Welcome

It is our pleasure to welcome students, faculty and guests to the PhD Day 2011. We warmly thank all those who have taken the time to participate and help make this PhD Day a leading event for our graduate students.

Science is deeply depending on financial resources and the competition for national as well as international economical support is increasing. It is also a political question how to distribute the available financial resources. Aarhus Graduate School of Health Sciences regards this aspect as a critical and very important matter for PhD students to consider in their future professional life as scientists. Therefore, the theme of the PhD day 2011 is: Financing Research. We have invited Anne Marie Engel, Lundbeckfonden, and Birgitte Nauntofte, Novo Nordisk Fonden, as representatives from private foundations, and Alain Peyraube, The European Research Council, as representative for an international foundation, to explain their view on how to finance research. As moderator of the discussion we have invited John Westensee from Aarhus University Research Support Office.

As is evident from the abstracts presented in this programme book the Aarhus Graduate School of Health Sciences provides a vibrant scientific environment ready to meet new challenges and offering many opportunities. The PhD students are central to research and the research environment and the Organizing Committee hereby acknowledge the contribution of the PhD students to the high quality research done at our Faculty.

The Organizing Committee and the faculty of Health Sciences are confident that the PhD day 2011 will be a success and we cordially welcome all participants.

Kimmo Jensen
Chairman, Organizing Committee

Lise Wogensen Bach
Vice-head, Aarhus Graduate School of Health Sciences

Allan Flyvbjerg
Dean, Faculty of Health Sciences, Aarhus University

Contents

- Information

Practical information:

- Lunch will be held in the Lake Auditorium Building.
- Posters will be shown in the Lake Auditorium Building; the Bartholin Building teaching wing room and auditoria 1 - 4; and the Victor Albeck Building.
- Posters should be hung between 4pm and 5pm on January 13th or between 7.15am and 8am on January 14th. All posters must be taken down immediately after the closing of the conference.
- Oral presenters for sessions O1-O4 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 H. Gravholt, Department of Endocrinology and Internal Medicine, and Department of Molecular Medicine, Aarhus University Hospital
- Grethe Elholm, PhD student, Department of Environmental and Occupational Medicine, School of Public Health, Aarhus University
- Maj Høygaard Nicolaisen, PhD student, Department of Prosthetics, School of Dentistry, Aarhus University
- Martin Skøtt, PhD student, Department of Anatomy, Aarhus University
- Mie Hessellund Samson, PhD student, Department of Clinical Biochemistry, Institute of Clinical Medicine, Aarhus University
- Iben Møller Jønsson, PhD student, Department of Paediatrics, Institute of Clinical Medicine, Aarhus University
- Kimmo Jensen, Department of Physiology and Biophysics, Aarhus University
- Lise Wogensen Bach, Research Laboratory for Biochemical Pathology, Institute of Clinical Medicine, Aarhus University
- Thomas Vorup-Jensen, Department of Medical Microbiology and Immunology, Aarhus University
- Vivi Schlünssen, Department of Environmental and Occupational Medicine, School of Public Health, Aarhus University
- Lene Birkegaard Pedersen, PhD Administration, Aarhus University
- Tanja Hansen, PhD Administration, Aarhus University

Secretariat:

Lene Birkegaard Pedersen (LBP@sun.au.dk) and Tanja Hansen (th@sun.au.dk) , Forskeruddannelsen, The Faculty of Health Scicences, Vennelyst Boulevard 9, 8000 Aarhus C

Graduate School of Health Sciences, Aarhus University

PHD DAY 14 JANUARY 2011

Sessions held in Auditorium 1 in the Lake Auditorium unless otherwise indicated

Financing Research

8.15 Welcome by Allan Flyvbjerg, Dean of Faculty

8.20 Welcome by Anna Sellmer Sørensen, Chairman of the PhD Association

8.25 Kimmo Jensen, Chairman of the Organizing Committee on today's programme

8.30 Invited speakers on '**Financing Research**'

Moderated by John Westensee from Aarhus University Research Support Office

- Anne Marie Engel, Lundbeckfonden

- Birgitte Nauntofte, Novo Nordisk Fonden

- Alain Peyraube, European Research Council

9.45 Poster sessions part 1 (odd numbers) and coffee
Lake Auditorium (P01-P13), Bartholin Building (P15-P25), and Victor Albeck Building(P27-P29)

11.15 Oral presentations (parallel sessions O1-O4)

Session O1	Chairmen: Peter Vedsted and Ulla Christina Møller	Auditorium 1
Session O2	Chairmen: Bent Deleuran and Jenny Blechingberg	Auditorium 2
Session O3	Chairmen: Ebba Nexø and Michael Wintherdahl	Auditorium 3
Session O4	Chairmen: Jens Leipziger and Ruta Tuckuviene	Auditorium 4

12.45 Lunch

13.15 Poster sessions part 2 (even numbers) and coffee
Lake Auditorium (P02-P12), Bartholin Building (P14-P26), and Victor Albeck Building (P28-P30)

14.45 Skou Lecture by Nobel Laureate **John Walker**

Chaired by Allan Flyvbjerg, Dean of Faculty

15.45 Fogh Nielsen Prize Competition

Chaired by Søren Moestrup, Chairman of the Fogh Nielsen board, and Anna Sellmer Sørensen, Chair-man of the PhD Association

- Marianne Skals

- Mads Fuglsang Kjølby

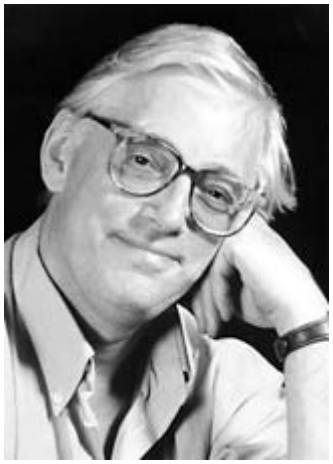
- Mette K. Hagensen

16.30 Closing remarks by Lise Wogensen Bach, Vice-Head of Graduate School

18.00 Dinner and presentation of prizes in 'Stakladen'. Festive speech by Professor Bent Deleuran.

22.00 Band and dance

The Keynote lecture



Professor Sir John Ernest Walker won the Nobel Prize in Chemistry in 1997. The prize was shared with Paul Boyer for their explanation of the enzymatic process that creates adenosine triphosphate (ATP). Another 1997 Nobel Prize winner was Jens Christian Skou – after whom the Skou Lecture is named – for the first discovery of an ion-transporting enzyme, Na+, K+-ATPase.

Walker received his BA in Chemistry in 1964 and in 1969 gained a DPhil from the Sir William Dunn School of Pathology, Oxford. In 1974, he attended a research workshop in Cambridge on the Sequence Analysis of Proteins, where he met Fred Sanger (chemistry laureate, 1958) who invited him to join the Protein and Nucleic Acid Chemistry Division at the Medical Research Council's Laboratory of Molecular Biology (MRC LMB) in Cambridge, UK.

It was here that Walker carried out his award-winning work. In 1978, he began to apply protein chemical methods to membrane proteins. The enzymes from the inner membranes of mitochondria had hardly been studied from a structural point of view. Therefore, Walker began a structural study of ATP synthase from bovine heart mitochondria and eubacteria. These studies resulted in a complete sequence analysis, and in the atomic structure of the enzyme, giving new insights into how ATP is made in the biological world.

John Walker is currently a director of the Medical Research Council Mitochondrial Biology Unit in Cambridge. Walker has received several international awards, and in 1995, was elected a Fellow of the Royal Society. In 1999 he was knighted for his services to molecular biology.

John Walker was born in Halifax, Yorkshire on January 7, 1941. He married Christina Westcott in 1963, and they have two daughters.

Text and picture from "Le Prix Nobel 1997" (1998) and "NOBELS Nobel Laureates photographed by Peter Badger" (2008)

Aarhus Graduate School of Health Sciences

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. Currently almost 600 PhD students are enrolled, with about 180 enrolled in 2010. The Graduate School is part of the Faculty of Health Sciences, which has four broad divisions: biomedical sciences, clinical sciences, public health and odontology. The Faculty has a total of about 400 professors and associate professors, with the clinical faculty members having joint appointments in the Aarhus University Hospital. The Graduate School has established twelve graduate programmes (GP) of high scientific quality which cover the whole range of the Graduate School's activities.

The Aarhus Graduate School of Health Sciences provides PhD training in all aspects of health sciences from basic research to the clinic. The integrated approach ensures that the overall aim of improving patient health care is obtained in a multidisciplinary manner without fragmentation of the research training process. Furthermore, this approach ensures a uniform quality of the PhD training program.

The Graduate School is led by a Head and vice-Head who are advised by the elected PhD Committee. The Heads of the Graduate School are assisted by the PhD administrator and the PhD office staff. The Graduate School holds about 100 courses each year, of which some are core courses taken by all PhD students, some are courses organized by the graduate programmes, and others are more general courses, including courses in transferable skills. In all cases the course programme is tailored according to the needs of the particular PhD student. The Heads of the Graduate School are responsible for monitoring the quality of the courses and initiating new courses as required in collaboration with the graduate programmes.

It is the aim of the Graduate School that the individual PhD student completes a project at the highest international level, and that the work can be seen as a part of health science in its broadest terms. This focus builds on the Faculty's international expertise which stretches from basic biomedicine and molecular biological research to patient-oriented clinical investigations into molecular understanding of pathogenesis, diagnosis and treatment. New discoveries in these areas will therefore have an advantage for society, but also an important commercial perspective directed towards the Danish pharmaceutical and biotechnological industry. It is within this large and exciting environment that the Graduate School is able to offer a wide range of challenging PhD programmes.

International networking is pivotal for progression in science – also among PhD students. With the aim to promote networking we have invited the following PhD students from abroad: Evelyne Furger (Paul Scherrer Institut, Zürich, Schwitzerland) (GP Laboratory Medicine), Andrew Siefert (Georgia Tech, Emory, USA) (GP Cardiovascular), Aishling Ahlstrøm (Sahlgrenska Akademin, Sweden) (GP Translational Molecular Medicine), Lin Yang (MRC Cambridge, UK) (GP Public Health), Anne Panhelainen (University of Helsinki, Finland) (GP Neuroscience), Matthew Gillum (Yale, New Haven, USA) (GP Endocrinology), Lily Jeng, Harvard Medical School, Boston, USA) (GP Laboratory Medicine), Rebecca Birch (The Royal Veterinary College, London, UK) (GP Membrane Transporters and Receptors) We all welcome our guests and wish them a pleasant stay.

Michael J. Mulvany, Head of Graduate School
Lise Wogensen Bach, vice-Head of Graduate School

International office

Aarhus University has an international focus and makes targeted efforts to attract researchers and students from abroad. The University wants to recruit PhD students from among the best students in the world. The University also wants Danish PhD students to go abroad.

This international focus and the wish for increased international mobility among PhD students are also encouraged by the Graduate School of Health Sciences.

The University has an International Centre (IC) which provides services to international PhD students. The International Centre provides practical and administrative assistance with solving problems arising in connection with the studies and work at Aarhus University, and residence in Denmark.

Furthermore, one can also obtain advice with regards to childcare and job-opportunities for spouses. The office provides a general service to all nine main academic areas, and refers questions to experts within or outside the University for more specific information.

One of these experts is the international officer at the Graduate School of Health Sciences. The international officer is a key person in the communication between the International Centre and the many institutes at the Faculty of Health Sciences, and can assist with more specific questions. Most importantly the officer will communicate with the international PhD student before arrival in Aarhus, giving information about legalisation, forwarding our welcome package. The PhD student will also be offered a free Danish course as soon as possible after arrival.

Since we are also encouraging Danish PhD students to work for shorter or longer periods of time in a laboratory abroad, we are planning to develop 'what shall I do' or 'how to go abroad' packages, which, hopefully, will avoid some of the problems the PhD students come across when planning their stay abroad. From 1 October 2009 it has been possible to earn ECTS points from your stay abroad if you hand in a report (1-3 months, 2 ECTS, 4-6 months, 4 ECTS).

For more information please look at our homepage: http://phd-health.au.dk/en/

The international officer can be contacted at: lbp@sun.au.dk

Lene Birkegaard Pedersen

Phdassociation.dk

All PhD students at SUN, AU are members

Including You!

We work on issues concerning Your PhD:

Overall, the Phd association works on improving the PhD study at SUN, AU.

We lobby for issues like PhD courses, teaching load, studying abroad etc.

Main activities include:

- Collaboration with the Graduate School of Health
- Science Organizer of ”After Work Meetings”
- Co-organizer of the annual PhD day

If you are interested in joining our work and getting involved,

please contact us by mail: kontakt@phdforeningen.dk

Phdforeningen.dk

Studenterforskning.dk

Selskab for Medicinsk Studenterforskning

Selskab for Medicinsk Studenterforskning

Selskab for Medicinsk Studenterforskning (SMS, *Society of Pregaduate Medical Research*) is an independent organisation 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 will March 2010 host the second national Danish conference for pregraduate medical research, where pregraduate researchers nationwide are invited to present their research and network with other students. Find more information on www.kms2010.dk

At the annual general assembly, medical students and doctors who have carried out a pregraduate Research Year are elected to the board of the *Society of Pregaduate Medical Research.*

The society manages a web-site that coordinates research year projects and distributes contact between supervisors and potential prospective research year students.

www.studenterforskning.dk

Studenterforskning.dk

Selskab for Medicinsk Studenterforskning

Student counsellor for PhD students

Personal contact: Sanne Angel

phdstudievejleder@sun.au.dk

Phone: 8942 4452

Surviving you dissertation

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

In the knowledge that a PhD-study can be an overwhelming challenge, the Faculty of Health Science has established a student counsellor for Ph.D 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 or for 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 in making competent decisions on deliberate basis.

You are always welcome to contact the PhD student counsellor!

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

Det Sundhedsvidenskabelige Bibliotek – Library of Health Sciences

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Session Chairmen

Fogh Nielsen session	Søren Moestrup & Anna Sellmer Sørensen
O1	Peter Vedsted & Ulla Christina Møller
O2	Bent Deleuran & Jenny Blechingberg
O3	Ebba Nexø & Michael Wintherdahl
O4	Jens Leipziger & Ruta Tuckuviene
P1	Albert Gjedde, Stine Chistiensen & Vivien Schack
P2	Kristian Stengaard-Pedersen, Iva S. V. S. Thomsen & Lene Sundahl Mortensen
P3	Toke Bek, Lotte Ørneborg Rodkjær & Pia Kirkegaard
P4	Jan Alsner, Magdalena Julia Dabowska & Jeppe Grøndahl Rasmussen
P5	Rikke Katrine Jentoft Olsen, Asgar Granfelt & Sine Nygaard Langerhuus
P6	Bente Jespersen, Rikke Vestergaard & Marta Bauerek
P7	Karin Lykke-Hartmann, Casper Nielsen & Anders Knudsen
P8	Anders D. Børglum, Nis Borbye Pedersen & Rune Thomsen
P9	Karen Dybkær, Claus Tvedesøe & Fillippo Peder D.Andrea
P10	Jens Otto Lunde Jørgensen, Gitte Dam & Nicklas Heine Staunstrup
P11	Karin Birkenkamp-Damtroder, Michael Kjeldager Tjørnild & Thomas Maribo
P12	Tine Brink Henriksen, Pernille Kure Vandborg & Marie Bagger Bohn
P13	Henrik Kolstad, Morsi Abdallah
P14	Mette Nyegaard, Tanja Tvistholm Sikjær & Anna Pietraszek
P15	Henrik Støvring, Dorte Rytter & Michael Smærup Brandt
P16	Flemming W. Bach, Eduardo Adrian Garza Villarreal & Ivana Konvalinka
P17	Robert A. Fenton, Simon Rasmussen & Emil Kofod-Olsen
P18	Birgitte Mønster Christensen, Martin Majlund Mikkelsen & Thais A. Pedersen
P19	Lise Lotte Hansen, Tina Storm, Kasper Toustrup
P20	Mette Madsen, Jasna Furtula & Jeppe Grøndahl Rasmussen
P21	Lone Sunde, Camilla Molich Hoff & Stefan W. Harders
P22	Marianne Hokland, Lisbeth Venø Kruse & Iben Blaabjerg Sundtoft
P23	Natalya Fedosova, Anne-Cathrine Bareid Østby & Maria Louise Salskov-Ivarsen
P24	Jens Cosedis Nielsen, Chumsen Wu & Vibeke Bregnballe
P25	Povl Munk-Jørgensen, Lene Bastrup Jørgensen & Flemming Bandholm Jakobsen
P26	Helle Prætorius, Birgitte S. Kousholt & Kristian Havmand Mortensen
P27	Lene Braad Hansen, Kathrine Kleis Tilma, Hans Henrik Møller Nielsen
P28	Michael John Hasenkam, Krista Dybtved Kjærgaard & Jesper Brink Askov
P29	Kirsten Lomborg, Anders Jensen, Thomas Greve

Session overview

Fogh Nielsen session. Chairmen: Søren Moestrup & Anna Sellmer Sørensen (Chairman of the PhD association)

FN	Marianne Skals. ALPHA-HAEMOLYSIN FROM ESCHERICHIA COLI INDUCES ATP RELEASE PRIOR TO CELL LYSIS
FN	Mads Fuglsang Kjølby. A NOVEL DRUG TARGET FOR THE TREATMENT OF HYPERCHOLESTEROLEMIA?
FN	Mette K. Hagensen. ENDOTHELIAL AND SMOOTH MUSCLE CELLS IN ALLOGRAFT VASCULOPATHY DO NOT DERIVE FROM CIRCULATING PROGENITOR CELLS BUT MIGRATE INTO THE GRAFT FROM THE RECIPIENT VASCULATURE

Oral session 01. Chairmen: Peter Vedsted & Ulla Christina Møller (PhD student)

O01.01	Britt Christensen. ERYTHROPOIETIN ADMINISTRATION ACUTELY STIMULATES RESTING ENERGY EXPENDITURE IN HEALTHY YOUNG MEN
O01.02	Jens Ølholm. SIRT1 DEPENDENT ANTI-INFLAMMATORY EFFECT OF RESVERATROL ON MCP-1 EXPRESSION AND SECRETION IN HUMAN ADIPOSE TISSUE
O01.03	Jens Holmer- Jensen. ACUTE DIFFERENTIAL EFFECTS OF DIETARY PROTEIN QUALITY ON POSTPRANDIAL LIPAEMIA IN OBESE NON-DIABETIC SUBJECTS
O01.04	Marie Louise Tørring. TIME TO DIAGNOSIS AND MORTALITY IN COLORECTAL CANCER: A COHORT STUDY IN PRIMARY CARE
O01.05	Ane Bærent Fisker. ADVERSE EVENTS AFTER ADMINISTRATION OF VITAMIN A WITH EPI VACCINES AFTER 6 MONTHS OF AGE IN GUINEA-BISSAU
O01.06	
O01.07	Bodil Bjørnshave. CAN COMPLETING REHABILITATION AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) BE PREDICTED, - AN EXPLORATIVE STUDY OF A COPD POPULATION TREATED AT HORSENS REGIONAL HOSPITAL
O01.08	Christian Fynbo Christiansen. TYPE 2 DIABETES, ANTIDIABETICS AND MORTALITY AMONG INTENSIVE CARE PATIENTS: A DANISH COHORT STUDY

Oral session 02. Chairmen: Bent Deleuran & Jenny Blechingberg (PhD student)

O02.03	Ole Schmeltz Søgaard. IMPROVING THE IMMUNOGENICITY OF PNEUMOCOCCAL CONJUGATE VACCINE IN HIV-INFECTED ADULTS WITH A TOLL-LIKE RECEPTOR 9 AGONIST ADJUVANT: A RANDOMIZED, CONTROLLED TRIAL
O02.04	Rasmus Boye Kjellerup. THE EXPRESSION OF DUAL SPECIFICITY PHOSPHATASE 1 IS DYSREGULATED IN PSORIASIS VULGARIS
O02.05	Ulla Schierup. HEPATITIS A AMONG DANISH TRAVELLERS 1980-2007
O02.06	Mette Handrup Møller. BIOFILM FORMATION IN CENTRAL VENOUS CATHETERS IN CHILDREN WITH CANCER: A RANDOMIZED CONTROLLED TRIAL OF TAUROLIDINE VERSUS HEPARIN
O02.07	Lise Saksø Mortensen. UTILIZING THE EPPENDORF OXYGEN ELECTRODE AND FAZA PET IMAGING TO PREDICT RADIATION RESPONSE IN EXPERIMENTAL TUMORS
O02.08	Ulrik Elstrøm. CONE-BEAM CT BASED TREATMENT PLANNING IN ADAPTIVE RADIOTHERAPY OF HEAD AND NECK CANCER

