the impact of protein conformations on ligand binding.

We here characterize a battery of introduced extracellular cysteines and their impact on transport activity. We also show how cysteine crosslinking can be used to manipulate transporter conformation and how this affects ligand binding.

P18.11 Anne Virring Sørensen

SLEEP IN CHILDREN WITH ADHD BEFORE AND AFTER TREATMENT WITH METHYLPHENIDATE

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Background: In addition to ADHD core symptoms, co-morbid conditions occur in up to 75% of patients with ADHD. Parents to children with ADHD and the children themselves also frequently report sleep problems of

significant importance. Both objective and subjective studies have been performed, and the findings are ambiguous. Sleep problems are reported in clinical practice in 25-50% of children and adolescents with ADHD.

Methylphenidate causes increasing activity of the central nervous system and increases or maintains alertness, combats fatigue, and improves attention. The impact of Methylphenidate on sleep is not well investigated.

Design: A clinical trial:

1. Reported sleep problems in an ADHD cohort within 1 year vs. 100 normal controls.

2. Objective sleep investigation (PSG and MSLT) in:

Children with ADHD and reported excessive daytime sleepiness (EDS)

Children with ADHD and no reported EDS

Normal controls

3. Pre-post analysis of the impact of Methylphenidate on sleep.

Methods and material: All referred medicine naïve children age 8-12 diagnosed with ADHD at department D, BUC-Risskov within a 12 month period.

Purpose: To describe sleep problems and sleep patterns in a cohort of newly referred patients with ADHD during a 12 month period. The study will also contribute to the knowledge of objectively measurable sleep patterns in children with ADHD and in the subtypes and be correlated to co-morbidity. Furthermore, the influence of medical treatment on sleep patterns will be evaluated.

Hypotheses: A group of children with ADHD are sleep disturbed and Methylphenidate does not have a negative effect on this group.

P19.01 Pernille Lühdorf

FISH, MARINE N-3 POLYUNSATURATED FATTY ACIDS AND STROKE.

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Background: Marine n-3 polyunsaturated fatty acids (PUFA) have several effects that could decrease the risk of stroke. Marine n-3 PUFA reduces the activity of platelets, decreases blood pressure, reduces plasma viscosity and plasma triglycerides, stabilizes heart rhythm and could stabilize plaques in the internal carotid arteries. Epidemiologic studies have shown that intake of fish particularly fat fish and intake of marine n-3 PUFA decreases the overall risk of stroke, decreases the risk of thromboembolic strokes but does not influence the risk haemorrhagic strokes. In this study the content of marine n-3 PUFA in fat tissue will be analysed as an objective measure of the intake of marine n-3 PUFA over the last 3 months. Furthermore this study has a size allowing analysis of different subgroups of thrombosis.
Hypotheses: There is a negative association between fat fish in the diet, the content of marine n-3 PUFA in the diet, the content of marine n-3 PUFA in fat tissue and the risk of strokes, not influence the risk of haemorrhagic

strokes. Method: The Danish prospective study Diet, Cancer and Health consists of 57000 men and women age 50-64 years at inclusion. At inclusion information about diet and lifestyle together with biologic material was collected. The study population was followed for more than 14 years. For every person in the study population who was admitted to a Danish hospital or emergency room with diagnose of stroke the case record were examined and diagnose was validated and characterized based on clinical appearance, brain scan, blood samples and other tests. Results: 2292 strokes are validated and characterized but further analysis is ongoing.

P19.02 Adjmal Nahimi

A COMMON NORADRENERGIC MECHANISM OF DEPRESSION AND L-DOPA INDUCED DYSKINESIA IN PARKINSON&ACUTE;S DISEASE IN VIVO?

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Aims: The aims of this proposal include tests of hypotheses of the pathogenetic mechanisms of noradrenergic neurotransmission in Parkinson's disease in vivo, using positron emission tomography of patients with early and advanced Parkinson's disease with or without L-DOPA-induced dyskinesia or co-morbid depression, and evaluation of whether these mechanisms can be influenced therapeutically.

Hypotheses

1. We argue that release in human cortical and subcortical brain regions of norepinephrine derived from metabolism of exogenous L-DOPA is greater in Parkinson's disease patients with L-DOPA-induced dyskinesia than in patients without this complication. This hypothesis will be tested by measuring antagonist [^{11}C]yohimbine binding to alpha-2 adrenoceptors before and after L-DOPA challenge.

2. If so, we argue that the greater rise of norepinephrine, measured as [^{11}C]yohimbine displacement after L-DOPA challenge, is the result of down-regulation or loss of norepinephrine transporters. This hypothesis will be tested by measuring the binding of [^{18}F]FMeNER-D_2, a tracer of norepinephrine transporters.

3. If so, we argue that the greater decline of [^{18}F]FMeNER-D_2 binding is significantly correlated to the symptoms of Parkinson's disease, as proof that patients with more severe loss of noradrenergic terminals exhibit more severe motor deficits

P19.03 Jafar Hyder Ali Shaik

DJ-1 PROTECTS AGAINST P25 INDUCED ALPHA-SYNUCLEIN CYTOTOXICITY

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Parkinson's disease (PD) is characterized by progressive degeneration of dopaminergic neurons in the substantia nigra and the intracellular deposition of Lewy bodies that are predominantly composed of α-synuclein.

Alpha synuclein is a 140 amino acid protein that is widely distributed throughout the brain and highly expressed in neurons. Aggregation of α-synuclein is involved in the pathogenesis of PD and variety of related neurological disorders. DJ-1 is a homodimeric, 189 amino acid protein which is cytoprotective in function against different types of stress. Mutations in DJ-1 result in early on-set PD. However it is not clear whether DJ-1 protects against a-synuclein cytotoxicity. In our rat oligodendroglial cell model AS-7, over expressing α-synuclein, we demonstrate that DJ-1 protects against p25 induced α-synuclein cytotoxicity. Various DJ-1 PD mutants were also studied in our cell model under toxic conditions and it was observed that mutations in DJ-1 abrogate protection against α-synuclein cytotoxicity. Results from Western blot analysis from the above experiment suggest that loss of protection in DJ-1 PD mutant proteins might be due to rapid degradation of DJ-1 by the host proteolysis machinery. DJ-1 dose dependent cytoprotection studies were also carried out and the data obtained from these experiments suggests that high dose of DJ-1 is required to protect against α-synuclein cytotoxicity. Human neuroblastoma cells SH-SY5Y are insensitive to alpha synuclein cytotoxicity. Western blot analysis of cell lysate from SH-SY5Y cells shows high levels of endogenous DJ-1 protein, which might be the reason for the non-sensitivity of these cells to α-synuclein toxicity.

P19.04 Louise Ørum Olesen

SEROTONERGIC MODULATION OF ALZHEIMER-LIKE DISEASE IN MICE

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Using a double transgenic mouse model of Alzheimer's disease (AD), APPswe/PS1dE9, developing amyloid plaques from 6-9 months of age, we want to investigate into the role of the neurotransmitter serotonin (5-HT) in the progression of Alzheimer's dementia. The focus of this study being on both neurodegeneration in the hippocampus, a structure essential in memory formation and retrieval, and on cognitive and behavioural changes in our mouse model. In patients with AD, post mortem studies have shown degeneration of 5-HT-ergic afferents to the neocortex as well as the hippocampus. This has been linked to some of the changes in behaviour and personality, especially emotional behaviour, seen in AD patients. Reduced fibre density has also been shown in APP/PS1 Tg mice. Our mouse model allows for manipulation of 5-HT levels by long-term pharmacological treatment with SSRI (increasing 5-HT levels) and by depletion of 5-HT, obtained by unilateral injection into the ventricles of a neurotoxin, 5.7-dihydroxytryptamin, partially killing serotonergic neurons. In 18-month-old APP/PS1 mice we observe a significant cognitive decline as well as behavioural changes in TG mice. After treatment with SSRI we no longer observe any difference between WT and treated TG mice in a wide range of behavioural and cognitive parameters. Currently, the rate of neurogenesis in the dentate gyrys (DG) as well as the total number of granule cells is being assessed by stereological methods. At the same time behavioural studies prior to and after surgical manipulation are being conducted, later followed by histological studies.

P19.05 Jeanette Springer

CHRONIC PAIN AND ALTERED SENSATION AFTER THORACOTOMY: IS INTRAOPERATIVE NERVE IMPAIRMENT A RISK?

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Background: Chronic pain is frequent after surgical procedures such as amputation, mastectomy and thoracotomy (Crombie et al. 1998; Wildgaard et al. 2009; Guastella et al. 2011). According to a recent Danish study with a follow-up period of 22 months, 33% of the patients developed pain after thoracotomy, and 4-12% of the patients experienced strong pain (Wildgaard et al. 2011). The mechanisms underlying chronic pain after surgery are not fully known, but several risk factors have been identified: sex (increased risk for women), age (smaller risk for children/adolescents and elderly people), genetic constitution, psychosocial factors, pain before surgery, intraoperative nerve damage and acute postoperative pain (Kehlet et al. 2006).

Aim: The PhD project will study if intraoperative nerve damage is responsible for the development of pain and sensory abnormalities after thoracotomy.

Hypotheses:

- Intraoperative nerve damage is correlated to acute and chronic pain after thoracotomy.

- The number of nerve fibres is reduced in skin biopsies on the operated side.

- Patients with pain after thoracotomy have an inverse relation between loss of nerve fibres and loss of cold and heat sensation, whereas patients without pain have a direct relation.

- Patients with pain have an increased response to capsaicin, and patients without pain have a reduced response to capsaicin compared to healthy individuals.

Methods: Pain questionnaires, Quantitative Sensory Testing (QST), intraoperative neurophysiology, skin biopsies and laser doppler imaging will be used in the project.

P19.06 Anne Hansen

POST-STROKE HEADACHE: A 3-YEAR FOLLOW-UP STUDY

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Background: Headache in the acute phase of stroke is only described in a few studies with an incidence of 17-34%. The continuation of headache following the acute phase of stroke has been described to a lesser extent and the incidence of chronic headache following stroke has yet to be well-

established.

Aim: To examine the incidence of headache 3 years following a stroke.

Methods: All consecutively eligible patients admitted to the Stroke Unit at Aarhus University Hospital from February 1 to October 1, 2007 and from February 1 to August 1, 2008, were included in the study and they were interviewed about their pain prior to and at stroke onset. Follow-up was conducted by phone 3 and 6 months after stroke and by mail 3 years after stroke using standardized questionnaires.

Preliminary results: A total of 640 patients were assessed at stroke onset of which 299 met the inclusion criteria and 220 patients completed the 3-year follow-up. There was reported headache at stroke onset by 34.9% and 3 years following stroke by 11.8% of the patients. The headache was experienced unilaterally by 57.7% while the remaining 42.3% experienced the headache bilaterally. The frequency of headache was reported to be between 2 to 14 days a month by 80.8% while 3.8% reported headache more than 14 days a month and 15.4% reported a daily headache . Mean intensity of headache was 5 (range 2-9) on the numeric rating scale. Headache duration varied; 19.2% reported headache to last less than 1 hour a day, 23.1% reported duration time of a day, 15.4% reported duration of 1 to several days, 11.5% reported a constant headache and 30.8% reported the duration time to be changing.

P19.07 Jin Zheng

P25 INDUCED ALPHA-SYNUCELIN DEPENDENT TOXICITY IN PRIMARY CULTURED HIPPOCAMPAL NEURONS

J. ZHENG

Department of Biomedicine

Parkinson's disease is the second most common neurodegenerative disease. The pathological hallmark of Parkinson's disease is Lewy bodies, which are composed of aggregated proteins. One of these proteins is referred to as alpha-synuclein (AS). Physiologically, AS is found in its monomeric form, but under pathological conditions, like in Parkinson's disease, AS is found in its aggregated form. However, the mechanisms underlying AS aggregation and how this aggregation induces neuronal cell death are not clear.

Previously, we found that the protein named p25, can induce AS aggregation and cell death in an oligodendrocyte cell line. However, the effect of p25 on primary neurons and in AS transgenic mice models is not clear. The aim of this study is to test the effect of P25 in both primary neurons and AS mice models.

In the cell model, cultured primary hippocampal neurons will be transected with the p25, and after certain period of time, we will study neuron morphology, neuron survival, and the expression levels of specific genes and proteins. AS aggregation and phosphorylation during the effect of p25 expression will also be investigated. The effect of AS on aggregation and phosphorylation will also be investigated.

In an animal experiment, human AS transgenic mice will be crossed with p25 transgenic mice. Firstly, a behavior test will be applied to these mice. Firstly, these mice will be given a behavior test. Then, these mice will be

sacrificed; immunohistochemistry will be used to study the pathological changes in certain locations in the brain. Real time PCR and western blot will also be used to detect mRNA expression and protein expression, respectively.

P19.08 Signe Rode Andreasen

NEUROPHYSIOLOGICAL IMPACT OF NORMAL AND MUTATED SODIUM-POTASSIUM PUMP IN THE MOUSE BRAIN

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BACKGROUND: Normal neuronal activity highly depends on the ability of the sodium-potassium (Na/K)-pump to establish the resting membrane potential after membrane hyperpolarization, which occurs subsequently to an action potential. Dysfunction of the Na/K-pump and thus inability to maintain a normal membrane potential has many neurological consequences. Mutations in the a_2 ($ATP1\alpha_2$) and a_3 ($ATP1\alpha_3$) isoforms are associated with Familial Hemiplegic Migraine type 2 and Rapid-onset Dystonia Parkinsonism, respectively. Interestingly, the a2 and a3 isoforms display distinct expression patterns in the brain, where a_2 is enriched in astrocytes (although not restricted to), and the a_3 isoform is neuron-specific.

HYPOTHESIS: Altering the α subunits could disturb neuronal and/or astroglial function and thereby alter the neuronal and synaptic function. Through electrophysiological recordings this project can reveal important influences of the Na/K-pump in living neurons in brain tissues.

METHOD: We will take advantage of two mouse models with perturbed Na/K-pump functions. The missense knock-in mice carry a specific point mutation in either the a_2 or the a_3 isoform of the pump. Using electrophysiological recordings from neurons in brain slices, we will investigate the physiological consequences of "loss-of-function" mutations in the hippocampus. Brain slices will be prepared from wild type and knock-in mice, and extracellular recordings will be used to reveal the neurophysiological consequences of perturbed Na/K-pump function.

P19.09 Morten Jønsson

INFLUENCE OF DOPAMIN ON GAMMA SYNCHRONIZATION - A MEG STUDY

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It has previously been shown (Lou, Gross 2010) that the degree of self reference is positively correlated to the synchronization in a paralimbic network consisting of Anterior Cingulate Cortex (ACC), Pulvinar Thalamus (Thal) and Posterior Cingulate Cortex (PCC). It was found that the biggest change in synchronization took place in the gamma spectrum and previous

studies indicate that this activity is regulated by GABA interneurons controlled by dopamine and acetylcholine (Changeux,Lou 2011).

In the present study a group of healthy right handed males is given either a Placebo or L-Dopa in a blinded design (2x12). They are scanned in a MEG scanner in a task where they rate how fitting a given adjective (e.g. clever) is to themselves in one series or to the Danish Queen in another series and finally a control condition where the number of vowels is counted. Approximately 5 minutes later they are required to recall their previous judgment of the adjectives. The MEG data is co-localized using a 3T structural MR. We hypothesize that the dopamine group will have a significant increase in gamma synchronization relative to the control group during the self awareness condition.

P19.10 Justyna Zareba

STUDY OF THE ROLE OF CALCIUM IN THE ALPHA-SYNUCLEIN INDUCED NEUROPATHOPHYSIOLOGY

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Parkinson's disease (PD) is mainly characterized by the progressive neurodegeneration of dopamine producing neurons of the substantia nigra (SN) and the presence of Lewy bodies in surviving cells. α-synuclein (α-syn) is a protein that plays a central role in the disease. It has been shown that mutations in the α-syn gene, as well as overexpression of the normal protein can lead to PD. Our hypothesis is that mishandling of α-syn in neurons leads to cellular dysfunctions that may be important for fully understanding PD. The goal of my research is to study the pathophysiological impact of α-syn overexpression in cells with a special focus on calcium homeostasis. Our preliminary data suggests that a-syn induces changes in calcium in the cytosol that could contribute to disease progression. The project aims to modulate calcium homeostasis in neurons as a potential therapeutic strategy in PD.

For an in vivo study, we use a rAAV (recombinant adeno-associated viral vector) tool encoding for h-α-synuclein (h-α-syn) or EGFP as control protein. Thus, a rat model of PD is achieved by local stereotactical viral vector injection into the right side of brain, leading to overexpression of h-α-syn in the rat midbrain. In an in vitro study, we use cortical cell cultures from the ASO transgenic mice to make calcium imaging. This mouse line overexpresses h-α- syn under the Thy1 promoter in selected brain regions but not in dopaminergic cells of the SN. Using Fura-2 as a calcium indicator and GABA to depolarize neurons, the resulting fluorescence Ca2+ transients are analyzed to determine resting calcium concentration, risetime, peak amplitude, and decay kinetics.

P19.11 Kim Henningsen

HIPPOCAMPAL BIOMARKERS OF SUSCEPTIBILITY AND RESILIENCE TO STRESS IN A RAT MODEL OF DEPRESSION

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Susceptibility to stress plays a crucial role in the development of psychiatric disorders such as unipolar depression and post-traumatic stress disorder. In the present study the chronic mild stress (CMS) rat model of depression was used to reveal stress-susceptible and stress-resilient rats. Large-scale proteomics was used to map hippocampal protein alterations in different stress states. Membrane proteins were successfully captured by two-phase separation and peptide based proteomics. Using iTRAQ labeling coupled with mass spectrometry, more than 2000 proteins were quantified and 75 proteins were found to be differentially expressed. Stress susceptibility was associated with increased expression of a sodium-channel protein (SCN9A) currently investigated as a potential antidepressant target. Differential protein profiling also indicated stress susceptibility to be associated with deficits in synaptic vesicle release involving SNCA, SYN-1 and AP-3. Our results indicate that increased oxidative phosphorylation (COX5A, NDUFB7, NDUFS8, COX5B and UQCRB) within the hippocampal CA regions is part of a stress-protection mechanism.

P19.12 Annemette Bondo Lind

LONGING FOR EXISTENTIAL RECOGNITION: A QUALITATITVE STUDY OF EVERYDAY CONCERNS FOR PEOPLE WITH SEVERE SOMATOFORM DISORDERS

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Background: Studies indicate that patients with somatoform disorders (SD) might be vulnerable to stressors and have difficulties coping with stress. Aim: To investigate what persons with SD daily experienced as stressful and how they dealt with this.

Methods: A constructivist grounded theory approach was used to collect and analyse textual data from 24 patients with SD.

Results: A major concern to patients was their longing for existential recognition and determining to patients' stress appraisals. Patients had difficulties with existential self-recognition of bodily sensations, vulnerability and needs which made it especially important to receive existential recognition in social interactions. We identified three different categories related to longing for existential recognition: existential misrecognition covering experiences where patients expressed to be meet by

distrust and disrespect; uncertain existential recognition where patients due to unclear communication were uncertain that they were totally recognized; and successful existential recognition where patients' experiences were meet by existential recognition.

Conclusions: Existential recognition was of vital importance and associated to patients' stress appraisals. Misrecognition and uncertain recognition were related to avoidant coping, increased stress appraisal and maintenance/aggravation of symptoms. Whereas successful recognition was related to more active coping, decreased stress appraisal and symptom reduction. The findings imply that future research and treatment of SD should address patients' ability to identify and express vulnerability and needs in both self-interactions and social interactions.

P20.01 Stine Karlsen GASTROINSTESTINAL TRANSIT TIMES IN PATIENTS WITH LIVER CIRRHOSIS AND PORTAL HYPERTENSION

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BACKGROUND: Patients with liver cirrhosis and portal hypertension have high morbidity and mortality, and gastrointestinal malfunction may be partly involved in development of complications. Studies have suggested both prolonged and shortened gastrointestinal transit times.

AIMS: We wished to study the transit times through the stomach, small intestine and colon in patients with liver cirrhosis and in healthy subjects. Further, we wanted to compare intestinal contraction patterns before and after meals and finally, we aimed at describing a possible correlation between transit times and the degree of portal hypertension.

METHODS: We used the Motility Tracking System (MTS) for determining gastric emptying time, small intestinal transit times and motility patterns in the small intestine during eight hour recordings. Magnet position and contraction patterns in three different gastrointestinal segments (stomach, small intestine and colon) were determined and segmental transit times calculated. The colonic transit time (CTT) was determined using radiopaque markers ingested for 6 consecutive days followed by an abdominal radiograph.

PRELIMINARY RESULTS: 13 patients have undergone the MTS investigation. The velocity through the proximal small intestine is significantly higher in cirrhotic patients group (median 1.28 m/hour, range 1.07-1.31) than in the 15 healthy controls (median 0.84 m/hour, range 0.72-1.07), p = 0.007. No correlation was found between portal pressure and velocity. There was no significant difference in either CTT or gastric emptying time between the patients and controls.

P20.02 Lise Haubjerg Nielsen HOSPITALIZATION FOR PNEUMONIA AMONG INDIVIDUALS WITH AND WITHOUT END STAGE RENAL DISEASE: A DANISH NATIONWIDE, POPULATION-BASED COHORT STUDY

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Introduction
Pneumonia is one of the most frequent life-threatening infections among renal transplant candidates and recipients.
We compared incidence rates of first hospitalization for pneumonia among individuals with and without end-stage renal diseases (ESRD) and explored risk factors for pneumonia in renal transplant recipients (RTR).

Methods
This observational cohort study was conducted from 1 January 1990 to 31 December 2009. Each member of a Danish population-based, nationwide cohort of RTR was matched with 19 control individuals from the general population. Data on age, mortality, emigration and hospital discharge diagnoses from 1977 onward were obtained from nationwide administrative databases. Pneumocystis jiroveci pneumonia is not counted as an episode of pneumonia. Risk factors were assessed by Poisson regression.

Results
The study included 4973 individuals with ESRD and 85899 control individuals without ESRD, providing 26,849 person-years and 734,061 person-years of observation, respectively.
Incidence rates of first hospitalization for pneumonia were 46.1 per 1000 person-years (95% (CI), 40.6-52.4) in waitlisted patients, 31.8 per 1000 person-years (95% CI, 29.3-34.4) in RTR, and 62.8 per 1000 person-years (95% CI, 54.3-72.7) in patients with graft loss.
Among RTR male sex, age ≥50 years, receiving a living donor kidney, and ≥1 year or more in dialysis prior to transplantation increased the risk of pneumonia.

Conclusions
The risk of first-time hospitalization for pneumonia among renal transplant candidates and recipients is very high. The risk of pneumonia has remained high during the entire study period and is of great clinical and public health concern.

P20.03 Lærke Valsøe Munk-Petersen ANTIGEN SPECIFIC POLYFUNCTIONAL T-CELL POPULATIONS IN HIV-1 INFECTED PATIENTS BEFORE AND AFTER TLR9-ADJUVANTED PNEUMOCOCCAL VACCINATION

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Introduction: T cell immunity can be characterized by the proportion of antigen specific secretion of proinflammatory cytokines. Using a unique vaccination cohort, we investigate the effect of a novel vaccine adjuvant (CPG 7909, a toll-like receptor9 (TLR9) agonist) on T cell immunity against the protein-carrier of the 7-valent pneumococcal conjugate vaccine (Prevenar®).

Methods: The project is a substudy to the clinical vaccine trial “Immune Response to Toll-Like Receptor 9-Agonist Adjuvanted Pneumococcal Vaccination in HIV Infected Adults”(ITAP). The study is approved by the Danish Data Protection Agency, The Danish National Committee on Biomedical Research Ethics and Danish Medicines Agency.

In short, 91 HIV-infected persons completed immunization twice with the 7-

valent conjugated pneumococcal vaccine (Prevenar, Wyeth), followed by a booster vaccination with the 23-valent pneumococcal vaccine (Pneumo Novum, Sanofi Pasteur MSD). The participants were randomized to receive a TLR9-agonist (CPG7909) or placebo as an adjuvant.

Using a six-colour flow cytometry intracellular cytokine stain procedure the longitudinal development of the proportions and magnitude of antigen specific CD4+ T cells are investigated in 40 participants from the ITAP trial (20 from each group).

Perspective: The objective of this project is to investigate the quality of the T cell response after pneumococcal vaccination with or without the TLR9 adjuvant (CpG7909) in HIV-1-infected adults.

This study will increase our understanding of the development of cellular immunity and the adjuvant effect of CPG7909 on vaccine responses. It will also evaluate the effect of CPG7909 on cellular HIV immune recognition.

P20.04 Nis Brix Lauridsen

PREDICTING FAILURE TO EXTUBATE AFTER INSURE IN NEWBORNS BORN BEFORE 32 WEEKS GESTATION

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Background: Respiratory distress syndrome (RDS) is the major cause of perinatal morbidity and mortality in preterm infants. The standard treatment is surfactant replacement immediately followed by extubation to nasal continuous positive airway pressure (nCPAP) — the INtubation-SURfactant-Extubation procedure (INSURE). Some infants need more respiratory support following INSURE than nCPAP, resulting in failure to extubate, i.e. the need for re-intubation with mechanical ventilation (MV).

Objectives: Our aim is to investigate if risk factors, such as gestational age (GA) at birth, PaO_2 and $PaCO_2$ prior to surfactant, low birth weight for GA, gender, infection, and RDS-grading on chest X-ray, are associated with failure to extubate.

Methods: A total of 438 preterm infants with a GA of less than 32 weeks born during 1998-2010 are included. Data on the hypothesized riskfactors, intubations, and MV will be systematically retrieved from medical records. Univariate, stratified and multivariate analyses will be carried out. The outcome is failure to remain extubated for 48 hours following INSURE, i.e. failure to extubate.

Perspectives: If we can predict infants at high risk of failure to extubate, we may prevent a high-risk re-intubation procedure by keeping them intubated with MV for a period of time after surfactant replacement. This would potentially decrease the morbidity and mortality in this sub-population of fragile premature infants.

Status: The project began September 2011 and some data will be ready for presentation in January 2012.

P20.05 Michelle Heidner

DISCREPANCY IN GESTATIONAL AGE BASED ON DATE OF LAST MENSTRUAL PERIOD AND ULTRASOUND AND NEWBORN DISEASE

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Background

The gestational age (GA) of the fetus and estimated date of delivery can be calculated by use of the first day of menstrual bleeding in the last menstrual period (LMP) by Nägele's rule or by ultrasound (US) measures of fetal biometries early in pregnancy. US measures thus convert a size to an age and fetuses with a slow growth in early pregnancy are consequently assigned a younger GA than their true chronological age. A discrepancy between a reliable LMP estimated age and a US measured age might be due to genetically slow growth or very early growth restriction from other causes. This can cause problems in etiological research as well as clinical decision making related to GA.

Objective

We set out to evaluate the association between discrepancy in GA estimated by reliable menstrual data and early ultrasound and newborn morbidity.

Methods

Some 40,000 women from the Aarhus Birth Cohort had their due dates estimated by both aforementioned methods and the difference between these was calculated. This variable will be categorized into three groups depending on the magnitude of the discrepancy (d) in days: d<7, 714. Newborn morbidity will be measured as the need for hospitalisation within the first 24 hours of life. Univariate, stratified and multivariate analyses will be performed.

Perspectives

This study may contribute to the understanding of diseases during the newborn period. An association between GA discrepancy and specific newborn illness indicates a role of very early fetal growth. The results may also warrant clinical awareness of the risks that newborns are facing and aid early diagnosis, timely treatment and improve parental counseling.

P20.06 Christina Mikkelsen - stud

HUMAN MANNAN-BINDING LECTIN AND FICOLINS: INTERACTIONS WITH VIRUSES

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Pattern recognition molecules (PRMs) of the innate immune system are an important part of the body's first line of defence against invading micro-organisms. These PRMs can either be cell bound or soluble (sPRM) in plasma. Examples of sPRM are the four lectins: mannan-binding lectin (MBL) and H-, L- and M-ficolin.

These lectins can, upon binding to pathogen associated molecular patterns,

via the MBL-associated serine proteases 1, 2 and 3, activate the lectin pathway of the complement system by cleaving and activating C4 and C2, thereby generating the C3 convertase C4b2a. Activation of C3 leads to the opsonisation of micro-organisms with C3b and formation of the membrane attack complex, which may result in the lysis of the micro-organisms.

While the interaction between the MBL and different types of virus is described, not much is known about the ficolins interactions with viruses. To extend the knowledge about the role of the innate immune system in viral infections, we studied the three ficolins as well as MBL. The binding of lectins to viruses was examined by coating microtitre wells with viruss, either directly or by use of anti-virus antibodies. The interactions were also studied in suspensions of viruses, as well as by virus neutralization assays, where viruses were incubated with the different lectins before plating on human cells. The number of plaques in the cell layer caused by viral mediated cell lysis was then evaluated.

The poster will present new knowledge about the interactions between viruses and the lectins of the innate immune system.

P20.07 Sidsel Hyldgaard Støy

THE TH17-CELL PATHWAY IN THE COURSE OF ACUTE ALCOHOLIC HEPATITIS.

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Alcoholic liver disease is the most common cause of cirrhosis in the Western world and associated with high morbidity and mortality. A subset of these patients will develop a condition with a particular adverse prognosis known as acute alcoholic hepatitis (AH). AH is characterized by an exaggerated inflammatory response of both innate and adaptive origin, but the fundamental pathological mechanisms are poorly understood. Th17 cells, a subgroup of CD4+ T cells, have been implicated in a variety of disease states in which immune dysregulation is a central feature. The proinflammatory cytokines IL-1beta and IL-6, involved in the differentiation of Th17 cells, are elevated during AH. Th17 cell are proinflammatory and have, via e.g. the production of IL-17, been shown to recruit neutrophils - a hallmark in AH. Furthermore, Th17 cells produce another cytokine, IL-22, that aids hepatocytes in resisting injury during inflammation. Our aim was to investigate how the level of circulating Th17 cells and their related cytokines fluctuate during an episode of AH and whether these changes correlate with disease activity and/or mortality.

We further studied the relationship between the production of IL-17A and IL-22 in respect to disease outcome. In the current study 22 patients diagnosed with AH, 10 patients with stable alcoholic cirrhosis and 10 healthy subjects were included. Peripheral mononuclear cells (PBMC's) were stimulated and stained intracellularly with fluorescence conjugated antibodies against IL-17A, IL-21 and IL-22 and were analyzed by flow cytometry to quantify circulating Th17 cells. The concentrations of IL-17A, IL-21, IL-22 and IL-23 in plasma were measured by ELISA.

P20.08 Morten Bue Svendsen

THE RELATION BETWEEN PERIPHERAL VASCULAR RESISTANCE AND PULSE WAVE VELOCITY

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Background: Essential hypertension (EH) is an important risk factor for development of cardiovascular disease. EH is associated with changes in the vascular wall in large as well as small arteries. The changes found in the small resistance arteries in patients with EH results in increased wall thickness and decreased lumen diameter. The consequence of this is reduced vasodilatory capacity and an increased vascular resistance. In large arteries hypertension results in increased wall thickness and a loss of elastic properties. The stiffening of the arterial wall leads to an increased pulse wave velocity (PWV) through the large arteries. When the pulse wave travels through the vascular tree it reaches the smaller resistance arteries. Increased peripheral resistance due to a decreased lumen may therefore influence augmentation of the pulse wave. Since PWV is an established independent risk factor for cardiovascular disease this could potentially affect patient outcome.

Method & Aim: No studies have yet determined the relationship between peripheral vascular resistance and PWV. This research year project will examine this relationship through measurements of peripheral vascular resistance using forearm venous occlusion plethysmography and through measurements of PWV in large arteries using tonometry equipment. With measurements on 50 healthy controls and 20 patients with newly diagnosed untreated EH, we aim to demonstrate a possible association, taking into account the role of age and blood pressure.

Results: The study is ongoing.

P20.09 Niels Johansen

BRAIN SWELLING DURING DIALYSIS (BRASE). ACUTE BRAIN VOLUME CHANGES IN HAEMODIALYSIS: COMPARISON OF LOW FLUX HAEMODIALYSIS WITH PRE-DILUTION HAEMODIAFILTRATION

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BACKGROUND: Previous studies have shown that haemodialysis (HD) can lead to a range of immediate side effects such as headache, nausea and even brain swelling.

HD-patients who suffer from these side effects are often treated with haemodiafiltration (HDF) instead of HD. However, there is little evidence that HDF is superior to HD since no studies have compared low flux HD and pre-dilution HDF with respect to subsequent cerebral swelling.

AIM: To investigate the effect of HD and HDF on brain swelling after dialysis.

METHOD: Five healthy individuals and sixteen stabile HD patients will be recruited. Exclusion criteria are contraindications against magnetic resonance imaging (MRI), steroid treatment, neurological disease and acute illness.

HD patients will receive both HD and HDF in a random order during two examination days. MRI of cerebrum, blood sampling and bioelectric impedance measurements will be performed before and after dialysis. The five healthy subjects will go through a similar program except for dialysis. Assuming no brain swelling, data from the healthy patient will indicate accuracy of the method and serve as a reference. MRI data will be processed with dedicated neuro-analysis software allowing for automatic segmentation of the cerebral area, providing quantitative estimation of the brain volume before and after dialysis treatment.

RESULTS: The study is still in progress.

P20.10 Marie Maagaard Sørensen

CARDIOVASCULAR FUNCTION FOLLOWING THE NUSS PROCEDURE FOR PECTUS EXCAVATUM - 3 YEARS FOLLOW-UP. A PROSPECTIVE, CONTROLLED STUDY.

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Objectives: Patients with pectus excavatum have compromised cardiac function during exercise. We hypothesized that the Nuss technique would improve cardiopulmonary function during exercise.Methods: We investigated 75 teenagers (49 patients, 26 controls) at rest and during bicycle exercise before surgery, 1 year postoperative and currently 3 years postop. (after pectus-bar removal). Echocardiography determined cardiac function at rest. Cardiac output, heart rate and aerobic exercise capacity was measured using a photo-acoustic gas-rebreathing technique during rest and exercise. Lung function was measured using spirometry.Results: Before surgery patients had lower cardiac index 6.6 ±1.1l/min/m^{2}as compared to controls 8.1 ±1.0 l/min/m^{2}during submaximal exercise, p=0.0001. No difference in heart rate or heart rate increase between the two groups. One year postop., cardiac index had significantly increased in patients although cardiac index was still significantly lower 7.2 ±1.0 l/min/m^{2}as compared to controls 8.5 ±1.6 l/min/m^2, p= 0.0008. Both patients and controls increased VO_2max during the first year although controls increased the most. Right ventricular diastolic dimension increased in both groups over the one year and left ventricular dimensions increased in patients. Before operation, patients had lower $FEV_1$86 ±13 % as compared to controls 94 ±10 %, p=0.009. About half of the teenagers have completed the 3 year study. Preliminary results will be presented on the poster.Conclusion: Patients with pectus excavatum have lower cardiac index at submaximal exercise as compared to age-matched controls. Their cardiac index and $FEV_1$are increased one year after operation.

P20.11 Peter Hjertholm

DIAGNOSTIC VARIABILITY IN DANISH GENERAL PRACTICE AND PROGNOSIS OF CANCER PATIENTS

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Background: Regarding survival of cancer Denmark is inferior to the countries we normally compare ourselves with. The general practitioners' (GPs) role as gatekeepers in Denmark might affect this. Little is known about the consequences of the observed wide variations in GPs' referral patterns and use of diagnostic procedures. Do cancer patients benefit from earlier diagnosis and better prognosis if they are registered with a diagnostic active GP compared to a GP who refer less and order fewer tests?

The aim is to investigate whether referral patterns and use of diagnostic tests among GPs affect the prognosis of cancer patients.

Methods: In a population based cohort, we will group GPs according to their use of referrals and diagnostics tests and construct a statistical model controlling for patient characteristics such as age, sex and sociodemographic factors. In addition two different measures of morbidity will be tested and included in the model, Charlson Co-Morbidity Index and Rx-defined Morbidity Groups. Finally, we will evaluate whether the survival of cancer patients depends on the referral and diagnostic activity of the GPs by using Cox regression.

Perspectives: Whether or not cancer patients' prognosis is correlated to the GPs' activity, this project will provide a contribution for more scientifically based reflections on GPs' access to and use of diagnostic testing. This may have implications for both politicians and the education of GPs.

P20.12 Caroline Emma Hedsund

A GASTROINTESTINAL TRANSIT TIME STUDY: HEALTHY CHILDREN INVESTIGATED WITH MOTILITY TRACKING SYSTEM

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Background

Description of small intestinal transit time in healthy children is lacking and normal values for gastric emptying (GE) and colonic transit time are sparse. Conventional methods such as radiopaque markers, scintigraphy, and PillCam either involve radiation or require the child to swallow a large pill. We present a minimally-invasive, radiation-free method, Motility Tracking System – 1 (MTS-1).

Aims

To evaluate the MTS-1 for use in children and describe normal values for segmental gastrointestinal transit times in healthy children.

Materials & Methods

19 healthy children (9 females), median age 10 (7-12) years, were included.

A small magnet pill was ingested and tracked by a matrix of sensors. Position and movement of the pill was recorded through the GI tract. Motility, frequencies of contractions and velocity of the pill was described. Specific contraction patterns were identified for the stomach, small intestines and colon. GE, small intestinal and colonic transit times were calculated.

Results

A majority of the children ingested the pill without problems. No side effects was seen during or after investigations. Median total gastrointestinal transit time: 38 hours (9-96). Median GE: 37 minutes (2-111). In 15 subjects, pill passed from terminal ileum into caecum during recordings, median small intestinal transit time (SITT): 302 minutes (164-397). 4 subjects did not pass pill from terminal ileum into caeum during recordings, SITT >331, >428, >454, >427 minutes. Median colonic transit time: 38 hours (6-90).

Conclusions

MTS is a safe method for examination of GI transit times in children and has good potential for future studies in pediatric patient groups.

P21.01 Randi Berg

GENOMIC HIV RNA INDUCES INNATE IMMUNE RESPONSES THROUGH RIG-I-LIKE-RECEPTOR-DEPENDENT SENSING OF SECONDARY STRUCTURED RNA

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Background: To date little is known about the role of the innate immune response during HIV infection. Recent studies suggest that innate immune activation by HIV may be partly responsible for the dysregulation of adaptive immunity and the development of immune deficiency observed during the course of the disease. It has been proposed that continuous immune activation induced by HIV is mediated through pattern recognition receptors (PRR)s expressed by cells of the innate immune system recognizing viral structures termed pathogen associated molecular patterns (PAMP)s. In this study we focus on HIV-derived RNA as possible PAMPs and identify PRRs and signalling pathways involved in innate immune activation by HIV.

Methods: Human peripheral blood mononuclear cells (PBMC)s were transfected with full-length genomic and HIV-derived RNA. Immune activation was measured as induction of interferon stimulated genes (ISG)s by ELISA and PCR. Involvement of PRRs was investigated by using PRR inhibitors and bone-marrow-derived macrophages from mice deficient in the adaptor MAVS. Signalling pathways were analyzed by luminex, trans AM, and confocal fluorescence microscopy.

Results: We demonstrate that full-length genomic and HIV-derived RNAs induce innate immune activation in human PBMC's measured as induction of ISGs . We identify the RIG-I-like receptors (RLR)s and MAVS to play an essential role in the recognition of HIV-derived RNA, and further show that the NF-kB, MAP kinase and IRF3 pathways are activated by HIV RNA. We are currently investigating if replication competent virus employ the same molecular receptors and pathways for activation of innate immune responses.

P21.02 Anders Jul Kjærgaard

DO SOLUBLE LEVELS OF ENDOTHELIAL ADHESION MOLECULES REFLECT ENDOTHELIAL EXPRESSION?

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Introduction

Endothelial dysfunction contributes to the pathophysiology of sepsis. This includes an up-regulation of Cellular Adhesion Molecules (CAMs) in response to pro-inflammatory cytokines.

Up-regulation of E-selectin, VCAM-1, ICAM-1 and PECAM-1 stimulate transmigration of leukocytes from the circulation into extravascular tissue, where they contribute to inflammation and tissue damage.

Soluble (s)CAMs has been shown to correlate to disease severity, but it is unknown if levels of sCAMs reflect the endothelial surface expression of CAMs. This would substantiate that it is reasonable to use sCAMs as markers of endothelial activation.

Hypothesis

1) TNF-a increases surface-bound CAMs in Human Umbilical Vein Endothelial Cells (HUVECs) and sCAMs in matching culture medium in a dose-dependent manner.

2) sCAMs correlate to surface bound CAMs.

Methods

HUVECs were cultured with various concentrations of TNF-α (0, 0.625, 1.25, 2.5, 5 and 10 ng/ml) for 8 hours.

Soluble and surface-bound PECAM-1, E-selectin, VCAM-1 and ICAM-1 expression were determined using flow cytometry.

Statistical analysis was done using Spearman´s correlation.

Results

TNF-a increased soluble and surface bound CAMs in a dose-dependent manner.

We found a correlation between E-selectin and sE-selectin, ICAM-1 and sICAM-1, and VCAM-1 and sVCAM-1, while there was no correlation between PECAM-1 and sPECAM-1

Conclusions

The use of sCAMs as markers of endothelial activation is partly supported by this study. There is a need for a surrogate marker of endothelial activation. We anticipate that sCAMs can accommodate this need.

P21.03 Mariane Høgsbjerg Schleimann

THE DIRECT REPEAT 6 PROTEIN FROM HUMAN HERPES VIRUS-6B ACCUMULATES IN VIRAL REPLICATION COMPARTMENTS

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Background: Human herpes virus 6A (HHV-6A) and 6B have been suggested to provide co-factors during malignancies. HHV-6A encodes a protein Direct Repeat 7 (DR7), which induces fibrosarcomas when injected into nude mice, transforms NIH3T3 cells in vitro, and interacts with and inhibits the function of the tumor suppressor p53. P53 is deregulated during infection with both HHV-6A and -6B. In HHV-6B, the gene homologous to dr7 from HHV-6A is named dr6.

Methods: To investigate the function of DR6 during HHV-6B infection, we characterized mRNA (by qPCR), protein expression in cytoplasm and nucleus (by Western blotting), cellular localization (by confocal microscopy), and interactions with cellular or viral proteins (by co-immunoprecipitation and confocal microscopy).

Results: Dr6 was expressed as a herpes virus early/late gene, since its mRNA expression was inhibited by cycloheximide and partly by phosphonoacetic acid. DR6 was localized to the nucleus in dots resembling viral replication compartments at 24 hours post infection (hpi) and accumulated to high levels at 48 and 72 hpi. However, DR6 and p53 were found at distinct subcellular locations as p53 accumulated in the cytoplasm during infection. In contrast, a novel interaction between DR6 and the viral DNA processivity factor, p41, and DR6 and the cellular TATA-binding protein (TBP) could be detected in the nucleus.

Conclusions: Our data implies a novel function of DR6 during HHV-6B replication and suggest that other viral proteins are important for deregulating p53 during infection.

P21.04 Srikanth Chiliveru

IFI16 AND ACTIVATION OF INFLAMMATION IN PSORIASIS

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Interferon gamma-inducible protein 16 (IFI16) is a PYHIN protein identified as an intracellular DNA sensor that mediates induction of interferon-β(IFN-β). Cytosolic localization of DNA has recently emerged as a critical activator of early innate defense, but the molecular mechanisms of recognition and immune activation remain largely unexplained. DNA detection in the cytoplasm leading to IFN-β induction is thought to be one of the triggers for

autoimmune and inflammatory conditions. The detection process is critical to understanding the cellular response to DNA viruses, immune-stimulatory bacterial and self DNA. Psoriasis is a chronic inflammatory skin disease affecting 2-3% of the European population and is characterized by infiltration of immune cells into the dermis and leading to hyper-proliferation of epidermal keratinocytes.

In this project, preliminary findings demonstrated the cytosolic expression of IFI16 in psoriatic lesions both at the transcript and protein levels supported by confocal microscopy. Transfection of keratinocytes with a 60-base pair dsDNA oligonucleotide derived from the HSV-1 genome (HSV 60mer) resulted in the induction of IFN-β and IFI16. The siRNA knock down of IFI16 gene in keratinocytes altered the production of CCL20, a chemokine abundant in psoriatic plaques and furthermore the IFI16 siRNA transfection followed by HSV60mer stimulus resulted in the alteration of various keratinocyte and psoriasis specific inflammatory cytokines and chemokines. This data gives the impetus to delve deeper into the relationship between IfI16 and psoriatic condition with emphasis on DNA recognition.

P21.05 Steffen Bank CAN GENETIC MARKERS PREDICT THE RESPONSE OF TNF INHIBITOR THERAPY?

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Background

Inflammatory bowel disease (IBD), including Crohns disease (CD) and ulcerative colitis (UC), is an autoimmune disease characterized by a dysregulated inflammatory response. Antibodies targeted against the pro-inflammatory cytokine tumor necrosis factor-α (TNF-α) are currently a mainstay of biologic therapy in IBD. However, approximately one-third of the patients have minimal or no response to these agents. A test predicting response would be a very important and useful tool providing basis for a more personalized medicine.

Methods

Blood samples from the patients have been collected at Statens Serum Institut (SSI) during a required screen for tuberculosis (TB) prior to initiation of the TNF inhibitor treatment. A total of 2659 patients with a diagnosis code of K50-63, and therby potential IBD patients, were identified by "Landspatientregistret". Clinical data are being registred in a web-database (https://trialpartner.dk). DNA from the IBD patients will be extracted and 50 functional single nucleotide polymorphism (SNP) in the TNF-alpha pathway will be examined.

This will make it possible to study the effect of genetic variants in a large, well-characterized groups of patients undergoing TNF inhibitor treatment and thereby identify genetic markers predictive for treatment response by comparing responders and non-responders to TNF inhibitor treatment.

Conclusion

This will hopefully benefit patients by improving the identification of an effective treatment for the individual patient (personalized treatment) and minimizing adverse effects by avoiding ineffective treatment and avoiding treating persons genetically predisposed for adverse affects.

P21.06 Winnie Ridderberg

MARKED INCREASE IN INCIDENCE OF INFECTIONS CAUSED BY SPORADIC ACQUISITION FROM THE ENVIRONMENT

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Background: An increased incidence of A. xylosoxidans infections has been observed at the Cystic Fibrosis Centre at Aarhus University Hospital, as the proportion of patients colonised with A. xylosoxidans increased from 6 to 10% from 2005 to 2009.

Method: Pulsed field gel electrophoresis (PFGE) was used to type isolates of A. xylosoxidans.

Results: A. xylosoxidans was cultured from 15 of 143 (10%) CF patients at Aarhus University Hospital during 2009. Five patients had been infected for more than 6 years and 5 patients had been infected for 2 to 3 years. However, five patients experienced a first-time identification of A. xylosoxidans in their respiratory cultures during 2009. Four patients infected for 2–7 years were part of a larger epidemic spread involving both Danish CF centres, while 11 patients, including the five incident cases from 2009, carried strains with unique genotypes. Longitudinal analysis of isolates from 10 patients with multiple preserved isolates showed that each patient persistently carried isolates of a single genotype. Following lung transplantation, two patients showed re-colonisation of the lung grafts with the pre-transplant A. xylosoxidans strain.

Conclusions: A. xylosoxidans has been transmitted between patients from our clinic, but the recent increase in incidence is not caused by cross infection. Cystic fibrosis patients colonised with A. xylosoxidans persistently carry a single clone. A. xylosoxidans is able to re-colonise lung grafts following transplantation.

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P21.07 Babak Jalilian

THE COORDINATED ROLES OF CD18 INTEGRINS AND MATRIX METALOPROTEINASE-9 IN RHEUMATOID ARTHRITIS

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Integrins are receptors expressed on the cell surface where they support cell-cell, cell-extracellular matrix, and cell-pathogen adhesion. CD18 integrins play a crucial role in the immune system through binding of intercellular adhesion molecules (ICAM) and complement factor C3. Recent studies

reported that CD11a/CD18 is shed from leukocytes in models of inflammation and CD18 is a substrate for MMP-9. A role of MMP-9 in a diverse range of inflammatory diseases, including arthritis and multiple sclerosis is emerging, yet insight on the connection between the enzymatic activity of MMP-9 with regard to CD18 integrins and disease is lacking. Previous studies in our laboratory have shown that the CD11a/CD18 complexes are shed as large oligomers consisting of 2xCd11a/CD18 and 4xCD11a/CD18 complexes. In terms of cellular factors regulating shedding of sCD11/CD18 and the SpA patients in therapy targeting the function of TNF-alfa showed a lowering of the sCD11/CD18 concentration in synovial fluid. The in vitro experiments show that incubation of MNC with TNF-alfa increased the concentration of sCD11/CD18 in the culture medium. While the role of TNF-alfa in shedding of CD11/CD18 has not previously been reported, it adds an interesting perspective on the recently established role of this cytokine in activation of MMP-9. The same influence of TNF-alfa was found on a K562 cell line with recombinant expression of CD11a/CD18 establishing this system as a tool for investigating the shedding of CD11a/CD18. Based on this work together with the above mentioned experimental findings we want to connect the function of IL-20 and TNF-alfa with the shedding of sCD11/CD18 in arthritis patients.

P21.08 Sanne Jespersen

VACCINATION SCARS IN HIV INFECTED PATIENTS - DOES VACCINIA VACCINATION CONFER PROTECTION AGAINST AIDS?

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Background: Vaccines may have non-specific effects. Studies from Guinea-Bissau have shown that the live vaccines vaccinia and BCG are associated with lower mortality than can be explained by prevention of smallpox and tuberculosis. Vaccinia vaccination was stopped in 1980 before the first case of HIV-1 was seen. The aim of this study was to study the association between vaccinia scarification and HIV status in Guinea-Bissau.

Methods: In this retrospective cohort study we included all patients born before 1980 from an HIV cohort in Guinea-Bissau. Presence of scars was assessed by a health professional and classified as vaccinia, BCG, or unclassified based on the information from the patient about previous vaccinations and the size of the scar.

Results: By May 2011, 1895 patients born before 1980 (1203 HIV-1, 396 HIV-2, 270 HIV-1/HIV-2, and 26 with unknown HIV-type) had been included in the cohort. The prevalence of vaccinia scars was 42% compared with 63% in the general population (p<0,001). Patients with vaccinia scars had higher middle upper arm circumference (270 mm vs. 263 mm p=0.001) and BMI (21.0 vs. 20.5 p=0.007). Time to initiation of anti-retroviral treatment was longer for patients with a vaccinia scar than for patients without after adjustment for sex, age and HIV-type, although this finding was not statistically significant HR=0.89 (CI: 0.77-1.03 p=0.11).

Conclusions: The prevalence of vaccinia scars was lower in the HIV cohort than in the general population. Vaccinia vaccinated patients were less affected nutritionally. Vaccinia vaccinations may have non-specific effects reducing susceptibility to HIV infection and slowing the disease progression.

P21.09 Caroline Winther Tørring

SPONTANEOUS LYMPHOCYTE TRANSFORMATION IN MULTIPLE SCLEROSIS

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Background:

Epstein-Barr virus (EBV) shows a strong association with multiple sclerosis (MS) on the basis of epidemiological and serological evidence, but it is not clear how EBV may initiate MS. Lymphoblastoid cell lines (LCL) can arise spontaneously in vitro from EBV-infected B cells, and it has previously been shown that this phenomenon occurs with an increased frequency in B cells from active MS patients. The mechanism behind this phenomenon remains to be elucidated.

Hypothesis and Aim:

We hypothesize that an increased propensity to spontaneously form LCLs in MS may be due to differences in EBV-load, expression of EBV and/or immune control of EBV-infected B cells. In this study, we investigated the relation between B-cell transformation and EBV-load in MS patients and controls by determining the frequency of spontaneous lymphocyte transformation and the load of EBV.

Methods:

Peripheral blood mononuclear cells (PBMC) were isolated from blood drawn from age and gender matched MS patients and controls. Cultures were established in microtiter plates and examined microscopically for clonal growth for 13 weeks. Growth-positive wells were confirmed by EBNA-1-specific PCR on supernatant and cells, and by immunofluorescence analysis. The frequency of EBV-infected B cells in PBMC was determined by EBNA-1-specific Q-PCR.

Results:

Although LCL was observed in 6 out of 11 MS patient and 5 out of 11 controls, the transformation was observed in 105 wells in MS patients compared with only 34 wells in control persons. Our data confirm and extend previous studies indicating an increased tendency to spontaneous lymphocyte transformation in vitro in MS patients.

P21.10 Stine Maria Andersen

VALRUBICIN TARGETS AND ACTIVATES PROTEIN KINASE C A IN KERATINOCYTES.

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Valrubicin is a semisynthetic anthracycline originally developed as an anti-

cancer drug. The absence of skin toxicity and the lipophilic characteristics allow the use of valrubicin as topical treatment. Recently, we showed that valrubicin has a beneficial effect in treating psoriasis and non-melanoma skin cancer (NMSC) by local application in animal models. Valrubicin localizes mainly in the cytoplasm, affects cell proliferation, and induces apoptosis.

Protein kinase C (PKC) is a family of cytoplasmic serine/threonine protein kinases that take part in cellular processes by playing a crucial role in the initial events of signal transduction. PKCa, which is activated by calcium and the second messenger diacylglycerol (DAG), is observed in the suprabasal layers of normal skin and is associated to differentiation processes.

Valrubicin possesses a valerate side chain resembling DAG in structure, thus, we hypothesized that the effect of topically applied valrubicin observed in skin inflammatory diseases is mediated through interaction with PKCa.

The aim of the present study was to investigate valrubicin's mode of action in keratinocytes by studying its effect on PKCa activation.

The characteristic of PKCa to translocate from the cytoplasm to the cellular membrane when activated was observed both by confocal microscopy and by western blot of the soluble and membrane-bound cellular proteins. Downstream signaling was confirmed by phosphorylation of extracellular signal-regulated kinases (ERK1/2).

Hence, valrubicin interacts with PKCa as observed by the increased PKCa activity. This increased activity may explain valrubicin's effect observed in treating psoriasis and NMSC.

P21.11 Johannes Martin Schmid

IN SUBJECTS ALLERGIC TO GRASS POLLEN, BASOPHIL SENSITIVITY DECREASES DURING SUBCUTANEOUS IMMUNOTHERAPY DUE TO BOTH HUMORAL FACTORS AND CELLULAR DESENSITIZATION

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Background: SCIT reduces the type-1 allergic response and causes a relief of symptoms. Basophil sensitivity defined as half maximum activation (LC50) after crosslinking of specific IgE, reflects clinical intensity of allergic disease. We hypothesized that changes in basophil sensitivity are caused by both humoral factors and cellular desensitization.
Methods: We measured changes in basophil activation in 24 grass pollen allergic subjects (18 on SCIT, 6 in control group) by flowcytometry as percentage of CD63 expression on the surface of CD193+ basophils activated by 8 $\log_{10}$ dilutions of grass pollen extract. Once annually allergen challenge was performed and participants completed symptom scores.
Results: In the treatment group, the LC50 in the present plasma samples changed from a mean of -0,52 at baseline to 1,64 after 15 months of treatment (n=24, p<0,001). Looking at the cellular changes, we found a 10-fold decrease of basophil sensitivity (ΔLC50: 0,98, n=16, p=0,0003) and a 10-fold decrease in the humoral component as well (ΔLC50: 1,03, n=16, p=0,026). The median concentration at positive nasal allergen challenge increased from 7.943 to 79.433 SQU/ml, while a positive skin prick test was found at a median concentration of 1.995 SQU/ml at baseline and 25.118 SQU/ml after one year. In the same period, the maximum symptom score decreased from 10,6 to 5,6. No significant changes were seen in the control group.

Conclusion: In the treatment group, there was a fast development of humoral protection and a slow cellular desensitization. This results in a 100-fold decrease in basophil sensitivity, which is paralleled by a significant improvement of clinical outcome.

P21.12 Søren Behrndtz Brandsborg

ILEO POUCH-ANAL ANASTOMOSIS IN PATIENTS WITH ULCERATIVE COLITIS: POUCH FUNCTION, QUALITY OF LIFE AND RISK OF CANCER

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Introduction

Since the early 1980's restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) has been the surgical procedure in Denmark when patients with ulcerative colitis (UC) require colectomy. Although many international studies have concluded that the short-term functional results are satisfactory and remain constant, others have suggested that function deteriorates over time. Furthermore, no national studies on pouch function, quality of life and the risk of developing cancer in the ileal pouch have been published.

The present study is performed in order to further document these issues in the total Danish cohort of IPAA patients because of ulcerative colitis.

Materials and Methods

The study includes 2624 patients who have been identified in the National Health Registry using relevant search criteria. In order to precisely specify the total group of IPAA patients we have performed a questionnaire survey in order to obtain information on possible pouch-surgery. Of the 2624 patients, 1881 were alive and could receive questionnaires regarding pouch surgery, pouch function and quality of life. For the remaining group a comprehensive review of medical records was performed to clarify type of surgery.

The cancer study includes all the Danish IPAA patients identified through the survey and the medical records.

Data from the National Health Registry, Cancer Registry and Pathology Database are used as well as questionnaires and review of medical records.

Results

1560 patients (83%) have returned the questionnaires. The statistical analysis of data has not been finished

P22.01 Anne Brosbøl-Ravnborg

CONTROL OF DENDRITIC-CELL FUNCTION BY VITAMIN D_3

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Background: Dendritic cells (DCs) are antigen-presenting cells initiating adaptive immune responses by activating naïve T cells. Immature DCs are important for induction of regulatory T cells. DC differentiation is influenced by 1,25-dihydroxyvitamin D_3 (vD_3) and low serum level of vD_3 is associated with various autoimmune diseases.

Hypothesis: We hypothesize that vD_3 is important for maintaining peripheral tolerance by inhibiting DC maturation and function.

Methods: DCs were differentiated and matured from human monocytes in the presence or absence of vD_3. DC differentiation and maturation were monitored by expression of surface molecules (HLA-DR, CD80, CD83, CD86, CD40 and CD14) by flow cytometry and morphology was examined by microscopy. Supernatants from cultures were analysed by ELISA for the presence of IL-6, IL-8, IL-10, TGF-b1 and IL-23.

Results: The presence of vD_3 influenced both the differentiation and maturation of DC. Microscopic examination showed that vD_3 inhibited formation of dendrites on DCs consistent with the phenotype of immature DCs. Maturation of DCs was repressed by vD_3 as judged by LPS-induced HLA-DR, CD80 and CD83 expression. Furthermore, vD_3 repressed the ability of DCs to induce growth of naïve T cells. DCs treated with vD_3 secreted IL-6, whereas control DCs did not.

Conclusions: The presence of vD_3 inhibited DC differentiation and maturation. VD_3 induced IL-6 secretion in DCs. Elucidating the mechanisms behind this may be of importance for understanding the role of vD_3 during induction of peripheral tolerance.

P22.02 Rie Io Glerup SUBCLINICAL BACTERAEMIA AND MORTALITY AMONG HAEMODIALYSIS PATIENTS - HD-BACT

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Introduction:

Mortality in the population of hemodialysis patients remains high. The annual mortality exceeds 20%. Cardiovascular disease (CVD) is the major course of mortality, accounting for half of all deaths in this population. There is a close relationship between inflammation and development of CVD. 30-60% of hemodialysis patients have chronically elevated markers of inflammation.

Hypothesis:

Chronic inflammation in hemodialysis patients may be caused by subclinical infection expressed by circulating bacterial DNA in the blood stream causing higher mortality and morbidity.

Aim of the study:

To investigate the influence of circulating bacterial DNA on mortality

morbidity and levels of inflammatory markers among a group of hemodialysis patients.

Material and Methods:

Hemodialysis patients treated at five facilities are included (Aalborg, Skejby, Horsens, Randers and Hjørring Hospital; in total approximately 420 patients).

Programme:

Physical examination. Blood sample drawn from peripheral vein and from hemodialysis access. Nasal wipe. Dialysate samples.

A group of approximately 100 hemodialysis patients will be examined again one week later with blood sampling to evaluate the expected continuous nature of circulating bacterial DNA.

Blood samples:

Bacterial DNA is detected by using broad range 16S rDNA PCR.

Blood cultures: 3 culture bottles are drawn for 7 days of automated incubation.

Inflammation markers: various cytokines, hsCRP, procalcitonin etc.

Baseline parameters.

Study participants will be followed for 2 years. The primary end point is all cause mortality and secondary end points: bacteraemia, cardiovascular death, cardiovascular events, and hospital admissions.

P22.03 Hanne Vinter IMIQUIMOD INDUCED SKIN INFLAMMATION: A HUMAN MODEL OF PSORIASIS

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INTRODUCTION AND AIM: The study of psoriasis is limited by the fact that psoriasis affects humans only. Recently, a new mice model of psoriasis-like skin inflammation induced by topical application of imiquimod has been introduced. Our aim is to test this model in a human context by applying imiquimod to non-lesional skin in psoriasis patients.

MATERIALS AND METHODS: Untreated psoriasis patients are treated with imiquimod and vehicle occluded by Finn Chambers for 48 hours or for 7 days. Prior to the treatment the skin is tape-stripped to ensure sufficient imiquimod/vehicle absorption. On day 2, 4, 7 and 10 or on day 7, 10 and 21, respectively, a clinical assessment of the skin inflammation was made and skin biopsies taken.

RESULTS: Thirteen patients have been included in the study. Of six patients (10-fold tape stripped and treated with Imiquimod for 2 days) five developed skin inflammation in the treated areas. HE-stained tissue sections of skin biopsies showed hyperplasia of epidermis, parakeratosis and a superficial

perivascular infiltrate in the dermis. One developed no skin reaction. Tape stripping was increased to 15-fold in three patients inducing spongiosis. Three patients were treated under occlusion for 7 days (10-fold tape-stripped). One developed a skin reaction similar to the patients treated for 2 days, one developed psoriasis in the treated areas probably due to Köbner phenomena and one developed no reaction. PCR is being evaluated at the moment.

PERSPECTIVES: If successful this study will improve the understanding of the pathogenesis of psoriasis and facilitate the identification of new targets in the treatment of psoriasis and other inflammatory diseases.

P22.04 René Østgård INTESTINAL INFLAMMATION IN ANKYLOSING SPONDYLITIS ASSESSED BY FECAL CALPROTECTIN, CAPSULE ENDOSCOPY, AND COLONOSCOPY AND THE EFFECT OF ADALIMUMAB ON MUCOSLA HEALING

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Background:

Studies of patients with Spondyloarthritis (SpA) but asymptomatic abdominal wise who underwent ileocolonoscopy demonstrated frequent subclinical gut inflammation. The changes seen in these patients could not be further classified histologically but immunological studies links SpA with Crohn's disease. Furthermore only Tumor Necrosis Factor – alpha (TNF-alpha) inhibitor and NSAID treatment are effective SpA but NSAID is harmful in intestinal disease. Routine colonoscopy is not recommended in these patients.

Hypothesis:

We expect to find increased intestinal inflammation in the small intestine in patients with active SpA and subsequent mucosal healing after treatment with adalimumab.

Purpose:

To establish the proportion of otherwise intestinally low-symptomatic patients with intestinal ulcers in patients diagnosed with active SpA and to illustrate the healing rate intestinally and inflammatory changes following TNF-alpha inhibitor treatment.

Materials and methods:

40 SpA patients with active disease. 25 patients with elevated feces calprotectin despite discontinuation of NSAID and 15 with normal levels are included. The patients are treated with adalimumab and are examined with capsular endoscopy, colonoscopy and MRI before and after treatment. In addition blood samples are drawn before treatment and after 12, 20 and 52 weeks for inflammatory analysis.

Perspective:

Elucidating the extent of intestinal inflammation and inflammatory in SpA clues for further unraveling of the pathogenesis of the disease. Calprotectin screening in SpA may be indicated

Status: 6 positive patients included. All with small bowel ulcers. No ulcers seen in the first control patient

P22.05 Julie Prahl PREVALENCE OF, RISK FACTORS FOR AND CONSEQUENCES OF LOW PLASMA CONCENTRATIONS OF FIRST-LINE TB DRUGS

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Background:

Tuberculosis (TB) is a global pandemic, with 9 million new cases of TB disease and approximately 2 million deaths each year. Cure rates exceed 95% with appropriate therapy, and death is a consequence of delayed diagnosis and ineffective or incomplete treatment. In treatment-compliant patients ineffective treatment could be a consequence of lower than expected plasma levels of one or more of the first-line antituberculosis drugs possibly caused by malabsorption, inaccurate dosing, altered metabolism, drug-drug interaction etc. In most cases low plasma levels can be corrected by dose adjustment.

Objective:

To assess the prevalence of, risk factors for and consequences of lower than expected drug concentrations in plasma of first-line drugs in Denmark.

Design:

Plasma concentrations of isoniazid, rifampicin, ethambutol and pyrazinamide were measured among 32 patients with active TB and 3 patients in prophylactic treatment.

Preliminary results:

Of the 35 patients enrolled 21 (60%) were inpatients. 21 (66%) of the 32 patients with active TB had pulmonary TB. 4 (11%) had a history of earlier TB, 5 (14%) had concomitant diabetes and 2 (6%) were HIV positive. 3 (9%) were lost to follow-up, and at present relapse has been observed in 2 patients (7%) and death during treatment in 3 (9%) patients.

The following numbers of patients had low plasma concentrations of the following drugs: isoniazid 25/35 (71%), rifampicin 19/33 (58%), ethambutol 10/28 (36%), pyrazinamide 3/29 (10%), both isoniazid and rifampicin 15/33 (45%).

Low serum albumin at time of diagnosis were associated with having rifampicin concentrations lower than the median rifampicin concentration ($p=0.11$).

P22.06 Nis Pedersen Jørgensen

BIOFILM FORMATION BY (SA) ON ORTHOPEDIC IMPLANTS IN A NOVEL MURINE INFECTION MODEL MIMICKING A CHRONIC, IMPLANT ASSOCIATED OSTEOMYELITIS (OM)

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Background Staphylococci are the most common pathogen causing infections on orthopedic implants, with SA accounting for nearly 35% of all implant associated OM. Implant associated OM is often characterized by the formation of bacterial biofilms, greatly increasing antibiotic resistance. Treatment options are hindered by the lack of an animal model.

Methods: 2 strains of SA, 1 MSSA (Xen29) and 1 MRSA (Xen30) were used to infect female C57Bl/6 mice. The implant-associated OM was established by a transcortical implantation of a stainless steel pin through the tibia. Prior to surgery, the pins were incubated in PBS containing 25% murine serum for 24 hours. Afterwards the pins were removed and placed in a MH bouillon containing 3.5% NaCl and 10^6 cfu/ml and incubated for additional 24 hours.

Animals were divided into two groups, one receiving MSSA and the other MRSA. At 5 defined time points, 5 animals from each group were sacrificed. Quantification of bacterial kinetics were done by CFU counts from both tibia and implant samples. Bacteria were extracted from the tibia by tissue homogenization and from the implants by ultrasonication. Assessment of biofilm formation on the implant was done by epifluorescent microscopy.

Results: A localized, clinical infection was developed in all animals. Epifluorescent microscopy confirmed the presence of a biofilm by day 4 after the implantation of the colonized pins. Bacterial load at the time of sacrifice were quantified in both tibia and implant samples.

Conclusion: We have established an animal model wherein it is possible to induce implant associated OM caused by SA.

P22.07 Thomas Aagaard Rasmussen

COMPARISON OF HISTONE DEACETYLASE (HDAC) INHIBITORS IN CLINICAL USE: POTENTIAL FOR DISRUPTING HIV-LATENCY AND EFFECT ON T-CELL ACTIVATION

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Background

To eradicate HIV-infection, the reservoir of latently infected resting T-cells must be depleted. We investigated the potential for disrupting HIV-latency of histone deacetylase inhibitors (HDACi) in clinical use.

Methods

The latently infected cell lines ACH2 and U1 were treated with the HDACi ITF2357 (givinostat), PXD101 (belinostat), SAHA (vorinostat), and valproic acid (VPA) across a broad range of concentrations. We estimated viral

replication by p24 production in culture supernatant using enzyme linked immunosorbent assay (ELISA). The potency of reversing HIV-latency was defined as p24 fold-increase above background. Peripheral blood mononuclear cells (PBMCs) from healthy donors were treated with the HDACi and the expression of T-cell phenotype and activation markers and HIV co-receptors were measured using flow cytometry.

Results

Both ITF2357 and PXD101 displayed significantly higher potency in stimulating HIV-1 expression than SAHA and VPA in the clinically relevant concentration range 125-500nM. Compared to untreated cultures, ITF2357 increased p24 levels 30.0-fold and 217-fold, PXD101 6.4-fold and 40.7-fold, and SAHA 3.2-fold and 14.1-fold at 125 and 250nM, respectively. The proportion of primary T-cells expressing CD69 increased from 39.5% in untreated cells to 85.9% in ITF2357-treated cells, 83.4% in PXD101-treated cells, 65.1% in SAHA-treated cells, and 50.1% in VPA-treated cells.