Oral session 03. Chairmen: Ebba Nexø & Michael Wintherdahl (PhD student)

O03.01	Aygen Øzbay. CALCINEURIN INHIBITORS ACUTELY IMPROVE INSULIN SENSITIVITY WITHOUT AFFECTING INSULIN SECRETION
O03.02	
O03.03	Anja Høegh Brugmann. HER4 IS DOWNREGULATED IN LYMPH NODE METASTASES COMPARED TO THE PAIRED PRIMARY BREAST CARCINOMA
O03.04	Samir Munir. HYPOXIC CHONDROGENIC DIFFERENTIATION OF HUMAN CORD BLOOD STEM CELLS IN STRUCTURALLY-GRADED POLYCAPROLACTONE SCAFFOLDS
O03.05	Tine Quistgaard. MESOANGIOBLASTS AS THERAPEUTIC STEM CELLS

O03.06 Dang Quang Svend Lee. EX VIVO BIOREACTOR-BASED PLATELET PRODUCTION
O03.07 Mette Juul Koefoed. GENE TRANSFER FOR BONE HEALING USING IMMOBILIZED FREEZE DRIED ADENO-ASSOCIATED VIRAL VECTORS
O03.08 Nina Dyrberg Lorenzen. EVALUATION OF BLOOD FLOW AND METABOLISM IN THE FEMORAL HEAD. A RANDOMISED COMPARISON OF SURGICAL APPROACHES IN RESURFACING HIP ARTHROPLASTY

Oral session 04. Chairmen: Jens Leipziger & Ruta Tuckuviene (PhD student)

O04.01 Thaneas Prabakaran. RECEPTOR-MEDIATED UPTAKE OF ALPHA-GALACTOSIDASE A IN HUMAN PODOCYTES IN FABRY DISEASE
O04.02 Anders Etzerodt. IMPROVED DRUG DELIVERY TO DISEASE-ASSOCIATED MACROPHAGES USING CD163 TARGETED LIPOSOMES.
O04.03 Christian Møller Pedersen. REMOTE ISCHEMIC PRECONDITIONING IS NOT MEDIATED BY ENDOGENOUS BRADYKININ IN HUMANS
O04.04 Mads Kronborg. HIS AND PARA-HIS PACING IN AV-BLOCK: FEASIBILITY AND ELECTROCARDIOGRAPHIC FINDINGS
O04.05 Thomas Wittenborn. IMAGING ANGIOGENESIS IN NOVEL MOUSE MODEL
O04.06 Christina Bisgaard. COMPARATIVE PROTEOMICS IN THE CHRONIC MILD STRESS MODEL OF DEPRESSION - A SEARCH FOR BIOMARKERS OF DEPRESSION IN HIPPOCAMPAL SUBREGIONS
O04.07 Trine Veje Axelsen. TRIGGERING ANTIBODY RESPONSE AGAINST A&BETA;42 BY LOW DOSE IMMUNIZATIONS OF A&BETA;1-42/PMP8-A&BETA;1-30 IN DOUBLE TRANSGENIC AD MICE
O04.08 Louise Munk Rydtoft. NEURITE DENSITY IN AN ALZHEIMER'S DISEASE MOUSE MODEL FROM DIFFUSION WEIGHTED MAGNETIC RESONANCE (MR)

Poster session 01. Chairmen: Albert Gjedde, Stine Chistiensen, Vivien Schack

P01.01 Pernille Munk Frandsen. ACTIVATION AND RECEPTOR STUDIES OF HUMAN MAST CELLS IN HEALTHY INDIVIDUALS AND PATIENTS WITH ASTHMA AND ALLERGY
P01.02 Sabina Jelen. AQUAPORIN-9 EXPRESSION IN MALIGNANT GLIOMA
P01.03 Rita Marques. ATP INHIBITS NACL ABSORPTION VIA BASOLATERAL P2X RECEPTORS IN MOUSE MEDULLARY THICK ASCENDING LIMB (MTAL)
P01.04 Randi Groslier Bjælde. CHARACTERISING THE PATHWAY FOR NUCLEOTIDE-RELEASE IN RENAL EPITHELIA
P01.05 Louise Lund Andersen. DOES CUBILIN PLAY A ROLE IN DEVELOPMENT OF MAMMACANCER?
P01.06 Lena Lindtoft Rosenbæk. REGULATION OF THE RENAL ION TRANSPORTER NCC BY PHOSPHORYLATION
P01.07 Muhammad Umar Cheema. STOICHIOMETRY ANALYSIS OF MULTIMERIC PROTEIN COMPLEXES USING BIOLUMINESCENCE RESONANCE ENERGY TRANSFER (BRET)
P01.08 Mette Laursen. STRUCTURAL INSIGHT INTO THE HIGH AFFINITY BINDING OF CARDIOTONIC STEROIDS TO THE NA+,K+-ATPASE
P01.09 Niklas Telinius, THE ROLE OF THREE VASOACTIVE SUBTABCES AND ENDOTHELIUM ON HUMAN THORACIC DUCT CONTRACTILITY IN VITRO
P01.10 Thala Marie Ørtoft Snerum, IRREGULAR MENSTRUAL CYCLE, OBESITY AND PRETERM BIRTH

Poster session 02. Chairmen: Kristian Stengaard-Pedersen, Iva Susanna Vio Streym Thomsen, Lene Sundahl Mortensen

P02.01 Louise Wamberg. 1,25-OH-VITAMIN D HAS ANTI-INFLAMMATORY EFFECTS IN HUMAN ADIPOSE TISSUE IN VITRO
P02.02 Zhulin Ma. A COMPARISON OF PHARMACODYNAMICS AND PHARMCOKINETICS OF INSULIN ASPART, BIPHASIC INSULIN 70 AND 50, AND FAST-ACTING HUMAN INSULIN IN PATIENTS WITH TYPE 1 DIABETES, A RANDOMISED, QUADRUPLE CROSS-OVER TRIAL
P02.03 Esben Laugesen. ARTERIAL STIFFNESS AND ISCHEMIC CEREBRAL DISEASE IN PATIENTS WITH TYPE 2 DIABETES

P02.04 Thomas Svava Nielsen. DIFFERENTIAL REGULATION OF ADIPOSE TISSUE LIPOLYSIS IN HUMANS DURING FASTING AND EXERCISE - A POSSIBLE LINK TO INSULIN RESISTANCE
P02.05 Michael Gejl Jensen. DIFFERENCES AMONG LONG-ACTING INSULINS FOR THE TREATMENT OF TYPE 2 DIABETES (T2D)?
P02.06 Xiaoping Chen. DOES ISOSTEVIOL (ISO) HAVE A BENEFICIAL EFFECT ON GLUCAGON SECRETION AND TREATMENT OF TYPE 2 DIABETES (T2D)?
P02.07 .
P02.08
P02.09
P02.10 Mikkel Vendelbo. INSULIN RESISTANCE DURING PROLONGED FASTING IS ASSOCIATED WITH IMPAIRED AS160 PHOSPHORYLATION AND GLYCOGEN ACCUMULATION IN HUMAN SKELETAL MUSCLE

Poster session 03. Chairmen: Toke Bek, Lotte Ørneborg Rodkjær, Pia Kirkegaard

P03.01 Anne Sophie Ågård. AFTER INTENSIVE CARE &NDASH; THEN WHAT? PATIENT AND PARTNER PERSPECTIVES
P03.02 Morten Søndergaard Jensen. AGE AT CRYPTORCHIDISM DIAGNOSIS AND ORCHIOPEXY IN DENMARK: A POPULATION-BASED STUDY OF 508,964 BOYS BORN FROM 1995 TO 2009
P03.03 Sofie Gry Pristed. ASSOCIATION BETWEEN ANTHROPOMETRIC MEASURES AND HEALTH RELATED QUALITY OF LIFE IN THE DANISH DIET, CANCER AND HEALTH STUDY
P03.04 Kirsten Krabek Frantzen. CARING FOR THE CAREGIVER - A QUALITATIVE STUDY OF PARENTS' PREFERENCES FOR TREATMENT OF THEIR CHILD WITH AUTISM
P03.05 Jette Ahrensberg. CHILDHOOD MALIGNANCIES. SYMPTOMS AND DIAGNOSTIC INTERVAL
P03.06 Dorthe Sørensen. COMMUNIKCATION AND COLLABORATION WITH COPD PATIENTS IN NON-INVASIVE VENTILATION
P03.07 Priscila Corraini. DEFINING AND DIAGNOSING CASES OF PERIODONTITIS
P03.08 Kirsten Hansen. CONCERNING CHILDREN OF PARENTS WITH MAJOR DEPRESSION
P03.09 Zhanna Tairova. DISRUPTION OF RETINOID AND CYP SYSTEMS AND EMBRYO DEVELOPMENT IN MARINE ORGANISMS &NDASH; A POTENTIAL MODEL FOR HUMANS
P03.10 Susanne Lemcke. EARLY SIGNS OF ADHD AND AUTISM IN TODDLERS

Poster session 04. Chairmen: Jan Alsner, Magdalena Julia Dabowska, Jeppe Grøndahl Rasmussen

P04.01 Eduardo Vázquez Garza. CHARACTERIZATION OF NK CELL SUBPOPULATIONS BY HCMV REACTIVATION IN IMMUNOCOMPROMISED PATIENTS, FOCUSING ON CD94/NKG2A- AND CD94/NKG2C POPULATIONS
P04.02 Maria Bro Kloster. DEREGULATED EXPRESSION OF PRDM1 ISOFORMS IN MALIGNANT B CELLS
P04.03 Torben L. Andersson. PROTEIN PROFILES OG CHEMORESISTANCE IN B-CELL MALIGNANCIES STUDIED IN MYELOMA CELL LINES AND THE MYELOMA HIERARCHY BY PROTEIN ARRAY ANALYSIS
P04.04 Kim Steve Bergkvist. STUDIES OF SMALL DISCRETE POPULATIONS OF B CELLS BY MICROARRAY TECHNOLOGY
P04.05 Niels Frost Andersen. THE IMPACT OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) GENE POLYMORPHISMS IN MULTIPLE MYELOMA PATIENTS TREATED WITH HIGH-DOSE THERAPY
P04.06 Anne Sørensen. BOLD MRI IN SHEEP FETUSES: A NON-INVASIVE METOD FOR MEASURING CHANGES IN TISSUE OXYGENATION.
P04.07 Michael Benros, AUTOIMMUNE DISEASES COMBINED WITH SEVERE INFECTIONS AS RESK FACTORS FOR SCHIZOPRENIA: A 30-YEAR POPULATION-BASED
P04.08 Olga Kudryavtseva, THE ROLE OF L-TYPE CALCIUM CHANNELS IN VASCULAR REMODELING AND SMOOTH MUSCLE PHENOTYPIC EXPRESSIONS

Poster session 05. Chairmen: Rikke Katrine Jentoft Olsen, Asgar Granfelt, Sine Nygaard Langerhuus

P05.01 Martin Skøtt. A NEW RODENT MODEL FOR STUDYING SUPERIMPOSED ACUTE KIDNEY INJURY ON CHRONIC KIDNEY DISEASE

P05.02 Johannes Martin Schmid. BASOPHIL SENSITIVITY DECREASES DURING THE UPDOSING PHASE OF SUBCUTANEOUS IMMUNOTHERAPY (SCIT) IN SUBJECTS ALLERGIC TO GRASS POLLEN
P05.03 Frederik Hvid-Jensen. BARRETTS ESOPHAGUS AND ADENOCARCINOMA: A NATIONWIDE 17-YEAR FOLLOW-UP STUDY ON 15102 PATIENTS DIAGNOSED WITH BARRETTS ESOPHAGUS IN DENMARK
P05.04 Hans Linde Nielsen. CLINICAL EPIDEMIOLOGY AND MANIFESTATIONS OF *CAMPYLOBACTER CONCISUS*
P05.05 Anne Brosbøl-Ravnborg. CONTROL OF DENDRITIC CELL FUNCTION BY VITAMIN D_3
P05.06 Kristian Ravlo. EFFECT OF REMOTE ISCHEMIC PRECONDITIONING ON DENDRITIC CELLS IN BLOOD AFTER RENAL TRANSPLANTATION - FLOW CYTOMETRY IN A PORCINE MODEL
P05.07 Karen Leth Nielsen. EXPRESSION OF HUMAN &BETA;-DEFENSIN 1 IN CORRELATION TO URINARY TRACT INFECTION
P05.08 Srikanth Chiliveru. HERPES SIMPLEX VIRUS EXPLOITS IFI16 TO PROMOTE ITS REPLICATION
P05.09 Anders Kirch Dige. HIGH REGULATORY T CELL PERCENTAGE PREDICTS CLINICAL RESPONSE OF ADALIMUMAB TREATMENT IN CROHN'S DISEASE
P05.10 Christian Ammitzbøll. HUMORAL PATTERN RECOGNITION MOLECULES IN PLASMA AND SYNOVIAL FLUID IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS
P05.11 Stine Maria Lund Andersen. VALRUBICIN ACTIVATES PKCA IN KERATINOCYTES

Poster session 06. Chairmen: Bente Jespersen, Rikke Vestergaard, Marta Bauerek
P06.01 Camilla Nyboe. ATRIAL SEPTAL DEFECT IN THE ADULT
P06.02 Jo Bønding Andreasen. CAN ROTEM® ANALYSIS BE APPLIED FOR HEMOSTATIC MONITORING IN PEDIATRIC CONGENITAL HEART SURGERY
P06.03 Jakob Stegger. BODY COMPOSITION AND BODY FAT DISTRIBUTION IN RELATION TO LATER RISK OF ACUTE MYOCARDIAL INFARCTION: A DANISH FOLLOW-UP STUDY
P06.04 Sidse Kringelholt. CARBONIC ANHYDRASE INHIBITORS INDUCE VASORELAXATION IN ISOLATED INTRAOCULAR PORCINE CILIARY ARTERIES
P06.05 Sophie Constantin Lütken. CARDIAC AND RENAL PARAMETERS IN LOW SODIUM DIET VERSUS STANDARD SODIUM DIET IN RATS WITH EXPERIMENTALLY INDUCED HEART FAILURE
P06.06 Jonas Agerlund Povlsen. CARDIOPROTECTION IN TYPE 2 DIABETES MELLITUS - SIGNIFICANCE OF THE MALATE-ASPARTATE SHUTTLE
P06.07 Christian Daugaard Peters. CARDIOVASCULAR EFFECT OF IRBESARTAN IN NEWLY STARTED HEMODIALYSIS PATIENTS: A SUBSTUDY WITHIN THE SAFIR-STUDY
P06.08 Niels Ramsing Holm. COMPARISON OF TWO-STENT TECHNIQUES FOR CORONARY BIFURCATION LESIONS. POOLED ANALYSIS OF THE BBC ONE STUDY AND THE NORDIC BIFURCATION STUDIES
P06.09 Rikke Esberg Kirkfeldt. COMPLICATIONS AND ASSOCIATED RISK FACTORS FOLLOWING PRIMARY PERMANENT PACEMAKER OR CARDIAC RESYNCHRONIZATION THERAPY IMPLANTATION. A POPULATION-BASED COHORT STUDY OF 28,860 DANISH PATIENTS
P06.10 Maria Skytte Tørring. DIFFERENTIAL CONTRACTILE RESPONSE OF SMALLER AND LARGER PORCINE RETINAL ARTERIOLES IN VITRO
P06.11 Frank Holden Christensen. THE EFFECT OF ATORVASTATIN ON THE NO-SYSTEM IN PATIENTS WITH TYPE II DIABETIC NEPHROPATHY, NEPHROPATHY AND HEALTHY PERSONS
P06.12 Vibeke Secher Dam. MOLECULAR CHARACTERIZATION OF CA^{2+} ACTIVATED CL-CHANNELS IN VASCULAR SMOOTH MUSCLE CELLS

Poster session 07. Chairmen: Karin Lykke-Hartmann, Casper Nielsen, Anders Knudsen
P07.01 Philipp Harbig. ADHERENCE IN TREATMENT WITH FUROSEMIDE IN OLDER ADULTS
P07.02 Casper Foldager. ADAPTION TO HYPOXIA IN MESENCHYMAL STEM CELLS IS ONLY PARTIALLY IMPROVED BY CHONDROGENIC STIMULATION
P07.03 Anders Peter Søndergaard. CORNEAL HYDRATION AND SWELLING PROPERTIES FOLLOWING UVA RIBOFLAVIN COLLAGEN CROSS-LINKING
P07.04 Trine Østergaard Nielsen. DIRECTING THE ALTERNATIVE SPLICING OF HER4 DECREASES CANCER CELL GROWTH

P07.05 Eva Greibe. DEVELOPMENT OF A VITAMIN B12 FOOD ABSORPTION TEST BY USE OF RAINBOW TROUT PROTEIN
P07.06 Solveig Klok Matthesen. EFFECT OF DIETARY POTASSIUM SUPPLEMENT ON BLOOD PRESSURE, AUGMENTATION INDEX AND THE RENIN-ALDOSTERONE SYSTEM IN HEALTHY HUMANS
P07.07 Kristina Bennet Emdal. HER4 IN ESTROGEN-RESPONSIVE AND ANTIESTROGEN-RESISTANT BREAST CANCER
P07.08 Evelyne Furger, Paul Scherrer Institute / ETH Zürich
P 07.09 Lily Jeng, Harvard Medical School

Poster session 08. Chairmen: Anders D. Børglum, Nis Borbye Pedersen & Rune Thomsen
P08.01 Caspar Skau Madsen. A DELTA AND C FIBER COMPONENTS OF CONTACT HEAT EVOKED POTENTIALS (CHEPS) IN CAPSAICIN INDUCED HEAT HYPERALGESIA
P08.02 Anna Tietze. ADVANCED MAGNETIC RESONANCE IMAGING TECHNIQUES; A TOOL TO PREDICT BRAIN TUMOUR TYPES AND GRADES AND TO ASSESS THERAPY RESPONSE
P08.03 Tina Birgitte Carstensen. ARE THERE GENDER DIFFERENCES IN COPING WITH NECK PAIN FOLLOWING ACUTE WHIPLASH TRAUMA? A 12-MONTH FOLLOW-UP STUDY
P08.04 Emilia Horjales. BRAIN IMAGING STUDIES ON THE RELATIONSHIP BETWEEN PAIN AND EMOTIONS
P08.05 Simon Hjerrild. CEREBRAL INVOLVMENT IN CHRONIC HEPATITIS C VIRUS INFECTION ASSESSED BY MRI
P08.06 Dariusz Orlowski. CHRONIC RESTRAINT STRESS CHANGES RAT HIPPOCAMPAL BRANCHING PATTERN AND SPINE DENSITY
P08.07 Mohit Kothari. COMPLEX TONGUE TRAINING- A NOVEL APPROACH IN REHABILITATION OF ORAL FUNCTION
P08.08 René Ernst Nielsen. COMPARING THE EFFECTS OF SERTINDOLE AND OLANZAPINE ON COGNITION (SEROLA)
P08.09 Leslie Foldager. CONDITIONAL LOGIC REGRESSION: IDENTIFYING SNP INTERACTIONS FROM INDIVIDUALLY TIME-MATCHED CASE-CONTROL DATA
P08.10 Karina Bendixen. DOUBLE-STRESS ALTERS EXPERIMENTAL MASSETER MUSCLE PAIN AND AUTONOMIC RESPONSE

Poster session 09. Chairmen: Karen Dybkær, Claus Tvedesøe, Fillippo Peder D.Andrea
P09.01 Johanne Lade Keller. ANALYSIS OF GENETIC CHANGES AND PROTEIN EXPRESSION PROFILES IN MELANOMA
P09.02 Jesper Kallehauge. APPARENT DIFFUSION COEFFICIENT (ADC) AS A QUANTITATIVE PARAMETER IN DIFFUSION WEIGHTED MR IMAGING IN CERVICAL CANCER. DEPENDENCE ON B-VALUES USED.
P09.03 Sidse Bregendahl. BOWEL DYSFUNCTION AFTER NEOADJUVANT THERAPY FOR RECTAL CANCER - PATHOPHYSIOLOGICAL MECHANISMS
P09.04 Anja Bille Bohn. CHANGES IN WATER AND SALT BALANCE IN RATS INDUCED BY COMBRETASTATIN
P09.05 Andreas Carus. CHRONIC INFLAMMATION AND CANCER - FOCUSING ON NEUTROPHILE LEUKOCYTES, MONOCYTES AND MACROPHAGES IN SOLID TUMORS
P09.06 Søren Haack. COMPARING MICROSTRUCTURAL INFORMATION USING DIFFUSION WEIGHTED MRI TO GEC ESTRO TARGETS USED FOR BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER
P09.07 Kasper Jarlhelt Andersen. CLINICAL AND ECONOMIC CONSEQUENCES OF WORK-UP WITHOUT LAPAROSCOPY IN PATIENTS WITH CRC LIVER METASTASES
P09.08 Thomas Reinert. COMPREHENSIVE GENOME METHYLATION ANALYSIS IN BLADDER CANCER; IDENTIFICATION AND VALIDATION OF NOVEL METHYLATED GENES AND APPLICATION OF THESE AS URINARY TUMOR MARKERS
P09.09 Bente Thoft Jensen. EFFICACY OF A MULTI PROFESSIONAL REHABILITATION PROGRAMME IN BLADDER CANCER
P09.10 Martin Skovmos Nielsen. IMAGE GUIDED RESPIRATORY GATED RADIOTHERAPY FOR LUNG CANCER PATIENTS: PRE CLINICAL EXPERIENCE ON GOTTINGEN MINIPIGS.

Poster session 10. Chairmen: Jens Otto Lunde Jørgensen, Gitte Dam, Nicklas Heine Staunstrup

P10.01 Torsten Bloch Rasmussen. A NOVEL RECESSIVE MUTATION IN DESMOPLAKIN CAUSING DILATED CARDIOMYOPATHY WITH SKIN AND HAIR ABNORMALITIES: NEW INSIGHTS INTO DISEASE MECHANISMS IN CAVAJAL SYNDROME

P10.02 Maria Jakobsen. AAV MEDIATED SHRNA EXPRESSION IN HUMAN SKIN

P10.03 Charlotte Uggerhøj Andersen. BIOMARKERS IN PULMONARY HYPERTENSION ASSOCIATED TO INTERSTITIAL LUNG DISEASE

P10.04 Trine Dalsgaard. DEVELOPMENT OF GENE THERAPY OF PKU

P10.05 Yonglun Luo. GENERATION OF A BRCA1 KNOCKOUT PIG MODEL BY RECOMBINANT ADENO-ASSOCIATED VIRUS-MEDIATED GENE TARGETING

P10.06 Maiken Kudahl Larsen. GENETIC ASPECTS OF FAMILIAL HYPERCHOLESTEROLEMIA AND ABUSE OF ANABOLIC ANDROGENIC STEROIDS AS AN ENVIRONMENTAL RISK FACTOR IN YOUNG ADULTS

P10.07 Terese K. Jeppesen. GENDER-DEPENDENT EXPRESSION OF MATRIX METALLOPROTEASES AND THEIR INHIBITORS IN THE KIDNEY

P10.08 Raffaella Mangnoni. HETEROZYGOUS HSP60 KNOCK-OUT MICE REPRESENT A MODEL OF HEREDITARY SPASTIC PARAPLEGIA TYPE13

P10.09 Jonas Jensen. IN VIVO TESTING OF STRUCTURAL GRADED POLYCAPROLACTONE SCAFFOLDS IN A PORCINE CALVARIA MODEL

P10.10 Steffen Møller-Larsen. IN-DEPTH ANALYSIS OF TOLL-LIKE RECEPTOR ASSOCIATION WITH ASTHMA AND RELATED ATOPIC DISORDERS

Poster session 11. Chairmen: Karin Birkenkamp-Damtroder, Michael Kjeldager Tjørnild, Thomas Maribo

P11.01 Louise Hauge Matzen. ACCURACY OF SCANOGRAPHY USING STORAGE PHOSPHOR PLATE SYSTEMS AND FILM FOR ASSESSMENT OF MANDIBULAR THIRD MOLARS

P11.02 Charlotte Hartig Andreasen. ASSEMENT OF FACTORS INFLUENCING THE SURGICAL OUTCOME OF PERIACETABULAR OSTEOTOMI IN ADULTS

P11.03 Maj Høygaard Nicolaisen. CLINICAL PERFORMANCE OF ZIRCONIA-CERAMIC AND METAL-CERAMIC POSTERIOR THREE-UNIT FIXED PARTIAL DENTURES: A RANDOMIZED CONTROLLED TRIAL

P11.04 Pernille Endrup Jacobsen. DENTAL ABNORMALITIES IN CHILDREN, EXPOSED TO ANTICONVULSANTS PRENATALLY

P11.05 Hans Gjørup. CRANIOFACIAL MORPHOLOGY OF PATIENTS WITH HYPOPHOSPHATEMIC RICKETS COMPARED TO HEALTHY CONTROLS

P11.06 Michael Skovdal Rathleff. EARLY INTERVENTION FOR ADOLESCENTS WITH PATELLOFEMORAL PAIN SYNDROME (THE EIAP-STUDY)

P11.07 Jan Rölfing. EPO'S EFFECT ON MSC IN VITRO

P11.08 Lone Ramer Nygaard Mikkelsen. FEASABILITY OF EARLY PROGRESSIVE RESISTANCE TRAINING AFTER TOTAL HIP REPLACEMENT

P11.09 Rubens Neto BONE ALLOGRAFTS IN HUMANS: IMMUNOLOGIC, TOMOGRAPHIC, HISTOLOGICAL AND HISTOMETRICAL EVALUATION OF ITS INCORPORATION AND CAPACITY OF OSSEOINTEGRATING DENTAL IMPLANTS

Poster session 12. Chairmen: Tine Brink Henriksen, Pernille Kure Vandborg, Marie Bagger Bohn

P12.01 Holger Borup Wemmelund. ASSOCIATION OF ACE INHIBITOR AND STATIN TREATMENT WITH SMALL ABDOMINAL AORTIC ANEURYSM PROGRESSION

P12.02 Yu Wang. DISTAL ADDING-ON PHENOMENON IN LENKE 1A SCOLIOSIS : RISK FACTOR IDENTIFICATION AND TREATMENT STRATEGY COMPARISON

P12.03 Morten Charles. EFFECTS OF EARLY DETECTION AND INTENSIVE TREATMENT ON PERIPHERAL ARTERIAL DISEASE &NDASH; ADDITION DENMARK

P12.04 Rune Erichsen. LONG-TERM STATIN USE REDUCES THE RISK OF GALLSTONE DISEASE - A POPULATION-BASED CASE-CONTROL STUDY

P12.05 Morten Schmidt. NONSTEROIDAL ANTI-INFLAMMATORY DRUG USE AND RISK OF VENOUS THROMBOEMBOLISM: A POPULATION-BASED CASE-CONTROL STUDY
P12.06 Mette Julsgaard Nielsen. POSTPARTUM ADHERENCE TO MEDICAL TREATMENT AMONG WOMEN WITH CROHN'S DISEASE
P12.07 Niels Henrik Krarup. QUALITY OF CARDIOPULMONARY RESUSCITATION IN OUT-OF-HOSPITAL CARDIAC ARREST IS HAMPERED BY INTERRUPTIONS IN CHEST COMPRESSIONS - A NATIONWIDE PROSPECTIVE STUDY
P12.08 Karin Biering. RETURN-TO-WORK (RTW) AFTER PERCUTAN CORONARY INTERVENTION (PCI)
P12.09 Efe Levent Aras. SURGICAL TREATMENT OF VERTEBRAL COMPRESSION FRACTURES VERSUS CONSERVATIVE TREATMENT. EVALUATION OF LONG-TERM OUTCOMES AND COST-EFFECTIVENESS.
P12.10 Palle Bager. WHAT'S CHEAPEST, INTRAVENOUS IRON SUCROSE- OR INTRAVENOUS IRON CARBOXYMALTOSE TREATMENT?

Poster session 13. Chairmen: Henrik Kolstad, Morsi Abdallah
P13.01 Rasmus Foldbjerg. SILVER NANOPARTICLES INDUCE OXIDATIVE STRESS IN A549 CELLS
P13.02 Malene Outzen. SELENIUM STATUS MEASURED IN BLOOD AFTER A HIGHER INTAKE OF FISH AND SHELLFISH - A RANDOMIZED DIETARY INTERVENTION STUDY
P13.03 Mona Lisa Idriss Kise. SOCIOECONOMIC AND DEMOGRAPHIC CHARACTERISTICS OF CANCER PATIENTS AS A PREDICTOR OF THE SEVERITY OF FIRST PRESENTED SYMPTOMS
P13.04 Susanne Lund Kristensen. THE ASSOCIATION BETWEEN ANTI-MULLERIAN HORMONE AND FEATURES OF POLYCYSTIC OVARY SYNDROME IN YOUNG WOMEN
P13.05 Peter Agergaard. THE DANISH NATIONAL PATIENT REGISTRY: A VALID DATA SOURCE REGARDING CONGENITAL HEART DISEASE
P13.06 Lene Søndergård Larsen. THE SIGNIFICANCE OF FELLOW PATIENTS DURING HOSPITALISATION; A RESOURCE OR A LIABILITY?
P13.07 Carina Henriksen. THE PATHOPHYSIOLOGY OF RAPID-ONSET DYSTONIA PARKINSONISM: CELL CULTURE STUDIES AND PORCINE MODEL
P13.08 Hanne Mainz. THE RELATIONSHIP BETWEEN NURSE STAFFING AND PATIENT OUTCOMES
P13.09 Jens Christian Jensen. WORK-RELATED PREDICTORS FOR MEDICAL CARE-SEEKING WITH UPPER EXTREMITY PAIN AND BACK PAIN IN A COHORT OF THE GENERAL WORKING POPULATION.
P13.10 Emma Tina Bisgaard Olesen. VASOPRESSIN INDEPENDENT PHOSPHORYLATION AND TRAFFICKING OF AQUAPORIN-2 BY SELECTIVE E-PROSTANOID RECEPTOR AGONISTS
P13.11 Annett Andersen. WORK RELATED SHOULDER LOADS: ESTABLISHMENT OF A JOB EXPOSURE MATRIX

Poster session 14. Chairmen:Mette Nyegaard, Tanja Tvistholm Sikjær, Anna Pietraszek
P14.01 Ulrick Espelund. INTERSTITIAL FLUID COLLECTED BY THE SUCTION BLISTER TECHNIQUE CONTAINS A HIGHER IN VITRO BIOACTIVITY THAN SERUM
P14.02 Jakob Østergaard. MANNOSE-BINDING LECTIN AND ACTIVATION OF COMPLEMENT SYSTEM IN TYPE 1 DIABETES
P14.03 Louise Jung Nørgaard Jensen. PLASMA CALPROTECTIN IN PATIENTS WITH CHRONIC HEART FAILURE
P14.04 Morten Møller Poulsen. RESVERATROL PREVENTS DEVELOPMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE BY A COMPENSATORY UPREGULATION OF MITOCHONDRIA NUMBER AND IN PARTICULAR UCP2
P14.05 Karina Bech Cullberg. RESVERATROL INHIBITS THE HYPOXIA-INDUCED INFLAMMATION AND ANGIOGENESIS IN HUMAN ADIPOSE TISSUE *IN VITRO*
P14.06 Lars Rolighed. STERNOTOMY IN THYROID OPERATIONS: RETROSPECTIVE STUDY OF 48 OPERATIONS.
P14.07 Merete Lindberg Hartvigsen. EFFECTS OF BIOFUNCTIONAL CARBOHYDRATES ON THE METABOLIC SYNDROME
P14.08 Ermina Bosnjak. ENDOTOXIN & CYTOKINES. DO PROTEIN LOSS AND METABOLIC EFFECTS DEPEND ON CNS ACTIVATION OF STRESS HORMONES OR ON LOCAL MECHANISMS IN MUSCLE AND FAT?

P14.09 Lea Brader. HEALTHY NORDIC DIET IN THE PREVENTION OF METABOLIC SYNDROME; THE AARHUS UNIVERSITY PART OF A MULTI-CENTRE STUDY (NORDKOST)
P14.10 Pernille Høyem, MRI of Carotid Arteries and Cerebrum in Patients with Type 2 Diabetes versus healthy Control Subjects – a preliminary analysis

Poster session 15. Chairmen: Henrik Støvring, Dorte Rytter, Michael Smærup Brandt
P15.01 Christian Wulff. EFFECT OF CASE MANAGEMENT IN COMPLEX CANCER PATHWAYS: A RANDOMIZED CONTROLLED TRIAL
P15.02 Anne Vested. EFFECTS OF IN UTERO EXPOSURE TO PFOA AND PFOS ON HUMAN SEMEN QUALITY AND HORMONE PROFILE
P15.03 Grethe Elholm. FARMING EXPOSURE LEADS TO LESS ALLERGIC SENSITISATION
P15.04 Ioanna Milidou. FIRST TRIMESTER NICOTINE EXPOSURE AND THE RISK OF INFANTILE COLIC
P15.05 Simon Grandjean Bamberger. GLOBALIZATION, ORGANIZATIONAL CHANGE AND PSYCHOSOCIAL WORK ENVIRONMENT: THE IMPACT ON MENTAL HEALTH
P15.06 Janne Fassov. FUNCTIONAL RESULTS OF SACRAL NERVE STIMULATION FOR IRRITABLE BOWEL SYNDROME
P15.07 Henriette Vind Thaysen. HEALTH RELATED QUALITY OF LIFE AFTER SURGERY FOR LOCALLY ADVANCED PRIMARY RECTAL CANCER OR RECURRENCE OF RECTAL CANCER
P15.08 Mette Vinther Skriver. HBA_{1C} AS PREDICTOR OF ALL-CAUSE MORTALITY IN INDIVIDUALS AT HIGH RISK OF DIABETES WITH NORMAL GLUCOSE TOLERANCE, IDENTIFIED BY SCREENING: A FOLLOW-UP STUDY OF ADDITION, DENMARK
P15.09 Kristina Grønborg Laut. HEALTH TECHNOLOGY DIFFUSION: THE EXAMPLE OF PRIMARY ANGIOPLASTY IN THE EU15 COUNTRIES
P15.10 Margrethe Smidth. IDENTIFICATION OF PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) FROM ADMINISTRATIVE DATA

Poster session 16. Chairmen: Flemming W. Bach, Eduardo Adrian Garza Villarreal, Ivana Konvalinka
P16.01 Kaare Meier. SEGMENTAL INNERVATION OF THE GOTTINGEN MINIPIG HIND LIMB
P16.02 Vibeke Fuglsang Bliksted. SOCIAL COGNITION IN FIRST-EPISODE SCHIZOPHRENIA: THEORY OF MIND AND SOCIAL PERCEPTION
P16.03 Mette Richner. SORTILIN IN NEUROPATHIC PAIN
P16.04 Kim Henningsen. THE ADULT RAT RESPONSE TO STRESS IS AFFECTED BY EARLY MATERNAL CARE QUALITY
P16.05 Annemette Bondo Lind. THE INFLUENCE OF MINDFULNESS-BASED COGNITIVE THERAPY FOR PEOPLE WITH SEVERE FUNCTIONAL DISORDER: A QUALITATIVE STUDY
P16.06 Louise Ørum Olesen. THE NEURAL BASIS OF COGNITIVE DEFICITS IN A MOUSE MODEL OF DEMENTIA
P16.07 Louise Brøndt Hartlev, A NEW UNBIASED STEREOLOGICAL APPROACH FOR ESTIMATING CHANGES IN ARTICULAR CARTILAGE AND SUBCHONDRAL BONE IN HUMAN OSTEOARTHRITIC FEMORAL HEADS
P16.08 Micah Allen. TRAINING THE BRAIN AT REST: MENTAL TRAINING AND PLASTICITY OF RESTING STATE NETWORKS

Poster session 17. Chairmen: Robert A. Fenton, Simon Rasmussen, Emil Kofod-Olsen
P17.01 Kristian Kjær Andersen. HYPOTHERMIA DURING OPERATION ON THE ASCENDING AORTA: COMPARISON OF TO METHODS
P17.02 Hanne Vinter. IMIQUIMOD INDUCED SKIN INFLAMMATION: A HUMAN MODEL OF PSORIASIS
P17.03 Tue Kruse Rasmussen. INCREASED IL-21 AND IL-23 ARE ASSOCIATED WITH INCREASED DISEASE ACTIVITY AND WITH RADIOGRAPHIC STATUS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS
P17.04 Rikke Fleron Leihof. INHIBITION OF INTRACELLULAR GROWTH OF UROPATHOGENIC E. COLI
P17.05 Christine Lodberg Hvas. INTRACRANIAL HEMORRHAGE - A NEW LARGE ANIMAL MODEL OF BRAIN DEATH

P17.06 René Østgård. INTESTINAL INFLAMMATION IN ANKYLOSING SPONDYLITIS ASSESSED BY FECAL CALPROTECTIN, CAPSULAR ENDOSCOPY AND COLONOSCOPY AND THE EFFECTS OF ADALIMUMAB ON MUCOSAL HEALING
P17.07 Lone Schmidt Sørensen. OMEGA-3 FATTY ACIDS AND COMPLICATIONS AFTER COLORECTAL SURGERY
P17.08 Ditte Andreasen Søborg. OCCURRENCE OF VIRULENCE GENES AMONGST NATURALLY OCCURRING ENVIRONMENTAL BACTERIA
P17.09 Julie Prahl. PHARMACOKINETICS AND PHARMACODYNAMICS OF FIRST LINE TUBERCULOSIS DRUGS IN HUMANS AND MICE WITH TYPE 2 DIABETES.
P17.10 Line Reinert. THE ROLE FOR TYPE I IFN AND TOL LIKE RECEPTOR INDUCED ANTIVIRAL ACTIVITY AGAINST HSV
P17.11 Frauke Rudolf. VALIDATION OF THE BANDIM TUBERCULOSIS-SCORE: RELIABILITY AND ABILITY TO PREDICT OUTCOME

Poster session 18. Chairmen: Birgitte Mønster Christensen, Martin Majlund Mikkelsen, Thais A. Pedersen

P18.01 Anna Sellmer Sørensen. DUCTUS ARTERIOSUS IS OPEN ON DAY FOUR IN HALF OF ALL NEONATES BORN BEFORE 32 WEEKS OF GA
P18.02 Helle Damgaard Zacho. DOES TC99M-MEBROFENIN GET METABOLISED IN THE INTESTINES?
P18.03 Asger Andersen. EFFECTS OF PHOSPHODIESTERASE-5 INHIBITION BY SILDENAFIL IN THE PRESSURE OVERLOADED RIGHT HEART
P18.04 Thomas Andersen Rix. FISH, MARINE N-3 POLYUNSATURATED FATTY ACIDS, AND THE DEVELOPMENT OF ATRIAL FIBRILLATION
P18.05 Charlotte Strandhave. HAPTOGLOBIN PHENOTYPE IS ASSOCIATED WITH ELEVATED LEVELS OF HIGH SENSITIVITY CRP AND INTERLEUKIN-6 IN PATIENTS WITH STAGE 3-5 CHRONIC KIDNEY DISEASE
P18.06 Rebekka Jensen. HUMAN DIABETICS RELEASE A CARDIOPROTECTIVE FACTOR.
P18.07 Peter Juhl-Olsen. HYPOXIC CARDIAC ARREST RESEMBLES ECHOCARDIOGRAPHIC INDICES OF PULMONARY EMBOLISM IN A PORCINE MODEL
P18.08 June Anita Ejlersen. IMPACT OF ULTRASOUND MICRO BUPPLE CONTRAST ON 2D-STRAIN ECHOCARDIOGRAPHY
P18.09 Lau Brix. INCREASED TEMPORAL RESOLUTION IN CARDIAC MR IMAGING
P18.10 Martin Bødtker Mortensen. IN-VIVO CELLULARIZATION OF PCL SCAFFOLDS IN JUVENILE PIG AORTA: A STEP TOWARDS CREATING PCL VASCULAR PROSTHESES

Poster session 19. Chairmen: Lise Lotte Hansen, Tina Storm, Kasper Toustrup

P19.01 Line Brøndum. STIMULATION OF THE IMMUNE SYSTEM AND INHIBITION OF ANGIOGENESIS IN PATIENTS WITH RENAL CELL CARCINOMA: A RANDOMIZED PHASE II STUDY.
P19.02 Peter Sandegaard Skyt. THE THERMAL DEPENDENCE OF PRESAGE DOSE RESPONSE: EFFECT OF IRRADIATION AND STORAGE TEMPERATURES
P19.03 Lotte Andreasen. THE PATHOGENIC FUNCTION OF MUTATIONS IN NLRP7 IN DIPLOID HYDATIDIFORM MOLES WITH BIPARENTAL GENOME
P19.04 Martin Mørck Mortensen. THE MOLECULAR SIGNATURE OF CLINICAL LOCALIZED PROSTATE CANCER
P19.05 Katja Maretty Nielsen. TREATMENT RESULTS AND PROGNOSTIC FACTORS IN SOFT TISSUE SARCOMA PATIENTS AT AARHUS SARCOMA CENTER, 30 YEARS EXPERIENCE
P19.06 Mette Bak Nielsen. TOTAL PELVIC EXENTERATION FOR PRIMARY ADVANCED AND RECURRENCE OF RECTAL CANCER
P19.07 Anders Christian Larsen. VENOUS THROMBOEMBOLISM IN PATIENTS RECEIVING PREOPERATIVE CHEMOTHERAPHY FOR GASTRIC CANCER
P19.08 Kåre Sanden Ettrup. UNILATERAL DEEP BRAIN STIMULATION OF THE VENTROMEDIAL HYPOTHALAMUS CAUSE TRANSIENT AGGRESSIVE BEHAVIOR AND SUPPRESSION OF APPETITE, IN THE GOTTINGEN MINIPIG