Conclusion

At physiological concentrations ITF2357 and PXD101 stimulates HIV-1 expression from latently infected cell lines more efficiently than SAHA and VPA. Given the safety profile ITF2357 emerges as an attractive candidate for purging of the latent HIV-reservoir.

P22.08 Lone Schmidt Sørensen

RAPID INCORPORATION OF OMEGA-3 FATTY ACIDS INTO PATIENTS COLONIC TISSUE AFTER ORAL SUPPLEMENTATION

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Rationale: Supplementation with omega-3 (n-3) fatty acids (FA) may alter postsurgical inflammatory response. The aim of this study was to investigate whether oral nutritional supplement (ONS) rich in n-3 FA, given for 7 days before surgery would be sufficient to incorporate n-3 FA into cell membranes of the colonic mucosa and colonic wall. Methods: A randomized, double-blind, placebo-controlled single centre intervention trial. 148 patients referred for colorectal cancer surgery received either an n-3 FA enriched ONS (Supportan®DRINK Fresenius Kabi 200 ml) twice daily, providing 2 g of eicasopentaenoic acid (EPA) and 1 g of docosahexaenoic acid (DHA) per day or a standard ONS for 7 days before surgery. Blood and tissue samples from a subgroup of 40 patients were taken. FA composition of tissues were analysed by gas chromatography. Results: 40 patients were included (female/male ratio 13/27) with a median age of 67 years (range 41-89). The two groups were comparable regarding demographics, surgical procedure, tumour stage, and nutritional risk status. We found a significant incorporation of EPA but not DHA into colonic mucosa (p=0.001) and colonic wall (p=0.004) in patients randomized to the n-3 FA supplement when compared to controls. Mean (SD) EPA mucosa: 0.8 (0.70) and EPA wall: 0.39 (0.29) in patients who received the n-3 FA supplement. EPA mucosa: 0.30 (0.31) and EPA wall: 0.16 (0.10) in the control group. FA are given as % of total amount of FA. Conclusion: EPA was incorporated into

colonic mucosa and colonic wall in patients receiving 7 days of n-3 FA supplementation.

P22.09 Lise Tornvig Erikstrup

DISK DIFFUSION ANTIMICROBIAL SUSCEPTIBILITY TESTING OF CLOSTRIDIUM DIFFICILE

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Objective: Reports of resistance and reduced susceptibility to metronidazole and vancomycin emphasize the need for surveillance of antimicrobial susceptibility of Clostridium difficile. The aim of our study was to evaluate disk diffusion for antimicrobial susceptibility testing of C. difficile by comparing our results with E-test.

Methods: Consecutive clinical isolates of C. difficile (n=118) collected from patients with diarrhea hospitalized at Aarhus University Hospital in 2008 were tested by E-test and disk diffusion. The media used were Brucella blood agar (Becton Dickinson, Europe). The plates were incubated in anaerobic atmosphere for 24 hours. Disk diffusion: Oxoid disks (Oxoid, UK) of vancomycin (5 ug) and metronidazole (5 ug) were used. The zone of inhibition was read in mm by a ruler. MIC determination by E-test: E-test strips (bioMérieux, France) with vancomycin and metronidazole were aseptically placed on the agar surface. The MIC was read at the point where the zone of complete inhibition intersected the MIC scale.

Results: For both vancomycin and metronidazole we found no resistant strains. For vancomycin the MIC ranged from 0.38-1.0 mg/L with an MIC_{50} of 0.5 mg/L and MIC_{90} of 0.75 mg/L. The zone diameter ranged from 21-27 mm. For metronidazole the MIC ranged from 0.023-0.75 mg/L with an MIC_{50} of 0.19 mg/L and MIC_{90} of 0.38 mg/L. The zone diameter ranged from 24-47 mm.

Conclusion: There was agreement between MIC values and zone diameter with an expectable and acceptable dispersion of one MIC value on 7-8 mm on the zone diameter. Therefore, we conclude that there is agreement between E-test and disk diffusion for vancomycin and metronidazole.

P22.10 Morten Leif Munding Stilund

SOLUBLE CD163 AS A DIAGNOSTIC MARKER IN MULTIPLE SCLEROSIS.

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Background

CD163 is a macrophage specific protein, which in its soluble form (sCD163) has been shown to be up-regulated in serum from patients with multiple sclerosis (MS).

Hypothesis and Aim:

We wanted to investigate if sCD163 was measurable in cerebrospinal fluid and whether it may serve as a novel diagnostic marker for MS.

Methods:

Paired samples of CSF and serum were drawn from 72 patients suspected for MS or other neurological disease at the Department of Neurology at Aarhus University Hospital. MRI scans were performed and the revised diagnostic criteria for MS used. CSF and serum levels of sCD163 were determined by ELISA. The control group consisted of 16 patients with neurological symptoms but yet had a normal MRI, normal CSF and a normal neurological clinical examination.

Results:

sCD163 was detectable in all CSF samples. The median level of sCD163 in CSF in 46 patients with MS was 0.091 mg/ml, which was significantly different from the control group, median level 0.068 mg/ml ($p<0.003$). A higher value was found in 10 patients with primary progressive MS (PPMS) (0.106 mg/ml) compared to 36 patients with relapse-remitting MS (0.087 mg/ml). Compared to the group of neurological patients without signs of CNS inflammation, patients with MS had significantly increased CSF levels of sCD163 ($p<0.003$) and patients with PPMS showed a tendency to have an even higher value ($p<0.043$).
 Conclusion:

sCD163 from macrophages is measurable in CSF and levels seem to be generally increased in MS. High values were especially found in PPMS. Inclusion of patients and controls is ongoing and further studies are planned to determine the diagnostic value of sCD163 and other markers in MS.

P22.11 Kresten Krarup Keller

INCREASING OSTEOCLASTIC BONE LOSS INSPITE OF FEWER OSTEOCLAST PRECURSORS DURING CHRONIC AUTOIMMUNE SKG-ARTHRTITIS EVALUATED BY 3D STEREOLOGICAL ESTIMATORS

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Objective

To investigate the arthritic and bone erosive changes, including the number of osteoclasts and osteoclast precursors in new SKG-model of inflammatory polyarthritis using 3D stereological estimators.

Methods

Arthritis was induced in female SKG-mice with Zymosan A. Quantitative histology was made in four control mice and four mice with arthritis euthanized after 6 and 12 weeks. Right hind paw was embedded undecalcified in methylmethacrylate and cut exhaustively generating vertical

uniform random sections. A computer controlled microscope and stereological software was used for histological quantification. Total volumes were estimated according to the Cavalieri principle, total surfaces were estimated using the vertical sections design, and the number of osteoclasts was counted in a physical fractionator.

Results

Arthritis score increased during the 12-week period and was paralleled by an increase in the volume of inflammatory tissue ($r=0.96$, $p<0.001$). The number of osteoclasts on bone ($r=0.77$, $p<0.05$) and osteoclast-covered bone surface ($r=0.62$, $p<0.05$) increased resulting in a decrease in volume of bone ($r=-0.65$, $p<0.05$). However, the number of osteoclast precursors declined between week 6 and 12 ($p<0.05$). The total cartilage surface ($r=-0.74$, $p<0.05$) and cartilage volume ($r=-0.74$, $p<0.05$) decreased during the 12 weeks of arthritis.

Conclusions

Bone erosion progressed although osteoclastogenesis was slowing. The decline in osteoclastogenesis in late stage disease may be uncoupled from both the inflammatory process and the development of bone erosions. This is the first time 3D quantitative histology has been applied in a mouse model of rheumatoid arthritis.

P22.12 Kristian Kjær Andersen

IS ENDOVASCULAR COOLING LESS STRESSFUL THAN SURFACE COOLING? STRESS, CEREBRAL, AND METABOLIC RESPONSES IN A PORCINE MODEL OF MILD HYPOTHERMIA.

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Introduction: Mild therapeutic hypothermia improves outcome after cardiac arrest. Endovascular or surface cooling methods can be used. The latter elicits a strong sympathoadrenal response, which can have adverse effects on muscle and brain, resulting in hypoxia or ischemia.

The effect of hypothermia per se on possible brain edema has not been investigated in a post cardiac arrest setting.

Objectives: To investigate whether endovascular cooling is superior to surface cooling during mild hypothermia in regards to eliciting a lower stress-response. To elucidate the effect of hypothermia on possible brain edema.

Methods: Eighteen 60 kg female pigs are randomised to endovascular cooling, surface cooling or control. Bloodsamples are obtained at discrete timepoints. MRI, mikrodialysis, near infrared spectroscopy and a probe measuring temperature, pressure and oxygen content is used to access intra cerebral parameters. Microdialysis is performed in muscle and skin.

Primary endpoint is the difference in plasma epinephrine between groups.

Secondary endpoints include p-norepinephrine, s-cortisol, s-ACTH, electrolytes, acid-base status, L/P ratio, and change in whole brain volume.

P23.01 Christina Kjærgaard Rasmussen

2- AND 3-DIMENSIONAL ULTRASOUND IN DIAGNOSING ADENOMYOSIS &NDASH; DIAGNOSTIC ACCURACY AND OBSERVER VARIATION

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Introduction: Diagnosing adenomyosis with 2-Dimensional (2D) transvaginal ultrasound (TVU) is highly dependent on the observer. Using 3-Dimensional (3D) TVU it is possible to visualize the junctional zone and to save 3D volumes. We wish to evaluate the use of 2- and 3D TVU as a tool to diagnose adenomyosis based on observer variation and accuracy. The findings will be controlled by the gold standard pathology. Furthermore, we wish to establish a consensus on the classification, grade and stage of adenomyosis using 2- and 3D TVU.

Methods: 120 premenopausal women scheduled for either hysterectomy or transcervical resection of the endometrium (TCRE) for benign reasons will be enrolled. The regional ethical committee has approved the project. Participating patients will go through a preoperational 2- and 3D TVU examination performed by an experienced and an inexperienced observer, blinded to each other. Additionally, a 30 sec 2D video sweep and 3D volumes will be saved for later evaluation. Results of these examinations will be correlated blindly to the presence of adenomyosis on histological specimens. All patients will fill out a validated questionnaire.

Perspectives: If 3D TVU combined with the normal 2D TVU examination improves the diagnostic accuracy for adenomyosis it can pave the way for future diagnosis of adenomyosis. Ideally a less experienced gynecologist will be able to do the examination and the stored 3D volumes can be sent electronically to an experienced gynecologist for the final judgment. If the diagnosis of adenomyosis by 2- and 3D TVU is highly accurate, it will be possible to test new minimal invasive treatments as alternatives to hysterectomy and TCRE.

P23.02 Anni Assing Winckelmann

CLINICAL USE OF TOLL-LIKE RECEPTOR 9 AGONIST CPG: EFFECT ON IMMUNE ACTIVATION AND PROVIRAL RESERVOIR IN HAART-TREATED HIV-INFECTED PATIENTS.

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Introduction:

Highly active antiretroviral therapy (HAART) today is able to suppress infection and restore immune function in HIV patients, but interruption of treatment results in a rapid rebound of infection. This is caused by activation of a reservoir of latently infected CD4+ T-cells. We wish to investigate the effect of TLR-9 agonist CpG 7909 on the size of the proviral reservoir and T-cell activation in HIV-infected individuals on HAART.

Methods:

We will use collected PBMCs from a randomized controlled trial, where HIV-infected patients were randomized to receive pneumococcal vaccine with or without CpG as adjuvant at 0, 3 and 9 months. Of 76 study participants on HAART, 70 completed the 10 months follow-up, whereof 32 received CpG as adjuvant and 38 received a placebo adjuvant. The Danish Research Ethics Committee and The Danish Data Protection Agency have approved the original clinical study. The viral reservoir is quantified by measuring the frequency of CD4+ T-cells carrying integrated HIV-DNA using real-time PCR. T-cell activation, T-cell phenotype and T-cell expression of HIV co-receptors will be measured using flow cytometry. Measurements will be made prior to and one month after the 3rd vaccination (at 9 and 10 months, respectively). Changes will be calculated for each patient and compared across the two study arms.

Perspectives:

This study will investigate the possible effects of CpG in reducing the proviral HIV-reservoir. The emerging perspective, should we find indications that treatment with CpG reduces the proviral reservoir, will be of a new clinical study with CpG in HIV-infected patients on suppressive HAART.

P23.03 Laura Laine Larsen

HMICL - A NOVEL MARKER FOR IDENTIFYING MPN PATIENTS AT RISK OF LEUKEMIC TRANSFORMATION?

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Background: Myeloproliferative neoplasms (MPN) constitute a heterogeneous group of pre-leukemic diseases including polycythaemia vera, essential trombocythaemia, myelofibrosis and chronic myeloid leukemia. Leukemic transformation occurs in 5-30% of cases with MPN.

Evidently, a single point mutation in the JAK2-gene explains the pathogenetic background of most MPNs, however the cause of leukemic transformation has yet to be unraveled.

Surface expression of human myeloid inhibitory C-type lectin-like receptor (hMICL) has proved reliable in diagnosing acute myeloid leukemia. This unique property of hMICL may also be applicable in MPN.

Aim: To quantify the hMICL+ progenitors in patients with MPN and correlate this to stage of MPN disease and progression. Furthermore, gene expression levels of mutated JAK2 in purified hMICL+ progenitors will be performed to elucidate the malignant nature of these putative leukemic stem cells. In addition, culturing of the hMICL+ progenitors will determine the proliferative potential of this subset.

Material and methods: Cell surface expression of hMICL on circulating progenitors in peripheral blood will be measured by flow cytometry. Isolation of hMICL+ cells will be performed using immunomagnetic beads and FACS-sorting. qPCR will be used for quantification of mutated JAK2 expression levels. Culturing of cells in methylcellulose will be performed to

unravel the leukemogenic potential of purified cell populations.

P23.04 Kira Schreiner Simonsen

HAPTOCORRIN - A NEW BIOMARKER FOR PRIMARY LIVER CANCER?

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Background:

Annually, 250 patients are diagnosed with hepatocellular carcinoma (HCC) in Denmark. HCC is fairly rare, but untreated the survival rate is very low. Treatment depends both on tumour characteristics and underlying liver function. Curative treatment in form of resection is often not an option, since most cases develop in patients with liver cirrhosis. The existing biomarker, alpha-fetoprotein (AFP), is deficient in 20% of HCC cases, and can be a false positive, as AFP is elevated in conditions with liver regeneration.

Haptocorrin has previously been described elevated in subtypes of HCC, and has been suggested to be related to HCC for some time. However, the literature on the subject is of an older date, and covers only smaller populations.

The aim of the study is to investigate Haptocorrin as a biomarker for HCC based on larger cross-sectional and prospective cohorts than previously described.

Hypotheses:

- Haptocorrin is elevated in patients with HCC and is correlated to tumor size and dissemination.

- Haptocorrin is unaffected by other liver diseases.

- Haptocorrin levels are reduced following tumor ablation.

Methods:

The study is based on two populations:

55 patients from Aarhus with HCC followed with blood samples and medical imaging before and after ablative treatment.

100 patients with HCC and 100 age and gender matched controls with cirrhosis from Melbourne, Australia.

The results will be compared with a group of healthy gender and age matched controls from a Danish biobank.

Blood samples will be analyzed for Haptocorrin, liver enzymes, kidney function, AFP, CP-score and MELD-score. For TNM-classification we have CT/MRI results.

P23.05 Lise Brehm Høj

CLINICAL DATABASE FOR PATIENTS WITH NEUROENDOCRINE TUMOURS

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Background:

Neuroendocrine tumours (NETs) develop from the diffuse neuroendocrine system. The tumours are rare but occur with increasing incidence. The SEER Programme has demonstrated an annual increase in incidence from 1.1/100 000 in 1973 to 5.3/100 000 in 2004. In particular the incidence of NETs in the bronchopulmonary system, small intestine and rectum has increased considerably.

Medical Department Aarhus University Hospital, is responsible for the treatment of NET patients in the Western part of Denmark with a population of approximately 1.9 million people.

Purpose:

In 2007 Medical Department V established a clinical database with data from patients with classical midgut carcinoids treated at the department from 1994 until 2003. During this research year we wish to create a new database including patients with all types of NETs seen at the Medical Department V from 1994 untill 2011. Almost 500 patients have been seen in this time period. With establishment of the database we will be able to study survival in our population of NET patients and thus be able to compare our treatment results with those from other NET Centers.

Methods:

We will make a retrospective evaluation of diagnostics and treatment of NET patients at Medical Department V. Clinical and biochemical data from patients will be extracted from hospital records and included in the database. Based on these data analysis of survival among the patients will be performed with use of the Kaplan-Meier analysis. Prognostic markers for survival (sex, age, primary tumour, Ki-67 index, TNM- and WHO-classification) will be evaluated.

P23.06 Heidi Buvarp Dyrop

EFFECTS OF A LAW BASED TIME SCHEDULE FOR DIAGNOSTICS AND TREATMENT IN SUSPECTED SARCOMA PATIENTS

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Introduction: Sarcomas represent less than 1% of all newly diagnosed cancers in Denmark. Definitive diagnostics and treatment are centralized to a small number of sarcoma centers. For cancer diseases an early treatment is vital, but it is still a big problem both nationally and internationally that patients go through a delay before getting the needed treatment. The cancer pathway for treatment of sarcomas were introduced on the 1st of January

2009, defining criteria for suspicion of cancer and process times for each phase, but the evidence for these criteria is only partially examined. The intention of cancer pathways is to bring attention to the diseases and also improve the effort of the hospital system through a faster diagnostic process, but it is virtually unknown to what extent they have contributed to a faster treatment.

Aims: 1) Study the frequency of sarcoma in patients referred to cancer pathways. 2) Investigate the occurrence of symptoms defined in the criteria for cancer suspicion. 3) Compare the process time from 1st contact to start of treatment before and after introduction of cancer pathways. 4) Investigate if the diagnostic program can be carried out on time, and whether delay is caused by justified supplementary diagnostics. 5) Examine whether cancer pathways have affected the time period from 1st symptom to treatment.

Materials and methods: The study population of approximately 1600 patients consists of patients referred from other hospitals to the Sarcoma centre with a suspicion of cancer, in the period 01.01.2007 – 31.12.2010. Patient records will be reviewed for data on symptoms, diagnostics and process times.

P23.07 Cecilie Ejerskov Pedersen

BOWEL FUNCTION IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1

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Background: Although special eating habits, altered bowel function and need of laxatives occur among children with neurofibromatosis type 1 (NF1), no systematic investigations of bowel function in children with NF1 have to date been published.

Aim: The study aims to compare bowel function in children with NF1 with that of healthy children of the same age and to investigate the hypothesis that children with NF1 have prolonged colonic transit time and an abnormally large rectum diameter.

Methods: We investigate 20 children with NF1 aged 4-11 years. The descriptive study includes the following investigations:

Rome III criteria: The child's gastrointestinal symptoms are classified based on category H diagnostic criteria.

Transabdominal ultrasound of rectal diameter: On the first visit the rectal diameter is measured three times and the mean calculated.

Dietary habits: A three-day diary analysis focusing on composition, energy intake and whether the diet is inducive of diarrhoea or constipation.

Bowel movements: A two week diary on the frequency of bowel movements and consistency of stools.

Colonic transit time (CTT): One capsule per day containing radiopaque markers is ingested on six successive days. An abdominal X-ray is taken on

day seven.

Collection: Data collection is expected to be finished by February 2012.

Results: Results from children with NF1 are compared to literature-based normative data on healthy same-age children.

P23.08 Jonas Franck Olesen

LOCAL EFFECTS OF AMINO ACIDS, ANDIN THE BILATERALLY PERFUSED HUMAN LEG

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Introduction: Protein loss during critical illness is an important problem and is shown to predict overall survival. In animal studies, infusion of leucine is shown to increase the synthesis of muscle protein by 30-40% and decrease protein degradation by 30%. Animal studies also show that after administrating 3-hydroxybutyrate (3-OHB), cardiac output increase, and O_2 consumption decrease. Humane studies show 10% increase in protein synthesis and 30% decrease in protein degradation after administration of 3-OHB.

Objectives: Compared to saline, an amino acid infusion in the femoral artery will promote protein synthesis and inhibit breakdown assessed with local a/v phenylalanine and tyrosine tracer kinetics in healthy volunteers. These effects will be further amplified by leucine and 3-OHB enrichment and will include distinct alterations in muscle signal events, in particular mTOR.

Methods: n = 4 x 8 healthy male subjects are equipped with catheters in aa. femorales and vv. femorales bilaterally under local anaesthetics. Each study comprises a 3-hour basal period and a 3-hour period with hyperinsulinaemic-euglucaemic clamp. During the test, samples of arterial and venous blood and 4 muscle biopsies are obtained. The 4 different studies contain continues saline infusion compared to either (i) amino acids (Vamin), (ii) Vamin + leucine, (iii) Vamin + 3-OHB or (iiii) Vamin + leucine + 3-OHB.

Perspectives: This study elucidates whether infusion of aminoacids, leucin and 3-hydroxybutyrate can diminish protein loss and thereby potentially improve the nutrition of all critically ill patients.

P23.09 Steen Kåre Fagerberg

α-HAEMOLYSIN FROM INDUCES SHRINKAGE AND PHAGOCYTOSIS OF ERYTHROCYTES BY THP-1 MONOCYTES

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The lysis produced by α-haemolysin (HlyA) from E. coli is surprisingly preceded by a volume reduction.(1) This volume reduction is a consequence of an increase in the intracellular Ca^{2+} concentration, which triggers activation of the K^+ channel $K_{Ca}3.1$ and Cl^- channel TMEM16A. These events

are associated with phosphatidyl serine (PS)-exposure, which is a signal for clearance of erythrocytes (RBCs) by monocytes from the blood stream. Calcein loaded RBCs were incubated with or without HlyA, and added to THP-1 cells on coverslips. Phagocytosis was measured as calcein positive THP-1 cells after 60 min. RBCs exposed to ionomycin was used as positive controls. Addition of HlyA and ionomycin both significantly increased the phagocytosis of RBCs with 126% and 120% respectively. The uptake of RBCs in THP-1 cells was verified by immunocytochemistry using an anti-haemolglobin antibody. By this method we could visualize the volume reduced RBC inside the THP-1 cell. HlyA is known to trigger ATP release, but the HlyA and ionomycin induced phagocytosis was not affected by extracellular ATP, neither did ATP by itself trigger RBC phagocytosis by THP-1 cells. These data suggest that HlyA is a strong signal for phagocytosis, which potentially will allow clearance of RBCs before substantial hemolysis is evident during gram-negative sepsis. This project was funded by The Danish Council for Independent Research, Medical Sciences.

1. M. Skals et al., Journal of Biological Chemistry 285, 15557 (2010).

P23.10 Eva Mikkelsen ELECTROMYOGRAPHIC CHARACTERIZATION OF LABOR

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Background: Better methods are needed for preterm labor diagnostication. We hypothesize 1) that depolarization of the myometrium propagates from fundus to isthmus, 2) that the propagation velocity (PV) is faster in labor than in non-labor, and 3) that PV can be determined by electromyography (EMG). PV may be the best EMG-predictor of preterm labor. Knowledge on how to determine PV is insufficient though.

Objective: To investigate EMG-signals from laboring myometrium and to develop a method for determining PV.

Method: We included 10 women in active labor. EMG-signals were obtained via three monopolar, abdominal surface electrodes placed vertically in the midline with a distance of 6.5-11.2 cm between the electrodes.

Labview software was used for signal visualization and data processing. We calculated the PV from the distance between the electrodes and the time displacement of similar signals. For calculating time displacement, we used cross-correlation to identify similar signals.

Results: Each contraction consisted of 25-45 fluctuations with variable amplitudes. Background fluctuations with smaller amplitudes were observed between contractions. The signal order was random and independent of the vertical electrode order.

Conclusion: Depolarization of the laboring myometrium may therefore not occur in the direction from fundus to isthmus. Further investigation is needed for PV determination.

P23.11 Katrine Pedersen

THYMIC OUTPUT AND PROGRESSION OF HIV IN CHILDREN

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Disease progression and response to therapy in children infected with HIV is different to that of adults. Immune reconstitution in children on antiretroviral therapy occurs predominantly via generation of naïve T-cells, largely due to higher thymic output, whereas in adults it is mainly memory T-cells. Until now thymic output could only be estimated by using thymic receptor excision circles (TRECS) and/or markers expressed on recent thymic emigrants. However, these are confounded by peripheral T-cell division and cannot in themselves be used as quantitative estimates of thymic output. My aim is to combine experimental data with a mathematical model, as described by colleagues at Institute of Child Health, to give explicit measures of thymic output in children infected with HIV. I will relate this to disease progression and response to treatment, and establish the importance of thymic output for maintaining the naive T-cell pool in children infected with HIV.

Blood samples are being collected from the HIV clinic at Great Ormond Street Hospital, as well as from age matched controls. Blood samples from thymectomised patients will also be used. The mathematical model combines measurements of TRECs and a marker for peripheral T-cell division, Ki67. The model was validated against estimates of thymic output from size and cellularity of thymuses obtained at autopsy in children. Naïve T-cells are being identified phenotypically by staining for CD3/CD4/CD45RA. Dividing cells are being determined by Ki67 staining. TRECs are being determined by Real Time PCR. TRECs and Ki67 measurements are being carried out on naïve $CD4^+$, $CD45RA^+$ T-cells isolated with Miltenyi bead separation kits.

P23.12 Line Mouritsen Underbjerg

HYPOPARATHYROIDISM, AUTOSOMALT DOMINANT HYPOCALCAMIA AND PSEUDOHYPOPARATHYROIDISM IN DENMARK - EPIDEMIOLOGY, CAUSES, SYMPTOMS AND PROGNOSIS

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BACKGROUND: Hypoparathyroidism (HypoPT) is a relatively rare disease, characterized by low levels of parathyroidea hormone, [PTH] and plasma calcium. The most common cause of chronic HypoPT is following neck surgery. Other rare causes are congenital HypoPT, autoimmune destruction of the parathyroid glands, autosomal dominant hypocalcaemia (ADH), or magnesium deficiency. Pseudohypoparathyroidism (pseudoHypoPT) caused by peripheral resistance to PTH may have identical symptoms and clinical findings. Neither in Denmark or anywhere else in the world reliable information regarding the frequency of HypoPT or its consequences are available.

AIM: The aim of the study is to identify the number of people in Denmark with HypoPT incl. ADH and pseudoHypoPT. Furthermore, we aim at

identifying possible complications, especially the prevalence of kidney-, cardiovascular- and neuropsychiatric disease, fertility, hospitalization required hypo- or hypercalcaemia, overall number of hospitalizations and mortality. Finally, we will perform detailed examination and clinical characterization of patients with idiopathic HypoPT and pseudoHypoPT including gene diagnostics and family tracing for hereditary forms.

METHOD: The study is primarily conducted as a case-finding study in order to identify patients with possible HypoPT through existing registers (The National Medical Register and The National Board of Health Register, Denmark) with subsequent validation of the diagnosis by reviewing the patients medical charts. Secondarily, a case-control-study and clinical characterization of patients with idiopathic HypoPT are performed.

P24.01 Lone Winther Lietzen

USE OF GLUCOCORTICOIDS AND RISK OF BREAST CANCER RECURRENCE

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Background: Synthetic glucocorticoids (GCs) are used to depress the immune response.GCs have many side effects and may be carcinogenic.The effect of GC use on breast cancer prognosis is not known.

Objectives: To assess the effect of GC use on breast cancer recurrence.

Methods: We will conduct a population-based cohort study of the risk of breast cancer recurrence associated with use of systemic GCs among incident female breast cancer patients(UICC stage I, II or III) aged >18 years in Denmark and diagnosed between 01/01/1996 and 31/12/2006. Data on breast cancer patients, clinical and treatment factors, follow-up (recurrence,vital status) and co-morbidities will be obtained from the Danish Breast Cancer Cooperative Group, Danish Civil Registry and Danish National Registry of Patients. Data on GC prescriptions will be retrieved from the Register of Medicinal Product Statistics (RMPS). Patients will be categorized as ever versus never GC use; ever users will be stratified by dose and temporality. Women will be followed-up for 10 years or until 31/12/2009. We will use Cox proportional hazards regression models to assess the risk of breast cancer recurrence among GC users compared with non-users, adjusting for potential confounders.

Results: The cohort will include approximately 19,000 breast cancer patients.We will present descriptive characteristics of the study cohort and potential associations between risk of breast cancer recurrence among women with no history of GC use and those with a history of GC use.

Conclusion: This study will extend the limited current knowledge and provide vital clinical information on the risk of breast cancer recurrence associated with GC use.

P24.02 Kristoffer Koch

IMPACT OF SOCIOECONOMIC POSITION ON ONE-YEAR MORTALITY AFTER BACTEREMIA. A POPULATION-BASED COHORT STUDY

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Background: Socioeconomic disparities in survival have been found for many diseases, even in countries providing publicly funded healthcare. However, the impact of socioeconomic position on survival after severe infection and the role of pre-existing chronic diseases in this association have not been thoroughly investigated.

Objective: To examine the associations between socioeconomic position and one-year mortality after hospitalization with bacteremia.

Methods: We will conduct a population-based cohort study in two Danish regions with a population of 2.3 million people. From region-based bacteremia registries we will identify all patients in the age group 30-65 years hospitalized with bacteremia from 2000 through 2009. We will obtain information on socioeconomic position for all bacteremia patients (income, level of education, affiliation to the work market) from registries maintained by Statistics Denmark. Information on the patient's pre-existing chronic diseases will be obtained from the National Patient Registry, which contains information on all diagnoses received by patients in hospitals and outpatient clinics in Denmark. The impact of socioeconomic position on mortality rates one year after hospitalization with bacteremia will be examined with and without sequential risk adjustment for age, sex, ethnicity, major pre-existing chronic diseases, and bacteremia type.

Perspectives: In this study, we aim to elucidate the role of socioeconomic position in survival after bacteremia. We believe that the study will advance our knowledge of the clinical course of bacteremia and may discover targets for effective prevention to improve the outcome after bacteremia.

P24.03 Ane Birgitte Telén Andersen

MATERNAL USE OF GASTRIC ACID-SUPPRESSIVE DRUGS DURING PREGNANCY AND RISK OF ASTHMA IN OFFSPRING: A POPULATION-BASED DANISH COHORT STUDY.

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Background: Proton pump inhibitors (PPIs) may activate the immune system and cause asthma.

Objective: To investigate the association of prenatal exposure to PPIs and histamine 2-receptor antagonists (H2RAs) with risk of asthma.

Methods: In this cohort study, 197,060 singletons born between 1996 and 2008 in northern Denmark was followed until the end of 2009. Data were obtained through the Danish medical registries. Asthma in offspring was defined as at least two prescriptions of both a β-agonists and an inhaled

glucocorticoids and/or a hospital diagnosis of asthma during the follow-up. Cox proportional-hazard regression was used to compute incidence rate ratios, adjusting for covariates.

Results: 2238 (1.1%) children were exposed in utero to PPIs and 24,506 (12.4%) children developed asthma during follow-up (median follow-up = 6.8 years). The adjusted IRR (aIRR) of asthma associated with prenatal exposure to PPIs was 1.41 (95% confidence interval (CI): 1.27-1.56), compared with those unexposed prenatally. The association did not vary by trimester of exposure, and prenatal exposure to H2RAs was associated with similar increase in risk. The aIRR for maternal PPI and H2RA use in the year after giving birth, but not during pregnancy, was 1.32 (95% CI: 1.20-1.46) and 1.13 (0.93-1.36) respectively, compared with non-use during pregnancy and in the year after giving birth.

Conclusion: Prenatal exposure to PPIs was associated with an increased risk of asthma. Given the similar results seen for prenatal exposure to H2RAs, the observed association may be a manifestation of a 'class effect'.

P24.04 Palle Bager FATIGUE PREVALENCE IN IBD OUTPATIENTS IN SCANDINAVIA

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INTRODUCTION/OBJECTIVES:

In the literature, estimates of fatigue in inflammartory bowel disease (IBD) are very sparse. For IBD patients in remission the fatigue prevalence is approximately 45% vs. 20% in a healthy background population.

AIMS:

The aim was to determine the prevalence of fatigue among IBD outpatients.

METHODS:

6 centres in Denmark, Sweden and Norway consecutively included approximately 5% of their entire IBD cohort. All patients diagnosed with Crohn's disease (CD) or ulcerative colitis (UC) were included. Patients were monitored with blood samples, disease and demographics assessments. Fatigue was measured using Multidimentional Fatique Inventory (MFI 20).

RESULTS:

A total of 429 patients were included. General fatigue (GF) score for the entire cohort was (mean ±SD): 66 ±21. No statistical significant (t-test) between: CD and UC patients; anaemic and non-anaemic patients (p=0.06); patients with disease activity and in remission; iron deficiency (ID) and not ID. Females had a significant higher GF score than males (p<0.001). Regression analysis shows similar findings. GF was higher compared to the background population (mean ±SD): 35 ±28 and also higher than findings in

the part of the background population with chronic disease (mean ±SD): 46 ±30.

CONCLUSION:

Patients with IBD express more fatigue than the background population, and seem to experience more fatigue than patients with chronic diseases in general. The general fatigue score was higher among females compared to men.

P24.05 Karin Biering

WHEN IS RETURN TO WORK SAFE RETURN TO WORK? COMPARING MEASURES OF RETURN TO WORK IN A COHORT OF PATIENTS FOLLOWING PERCUTANEOUS CORONARY INTERVENTION

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Return to Work (RTW) is a commonly used term, but with a vareity of definitions. RTW is traditionally measured as a dichotomous outcome measured at a specific point in time or as a time-to-event measure.

Previous reviews have highlighted the need to combine various measures of RTW in order to capture recurrences, emphasising that the most commonly used measures capturing “time to the end of first temporary work disability period” and “time to first RTW” have limited value on their own.

The purpose of this study was to compare different RTW measures from administrative data 12 months after PCI. We also aimed to describe predictors of recurrent sick leave after first RTW.

Based on data from a cohort of 1585 study participants admitted following PCI from Aarhus University Hospital, Skejby, merged with a national register of granted social transfer payments, different definitions of RTW were established and compared using Cohen’s Kappa. We defined a “Workability score” based on number of working-weeks over total number of weeks, to capture recurrent events. Furthermore, a time-to–event analysis was performed using new sick leave as event in the time following first return to work.

We found good to excellent agreement between RTW definitions. Associations with a well-known predictor (gender) were stable within methods.

The “Workability-score” gave additional information on recurrences compared to traditional cross-sectional and time-to-event measures. Predictors of relapse of sick leave were female gender, acute indication of PCI and low score of General Health (SF12).

P24.06 Charlotte K. Lautrup

FAMILIAL RISK OF COLORECTAL CANCER - METHODS FOR TRACING FIRST DEGREE RELATIVES IN DENMARK

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Background: Investigating familial risk of diseases requires a valid identification of first degree relatives (FRDs).

Aim: To describe a method for tracing first degree relatives of colorectal cancer (CRC) patients in Denmark. Methods: A pilot study of tracing FDRs of 138 CRC patients from a cohort of 1200 patients diagnosed with CRC in 1995-1998. From questionnaires completed by patients at time of diagnosis a total of 9780 FDRs were expected. The mean year of birth of the patients was 1925 (1900-1976). Only FDRs living with the patient in 1968 can be found through the Civil Registration System (CPR) founded in 1968. The remaining FDRs must be identified by other methods. Using information on name, date of birth, and place of birth (parish) of the patients, the following search algorithm was used. 1. Searching the CPR for each patient 2. Finding parents to the patients using church books. 3. Finding siblings and children by: a) Searching the CPR for unique last names. b) Looking through church books, but only in smaller parishes.

Results: In the pilot project, the 138 CRC patients had 947 FDRs, distributed as 276 mothers, 276 fathers, 391 siblings and 280 children. Using the algorithm, 129 fathers (93.5 %), 137 mothers (99.3%), 248 (63.4%) siblings and 231 (82.5%) children were traced. In total, 745 (78.6 %) of FDRs were found.

Conclusion: The algorithm is very good at finding, in particular, parents and children.

For the most part, the work can be done on-line with web access to the CPR, and most church books up to 1950 are available. The number of found FDRs can be increased by using Population Registry cards, available from 1924-1968 in national archives.

P24.07 Shallu Sharma PREVELANCE OF COMPLICATIONS IN NEUROMUSCULAR SCOLIOSIS SURGERY: WHAT DOES THE LITERATURE TELL US?

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Background: Neuromuscular scoliosis patients have higher risk of developing complications during and after surgical treatment because of various concurrent risk factors of disease pathology and associated co morbidities. These patients have higher morbidity and mortality rates compared to other scoliosis. The neuromuscular scoliosis has the highest rate of complications (17.9%) followed by congenital (10.6%) and idiopathic (6.3%) scoliosis. The aim of the current review was to report the rates of adverse effects associated wth scoliosis surgery and to present them in light of patient and surgery related categories for comprehensive understanding.

Methods: An electronic search (1997 to 2011) yielded 356 articles. 66 were include for the review. Data extraction and management was done at various levels (study methods, participants, interventions, follow-up, outcome measure and comparisons).

Preliminary results: Diagonosis of neuromuscular scoliosis itself is one of

the most significant risk factors. Neuromuscular patients have 7 times higher risk of loosing >50% of blood volume during surgery. The progression of spinal curves in these patients is associated with significant physiological and functional impairments. Prolonged preoperative hospitilisation, extended operation duration and blood loss are the risk factors for infection. The neurological cognitive impairment, severity of deformity, use of allografts and malnutrition are precursors of high chances of infection.

These patients have multisystem involvement with pulmonary complications being one of the prominent causes of morbidity/ mortality with complications rates as high as 39%.

P24.08 Nicoline Valentina Krogstrup

IMPROVED GFR AND RENAL BLOOD PERFUSION FOLLOWING REMOTE ISCHEMIC CONDITIONING IN A PORCINE KIDNEY TRANSPLANTATION MODEL

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Delayed graft function complicates ~25% of kidney transplantations from brain dead donors. Remote ischemic conditioning (rIC) involves brief repetitive ischemia in a distant tissue in relation to ischemia/reperfusion in the target organ. rIC has been shown to induce systemic protection against ischemic injuries. Using a porcine kidney transplantation model we investigated the effects of recipient rIC on early GFR and intrarenal blood perfusion.

Brain death was induced in donor pigs (n=8) and kidneys were removed and kept in cold storage until transplantation. Nephrectomized recipient pigs were randomized to rIC (n=8) or non-rIC (n=8) with one kidney from the same donor in each group. rIC consisted of 4 x 5 min clamping of the abdominal aorta.

Mean GFR was significantly higher in the rIC group than in the non-rIC group (7.17 ml/min vs 3.43 ml/min, 95%-CI: 0.3 - 7.2 ml/min, p=0.0379). Mean renal blood flow in both cortex and medulla measured by dynamic contrast-enhanced MRI was significantly higher over time in the rIC group compared to the non-rIC group. Our study demonstrates for the first time a positive effect of rIC on early graft function and perfusion in a large animal transplantation model.

P24.09 Anne Gulbech Ording

THE CHARLSON COMORBIDITY INDEX SCORE AND BREAST CANCER INCIDENCE: A DANISH NATIONWIDE CASE-CONTROL STUDY

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Background: Only a fraction of all breast cancer cases can be explained by established risk factors. Comorbid diseases with known risk factors may be related to breast cancer incidence, providing new ideas about breast cancer etiology. The association between the Charlson comorbidity index score (CCI) and breast cancer incidence has never been studied.

Methods: This case-control study was conducted in Danish women aged 45 to 85 years who were diagnosed with breast cancer between 1994 and 2008 and registered to the Cancer Registry. 10 control women without breast cancer were risk-set sampled with replacement and matched to each breast cancer case on year of birth and calendar time. Information on comorbid conditions was retrieved from the National Registry of Patients up to 10 years before the date of inclusion. With conditional logistic regression, the association between the original and updated CCI and breast cancer incident was evaluated.

Results: 46,324 breast cancer cases and 463,240 control women were included. With both the original and updated Charlson comorbidity index score, an increasing score was associated with a weak trend toward increased risk of breast cancer up to a score of six. Among the individual Charlson diseases, lymphoma (OR=1.43, 95%CI=1.15; 1.78), any tumor (OR=1.69, 95%CI=1.10; 1.24), and metastatic solid tumor (OR=1.78, 95%CI=1.42; 2.21), were associated with increased breast cancer risk.

Conclusion: Only a weak association was observed with the Charlson comorbidity index score. The associations between the individual Charlson diseases and breast cancer support current knowledge about breast cancer risk factors and etiology.

P24.10 Louise Hjort Nielsen

REDUCTION OF VIOLENCE AMONG MENTALLY ILL OFFENDERS IN DENMARK USING STRUCTURED RISK ASSESSMENT SCHEMES

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The past 20 years have witnessed a dramatic rise in the number of mentally ill offenders in Denmark. Several studies have established a robust relationship between major mental disorders and the risk of committing a violent crime. However, little is known about the actual violent recidivism in this population in Denmark. We know little about whom, why and when mentally ill offenders re-offend, and how to best prevent this. The aim of this PhD project is to evaluate whether the use of risk management plans and intervention strategies based on two structured risk assessment schemes, the Short-Term Assessment of Risk and Treatability (START) and the Historical Clinical Risk management-20 (HCR-20) can reduce violence in a sample of Danish forensic patients from a regional Danish department of forensic psychiatry. The following research questions will be raised:

What is the predictive validity of the HCR-20 in terms of assessing the risk of violent recidivism among mentally ill offenders? Which items in the

START and the HCR-20 correlate with the risk of violence? Does the use of risk management plans and intervention strategies based on the START and the HCR-20 reduce the prevalence, severity, frequency, and/or the rate of violent episodes among mentally ill offenders in the wards and in the community? What is the interrater reliability among the staff members utilizing the START and the HCR-20?

If the use of structured risk assessment schemes can successfully identify those at risk of violent recidivism and inform the clinicians of subsequent preventive and treatment measures, we expect that the schemes will find wider application in general psychiatry throughout the region.

P24.11 Jonathan Montomoli

LIVER DISEASE AND POST-OPERATIVE MORTALITY IN PATIENTS WITH COLORECTAL CANCER: A DANISH NATIONWIDE COHORT STUDY

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Objectives: Colorectal cancer (CRC) is the third most common cancer worldwide with surgery as the main curative treatment. Chronic liver disease prevalence has increased; however, there is a limited knowledge on postoperative mortality in patients with liver disease who undergo CRC surgery.

Methods: We conducted a nationwide cohort study of all patients undergoing CRC surgery in Denmark from 1996 through 2009 by individual-level linkage of medical databases. We searched for any previous diagnosis of liver disease and categorized patients into three groups by liver disease status: no liver disease, non-cirrhotic liver disease, and liver cirrhosis. We estimated 30-day mortality in each group and used a Cox regression model to compute hazard ratios as measures of the relative risk (RR) of death, adjusting for gender, age, cancer stage, timing, comorbidities, surgery and alcoholism. Postoperative mortality and RRs were estimated for patients stratified by colon and rectal cancer.

Results: A total of 39,837 patients undergoing CRC surgery were included in the study. Of these, 369 (0.9%) had non-cirrhotic liver disease, and 158 (0.4%) had cirrhosis. Mortality was 8.7% in patients without liver disease and 13.3% in patients with non-cirrhotic liver disease with an adjusted RR of 1.43 (95% confidence interval (CI): 1.08-1.90) compared to patients without liver disease. Among patients with cirrhosis, mortality was 24.1%, corresponding to an RR of 2.77 (95% CI: 1.99-3.87). Similar results were obtained after stratifying patients by cancer site.

Conclusion: Pre-existing liver disease was associated with a markedly increased 30-day mortality following CRC surgery.

P25.01 Mikkel Andreas Strømgaard Andersen

CRITERIA-BASED EMERGENCY MEDICAL DISPATCH OF AMBULANCES - FIRST EXPERIENCES IN DENMARK

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Introduction

In Denmark, Alarm 112 calls and Emergency Medical Dispatch (EMD) are two separate institutions. Alarm 112 calls are mainly answered by the police. In Aarhus, a new EMD centre for the Central Denmark Region (1.2 mio. people) opened on 1 December 2009. It was the first to employ healthcare professionals and to use a new tool for criteria-based dispatch called the Danish Index. The aim of the present study is, for the first time in Denmark, to describe the level of urgency of patients transported by ambulance based on the Danish Index categories A-E and to determine if ambulance response time target values were reached.

Methods

It is an observational cohort study based on consecutive, electronically collected data from the initial six months of operation (1 December 2009 to 31 May 2010) of the new EMD centre in Aarhus.

Results

A total of 73,484 patients were included. The distribution according to level of urgency was as follows: A 28.7% (n = 21,104), B 13.5% (n = 9,890), C 21.0% (n = 15,418), D 35.1% (n = 25,818), E 1.7% (n = 1,254). The median ambulance response time intervals for levels A and B were 6.5 and 11.9 min, respectively. Comparison of level A response time intervals with the equivalent target values showed that the 75, 92 and 98 percentiles were 10.0/10 min, 14.6/15 min, 18.6/20, respectively.

Conclusion

In a cohort of 73,484 patients, the highest level of urgency (A) was found in 28.7% of cases, while the largest group, 35.1% of patients, were level D cases – these patients had a need for transport, but not by ambulance. The level A target response time requested by Alarm 112 was achieved.

P25.02 Eva Bjerre Ostenfeld

USE OF GLUCOCORTICOIDS AND COLORECTAL CANCER RISK; A POPULATION-BASED CASE-CONTROL STUDY IN NORTHERN DENMARK, 1991-2010

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Background: Glucocorticoids have potent immunosuppressive properties, thus potentially inhibiting cancer prevention by host immunosurveillance. Nonetheless, inflammation has been suggested to predispose to colorectal cancer (CRC) and in this context, glucocorticoids may be chemopreventive. Knowledge of glucocorticoids as a risk factor for colorectal cancer (CRC) development is limited.

Methods: Using Danish medical databases, we conducted a case-control study to investigate the association between glucocorticoid use and CRC risk.

Cases were diagnosed with a first time CRC from 1991 through 2010. Using risk set sampling, 10 population controls were selected for each case, matched on age, gender and place of residence. We estimated odds ratios (ORs) and 95% confidence intervals (CIs) associating glucocorticoid use and CRC risk, adjusting for potential confounders.

Results: The study included 15,663 cases and 156,630 controls. We found no effect on CRC risk in users of more than two prescriptions of systemic glucocorticoids plus additional non-systemic glucocorticoids, if any (adjusted OR (aOR) = 1.01 (95% CI = 0.94-1.07)), systemic glucocorticoids only (aOR = 0.93 (95% CI 0.86-1.00)) or inhaled glucocorticoids only (aOR = 0.96 (95% CI 0.86-1.08)). Recent versus former use as well as duration of use had no impact on the null result. Dose of glucocorticoids (cumulative prednisone equivalent dose) showed no effect on CRC risk, regardless of duration of use.

Conclusions: We found no associations between glucocorticoid use and CRC risk

P25.03 Michael Dalager-Pedersen

MYOCARDIAL INFARCTION AND STROKE AFTER INCIDENT COMMUNITY-ACQUIRED BACTEREMIA: A 15-YEAR COHORT AND CASE SERIES STUDY

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Various infectious diseases have been associated with the development of acute myocardial infarction (AMI) and acute ischemic stroke (AIS). Still, the risk and underlying mechanisms are not well understood. Patients with community-acquired bacteremia (CAB) constitute a well-defined patient group for further studies of this association.

Our aim is to evaluate the risk of AMI and AIS up to one year after CAB.

The study will be based in North Jutland, Denmark, 1995-2009, and include a cohort design and self-controlled case series analyses. Information on blood cultured patients, and all events of hospitalized AMI and AIS in the region, will be ascertained from Danish population-based registries. Adults blood cultured ≤48 hours after admission to a medical department, and no recent hospital stay or previous bacteremia, will be eligible for the study. An estimated 5,000 patients exposed to CAB, and 40,000 blood culture-negative patients, will be available for further analyses. In addition, we will assemble an age, gender, and calendar-time matched comparison cohort of ~50,000 persons from the background population. The cohort design will be used to compare incidence and confounder-adjusted risk-ratios of AMI and AIS in CAB patients and comparison cohorts. Moreover, we will apply a self-controlled case series method to bacteremic patients for within-person comparisons of rates of AMI and AIS after CAB with patient's baseline risk.

Knowledge of risk factors for AMI and AIS are of utmost importance. Increasing awareness of the association between bacteremia, AMI and AIS

may lead to increased focus on preventive strategies, earlier detection and treatment of all three entities.

P25.04 Efe Levent Aras

PEDICLE SCREW FIXATION FOR UNSTABLE THORACIC SPINE FRACTURES: CLINICAL AND RADIOLOGICAL EVALUATION OF 120 CASES.

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Background: The stabilization of unstable thoracolumbar (TL) fractures with pedicle screws (PS) have been well documented in the literature, but the evidence of PS application for unstable thoracic spine fractures is still lacking.

Materials and Methods: After entering a certain diagnosis and surgery code to the hospital registry system, 120 prospective patients were recruited for the time period between January 2002 and October 2010. 61 patients (18 Female, 43 Male) met our inclusion criteria as unstable fractures between the Th1-TH11 levels. Th12 fractures were excluded due to anatomical position, which is considered as in TL region. Patient journals, operation notes and radiological examinations were investigated. Outpatient visits were obtained after 3 months, 1 and 2 years.

Results: The mean age was 43.34±2.12. Etiology of trauma varied from 61% traffic accidents to 39% fall accidents. In total, 454 PSs were administrated with 89% allo or auto-graft bone application. Mean operation time was 135.07±6.61 minutes. General and surgical related complication rates were 6% and 7% respectively. We did not obtain any significant difference, when we implied the subgroup analysis due to the injury mechanisms (p=0.13 and p=0.51). Only 1 (1.6%) patient had an implant removal surgery after 5 months due to screw engagement to the disc space. The mean segmental kyphosis angle was 22.6˚±1.7 preoperatively, 17.4˚±1.89 (p< 0.05) postoperatively and 21.7˚±1.6 at 2 years.

Conclusion: In the hands of an experienced institution, PS fixation is a safe and effective method to correct and prevent further kyphotic deformity after traumatic unstable thoracic spine fractures.

P25.05 Anne Fia Grann

MELANOMA: THE INFLUENCE OF COMORBIDITY ON SURVIVAL

A.F. Grann

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Background: The incidence of melanoma of the skin has increased more than any other cancer in most white populations during the last decades. In 2009, 1829 people in Denmark were diagnosed with melanoma.

The most important risk factor for melanoma is exposure to UV-light and the most important predictor is excessive UV exposure in childhood, recalled as sunburn.

Patients aged 65 years or older form more than half of melanoma patients. The elderly have more chronic diseases and are treated with more immunosuppressive medications than younger persons, which may add to the risk of skin cancer.

The effect of comorbidity has been investigated for different types of cancers and several studies have shown that more severe comorbidity present at diagnosis is associated with poorer survival after a diagnosis of cancer.

The prognostic importance of comorbidities in melanoma patients is largely unknown.

Objective: To evaluate whether there is an association among patients with melanoma between comorbid diseases and over-all mortality rates.

Methods: We will perform a population-based cohort study of patients diagnosed with melanoma from 1987 through 2009. Five patients will be matched to every melanoma patient on age, sex, calendar year and comorbidities. We will calculate interaction contrasts based on 1- and 5-year cumulative mortality.

Perspectives: From this study we expect to achieve new knowledge about comorbidity and how it influences the prognosis of melanoma; and thereby contribute to improve melanoma treatment strategies, i.e. treatment selection and counseling patients.

P25.06 Anne Nakano Jensen

QUALITY OF HOSPITAL CARE AND CLINICAL OUTCOME AMONG PATIENTS WITH INCIDENT HEART FAILURE IN DENMARK: A NATIONWIDE STUDY

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Background

Advances have been made in heart failure research in recent years with an increasing strength behind a range of evidence-based recommendations. Data on implementation of these recommendations in everyday clinical practice are however sparse.

Methods

We conducted a nationwide, population-based prospective study using data from a national heart failure registry (the Danish National Indicator Project). Registration in the database is mandatory for all hospital departments treating patients with incident heart failure. We identified all patients registered between February 2003 to February 2010 and obtained data on patient characteristics and processes of in-hospital care and rehabilitation.

Results

In total, 23,361 patients were identified. The use of a number of processes of care increased during the study period, including use of echocardiography/MUGA/Ventriculography (from 64.5% to 91%; $p<0.01$),

New York Heart Association-classification (from 29.3% to 84.1%; p<0.01), Betablockers (from 72.5% to 87.6%; p<0.01), physical training (from 5.7% to 20.7%; p<0.01) and participation in patient education program (from 48.6% to 81%; p<0.01). In contrast, the use of ACE/ATII inhibitors and aldosterone antagonists remained stable.

Non-planned re-admission within four weeks after discharge (only monitored from 2007-2010) dropped from 9.6% to 8.4% (p=0.86) whereas, 1 year mortality (2003 to 2008 inclusive) dropped from 20.7% to 16.55% (p<0.01)
Conclusion

Quality of in-hospital care to patients with incident heart failure has improved since systematic monitoring was initiated in Denmark. During the same period, a significant decrease in mortality has been observed.

P25.07 Gija Rackauskaite

RESPONDERS AND NON-RESPONDERS TO THE WEB BASED QUESTIONNAIRE AMONG PARENTS TO CHILDREN WITH CEREBRAL PALSY

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Background: Cerebral Palsy (CP) is a disorder of posture and motor control caused by a non-progressive lesion of the developing brain. Treatment of CP depends on child's gross motor function and needs a multidisciplinary approach. Therefore, all treatment methods are not available in one source of records.

Aim: To justify that parental questionnaire is a reliable source for gross motor function and treatment of children with cerebral palsy.

Method: The Gross Motor Function Classification System -Family Report (GMFCS-FR) is translated from the English GMFCS-FR into Danish after the *CanChild* guidelines. Reliability is tested by physiotherapist's interview. An original Treatment Questionnaire (TQ) is developed for study purpose by research group. Reliability test with 30 families and child's records is ongoing.

Results: The interrater agreement between the GMFCS-FR and physiotherapist's GMFCS is high (76%) and misclassification is minimal. Results from reliability testing of TQ questionnaire are not available yet.

P25.08 Eva Sædder

DEVELOPMENT OF AN ALGORITHM FOR DIFFERENTIATED INTERVENTION AGAINST MEDICATION ERRORS IN ACUTE HOSPITAL ADMISSIONS ON THE BASIS OF INDIVIDUALIZED RISK STRATIFICATION

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Background: A medication error is an error that causes damage or poses a threat to a patient. The risk of patients to be exposed to errors is related to patient age, comorbidities, individual drugs and polypharmacy. Medication review at hospital admission has been shown to reduce medication errors but it has not unambiguously been shown that this has an effect on length of hospital stay, readmissions or death. A reason may be that the patients receive the same intervention despite the complexity of their drug treatment and other risk factors.

Hypothesis: It is possible to develop an algorithm that stratifies patients regarding their risk for medication errors.

Aim: To develop an algorithm to be used for individual risk stratification of patients admitted to hospital with regards to their need for control and intervention to their drug treatment.

Methods: Risk factors for medication errors such as age, comorbidities, polypharmacy and individual drugs are found by literature search. Individual drugs will be assessed for risk potential by 50 experts in a delphi process. The risk factors will be assigned values on a numerical scale. An overall risk score will be attached to an intervention. The higher the score, the more specialized the intervention. The validity of the algorithm will be tested in a historic patient population where medication and medication errors are known.

Future perspectives: The algorithm will be implemented in IT systems to enable risk assessment of patients which allows for early intervention in drug treatment and thereby improve patient safety.

P25.09 Dorthe Krogsgaard Bonnerup

PHYSICIANS' ATTITUDES TOWARDS DRUG COUNSELLING FROM EXTERNAL HEALTH PROFESSIONALS

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Background: Medication errors lead to harm and death in up to 6 out of 100 admissions to hospital. Medication reviews performed on admission to hospitals reduce medication errors; however, the evidence of effect on morbidity and mortality is currently inconsistent.

To benefit from medication reviews it is necessary that the physicians at the ward adhere to the recommendations. Two Danish studies have revealed that the physicians only adhered to 20-40% of the provided recommendations. Reasons for disregarding external drug counseling have not been studied thoroughly in Denmark or abroad.

Objective: The objective is to investigate physicians' attitudes towards drug counseling from external health professionals.

Methods: Four focus group interviews are performed to reveal themes and items for a questionnaire survey. The members of the focus groups are both younger physicians and more experienced surgeons and medical physicians. The questionnaire is developed based on literature review and results from the focus groups. The questionnaire will be pilot tested in a group of 30

physicians before being emailed to approximately 200 physicians at Aarhus University Hospital.

Perspective: Based on results from this study it will be possible to perform medication reviews and delivery of the recommendations in closer accordance with the physician's wishes and demands. This may lead to a better adherence to the recommendations which may have an impact on acutely admitted patients' morbidity and mortality. The effect of a differentiated medication review based on knowledge from this study, among other things, should be tested in a randomized controlled trial.

P25.10 Henrik Gammelager

ONE-YEAR MORTALITY AMONG DANISH INTENSIVE CARE PATIENTS WITH ACUTE KIDNEY INJURY: A COHORT STUDY

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INTRODUCTION: Acute kidney injury (AKI) is associated with increased in-hospital mortality among intensive care unit (ICU) patients. However, there are only few studies on long-term mortality.

OBJECTIVES: To examine 1-year mortality of patients with and without AKI at ICU admission.

METHODS: We identified all adults admitted to any ICU in the counties of North Jutland and Aarhus between 2005 and 2008 using the Danish National Registry of Patients. We used a laboratory database to determine the AKI level at ICU admission for each patient using the RIFLE classification: No AKI, AKI Risk, AKI Injury, and AKI Failure. Patients with chronic kidney disease (3.9%) and patients without creatinine measurements at ICU admission were excluded (10.1%). We followed patients from ICU admission until death, emigration or for up to one year. We used Kaplan-Meier method to estimate 1-year mortality and Cox proportional hazards regression to compute hazard ratios (HR), controlling for potential confounders.

RESULTS: We identified 19,653 ICU patients. Among the 3,585 (18.2%) patients with AKI, 1,540 (7.8%) were classified as AKI Risk, 1,076 (5.5%) as AKI Injury and 969 (4.9%) as AKI Failure.

The 1-year mortality was 45.1% for the Risk group, 53.6% for the Injury group and 58.2% for the Failure group compared to 20.7% for patients without AKI. The adjusted HRs compared to patients without AKI were 2.0 (95% CI: 1.9-2.2), 2.7 (95% CI: 2.4-2.9) and 3.2 (95% CI: 2.9-3.5) for the Risk, Injury and Failure groups, respectively.

CONCLUSIONS: AKI at time of ICU admission is present in almost one fifth, and associated with markedly increased 1-year mortality compared with patients without AKI

P25.11 Malene Schou Nielsson

MORTALITY IN ELDERLY PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT: A DANISH ONE YEAR COHORT STUDY

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Objectives: To assess 30-day and 1-year mortality in patients admitted to the ICU in Northern Denmark in relation to age controlling for level of morbidity.

Methods: Through the Danish National Registry of Patients (DNRP) we identified a cohort of 34,246 patients admitted to an ICU in Northern Denmark from 2005-2008. We obtained information on surgical procedures performed within 7 days prior to ICU admission and comorbidity according to the Charlsons Comorbidity Index from DNRP. Information on time to death was obtained from the Civil Registration System. We used the Kaplan-Meier method to estimate survival and computed mortality rate ratios (MRRs) using a Cox proportional hazard model, stratified by type of admission (medical/surgical patients). We compared the mortality rates among patients aged 15-49, 50-64, 65-79, ≥ 80 years of age, adjusting for sex and comorbidity using Charlsons Comorbidity Index. We used the age group of 50-64 year old as reference.

Results: In medical patients 30-day mortality was 44.1% in patients aged ≥80 years compared with 18.7% in those aged 50-64 year (Adjusted MRR = 2.63 (95% CI, 2.36-2.94)). In surgical patients, 30-day mortality was 31.8% in patients aged ≥80 years (adjusted MRR= 3.96 (95% CI, 3.55-4.41)). The 1-year MRRs for patients aged ≥80 years were 2.59 (95%CI, 2.37-2.84) and 3.11 (95% CI, 2.86-3.37) for medical and surgical patients, respectively. For medical patients aged 65-79 the 30-day and 1-year MMRs were 1.6 (95% 1.5-1.8) and 1.6 (95% 1.5-1.8); surgical patients 1.5 (95% 1.4-1.7) and 1.4 (95% 1.3-1.5).

Conclusions: High age is a prognostic factor for 30-day and 1-year mortality after admission to an ICU

P26.01 Lene Rahr Wagner

IMPACT OF DIFFERENT GRAFT TYPES AFTER ACL RECONSTRUCTION: RESULTS FROM THE DANISH REGISTRY OF KNEE LIGAMENT RECONSTRUCTION

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INTRODUCTION: The choice of graft for Anterior Cruciate Ligament (ACL) reconstruction is still controversial. Since 2005 the Danish registry of knee ligament reconstruction (DKRR) has monitored the quality and development in ACL reconstruction. This database contains data from all

clinics in Denmark performing ACL reconstruction. The objective of this study was to report the results with two graft types in primary ACL reconstruction, bone-patellar tendon-bone (BPTB) graft and semitendinosus and gracilis (ST/GR) graft.

METHODS: We identified 10951 patients from the DKRR who underwent primary ACL reconstruction in the period from 2005 to 2010. The survival of different surgical techniques was determined using revision ACL reconstruction as primary endpoint. KOOS and scores were used as patient reported outcome measures.

RESULTS: The one year survival rate after ACL reconstruction with ST/GR graft and BPTB graft was 96% and 97%, respectively. KOOS score preoperatively and postoperatively was identical except for sports postoperatively where ST/GR performed slightly better than BPTB for the two groups.

CONCLUSION: Previously, randomised controlled trials have shown no difference in survival using BPTB vs. ST/GR grafts. This is confirmed in our study. This is the first nationwide population based study reporting the results with different surgical techniques after primary ACL reconstruction. Our study suggests limited impact of graft choice for the outcome after primary ACL reconstruction.

P26.02 Charlotte Hartig Andreasen

FACTORS PREDICTING FAILURE FOLLOWING PERIACETABULAR OSTEOTOMY: A 2-12 YEARS FOLLOW-UP STUDY OF 406 PERIACETABULAR OSTEOTOMIES

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Background

Periacetabular osteotomy (PAO) is used to prevent osteoarthritic development in dysplastic hips. Little is known about what factors predict failure following PAO. Refinement in selection of patients and treatment strategies may improve based on such information.

Aim of Study

This study reports the outcome of the largest PAO cohort ever. The aim of this study is to identify pre- and postoperative factors predicting failure after PAO defined as a WOMAC pain score > 10 or conversion to total hip replacement (THR).

Materials and Methods

Of the 462 hips treated with PAO from Dec 1998 to 2008 in Aarhus, 407 hips with complete pre- and postoperative radiographics were included in the study (median age: 34.1 yrs, range 13.2-61.4). Radiographic indices of hip dysplasia were assessed on conventional radiographs and on preoperative CT-scans. The WOMAC questionnaires were completed by 83% patients. By inquiry to the Danish Hip Arthroplasty Registry we assessed

conversions to THR.

Findings / Results

Defining THR as an end point the Kaplan-Meier analysis showed a hip survival rate of 78.1% (95% CI, 68.8%-84.9%) at 12.4 years. A WOMAC pain score of 10 or more was found in 47 of the preserved hip joints. Using Cox regression analysis the following statistically significant predictors of conversion to THR were identified: age at surgery > 45 yrs, severe preoperative dysplasia (CE-angle <0 deg), the presence of an os acetabuli, joint space width < 3.0 mm and a Tönnis grade of 2.

Conclusions

PAO is effective in treating hip dysplasia at long term follow-up. Preoperative signs of joint degeneration and severe hip dysplasia are to be considered when selecting patients for a successful PAO.

P26.03 Michael Skovdal Rathleff

PREVALENCE OF TRAUMATIC AND NON-TRAUMATIC ANTERIOR KNEE PAIN AMONG ADOLESCENTS.

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Introduction: Knee pain is common during adolescence. The proportions of adolescents reporting pain relating to sudden onset trauma versus insidious, slow-developing pain has not yet been investigated. The purpose is to investigate the prevalence of self-reported knee pain among adolescents between 15 and 19 years and to describe the proportions reporting pain related to trauma versus insidious onset. Secondly, to describe the most frequent physician-determined-diagnoses in those complaining of insidious anterior knee pain. Methods: Online questionnaires have been forwarded to 3,000 students aged 15-19. Localization of pain is quantified through a pain mannequin. Students who report knee pain will be telephoned and asked about pain localization, onset of symptoms and if the onset of pain was related to a traumatic event or insidious. Students who report anterior knee pain with an insidious onset will be offered a clinical examination by a rheumatologist.

Results: So far 1,277 students have answered the questionnaire (response rate of 42.6%). The prevalence of self-reported knee pain was 36.3%. Among those who were telephoned, 73 (21.5%) students reported knee pain with a traumatic onset while 267 (78.5 %) reported an insidious onset of pain. 129 students were invited to a clinical examination; 117 (90.7 %) accepted. Patellofemoral Pain Syndrome (PFPS) and patellar tendinopathy (PT) were the two most frequent diagnoses made. 91 (78%) were diagnosed with PFPS, and 7 (6%) were diagnosed with PT.

Conclusion: These preliminary data indicate a high prevalence of non-traumatic insidious anterior knee pain among adolescents and PFPS may

account for as much as 78% of all cases.

P26.04 Jannie Dahl Hald

OSTEOGENESIS IMPERFECTA - GENETICS, PHENOTYPE AND QUALITY OF LIFE

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Objectives: Osteogenesis imperfecta (OI) is an inherited disorder characterised by varying degrees of fragile bones and other signs of defect collagen type 1. The clinical spectrum is broad and although genetic background of the disease is well known, no clear relation is established between genotype and phenotype. With this project, we want to thoroughly describe an adult population with OI.

Methods: 100 adult patients with OI type I or IV will be included in this study. Recruitment taking place through the three centres treating OI in Denmark: Aarhus, Odense and Rigshospitalet/Hvidovre. Adults not followed at these centres will be informed through two national centres for rare diseases where the children with OI are seen; through regional hospitals where treating doctors are informed about the study; and through Danish OI patient Society.

Inclusion criteria: Patients with OI type I and IV, age 18 - 70 years, with informed consent.

Exclusion criteria: Treatment with glucocorticoids ≥ 5mg daily during the last 3 months; metabolic bone disease other than OI; vitamin D deficiency or liver- or kidney diseases; cancer.

Investigations: Bone quality (BMD by DXA, pQCT, QCT, X-ray, bone markers); collagen status; sequencing of COL1A1 and COL1A2; dental exam; degree of otosclerosis; eye exam; and quality of life (SF 36).

Results: Patients still being included in this trial. No results available.

Conclusion: This study will significantly increase the knowledge about OI among adults in Denmark in regard to genotype, skeletal and non-skeletal phenotype and quality of life. This knowledge is essential in order to target treatment strategies and good handling of adults with OI in the future.

P26.05 Anette Liljensøe

OBESITY INFLUENCES THE CLINICAL OUTCOME AND THE QUALITY OF LIFE FOLLOWING PRIMARY TOTAL KNEE ARTHROPLASTY.

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INTRODUCTION: In Denmark there is performed annually between 7-8000 primary total knee arthroplasties (TKA). The most frequent indication for TKA is osteoarthritis (80%). Investigations have shown that obesity is a

significant factor for the development of arthritis. The purpose of the study was to investigate whether there is an association between the preoperative BMI in TKA patients and the effect five years postoperative.

METHOD: 197 patients, who had undergone primary TKA, participated in a five years follow-up study. The outcome measures were patient reported outcome (SF-36), and the Knee Society Rating System (KSS).

RESULTS: With Ordinal logistic regression (adjusted for gender, age, basic disease and surgical procedure) were found statistically significant associations between BMI and nine of the fourteen outcome measures. For all outcome measures were found OR > 1. With a difference in BMI at 1 kg/m^2 increases the risk of lower scores from a minimum of 2% OR 1.02 (0.97-1.07) p = 0.5 ("mental component score") to maximum 14% OR 1.14 (1.08-1.21) p <0.001 (KSS function score). With a difference in BMI at 5 kg/m^2 mincreases the risk of lower scores from a minimum of 9% OR 1.09 ("mental components scores") to a maximum of 96% OR 1.96 (KSS function scores). With a difference in BMI of 10 kg/m^2 rises risk of worse score with minimum 19% OR 1.19 ("mental component score") to a maximum of 284% OR 3.84 (KSS function score).