P19.09 Shallu Sharma, PROSPECTIVE DYNAMIC FUNCTIONAL EVALUATIONOF GAIT, BALANCE AND POSTURE FOLLOWING SPINAL RECONSTRUCTIVE SURGERY IN ADULT SCOILIOSIS AND CONTROLS

Poster session 20. Chairmen: Mette Madsen, Jasna Furtula, Jeppe Grøndahl Rasmussen

P20.01 Kathrine Just Andersen. ELECTROPHYSIOLOGICAL RECORDINGS IN SUBTHALAMIC NUCLEUS IN AN ALPHA-SYNUCLEIN MODEL OF PARKINSON'S DISEASE.
P20.02 Cristine Betzer. FINDING LIGANDS FOR &ALPHA;-SYNUCLEIN OLIGOMERS
P20.03 Morten Jønsson. FUNCTIONAL CONNECTIVITY IN DEPRESSION: A MEG STUDY
P20.04 Zita Dósa. INCREASED TONIC GABA-A RECEPTOR MEDIATED SIGNALING IN DENTATE GYRUS OF SSADH DEFICIENT MICE
P20.05 Sanne Kjær Vandborg. IS TREATMENT OUTCOME ASSOCIATED WITH COGNITIVE FUNCTIONS IN OCD?
P20.06 Stephen Austin. METACOGNITION AND SCHIZOPHRENIA: AN INVESTIGATION OF METACOGNITIVE BELIEFS AND PSYCHOPATHOLOGY WITHIN THE OPUS COHORT AT 10 YEAR FOLLOW UP.
P20.07 Noomi Gregersen. MARKERS ON CHROMOSOME 19P13 ARE ASSOCIATED WITH PANIC DISORDER
P20.08 Martin Dietz. MISMATCH NEGATIVITY (MMN) AND NEGLECT SYNDROME
P20.09 Line Gebauer Josefsen. MUSICAL EMOTIONS IN PEOPLE WITH AUTISM AND ASPERGER'S SYNDROME
P20.10 Katja Anna Hybel. NEURO AND METACOGNITIVE MARKERS AND PREDICTORS OF TREATMENT RESPONSE IN CHILDHOOD OCD

Poster session 21. Chairmen: Lone Sunde, Camilla Molich Hoff, Stefan W. Harders

P21.01
P21.02 Franz-Joachim Kaiser. INITIAL RECOMBINATION IN THE TRACK OF HEAVY CHARGED PARTICLES
P21.03 Lasse Sommer Kristensen. INCREASED SENSITIVITY OF *KRAS* MUTATION DETECTION BY HIGH-RESOLUTION MELTING ANALYSIS OF COLD-PCR PRODUCTS
P21.04 Stine Elleberg Petersen. MORBIDITY IN PATIENTS WITH PROSTATE CANCER TREATED WITH RADIATION THERAPY
P21.05 Lotte Abildgaard. MINIMAL RESIDUAL DISEASE MONITORING IN CHILDHOOD ACUTE MYELOID LEUKAEMIA
P21.06 Maria Thor. RECTUM MOTION AND MORBIDITY PREDICTION: IMPROVING CORRELATION BETWEEN LATE MORBIDITY AND DVH PARAMETERS THROUGH USE OF RECTUM PLANNING ORGAN AT RISK VOLUMES
P21.07 Hanna Rahbek Mortensen. REDUCTION OF DYSPHAGIA-RELATED MORBIDITY IN HEAD AND NECK RADIOTHERAPY
P21.08 Patricia Switten Nielsen. SIMPLE IMMUNOHISTOCHEMICAL DOUBLE STAINS WITH STRONG DIAGNOSTIC CAPABILITIES IN MELANOCYTIC LESIONS
P21.09 Esben Schjødt Worm. SETUP ERRORS IN STEREOTACTIC BODY RADIATION THERAPY: RELATION TO TREATMENT TIME, TUMOR POSITION, AND BODY MASS INDEX
P21.10 Sara Thörnqvist. SENSITIVITY TO TARGET MOTION IN SIMULATED INTEGRATED BOOST TREATMENTS OF PROSTATE AND LYMPH NODES FOR DIFFERENT SET-UP METHODS AND TREATMENT DELIVERY TECHNIQUES

Poster session 22. Chairmen: Marianne Hokland, Lisbeth Venø Kruse, Iben Blaabjerg Sundtoft

P22.01 Mette Konow Bøgebjerg Dolberg. MAGNESIUM IN ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE
P22.02 Ming Sun. NANOMEDICINE IN BREAST CANCER BONE METASTASIS: TARGETING CANCER STEM CELL
P22.03 Maja Ludvigsen. OUTCOME-RELATED PROTEIN EXPRESSION PROFILE IN PATIENTS WITH CLASSICAL HODGKIN LYMPHOMA.
P22.04 Halldór Bjarki Einarsson. OSTEOCLASTS IN BONE TISSUE ENGINEERED ALTERNATIVE
P22.05 Kasper Lynghøj Christensen. NOVEL CARBONYL SCAVENGER?

P22.06 Miao Wang. PREDICTIVE VALUE OF THE TOKUHASHI SCORING SYSTEMS IN SPINAL METASTASES (EVALUATION OF 448 PATIENTS IN THE AARHUS SPINAL METASTASES DATABASE)
P22.07 Nanna Cornelius. RIBOFLAVIN-RESPONSIVE MULTIPLE ACYL-COA DEHYDROGENASE DEFICIENCY (RR-MADD); A SYNERGISTIC EFFECT OF RIBOFLAVIN AND TEMPERATURE
P22.08 Anders Britze Hansen. THE CHOLESTEATOMA PROTEOME
P22.09 Kirstine Kjær Kirkegaard. TIME-LAPSE IMAGING AND METABOLIC PROFILE OF HUMAN PRE-IMPLANTATION EMBRYOS AFTER BLASTOMERE REMOVAL
P22.10 Nynne Sharma. TRANSCRIPTIONAL REPRESSION OF TRANSGENES DELIVERED BY SLEEPING BEAUTY, PIGGYBAC AND TOL2 DNA TRANSPOSON VECTORS

Poster session 23. Chairmen: Natalya Fedosova, Anne-Cathrine Bareid Østby, Maria Louise Salskov-Ivarsen
P23.01 Jan Danz. GINGIVAL RECESSIONS AND TOOTH MOVEMENT
P23.02 Line Kjeldgaard Pedersen. INTRA- AND INTERRATER RELIABILITY OF PRESSURE PAIN THRESHOLD IN CHILDREN WITH ORTHOPEDIC DISORDERS.
P23.03 Merete Gregersen. MULTIDISCIPLINARY GERIATRIC INTERVENTION AMONG NURSING HOME RESIDENTS WITH HIP FRACTURE REDUCES MORTALITY
P23.04 Martin Svoldgård Vesterby. REMOTE REHABILITATION SUPPORT
P23.05 Dan Østergaard Pradsgaard. ULTRASONOGRAPHY IN JUVENILE IDIOPATHIC ARTHRITIS

Poster session 24. Chairmen: Jens Cosedis Nielsen, Chumsen Wu, Vibeke Bregnballe
P24.01 Peter Hjorth. PHYSICAL HEALTH OF RESIDENTS IN PSYCHIATRIC AND SOCIAL CARE FACILITIES
P24.02 Birgitte Blicher Pedersen. POSTSTROKE FATIGUE - DEVELOPING AND TESTING A PROGRAM TO REDUCE AND COPE WITH FATIGUE
P24.03 Kasper Grosen. PREVALENCE AND CHARACTERISTICS OF CHRONIC PAIN FOLLOWING VIDEO-ASSISTED THORACIC SURGERY AND ANTERIOR THORACOTOMY IN PATIENTS WITH PULMONARY MALIGNANCIES
P24.04 Rasmus Østergaard Nielsen. PROTOCOL FOR THE DANO-RUN STUDY: A 1-YEAR OBSERVATIONAL FOLLOW UP STUDY ON RUNNING RELATED INJURIES IN 1000 NOVICE RUNNERS.
P24.05 Matias Grynderup. PSYCHOLOGICAL DEMANDS, DECISION LATITUDE AND THE RISK OF INCIDENT DEPRESSION
P24.06 Connie Berthelsen. RELATIVES PARTICIPATION IN OLDER PATIENTS ACCELERATED TREATMENT PROGRAMME DURING TOTAL HIP OR KNEE REPLACEMENT. CONSTRUCTING GROUNDED THEORY.
P24.07 Palle Larsen. REHABILITATION NURSING RESEARCH IN PATIENTS HEART REHABILITATION IN PHASE III .
P24.08 Jakob Jakobsen. SACRAL NERVE STIMULATION FOR IDIOPATHIC FAECAL INCONTINENCE - EFFICACY AND PATIENT SATISFACTION -
P24.09 Mai-britt Guldin. RISK ASSESSMENT OF COMPLICATED GRIEF AMONG FAMILY CAREGIVERS OF DECEASED CANCER PATIENTS. A RANDOMIZED CONTROLLED STUDY.
P24.10 Helle Svenningsen. SEDATION - DELIRIUM - PTSD

Poster session 25. Chairmen:Povl Munk-Jørgensen, Lene Bastrup Jørgensen, Flemming Bandholm Jakobsen
P25.01 Lise Graversen. IDENTIFICATION OF PRESCHOOL CHILDREN AT HIGH RISK OF FUTURE OVERWEIGHT
P25.02 Zara Ann Stokholm. LONG-TERM OCCUPATIONAL NOISE AND ANTIHYPERTENSIVE MEDICATION: A REGISTER-LINKED STUDY
P25.03 Christina Malmose Stapelfeldt. MEASURING SICK LEAVE AMONG ELDERCARE WORKERS: ARE DANISH ADMINISTRATIVE DATA ON SICKNESS BENEFIT AS VALID AS DATA ON SICK LEAVE FROM COMPANY RECORDS?
P25.04 Rikke Jørgensen. MEANINGFUL CHANGE WITH THE METHOD GUIDED SELF-DETERMINATION &NDASH; A RANDOMISED CONTROLLED STUDY FOR PATIENTS DIAGNOSED WITH SCHIZOPHRENIA.

P25.05 Anette Werner. MENTAL TRAINING AND CHILDBIRTH - THE EFFECT ON PAIN EXPERIENCE, LENGTH OF BIRTH AND OTHER BIRTH OUTCOMES
P25.06 Lene Jacobsen. METABOLIC SYNDROME IN PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA - PREDICTION AND PREVENTION
P25.07 Bjarne Rittig-Rasmussen. NECK PAIN, NECK TRAINING AND CORTICAL PLASTICITY
P25.08 Anne-Birgitte Vogelsang. PARTNERS TO ICD RECIPIENTS A DISREGARDED RESOURCE? A DESCRIPTIVE CROSS-SECTIONAL RETROSPECTIVE MULTI-CENTRE QUESTIONNAIRE STUDY OF THE PSYCHOLOGICAL PROFILE OF ICD PARTNERS, DETERMINANTS OF THEIR REHABILITATION NEEDS AND SATISFACTION WITH INDIVIDUAL INFORMATION AND SUPPORT OFFERED.

Poster session 26. Chairmen: Helle Prætorius, Birgitte S. Kousholt, Kristian Havmand Mortensen

P26.01 Anne Dorte Blankholm. MR ANGIOGRAPHY WITHOUT GADOLINIUM CONTRAST AGENTS
P26.02 Steen Fjord Pedersen. MRI ASSESSMENT OF ENDOTHELIAL DAMAGE AND ANGIOGENESIS IN PORCINE CORONARY ARTERIES USING GADOFOSVESET
P26.03 Christoffer Laustsen. NON-INVASIVE METABONOMICS ON DIABETIC RATS BY HYPERPOLARIZED 13C MRI
P26.04 Anette Luther Christensen. POISSON REGRESSION MODELS OUTPERFORM THE GEOMETRICAL MODEL IN ESTIMATING THE INTENSITY OF SEASONAL VARIATION: A SIMULATION STUDY
P26.05 Christian Alcaraz Frederiksen. PREOPERATIVE ASSESSMENT OF CARDIAC FUNCTION BY SPECKLE TRACKING ULTRASOUND
P26.06 Sanne Bøjet Larsen. REDUCED PLATELET RESPONSE TO ASPIRIN IN PATIENTS WITH PREVIOUS MYOCARDIAL INFARCTION COMPARED WITH PATIENTS HAVING CORONARY ARTERY DISEASE WITHOUT PREVIOUS MYOCARDIAL INFARCTION
P26.07 Lars Jakobsen. SEX- AND AGE-RELATED DIFFERENCES IN OUTCOME AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION
P26.08 Bent Roni Ranghøj Nielsen. SHORT TERM HYPERGLYCEMIA IMPROVES LEFT VENTRICULAR SYSTOLIC FUNCTION AND INCREASES WALKING DISTANCE IN PATIENTS WITH TYPE 2 DIABETES AND HEART FAILURE.
P26.09 Thomas Larsen. SUPPRESSION OF PLASMA RENIN CONCENTRATION AND ANGIOTENSIN II AFTER INHIBITION OF SYSTEMIC NITRIC OXIDE SYNTHESIS IN HEALTHY SUBJECTS. A DOSE-RESPONSE STUDY.
P26.10 Torjus Skajaa. THE BIOLOGICAL PROPERTIES OF IRON OXIDE CORE HIGH-DENSITY LIPOPROTEIN IN EXPERIMENTAL ATHEROSCLEROSIS
P26.11 Carsten Stengaard. THE ROLE OF BIOMARKER ANALYSIS IN THE PRE-HOSPITAL DIAGNOSIS AND TRIAGE OF HEART ATTACK PATIENTS (THE PRE-HAP STUDY)
P26.12 Michael René Skjelbo Nielsen. THE EFFECT OF LOW-DOSE N-3 FATTY ACIDS ON LEUKOTRIENE BIOSYNTHESIS IN AN OVERWEIGHT POPULATION.

Poster session 27. Chairmen: Lene Braad Hansen, Hans Henrik Møller Nielsen, Kathrine Kleis Tilma

P27.01 Adjmal Nahimi. NEUROPROTECTIVE AND ANTIDYSKINETIC MECHANISMS OF NOREPINEPHRINE IN PARKINSON'S DISEASE
P27.02 Signe Groth Renvillard. NEUROPSYCHOLOGICAL IMPAIRMENT AND HIGH PREVALENCE OF PSYCHIATRIC MORBIDITY IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS
P27.03 Anne Hansen. PAIN FOLLOWING STROKE: A PROSPECTIVE STUDY
P27.04 Mette Buhl Callesen. PATHOLOGICAL GAMBLING IN PARKINSON'S DISEASE
P27.05 Kartheeban Nagenthiraja. PERFORMANCE OF LINEAR AND NON-LINEAR MODELS IN PREDICTING TISSUE OUTCOME IN ACUTE ISCHEMIC STROKE
P27.06 Tue Hartmann. PRETREATMANT MR-SCANNING IN OCD
P27.07 Kari Konstantin Nissen. RECONSTRUCTION OF HERV-F(C)1, ASSOCIATED WITH MULTIPLE SCLEROSIS
P27.08 Kristina Dupont Hougaard. REMOTE ISCHEMIC PERCONDITIONERING IN ACUTE STROKE; AN ENDOGENEOUS MODEL TO GENERATE NEUROPROTECTION.
P27.09 Mikkel Mylius Rasmussen. SCINTIGRAPHIC ASSESSMENT OF COLORECTAL MOTILITY AND EMPTYING FOLLOWING XIAOS PROCEDURE IN SPINAL CORD INJURY PATIENTS

Poster session 28. Chairmen: Michael John Hasenkam, Krista Dybtved Kjærgaard, Jesper Brink Askov

P28.01 Jacob Mørup Schlütter. THE NUMBER OF FETAL CELLS IN MATERNAL BLOOD IS ASSOCIATED TO EXERCISE AND FETAL GENDER

P28.02 Tina Rask Elmholdt. IS IMATINIB MESYLATE AN EFFECTIVE TREATMENT OF NEPHROGENIC SYSTEMIC FIBROSIS? AN OPEN-LABEL CLINICAL TRIAL

P28.03 Kathrine Kleis Tilma. TOPICAL TREATMENT FOR ONE WEEK WITH LATANOPROST BUT NOT DICLOFENAC REDUCES THE DIAMETER OF DILATED RETINAL ARTERIOLES IN PATIENTS WITH TYPE 1 DIABETES MELLITUS AND MILD RETINOPATHY

P28.04 Ole Halfdan Larsen. KAOLIN ACTIVATED THROMBOELASTOGRAPHY FAILS TO DISTINGUISH DILUTIONAL COAGULOPATHY FROM THROMBOCYTOPENIA

P28.05 Chris Bath Søndergaard. STEM CELL THERAPY OF SEVERE CORNEAL DISORDERS: TRANSCRIPTOME ANALYSIS OF DISCRETE CORNEAL SUBPOPULATIONS AND DEVELOPMENT OF ANIMAL ORIGIN FREE (AOF) CULTURE SYSTEMS

P28.06 Trine Borup Andersen. PREDICTION OF RENAL FUNCTION (GFR) FROM CYSTATIN C AND CREATININE IN CHILDREN: BODY CELL MASS INCREASES ACCURACY OF THE ESTIMATE.

P28.07 Mie Hessellund Samson. TREFOIL FACTOR FAMILY PEPTIDES IN HUMAN CYCLICAL CERVICAL MUCUS. METHOD EVALUATION AND RESULTS.

P28.08 Andrew Siefert, Georgia Tech/Emory

Poster session 29. Chairmen: Kirsten Lomborg, Thomas Greve, Anders Jensen

P29.01 Christian Dalgas. THE EFFECT OF FREE FATTY ACIDS ON AMINOOXYACETATE INDUCED CARDIOPROTECTION

P29.02 Hjördis Osk Atladõttir. NEONATAL COMPLICATIONS AND AUTISM SPECTRUM DISORDERS

P29.03 Mirela Dzeko, IPSILATERAL VERSUS DIAGONAL ASSESSMENT OF PULSE WAVE VELOCITY IN THE LARGE ARTERIES: IS THE RESULT DIFFERENT?

P29.04 Peter Bondeven Petersen, POST-OPERATIVE QUALITY ASSESSMENT IN PATIENTS WITH RECTAL CANCER BY MRI OF THE PELVIS

P29.05 Ninna Sønderby Lund, METALLOTHIONEINS AND BETA CELL FUNCTION DURING GLUCOSE OR PALMITATE STRESS

P29.06 Janus Adler Hyldebrandt, RIGHT VENTRICLE PHYSIOLOGY, METABOLISM AND PHARMACOLOGICAL RESPONSE IN HEALTHY NEWBORN PIGS IN ASSOCIATION WITH RIGHT VENTRICULAR ISCHEMIA, HYPERTROPHY AND DILATATION

P29.07 Johan Frederik Berg Arendt, HOW TO EXPLAIN AN ELEVATED LEVEL OF PLASMA VITAMIN B12

P29.08 Linn Berger Håkonsen, DOES WEIGHT LOSS IMPROVE SEMEN QUALITY AND REPRODUCTIVE HORMONES?RESULTSFROM A COHORT OF SEVERELY OBESE MEN

P29.09 Majbritt Jeppesen, INTERNETBASED INTERACTIVE DECISION SUPPORT IN THE TREATMENT OF TYPE 2 DIABETES

P29.10 Pall Karlsson, DETERMINATION OF INTRAEPIDERMAL NERVE FIBER DENSITY AND SMALL FIBER FUNCTION IN HEALTHY MEN AND IN PATIENTS WITH NEUROPATHY

Third year PhD students section 30.

30.01 Tanja Tvistholm Sikjær. REDUCED MUSCLE STRENGHT IN PATIENTS WITH LONG STANDING HYPOPARATHYROIDISM COMPARED TO HEALTHY CONTROLS.