Discussion: The association between BMI and the efficacy 5 years following primary TKA is clear. High BMI increases the risk of poor outcome following TKA.

P26.06 Jan Rölfing EPO DOES NEITHER STIMULATE PROLIFERATION NOR OSTEOGENIC DIFFERENTIATION OF HMSC-TERT CELLS

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Background: Erythropoietin (EPO) is an erythropoesis stimulating agent. It' s capability to induce angiogenesis and to promote ossification has been demonstrated in vivo. However, the mechanism is yet unknown. We aim to investigate the effect of EPO on telomerase-immortalized human mesenchymal stem cells (hMSC-TERT).

Hypothesis: EPO enhances hMSC-TERT cells' proliferation and osteogenic differentiation.

Methods: 4000 cells/cm2 hMSC-TERT cells were seeded on 96-wells plates in standard and osteogenic medium. After one day 5, 10, 50 and 100 IU/ml of Epoetin alpha or Epoetin beta were added. Negative control: standard medium without EPO treatment. Positive control: BMP2. On day four and seven the following assays were used to evaluate cell viability, cell number and osteogenic activity: MTT, SYBR Green and alkaline phosphatase activity.

Results: Neither EPO alpha nor EPO beta augmented osteogenic differentiation. No increase in proliferation was observed. Please refer to the poster for quantities and statistical analyses.

Discussion: Previous independent research groups report an increased proliferation rate and osteogenic differentiation of primary human MSC when exposed to EPO alpha. We did not observe a similar effect. The most likely explanation is that hMSC-TERT react differently to EPO treatment compared to primary human MSC. Therefore, we are going to repeat the

setup with primary hMSC.

P26.07 Karen Toftdahl Bjørnholdt

ACUTE AND CHRONIC PAIN AFTER SHOULDER SURGERY: TREATMENT AND EPIDEMIOLOGY

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Background: Pain following shoulder surgery is often considerable. In other types of surgery, new treatments have been introduced which may also be beneficial to shoulder patients. These include local infiltration analgesia (LIA) and high dose dexamethasone. In some studies, a connection is seen between severe acute postoperative pain and chronic pain. These treatments and this connection have not been explored for shoulder surgery.

Purpose: To assess postoperative pain treatment after shoulder arthroplasty by LIA compared to interscalene block, and after arthroscopic shoulder surgery by high dose dexamethasone. To identify prevalence and risk factors (especially acute pain) for chronic postoperative pain after shoulder surgery.

Methods: 1. Randomised controlled trial (RCT) with 80 patients from Horsens Hospital and Aarhus University Hospital undergoing shoulder arthroplasty. They are randomised to LIA (300 mg ropivacain infiltrated during surgery) or interscalene block (ropivacain, continuous for 48 hours).

2. Double blind RCT with 75 patients from Horsens Hospital undergoing arthroscopic day-case surgery (decompression and/or acromioclavicular resection). They are randomised to placebo, 8 or 40 mg dexamethasone as a single dose preoperatively. Pain scores, analgesics and side effects are recorded for 3 days.

3. Patients registered in the Shoulder Arthroplasty Register in 2007-2009 are sent a questionnaire regarding current state and recalling their acute postoperative pain. Data in the register regarding other possible risk factors for chronic pain are assessed.

Status: The clinical studies include from July 2011 and October 2011; the third study will begin in 2012.

P26.08 Morten Christian Bay Grauballe

THE ROLE OF TNF-α AND AGES IN RATMODEL WITH DIABETES AND PERIODONTITIS

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Background:

The relationship between diabetes and periodontitis (MP) is described as a cycle in which diabetes predisposes MP and the presence of MP conversely affects diabetic status. In diabetic patients there is a correlation of elevated

levels of Advanced Glycation End Products (AGE) with the development of diabetic complications. The amount of AGEs is influenced by inflammation, properly mediated by Tumour Necrosis Factor-alpha (TNF-α), which is a proinflammatory cytokine found at elevated levels in patients with MP. TNF-α is also an important factor in glucose metabolism and hyperglycemia leads to the formation of AGE resulting in an inflammatory response.

There is strong evidence that both type 1 and type 2 diabetes are risk factors for development of MP. However, there is limited knowledge about the inverse relationship. In the present study we want to elucidate the role of TNF-α and of AGEs in rats with diabetes and MP by investigating inflammation markers, diabetic status and alveolar bone loss.

Methods:

Diabetic Zucker rats (N=60) and their lean littermates (N=30) are divided into 6 treatment groups of 15 Lean Zucker rats without MP, Lean Zucker rats with MP, diabetic Zucker rats, diabetic Zucker rats with MP, diabetic Zucker rats with MP plus anti-TNF-α treatment, diabetic Zucker rats with MP plus anti-rAGE treatment. MP is ligature induced for 4 weeks. After 5-weeks, glucose tolerance, insulin resistance, free fatty acids, cytokines and bone loss are recorded.

Results:

To come

P26.09 Pernille Endrup Jacobsen

DENTAL ABNORMALITIES IN CHILDREN EXPOSED TO ANTICONVULSANTS PRENATALLY

P.E. Jacobsen

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Background: Every year, 200 women with epilepsy give birth in Denmark, and previous studies have shown that their children have a 2-3 times higher risk of congenital abnormalities.

Dental aspects: Previous studies have shown that prenatal exposure to drugs such as dioxin or tetracycline can induce dental hypomineralization in the child. Dental agenesis is known to have a genetic background, and recent studies have shown that several genes are involved. MSX1 is one of the genes responsible for the tooth development as well as the birth defects we see in children exposed to anticonvulsants prenatally.

Methods:

The study is conducted as a follow-up study based on information from the medical birth register, the birth cohort from Aarhus and the prescription database. Information on the mother's health condition, medication use, alcohol or smoking habits during the pregnancy will be registered. Likewise, gestational age, birth weight and congenital abnormalities of the child will be registered.

Children 6-10 years of age: 80 exposed children and 250 non-exposed children. Outcome measurement (hypomineralization) will be a clinical examination of permanent as well as primary teeth. Questionnaire survey of

medical condition, lifestyle habits and breast feeding habits of the mother during pregnancy. Ethical approval has been obtained from the The Scientific Ethical Committee

Children 12-18 years of age: 200 exposed children and 250 non-exposed children. Outcome measurement (dental agenesis) will be collected from the children's dental chart. Correlation between agenesis and other congenital abnormalities will be explored.

P26.10 Lars Bo Petersen

POSTOPERATIVE COMPLICATIONS AFTER MANDIBULAR THIRD MOLAR REMOVAL BASED ON PANORAMIC RADIOGRAPHY OR CONE BEAM CT-SCANNING: A RANDOMISED CONTROLLED CLINICAL STUDY

L.B. Petersen

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Background: Removal of the third molar in the lower jaw is the most common surgical procedure in dentistry. Injury to branches of the trigeminal nerve during surgery is a rather common complication and though most disturbances are temporary, there is an ongoing search for methods to reduce the incidence. The introduction of cone beam CT scanning (CBCT) a decade ago allows a 3D display of the relationship between the third molar and the mandibular canal, but the costs and radiation dose are higher than for panoramic radiography, the traditional method before surgery. The aim of this study is to assess the complications after removal of the third molar in the lower jaw when using either a panoramic image or CBCT as the presurgical radiographic method.

Methods: The study is conducted as a randomized controlled double-blinded trial. The patients are randomized to either test or control group with 200 patients in each group. In the test group a panoramic image and a CBCT is available whereas in the control group the patients are examined by panoramic radiography and a simulated CBCT. The procedure is blinded for both patient and examiner. Presurgically, baseline clinical and neurosensoric registrations are performed. The removal of the tooth follows in an external set-up executed by specialized surgeons. Postsurgically, the examiner repeats the clinical and neurosensoric registrations. Costs and resources in a health-economical perspective are also recorded.

Results: The project is ongoing and expected to be finished in autumn 2013.

P27.01 Steffen Jensen

EVALUATION OF TWO COMMERCIAL GLOBAL MIRNA EXPRESSION PROFILING PLATFORMS FOR DETECTION OF LESS ABUNDANT MIRNAS

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BACKGROUND:

microRNAs (miRNA) are short, endogenous transcripts that negatively

regulate the expression of specific mRNA targets. miRNAs are found both in tissues and body fluids such as plasma. A major perspective for the use of miRNAs in the clinical setting is as diagnostic plasma markers for neoplasia. While miRNAs are abundant in tissues, they are often scarce in plasma. For quantification of miRNA in plasma it is therefore of importance to use a platform with high sensitivity and linear performance in the low concentration range. This motivated us to evaluate the performance of three commonly used commercial miRNA quantification platforms: GeneChip miRNA 2.0 Array (Affymetrix), miRCURY Ready-to-Use PCR (Exiqon), Human panel I+II V1.M, and TaqMan Human MicroRNA Array v3.0 (Applied Biosystems Inc.).

RESULTS:

Using synthetic miRNA samples and plasma RNA samples spiked with different ratios of 174 synthetic miRNAs, we assessed the performance characteristics' reproducibility, recovery, specificity, sensitivity and linearity. It was found that while the qRT-PCR based platforms from ABI and Exiqon were sufficiently sensitive to reproducibly detect miRNAs at the abundance levels found in human plasma, the array based platform from Affymetrix was not. At high miRNA levels both qRT-PCR based platforms performed well in terms of specificity, reproducibility and recovery. At low miRNA levels, as in plasma, the Exiqon platform showed better sensitivity and linearity than the ABI platform.

CONCLUSIONS:

For profiling clinical samples with low miRNA abundance, such as plasma samples, the Exiqon platform with its better sensitivity and linearity would probably be superior.

P27.02 Lea Hougaard Pedersen

TREATMENT OF CHRONIC KIDNEY DISEASE WITH SIRNA NANOPARTICLES TARGETING MMP-2, MT1-MMP, AND TIMP-2

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Renal failure is seen primarily as idiopathic or can arise as a consequence of diabetes mellitus. Today, no curing treatment can be provided. We have examined the molecular mechanisms which are fundamental for the development of chronic kidney disease (CKD). Our focus is MMP-2, MT1-MMP, and TIMP-2, which are shown to play an important role in extracelluar matrix deposition and thereby fibrosis, a hallmark in CKD. We hypothesize that specific downregulation of these molecules will either inhibit or reverse the progress towards nephropathy in vivo.

Our studies will be conducted by administration of chitosan/siRNA nanoparticles in a transgenic mouse model that overexpresses TGF-β1 locally in the kidneys. This model develops thickening of the glomerular basement membrane, deposition of mesangial matrix and mild interstitial fibrosis at the age of 2 months. The fibrosis is manifest at the age of 4 months. An inhibitory effect of siRNA treatment (6 weeks) will be initiated

at 2 months of age, whereas reversibility will be tested in 4-month-old mice with manifest fibrosis. The efficiency of siRNA to knock-down MMP-2, MT1-MMP, and TIMP-2 RNA expression is tested in vitro. The intervention experiments will be preceded by pharmacokinetic analyses to clarify the distribution of siRNA particles in the mice. This will form the basis for verifying the hypotheses; preventing the fibrosis in 2-month-old mice and reversing it in 4-month-old mice.

The results will clarify if inhibition of relevant molecules by siRNA nanotechnology will stop the progress towards nephropathy. If this is the case, this will clear the way for new treatment strategies of patients suffering from nephropathy.

P27.03 Dennis Kjølhede Jeppesen

IDENTIFICATION AND CHARACTERIZATION OF CIRCULATING EXOSOMES IN BLADDER CANCER

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Background: Exosomes are small membrane vesicles (40-100 nm) of endocytotic origin that are secreted from cells to the extracellular space and body fluids. In various cancers, exosomes of tumor origin have been detected in plasma or serum from patients. Circulating exosomes contain a large number of proteins and lipids as well as RNA (mRNA and miRNA).

Aim: This project aims to examine not only the fundamental structure and function of exosomes, but also to develop potential clinical applications by discovering exosome-derived biomarkers for bladder cancer.

Methods: Bladder cancer cell lines FL3 and T24 with and without metastatic potential, respectively, were cultivated in CELLine AD 1000 Bioreactors for increased exosome yield. Cell viability was assessed by the trypan blue exclusion method and exosome isolation was subsequently conducted by differential centrifugation, including a 100,000 x g step to pellet the exosomes. For quantification of exosomes, Bradford protein assays and a novel acetylcholinesterase activity assay were assessed. For visualization of FL3-derived exosome vesicles, stable over-expression of GFP-Hsp70 was conducted as Hsp70 was identified as an exosome marker by proteomic analysis.

Results and perspectives: The yield of exosomes was 10-fold higher from the bioreactor system compared to that obtained from conventional cell culture flasks. Exosome vesicles were visualized by dynamic light scattering analysis. Stable cell populations of GFP-Hsp70 expressing cells were obtained. Future work will focus on further purification methods for exosomes in plasma samples from bladder cancer patients, as well as vesicular uptake of exosomes in recipient cells.

P27.04 Juan Manuel Shiguetomi Medina

EPIPHYSIODESIS MADE WITH RADIOFREQUENCY ABLATION: FIRST RESULTS FROM A PILOT STUDY

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Anisomelia is a condition of leg length discrepancy.In children, it is often treated with epiphysiodesis. Current techniques involve opening cortical windows on both the lateral and medial sides of the bone where the growth plate is manually destroyed with curettes and/or drills. Complications such as breaching the anterior or posterior cortex of the treated bone have potentially serious consequences with risk of vascular and/ or nerve injury, and/or damage to the metaphyseal region of the bone. Therefore, there is a need for a reliable and precise procedure which overcomes the complications.

Aim: Development of a new technique for epiphysiodesis using radiofrequency ablation on an animal modelthat involves less scarring, less exposure to X-rays, and reduces the risk of injuring the surrounding structures compared to current methods.

4 non-mature pigs were used.A control leg was randomly selected and the contralateral one was treated at two ablation sites (lateral and medial).We identified at the proximal tibia growth plate using x-ray. A probe was inserted and the ablation performed. MR images were performed right after the procedure and 12 weeks later.

At the end of the study we measured the length of both tibiae on each animal.We found that both legs were equal at the beginning of the study and there was a leg length difference in average of 3.5mm (SD=0.48) at the end.No damage to the surrounding cartilage structures was found.

Epiphysiodesis using radio frequency ablation is an innovative technique that may represent an alternative way of treatment.These results show that this technique can arrest growth in a safe effective way.

P27.05 Anne Louise Askou

REDUCTION OF CHOROIDAL NEOVASCULARIZATION IN MICE BY AAV-DELIVERED ANTI-VEGF SHRNA

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VEGF plays an essential role in ocular angiogenic diseases including the late-stage form of AMD, the primary cause of vision loss in the western world. Over-expression of VEGF leads to development of vasculature emanating from the choroid, invading the subretinal space through breaks in Bruch's membrane. Strategies leading to long-term suppression of inappropriate ocular angiogenesis are required.

A panel of 10 shRNAs targeting the coding region of human $VEGF_{165}$ was tested in HEK293 cells and in the human retinal pigment epithelial cell line,

ARPE-19. VEGF knock-down up to 92% was achieved by co-transfecting shRNA-expressing constructs with plasmid encoding the Renilla luciferase gene fused to the $VEGF_{165}$ sequence. For in vivo delivery of the most potent shRNA cassette, both single-stranded and self-complementary rAAV vectors were packaged in serotype 8 capsids. Intramuscular administration in mice led to localized expression and 96% knock-down of endogenous VEGF. Using eGFP as a marker, efficient gene transfer of retinal pigment epithelial cells, the cells thought to be responsible for the abnormal VEGF production, was obtained by subretinal delivery of rAAV2.8 vectors. The capacity of rAAV-encoded shRNAs to silence endogenous VEGF gene expression was evaluated in the laser-induced murine model of choroidal neovascularization (CNV). In this mouse model of AMD, sizes of the CNV were found to be significantly reduced following rAAV-shRNA subretinal delivery. Thus, our results indicate that gene transfer combining AAV-mediated delivery with triggering of the endogenous RNAi pathway can be used for anti-VEGF therapy and holds great promise for the treatment of AMD.

P27.06 Anne Skakkebæk Jensen

NEUROCOGNITIVE OUTCOME AND PSYCHOPATHOLOGY IN MEN WITH KLINEFELTER SYNDROME

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BACKGROUND Klinefelter Syndrome affects 1:660 men and is the most common sex-chromosome disorder in men. Men with Klinefelter syndrome have an extra X chromosome giving rise to the 47, XXY chromosomal pattern. The X chromosome contains many genes which are involved in cognition and mental function, and it is well-known that Klinefelter syndrome is associated with a variable cognitive and behavioral dysfunction. The risk of psychopathology also seems to be higher in men with Klinefelter syndrome. Furthermore, hypogonadism is common in men with Klinefelter syndrome, and the many of these men receive testosterone therapy, when they reach adolescence/adulthood.

AIM To investigate the neurocognitive abilities, symptoms of psychopathology, personality and autistic traits in a large sample of adult men with Klinefelter syndrome and to access the effect of testosterone therapy.

METHODS A total of 60 men with Klinefelter syndrome and 60 age- and education-matched control subjects participated. All participants were tested with standardized neuropsychological test. The revised NEO Personality Inventory (NEO PI-R) and the Symptom Checklist-90 (SCL-90) were used to evaluate personality traits and symptoms of psychopathology, respectively. Autism traits were assessed with the Autism Spectrum Questionnaire (AQ).

P27.07 Maja Ludvigsen

TRANSLATIONAL RESEARCH IDENTIFIES PROGNOSTIC MARKERS INCLUDING GALECTIN-1 IN THE TUMOR MICROENVIRONMENT OF CHL PREDICTIVE FOR RELAPSED /REFRACTORY DISEASE

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No prognostic marker of classical Hodgkin lymphoma (cHL) has yet been identified even though considerable effort has been spent trying to. In this study, we have used a proteomic approach to generate a set of putative markers that can work as possible prognostic parameters in advanced stage cHL. Fast frozen pretreatment tumor tissue from 14 younger advanced stage patients were grouped according to treatment response and analysed using 2-dimensional polyacrylamide gels. Differential expressed protein was identified by liquid chromatography mass spectrometry. So far, desmoplakin (DSP), a G-protein (GNAI3), proteasome activator (PSME1), peroxiredoxin 1 (PRDX1) and galectin-1 (GAL1) have been verified by Western blot analysis. Additionally, GAL1 was further analyzed using immunohistochemistry on 143 advanced stage cHL and its expression was correlated with clinico-pathological and outcome parameters. Among younger (≤ 61 yrs) patients, a high GAL1 correlated with poorer overall and event-free survival (both p= 0.007), at the univariate level and at the multivariate level, high GAL1 expression retained a significant predictive impact on event-free survival. Thus, in addition to its functional role in cHL-induced immunosuppression, Gal-1 is also associated with an adverse clinical outcome in this disease (Kamper et al., 2011).

Reference

Kamper P, Ludvigsen M, Bendix K, Hamilton-Dutoit S, Rabinovich GA, Møller MB, Nyengaard JR, Honoré B, d'Amore F. Proteomic analysis identifies galectin-1 as a predictive biomarker for relapsed /refractory disease in classical Hodgkin lymphoma. Blood 2011; 117(24): 6638-49.

P27.08 Yujia Cai

TRANSPOSON-BASED LENTIVIRAL VECTOR TECHNOLOGY FOR GENE DELIVERY AND PERSISTENT TRANSGENE EXPRESSION

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Department of biomedicine

With the revived Sleeping Beauty (SB) DNA transposon as a driving force, vectors derived from transposable DNA elements have emerged as new

promising gene vehicles in therapeutic gene transfer. Transgenes carried by transposon-based vectors are efficiently inserted into the genomic DNA of vector-treated cells by the action of the transposase, facilitating long-lasting gene expression and a prolonged therapeutic effect in dividing cells. As opposed to conventional integrating viral vector systems, transposon vectors are inserted into genomic DNA with a random integration profile and do not preferentially target active transcriptional units. Genomic integration of the transgene is pivotal in many applications of viral gene transfer. Genetic treatment of hematopoietic stem cells, for example, depend on the gene insertion and persistency of expression during proliferation and differentiation. Much effort, therefore, has been assigned to the development of viral vectors that home preferentially to 'safe harbors' in the genome. The present PhD project explores new approaches for combining lentiviral gene delivery with alternative gene insertion. Previous findings have documented that foreign nonviral proteins can be incorporated into and transferred by lentiviral particles. We hypothesize that lentiviral particles may therefore be able to package nonviral gene-inserting proteins that may eventually facilitate genomic insertion of reverse-transcribed lentiviral DNA in relevant target cells. By this approach it will be possible to disengage the DNA insertion process from the normal integration machinery and benefit from the properties of a heterogenous integration machinery.

P27.09 Terese K. Jeppesen

ABSENCE OF A GENERAL BENEFICIAL EFFECT OF RENAL SMAD3 BLOCKAGE

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TGF-β1 has a pivotal role in the pathogenesis of kidney diseases characterized by fibrosis. The main intracellular mediator of TGF-β1 signaling is the Smad system, where Smad2/3 plays a central role in transcription of target genes involved in extracellular matrix (ECM) metabolism. We have created a transgenic mouse model with overexpression of TGF-β1, which develops renal morphological changes similar to nephropathy in man.

We hypothesize that blockade of Smad3 protects against the development of TGF-β1-driven kidney fibrosis. To block TGF-β1 signaling our TGF-β1 transgenic mice were backcrossed with Smad3-gene-deficient mice. Glomerulopathy was assessed by electron microscopy, whereas interstitial fibrosis was assessed by measurement of the total collagen content and expression and localization of individual ECM components. In in vitro experiments we explored the response of mesangial and glomerular endothelial cells to TGF-β1 with and without inhibitors of the Smad2/3 pathways.

Deletion of Smad3 reduces ECM accumulation in the mesangial area and in the tubulointerstitial space but does not prevent TGF-β1-induced glomerular basement membrane (GBM) thickening in vivo. This questions whether

Smad3 inhibition has the potential to exert general beneficial effect on renal diseases. In vitro experiments demonstrate that mesangial and glomerular endothelial cells exhibit clear cell-specific responses to TGF-β1 and Smad2/3 blockage, which may explain the lack of a positive effect on the GBM.

Our findings support the view that beneficial effects of gene-targeting are dependent of the context of TGF-β1 expression and further emphasizes the complexity of TGF-β1 signaling in vivo.

P27.10 Ulla Munksgaard Stahlschmidt

FUNCTIONALIZED BI-PHASIC OSTEOCHONDRAL PLUG FOR CARTILAGE REPAIR

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Aim

The aim of the Ph.D. project is to develop a 3D biphasic cell-free scaffold to rebuild damaged cartilage and bone tissue. The scaffolds will be designed to control stem cell differentiation into bone and cartilage forming cells. To functionalize the scaffold it will be coated with collagens and small interfering RNA (siRNA)-loaded nanoparticles targeting osteogenic and chondrogenic differentiation, respectively.

We will investigate the response of mesenchymal stem cells (MSC) first in vitro and then in vivo in a goat model.

Hypotheses

1: siRNA nanoparticle functionalized scaffolds coated with collagen can be used as a delivery system directing hMSC's into either bone or cartilage in vitro.

2: Biphasic scaffolds coated with collagen and functionalized with siRNA enhancing a chondrogenic and osteogenic end can be used for osteochondral repair in vivo.

Materials and Methods

The scaffold itself consists of polycaprolactone (PCL) and is produced in collaboration with iNANO, Aarhus University.

The project is divided into two studies:

Study 1) Development of scaffolds

a) Functionalizing the scaffold by coating with collagen I and siRNA (BCL2L2) and study osteogenic differentiation of human mesenchymal stem cells (hMSC's) and goat MSCs in vitro

b) Functionalizing the scaffold by coating with collagen II and siRNA (Sox9) and study chondrogenic differentiation of hMSC's and goat MSCs in vitro

c) Combining scaffold to a biphasic scaffold and study osteogenic and chondrogenic differentiation of hMSCs and goat MSCs in vitro

Study 2) In vivo study of biphasic scaffolds in an osteochondral goat model

P27.11 Shivani Shivprasad Joshi

NOVEL MUTATION CAUSING CNDI IN SWEDISH PATIENT.

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Congenital Nephrogenic Diabetes Insipidus (CNDI) is a rare inherited disorder characterized by reduced ability to reabsorb water in response to the antidiuretic effect of vasopressin on renal collecting duct cells. Patients exhibit polyuria, nocturia, hypernatremic dehydration, failure to thrive, irritability, and fever. CNDI is genetically heterogeneous and may be inherited in an X-linked or autosomal recessive manner. The proband (7.5 years Swedish male), was identified to have CNDI at 1 month of age and diagnosed at 6 months of age during an episode of gastroenteritis. There was no family history of diabetes insipidus. We sequenced coding regions of arginine-vasopressin receptor-2 gene - AVPR2 gene in patient and 4 unaffected family members. We identified a novel de novo mutation (80bp duplication) in Exon 2 of AVPR2 gene in the patient. Duplication begins from nucleotide 1312 (gDNA sequence) and consists of 80bp that are identical to nucleotide sequence from 1232-1311. This duplication leads to a frame shift and a stop codon- 4 codons downstream (AAWD 294-297>PRLX). There were no mutations in coding regions of AVPR2 gene, in other family members. In this case, clinical data including the water deprivation test and duplication mutation will aid in understanding the pathophysiology of CNDI. Identification of such mutations will facilitate in early diagnosis of CNDI, genetic counseling and early intervention aimed at reducing morbidity with reference to diagnostic testing.

P28.01 Anto Praveen Rajkumar Rajamani

T(9;17) (Q33.2;Q25.3) TRANSLOCATION REVEALS THE ASSOCIATION BETWEEN BIPOLAR DISORDER AND AS WELL AS GENES

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Background: Chromosomal aberrations increase the risk for major psychotic disorders. Cross linking Danish Psychiatric Case Registry and Danish Cytogenetic Case Registry identified a patient with t (9;17) (q33.2;q25.3) translocation and bipolar affective disorder (BD).

Methods: We employed Fluorescent In Situ Hybridization (FISH) to narrow down the breakpoint regions in that patient. We used Ensembl and Biomart web tools to identify the known genes within those regions, which are expressed in brain. We accessed WTCCC, UCL and STEP-BD data and

analyzed the allelic and genotypic associations between BD and the single nucleotide polymorphisms (SNPs) of those genes, using Plink v1.07.

Results: We narrowed down 9q33.2 and 17q25.3 breakpoint regions to 112 KB (124,202,476-124,315,433) and 3l8 KB (78,267,202-78,585,422). We identified four protein coding genes (FLJ35220, NPTX1, RNF213 and RPTOR) in the 17q25.3 breakpoint region. When we analyzed the WTCCC data, rs8072229, rs4602089 and rs12601089 in RPTOR had significant allelic and genotypic associations with BD. While analyzing WTCCC, UCL and STEP-BD data together, rs7223701 and rs8359 in RNF213 and rs4561525, rs11150864, rs8072229, rs4602089, rs12601089, rs2138125, rs9911574 and rs7216306 in RPTOR were significantly associated with BD.

Conclusions: Chromosomal breakpointregions help to identify the candidate genes for psychiatric genetic association studies. Follow-up studies of RPTOR and RNF213 as candidate genes in BD are warranted.

P28.02 Aida Solhøj Hansen

SIGNIFICANCE OF CD46 ISOFORMS ON THE REGULATION OF CELLULAR RESPONSES

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Background: CD46 is a transmembrane glycoprotein expressed on all nucleated human cells and is involved in innate (regulation of the complement system) and adaptive (induction of Tr1 cells) immune responses. In addition, CD46 acts as a receptor for several micro-organisms. Alternative splicing produces multiple isoforms of CD46.

Hypothesis: We hypothesize that CD46 exerts distinct and different functions according to the isoform expressed. To test this hypothesis, the expression of the different isoforms on multiple immune cells, the functional significance of the CD46 isoforms, and the regulation of the alternative splicing of the receptor will be examined.

Methods: Subtypes of immune cells will be isolated by fluorescence-activated cell sorting (FACS) and characterized for their expression of CD46 isoforms by real-time PCR. The most common isoforms will be cloned and expressed, and the functional significance of each isoform will be investigated after infection with human herpesvirus 6A/6B. The significance of Ser/Arg-rich proteins (SR-proteins) and heterogeneous nuclear ribonucleoprotein (hnRNP) involved in alternative splicing will be investigated by knock-down of these factors by a high-throughput RNA interference screen.

Perspectives: Detection of specific functions associated with alternative spliced isoforms of CD46 is important for understanding the regulation of immune responses. Identification of factors controlling CD46 splicing will enhance the understanding of immune regulation and thereby elucidating the regulatory balance between inflammation and tolerance.

P28.03 Siri Strand

LONG NON-CODING RNAS IN PROSTATE CANCER: REGULATION, FUNCTION AND BIOMARKER POTENTIAL

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Prostate cancer (PC) is the most commonly diagnosed malignancy in the Western world, causing ~ 10 % of all male cancer deaths. The primary aim of this project is the identification of new molecular biomarkers for PC, focusing on changes in DNA methylation patterns and long non-coding RNA (ncRNA) expression. The intention is to help increase the specificity of PC diagnosis and prognosis, thus contributing to improved cancer treatment.

The genetic and epigenetic basis of PC biology is investigated in clinical samples and PC cell lines by means of genome wide profiling of DNA methylation patterns and custom array-based ncRNA expression profiling. Transposon-based insertional mutagenesis (TIM) allows rapid identification of cancer causing genes in vitro. By comparing TIM mutated genes and candidate long ncRNAs identified through expression- and methylation profiling, we aim to distinguish driver mutations from passenger mutations, thus identifying long ncRNAs that, by means of their function in PC tumorigenesis, can work as biomarkers as well as potential drug targets. The biological role of the candidate long ncRNAs will be studied by means of functional knock-down and overexpression studies in vitro and in vivo.

P28.04 Ming Sun

NANOMEDICINE IN BREAST CANCER BONE METASTASIS: TARGETING CANCER STEM CELL

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Background: Metastasis accounts for over 90% of lethality in cancer patients. In recent years, with the discovery of cancer stem cells (CSCs) in solid tumors, a CSC-based theory for both tumor-initiationand metastasis has been proposed. This could have fundamental and profound implications for cancer therapy.

Aims: The aim of the present study is: i) to isolate and identify CSCs from bone metastasis sites in individual patients, ii) to design a new drug delivery system in targeted therapy for cancer stem cell and iii) evaluate the effect of this system in vivo. study.

Hypotheses: To significantly increase the efficacy of chemotherapy against potentially resistant breast cancer bone metastasis stem cells, an anticancer agent is delivered simultaneously in one multifunctional drug delivery system in combination with other active ingredients that perform different specific functions for enhancing cellular uptake and efficiency of the main

drug specifically in cancer stem cells and preventing the development and/or suppression of the existent drug resistance.

Materials and methods:Study 1 - Isolation and identification of cancer stem cells from breast cancer bone metastasis: Collection of CSCs from breast cancer bone metastasis specimens; Isolation of CD44+/CD24– Populations by Flow Cytometry. Study 2 - Co-delivery of siRNA and anticancer drug for CSCs-targeted treatment of breast cancer bone metastasis in vitro. Study: encapsulation of chemotherapeutic agents; Intracellular test; Cytotoxicity and apoptosis analysis; gene and protein expression. Study 3 - Drug delivery system for treatment of breast cancer bone metastasis in vivo. study.

P28.05 Miao Wang

NEUROLOGICAL FUNCTION AND SURVIVAL OUTCOME OF AARHUS ALGORITHM IN PATIENTS WITH SPINAL SOLITARY PLASMACYTOMA OR MULTIPLE MYELOMA

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Summary of background data. Solitary plasmacytoma and multiple myeloma are the most frequent malignant spinal tumors, and they are most frequently localized in the spinal vertebral body. Patients often suffered from severe back pain, pathological fracture, and cord compression.

Patients and methods. This study included 33 patients (19 men, 14 women, mean age of 59 years, range from 30 to 84 years). The solitary plasmacytoma group contained 12 patients; multiple myeloma group contained 21 patients. All the patients underwent surgical treatment after complete diagnostic evaluation during December 1994 to November 2009 at the Aarhus University Hospital in Denmark. All the information was prospectively collected into the Aarhus Spinal Tumor Database.

Results. Thirty patients (91%) had local symptoms before operation. Twenty-five patients (82%) had radicular symptoms. Twenty-one of the cases (64%) were identified as Tomita Type 7. Ten patients (30%) were located between Tomita Type 4 to 6. Thirteen of the cases (39%) had chemotherapy, and 5 Patients (15%) had radiotherapy prior to surgery. The neurological status was improved in 14 Patients out of 24 patients (58%), maintained in 16 cases and decreased in 3 patients. At the end of study, 29 patients died. The mean survival duration was 25±20 months (range from 1.4 month to 72 months).

Conclusion. The surgical treatment of spinal solitary plasmacytoma and multiple myeloma based on Aarhus Algorithm is an effective method of treatment with respect to neurological function.

P28.06 Anders Britze Hansen

THE CHOLESTEATOMA PROTEOME

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Background: Middle ear cholesteatoma is a squamous cell tumor affecting around 380 persons per year in Denmark. Although benign by definition many of the characteristics e.g. its destructive behavior, complication rate and extensive treatment regime share similarities with conditions of malignant nature. Being the only treatment modality surgery shows disappointing cure rates and additional or alternative, preferably medical, treatment options are needed. Methods: Biopsies from cholesteatoma and the surrounding tissues are acquired from patients undergoing cholesteatoma surgery at Aarhus University Hospital. By nano-LC-MS/MS an overview of the cholesteatoma proteome is presented and compared to that of the neighboring tissues. Luminex Multiplex bead-based antibody assay will be applied on the same tissues for specific examination of the cytokine inflammation profile. Objectives: To investigate the interrelation and discrepancies between cholesteatoma and surrounding tissue, to thereby indicate the origin of the tumor and to detect key proteins for the pathogenesis that might serve as targets for future treatment. The first full large-scale proteomic analysis has led to the identification and quantization more than 1400 proteins. Bioinformatics has pointed out clusters of proteins representing interesting biological processes that are differentially expressed in cholesteatoma tissue compared to the tissues from which the cholesteatoma is believed to originate. The succeeding analyses will consolidate this expression map and pick the candidates for further investigation in the search for biomarkers of the disease.