30.02 Magdalena Julia Dabrowska. IMPACT OF GROWTH FACTOR INDEPENDENCE 1 IN HUMAN T-CELL LYMPHOMAS; PATHOGENIC POTENTIAL IDENTIFIED BY INSERTIONAL MUTAGENESIS IN A MURINE T-CELL LYMPHOMA MODEL

30.03 Vivien Schack. A REDUCED PHOSPHORYLATION RATE ACCOUNTS FOR THE FUNCTIONAL DISTURBANCE OBSERVED FOR SEVEN NA^+,K^+-ATPASE MUTATIONS ASSOCIATED WITH THE NEUROLOGICAL DISORDER: FAMILIAL HEMIPLEGIC MIGRAINE TYPE-2 (FHM-2)

30.04 Jimmi Søndergaard. INTER- AND INTRA-FRACTION MOTION OF THE BLADDER TUMOR BASED ON PERITUMORAL LIPIODOL INJECTIONS IN THE BLADDER WALL.
30.05 Lise Juul. INVOLVEMENT OF NURSES IN TYPE 2 DIABETES CARE IN DANISH GENERAL PRACTICE
30.06 Anders Jensen. MICROBIAL DIVERSITY OF INFECTED AND HEALTHY TONSILS
30.07 Ivana Konvalinka. NEURAL OSCILLATIONS OF INTERPERSONAL COORDINATION: DUAL EEG AND MEG STUDIES OF JOINT TAPPING
30.08 Stine Christensen. SORLA REGULATES LIPOPROTEIN LIPASE ACTIVITY BY INTRACELLULAR TRAFFICKING
30.09 Jenny Blechingberg Friis. REGULATION OF GENE EXPRESSION BY THE FET-PROTEIN FAMILY
30.10 Thais A. Pedersen. LATE CARDIOVASCULAR MORBIDITY IN REPAIRED AORTIC COARCTATION: NO CURE FOR THE AORTIC COARCTATION SYNDROME
30.11 Ruta Tuckuviene. PEDIATRIC THROMBOEMBOLISM IN DENMARK 1994-2006: A NATIONWIDE POPULATION-BASED STUDY
30.12 Vibeke Bregnballe. PARENTING ADOLESCENTS WITH CYSTIC FIBROSIS: ADOLESCENTS' POINTS OF VIEW
30.13 Gitte Dam. ACUTE EFFECTS OF INGESTION OF BRANCHED-CHAIN AMINO-ACIDS ON MUSCLE AMMONIA METABOLISM
30.14 Thomas Greve. IS THE *LYTA*-GENE IN THE MITIS GROUP OF THE VIRIDANS STREPTOCOCCI IN GENERAL DIFFERENT IN EACH GROUP MEMBER?
30.15 Birgitte S. Kousholt. NATRIURETIC PEPTIDE INFUSION IN MYOCARDIAL ISCHEMIA/REPERFUSION IS ASSOCIATED WITH REDUCED MYOCARDIAL DAMAGE AND INVERSED ENDOGENOUS RELEASE OF NATRIURETIC PEPTIDE IN PIGS
30.16 Kaspar Renÿ Nielsen. POLYMORPHISMS IN INFLAMMATORY MEDIATORS - RELATION TO DISEASE ACTIVITY IN B-CELL DISEASES
30.17 Asger Granfeldt. 7.5% NACL WITH ADENOSINE, LIDOCAINE AND MG2+ REDUCES FLUID REQUIREMENT AND IMPROVES KIDNEY FUNCTION FOLLOWING 70% BLOOD LOSS IN A PIG MODEL OF SEVERE HEMORRHAGIC SHOCK
30.18 Flemming Bandholm Jakobsen. THE LONG TERM IMPACT OF HEALTH PROFESSIONAL STUDENTS LEARNING IN AN INTERPROFESSIONAL TRAINING UNIT
30.19 Lene Bastrup Jørgensen. TITLE: INNOVATIVE METHOD FOR INVESTIGATING COPD PATIENTS' STRATEGIES FOR COPING WITH BREATHLESSNESS
30.20 Nis Borbye Pedersen. IDENTIFICATION OF REGULATORY PROTEINS OF THE KIDNEY SPECIFIC NA-CL COTRANSPORTER, NCC
30.21 Malene Bek-Thomsen. EVOLUTION OF *STREPTOCOCCUS PNEUMONIAE* INTO FUNCTIONALLY DISTINCT SUBPOPULATIONS
30.22 Marie Bagger Bohn. THREE-DIMENSIONAL KINEMATIC ANALYSIS OF KNEE ROTATIONAL STABILITY IN ACL-DEFICIENT PATIENTS DURING PIVOTING.
30.23 Janne Lund Helverskov. EMPIRICAL SUPPORT FOR A RECLASSIFICATION OF EATING DISORDERS NOT OTHERWISE SPECIFIED
30.24 Lisbeth Venø Kruse. THE HERITABILITY OF ATOPIC DISEASE - ESPECIALLY ALLERGIC RHINITIS
30.25 Camilla Molich Hoff. THE IMPORTANCE OF HAEMOGLOBIN LEVEL AND EFFECT OF TRANSFUSION IN HNSCC PATIENTS TREATED WITH RADIOTHERAPY - EVALUATED IN THE RANDOMIZED DAHANCA 5 STUDY
30.26 Jeppe Grøndahl Rasmussen. TRYPSINIZATION AND PROLONGED HYPOXIC CULTURE INCREASES THE EXPRESSION OF GENES RELATED TO ANGIOGENESIS IN HUMAN ADIPOSE TISSUE-DERIVED STEM CELLS
30.27 Maria Luise Salskov-Iversen. THE CASPASE-5 EXPRESSION IS UPREGULATED IN PSORAISIS
30.28 Lotte Ørneborg Rodkjær. DISCLOSURE DECISIONS: A GROUNDED THEORY OF HIV-POSITIVE PERSONS COPING WITH DISEASE-RELATED STRESSORS
30.29 Eduardo Adrian Garza Garza Villarreal. SONATA ANALGESICA: MUSIC, PAIN AND THE PLACEBO EFFECT
30.30 Hans Henrik Møller Nielsen. SINGLE CENTRE TRANSCATHETER AORTIC VALVE IMPLANTATION USING THE EDWARDS SAPIEN VALVE
30.31 Anders Knudsen. STEREOLOGICAL ASSESSMENT OF ISCHEMIA/REPERFUSION INJURIES IN THE RAT LIVER. EFFECTS OF ISCHEMIC PRE- AND POSTCONDITIONING

30.32 Jasna Furtula. TRIPLE STIMULATION TECHNIQUE APPLIED ON ALS PATIENTS AND CONTROL SUBJECTS

30.33 Michael Winterdahl. TRACER INPUT FOR KINETIC MODELLING OF LIVER PHYSIOLOGY DETERMINED WITHOUT SAMPLING PORTAL VENOUS BLOOD IN PIGS

30.34 Rikke Vestergaard. BONE HEALING AFTER MEDIAN STERNOTOMY: IS OSTENE® SUPERIOR TO BONE WAX?

30.35 Sine Nygaard Langerhuus. DIETARY FISH OIL REDUCES PLASMA PGE_2 METABOLITE CONCENTRATION AND WEIGHT-GAIN SUPPRESSION IN A PORCINE MODEL OF EARLY AORTIC VASCULAR PROSTHETIC GRAFT INFECTION

30.36 Iva Susanna vio Streym Thomsen. ASSESSING VARIABILITY OF PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY OF TIBIA IN 9 MONTH OLD INFANTS.

30.37

30.38 Rune Thomsen. DEVELOPING THE BOYDEN CHAMBER ASSAY FOR PURIFICATION OF LOCALIZED RNAS IN ASTROCYTIC CELLS

30.39 Iben Blaabjerg Sundtoft. CERVICAL INSUFFICIENCY CAUSING PRETERM BIRTH DUE TO LOW CERVICAL COLLAGEN CONCENTRATION

30.40 Pia Kirkegaard. DEVELOPMENT OF A COMPLEX INTERVENTION IN RISK COMMUNICATION USING ACTION RESEARCH AS METHODOLOGY

30.41 Anna Pietraszek. POSTPRANDIAL DYSMETABOLISM - THE EFFECTS OF MONOUNSATURATED VS. SATURATED LIPIDS ON LIPID AND CARBOHYDRATE METABOLISM AND INFLAMMATION IN HEALTHY 1^{ST} DEGREE RELATIVES OF PATIENTS WITH TYPE 2 DIABETES

30.42 Filippo Peder D'Andrea. CANCER STEM CELLS INTRINSIC RADIOSENSITIVITY IN A MESENCHYMAL MOUSE MODEL FOR SOFT TISSUE SARCOMA

30.43 Nicklas Heine Staunstrup. A TRANSGENIC PORCINE MODEL FOR PSORIASIS AND A NOVEL SKIN-SENSOR SYSTEM

30.44 Lene Sundahl Mortensen. EFFECTS OF DIFFERENT FRACTIONS OF WHEY PROTEIN ON POSTPRANDIAL LIPID AND HORMONE RESPONSES IN TYPE 2 DIABETES

30.45

30.46 Kasper Toustrup. HYPOXIC GENE EXPRESSION CLASSIFICATION WITH PROGNOSTIC AND PREDICTIVE IMPACT IN HEAD AND NECK SQUAMOUS CELL CARCINOMAS (HNSCC)

30.47

30.48 Francesco Trepiccione. ACUTE LITHIUM EFFECT ON INNER MEDULLARY COLLECTING DUCT

30.49 Kristian Havmand Mortensen. HAEMOSTATIC BALANCE IN TURNER SYNDROME

30.50 Janne Lebeck. GENDER SPECIFIC REGULATION OF AQUAPORIN-9 AND GLYCEROL KINASE IN STARVED RATS

30.51 Dorte Rytter. MATERNAL INTAKE OF FISH OIL DURING PREGNANCY AND BLOOD PRESSURE IN THE 19 YEAR OLD OFFSPRING

30.52 Claus Tvedesøe. ENHANCEMENT OF ANTI-TUMOR ACTIVITY BY USING IL-2 IN COMBINATION WITH CANCER THERAPY

30.53 Marta Bauerek. EFFECT OF DIETARY CHOLESTERYL ESTERS ON THE PLASMA LIPID LEVELS IN LDLR-DEFICIENT MICE

30.54 Emil Kofod-Olsen. HUMAN HERPESVIRUS-6B PROTEIN U20 IS A NOVEL INHIBITOR OF TNF RECEPTOR SIGNALLING

30.55 Krista Dybtved Kjærgaard. RELIABILITY OF ^{51}CR-EDTA PLASMA AND URINARY CLEARANCE AS A MEASURE OF RESIDUAL RENAL FUNCTION IN DIALYSIS PATIENTS

30.56 Stefan W. Harders. LIMITED VALUE OF ^{99M}TC DEPREOTIDE SPECT COMPARED TO CT FOR THE EVALUATION OF PULMONARY LESIONS

30.57 Pernille Kure Vandborg. RELATIONSHIP BETWEEN ACUTE INTERMEDIATE-ADVANCED BILIRUBIN ENCEPHALOPATHY, SERUM BILIRUBIN LEVELS AND CHRONIC BILIRUBIN ENCEPHALOPATHY IN LATE PRETERM AND TERM NEONATES

30.58 Casper Nielsen. A NEW SAMPLE PREPARATION METHOD TO PREVENT INTERFERENCES FROM L-LACTATE DEHYDROGENASE IN THE QUANTITATIVE DETERMINATION OF D-LACTATE IN PLASMA.

30.59 Simon Rasmussen. INDUCTION OF AUTOPHAGY DURING HERPES SIMPLEX VIRUS INFECTION BY A POTENTIAL NOVEL MECHANISM

30.60 Tina Storm. NOVEL CUBN MUTATION REVEALS NO DETECTABLE RENAL CUBILIN AND SUGGESTS THAT IT IS NOT VITAL FOR HUMAN EMBRYONIC DEVELOPMENT

30.61 Michael Smærup Brandt. IT-SUPPORT IN HOME REHABILITATION OF GERIATRIC PATIENTS WITH VESTIBULAR DYSFUNCTION

30.62 Thomas Maribo. POSTURAL STABILITY IN LOW BACK PAIN PATIENTS: RELIABILITY OF SWAY MEASURES ON A PORTABLE FORCE PLATFORM

30.63 Martin Majlund Mikkelsen. INSULIN RESISTANCE, ADIPONECTIN AND ADVERSE OUTCOMES FOLLOWING ELECTIVE CARDIAC SURGERY: A PROSPECTIVE FOLLOW-UP STUDY

30.64 Jesper Brink Askov. NOVEL PAPILLARY MUSCLE FORCE TRANSDUCER: INITIAL TESTS AND RESULTS

30.65 Anne-Cathrine Bareid Østby. MULTIPLEX PCR DIAGNOSTICS OF 12 COMMUNITY RESPIRATORY VIRUSES THROUGH FOUR YEARS

30.66 Michael Kjeldager Tjørnild. REPEATABILITY AND DETECTION QUALITY IN DOUBLE DXA-SCANS - A CLINICAL COMPARISION OF 2 SOFTWARES

30.67 Chunsen Wu. RISK OF CANCERS AND CARDIOVASCULAR DISEASES IN OFFSPRING EXPOSED TO A DIABETIC ENVIRONMENT IN UTERI

30.68 Morsi Abdallah. INTRAUTERINE INFLAMMATION AND AUTISM: MEASUREMENTS OF SELECTED NEUROTROPHINS AND CYTOKINES LEVELS IN AMNIOTIC FLUID SAMPLES FROM A DANISH HISTORIC BIRTH COHORT

Abstracts

Abstracts for Fogh Nielsen prize competition, oral presentations (O1-O4) and poster sessions (P01-P29), including abstracts not presented as poster (30.01 – 30.68 - third year students participating as chairmen and the like).

Marianne Gerberg Skals

ALPHA-HAEMOLYSIN FROM ESCHERICHIA COLI INDUCES ATP RELEASE PRIOR TO CELL LYSIS

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The pore forming α-haemolysin from E. coli (HlyA) uses P2X-receptor activation to induce lysis of human, murine and equine erythrocytes. The HlyA-induced activation of P2X receptors is a consequence of ATP release, as scavengers of ATP abolish the haemolytic effect of HlyA. Haemolysis caused by HlyA is preceded by considerable cell shrinkage, during which the erythrocytes are provoked to expose phospatidylserine (PS) in the outer leaflet of the cell membrane. Interestingly PS exposure is known to be triggered by ATP alone in human erythrocytes, and is believed to be an important factor for recognition and fagocytosis of erythrocytes by monocytes and macrophages. Here we investigate the HlyA induced ATP release of erythrocytes. ATP release is measured via the luciferine/luciferase method. Addition of HlyA, in concentrations that does not produce any detectable haemolysis within 30 minutes, produced a significant ATP release from human erythrocytes. This rise in extracellular ATP was apparent already few minutes after application of HlyA and was partially inhibited with the non-selective pannexin blocker carbenoxolone. The released ATP is involved in the HlyA-induced shrinkage as P2 receptor antagonists significantly reduced the HlyA-induced erythrocyte shrinkage and PS-exposure. In conclusion, the pore-forming toxin HlyA releases significant amounts of ATP long before any lysis can be detected. This ATP can for the main part be ascribed to pannexin channel activation, although we cannot exclude that a smaller amount of ATP is released through the HlyA pore itself. The releases ATP is important for the following erythrocyte swelling and PS exposure.

Mads Fuglsang Kjølby

A NOVEL DRUG TARGET FOR THE TREATMENT OF HYPERCHOLESTEROLEMIA?

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Introduction: Many risk factors for developing atherosclerosis have been identified over the years. Despite of this, diseases related to atherosclerosis are still the leading cause of death in the western world. However, genome-wide analysis (GWAS) have now allowed for the identification of novel genes, so-called modifier genes, involved in multifactorial diseases. A locus on chromosome 1p13 has recently been identified having strong association to coronary artery disease and high LDL-cholesterol levels. Because this locus covers three genes, CELSR2, PSRC1, and SORT1, respectively, the responsible gene remained elusive.

Methods and Results: To investigate if SORT1, encoding the receptor sortilin, is the gene responsible for modifying LDL-cholesterol metabolism, we used sortilin-deficient mice. Sortilin is, among other tissues, expressed in the liver; an organ critical to lipoprotein metabolism. We found that sortilin attenuates the LDL-cholesterol elevation1observed in the LDL-receptor knockout mice by 20-30% ($P<0.009$), and that absence of sortilin expression reduces secretion of lipoproteins by 22% ($P=0.006$). Importantly, this reduction in plasma cholesterol translated into a 60% reduction in atherosclerosis.

Conclusion: We conclude that sortilin directly affects plasma cholesterol. This

finding together with the results of GWAS studies in humans show a novel connection between the receptor sortilin and coronary artery disease and LDL-cholesterol. Sortilin may, thus, prove to be a drug target in future treatment of hypercholesterolemia.
1) Kjolby et al., Cell Metabolism, 2010.

Mette Hagensen

ENDOTHELIAL AND SMOOTH MUSCLE CELLS IN ALLOGRAFT VASCULOPATHY DO NOT DERIVE FROM CIRCULATING PROGENITOR CELLS BUT MIGRATE INTO THE GRAFT FROM THE RECIPIENT VASCULATURE

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Background - Current hypotheses suggest that circulating progenitor cells contribute to endothelial cells (ECs) and smooth muscle cells (SMCs) in allograft vasculopathy (AV), but this remains controversial because studies so far have been unable to distinguish between cells migrating into allografts from the flanking vasculature and those homing from the blood. In the present study, we developed a double-transplantation technique to overcome this problem and applied it to a model of hyperlipidemia-accelerated AV.
Methods and Results - As expected, cells of BALB/c carotid allografts were eradicated when transplanted into $eGFP^{+}apoE^{-/-}$ C57BL/6 (B6) mice without immunosuppression, and AV lesions formed by recipient-derived $eGFP^{+}$ ECs and SMCs. To analyze whether the $eGFP^{+}$ cells migrated into allografts from the flanking vasculature, we inserted BALB/c allografts into segments of $eGFP^{+}apoE^{-/-}$ B6 carotid artery that were previously transplanted into $apoE^{-/-}$ B6 mice. Again, SMCs and ECs of AV lesions were $eGFP^{+}$indicating massive migration of recipient cells through the anastomosis sites. Conversely, to track progeny of circulating progenitor cells, we inserted BALB/c grafts into segments of $apoE^{-/-}$ B6 carotid artery that were previously transplanted into $eGFP^{+}apoE^{-/-}$ B6 mice. Among 672 ECs and 3162 SMCs analyzed in AV lesions, we did not find a single $eGFP^{+}$ cell.
Conclusion – Migrating cells from the flanking recipient vasculature, rather than circulating progenitor cells, constitute the main if not the only source of SMCs and ECs in this murine model of AV.

O01.01 Britt Christensen

ERYTHROPOIETIN ADMINISTRATION ACUTELY STIMULATES RESTING ENERGY EXPENDITURE IN HEALTHY YOUNG MEN

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Treatment with recombinant human erythropoietin (rHuEpo) improves insulin sensitivity in patients with end-stage renal disease, and animal studies indicate that Epo increases fat oxidation. However, the metabolic effects of rHuEpo have never been experimentally studied in healthy humans. The objective was to investigate the effects of an acute rHuEpo bolus on substrate metabolism and insulin sensitivity in health young men.
Ten healthy young men were studied in a single-blinded, randomised cross-over design with a 2-wk wash-out period receiving 400 IU/kg rHuEpo or placebo on two separate occasions. Substrate metabolism was evaluated by indirect calorimetry and tracer infusions, insulin sensitivity by a hyperinsulinemic euglycemic clamp, and levels of uncoupling proteins (UCP) by PCR.
Resting energy expenditure (REE) increased significantly after rHuEpo [Basal; 1863.3 + 67.2 (placebo) vs. 2041.6 + 81.2 (rHuEpo) $p<0.001$, Clamp; 1903.9 + 68.3 (placebo) vs. 2015.7 + 114.4 (rHuEpo), $p=0.03$]. This increase in REE could not be explained by changes in mRNA levels of UCP2 or UCP3 levels. Fat oxidation in the basal state tended to be higher after rHuEpo ($p=0.05$), whereas the suppression of fat oxidation during the clamp was significantly higher after rHuEpo ($p=0.03$). Insulin stimulated glucose disposal and glucose metabolism did not change

significantly in response to rHuEpo. Likewise, whole-body and forearm protein metabolism was unchanged throughout the study.
In, conclusion, a single injection of rHuEpo acutely increases REE in healthy human subjects. This calorigenic effect is not accompanied by distinct alterations in the pattern of substrate metabolism or insulin sensitivity.

O01.02 Jens Ølholm

SIRT1 DEPENDENT ANTI-INFLAMMATORY EFFECT OF RESVERATROL ON MCP-1 EXPRESSION AND SECRETION IN HUMAN ADIPOSE TISSUE

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OBJECTIVE: Human obesity is characterized by increased production of pro-inflammatory substances from the adipose tissue. Another hallmark of inflammation is increased adipose tissue macrophage infiltration and Monocyte Chemoattractant Protein (MCP)-1 play an essential role in the early events in this process.
Calorie restriction improves metabolic profile. These effects are dependent upon activation of the Sirt1 enzyme and can be mimicked by a natural phytoalexin, resveratrol (RSV), which is a potent Sirt1 activator. Sirt1 has recently been found in human adipose tissue and we surmise that the beneficial role of RSV in improving metabolic profile are at least in part due to altering MCP-1 expression and secretion through Sirt1 dependent pathways.
DESIGN: The effect of RSV on IL1β induced change of MCP-1 mRNA gene expression and secretion were measured in human adipose tissue explants and in differentiated human adipocytes in primary culture.
RESULTS: Exposure to IL1β for 24 hours increased secretion of MCP-1 ($p<0.05$) and increased mRNA expression ($p<0.05$) accordingly. Concomitant incubations with RSV reversed the IL1β-stimulated secretion and gene expression.Incubation with sirtinol (an inhibitor of the SIRT-1 enzyme activity) was able to diminish the anti-inflammatory effect of RSV ($p<0.05$) in cultured adipocytes, indicating that the anti-inflammatory effects of RSV are mediated through the SIRT-1 enzyme
CONCLUSION: Inhibition of MCP-1 expression in human adipose tissue may represent a novel mechanism of resveratrol in preventing obesity-related pathologies.

O01.03 Jens Holmer-Jensen

ACUTE DIFFERENTIAL EFFECTS OF DIETARY PROTEIN QUALITY ON POSTPRANDIAL LIPAEMIA IN OBESE NON-DIABETIC SUBJECTS

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Objective: To evaluate the acute effect of dietary protein quality on postprandial lipaemia in obese non-diabetic subjects
Methods: 11 obese non-diabetic subjects participated in a single-blinded, randomized, acute clinical intervention study with cross-over design. All participants consumed four fat-rich meals on four different days. All meals consisted of an energy-free soup + 80g of fat served with 45g of carbohydrate and 45g of protein from one of four dietary protein sources (Cod protein (COD), whey isolate (WHEY), gluten (GLU) and casein (CAS)). Blood samples were drawn during the 8h postprandial period.
Results: We found significantly higher plasma triglyceride (p-tg) net iAUC after GLU-meal (42%, $p=0.017$) compared to WIS-meal. P-tg net iAUC was also higher after COD-meal (29%, $p=0.078$) and CAS-meal (14%, $p=0.43$) compared to WHEY-meal. P-insulin net iAUC after 240 minutes was higher after WHEY-meal than after COD-meal (65%, $p<0.001$), GLU-meal (77%, $p<0.001$) and CAS-meal (34%, $p=0.002$), respectively. The free fatty acids net iAUC was suppressed more potently after CAS-meal (-47 mmol/L) than after COD-meal (-2.6 mmol/L, $p=0.01$) and GLU-meal (+5 mmol/L, $p=0.007$)
Conclusion: In obese non-diabetic subjects, plasma triglycerides were lower after a fat rich meal supplemented with whey isolate compared to supplementation with gluten, cod or casein. Interestingly, whey isolate is more insulinotropic than the

three other dietary proteins. Free fatty acids were suppressed more pronounced by the casein supplemented meal than after cod and gluten meals. Dietary supplementation with whey isolate may prove beneficial in reducing cardiovascular risk in obese non-diabetic subjects

O01.04 Marie Louise Tørring

TIME TO DIAGNOSIS AND MORTALITY IN COLORECTAL CANCER: A COHORT STUDY IN PRIMARY CARE

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BACKGROUND: Several studies of delay and mortality in colorectal cancer (CRC) patients have shown a 'waiting time paradox' where patients with short waiting times have higher mortality than other patients. This has led some clinicians to doubt the benefits of expediting diagnosis for CRC patients. However, failure to account for clinical triage may have led to false conclusions.

OBJECTIVE: To analyse the association between the diagnostic interval (time from first presentation of symptoms until diagnosis) and 3-year mortality after diagnosis of CRC while making patients comparable at the time of first presentation in primary care.

DESIGN: Population-based prospective cohort study.

SETTING: Danish county between 2004 and 2005.

PARTICIPANTS: 268 CRC patients who attended primary care before diagnosis.

RESULTS: Compared to patients presenting with symptoms suggestive of cancer or any other serious illness, the odds of experiencing ≥12 weeks versus 5-11 weeks of diagnostic interval were 3.72-fold (95%CI: 2.04, 6.78) higher for patients presenting with vague symptoms not directly relating to cancer or any other serious illness. In patients with alarm or serious symptoms, the adjusted 3-year mortality odds ratio decreased with diagnostic intervals up to five weeks and then increased with longer diagnostic intervals (p=0.002). A reverse association was seen for patients with vague symptoms, although not statistically significant.

CONCLUSION: The study shows the waiting time paradox together with an increasing mortality with longer diagnostic intervals, but only in patients presenting with alarm or serious symptoms, i.e. when advanced disease and rapid investigations are expected.

O01.05 Ane Bærent Fisker

ADVERSE EVENTS AFTER ADMINISTRATION OF VITAMIN A WITH EPI VACCINES AFTER 6 MONTHS OF AGE IN GUINEA-BISSAU

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Background: We are currently testing the effect of the WHO policy of providing vitamin A supplementation (VAS) at vaccination contacts. Based on prior observations we expect beneficial effects of VAS with live (measles and/or yellow fever) vaccines, but negative effects with inactivated (diphtheria-tetanus pertussis (DTP) or pentavalent (DTP-HiB-HBV)) vaccines; the effects being strongest in girls. In a subgroup we investigated whether VAS had sex-differential adverse events, and whether VAS had sex-differential effects on known adverse events after the vaccines.

Methods: Children were randomised to VAS or placebo at the vaccination contact (day 0) and visited on day 1,2,3,7,14,12 and 31. We interviewed the caretaker, assessed the fontanel and measured temperature. We defined adverse events after VAS as signs of increased intracranial pressure (ICP) on day 1; after a killed vaccine as fever on day 1-3; after live vaccines as fever on day 14.

Results: We obtained information on 1672 children; 1143 had received live and 529 inactivated vaccines. VAS was associated with signs of increased ICP in boys

(Prevalence Ratio (PR):1.59 (95%CI: 1.08-2.33), but not in girls (p=0.004 for interaction between sex and VAS)). VAS had no effect on adverse events after an inactivated vaccine. VAS was associated with more adverse events after a live vaccine in girls (PR:2.48 (1.21-5.08), but tended to be associated with less adverse events in boys (p=0.004 for interaction between sex and VAS).
Conclusion: VAS seems to increase ICP in boys and potentiate adverse events of live vaccines in girls. The results support that the effect of VAS on the immune system vary depending on sex and vaccine type.

O01.06 Lene Hjort

LOW BIRTH WEIGHT DEFINE DESTINCT ETIOLOGIC SUBGROUPS IN AUTISM

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Background
Autism is a neuro-developmental disorder often complicated by co-existing developmental disabilities (CDDs) like mental retardation, epilepsy and birth defects. The autism CDD profile vary by sex since CDDs are more common in girls than in boys. The autism sex ratio is 4:1.
Autism is highly heritable, but specific etiologic pathways are largely unknown and are believed to vary in autism subgroups. Researchers currently struggle to define subgroups based on phenotypic characteristics to yield distinct etiologic pathways.
Low birth weight (<2500g, lbw) is associated with an increased autism risk. Recently, however, one subgroup study reported that lbw is a stronger autism risk factor in girls and in autism with CDDs than in other autism subgroups. This suggest lbw define subgroups in autism with distinct etiologic pathways.
Objectives: To confirm and extend previous findings suggesting lbw define distinct etiologic subgroups in autism
Methods: We conducted a register-based, population-based follow-up study: National birth cohorts 1990-2007 and information on 1. Birth weight, 2. Covariats, 3. Autism and CDD diagnoses in cohort members were retrieved from Danish health registers.
We assessed 1. The overall hazard ratio (HR) of autism and 2. The sex-specific HRs of autism following lbw when compared to a normal birth weight in autism subgroups stratified by CDDs.
Results: Preliminary analyses confirmed a stronger lbw-autism association in girls than in boys, and a stronger lbw-autism association in autism with selected CDDs than for other autism subgroups.
Conclusion: Our results support that lbw, sex and CDDs define distinct etiologic subgroups in autism.

O01.07 Bodil Bjørnshave

CAN COMPLETING REHABILITATION AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) BE PREDICTED, - AN EXPLORATIVE STUDY OF A COPD POPULATION TREATED AT HORSENS REGIONAL HOSPITAL

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Introduction: Denmark offers COPD rehabilitation programs to enable patients to tackle the consequences of COPD, but only a minority of the patients complete these programs. To increase the completion rate, an explorative study was performed, to characterize COPD patients and to identify differences between patients who complete and those who do not complete rehabilitation.
Methods: In- and outpatients with COPD were investigated and those who participated in baseline tests were compared in terms of completion of rehabilitation, drop-out, and no rehabilitation offer.
We obtained data on basic characteristics, co-morbidity, lung-function (FEV1),

dyspnea (MRC), six-minute walking-distance (6MWD), and quality of life (SF36).
Result: The source population counted 521 COPD patients of whom 256 were excluded (diagnosis withdrawn, death, moved away, long-term oxygen, severe illness). The most obvious difference between “completers” and those with no rehabilitation offer was a shorter 6MWD (350 (CI:322;379) metre among those with no rehabilitation offer vs 413 (CI: 379;447)) and a lower perception of their own physical performance despite a higher lung function (FEV1 37% (CI:32;41)) among completers versus 44%(CI:40;48). This difference suggests that lower physical and psychological performance with the same lung function indicates a lower chance of completion.
Conclusion: COPD patients who could potentially benefit most from completing rehabilitation seem to be deselected. A mere 9% completed rehabilitation within the study period and 23% ever completed. This demonstrates that the political target that 60% of COPD patients should be offered rehabilitation is still far away.

O01.08 Christian Fynbo Christiansen

TYPE 2 DIABETES, ANTIDIABETICS AND MORTALITY AMONG INTENSIVE CARE PATIENTS: A DANISH COHORT STUDY

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Introduction: Although patients with diabetes may be at increased risk of critical illness, recent studies suggest mortality similar to non-diabetics. However, none of the studies included information on type of diabetes or on antidiabetic treatment. We therefore examined mortality among ICU patients with and without T2DM, and studied the impact of preadmission antidiabetic treatment on mortality by linking population-based medical databases.
Methods: We identified all adult patients admitted to ICUs at the hospitals in Northern Denmark (population~1.8 million). Diabetics were identified by previous hospital diagnosis of diabetes, diabetes complications, or by redemption of any prescription for antidiabetic drugs within 90 days. Data on ICU treatments and comorbidity were also obtained from medical databases. We used Kaplan-Meier to estimate 30-day and 1-year mortality, and Cox regression analyses, controlling for age, gender, and comorbidity, to compare mortality rates.
Results: We included 33,960 ICU patients, 3,752 (11.0%) had T2DM and 30,208 (89.0%) did not have diabetes. T2DM patients were older and had more comorbidities than non-diabetics.
The crude 30-day mortality was higher in patients with T2DM compared with non-diabetics (15.0% vs. 22.7%). The adjusted hazard ratio was 1.2 (95% 1.1-1.3), but lower in users of metformin (HR=1.0, 95%CI: 0.8-1.3) or users of any antidiabetic combination (HR=1.0, 95%CI: 0.9-1.2). A similar pattern was found for 1-year mortality.
Conclusions: Among ICU patients, type 2 diabetes was associated with an increased 30-day and 1-year mortality compared with non-diabetics; however, metformin users had mortality similar to non-diabetics.

O02.02 Anne Stidsholt Roug

FLOW CYTOMETRIC DETECTION OF MINIMAL RESIDUAL DISEASE IN ACUTE MYELOID LEUKEMIA - THE ADDITION OF HMICL AND CD123 ADD TO SENSITIVITY AND APPLICABILITY

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The outcome of acute myeloid leukemia (AML) is strongly correlated to the extent of minimal residual disease (MRD) at remission. Fusion transcripts, over-expressed genes and mutated genes have been employed in MRD quantification by RQ-PCR and are applicable for 30% - 80% of all patients. More recently, flow cytometry (FCM) has been implemented as an additional tool for MRD detection employing

strict gating criteria in detection of leukemia associated aberrant immunophenotypes (LAIPs). We have identified human Myeloid Inhibitory C-type Lectin (hMICL) as a candidate for AML marking at diagnosis and relapse in a study of more than 150 patients. Importantly, we found expression of hMICL in the progenitor populations (defined as CD34+CD38- or CD117+CD38-) in AML cases contrary to healthy donors. CD123 is myeloid progenitor marker expressed in the majority of AML cells at diagnosis. We hypothesized that the combination of hMICL and CD123 might serve as widely applicable MRD markers in AML and as such improve sensitivity for this approach. We performed a prospective study encompassing 38 patients with 74 follow up samples. Importantly, the assay was performed in strict parallel with other LAIPs, i.e. with no special provisions for the new markers. The FCM assay correlated to available data from the most sensitive RQ-PCR marker of a series of molecular aberrations (p=0.37, McNemars chi^2 test). Qualitative discordance was reduced due to a fourfold reduction of patients with FCM negative results but positive RQ-PCR result. The quantitative correlation coefficient between RQ-PCR and FCM increased from 0.46 to 0.7 by addition of hMICL and CD123.

O02.03 Ole Schmeltz Søgaard

IMPROVING THE IMMUNOGENICITY OF PNEUMOCOCCAL CONJUGATE VACCINE IN HIV-INFECTED ADULTS WITH A TOLL-LIKE RECEPTOR 9 AGONIST ADJUVANT: A RANDOMIZED, CONTROLLED TRIAL

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Background. Persons infected with human immunodeficiency virus (HIV) are often hyporesponsive to immunization, including pneumococcal vaccines. We hypothesized that adding CPG 7909, a toll-like receptor 9 (TLR9) agonist and vaccine adjuvant, to 7-valent pneumococcal conjugate vaccine (7vPnC) would increase its immunogenicity in HIV-infected adults.

Methods. We performed a double-blind, placebo-controlled, phase 1b/2a trial randomizing HIV-positive patients to receive double doses of 7vPnC (Prevnar) at 0 and 3 months and 1 dose of 23-valent pneumococcal polysaccharide vaccine (PPV-23; Pneumo Novum) at 9 months, with experimental patients receiving 1 mg of CPG 7909 added to each of their 3 vaccine doses. Immunogenicity and safety were evaluated for up to 10 months. The primary end point was the proportion of vaccine high responders at 9 months, defined as a 2-fold increase in IgG levels to ≥ 1 μg/mL for at least 5 of 7 of the 7vPnC serotypes.

Results. Ninety-seven participants were included in the study. The proportion of vaccine high responders was higher in the experimental group (n=48) than among controls (n=49; 48.8% vs 25.0%; P=0.02) at 9 months. Greater proportions of high responders were also observed at 3 (51.1% vs 39.6%; P=0.26), 4 (77.3% vs 56.3%; P=.03), and 10 months (87.8% vs 51.1%; P<0.001). Mild systemic and injection site reactions to 7vPnC were more common in the experimental group than the control group (100% vs 81.3%; P=0.002). No adverse effects on CD4+ cell count or organ functions occurred in either group.

Conclusions. The addition of a TLR9 agonist to 7vPnC significantly enhanced the proportion of vaccine high responders.

O02.04 Rasmus Boye Kjellerup

THE EXPRESSION OF DUAL SPECIFICITY PHOSPHATASE 1 IS DYSREGULATED IN PSORIASIS VULGARIS

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The dual specificity phosphatase 1 (DUSP1) is an important negative regulator of p38 MAPK activity. The purpose of this study was to investigate DUSP1 in psoriasis. The experimental setup included in vitro culturing of normal human epidermal keratinocytes (NHEKs), punch biopsies from nonlesional and lesional skin from patients with psoriasis or nickel-induced allergic contact dermatitis, and RT-qPCR.

We found that the DUSP1 mRNA expression was significantly induced in NHEKs in response to stimulation with IL-1beta (36 fold) or TNF-alpha (9 fold). For both stimuli the DUSP1 mRNA expression peaked after 1 hour and returned to baseline after 3 hours. Using chemical inhibitors, we demonstrated that the IL-1beta-induced expression of DUSP1 was mediated through the p38 MAPK-MSK1/2 signaling pathway. Both the IL-1beta level as well as the activity of the p38 MAPK-MSK1/2 pathway are increased in psoriasis. Nevertheless, in chronic plaque-type psoriatic skin from 17 patients we found that 12 patients displayed a decreased expression of DUSP1 mRNA whereas 5 patients showed an increase. The overall difference was a significant reduction of approximately 26 percent. In contrast, in skin biopsies from 9 patients with a positive nickel patch test after 72 hours, we found a 1.7 fold increase in the expression of DUSP1 mRNA. Thus, it appears that the apparent compensatory upregulation of DUSP1 as seen in nickel-induced allergic contact dermatitis is deficient in psoriasis. Dysregulation of DUSP1 is therefore likely to contribute to the ongoing inflammatory response seen in psoriasis.

O02.05 Ulla Schierup Nielsen

HEPATITIS A AMONG DANISH TRAVELLERS 1980-2007

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Objectives: Hepatitis A is regarded as the most frequent vaccine-preventable disease in travellers, but improved sanitary conditions at many travel destinations may have reduced the travel related incidence over the last decades. Little data is available on the present risk of disease when travelling non-immune.
This study presents destination-specific incidence rates and time trends of travel related hepatitis A, and relative risks in immigrants versus native Danish travellers.
Methods: An Internet based survey among 26.640 Danes was carried out in July 2007 which provided data on journey time, destinations and proportion of non-immune travellers. Retrospective data on travel activity in the Danish population since 1980 were retrieved from Danish Statistics. These data were combined with national surveillance data on hepatitis A cases registered in Denmark 1980-2007.
Results: Time trends 1980-2007 show a 10-fold decline in hepatitis A incidence rates among travellers. The overall incidence rate in 2002-2006 was 39 (95% CI 34-46) per 100,000 nonimmune travel months when travelling outside Europe. 9.3% of the Danish population had travelled to such areas during the previous 12 months. 75% were immune when travelling. In 2002-2006, 8% of the population and 80% of cases were immigrants/children of immigrants. Immigrants visiting their countries of origin had higher per month risks than native Danish tourists visiting the same destinations.
Conclusions: Hepatitis A incidence is declining at most travel destinations worldwide, and the targeted immunization strategy works well for native Danes. Special focus on hepatitis A prophylaxis in immigrants and their children is warranted.

O02.06 Mette Møller Handrup

BIOFILM FORMATION IN CENTRAL VENOUS CATHETERS IN CHILDREN WITH CANCER: A RANDOMIZED CONTROLLED TRIAL OF TAUROLIDINE VERSUS HEPARIN

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Background: Most children with cancer need a central venous catheter (CVC). Infections continue to be one of the major complications of CVC. Catheter-related infections cause an increase in morbidity and mortality both due to the infection itself but also because it causes delay in the chemotherapy. Formation of an intraluminal biofilm plays a substantial role in the pathogenesis of catheter-related infections. Taurolidine, an antimicrobial agent derived from the naturally occurring aminosulphonic acid taurinamide and formaldehyde, has demonstrated in vitro

prevention of biofilm formation. The aim of this study was to compare the influence of catheter locking with taurolidine and heparin on the in vivo biofilm formation in CVC in children with cancer.
Methods: A total of 40 children with cancer were randomized to heparin(n=20) or taurolidine(n=20) for catheter locking. The children were studied from the time of catheter insertion and until removal of the catheter. After removal, catheters were examined by standardized scanning electron microscopy (SEM) to assess quantitative biofilm formation. Biofilm was considered to be present if morphologically typical structures and bacterial cells were identified. Adherent biological material (ABM) was defined to be present if morphologically typical structures were identified but with no bacteria present. Furthermore, quantitative and semi-quantitative cultures were also conducted to determine the catheters' colonization status.
Results: The study is ongoing and will be ready for data presentation in January.