P28.07 Kim Blauenfeldt Gosmer

CHEMICAL PROFILING OF ILLEGAL DRUGS AS A FORENSIC TOOL

K.B. Gosmer

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Impurities can be found in any illegal drug whether it is naturally occurring or made in a laboratory. The impurities can either be structurally related to the drug or traces of organic solvents used during manufacturing. Due to the clandestine nature and the lack of quality control in illegal drug production, the relative ratios of these impurities will vary from batch to batch thereby providing a chemical profile, or a chemical fingerprint, that is unique for every single production.

By comparing the chemical profiles of seized drugs it is therefore possible to identify samples that have a common origin meaning that the suspects have had a connection either directly from dealing with each other or indirectly through a common supplier. Obtaining this type of information through regular police investigations can be laborious and it can be impeded by cautious drug dealers whereas chemical profiles are always present.

The chemical profiles are obtained by using gas chromatography-mass spectrometry (GC-MS) to separate, identify and relatively quantify the impurities, and compared by correlation methods such as Pearson's Correlation Coefficient and the Squared Cosine. Results are reported to the Department of Organized Crime and evaluated on the usefulness of the information.

The main purpose of the project is thus to implement and evaluate the use of chemical profiling as a means to obtain new intelligence on the distribution networks of illegal drugs in Denmark and as scientific evidence during trials. Furthermore, development and implementation of analytical methods to

chemically profile anabolic steroids and a range of new but rarely seized drugs is also part of the project.

P28.08 Inge Gram Carlsen

REGULATION OF HSP27 IN UNILATERAL OBSTRUCTED KIDNEY AND IN RMIC SUBJECTED TO MECHANICAL AND INFLAMMATORY STRESS.

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In vivo, renal medullary interstitial cells (RMIC) are subjected to mechanical and inflammatory stress as a resultof ureteral obstruction. It has previously been demonstrated that heat shock protein (HSP) 27 is expressed in RMIC in vivo and in vitro. HSP27 exists in a phosphorylated active form (pHSP27) which plays a role in stabilization of actin filaments and has anti-apoptotic function.

In vivo studies using rats subjected to unilateral ureteral obstruction for 6h and 12h; showed unchanged HSP27 mRNA and protein level in kidney inner medulla (IM). However, pHSP27 protein level was increased in obstructed kidney IM compared to both sham and contralateral kidney. To further examine the activation of HSP27 in response to mechanical and inflammatory stress in vitro we subjected RMIC to pressure and stimulation with interleukin 1β (IL-1β). During inflammatory stress, stimulation with IL-1β over time (2-24h) showed increased HSP27 and pHSP27 protein level in response to 8h stimulation. Using a novel pressure apparatus, pressure of 60 mm Hg over time (2h-24h) was explored directly in RMIC which displayed an unchanged expression of HSP27 and pHSP27 protein level.

These data indicate that acute unilateral obstruction increase the active phosphorylated form of HSP27 in the obstructed rat kidneys, and as well in renal medulla interstitial cells stimulated with IL-1β. Various forms of cellular stress change HSP27 and pHSP27 protein expression differently and this may affect the ability of RMIC to mount an effective cytoprotective response to stress.

P28.09 Paula Fernandez Fernandez Guerra

ANALYSIS OF MITOCHONDRIAL RESPONSE TO INDUCED OXIDATIVE STRESS IN NORMAL HUMAN DERMAL FIBROBLASTS USING NUCLEOCOUNTER NC-3000

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Oxidative stress has been proposed as an important contributing pathogenic feature in inherited mitochondrial enzyme disorders. Given the critical role that mitochondria play in different metabolic pathways the functional disruption of these is associated with mitochondrial dysfunction. Mitochondrial dysfunction is characterized with changes in mitochondrial membrane potential, cellular redox state and cellular viability, among others. These parameters can be analyzed in cultured patients' cell lines. In

many cases the only tissue material readily available is human skin fibroblasts. A wide range of protocols have been described to study mitochondrial function in fibroblasts, but most of these protocols have several drawbacks and limitations.

The NucleoCounter is a novel, portable image cytometer device based on the principle of fluorescence microscopy. The main advantage is its ability to handle a large number of samples with a high degree of precision. The present work establishes its use with normal human dermal fibroblast (NHDF) to check its reliability, consistency and accuracy for measuring mitochondrial function.

This study describes a methodology for detection of effects in mitochondrial function after treatment with hydrogen peroxide (H_2O_2). Studies in NHDF treated with 2mM and 4mM H_2O_2 during 2 hours show a detectable change in three parameters: cellular redox state, mitochondrial membrane potential and percentage of viable cells. We could observe a low intra-observer variation as well as consistency in repetitive analysis. That establishes it as an efficient and highly potential device for monitoring mitochondrial function in human skin fibroblasts.

P28.10 Helle Kristensen

EPIGENETIC SILENCING AND BIOMARKER POTENTIAL OF , AND THEIR HOST GENE IN PROSTATE CANCER

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Among men, prostate cancer (PC) is the most frequently diagnosed type of cancer in the Western world and the second most frequent cause of cancer related death. The approach whereby PC is diagnosed today, plus the opportunities to give a precise prognosis, are not satisfying. Thus, identification of novel molecular biomarkers for improved accuracy of PC diagnosis and prognosis is important. This study investigates the expression and biomarker potential of miR-224, miR-452 and their host gene gamma-aminobutyric acid (GABA) A receptor family epsilon subunit (GABRE) in PC by transcriptional profiling and DNA methylation studies of the GABRE promoter associated CpG island. Compared to nonmalignant prostate epithelial cells, miR-224, miR-452 and GABRE transcript levels are significantly reduced in PC cells. Bisulfite sequencing and quantitative methylation-specific PCR reveal frequent promoter hypermethylation of GABRE in both PC cell lines and PC tissue samples, suggesting epigenetic silencing of the genomic GABRE locus in PC. GABRE methylation accurately distinguishes nonmalignant from PC samples ($p<0,001$), thus potentially allowing the detection of PC through methylation analysis. By univariate analysis in a radical prostatectomy sample set for PC, high GABRE methylation significantly predicts PSA recurrence after radical prostatectomy ($p=0.0005$). Furthermore, in multivariate models, GABRE methylation adds significant independent value to established prognostic factors ($p=0.017$). In summary, our results show that down-regulation of miR-224, miR-452 and GABRE is associated with PC, and identifies GABRE

as a new methylation marker candidate for PC detection and prognosis.

CH.01 Martin Gottliebsen

LONG BONE GROWTH CONTROL CAN BE ACHIEVED WITH TOTALEPIPHYSIODESIS USING 8-PLATES

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Introduction: Epiphysiodesis is an established method to correct leg length discrepancy (LLD) between 2 and 5 cm. At least two techniques are available to obtain permanent fusion of the growth plate; Phemisters open procedure and Canales technique using power drills percutaneously. The 8-plate technique (using a small plate and 2 screws) is widely used for reversible hemiepiphysiodesis and may be used to obtain total reversible epiphysiodesis in treatment of LLD thus avoiding the need for timing of the procedure.

Methods: A paired randomised animal study was conducted to establish a model on treatment of LLD with 8plates. 40kg pigs (n=5) were randomised to either total epiphysiodesis on right proximal tibia with medial and lateral 8plates or no treatment. The left side received the opposite treatment. Implants were removed after 10 weeks treatment. After additional 5 weeks of housing the animal was euthanised. A 1.5 Tesla clinical magnetic resonance (MR) scanner was used to examine both tibias at baseline (before surgery), after 10 weeks (implants removed) and after 15 weeks.

Results: At baseline the interphyseal distances were equal in all animals left and right legs. We measured a mean discrepancy in interphyseal distance of 11.1 mm after 10 weeks and 9.3 mm after 15 weeks with the treated leg being shortest in all cases (P = 0.031). Reversibility of growth was observed after removal of 8plates.

Conclusion: Total reversible epiphysiodesis can be obtained in this animal model. The technique is still an undocumented practice in clinical settings but could potentially avoid the need for timing of epiphysiodesis.

CH.02 Randi Groslier Bjælde

AGONISTS THAT INCREASE $[CA^{2+}]_I$ HALT THE MOVEMENT OF ACIDIC CYTOPLASMATIC VESICLES IN MDCK CELLS

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Translocation of vesicles within the cytoplasm is essential to normal cell function. The vesicles are typically transported along the microtubules to their destination. The aim of this study was to characterize the vesicular movement in resting and stimulated renal epithelial cells. MDCK cells loaded with dyes taken up by acidic vesicles (quinacrine or acridine orange) revealed vigorous movement of the labeled vesicles at 37°C. These movements seem to require intact microtubules, since nocodazole leads to a considerable reduction of the vesicular movements. Interestingly, we found that extracellular ATP caused the vesicular movement to cease. This observation was very obvious in time lapse. Similarly,other stimuli known to increase the intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) in MDCK cells (increment in the fluid flow rate or arginine vasopressin) also reduced the

vesicular movement. These findings were quantified by analysis of single vesicular movement patterns. In this way, ATP was found to reduce the lateral displacement of the total population of vesicles by 40%. As all these perturbations increase $[Ca^{2+}]_i$, we speculated that this increase in $[Ca^{2+}]_i$ was responsible for the vesicle arrest. Therefore, we tested the effect of the Ca^{2+} ionofore, ionomycin (1µM), which in the presence of extracellular Ca^{2+} resulted in a considerable and sustained reduction of vesicular movement amounting to a 58% decrease in average lateral vesicular displacement. Our data suggest that vesicles transported on microtubules are paused when subjected to high intracellular Ca^{2+} concentrations. This may provide an additional

explanation for the cytotoxic effect of high $[Ca^{2+}]_i$.

CH.03 Esben Laugesen

INCREASED ARTERIAL STIFFNESS IS INDEPENDENTLY ASSOCIATED WITH RISK OF ISCHEMIC CEREBRAL DISEASE IN PATIENTS WITH TYPE 2 DIABETES DESPITE GOOD BLOOD PRESSURE AND LIPID CONTROL

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Type 2 diabetes (T2D) patients have increased risk of cardiovascular disease (CVD) including stroke. CVD-risk is traditionally assessed using clinical blood pressure (BP) and lipid profile. Increased arterial stiffness (AS) predicts CVD in the general population. We investigated if AS was associated with indices of cerebrovascular disease risk in T2D´s and sex- and age-matched controls.

Methods:

91 T2D patients and 91 sex- and age- matched controls were examined. AS was assessed by aortic pulse wave velocity (aPWV), and risk of cerebrovascular disease by severity of white matter lesions (WMLs) on MRI scans. WMLs were rated a.m. Breteler (no/slight changes=0, moderate=1, severe=2).

Results:

Despite lower clinical BP (126 vs 131 mmHg systolic) and lower lipid levels, T2D patients had significantly higher aPWV than controls, (9.1(8.7; 9.4) vs 7.9 (7.5;8.2) m/s (median(range)), p<0.0001. aPWV increased across Breteler categories (8.0(7.7;8.3) vs 9.1 (8.5;9.6) vs 9.2 (8.3;10.0) m/s, p<0.001 for trend.

In diabetics, pairwise comparisons showed significant aPWV differences between all Breteler categories (8.5 (8.1;9.0) vs 9.5 (8.8;10.2) vs 10.9 (9.8;12.2)) m/s, p<0.05 for all, and, in controls, between category 0 and 1 (7.5(7.1;7.8) vs 8.6 (7.9;9.4) m/s, p<0.01). After adjustment for covariates in multivariate regression, aPWV remained independently associated with severity of WMLs in the diabetic population, p<0.01.
Conclusion:

Despite good BP and lipid control, aPWV was substantially higher in patients with T2D and independently associated with severity of WMLs. Increased AS might be involved in the pathophysiology underlying the increased risk of stroke seen in the T2D population.

CH.04 Annette Langager Høgh

USE OF ACE-INHIBITORS AND CLINICAL OUTCOME AFTER PRIMARY VASCULAR SURGICAL RECONSTRUCTION: A PROPENSITY SCORE MATCHED NATIONWIDE FOLLOW-UP STUDY

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Objective:

To examine the association between ACE inhibitor use and clinical outcome (MI, recurrent vascular surgery, death, stroke and/or major amputation) after primary vascular reconstruction in a population-based long-term follow-up study.

Methods:

All patients undergoing primary vascular surgical reconstruction between 1996 and 2007 were identified in the Danish Vascular Registry. We obtained data on all filled prescriptions, clinical outcomes and confounding factors by linkage to other health care registries.

For each ACE inhibitor user one non-user was identified using propensity score matching (Greedy method), followed by Cox-regression to estimate adjusted hazard ratios (Adj. HR).

Results:

We included 17495 matched patients (4912 ACE inhibitor users and 12583 non-users) with a median follow-up period of 582 days (range 30 to 4379 days). The cumulative risk of MI was 6.2% for ACE inhibitor users and 4.7% for non-users (adj.HR 1.20, 95% CI 1.03-1.39). Cumulative risk of new vascular surgery was 24.0% for ACE inhibitor users and 23.1% for non-users (adj.HR 1.21, 95% CI 1.13-1.30). All cause mortality was 20.4% for ACE inhibitor users and 24.9% for non-users (adj.HR 0.88, 95% CI 0.81-0.96). No differences were seen concerning stroke and major amputation.

Conclusion:

We found use of ACE inhibitors to be associated with lower all-cause mortality but also an increased long-term risk of recurrent vascular reconstruction. This may imply that through improvement of patient survival, ACE inhibitor use also extends the time the patients are at risk of requiring recurrent vascular reconstruction.

CH.05 Jakob Jakobsen

RELATION BETWEEN MOTOR AND SENSORY THRESHOLD DURING PERCUTANEOUS NERVE EVALUATION

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This study aimed to determine the relationship between the amplitude necessary to elicit a motor/sensory threshold during the Percutaneous Nerve Evaluation(PNE-test) and to evaluate early lead displacement.

Method: 14 patients had a PNE-test in deep sedation. Motor threshold was tested with a test-needle and test-electrode placed anteriorly to the sacrum. The position was verified by fluoroscopy. Sensory threshold was determined in the fully awake patient after the Propofol infusion was stopped and secondly, the day after surgery where the temporary pacemaker was activated. A Pelvic-CAT-scan was performed the day after surgery to verify exact electrode-tip location.

Results: In total 40 temporary electrodes were inserted. A significantly higher (p-value:<0.001) amplitude was necessary to elicit a motor response on test-electrodes than on test-needles 2 volt(0.5-5) versus 1 volt(0.5-4). Sensory threshold increased from 1.75 volt (0.5-8) to 2 volt (0.5-9.9) the day after surgery (p-value:0.008).

Seventeen(42.5%) electrodes were displaced posteriorly 24-hour postoperative. Delta-amplitude to elicit a sensory response had increased significantly (p-value:<0.001) compared to the non-displaced electrodes (2volt (0-7) versus 0volt (-2-1.5)).

Conclusions: The amplitude necessary to elicit a motor response on the test-lead was significantly higher compared to the test-needle. Posterior lead-displacement is common and associated with an increase in sensory threshold.

CH.06 Maiken Kudahl Larsen

MOLECULAR AUTOPSY; GENETIC INVESTIGATION OF SUDDEN UNEXPLAINED DEATH

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Sudden cardiac death is a major cause of premature death in children and young adults in developed countries. Standard forensic autopsy procedures can be unsuccessful in determining the cause of death. Molecular autopsy (postmortem molecular genetic screening), however, has revealed that a number of these deaths are caused by inherited cardiac diseases. The study material consisted of 161 cases of sudden death aged 0-40 years that died in the period 1998-2008. They were screened for inherited heart diseases including premature coronary heart disease, cardiomyopathies and malignant channelopathies using molecular genetic methods. The material was selected from the forensic database by age and cause of death categorized as cardiovascular or unknown cause of death at autopsy. Manual selections of cases were then performed based on autopsy findings and patient histories were provided from autopsy-, police-, and, in some cases, from hospital reports. Genomic DNA was isolated from whole blood. Mutational screening was performed by DNA sequencing, high resolution melting and PCR-based SNP genotyping.

Approximately 10% of the examined cohort had a pathogenic mutation. Family follow-up are ongoing.

Based on our results and the ongoing development in technology for identifying the causes of sudden unexplained death we recommend regional centres for autopsy of sudden unexplained death victims. These centres should serve as centres for expert pathological evaluation and molecular autopsy. National and international guidelines concerning molecular autopsy and transmission of the results to the family members should be proposed for cases of sudden cardiac death.

CH.07 Matias Grynderup

PHYSIOLOGICAL STRESS AND THE RISK OF DEPRESSION

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Aim

Stress is a suspected cause of depression and high cortisol concentration is a well replicated finding in depressed patients. The aim of this study was to determine if physiological stress, measured as high levels of salivary cortisol, increase the risk of depression.

Methods

In 2007, we enrolled 4467 public employees. Morning and evening salivary cortisol concentration was measured for each participant. Participants reporting high levels of depressive, burnout or stress symptoms went through a psychiatric interview where 98 participants with depression were excluded. Two years later in 2009, 3031 (72%) participated at follow-up. The psychiatric interviews were repeated and 63 cases of newly onset depression were diagnosed. Odds ratios of depression were estimated for every 1 nmol/l increase in morning and evening cortisol concentration, as well as for the difference between morning and evening cortisol concentration (slope).

Results

The risk of depression decreased by increasing morning cortisol concentration and by increasing slope, while the risk was not related to evening cortisol concentration. The adjusted odds ratio for 1 nmol/l increase in morning and evening cortisol concentration were 0.61 (95% CI: 0.37, 0.99) and 0.90 (95% CI: 0.62, 1.31), respectively. The adjusted odds ratio for 1 nmol/l increase slope were 0.60 (95% CI: 0.40, 0.90).

Conclusion

This study did not support our a priori hypothesis that physiological stress is a risk factor for depression. On the other hand, our findings are in line with several recent reports showing that long term stress may lower cortisol

concentration and thereby increase the risk of depression.

CH.08 Dariusz Orlowski

SEMI-AUTOMATIC ESTIMATION OF DENDRITE SPINE DENSITIES COMPARED TO MANUAL COUNTING

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Dendritic spines are the sites for excitatory connections. The spine number may therefore reflect neural connectivity and provide knowledge about neuroplasticity. Spine density estimations based on analysis of neurons impregnated with different variants of the Golgi method are often used to quantify changes in neuroplasticity occurring during health, brain diseases, and different treatment paradigms. Manual spine counting is, however, time consuming and is a source of inter-observer variation; moreover, the exact spine number is usually not very informative and difficult to obtain.

We present a quick and simple method based on the irregularity of the dendrite surface to estimate spine density. Using the ImageJ program microphotographs of Golgi impregnated dendrites were binarized, skeletonized and the skeleton terminal endings, which approximately represent the spine positions, were counted and divided by dendrite length to reveal spine density. Results based on more than 700 dendritic fragments, from the hippocampus of the control rats and rats submitted to 21 days of chronic restraint stress were compared with manual spine counting using the Bland-Altman method.

Results from both methods are correlated ($r=0.6$, $p<0.0001$), and both methods showed similar significant differences between the groups in the CA1 area, and no differences in the CA3 area.

In conclusion, the presented semi-automatic method yields consistently a higher spine density number than manual counting resulting in similar significance between groups. The proposed method may therefore be a reproducible, time saving and useful approach in neuroplasticity studies requiring analysis of hundreds of dendrites.

CH.09 Anders Kirch Dige

INFLIXIMAB INDUCES CLONAL EXPANSION OF γδ-T CELLS IN CROHN'S DISEASE: A PREDICTOR OF LYMPHOMA RISK?

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Background: Concominant with the use of combined immunotherapy in Crohn's disease (CD), the incidence of hepato-splenic gamma-delta (γδ)-T cell lymphoma has increased sharply. We hypothesised that repeated infusion of anti-TNF-α agents may induce clonal selection.

Methods: We investigated dynamic changes in the γδ-T cells of 46 patient with CD following treatment with anti-TNF-α (inflimab: n=20; adalimumab: n=26) using flow cytometry. In patients with a high γδ-T cell level, the γδ-T

cells were assessed for clonality.

Results: 35 patients had a γδ-T cells level (mean 1.6%) comparable to healthy individuals (mean 2.2%). 11 CD patients (24%) exhibited an increased level of γδ-T cells (5–15%). In the 18 patients also receiving thiopurines or methotrexate, the average baseline γδ-T cell level was 4.4%. In three male CD patients with a high baseline value, γδ-T cell population increased dramatically following infliximab. A fourth male patient on infliximab monotherapy presented with 20% γδ-T cells, which increased to 25% shortly after treatment. Clonality studies revealed an oligoclonal γδ-T cell pattern with dominant γδ-T cell clones. In vitro experiments showed a dose-dependent proliferative effect of anti-TNF-α agents on γδ-T cells.

Conclusion: CD patients treated with immunomodulators had constitutively high levels of γδ-T cells. Infliximab exacerbated clonal γδ-T cell expansion in vivo and induced γδ-T cell proliferation in vitro. Overall, young, male CD patients with high baseline γδ-T cell levels may be at an increased risk of developing malignant γδ-T cell lymphomas following treatment with anti-TNF-α agents.

CH.10 Niels Fristrup

CATHEPSIN E, MASPIN, PLK1, AND SURVIVIN ARE PROGNOSTIC PROTEIN MARKERS FOR PROGRESSION IN NON-MUSCLE INVASIVE BLADDER CANCER - A LARGE SCALE TISSUE MICROARRAY VALIDATION STUDY

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Background:The histopathological parameters currently used in the clinic cannot predict the individual disease course precisely. Consequently, non-muscle invasive bladder cancer patients have to be monitored thoroughly for disease recurrence and progression by urine and cystoscopy examinations. Here we investigate the prognostic value of Cathepsin E, Maspin, PLK1, and Survivin.

Material and Methods: Three different tissue microarray cohorts with long-term follow-up were used. In total 693 non-muscle invasive urothelial carcinomas from Denmark, Sweden and Spain. Protein expression was measured by immunohistochemistry and antibody specificity was validated by Western blotting.

Results: In the Danish patient cohort we found the expression of Cathepsin E, Maspin, PLK1, and Survivin to be significantly associated with progression to stage T2-4 bladder cancer (for each marker: log-rank test;

p<0.001). Multivariate Cox regression analysis identified Cathepsin E (p<0.001), PLK1 (p=0.018), Maspin (p=0.001), and Survivin (p=0.001) as independent prognostic markers. Furthermore, the expression of Maspin, Survivin and Cathepsin E significantly sub-grouped patients already stratified by EORTC risk scores. Finally, we successfully validated the prognostic findings in tumors from 410 patients from Sweden and Spain.

Conclusions: Cathepsin E, Maspin, PLK1, and Survivin are strong prognostic markers in non-muscle invasive bladder cancer. All four protein markers may be clinically relevant markers for guiding optimal treatment of patients with non-muscle invasive urothelial carcinoma. Additional prospective studies are needed to further validate the clinical relevance of the marker panel.

CH.11 Muhammad Umar Cheema

ALDOSTERONE INDUCES ACCUMULATION OF AN ALPHA ENAC IMMUNEREACTIVE PEPTIDE IN PROTEOSOMES OF DISTAL RENAL TUBULES

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The epithelial sodium channel, ENaC, is a protein complex formed by α-, β-, and γ- subunits. Renal ENaC plays a crucial role in Na^+ homeostasis and extracellular fluid volume control. Regulation of ENaC is multifaceted and includes differential protein expression of the individual subunits and redistribution of ENaC containing vesicles to and from the apical plasma membrane. Using an antibody against the NH2-terminus of αENaC, we previously demonstrated increased apical αENaC expression in connecting tubules and collecting duct in rats receiving 50 µg aldosterone/kg body weight/24 hrs for 7 days as compared to vehicle treated controls. In this study, using an antibody against the extracellular loop of αENaC there was marked labeling of spherical intracellular structures in connecting tubules of the aldosterone treated rats with no labeling in untreated animals. Double-labeling immunofluorescence analysis revealed low level of colocalization of the αENaC immunoreactivity with cathepsin D (lysosomes), less with early endosomes (EEA1) and minimal with recycling endosomes (rab11). By contrast, the structures colocalize to a high degree with protesomes specifically in distal convoluted and connecting tubules. The results suggest that aldosterone infusion is accompanied by an increased endocytosis of anti-αENaC reactive peptide, which eventually ends up in proteosome for proteolytic degradation.

CH.12 Carina Henriksen

THE PATHOPHYSIOLOGY OF RAPID-ONSET DYSTONIA PARKINSONISM: CELL CULTURE STUDIES AND PORCINE MODEL

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Rapid-onset Dystonia Parkinsonism (RDP) is an autosomal dominantly inherited neurological disorder characterized by abrupt onset of dystonia, usually with signs of Parkinsonism. RDP is caused by missense mutations in the a3-isoform of the Na^+,K^+-ATPase. a3 is the major isoform of Na^+,K^+-ATPase expressed in neurons, but a convincing hypothesis for the

pathophysiological mechanism underlying the development of the disease is missing and a contribution to a better understanding of this mechanism is the aim of the Ph.D. project. It is possible that the pathogenesis is entirely related to lack of Na^+,K^+-ATPase function, but it is also possible that dominant negative interactions from the mutated protein may be important. By use of cell culture, RDP mutations will be analyzed to evaluate their influence on the function of the Na^+,K^+-ATPases. Some mutations have been found to reduce the Na^+ affinity of the Na^+,K^+-ATPase. It is a goal to establish transgenic mini pigs overexpressing Na^+,K^+-ATPase a3 with a RDP mutation causing reduced Na^+ affinity, thus allowing us to test the negative dominance hypothesis. The first litter of six piglets has just been born and only one piglet is still alive. All six piglets will be analysed for the transgene. The promoter was the porcine promoter of ATP1A3, which has been cloned. The function of the ATP1A3-promoter has been tested in cell lines, and its neuron specificity has been analysed in zebra fish. The tissue specific expression patterns of the isoforms (a1, a2 and a3) of the Na^+,K^+-ATPase at the transcriptional level has been investigated, including expression in specific parts of the porcine brain as well as the developmental pattern

CH.13 Sabina Jelen

TWO UREA CHANNELS, AQP9 AND A UT-A GENE PRODUCT, FACILITATE HEPATOCYTE BASOLATERAL MEMBRANE UREA PERMEABILITY.

S. J, M. R

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In mammals, nitrogen from protein degradation is disposed as urea. Many studies have investigated expression of urea transporters in hepatocytes, where urea is produced. Nevertheless, the role of protein facilitated urea transport in liver and the involved molecules remain unknown. Here we have utilized stopped flow light scattering measurements to determine urea permeability in isolated hepatocyte basolateral membranes. The promiscuous urea channel inhibitor phloretin and the competitive UT family channel inhibitor dimethylurea reduced urea permeability of these membranes by 70% and 40%, respectively. This suggested involvement of both, UT family proteins as well as other phloretin sensitive channels. In membranes isolated from AQP9 (AQP9-/-) and UT-A (UT-A-/-) single knockout mice, respectively, urea permeability was decreased by 30% and 40%, respectively, compared to wild type mice. These experiments identified AQP9 and a UT-A gene product as hepatocyte urea channels. At present, the physiological role of AQP9 in hepatocyte function was investigated following exposure of mice to high oral glutamine doses or high protein diet. These conditions did not affect the concentrations of urea or its precursor ammonia, in AQP9-/- mouse tissues. In a similar study, hepatocyte function of UT-A-/- mice in urea synthesis appeared normal. We conclude that both, AQP9 and a UT-A gene product, constitute redundant urea channels in hepatocytes. We plan to investigate hepatocyte membrane urea permeability and hepatocyte function in AQP9-/- UTA-/- double knockout mice.

CH.14 Louise Wamberg

DIFFERENTIAL EXPRESSION OF VITAMIN-D-METABOLIZING CYTOCHROMES P450 IN HUMAN ADIPOSE TISSUE DEPOTS

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Objective: The activation of vitamin D_3 is a two-step process catalysed first by the 25-hydroxylases (CYP2R1, CYP2J2 and CYP27A1) and secondly by the 1α-hydroxylase (CYP27B1) classically confined to the liver and kidney, respectively. Vitamin D is stored in adipose tissue (AT), and circulating levels of 25-vitamin D are commonly low in obesity. We aimed to determine whether the activating CYPs are expressed in AT, and whether their expression differs in lean and obese women.

Methods: Paired samples of visceral (VAT) and subcutaneous (SAT) adipose tissue biopsies were obtained from 20 obese women (BMI: 46.1 (44.0 – 48.2) kg/m^2) undergoing laparoscopic gastric banding for obesity and from 20 lean women (BMI: 23.4 (22.3 – 24.5) kg/m^2) undergoing laparoscopic surgery for benign gynecological reasons. Relative gene expressions were measured using RT-PCR.

Results: CYP2R1, CYP2J2 and CYP27A1 were all expressed in AT. The CYP27B1 was also expressed in AT. The degrading enzyme CYP24A1 was not expressed in AT. Expression of CYP2R1 and CYP2J2 were highest in SAT of lean women (P=0.02 and p= 0.004, respectively), with no differences in obese women. Interestingly, CYP27A1 was higher in VAT of obese women (p =0.01) and tended to be so in lean women p= 0.07). CYP27B1 was higher in SAT than VAT of both lean and obese women (p= 0.02 and p= 0.03, respectively).

Conclusion: All three of the 25-hydroxylases and the 1α-hydroxylase were expressed in adipose tissue. Expression differed in SAT and VAT and in lean and obese women. This implies depot-specific, local activation of vitamin D is possible within AT causing paracrine or autocrine effects on AT metabolism.

CH.15 Carina Agerbo Rosenberg

CHARACTERISATION OF AGE SPECIFIC T CELL RESPONSES FOLLOWING VACCINATION AGAINST HEPATITIS B VIRUS INFECTIONS

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Virus infections are a major source of morbidity. Although many viral vaccines, including those protecting against hepatitis virus, have been successful in reducing the incident of disease it is nevertheless the case that as many as 10% of the vaccine recipients do not respond to the vaccine and consequently are left unprotected.

Here, we propose to study the molecular mechanisms involved in the immune response to vaccination against hepatitis B infection. The study cohort contains samples from 28 healthy vaccine recipients younger than 35 and 28 healthy vaccine recipients older than 55. Preliminary data collected

so far indicated a differential immune response towards the HBV vaccine in young and elderly donors. Evaluation of the antibody titer showed a significantly higher prevalence of non-responders ((HBsAg specific antibodies < 10 IU/L) among elderly donors and a significantly higher proportion of high responders (HBsAg specific antibodies > 1000 IU/L) among younger donors ($p < 0.0361$).

We suggest that an analysis of the vaccine response in elderly recipients may throw new light on the more general issue of non-responding vaccine recipients. By comparison of donor-derived samples we aim at identifying the mechanism that support protection against the infection and hence may play a role in differential response to vaccination. A comprehensive analysis using flow cytometry is applied to characterise the role of T cells in the regulation of antibody formation following in vitro re-stimulation assay. Markers such as cytokine synthesis and immunosenescence indicators will be tested in parallel.

CH.16 Xiaoping Chen ISOSTEVIOL HAS A BENEFICIAL EFFECT ON FATTY ACID-INDUCED GLUCAGON SECRETION

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Abstract

Aims/hypothesis: Long-term exposure to high fatty acid levels impairs insulin secretion and exaggerates glucagon secretion. The aim of this study was to explore the potential modifying action of Isosteviol (ISV), an antihyperglycaemic agent, on palmitate-induced effects on alpha cells.

Methods: Long-term incubation studies of alpha TC1-6 cells in the presence of 0.5 mM palmitate with/without a range of concentrations of ISV were performed. Here we investigated the effect of ISV on glucagon secretion as well as on gene expression in these cells. We also examined the effect of ISV on glucagon and insulin secretion from isolated mouse islets after long-term palmitate exposure.

Results: Culturing the cells for 72-h with 0.5 mM palmitate, followed by a 2-h incubation with 2 mM glucose and 18 mM glucose, resulted in 34% ($p<0.05$) and 56% ($p<0.01$) increase in glucagon secretion, respectively. At 2 mM glucose, ISV (10^{-8} M) reduced palmitate-stimulated glucagon release by 18% ($p<0.05$). At 18 mM glucose, ISV at 10^{-8} and 10^{-6} M each reduced palmitate-stimulated glucagon release by 27% ($p<0.05$). Palmitate increased Pcsk2, Irs2, Fasn, Srebf2 ($p<0.001$), Acaca ($p<0.01$), Pax6 ($p<0.05$) and glucagon mRNA ($p<0.05$) levels in the cells. ISV significantly ($p<0.05$) up-regulated Insr, Irs, PIK3r1, and Akt1 gene expression in the presence of palmitate. Furthermore, 72-h exposure of mouse islets to palmitate resulted in hypersecretion of glucagon ($p<0.001$) and reduction of glucose-induced insulin secretion ($p<0.01$), whereas ISV was found to reverse palmitate's

effects.

Conclusion: ISV counteracts the αlpha cells hypersecretion caused by long-term palmitate exposure.

CH.17 Anders P. Søndergaard

UVA RIBOFLAVIN COLLAGEN CROSS-LINKING LOWERS STROMAL SWELLING PRESSURE

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Purpose: To evaluate whether UVA riboflavin cross-linking reduces stromal swelling pressure in porcine corneal segments.

Methods: In 14 porcine eyes ex vivo, the central corneal thickness (CCT) was determined by ultrasound pachymetry. Mounted in an artificial anterior chamber, anterior and posterior segments of 230 μm were cut with a femto-second laser. With the flaps in situ, the treatment group (n=7) underwent a UVA riboflavin cross-linking procedure (CXL). In the control group (n=7) only riboflavin solution was applied. The segments were removed and the weights measured. After a 2-hour pre-swelling period, the swelling behavior of the segments in isotonic saline was measured in a biomechanical setup. The swelling force exerted by the corneas in the anterior-posterior direction was recorded at different thicknesses and the swelling pressure was calculated. Dry weights were obtained for solids correction.

Results: No significant difference in mean dry weight was observed between groups. The hydration change in the CXL group compared to the control group after the pre-swelling period was significantly lower in anterior segments ($p = 0.0026$), but insignificant in posterior segments ($p=0.0595$). Non-linear regression parameters of CCT vs. swelling pressure were significantly different in the two groups.

Conclusions: The stromal swelling pressure in the anterior part is lowered after the CXL procedure ex vivo, suggesting that this treatment can reduce corneal edema in vivo. The results agree with previous biomechanical findings; CXL primarily affects the anterior segment of the stroma.