O02.07 Lise Saksø Mortensen

UTILIZING THE EPPENDORF OXYGEN ELECTRODE AND FAZA PET IMAGING TO PREDICT RADIATION RESPONSE IN EXPERIMENTAL TUMORS

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Purpose: The purpose of this pre-clinical study was to investigate if hypoxia (measured by Eppendorf polarographic needle electrode and ^{18}F- fluoroazomycin arabinoside (^{18}F-FAZA) PET) prior to radiation therapy can predict outcome.
Material/methods: Subcutaneous C3H mammary carcinomas grown in CDF1 mice were used. Oxygenation status of the tumors was assessed by the Eppendorf oxygen electrode and ^{18}F-FAZA PET imaging, followed by irradiation with a single dose of 55 Gy. Eppendorf pO_2 measurements were analyzed using the fraction of pO_2 values ≤2.5 mmHg. ^{18}F-FAZA-uptake was quantified by calculating tumor-muscle-ratios (T/M). Response was determined as local tumor control 90 days after treatment. In the Eppendorf experiments the time to tumor recurrence (TTR) was expressed depending on whether the percentages of pO_2 values≤ 2.5 mmHg was above (more hypoxic) or below (less hypoxic) the median value. In the ^{18}F-FAZA experiments TTR was expressed depending on whether T/M was above (more hypoxic) or below (less hypoxic) the median value.
Results: Eppendorf estimates of tumor pO_2 in 110 tumor bearing animals showed that the median percentage of pO_2 values≤ 2.5 mmHg was 49 %. Separating the animals into 2 groups based on this value resulted in a highly significant difference in local tumor control. So far ~30 animals have been ^{18}F-FAZA scanned and initial analysis indicates the animals can be separated in 2 groups based on the median ^{18}F-FAZA T/M.
Conclusion: Hypoxia measured by Eppendorf oxygen electrodes was found to be predictive of radiation response.Initial analysis suggests that there is a relationship between hypoxia as quantified by ^{18}F-FAZA PET and tumor control probability

O02.08 Ulrik Vindelev Elstrøm

CONE-BEAM CT BASED TREATMENT PLANNING IN ADAPTIVE RADIOTHERAPY OF HEAD AND NECK CANCER

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Purpose: To perform a quantitative evaluation of image quality and dose-computational properties in cone-beam CT (CBCT) compared to the conventional CT used in the clinical practise for patient treatment planning and explore the consequences of CBCT-based treatment plan adaptation.
Methods and Materials: The material consisted of commercial phantoms, a homemade phantom to simulate changes in patient anatomy (i.e. changes in scatter radiation) and more than 150 consecutive head and neck cancer (HNC) patients having undergone daily CBCT-guided treatment. Five different CBCT acquisition modes on linear accelerators were compared to two CT scanners addressing image

quality parameters like noise, contrast, uniformity and accuracy of CT numbers using different image-reconstruction settings. Different methods to calibrate the relationship between CT numbers and tissue electron densities used by treatment systems to perform dose calculations were applied. The impact was evaluated by comparing electron density distributions in selected organs and regions-of-interest (ROIs), and the 3D dose distributions were analysed using the gamma-index method.
Results: Based on CBCT phantom measurements, all the image quality indicators could be improved by a factor of 4-5 compared to present clinical settings, however, still inferior to conv. CT. The effect of changes in patient size could be compensated by advanced calibration and reconstruction techniques. For various patient ROIs the electron density could be brought in concordance with conv. CT within 2% on average.
Conclusion: CBCT-based treatment planning could form the basis for direct evaluation of daily treatment performance.

O03.01 Aygen Øzbay

CALCINEURIN INHIBITORS ACUTELY IMPROVE INSULIN SENSITIVITY WITHOUT AFFECTING INSULIN SECRETION

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Introducing the calcineurin inhibitors (CNIs) cyclosporine (CsA) and tacrolimus (Tac) has improved the outcome of organ transplants, but complications such as New Onset Diabetes mellitus After Transplantation (NODAT) cause impairment of survival rates. The relative contribution of each CNI to the pathogenesis and development of NODAT remains unclear. We sought to compare the impact of CsA and Tac on glucose metabolism in human subjects. To this end10 healthy men underwent 5-hour infusions of CsA, Tac and saline in a randomized, double-blind, cross-over study. During infusion glucose metabolism was investigated using following methods: a hyperinsulinemic-euglycemic clamp, an intravenous glucose tolerance test (IVGTT), glucose-stimulated insulin concentration time-series and indirect calorimetry. Clamp derived insulin sensitivity was increased by 25 % during CsA ($p=0.003$) and 13 % during Tac administration ($p=0.04$), whereas the insulin sensitivity index k_G assessed by IVGTT was unaltered. Neither first phase insulin secretion nor pulsatile insulin secretion was affected during CNI treatment. Glucose oxidation rates increased, only non-significantly, while lipid oxidation and counterregulatory hormones remained unchanged. Mean blood levels of CNIs were 486.9±23.5 mg/l for CsA and 12.8±0.5 mg/l for Tac. In conclusion acute effects of intravenous CsA and to a lesser degree Tac infusions include increased insulin sensitivity, without any effect on first phase or pulsatile insulin secretion.

O03.02 Carolina Cannillo Graffe

THE EFFECT OF HIGH AND LOW SODIUM INTAKE ON RENAL TUBULAR FUNCTION AND VASOACTIVE HORMONES IN ESSENTIAL HYPERTENSION, DURING BASAL CONDITIONS AND AFTER HYPERTONIC SALINE INFUSION.

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Increasing evidence points to an abnormal regulation of the aquaporin-2 water channel (AQP2) and the epithelial sodium channel (ENaC) in the collecting duct principal cells in essential hypertension (EH). The function of these channels might be influenced by the sodium intake in EH.
We measured the effect of 4 days of high sodium (HS) intake (250-350 mmol day^{-1} ≈ 14.6-20.5 g salt day^{-1}) and 4 days of low sodium (LS) intake (25-35 mmol day^{-1} ≈ 1.5-2.0 g salt day^{-1}) on urinary excretion of AQP2 (u-AQP2), fractional sodium excretion (FE_{Na}), free water clearance, urinary excretion of prostaglandin E2 and cyclic AMP, and plasma concentrations of vasopressin, renin, angiotensin II, aldosterone, ANP and BNP in a randomized, single-blinded, cross-over study of 21 patients with mild to moderate EH and 20 healthy controls, during 24 h urine

collection and during hypertonic saline infusion.
During LS intake, the patients had significantly lower aldosterone (224 ± 18 vs. 405 ± 34 pmol l^{-1} (mean ± SEM), P=0.046) and significantly higher FE_{Na} (0.75 ± 0.13 vs. 0.43 ± 0.05%, P=0.025) compared with the healthy controls. Furthermore, during LS intake aldosterone decreased significantly less in response to the saline infusion in patients compared with controls (-27.31 ± 2.27 vs. -34.85 ± 2.12%, P=0.021). No difference was found in vasopressin or u-AQP2 between patients and controls. However, in both the patients and the controls u-AQP2 was lower during LS intake compared with HS intake, despite similar plasma vasopressin levels.
The results indicate an abnormally decreased ability of patients with EH to increase and decrease aldosterone in response to changes in sodium balance.

O03.03 Anja Høegh Brügmann

HER4 IS DOWNREGULATED IN LYMPH NODE METASTASES COMPARED TO THE PAIRED PRIMARY BREAST CARCINOMA.

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Introduction: The Human Epidermal Growth Factor Receptor 4 (HER4) of the EGF receptor family has been characterized in both normal and malignant human breast tissue and HER4 overexpression has been shown to predict prolonged survival compared to HER4 receptor negative disease.
In our study we investigated the HER4 expression in normal breast tissue, primary breast carcinoma and in ipsilateral metastatic axillary lymphnodes at the time of primary breast cancer surgery.
Material and methods: Paired tissue samples from normal breast tissue and primary breast carcinomas were obtained from 169 patients. Out of these a third sample was obtained from 66 patients with metastatic lymphnodes. The mRNA expression of HER4 was quantified with real time RT-PCR and expressed relative to the householdgene (HMBS) in arbitrary units (arb.u.).
Results: The mRNA expression of HER4 was significantly higher in breast carcinoma with a mean of 2.26 arb.u. [95% c.i.:1.87 to 2.65 arb.u.] than in the paired sample of normal breast tissue with a mean of 0.82 arb.u. [95% c.i.: 0.47 to 1.16 arb.u.] (p=0.0001). The mRNA expression of HER4 was also significantly higher in breast carcinoma than in the corresponding lymphnode mean 0.75 arb. u. [95% c.i.: 0.43 to 1.07 arb.u.] (p=0.015).
Conclusion: The HER4 expression was high in the primary tumour as compared to normal breast tissue and the corresponding lymphnode. In view of previously published relations between a low expression of HER4 and a poor prognosis our results warrant further studies in order to evaluate whether suppression of HER4 in tumour cells could be involved in lymphogenic metastatic spread.

O03.04 Samir Munir

HYPOXIC CHONDROGENIC DIFFERENTIATION OF HUMAN CORD BLOOD STEM CELLS IN STRUCTURALLY-GRADED POLYCAPROLACTONE SCAFFOLDS

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There is an increasing interest in investigating alternative treatments for cartilage injuries. This study demonstrated the chondrogenic potential of human cord blood-derived Multi-Lineage Progenitor Cells (MLPCs) under different oxygen tensions. Second, MLPCs were seeded on a novel, structurally graded polycaprolactone (SGS-PCL) scaffold and chondrogenesis was evaluated.
MLPCs obtained from BioE Inc (St. Paul, MN, USA) were expanded, and subsequently cultured in a standard micromass pellet system. Pellets were cultured in control or chondrogenic induction medium under 5% or 21% oxygen tension. Chondrogenic potential was evaluated by histology (alcian blue, safranin O), glycosaminoglycan (GAG) protein secretion, and gene expression of cartilage markers. Based on this data, MLPCs were seeded in SGS-PCL scaffolds and cultured

at 5% oxygen tension for 21 days followed by chondrogenic evaluation as above. GAG production in induced pellets was observed to be located centrally in 21%-, and peripherally in 5%-oxygen tensions. Histological sections revealed a cartilaginous structure as recognized by chondrocyte-like cells embedded in lacunae.
When cultured at 5% hypoxia as a pellet system increased gene expression for Collagen-II is observed. Decreased gene expression for collagen-I, collagen-X and aggrecan. Increased GAG production is observed when cultured at hypoxia.
Culturing on SGS-scaffold revealed increased gene expression of aggrecan, collagen-II and SOX9 and decreased expression on collagen-I. GAG production on SGS is significantly increased.
Conclusion: SGS has chondrogenic potential. In further studies this novel scaffolds mechanical properties will be evaluated.

O03.05 Tine Qvistgaard

MESOANGIOBLASTS AS THERAPEUTIC STEM CELLS

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Introduction: Mesoangioblasts are mesodermal stem cells. They are easy to expand, they retain high differentiation potential, and they are obvious candidates for therapeutic intervention. This project explores the osteogenic and skeletal myogenic potentials of mesoangioblasts. The aim is to use these cells for experimental reconstruction of oro-facial bone defects and regenerative treatment of Duchenne Muscular Dystrophy.
Methods: Mesoangioblasts are evaluated in vitro for attachment, proliferation and differentiation on granules of calcium phosphate (HA/TCP). Mesoangioblasts (+/- BMP2) attached to such granules are inserted in vivo or in situ to assess osteogenic differentiation. For therapeutic application against Duchenne Muscular Dystrophy, mesoangioblasts are engineered into retroviral packaging cells for in situ transduction of dystrophic fibers with microdystrophin. Methods for delivery of cells are monitored histochemically to deliver cells efficiently to all affected sites of the body. All in vivo work is done on mice.
Results: Mesoangioblast attachment to HA/TCP granules was observed to depend on serum levels, granula size, and composition. Cells expressing BMP2 have been developed and are compared with original mesoangioblasts in vitro et vivo. Mesoangioblast packaging cells have been engineered and are currently tested for their efficiency using an egfp-expressing retroviral vector. We found intracardial injection of labeled mesoangioblasts to distribute cells systemically, including delivery to oro-facial bone.

O03.06 Dang Quang Svend Le

EX VIVO BIOREACTOR-BASED PLATELET PRODUCTION

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From a transfusion viewpoint, the most important cells in blood are the oxygen-carrying red cells and the blood platelets, which are essential for hemostasis. In 2008, Danish hospitals performed 328.036 red cell transfusions and 33.070 platelet transfusions. Platelet treatment is indicated for patients undergoing invasive surgery, low platelet count, or diseased platelets. The latter conditions, thrombocytopenia and thrombocytopathy, commonly arise from malignancies such as leukemia.
Once harvested, platelets have a shelf-life of maximum 5 days, which complicates blood banking to a much wider extent than stocking up on red cells that have a shelf-life of 2 months. And while sporadic treatment with platelets does not pose great immunological complications to the patient, the surface expression of MHC class I molecules can lead to alloimmunization and refractoriness in prolonged treatment.
Clinical scale ex vivo platelet and red cell production based on a tissue engineering

approach will significantly mitigate supply problems, costs of donor screening and blood product preparation, and immunization events. In this study, we use a revolutionizing novel perfusion bioreactor to produce a high yield of plateletoid fragments from differentiated K562 cells seeded in porous polyester matrices. The fragments express platelet markers CD41, Neurogranin, and PF4 and are activated in the presence of ADP or collagen. While designing the setup, we have given special attention to experimental costs and process simplicity to further increase relevance to translational medicine.

O03.07 Mette Juul Koefoed

GENE TRANSFER FOR BONE HEALING USING IMMOBILIZED FREEZE DRIED ADENO-ASSOCIATED VIRAL VECTORS

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Bone allografts are widely used clinically although they often heal insufficiently leading to risk of fracture. These problems may be alleviated using allografts coated with freeze-dried AAV vectors carrying genes for osteogenic stimuli. We have evaluated the kinetics of the gene delivery from bone allografts and potential effects of stimulation of new bone formation.
For the in vitro studies AAV-GFP coated allografts were placed onto confluent layers of HEK 293 cells. Subsequently the grafts were moved to a new cell layer every minute, and GFP positive cells measured 2 days later. We show that within the first minute most of the viral vectors (88%) from the bone grafts were released.
A murine critical size fracture model was used for in vivo studies. Allografts coated with AAV-luciferase were implanted and bioimaging was used to assess luciferase activity. New bone formation was stimulated by VEGF and bFGF2 and evaluated after 10 weeks using micro-CT and histomorphometry.
Bioluminescence imaging showed localized gene expression reaching a plateau from 51 to 70 days. Interestingly VEGF coated allografts lead to an approx. 5 fold increase in total bone volume compared to bFGF2, a combination of VEGF and bFGF2 and controls, although with large variation within each group.
In conclusion allografts with freeze-dried AAV vectors on the surface is a promising new tool for enhancement of the formation of new bone. The positive effect of VEGF on bone formation points to new blood vessels as a critical step in the healing process.

O03.08 Nina Dyrberg Lorenzen

EVALUATION OF BLOOD FLOW AND METABOLISM IN THE FEMORAL HEAD. A RANDOMISED COMPARISON OF SURGICAL APPROACHES IN RESURFACING HIP ARTHROPLASTY.

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Background: Osteonecrosis of the femoralhead in resurfacing hip arthroplasty (RHA), may be the result of a decreased bloodflow during surgery. Changes in bloodflow may be visualized by Laser Doppler Flowmetry. The effect of a change in the bloodflow can be seen by monitoring the metabolic markers in the bone, using microdialysis. The purpose of this study is to investigate the influence of the surgical approach on the bloodflow and the metabolism in the femoralhead in RHA. We hypothesized that an antero-lateral approach would result in less reduction in bloodflow during surgery and less ischemia after surgery.
Material: Fifty patients are randomised to RHA by either an anterolateral (AL group) or a posterior approach (PO group). The bloodflow to the femoralhead is measured before and after insertion of the implant. Metabolism in the femoralhead is monitored in three days by microdialysis, then analysed regarding the content of:glucose, lactate, pyruvate and glycerol. The patients are evaluated by Visual Analogue Scale (VAS) and Harris Hip Score (HHS) before and after surgery.
Results: Preliminary results for the first 30 patients are presented. We found no statistical significant difference in blood flow reduction between the groups ($p=0.88$). The results of the microdialysis are based on 21 patients. We have found a

more pronounced sign of ischemia in the PO group seen by a low glucose value and a high lactate value. The mean pre- and post-operative HHS and VAS scores improved significantly in both groups ($p < 0.01$).
Discussion: To our knowledge, a RCT comparing two surgical techniques in RHA by assessment of the blood supply and metabolism has not previously been performed.

O04.01 Thaneas Prabakaran

RECEPTOR-MEDIATED UPTAKE OF ALPHA-GALACTOSIDASE A IN HUMAN PODOCYTES IN FABRY DISEASE

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Introduction: Injury of glomerular podocytes is prominent in Fabry disease, caused by progressive lysosomal accumulation of glycosphingolipid in form of globotriaosylceramide (GL-3). Podocyte repair is therefore an important therapeutic target in Fabry patients.
Aim: To determine how recombinant α-galactosidase A (α-Gal A) (Fabrazyme) designed for enzyme replacement therapy in Fabry disease is taken up by human podocytes.
Methods: The mechanism of α-Gal A uptake in cultured podocytes and in vivo was investigated using affinity chromatography, immunocytochemistry, laser capture microdissection, RT-PCR and Western blotting analyses.
Results: The present study identifies three endocytic receptors, mannose 6-phosphate receptor, megalin, and sortilin, with drug delivery capabilities in human podocytes. All receptors are localized on the surface membrane of cultured podocytes indicating their endocytic capabilities. Furthermore, the receptors were found to mediate the uptake and lysosomal targeting of recombinant α-Gal A in cultured podocytes.
Conclusions: The present findings highlight the importance of receptor-mediated endocytosis as a key mechanism in podocyte maintenance by delivering α-Gal A to lysosomes for degradation of GL-3 deposits. This study provides the molecular basis for the renal effect of treatment with α-Gal A and identifies possible pathways for future non-carbohydrate based drug delivery to the glomerular podocytes and other tissues.

O04.02 Anders Etzerodt

IMPROVED DRUG DELIVERY TO DISEASE-ASSOCIATED MACROPHAGES USING CD163 TARGETED LIPOSOMES.

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The hemoglobin scavenger receptor CD163 is exclusively expressed on cells of the monocytic lineage. Expression of CD163 is highly regulated and increased in macrophages associated with various inflammatory conditions such as rheumatoid arthritis, Chron's disease and atherosclerosis. Moreover, recent evidence relates the expression of CD163 in breast and rectal cancer with early recurrence and poor outcome.
In the present study we have developed a nanoscale drug carrier for specific macrophage targeting by modifying PEGylated liposomes (stealth® liposomes) with a CD163 targeting moiety. Besides protecting encapsulated hydrophilic drugs from unwanted interactions and degradation, liposomes accumulate passively in solid tumors and inflamed tissue by means of the enhanced permeability and retention effect (EPR). Using a mouse model for rheumatoid arthritis and glucocortiod as encapsulated drug early in vivo data suggest improved effect compared to controls. This supports our hypothesis predicting that the combination of liposome characteristics with macrophage targeting will efficiently deliver drugs

to affected tissue and thereby enhance tissue distribution and pharmacokinetics of the drugs in question.

O04.03 Christian Møller Pedersen

REMOTE ISCHEMIC PRECONDITIONING IS NOT MEDIATED BY ENDOGENOUS BRADYKININ IN HUMANS

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Ischemia reperfusion injury (IR) induces endothelial dysfunction with attenuation of acetylcholine-induced vasodilatation in man. Remote ischemic preconditioning (RIPC) preserves endothelium-dependent vasodilatation following IR injury. Given that exogenous bradykinin protects against IR injury, we hypothesised that endogenous bradykinin mediates the vascular protective effects of RIPC.

In a double blind crossover study, 20 subjects were randomised to receive an intravenous infusion of the bradykinin B2 receptor antagonist, HOE-140 (0.1 mg/kg body weight) or saline placebo. IR injury (20 min upper arm cuff inflation to 200 mmHg) was induced in the non-dominant arm in all subjects. Prior to induction of IR injury 10 of the subjects also received 3 cycles of 5 min RIPC in the dominant arm. Using bilateral forearm venous occlusion plethysmography, blood flow was measured during intra-brachial infusion of acetylcholine (ACh; 5-20 µg/min) at baseline and following IR injury.

Compared to baseline, acetylcholine-induced endothelium-dependent vasodilatation was reduced at 15 and 45 min following IR injury, both in the presence (P=0.0002) and absence (P=0.04) of HOE-140. RIPC prevented the reduction in ACh-induced vasodilatation associated with IR injury, irrespective of the presence or absence of HOE-140 (P>0.05 for both).

Endothelial vasomotor dysfunction is induced by IR injury and can be prevented by RIPC. Our findings suggest that endogenous bradykinin does not play a major role in the induction of IR injury or its prevention by RIPC

O04.04 Mads Kronborg

HIS AND PARA-HIS PACING IN AV-BLOCK: FEASIBILITY AND ELECTROCARDIOGRAPHIC FINDINGS

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Purpose: Chronic RV pacing reduces the left ventricular ejection fraction and is associated with adverse clinical outcome, due to an abnormal activation of the left ventricle. Patients with AV-block and QRS <120 ms have preserved interventricular conduction system and forms the major group of potential candidates for chronic His pacing. We aimed to establish stable, direct His-bundle pacing (DHP) or para-His pacing (PHP) in patients with AV-block and QRS <120 ms.