CH.18 Chris Bath Søndergaard

OXYGEN AS A KEY REGULATOR OF LIMBAL EPITHELIAL STEM CELL GROWTH AND DIFFERENTIATION

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Transplantation of ex vivo cultured Limbal Epithelial Stem Cells (cLESCs) is emerging as the new treatment of choice for ophthalmologic diseases with concurrent Limbal epithelial Stem Cell Deficiency (LSCD). It is expected that physiological epithelial oxygen concentrations vary from below 5% in the stem cell niche to about 17% below the tear film.

We hypothesized that environmental exposure to a gradient of different oxygen concentrations during cLESC expansion could selectively promote

different epithelial cell phenotypes.

Human corneoscleral discs were obtained from the Danish Cornea Bank. Growth and phenotype of cLESCs were compared between oxygen concentrations of 2%, 5%, 10%, 15%, and 21%. Two culture systems were compared using either serum-containing medium and NIH/3T3 feeder cells or EpiLife® (serum-free medium without feeder-cells as support). Immunocytochemistry was done using Hoechst 33342 and antibodies against ABCG2, ΔNP63α, and cytokeratin 3. Cell cycle analysis was performed using staining intensities of Hoechst 33342.

In both culture systems a bimodal growth pattern of cLESCs was detected. Slowest growth was found in 2% and 15% oxygen concentrations. In both systems ABCG2 expression was highest in low oxygen concentrations of 2-5%. CK3 expression started to increase at 5-10%. ΔNP63α intensities were highest at 10%. The highest fractions of 4n DNA cells were seen at 2% and 15%.

We conclude that cLESCs is selectively expanded in 2%, TACs at 5%-10% and PMCs at 15%. ABCG2 seem to be a better marker for stem cells than the commonly used transcription factor ΔNP63α. As 2% seem to promote stemness in culture, this could be important for future clinical outcome.

CH.19 Regina Gonzalez Dosal

HSV INFECTION INDUCES PRODUCTION OF ROS, WHICH POTENTIATE SIGNALING FROM PATTERN RECOGNITION RECEPTORS: ROLE FOR S-GLUTATHIONYLATION OF TRAF3 AND 6

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The innate immune response constitutes the first line of defense against infections. Pattern recognition receptors recognize pathogen structures and trigger intracellular signaling pathways leading to cytokine and chemokine expression. Reactive oxygen species (ROS) are emerging as an important regulator of some of these pathways. ROS directly interact with signaling components or induce other post-translational modifications such as S-glutathionylation, thereby altering target function. Applying live microscopy, we have demonstrated that herpes simplex virus (HSV) infection induces early production of ROS that are required for the activation of NF-κB and IRF-3 pathways and the production of type I IFNs and ISGs. All the known receptors involved in the recognition of HSV were shown to be dependent on the cellular redox levels for succesful signaling. In addition, we provide biochemical evidence suggesting S-glutathionylation of TRAF family proteins to be important. In particular, by performing mutational studies we show that S-glutathionylation of a conserved cysteine residue of TRAF3 and TRAF6 is important for ROS-dependent activation of innate immune pathways. In conclusion, these findings demonstrate that ROS are essential for effective activation of signaling pathways leading to a successful innate immune response against HSV infection.

CH.20 Dorte Guldbrand Nielsen

THE RELATIONSHIP BETWEEN IMMEDIATE RELEVANT BASIC SCIENCE KNOWLEDGE AND CLINICAL KNOWLEDGE: PHYSIOLOGY KNOWLEDGE AND TRANSTHORACIC ECHOCARDIOGRAPHY IMAGE INTERPRETATION

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Background: Two major views on the relationship between basic science knowledge and clinical knowledge stand out; the two-world view seeing basic science and clinical science as two separate knowledge bases and the encapsulated knowledge view stating that basic science knowledge plays an overt role being encapsulated in clinical knowledge. However, recent research has implied that a more complex relationship between the two knowledge bases exists. This study explores the relationship between immediate relevant basic science (physiology) and clinical knowledge within a specific domain of medicine (echocardiography).

Methods and results: 28 medical students in their 3rd year and 45 physicians (15 interns, 15 cardiology residents and 15 cardiology consultants) took a multiple-choice test of physiology knowledge. The physicians also viewed images of a transthoracic echocardiography (TTE) examination and completed a checklist of possible pathologies found. A total score for each participant was calculated for the physiology test, and for all physicians also, for the TTE checklist. Consultants scored significantly higher on the physiology test than did medical students and interns. A significant correlation between physiology test scores and TTE checklist scores was found for the cardiology residents only.

Conclusion: Basic science knowledge of immediate relevance for daily clinical work expands with increased work experience within a specific domain. Consultants showed no relationship between physiology knowledge and TTE interpretation indicating that experts do not use basic science knowledge in routine daily practice, but knowledge of immediate relevance remains ready for use.

CH.21 Peter Hjorth

PHYSICAL HEALTH OF RESIDENTS IN PSYCHIATRIC AND SOCIAL CARE FACILITIES

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Background

Prevalence of physical illness among patients suffering from psychiatric illness is higher than in the average population.

Hypothesis

There is a correlation between the awareness of physical health and the physical health.

Design: Randomised intervention study with follow-up after 12 months.

The population consists of 174 patients living in six long-term facilities for severe mentally ill patient. The 330 staff members were also participating. Measurement of patients: blood test, ECG, BMI, waist, lung peep, blood pressure, physical fitness, tobacco and alcohol consuming.

Intervention

Sessions with each participants were held to collect the data. The method of Motivational Interviewing was used. Focus group discussions were carried out. There was teaching sessions to the staff about smoking cessation, and discussions about correct use of antipsychotic medicine. Improvement in the structural conditions in the facility to maximise the physical exercise and in healthy food. In the control facilities there were treatment as usual during the study period.

Results

The intervention results in a statistical significance reduction in the unhealthy waist circumference both among patients and staff. There are improvements in the blood values of cholesterol, LDL and fasting glucose among patients.

Conclusions

Active awareness on the physical health has a positive effect of the physical health of the patients and staff. There are excess physical health problems in people with severe mental illness. The potential and needs for prevention and treatment are considerably

CH.22 Anne Sophie Ågård

LIFE AFTER ICU: TRAJECTORIES OF ICU-SURVIVORS AND THEIR PARTNERS POST ICU

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INTRODUCTION: Critical illness and admission to ICU radically affects both patients and their relatives during hospitalization and after discharge. Little is known, however, about the challenges facing them after ICU discharge.

OBJECTIVES:To describe the trajectories of ICU-patients and their partners and identify their use of health care services and loss of work during the first year after ICU-discharge.

METHODS: Observational, longitudinal design. Data from population registers and interviews at three and 12 months post ICU-discharge. ICU-survivors intubated > 96 hours aged 25-70 years and their partners from five ICUs were included. We excluded patients with appreciable chronic conditions prior to admission.

MAIN RESULTS: Eighteen patients and their partners participated in the study. After hospital discharge ten patients were transferred to a rehabilitation facility for intensive physical training or neurorehabilitation, median length of stay 52 days (range 15-174). Subsequently, 13 patients participated in community-based physical training for median 12 weeks (range 3-34). Patients had 265 visits to out-patient clinics and GP 12 months before ICU and 444 in the year after. Three patients had returned to their pre-ICU employment rate after 12 months. In ICU partners' mean (range) sick leave was 11 days (4-42) full time and 9 days (0-44) part time. After ICU, partners' sick leave was 17 days (0-124) full-time and 21 days (0-106) part-time.

CONCLUSIONS: Even after months of extensive training some patients failed to fully recover and return to work 12 months after ICU discharge. The partners needed extensive sick leave to fill their role as informal caregivers.

CH.23 Connie Berthelsen

RELATIVES' PARTICIPATION IN OLDER PATIENTS' FAST-TRACK TREATMENT PROGRAM DURING HIP OR KNEE REPLACEMENT - CONSTRUCTING GROUNDED THEORY

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In Denmark, there is annually performed (year 2008) 7473 hip- and 7416 knee replacement surgeries, and 49 % of patients are over the age of 70. Indications for hip and knee replacement are often arthritis and excruciating pain, which can lead to loss of ability to function. Hence, older people are expected to have some need for help and support in their daily living by relatives, both before, during and after hospital admission. The relatives´ role in the fast-track treatment program is presumed to be important but has never before been examined.

Overall aim:

To generate a grounded theory explaining the pattern of behaviour in relative's role in older patients fast-track treatment program during hip or knee replacement.

The study rests on a classic grounded theory approach by Glaser and Strauss (1967) and the further work of Glaser. Through all three studies, data is collected through theoretical interviews, non-participant observations, subsequent conversations, informal conversations and written material of information from the wards.

The research will provide an improved foundation for health professionals to include and cooperate with relatives. Hence it is likely to bring evidence based knowledge about the importance of relatives as potential resources in the fast-track treatment program and be an opportunity for improvement of quality in clinical practice.

CH.24 Marie Louise Svendsen

HIGHER STROKE UNIT VOLUME ASSOCIATED WITH IMPROVED QUALITY OF ACUTE STROKE CARE AND POTENTIAL COST SAVINGS

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Background and Purpose: Specialized stroke unit care improves outcome among stroke patients, but it is unclear whether there are any "scale advantages" from treating a larger number of patients. We examined whether stroke unit volume was associated with quality of acute stroke care, mortality, and hospital bed-day use (determines a substantial part of costs in stroke care).

Methods: In a nationwide population-based cohort study, we identified 63,995 patients admitted to stroke units between 2003 and 2009. Data on exposure, outcome, and covariates was collected prospectively. Comparisons were clustered within stroke units, and adjusted for patient- and hospital characteristics.

Results: Patients who were admitted to high-volume stroke units received more recommended processes of acute stroke care compared with patients in low-volume stroke units (unadjusted difference 9.84 percentage points (95% CI 3.98-15.70)). Higher volume was associated with shorter length of initial hospital stay (adjusted ratio 0.49 (95% CI 0.41-0.59)) and reduced total bed-day use in the first year after stroke (adjusted ratio 0.79 (95% CI 0.70-0.87)). No association was found with mortality.

Conclusions: Patients admitted to high-volume stroke units received a higher quality of acute stroke care, potentially at lower costs. We observed no association between volume and mortality.

CH.25 Berit Hvass Christensen

MOTHERS' WORK EXPOSURE DURING PREGNANCY AND ASTHMA IN THEIR CHILDREN, A PROSPECTIVE COHORT-STUDY

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Prenatal exposures may add to the worldwide increase in asthma prevalence. We estimated the association between maternal work and asthma prevalence among 7 year old offspring.

Methods: Analysis included 42,696 children from Danish National Birth Cohort and their mothers. Job title (DISCO codes) was classified by exposure agents: high molecular weight exposure (HMW), low molecular weight/irritant exposure (LMW), mix of HMW and LMW exposure, farmers, unclassifiable exposure, students and references. Children's asthma was defined as even asthma and/or wheeze in the last 12 months. Atopy was

defined as atopic dermatitis ever.

Results: The overall prevalence was 15.8%. The highest asthma prevalence was among children of mothers exposed to LMW/irritant agents during pregnancy (18.6%). Adj. logistic regression analysis and stratifying for atopic status in the children showed association between mother's occupational exposure to LMW/irritants and asthma in the child (OR 1.13 (95% CI 0.94;1.35) and 1.14 (1.01;1.28) for atopic and non-atopic children respectively). The same tendency was seen for HMW (OR 1.21 (95% CI 0.75;1;97) and 1.08 (0.77;1.51) respectively). Adjusted models included: mother's age, BMI, atopy, smoking, use of medication, pets, SGA and gender. Adjusting for postnatal exposure, the same tendencies were seen for HMW and LMW/irritant in atopic children. For the non-atopic children, postnatal exposure showed to be more important in the LMW group. No significant associations to asthma were seen in the other exposure groups.

Conclusion: The results indicate an association between maternal occupational work exposures and the risk of asthma in the child at age 7 years.

CH.26 Sofie Gry Pristed

ASSOCIATION BETWEEN ANTHROPOMETRIC MEASURES AND HEALTH-RELATED QUALITY OF LIFE - DATA FROM THE DANISH DIET, CANCER AND HEALTH STUDY

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AIM

To examine associations between anthropometric measures and health-related quality of life (HRQoL).

METHODS

A cross-sectional study based on the Danish prospective study Diet, Cancer and Health. Invited to participate were individuals aged 50-64 years, born in Denmark, living in Copenhagen or Aarhus County, not previously diagnosed with cancer.

At five years of follow-up information about HRQoL and anthropometric measures were questionnaire-based. Short Form 36 assessed HRQoL and the scores were summarised into a physical and a mental component score.

Associations were analysed by linear regression for men and women separately.

RESULTS

In total 18,859 men with a median body mass index (BMI) of 26 (10-90% percentile 22.5-30.6) and 21,478 women with a median BMI of 24.6 (10-

90% percentile 20.7-30.7) were included.

For an additional unit in BMI, the mean physical component summary was 0.40 (95% CI 0.38-0.43) lower in women and 0.31 (95% CI 0.28-0.34) lower in men.

BMI was not associated with the mental component summary.

For a one centimetre larger waist circumference, the mean physical component summary was 0.14 (95% CI 0.13-0.15) lower in both genders.

For a one centimetre larger waist circumference, the mean mental component summary was 0.03 (95% CI 0.02-0.04) lower in women and 0.02 (95% CI 0.01-0.04) lower in men.

CONCLUSION

For both genders; the physical component summary was inversely associated with BMI and waist circumference; the mental component summary was not associated with BMI, but it was inversely associated with waist circumference.

Due to the large number of participants, even weak associations without clinical interest were statistically significant.

CH.27 Morsi Abdallah

IMMUNOLOGIC DYSFUNCTION IN AUTISM SPECTRUM DISORDERS: FINDINGS FROM A DANISH HISTORIC BIRTH COHORT

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Introduction

Autism Spectrum Disorders (ASD) refers to a group of heterogeneous neurodevelopmental disorders characterized by qualitative impairments in social interaction, communication and repetitive stereotypic behavior. Mounting evidence has suggested a potential role of immunologic dysfunction in the pathophysiology of ASD. In this project markers of immunologic dysfunction (inflammatory cytokines, chemokines) and alpha fetoprotein levels were measured perinatally utilizing a unique Danish Historic Birth Cohort (HBC) maintained at Statens Serum Institute (SSI).

Materials and Methods

Amniotic fluid, maternal serum and dried blood spots samples from the HBC and the Danish Newborn Screening Biobank were utilized. Using data from Danish nation-wide health registers, a case-control study design of 414 cases and 820 controls was adopted. Levels of different cytokines, neutrophins and alpha-fetoprotein (AFP) were analyzed at SSI using

Luminex xMAP technology and radioimmunoassay techniques. Case-control differences were assessed as categories (logistic regression) or continuous measures (tobit regression).

Results and Conclusions

Elevated levels of number of pro-inflammatory (i.e. TNF, MCP-1) and anti-inflammatory (i.e. IL-4, IL-10) cytokines and matrix metalloproteinases (MMP-9) were found in ASD cases compared to controls. Also, ASD cases were more likely to have abnormally elevated levels of AFP. While findings in this study confirmed the role of immune dysfunction in ASD, to the best of our knowledge this is the first study to show that such a dysfunction is initiated intrauterinely. Further studies to examine the specificity of these findings to ASD are necessary.

CH.28 Anette Werner MENTAL TRAINING AND CHILDBIRTH - THE EFFECT ON PAIN EXPERIENCE, LENGTH OF BIRTH AND OTHER BIRTH OUTCOMES

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Background:

Experiencing labour pain is a challenge to the parturient woman. Pharmacological pain relief methods to relieve birth pain are limited and often associated with side effects.

Several studies indicate that hypnosis has a positive impact on labour pain and several other birth outcomes. However, many of these studies may be prone to bias and confounding.

Aim:

The aim of this study is to examine the effect of a short antenatal course in self-hypnosis on several endpoints:

Primary endpoint:

The use of epidural analgesia during birth

Secondary endpoints:

Duration of birth

Birthprogression at admission

Birth experience

Medical interventions during birth

Hemorrhage during birth

Saliva cortisol profile

Infection (mother and child)

Postnatal depression

Breastfeeding duration

Child's condition and wellbeing

Future mode of delivery

Methods:

The study is designed as a randomised, controlled, single-blinded trial using a 3 arm group design.

The intervention group: receives 3 antenatal classes in self-hypnosis including audio compact discs for homework.

The active comparator group: receives 3 antenatal classes containing a mixture of different relaxation methods and Mindfulness. This course also includes audio compact discs for homework.

The control group: receives ordinary antenatal care and no additional interventions.

The data collection is based on questionnaires, register data, medical records and biological material.

Status:

We started including participants July 2009 and completed recruitment May 2011. We included in total 1222 pregnant women and expect the data collection to be completed March 2012

CH.29 Anne-Birgitte Vogelsang

LIVING TOGETHER WITH A RECIPIENT OF AN MPLANTABLE ARDIOVERTER EFEBRILLATOR A CHALLENGE?

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Background: Little is known about the impact of an ICD implantation on partners. A Danish study (n=161) has shown that 70% want the individual support to improve significantly, 50% do not know how to react to shock-therapy and 47% worried highly when the ICD recipient was physically active.

Method: A cross-sectional, retrospective questionnaire study. Inclusion: all adult ICD recipients, who for the first time had an ICD implanted in the period from 1 January 2005 until 1 January 2008 (N=1575, eligible n=1305), and their possible partner.

Objective: To identify partners' need for support during rehabilitation and exposure factors. To identify fears and concerns of the recipient and the partner. To evaluate the psychological impact of an ICD treatment on

partners and recipients.

Results: 71% of the eligible ICD recipients answered; of those who had a partner, 94% of the partners (n=578) answered. Compared to the general population in Denmark, adjusted for age and gender, partners to ICD recipients had statistically significantly higher stress level (diff mean 1.87 (0.94;2.80)), affection on family life (p<0.005) and statistically significantly lower self-rated mental quality of life (p< 0.005). Looking at ICD specific worries we found that 64 (60;68)% worried when the ICD recipient was physically active, and 54 (50;59)% worried if the ICD recipient should get shock-therapy. Only 46(44;51)% knew what to do if shock therapy was introduced. 74 (72;77)% wanted the individual support to improve significantly.

Conclusion: Partners to ICD recipients are highly affected in their personal lives and are not sufficiently supported in the process.

CH.30 Lisa Gregersen Østergaard

THE EFFECT OF EARLY INITIATION OF REHABILITATION AFTER LUMBAR SPINAL FUSION - A RANDOMIZED CLINICAL TRIAL

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Background: Despite of the increase in lumbar spinal fusions, and the fact that spinal fusion procedures have been performed for more than 70 years, only few studies have examined rehabilitation strategies for this patient group. Group-based rehabilitation has proven to be both efficient and cost-effective for lumbar spinal fusion patients. The most current practice is that patients visits their surgeon 12 weeks after the surgery and start their rehabilitation at this point in time. We hypothesise that patients starting rehabilitation already 6 weeks after the surgery, will recover as least as well as patients starting their rehabilitation 12 weeks after surgery.

Purpose: The aim of the present study is to comparing the effect of rehabilitation when starting the rehabilitation either 6 weeks or 12 weeks after a lumbar spinal fusion, focusing on ADL, functional mobility, and return to work.

Methods: The study is a multicenter clinical randomized study including 82 patients. The patients were randomly assigned to a 6-weeks-group starting their rehabilitation 6 weeks post surgery or a 12-weeks-group starting their rehabilitation 12 weeks post surgery. The patients in the two groups received the same group-based rehabilitation. Primary outcome was the Oswestery Disability Index (ODI). Secondary outcome was the Dallas Pain Questionnaire (DPQ), the Low Back Pain Rating Scale and absence from work. The Wilcoxon rank sum test was used to test any differences between the groups, looking at the difference from baseline to 6 months and 12 months follow up (significance level: 0.05).

Results: Data at 6 months and 12 months follow-up will be presented at the Ph.d. day.

CH.31 Christina Malmose Stapelfeldt

PATTERNS OF SICK-LEAVE'S ASSOCIATIONS WITH WORK CHARACTERISTICS AMONG EMPLOYEES IN THE MUNICIPAL ELDERCARE IN AARHUS

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Background: Divergent associations between work environment factors and sick leave have been suggested to be due to different measures of sick leave. Sick leave patterns may be more comprehensive than total workdays absent. Aim: To analyse associations between sick leave spells and workplace factors. Material and methods: Employees from the municipal eldercare in Aarhus employed throughout 2005, who responded to the questionnaire "Working in the eldercare" containing work factor scales ranging from 0-100, were included. Workplace-derived sick leave records started and/or ended in 2005 were defined in different patterns (no sick leave at all, solely 1 to 11 short spells (less than 14 days), solely long spells (at least 15 days) and a mix of short and long spells). Linear regression models were used to find statistical associations, adjusted for age, occupation and seniority. Results (preliminary): Response rate 77% (2,584 employees), 96% being female. Median absence 5 (min-max: 0-581) calendar days. Median number of spells 2 (min-max: 0-13). Associations between number of spells and demands for hiding emotions (β=0.5; 95%CI: -0.2 - 1.3), influence (β=-0.8; 95%CI: -1.5 - -0.1) and quality of leadership (β=-0.9; 95%CI: -1.9 - 0.02). Type of spell acted as an effect modifier; employees with solely long spells reported more influence and better quality of leadership the more spells (the latter being significant). Discussion: Number and duration of spells seems to be important when associations with the working environment are appraised.

CH.32 Tue Fryland

A FUNCTIONAL CHARACTERIZATION OF BRD1 IN RELATION TO PSYCHIATRIC DISEASES.

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The bromodomain containing 1 (BRD1) gene has been implicated with brain development and susceptibility to schizophrenia and bipolar disorder. The BRD1 protein is essential to H3K14 acetylation and plays a keyrole in embryonic development and survival. To clarify the role of BRD1 in psychiatric diseases we

developed an approach to investigate the chromatin and protein interactions

of the BRD1-S and BRD1-Lisoforms. Co-IP mass spectrometry analysis confirmed the interactions with ING4, ING5, EAF6 and HBO1. Additionally, 9 new interactions with BRD1 were identified, including 2 unique interactions for BRD1-S and 3 unique interactions for BRD1-L. The strongest new interaction has recently been identified as genomewide significant in a schizophrenia and bipolar disorder meta-analysis. ChIP sequencing revealed that both BRD1 isoforms predominantly bind promoter regions and the transcription start site of a specific subset of genes. In total, 1967 target genes for BRD1-S and 1431 target genes for BRD1-L were discovered. Microarray expression analysis of these target genes suggests a function in activation and repression ofgenes. A bioinformatics approach based on simulations of the ChIP sequencing data identified BRD1 as a major regulator of genes associated with hematological disease, cardiovascular disease and psychological disease. The mRNA expression levels of BRD1 target genes associated with psychological diseases were measured in the brains of Brd1 knockout mice and wild type mice. Several genes had a significant increase in expression in Brd1 knockout mice. These results clearly suggests a key role of BRD1 in the pathophysiology of psychological illnesses.

CH.33 Stefan W. Harders

CT PERFUSION FOR SOLITARY PULMONARY NODULES. DISSENTING RESULTS.

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Purpose

CT Perfusion (CTP) is a CT technique which may in theory quantify the actual perfusion of tissues, including cancers. In this study CTP was used to examine patients with suspected lung cancer. Two different methods of drawing tissue regions of interest (ROIs) were applied, and it was examined if they could be used interchangeably. It was also examined whether the methods could be used to discriminate malignant from benign nodules.

Methods

Fifty-nine patients were included. Blinded CTP images were reviewed. Small ROIs (sROIs) and large ROIs (lROIs) were drawn and perfusion parameters were computed. Analyses were made on the log scale. Differences between the methods were presented as median ratios ($median_{sROI}/median_{lROI}$) with 95% limits of agreement, and supplemented by paired t-tests. The ability to discriminate malignant from benign nodules was assessed by unpaired t-tests. Histopathology was used as reference standard.

Results

The median ratio of perfusion was 2.8 (0.24 – 32); peak enhancement intensity was 2.1 (0.32 – 14); time to peak was 0.82 (0.13 – 5.2); blood volume was 2.5 (0.13 – 49); respectively. The differences were highly significant ($p < 0.001$). Neither sROIs ($0.084 < p < 0.73$) nor lROIs ($0.13 < p$

< 0.76) could be used to discriminate malignant from benign nodules.

Conclusion

Firstly, there were highly significant differences between sROIs and lROIs. Therefore the methods should not be used interchangeably. Second, neither sROIs nor lROIs could be used to discriminate malignant from benign lung nodules. Therefore focus should be changed toward staging and therapy monitoring.

CH.34 Peter Sandegaard Skyt

THREE DIMENSIONAL MEASUREMENTS OF THE EFFECT OF TUMOR TRACKING IN RADIOTHERAPY

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Purpose: Complex treatment methods such as rotational intensity modulated radiotherapy (rIMRT) offer highly conformal dose delivery but can be compromised due to target motion which has led to the development of tumor tracking. Due to the complex 3D patterns of tumour motion, tracking would benefit from a full 3D dosimetric verification. In this study we have therefore investigated the use of 3D dosimetry for measuring the effect of tracking on 3D dose distributions with the use of a clinically measured prostate motion.

Method and Materials: Two gel dosimeters were irradiated with the same prostate rIMRT treatment plan, delivered with and without tracking while moved with a prostate motion. A reference gel dosimeter was irradiated without motion or tracking. Tracking was performed using a transponder system (RayPilot, MicroPos AB, Sweden). After experiments the 3D dose distributions were read-out using an optical CT scanner.

Results: 3D 3%/3mm gamma analysis were performed between the motion and the reference dosimeters. The gamma fail-rate was found to improve from 23% to 8% by tracking compared to treatment without tracking. The failed points in the tracking treatment were located within a region of the dosimeter while the motion treatment without tracking revealed failed points at most dose gradients in the dosimeter.

Conclusion: Optical 3D dosimetry is a valuable tool to quantify the impact of motion and motion compensation on the delivered dose distribution to a moving target. Improved knowledge about the dose distribution is obtained due to (i) the three-dimensional nature of the measurements and (ii) the high resolution compared to competing techniques.

CH.35 Anette Luther Christensen

IS THE SEASONAL VARIATION IN HOSPITALISATION RATES OF ATRIAL FIBRILLATION RELATED STROKES IN DENMARK DYNAMIC?

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Atrial fibrillation (AF) is the most common cardiac arrythmia and hospitalisations with AF have increased during the last two decades. The frequency of AF increases with age and considering the population demographic it is expected that the number of people with AF will be increasing remarkably. AF is considered an independent risk factor for stroke. The consequences of stroke on patients are crucial and may be a considerable burden on society regarding rehabilitation. It has been reported that hospitalisations with stroke exhibit seasonal variation during the calendar year, however seasonality in AF related strokes has not been investigated.

Changes in seasonality of AF related stroke hospitalisations have not been investigated. Knowledge of seasonality of AF related stroke, and possible changes over time, may contribute to knowledge of the etiology of AF and may improve prophylaxis treatment and prognosis for AF patients.

Using a state space model to fit hospitalisation rates of AF related strokes, accounting for a secular trend and modelling the seasonality as a sum of four sinusoids, it is possible to investigate whether hospitalisations of AF related strokes exhibit seasonal variation. Furthermore, we may be able to investigate the dynamic nature of the seasonal variation over time. However, modelling hospitalisation rates of AF related strokes as being Poisson distributed using a state space model is not trivial in regards to estimation algorithms.

We identified 249,411 AF hospitalisations using the Danish National Patients Registry from 1977 to 2008. During follow-up 33,345 were hospitalised with stroke.

All analyses will be performed in R using the package sspir.

CH.36 Christian Alcaraz Frederiksen

POINT-OF-CARE ULTRASOUND REVEALS IMPORTANT HEART PATHOLOGY

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Introduction

A standard preoperative assessment is unlikely to identify impaired cardiac function or significant pathology. A full cardiological examination including echocardiography will provide the information needed for proper safety during surgery and anesthesia, but is often unrealistic due to limited resources. Similar issues in the emergency units and the critical care setting has given rise to different point-of-care ultrasound protocols like focus assessed transthoracic echocardiography (FATE). However, little is known about the diagnostic accuracy of FATE among inexperienced examiners.

Objective

The purpose of this study was to examine the diagnostic accuracy of FATE.

Method

25 patients with or without significant cardiac pathology were included. FATE was performed by an inexperienced examiner at the bedside and images were interpreted with dichotomous outcomes in regard to seven entities. Interpretations were compared with ultrasonic diagnosis made by a specialist in cardiology.

Results

175 assessments were made with a total of 5 discrepancies between the FATE examiner and the specialist; two with regard to right ventricular dilatation, two with regard to tumors and masses and one with regard to left ventricular hypertrophy. Overall sensitivity was 97.4% and specificity 97.1%. Positive predictive value was 90.5% and negative predictive value was 99.2%. Kappa statistics showed good agreement between observers (k=0.92).

Conclusions

These preliminary results show good diagnostic performance of bedside ultrasound performed by an inexperienced examiner and shows potential for screening in the perioperative period.

CH.37 Niels Ramsing Holm

FINAL KISSING BALLOON DILATATION IN SIMPLE STENTING OF CORONARY BIFURCATION LESIONS. POOLED ANALYSIS OF THE BBC ONE STUDY AND THE NORDIC BIFURCATION STUDIES

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Background

It is unknown whether to perform final kissing balloon dilatation (FKBD) after simple stenting of coronary bifurcation lesions.

Methods

We performed a patient level meta-analysis of 9 month clinical outcome of FKBD versus no-FKBD after stenting the main vessel in a pool of the British Bifurcation Coronary Old New and Evolving strategies study (BBC ONE) and The Nordic Bifurcation Studies.

Results

Nine month clinical follow-up were available for a total of 934 patients treated by the simple strategy. FKBD was performed in 343 of the patients. Mean age was 64±11 in the FKBD group and 63±10 yrs in no-FKBD group. 28% were females in both groups. In both groups, 60% of the lesions were "true" bifurcation lesions. Procedure time (67±76 vs. 56±65, p=0.01), fluoroscopy time (17±11 vs. 13±10, p<0.0001) and contrast volume (246±110 vs. 230±128, p=0.04) were all increased by FKBD. Major Adverse Cardiac Events (MACE) rate was 7.3% after FKBD vs. 5.1% (HR 1.54 [95% CI 0.9 to 2.6], p= 0.16) after no-FKBD. MACE was a composite endpoint of total death, non-procedural myocardial infarction and target vessel revascularization. In the true bifurcation lesion subgroup (n=555) MACE was 5.3% after FKBD vs. 5.8% for no-FKBD (HR 1.02 [95% CI 0.5 to 2.5], p= 0.94). In the non-true bifurcation subgroup (n=379), MACE rates were 10.3% after FKBD versus 4.1 % in the no-FKBD group (HR 2.53 [95% CI 1.1 to 5.8], p= 0.03).

Conclusion

Final kissing balloon dilatation after stenting the main vessel for treatment of coronary bifurcation lesions in BBC ONE and the Nordic Bifurcation studies did not improve 9 month clinical outcome in neither true nor non-true bifurcation lesions.

CH.38 Lars Jakobsen DIMENSIONS OF SOCIOECONOMIC STATUS AND CLINICAL OUTCOME AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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Background: The association between low socioeconomic status (SES) and high mortality from coronary heart disease (CHD) is well known. However, the mechanisms underlying the SES-related differences in outcome in patients with CHD remains poorly understood.

Design: Population-based follow-up.

Methods: We included 9070 patients treated with primary PCI (PPCI). They were divided into high- and low-SES groups according to income, education, and employment status. The primary outcome was major adverse cardiac events (MACE) (cardiac death, recurrent myocardial infarction, and target vessel revascularization) at 30 days, 1, and 2 years.

Results: Overall, low-SES patients were older and had a more adverse baseline risk-profile than high-SES patients. Compared to high-SES patients, low-SES patients had a higher cumulative risk of MACE when using income and employment status as the indicator of SES (2 years HR=1.65 (1.46-1.86) and HR=1.92 (1.71-2.17) respectively). After adjustment for patient characteristics, the differences were attenuated (2 years HR=1.18 (1.01-1.37) and HR=1.14 (0.96-1.35)). Further adjustment for admission findings, procedure-related data and medical treatment during follow-up

had no significant effect on the associations. With education as the indicator of SES, no differences were seen in the crude HRs of MACE between the 2 groups.

Conclusions: Even in a tax-financed health care system, low-SES patients treated with PPCI face a worse prognosis than high-SES patients. The poor outcome appears to be explained by differences in baseline patient characteristics. Poor clinical outcome was associated with employment status and income but not educational level.

CH.39 Stephen Austin

METACOGNITIVE BELIEFS AND COURSE OF ILLNESS WITHIN SCHIZOPHRENIA SPECTRUM DISORDERS - OPUS COHORT 10 YEAR FOLLOW-UP.

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The OPUS trial is the largest randomized clinical trial comparing intensive early intervention versus standard treatment in people with first episode schizophrenia spectrum disorder, which ran from 1998 to 2000 and recruited 547 newly diagnosed people with schizophrenia. One of the purposes of the 10 year follow up is to examine the relationship between metacognitive processes, psychopathology and course of illness. Metacognitive beliefs cover the awareness/knowledge of cognition and the strategies used to regulate cognition. Numerous studies have shown people with schizophrenia often experience elevated levels of metacognitive beliefs which may lie on a continuum ranging from “healthy” to “at risk” to “psychotic”. Maladaptive metacognitive beliefs may be implicated in the vulnerability, transition and maintenance of psychotic symptoms. All participants from the original OPUS trial were invited to participate in the 10 year follow-up. Diagnosis and psychopathology was measured using SCAN, SAPS/SANS, metacognitive beliefs with MCQ-30 and course of illness using the Lifechart Schedule. A total of over 70% of the original sample participated in the study and revealed significant correlations between levels of metacognitive beliefs and severity of delusions and hallucinations. The more elevated metacognitive beliefs were, the greater the severity of psychopathology. All categories of metacognitive beliefs contributed significantly in discriminating between continually psychotic and non-psychotic course of illness. The clinical implications of these results will be discussed.

CH.40 Kari Konstantin Nissen

EXPRESSION OF GAG AND POL FROM RECONSTRUCTED HERV-FC1, ASSOCIATED WITH MULTIPLE SCLEROSIS

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Background

Recently, our group found genetic evidence for association of multiple sclerosis with an endogenous retrovirus located on chromosome X, HERV-Fc1 [1]. The HERV-Fc1 sequence contains the general retrovirus structure of

LTRs and the genes gag, pol and env. The env gene has an open reading frame (ORF). The gag ORF is terminated by two stop codons (single stop in exogenous retroviruses). The pol frame is interrupted by a frameshift and a premature stop-codon. HERV-Fc1 is only sparsely characterized and we therefore aimed to investigate this provirus, especially in relation to potential involvement in autoimmunity.

Materials and methods

The HERV-Fc1 gag and gag-pol genes were cloned into expression vectors. For one vector, the pol ORF was restored by point mutations. All clones were fully sequenced to ensure correct sequence, before cellular expression. Protein expression was determined by WB and IHC.

Results and conclusion

The HERV-Fc1 gag gene has potential for immediate expression; this expression is dependent on the 5'UTR region of gag. Expression of Fc1 GagPol polyprotein could be achieved upon only three point mutations, with read-through of one stop-codon. Both high molecular weight (>140kDa) GagPol and lower (~40kDa) was found. Pelletable Fc1 Gag could be detected in the culturing media, suggesting particle formation and export.

These vector constructs can be used in future characterization of HERV-Fc1, e.g. tropism determined by host restriction factors, drug sensitivity etc.

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CH.41 Kathrine Just Andersen

ELECTROPHYSIOLOGICAL RECORDINGS IN THE BASAL GANGLIA IN AN ALPHA-SYNUCLEIN MODEL OF PARKINSON'S DISEASE

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Parkinson's disease (PD) is a progressive illness characterized by the neurodegeneration of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNc). The consequent loss of DA tone in the striatum results in an imbalance of the basal ganglia (BG), which play an essential role in movement coordination.

Interestingly, the presence of intracellular aggregated α-synuclein (α-syn) like the one found in Lewy Bodies in DA neurons in SNc of PD patients is believed to contribute to the initiation and progression of neurodegenerative mechanisms.

The aim of our studies is to investigate whether viral-mediated overexpression of α-syn in the SNc in rats induces changes in neuronal activity in BG nuclei, i.e. STN, SNc and SN pars reticulata (SNr).

Overexpression of α-syn in DA neurons of the SNc in rats was induced by unilateral viral vector injections, which resulted in progressive pathological

accumulation of α-syn resembling what is found in PD patients. Extracellular single unit recordings were conducted in anesthetized rats 5 and 12 w after viral injection for STN neurons, and 12 and 24 w post-injection for SN neurons.

α-syn overexpression was found to affect STN firing pattern 12 w post-virus injection, as indicated by an increase of neurons firing in bursts. In addition, preliminary results indicate a similar change in firing pattern in the SNc with increased burstiness in α-syn rats compared to GFP/naïve rats.

Furthermore, pilot studies revealed a trend for an increased firing rate of SNr neurons in α-syn rats. Interestingly, these changes within the BG, seems to precede any DA neuronal loss, indicating that α-syn overexpression may induce BG dysfunction.

CH.42 Karina Bendixen

EFFECT OF A SINGLE DOSE PROPRANOLOL ON HYPERTONIC SALINE-EVOKED MASSETER MUSCLE PAIN AND AUTONOMIC RESPONSE IN HEALTHY WOMEN

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Aims: There is a strong relationship between the autonomic nervous system and pain. This study tested the effect of propranolol (40 mg) on hypertonic saline (HS) evoked masseter muscle pain and autonomic measures in combination with modulation from a mental arithmetic task (Paced Auditory Serial Addition Task, (PASAT) in a randomized, double-blinded, placebo-controlled, and crossover study.

Methods: Sixteen healthy women participated in two sessions each in which propranolol or placebo was administered 1½ hours prior to two infusions (30 minutes apart) of 5% painful HS in the masseter muscle. The second HS-infusion was combined with PASAT. HS-induced pain was scored on a 0-10 numerical rating scale. Task Force® Monitor was used to obtain autonomic measures - electrocardiogram, blood pressure, impedance cardiography and respiration - to estimate autonomic nervous systems activity during rest and during mental stress.

Results: HS-pain was reduced by PASAT ($P < 0.05$), but with no differences between propranolol and placebo ($P > 0.05$). Propranolol induced significant autonomic changes with reduced heart rate and systolic blood pressure and increased baroreceptor sensitivity and heart rate variability (SD of all normal RR-intervals; root mean square successive differences; frequency power).

Conclusion: A stressful mental arithmetic task reduces HS-evoked muscle pain. The propranolol dose was effective with significant effects on the

autonomic nervous system causing a desirable autonomic profile but without any effect on HS-evoked pain levels. The lack of effect of propranolol on HS-pain in this group of women could be due to enzymatic activities of catechol-O-methyltransferase.

CH.43 Louise Buur Lund

SIGNALLING PATHWAYS INVOLVED IN α-SYNUCLEIN AGGREGATION DEPENDENT CELL DEATH

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Aggregation of α-synuclein is a pivotal point in a range of neurodegenerative diseases including multiple system atrophy (MSA), Parkinson's disease (PD), and dementia with lewy bodies (DLB). However, the cellular mechanism causing this phenomenon and consequently leading to cell death is still unclear.

Every function of the cell is mediated and regulated via signal transduction pathways and constitutes a highly complex system. We present a cellular model of α-synuclein aggregation dependent cell death. The brain specific protein p25/TPPP acts, by co-expression, as a potent inducer of α-synuclein aggregation leading to microtubule degradation, retraction of the cytoskeleton to the perinuclear region, and finally apoptosis. We have developed a high throughput image based algorithm by the use of the Cellomics Array Scanner, performed a screen of 160 small molecule kinase inhibitors, and we have identified pathways able to rescue affected cells by inhibiting the ongoing cell death.

By characterising the effect of such players it may be possible to elucidate what leads to the toxic formation of α-synuclein-species or the fatal consequences hereof and thereby open up for new cytoprotective strategies. Among other hits we demonstrate a positive effect of Casein kinase II inhibitors that suggests a toxic implication of Serine 129 phosphorylation in α-synuclein dependent toxicity. Furthermore we have observed effects of key kinases involved in stress responses to oxidative stress, ER-stress and translational initiation. Presently, the positive hits are being validated by si-RNA based technology and the pathways further investigated.

CH.44 Jan Danz

GINGIVAL RECESSIONS AND TOOTH MOVEMENT

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Expansive tooth movement is common in orthodontic treatments to align crowded teeth or to compensate dentoskelettal discrepancies. Negative side effects are the development of bone dehiscences and in some cases gingival recessions, if a tooth is moved beyond its alveolar bone housing. To investigate prameters of possible importance on the development of gingival recessions by expansive tooth movement, an animal model was established to move teeth buccaly with different distances of movement (to the alveolar border; beyond the alveolar border), with different force magnitudes (high vs. low) and with a retention period to allow tissue reorganization. The

distances of the movement and the location for histological cuts were measured on microCT scans. On these slices histomorphometry will be perfomed regarding gingival tissues (transversal cuts) and root resorption (horizontal cuts). Blood samples were taken during the initial phase of tooth movement to investigate systemic inflammatory reactions by expansive tooth movement.

CH.45 Marie Bagger Bohn

THREE-DIMENSIONAL KINETIC AND KINEMATIC ANALYSIS OF KNEE ROTATIONAL STABILITY IN ACL-DEFICIENT PATIENTS.

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Background:

During the last five years there has been a shift towards more anatomic ACL reconstruction, with the purpose of restoring natural knee biomechanics. There is a need to have precise methods for evaluation of knee kinematics and kinetics to evaluate the outcome of the new surgical methods. 3D-motion analysis is such a method.

Aim:

The aim of the study was to determine the functional knee rotation of ACL deficient knees (ACLD) and to compare results with healthy knees using 3D motion analysis.

Methods:

42 ACLD patients and 16 healthy subjects were included in the study. Motion data was captured using 8 cameras and QTM software. All data was analyzed by Visual-3D and Matlab. Reflective markers were attached to bony landmarks of the lower limb and clusters of markers placed on the shank and thigh. A pivoting task was conducted by descending a stairway and immediately pivot on the landing leg.

Results:

The average rotational stiffness (moment/angle rotation ((Nm/g)/deg) of the ACL-deficient and ACL-intact knee was 5.9 (95% CI: 3.8-7.9) and 6.7 (95% CI: 6.0-7.5), respectively ($p<0.001$). The average rotational stiffness of the healthy control group was 7.0 (95% CI: 5.9-8.0). No statistically significant difference, as found between the ACL-intact knee and the control group (both legs) ($p=0.702$).

Conclusion:

3D-motion analysis of the knee revealed a significant lower rotational stiffness of the ACL-deficient knee compared to the contra-lateral intact knee. No significant difference in rotational stiffness was seen between the ACL intact knee and the healthy control group. 3D-motion analysis is a valid method to measure rotational stability of the knee.

CH.46 Thomas Damgaard Sandahl

VALIDATION OF PROGNOSTIC SCORES FOR CLINICAL USE IN PATIENTS WITH ALCOHOLIC HEPATITIS

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Objective. In patients with alcoholic hepatitis, assessment of mortality risk is a key factor in clinical management. Within the last decade, several prognostic scores have emerged. We aimed to evaluate and compare the predictive performances of the Glasgow alcoholic hepatitis score (GAHS); the model of end-stage liver disease (MELD); the MELD-Na; the Lille model; and the age, bilirubin, international normalized ratio, and creatinine (ABIC) score in a population-based unselected cohort of patients with alcoholic hepatitis. Material and methods. We applied the scoring systems to all 274 patients hospitalized and diagnosed with alcoholic hepatitis (1999–2008) in a Danish region of 1.1 million inhabitants. The ability of each score to predict mortality was evaluated using receiver operating characteristics curves, and the area under the receiver operating characteristics curves (AUROCs) was used to compare the scores. Results. The 28-day mortality was 16%, 84-day 27%, and 180-day 40%. The models had similar predictive properties with AUROC = 0.74–0.78 for 28-day mortality, 0.69–0.77 for 84-day mortality, and 0.65–0.75 for 180-day mortality. There were no statistically significant differences in the models' performances ($p > 0.9$). Re-scoring on day seven improved the AUROCs of the models (AUROC for 28-day, 0.75–0.83; 84-day, 0.75–0.79; and 180-day, 0.72–0.74). Conclusions. The MELD, the MELD-Na, the GAHS, the Lille-model, and the ABIC scores each predicted the 28-, 84-, and 180-day mortality of our patients with alcoholic hepatitis and to the same degree, although not as well as in the original cohorts. Re-scoring on day seven improved the models' predictions.

CH.47 Asger Granfeldt

RESUSCITATION WITH ADENOCAINE AND MAGNESIUM REDUCES FLUID REQUIREMENT AND IMPROVES CARDIAC FUNCTION FOLLOWING 72% BLOOD LOSS IN THE PIG

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Fluid therapy following hemorrhage triggers ischemia-reperfusion (I/R) injury and organ dysfunction. The combination of adenosine and lidocaine (adenocaine) and Mg^{2+} (ALM) has been shown to stabilize cardiac function after hemorrhage in the rat. Hypothesis: ALM in hypertonic 7.5%NaCl at resuscitation: 1) reduces fluid requirements and 2) improves post-resuscitation cardiac function.

Pigs (38kg) were randomized to: Sham(n=5), Sham+ALM(n=5), hemorrhage(n=11), and hemorrhage+ALM(n=9). Animals were subjected to pressure controlled hemorrhage at a MAP of 35mmHg. After 90min Ringers acetate and 20ml 7.5% NaCl with or without ALM was infused to maintain a

target MAP of 50mmHg (permissive hypotension). After 30min 75% of the shed blood was re-infused with or without ALM and the pigs were observed for 6 hrs. Cardiac function was evaluated by pressure-volume(P-V) analysis.

In the ALM group 40% less fluid was required to maintain a MAP of 50mmHg for 30min (hemorrhage: 41.5ml/kg CI: 27.7-61.8 vs ALM: 24.7ml/kg CI:19.4-31.5*). During permissive hypotension 7.5%NaCl+ALM significantly increased cardiac contractility (dP/dt_{max}) (hemorrhage: 2622 mmHg/sec±331 vs ALM: 4301 mmHg/sec±262*). Treatment with ALM at blood infusion reduced whole body O2 consumption by 27% lasting 30 min into infusion*. In addition, systolic function after blood reinfusion, evaluated by P-V analysis was significantly improved in the ALM group. Furthermore, ALM enhanced relaxation (dP/dt_{min}) during reperfusion (hemorrhage: -1578mmHg/sec±103 vs ALM -2178mmHg/sec±189*). Conclusion: Treatment with 7.5% NaCl ALM reduced fluid requirements by 40% during permissive hypotension and improved cardiac function. (* $p<0.05$).

CH.48 Anne-Cathrine Bareid Østby

COMMUNITY RESPIRATORY VIRUSES IN INTENSIVE CARE PATIENTS WITH ACUTE RESPIRATORY DISEASE

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BACKGROUND: Respiratory viruses are a major cause of respiratory tract infections and associated with chronic obstructive pulmonary disease (COPD) and incompensated mb. cordis. Few have studied the presence of these viruses in intensive care units (ICU).

AIM: To study common respiratory viruses in ICU patients, admitted with respiratory symptoms, and to review the epidemiology and microbiological data.

METHODS: Throat swabs from 122 ICU patients with respiratory symptoms were analysed using a multiplex real time PCR assay, detecting 12 common respiratory viruses. Clinical information and micobiological data was recorded.

RESULTS: 19 (16%) of the patients had a viral respiratory infection (Group 1), of whom 10 had influenza and 3 respiratory syncytial virus. Coinfections with viruses and bacteriae or fungi, were found in 10 patients. Underlying COPD was found in 8 (42%), a heart condition in 6 (32%). In the 103 patients with no virus (Group 2), the proportions were 32 (31%) and 43 (42%). Median age was 69 in Group 1, and 69.5 in Group 2. Mors within 30 days from the viral sample was seen in 11 (58%) in Group 1 and 48 (47%) in Group 2. Sepsis was diagnosed in 7 (37%), and ARDS in 2 (11%) in Group 1, and in 52 (51%) and 8 (8 %) in Group 2. Median ICU stay was 5 days in Group 1, and 6 days in Group 2. Statistical analyses revealed no significant differences between the groups for these variables.

DISCUSSION: This study's strength lies in comparing the viral PCR analyses with the concurrent microbiological and clinical data. The non-significance could imply that respiratory viruses in ICU patients has a low impact on the clinical course, but more, larger studies are needed.

CH.49 Rikke Olesen

DYNAMICS OF HIV SHEDDING AND CD8+ T CELL INFLUX INTO THE CERVICOVAGINAL SECRETIONS DURING HIV INFECTION IN BLT HUMANIZED MICE

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Background: During acute HIV infection in women there are high levels of HIV in cervicovaginal secretions (CVS) and secondary HIV transmission is high. Hence, knowledge about the dynamics of HIV shedding and hematopoietic cell populations (HCPs) in the CVS is critical for understanding sexual HIV transmission. Our objectives were to describe the dynamics of HIV shedding and HCPs in the CVS during acute HIV infection in BLT humanized mice (BLT mice).

Methods: We obtained CVS samples from BLT mice and HCPs were phenotyped by flow cytometry. BLT mice were infected by mucosal exposure with HIV-1_{JR-CSF}. HIV-RNA/DNA was measured by PCR.

Results: The main HCP in the CVS from BLT mice are memory T-cells with high CCR5 expression. The CVS from infected BLT mice contained high HIV-RNA levels as well as HIV infected cells. Analyses of the HCPs during acute HIV infection demonstrated a rapid decrease in the percentage of $CD4^+$ T cells in the CVS not observed in the peripheral blood. Further analyses demonstrated a gradual influx of both $CD8^+$ and $CD4^+$ T-cells into the CVS. However, the magnitude of $CD8^+$ T cell influx was higher than the $CD4^+$ T cell influx responsible for the apparent decrease in the percentage of $CD4^+$ T cells.

Conclusion: The CVS of BLT mice contain memory T cells with high CCR5 expression and we could detect HIV and infected cells. These results demonstrate the potential of BLT mice as an in vivo model to study the dynamics of HCPs as well as HIV and infected cell shedding into the CVS during HIV infection. This model can serve to study the role of hormones and genital tract infections in HIV transmission and to evaluate early inhibitors of HIV transmisison

CH.50 Louise Hauge Matzen

THE INFLUENCE OF CONE BEAM CT-SCANNING ON TREATMENT PLANNING BEFORE REMOVAL OF MANDIBULAR THIRD MOLARS

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Aim: To evaluate the influence of cone beam computed tomography (CBCT) on treatment planning (TP) before surgical removal of mandibular third molars and to identify decision factors predisposing for exclusive removal of the crown (coronectomy) versus removal of the entire tooth (amotio).

Methods: A total of 187 mandibular third molars with an indication for surgical intervention underwent a radiographic examination with three methods: panoramic imaging, stereo-scanography and CBCT. The TP was established after the radiographic examination. The first TP (TP1) was established on the basis of the panoramic image and stereo-scanogram.

Afterwards, the CBCT was available and a second TP (TP2) was established. Logistic regression analyses were performed to test factors predisposing for a change in treatment plan from amotio in TP1 to coronectomy in TP2 and to test factors predisposing for the decision: coronectomy.

Results: Overall the TP changed for 23 teeth after TP2 of those TP for 15 teeth changed from amotio to coronectomy. The most important factor for this changewas a close relationship between the roots of the third molar and the mandibular canal in CBCT images (OR = 8.2, P = 0.007). Age, sex, root morphology and relation to the mandibular canal had a statistically significant impact on the treatment decision for coronectomy, both when the plan (TP1) was based on panoramic images and stereo-scanograms ($P \leq 0.036$), and when it (TP2) was based on CBCT ($P \leq 0.04$).

Conclusion: TP changed in 8% of the cases from amotio to coronectomy, when CBCT was available. Close contact to the mandibular canal in CBCT sections was the most important factor for deciding coronectomy.

CH.51 Christina Bisgaard

NOVEL HIPPOCAMPAL PROTEINS IMPLICATED IN ANTIDEPRESSANT DRUG RESPONDANCE AND RESILIENCE TO STRESS

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Background: Depression is today one of the leading causes of disability. Treatments available today include antidepressive medication, however 40-50% of depressive patients do not respond to the first line of treatment and treatment resistant depression has become a common clinical problem and a major health concern. In the present study we use the Chronic Mild Stress (CMS) model of depression to investigate what defines antidepressant respondance and what defines resilience to stress on a protein level.

Methods and Results: To find what proteins are regulated in both the granular cell layer and synapses from the ventral hippocampus during development of anhedonic behavior, antidepressant drug respondance and resilience to stress we use a quantitative proteomic strategy that combines Laser Capture Microdissection (LCM), 2D Differential Gel Electrophoresis (DIGE), Isobaric Tags for Relative and Absolut Quantitation (iTRAQ) and Tandem Mass Spectrometry (MS/MS) to isolate, separate and identify proteins of interest. This approach allows for the identification of novel proteins involved in different aspects of this multifaceted affective disorder. Several regulated proteins have been identified and validated using Selected Reaction Monitoring (SRM).

Conclusion: We have identified several interesting proteins implicated in antidepressant drug respondance and stress resilience. This discovery-based study provides a greater understanding of depression etiology and pathophysiology and ultimately helps identify new treatment targets and pathways able to increase the percentage of treatment responders, induce a

rapid onset of action and improve the side effect profile.

CH.52 Mai-britt Guldin

A POPULATION-BASED CASE-CONTROL STUDY OF HEALTHCARE UTILIZATION AMONG RELATIVES TO CANCER PATIENTS IN BEREAVEMENT.

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Background: For a group of bereaved spouses adjustment to the loss of a spouse to cancer is prolonged and problematic, called 'complicated grief'. Thus, there might be an increased need for healthcare services relating to a range of physical and mental impairments. However, we have no valid and complete knowledge about such needs. The objective of this study was to investigate the effect of spousal bereavement due to cancer on healthcare utilization.

Methods: A case-control study conducted in a population-based cohort extracted from Danish registries covering two years pre loss and two years post loss. Cases were matched with 10 controls on the basis of age and gender, only cases experienced spousal loss. Data consisted of use of general practice, psychologist, admissions to hospital and use of medication (anxiolytics and antidepressants).

Results: A cohort of 6559 married persons was identified through The Danish Death Registry and the Danish Cancer Registry to have died from cancer in Denmark in the year of 2005. Via the Central Person Registry their spouses were identified. Preliminary results on utilization of general practice, hospital admittance, medicine consumption and referrals to psychological or psychiatric treatment among the bereaved spouses show elevated levels among the bereaved compared to the controls with a specific pattern of utilization in relation to the time of their bereavement.

Conclusions: The study will present estimates of the need of health care among bereaved spouses. Thus, this study provides new knowledge on needs and how to organise healthcare for bereaved spouses.

CH.53 Jens Christian Jensen

DO WORK-RELATED FACTORS AFFECT PRIMARY MEDICAL CARE-SEEKING FOR BACK PAIN OR UPPER EXTREMITY PAIN?

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Musculoskeletal pain (MP) is one of the most important reasons for care-seeking in primary care. Pain intensity and disability are important predictors of care-seeking, but looking beyond pain, other factors such as work-related factors or individual factors may have an impact on care-seeking. The aim of this study is to elucidate the effects of physical and psychosocial workloads on primary care-seeking for back pain and upper extremity pain within an eighteen month follow up.

Methods: baseline questionnaire and ensuing registration of all contacts by participants to eight general practitioners with either upper extremity or back pain using ICPC. 4325 working men and women were eligible. 445 (10.3%) paid a first time visit with upper extremity pain, the number being 498 (11.5%) for back pain. Cox proportional hazard regression analysis of time to first visit was performed. Adjustment for potential confounders was done, and two different statistical models were made, one model including self-rated general and mental health as indicators of comorbidity. Results were stratified by gender.

Results: Heavy lifting at work predicted care-seeking for both back pain as well as upper extremity pain among men, but not among women. Repetitive work did not predict care-seeking for any of the two conditions. No psychosocial factors contributed in any significant way. There was no difference between the two statistical models.

Discussion: This work implies that work-related factors to some extent contribute to care-seeking for MP. A better understanding of contributing factors could be an important instrument for the general practitioner when advising patients on return to work.

CH.54 Anders Jensen THE MICROBIOME OF HUMAN TONSILS IN HEALTH AND DISEASE

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Tonsils and especially the lymphoid follicles lining the tonsilar crypts are mucosal antigen handling sites and play a significant role in inducing immune reactions. The tonsils are also entry site for infections. To understand the processes and the interactions between the host and the microorganisms, an extensive mapping of the microbial flora in the tonsil crypts is essential. The aim of the study is to examine the microbial diversity in the tonsilar crypts of 5 infected and 5 healthy small children and 5 healthy and 5 infected adults. 16S rRNA gene tags were sequenced with 454 pyrosequencing using titanium chemistry. In total 1610000 sequences tags were analysed with the Mothur software. At a 3% sequence distance 81 to 436 different bacterial species were found per sample. Significant differences in bacterial composition and community structure were found between children and adults. However, no such significant differences could be detected between healthy and infected tonsils, although a trend in different community structure were observed for both adults and children. This is the first exstensive study of the microbiome of the human tonsils and the results gives an insight into the bacterial diversity of the tonsils and the importance of the tonsillar microbiota for the predisposition for tonsillitis, and will provide a background for understanding the importance of commensal bacteria in the regulation and initiation of local and systemic immune reaction patterns.

CH.55 Søren Beck Jensen IFI16 IS A CYTOPLASMIC DNA RECEPTOR WHICH SIGNALS THROUGH STING AND TBK1 TO ELLICIT A TYPE I IFN RESPONSE FOLLOWING HERPES SIMPLEX VIRUS INFECTION

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The innate immune system relies on germline encoded pattern recognition receptors (PRR) to recognize pathogen associated molecular patterns (PAMP) and danger associated molecular patterns (DAMP) to initiate immune responses. Groups of PRRs have been described over the past decade with AIM2-like receptors (ALR) recently proposed as a new group of receptors important in innate responses. IFI16 (and its murine homolog IFI204) and AIM2 are the two identified members of the ALRs, which have been shown to be involved in activation of immune responses. AIM2 and IFI16 both recognize cytoplasmic DNA. AIM2 activates an ASC-dependent inflammasome activating caspase-1 to generate bioactive IL1beta, IL18 and IL33. Our lab and collaborators have shown that IFI16/IFI204 induce a type I IFN response mediated by STING-dependent TBK1 activation in response to transfected DNA and herpes simplex virus infection. However the role of IFI16/IFI204 in vivo has not been described because IFI204 deficient mice are unavailable. Therefore we attempt to generate a genetically modified mouse strain with conditional deficiency in IFI204 by implanting LoxP sites around exons 2-5 of IFI204. In brief, a targeting vector for conditional knock out of IFI204 was generated and electroporated into embryonic stem cells (ESC). ESC clones bearing the resistance marker from the vector were picked and screened for clones where the targeting vector was inserted into the chromosome by homologous recombination was preformed. ESC clones in which the targeting vector had replaced the wild type allele were hence identified and injected into mouse blastocyst embryos.

CH.56 Annett Andersen

OCCUPATION AND RISK OF SURGERY FOR NON-TRAUMATIC SHOULDER DISORDERS – A NATIONWIDE DANISH REGISTER STUDY

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Objective-s

Shoulder disorders have been found to occur more frequently in some occupational groups than in others. This may indicate that work related risk factors increase the risk of shoulder disorders. The aim of this study is to describe the incidence of shoulder surgery in relation to occupation in Denmark, 2003-2008, and to investigate the risk of shoulder surgery in relation to cumulative physical work load.

Methods

We conduct a register-based cohort study comprising all people born in Denmark from 1940 to 1977 with at least five years of accumulated work experience. In the follow up period, 2003-2008, people with first-time operations for non-traumatic shoulder disorders will be identified. In order to describe the incidence of shoulder surgery in relation to occupation the cohort will be divided according to main occupation in 2000 and age standardized incidence rates will be calculated. To investigate the risk of

shoulder surgery in relation to cumulative physical load individual information on job titles since 1993 will be combined with a job exposure matrix based on expert ratings. Multivariate Cox proportional hazards models will be used, stratified by gender, and with age, administrative region and socioeconomic status as covariates.

Results

The study comprises 3,411,351 people including 16,792 first-time shoulder-operated patients. Findings will be presented.

Conclusions

The study will generate an overview of the incidence of shoulder surgery in relation to occupation at a population level and provide new insight into the importance of cumulative physical work load.

CH.57 Dan Østergaard Pradsgaard

JOINT CARTILAGE THICKNESS MEASURED BY ULTRASOUND IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Joint cartilage degradation is resulted by ensuing chronic inflammation in juvenile idiopathic arthritis (JIA). Since the primary goals of treatment are to prevent joint destruction, sensitive methods are needed to evaluate cartilage thickness (CTh). Ultrasonography (US) is a reliable tool in the assessment of joint cartilage in rheumatic disease. The purpose of this study was to investigate whether US is a sensible method in the evaluation of joint cartilage.

Methods: In a cross-sectional setting we included 73 patients diagnosed JIA. Subsets were 13 systemic onsets, 35 oligoarticular JIA and 25 polyarticular JIA. Mean age (range) 10.2 yrs (5-15), boys/girls: 17/32. A group of 394 healthy children were used for comparison, age 10.9 (6-16), boys/girls: 217/177. All were examined with grey-scale US of distal femural cartilage.

Results: Demographic data were comparable between groups. CTh decreased with increasing age ($p<0.001$). When controlling for age we found significant difference between CTh for boys and girls 3.0 mm (±0.6) vs. 2.5 mm (±0.6), $p<0.0001$). Degradation of knee CTh was less in oligoarticular JIA (2.9 mm (±0.6)) than in polyarticular JIA (2.4 mm (±0.6), $p<0.001$) and systemic onset JIA (2.7 mm (±0.6), $p=0.02$) when controlling for age and gender.There was a significant difference between healthy (3.5 mm ±0.5) and all three JIA subgroups.

Conclusion: We found differences in knee cartilage thickness between 3 subtypes of JIA and also between healthy children and JIA children. Our results shows that US is able to assess even small differences in joint cartilage thickness, which makes it valuable in the evaluation of joint diseases in childhood.

CH.58 Jeppe Barckman

ANTIBIOTIC IMPREGNATION OF ALLOGRAFT BONE AND THE EFFECT ON IMPLANT FIXATION

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INTRODUCTION: Hip and knee arthroplasty present surgeons with difficult bone loss. In these cases the use of morselized allograft is a well-established way of optimizing early implant fixation. In revisions, the surgical field is potentially infected. The use of allograft bone creates a “dead space” in which the immune system has impaired access, and even a small amount of bacteria may therefore theoretically increase the risk of infection. We hypothesized that the allograft bone could be used as a local antibiotic delivery vehicle without impairing the implant fixation, tested by mechanical push-out and histomorphometry.

MATERIAL AND METHODS: Following approval of the Institutional Animal Care and Use Committee we implanted a cylindrical (10x6 mm) porous-coated Ti implant in each distal femur of 12 dogs observed for 4 weeks. The implants were surrounded by a circumferential gap of 2.5 mm impacted with a standardized volume of morselized allograft. In the two intervention groups, a 0.2ml tobramycin solution of high (800mg/ml) and low (200mg/ml) concentration was added to the allograft, respectively. In the control group, 0.2ml saline was added to the allograft. Data was evaluated with Wilcoxon signed-rank test. P-values < 0.05 were considered statistically significant.

RESULTS: There was no significant biomechanical or histological difference between the three groups.

CONCLUSION: We found no disadvantage in terms of implant fixation or new bone formation when adding tobramycin to the allograft bone. Tobramycin impregnation of the bone graft seems safe, and the results warrant further studies to elucidate its potential effect on infection prophylaxis.

CH.59 Kirstine Kjær Kirkegaard

NOVEL TOOLS FOR EMBRYO SELECTION IN ASSISTED REPRODUCTIVE TREATMENT

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Selection of the most competent embryo is a cornerstone in improvement of assisted reproductive treatment. Assessment of embryo morphology is currently the choice of method, but exposes embryos to harmful environmental changes during inspection. High-frequency recording (time-lapse) overcomes this limitation and may even provide new markers of embryo competence. Other studies indicate that embryo competence is reflected in both embryo metabolism and gene expression. Accordingly, the

aim of this study was to correlate embryo kinetics, metabolism and gene expression to pregnancy potential.

The safety of the incubator was tested in a randomised study comparing embryo development in a standard incubator to the time-lapse incubator, demonstrating no differences. Patients fulfilling the following criteria were eligible: i) age<38, ii)≥8 oocytes aspirated and ii) no endometriosis. Patients consented to time-lapse culturing with trophectoderm biopsy prior to transfer at the blastocyst stage, along with collection of spent culture media.

13 genes were selected based on the literature and tested on donated oocytes. Of these, 2 genes (Cdx2 and Hoxb7) were selected for real-time Q-PCR analysis in 14 trophectoderm biopsies of 2-10 cells from transferred blastocyst where 7 resulted in pregnancies and 7 in non-pregnancies. A time-lapse scoring scheme was developed and tested for inter- and intra- observer variability. The scoring scheme was used to evaluate the morpho-kinetics on all embryos from 70 patients (still recruiting), in order to identify markers of developmental competence and pregnancy potential.

Data from the gene expression and time-lapse analyses will be presented.

CH.60 Torsten Bloch Rasmussen

DESMOSOMAL PROTEIN EXPRESSION IN MYOCARDIAL AND EPIDERMAL TISSUE FROM CARDIOMYOPATHY PATIENTS WITH DESMOPLAKIN MUTATIONS

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Arrhythmogenic right ventricular cardiomyopathy (ARVC) and Carvajal syndrome (CS) are hereditary cardiac conditions, which may be caused by mutations in the gene for desmoplakin (DSP). The DSP protein is abundantly expressed in both myocardial and epidermal tissue. Since it is difficult to obtain myocardial tissue for extensive protein studies, we investigated the expression of DSP mutations in epidermal tissue of affected families. Initial genetic investigations of 70 ARVC patients identified 3 heterozygous DSP mutations in addition to a homozygous mutation in one CS patient. DSP gene and protein expression in myocardial and epidermal biopsies were investigated by immunohistochemistry, while keratinocyte cultures established from skin biopsies obtained from individuals carrying DSP mutations were investigated by reverse-transcriptase-PCR, western blotting, and mass spectrometry. The results showed that mutation carriers with abnormal DSP expression had the same changes in both myocardial and epidermal tissue. Furthermore, the investigations revealed different disease mechanisms, which correlated with specific types of mutations (missense, deletion, nonsense, frameshift) and were characterized by haploinsufficiency, dominant negative effects, or a combination of these. The results suggested that cultured keratinocytes obtained from patients with

desmosomal gene mutations is a valuable resource to elucidate the effects of disease-causing mutations in patients with desmosomal cardiomyopathies.

CH.61 Christel Krøigaard

IMPAIRED EDHF-TYPE RELAXATION IN RAT PULMONARY ARTERIES DESPITE UPREGULATION OF SK3 CHANNELS IN CHRONIC HYPOXIC RATS

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Ca^{2+}-activated K^+ channels of small (SK) and intermediate (IK) conductance are involved in endothelium-dependent relaxation of pulmonary arteries. We hypothesized that SK and IK function and expression were increased as a compensatory mechanism to counteract hypoxia-induced pulmonary hypertension in rats. Isolated pulmonary arteries from normoxic (nPAs) and hypoxic (hPAs) rats were mounted in microvascular myographs for isometric tension recordings. Acetylcholine (ACh) relaxations were similar in nPA and hPAs. ACh relaxation was abolished by the combined inhibition of nitric oxide synthase (L-nitro-arginine, L-NOARG), cyclooxygenase (indomethacin) and soluble guanylate cyclase (ODQ) in hPAs (-1±4 %, n=8), whereas 20±6 % relaxation persisted in nPAs. Inhibition of Na^+/K^+ ATPase with ouabain or blocking SK (apamin) and IK (charybdotoxin) channels reduced the persisting relaxation. A novel activator, NS4591 induced relaxations which were reduced by blocking SK or IK channels. In the presence of L-NOARG and indomethacin, NS4591 relaxation was markedly reduced in hPAs compared to nPAs. In endothelium-denuded nPAs and hPAs, extracellular K^+ (2-6 mM) induced relaxations. BKβ1, BKα and SK3 protein was upregulated in hPAs. Treatment with NS4591 did not prevent the development of pulmonary hypertension and right ventricular hypertrophy in chronic hypoxic rats. In conclusion, EDHF type relaxation occurs through IK and SK3 channel activation followed by Na^+/K^+ channel opening. Despite upregulation of SK3 and BK, the EDHF-type relaxation is impaired in hPAs, and modulation of SK3 and IK channels failed to prevent pulmonary hypertension in chronic hypoxic rats.

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