Method: We included consecutive patients with 2nd or 3rd degree AV -block, LVEF > 0,40, QRS duration <120 ms, and sinus rhythm. All patients received a biventricular pacemaker with one atrial lead, one right ventricular lead mid-septal and one lead in the His bundle or in the para-His area. Pacing from apex was performed temporarily during the implantation. Patients were followed-up after 3 months.

Results: We included 38 patients (mean age 67(±10), 30(79%) male) with a mean intrinsic QRS of 92 (±13) ms. The mean implantation time was 85 (±31) min, the mean fluoroscopic time was 23 (±12) min and the mean position attempts was 8 (±5). We achieved DHP in 4 patients with a mean QRS of 100 (±19) ms, in 28 patients stable PHP was achieved with a mean QRS of 112 (±18) ms in 6 patients neither DHP nor PHP were achieved. The mean QRS duration was 153 (±12) ms with mid-septal pacing and 161 (±15) ms with apical pacing both significantly longer than DHP and PHP pacing (<0.001).

Conclusion: Stable DHP or PHP are feasible in 84 % of patients with narrow QRS and AV-block, and leads to a reduction of the paced QRS duration and a more physiological activation pattern of the left ventricle, compared with RV septal or

apical pacing.

O04.05 Thomas Wittenborn

IMAGING ANGIOGENESIS IN NOVEL MOUSE MODEL

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As a common denominator for many pathological conditions including progression of atherosclerosis and solid tumors, the angiogenesis process can serve as a target for diagnosis and treatment when investigating these diseases. Developing blood vessels are known to be fragile and leaky, introducing an opening into the Extravascular Extracellular Space (EES). This opening may be exploited to introduce Ultrasmall Superparamagnetic Iron Oxide (USPIO) particles into the EES. By attaching different ligands to the particle surface these can be functionalized to target matrix proteins, proteoglycans or other components of the EES and hence identify areas with leaky vessels/angiogenesis.

We have been able to observe the process of neovascularization within PCL-implants ranging from 1-6 weeks. DCE-MRI revealed rapid signal increase in the perifery of ”young” implants (1-2 weeks) followed by signal diffusion throughout the entire implant. ”Older” implants (5-6 weeks) showed rapid signal increase throughout the implant indicating full vascularization of the implants. Histology confirmed the presence of vessels in the perifery of ”young” implants and throughout the entire area of the ”older” implants. Functionalized iron oxide nanoparticles targeted to the extracellular matrix have been testet in this model alongside control particles, reference particles and saline. Ultra high-field MR images have been recorded before and 24 hours after injection of the particles and are now being analyzed for particle accumulation.

O04.06 Christina Bisgaard

COMPARATIVE PROTEOMICS IN THE CHRONIC MILD STRESS MODEL OF DEPRESSION - A SEARCH FOR BIOMARKERS OF DEPRESSION IN HIPPOCAMPAL SUBREGIONS

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Extensive research has focused at unraveling the underlying molecular mechanisms leading to depression and recovery. These mechanisms are, however, still unknown, but most likely accompanied by changes in protein expression profiles and the aim of this study is to quantitatively investigate these protein expression differences.

The chronic mild stress rat model of depression is our animal model. This model induces anhedonic behavior, a major symptom of depression, by exposing rats to a series of mild stressors. A significant decline in the intake of a sucrose solution is observed in stressed animals compared to non-stressed animals. This is reversed by antidepressant treatment. Six different groups emerge from our depression model; stress resilience, drug-responders, drug-nonresponders, stress vehicle, control drug, control vehicle.

To identify hippocampal granular cell layer proteins important in development of depression and recovery we used a proteomic strategy that combines Laser Capture Microdissection (LCM), 2D Differential Gel Electrophoresis (DIGE) and Tandem Mass Spectrometry (MS/MS) to isolate, separate and identify proteins of interest. The coupling of LCM, 2D DIGE and MS/MS is a brand new approach to investigate neurobiological aspects of depression.

We have identified several interesting proteins implicated in the development of anhedonic behavior, antidepressive drug respondance and stress resilience. This provides a greater understanding of depression etiology and pathophysiology and ultimately helps identify new treatment targets able to increase the percentage of treatment responders, induce a rapid onset of action and improve the side effect

profile.

O04.07 Trine Veje Axelsen

TRIGGERING ANTIBODY RESPONSE AGAINST A&BETA;42 BY LOW DOSE IMMUNIZATIONS OF A&BETA;1-42/PMP8-A&BETA;1-30 IN DOUBLE TRANSGENIC AD MICE.

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The neuropathology of Alzheimer's disease (AD) is characterized by the presence of senile plaques and neurofibrillary tangles. The senile plaques are composed of β-amyloid (Aβ) -peptides, largely Aβ40 and Aβ42. Aβ42 is characterized as neurotoxic, and therefore the target of many immunization studies [1].
To generating an antibody response against Aβ42 high doses of either Aβ1-42 or fragments of the Aβ-peptide were used in immunizations of transgenic AD mice. Transgenic AD mouse models express a mutated form of Amyloid precursor protein (APP), which leads to increased levels of Aβ-peptide in the brain [2]. Therefore transgenic AD mice may recognize the Aβ-peptide as a "self molecule" which makes it difficult to generate an antibody response towards Aβ42. Thus, high amounts of Aβ must be used to generate a substantial immune response to Aβ42 [3].
Here we show that it is possible to generate an antibody response against Aβ42 using only 30 µg of antigen in the AD mouse model expressing APPsw and PS1dE9 [4]. The antigen used was Aβ1-42 mixed with the T-cell epitope Pmp8 [5] synthesized in connection with Aβ1-30. The mixed peptides were, denatured, lyophilized and dissolved again to incorporate pmp8-Aβ1-30 into the aggregated structure of Aβ1-42.
Boosting the immune system with a highly immunogenic T-cell epitope as Pmp8 makes it possible to generate an antibody response against Aβ42 in APPsw X PS1dE9 mice using 30 µg antigen, even though Aβ42 may be regarded as a "self molecule" in APPsw X PS1dE9 mice.
[1] Lemere CA Nat Rev Neurol 2010 [2] Duyckaerts C Acta Neuropathol 2008 [3] Schenk D Nature 1999 [4] Jankowsky JL Neurobiol Aging 2004 [5] Mygind T Immunol Med Microbiol 2004

O04.08 Louise Munk Rydtoft

NEURITE DENSITY IN AN ALZHEIMER'S DISEASE MOUSE MODEL FROM DIFFUSION WEIGHTED MAGNETIC RESONANCE (MR)

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Measuring neurodegeneration has great interest. To date, achieving such a measure can only be done through elaborate histological and stereological analysis. An alternative, non-invasive method based upon diffusion weighted magnetic resonance imaging and computer modelling has previously presented (Jespersen et al, NeuroImage 2007). The pathological hallmark of Alzhimers disease is plaques, tangles, and neurodegeneration. Several studies show that plaque deposition precedes tangle formation, but the timing of neurodegeneration remains to be elucidated. It is interesting to investigate probable neurodegeneration in an AD mouse model, and potentially the relative timing and position of plaque development and neurodegeneration. However, such experiments necessitate extreme diffusion gradient power and signal values only obtainable with ultra-high-field MR. Four male APPswe/PS1dE9 and two wild type mice has to date been scanned on a 16,4 Tesla BRUKER MR scanner and their neurite densities calculated (see table 1). Based upon this data, no statistical significant conclusion can be made regarding the neurite density in the AD mouse model compared to wild type mice, because of the low number of mice in each group, the study is ongoing. In addition, since the sensitivity of the MR coils used in this preliminary study only allows resolutions below the desired, focus is now on implementing a newer and smaller coil. This should allow investigation of the entorhinal cortex and insight to the

timing of plaque and neurodegeneration should be obtainable. However, these studies require implementation of newly purchased micro coil, which at present is still ongoing.

P01.01 Pernille Munk Frandsen

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

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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. Mast cells express several receptors including the high affinity receptor (FcεRI) and Toll like receptors (TLRs). These receptors can activate the mast cell and are thus considered important in mediator release causing asthma. The objectives of this study are 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 like prostaglandin D2, histamine and several cytokines.
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. From this study we expect to achieve new knowledge about some of the differences between mast cells from healthy and allergic individuals.

P01.02 Sabina Jelen

AQUAPORIN-9 EXPRESSION IN MALIGNANT GLIOMA

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Glioblastoma mulitforme is the most common form of malignant brain tumor accounting for more than 50% of all primary brain tumors and has poor prognosis. Recent studies described enhanced expression of the water channel aquaporin 9 (AQP9) in high-grade glioma patients, possibly indicating a function for AQP9 in the pathophysiology of glioma. The aim of my studies is to evaluate the expression pattern of AQP9 in gliomas using human and mouse models. The mouse glioma model was developed by intracranial injection of Gl261 cells into C57BL/6 mice. We evaluated the AQP9 expression with immunofluorescence in both, human tissue and the mouse model. Human tissue revealed positive AQP9 labeling in the tumor cells in a subpopulation of tumor cells. Moreover, we discovered strong immunolabeling of AQP9 co-localized with the neutrophil marker CD15. The mouse glioma model did not show AQP9 expression in glioma cells. However, like in human tissue, AQP9 was detected in neutrophils. Further analysis has to be done for a more detailed characterization of AQP9 expression and to hypothesize on a potential function. In conclusion, the water channel AQP9 is expressed in human glioma and may be important for brain tumor progression.

P01.03 Rita Marques

ATP INHIBITS NACL ABSORPTION VIA BASOLATERAL P2X RECEPTORS IN MOUSE MEDULLARY THICK ASCENDING LIMB (MTAL)

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Renal epithelia express multiple luminal and basolateral P2 receptors that mediate inhibition of solute absorption. Previously we identified luminal and basolateral $P2Y_2$ receptorsin the medullary thick ascending limb (mTAL) as well as evidence for a basolateral P2X receptor. Recently was sugested that extracellular nucleotides influence ion transport in this segment. The main aim was to investigate how extracellular ATP influences NaCl absorption in mTAL. In this study, we used isolated, perfused mouse mTAL to electrically measure Na^+ absorption. We

characterized the transepithelial voltage (V_{te}), transepithelial resistance (R_{te}) and via these the transepithelial Na^+ absorption (I_{sc}). Non-stimulated mTALs show a V_{te}: +9.03±0.44 mV, a R_{te}: 8±1.1 Ω cm² and a I_{sc}: 1404±21.4 µA/cm² (n=16). Basolateral ATP (100 µM) acutely and reversibly reduced the absorptive I_{sc}. After 2 minutes a maximal reduction measured amounted to 19.6±2.8% (n=8). In the presence of ATP transport inhibition was sustained. Suramin (P2 receptor antagonist) inhibited the ATP effect. Basolateral UTP, a $P2Y_2/P2Y_4$ receptor agonist was without effect. Via pharmacological tools, we were able to isolate two possible P2X receptor candidates, mainly $P2X_2$ and $P2X_7$. In $P2X_7$ receptor knock-out mice, ATP-mediated transport decrease was still present. Futhermore, the use of ivermectin ($P2X_4$activator) slightly potentiated the ATP effect. These data indicate that basolateral ATP exerts a significant inhibition of Na^+ absorption in mouse mTAL via a P2X receptor-mediated mechanism. Further studies in mice lacking the $P2X_2$ and $P2X_4$ receptors are needed and may point to a complex system where several receptors interplay.

P01.04 Randi Groslier Bjælde

CHARACTERISING THE PATHWAY FOR NUCLEOTIDE-RELEASE IN RENAL EPITHELIA

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Extracellular ATP is via P2 receptors a significant modulator of the epithelial transport. Nucleotides are constitutively released by renal epithelial cells. Nucleotide release has been suggested to occur either via a conductive pore or by exocytosis. The aim of the present study is to define the nucleotide release pathway in renal epithelial cells.

We use various techniques using MDCK cells as a model system: (1) We have established that spontaneous $[Ca^{2+}]_i$ increments in renal epithelia reflect nucleotide release. (2) Live cell imaging of quinacrine stained vesicles in MDCK cells. (3) Luciferin-luciferase lumeometry.

Inhibition of the vesicular H^+-ATPase with Bafilomycin (1 µM) reduced the spontaneous nucleotide release with 78.8%. Bafilomycin also diminished the hypotonically (80%) and the flow-induced $[Ca^{2+}]_i$-response by 67.3% and 61.8% respectively. Interference with vesicular fusion by N-ethylamide (100 µM) dramatically lowered the spontaneous nucleotide release (88.5%) and the flow induced $[Ca^{2+}]_i$-response (63.3%). Inhibitors of the Golgi apparatus, microfilament as well as gap-junctions did not affect neither the spontaneous nor the flow-induced $[Ca^{2+}]_i$-response. In time laps studies on living MDCK cells showed that vesicles stained with quinacrine moved vigorously around in the cytoplasm. After mechanical or agonist stimulation the vesicle movement ceases and the overall fluorescence decreased with 5.8 % and 7.6 % respectively, as a measure of vesicular release. In summary, these data support that spontaneous and mechanically induced ATP release occurs via exocytosis in renal epithelia.

P01.05 Louise Lund Andersen

DOES CUBILIN PLAY A ROLE IN DEVELOPMENT OF MAMMACANCER?

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Mammacancer is the form of cancer which affects the majority of the women getting cancer in Denmark. This projects aims to investigate the role of a multiligand receptor protein named cubilin in the development of mammacancer.

Cubilin forms in complex with amnionless (AMN) the receptor complex cubam, which is expressed at the apical surface of different polarized epithelia. In the terminal ileum it binds and promotes cellular uptake of the complex intrinsic factor-vitamin B12, and in the proximal tubules of the kidney cubam is involved in reabsorption of various ligands from the glomerular ultrafiltrate.

Cubilin is a ~460 kDa peripheral membrane protein, composed of a ~110 amino acid N-terminal tail including a trimerization domain followed by eight EGF-like repeats and 27 contiguous CUB domains. The N-terminal part of cubilin binds to AMN, and a physiological explanation for the trimerization of cubilin is speculated

to be the need for a strong interaction between extracellular cubilin units and membrane anchoring AMN units. Both in ileum and kidney, the ~45 kDa partner AMN is required for correct processing and anchorage of cubilin at the cell surface, and for internalization of ligands by endocytosis via clathrin-coated pits.
Cubilin expression has also been reported elsewere, as in human mammacancer cell lines. This information did not prove important to us, until we discovered the binding of fibroblast growth factor 8 isoform b (considered to be involved in the development of mammacancer to cubilin with high affinity (Andersen, L.L., Kozyraki, R. and Madsen, M., unpublished). This project therefore aims to investigate the link between cubilin and Fgf8b in mammacancer.

P01.06 Lena Lindtoft Rosenbæk

REGULATION OF THE RENAL ION TRANSPORTER NCC BY PHOSPHORYLATION

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Dysregulation of salt transport results in a number of clinical disorders, including hypertension. A current medication used to lower blood pressure is thiazide, which directly targets the renal NaCl co-transporter (NCC). NCC is a member of the cation-chloride co-transporter family and localizes to the distal convoluted tubule (DCT). NCC reabsorbs a substantial part of NaCl delivered from the loop of Henle. Conserved phosphorylation sites are located in the amino-terminal of NCC. Phosphorylation of these residues can occur via the WNK-SPAK/OSR1 pathway, resulting in increased co-transporter activity. Recent reports suggest that angiotensin II (ANGII) and aldosterone can signal through the WNK-SPAK/OSR1 pathway to activate NCC by phosphorylation. It is determined by our group that phosphorylation of NCC can be regulated by vasopressin (AVP) independently of ANGII, and a novel phosphorylation site (S124) has been identified. Bioinformatic studies confirmed the S124 site as a true phosphorylation site. Immunoblotting using phosphospecific antibodies showed a band of ~160 kDa in the kidney cortex and not in the inner medulla. Electron and confocal microscopy revealed pS124-NCC to be located in apical and subapical regions of DCT cells and do not appear in other cells throughout the nephron. Rats treated with aldosterone and/or ANGII or AVP significantly increased the abundance of pS124-NCC. Future studies will involve functional examinations of wildtype NCC and phosphorylation-deficient mutants in oocytes additional to studies of NCC trafficking in DCT cell lines.

P01.07 Muhammad Umar Cheema

STOICHIOMETRY ANALYSIS OF MULTIMERIC PROTEIN COMPLEXES USING BIOLUMINESCENCE RESONANCE ENERGY TRANSFER (BRET)

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Objective: The precise subunit composition of functional protein complexes is unknown for some important membrane proteins. For example, although the epithelial sodium channel (ENaC) was first described as a heterotetrameric complex of two αENaC, one βENaC and one γ ENaC subunit, both higher order complexes and trimeric structures have been proposed recently. Our study aims to improve the methodology for determining subunit composition.
Methods: A bioluminescence resonance energy transfer (BRET) technique is being established in living cells to study close proximity of two proteins of interest. One protein is tagged with Renilla luciferase (Rluc) that activates the bioluminescent substrate Colentrazine H (ColH) acting as a BRET donor (emitting 480-500 nm light). The second protein carries an EYFP fluorescent-tag, which is a BRET acceptor (here excited at 480-500 nm and emitting at 525 nm). At 37°C, biolumiescence and fluorescence signals from living cells are recorded in a cuvette by photomultiplier (PMT) based spectrometry and by microscopy using an electron multiplying charged coupled device (EM-CCD camera).
Results: Bioluminescence and fluorescence spectrometry of control Rluc-EYFP constructs transiently transfected into HEK cells was used to determine excitation and emission spectra. Robust increases in both signals (200 to 1000 fold) were observed immediately after addition of 5 µM ColH. Similar results were obtained at

the single cell level by microscopy, with an observed 20-100 fold increase in EYFP signal after ColH addition.
Conclusion: We have established a live cell microscopical BRET technique in the laboratory for the study of multiprotein complexes.

P01.08 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 a specific target for cardiotonic steroids (CTS), a family of naturally derived compounds used for centuries in the medical treatment of congestive heart failure and atrial fibrillation, i.e. digoxin (digitalis). Despite a long history and an intensive therapeutic application of CTS, the structural basis for their high affinity binding to the Na+,K+-ATPase is still unknown. In addition to a well-established inhibiting effect on the Na+,K+-ATPase activity, CTS binding is now further believed to initiate several intracellular signaling pathways and have been related to several diseases, such as hypertension and cancer.

We present a crystal structure of the pig kidney Na+,K+-ATPase in its phosphorylated (E2P) form stabilized by high affinity binding of the CTS ouabain. The steroid binds to a site formed by the transmembrane segments aM1-aM6, plugging the ion pathway from the extracellular side. The structure reveals a new conformational state of the Na+,K+-ATPase, closely related to the genuine E2P state. Most importantly we find that aM1 and aM2 move towards aM3 and aM4, forming a high affinity binding site for the CTS, and the A-domain is rotated in response to phosphorylation. The consequences of the observed re-arrangements of the Na+,K+-ATPase for the protein-protein interactions within the intracellular signal transduction network will be discussed.

P01.09 Niklas Telinius

THE ROLE OF THREE VASOACTIVE SUBTABCES AND ENDOTHELIUM ON HUMAN THORACIC DUCT CONTRACTILITY IN VITRO

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Introduction
The lymphatic system regulates tissue fluid balance and is in this way an important security factor to prevent oedema. Our current knowledge of the intrinsic contractions in lymphatic vessels is based primarily on animal studies.
Material & Methods
Thoracic ducts were harvested from 16 patients during oesophageal and cardia cancer surgery. Vessel segments were mounted in a wire myograph and normalized to 21 mmHg. Vessels were tested with noradrenaline (NA)(10-9-10-5M), the thromboxane analogue U46619 (10-12-10-7M) and endothelin-1 (ET-1)(10-12-10-7.5M). Endothelial function was assesed with acetylcholine (ACh) or bradykinin (BK).
Aims
The aim for this study was to investigate the role for adrenoceptors, thromboxane and endothelin receptors in human thoracic duct contractility and furthermore the role of the endothelium.
Results
The vessels produced an average peak tension of 2.6±0.4 Nm-1 after exposure to NA, 5.6±1.2 Nm-1 after U46619 and 5.3±1.3 after ET-1. Both ET-1 and U46619 produced significantly higher peak average tension than NA.
Transient and rhythmic contractions appeared with increasing concentrations, but at the highest concentration of U46619 and ET-1 a tonic contraction was seen.
On average, NA preconstricted vessels relaxed 25±4% and 41±5%, in the presence

of ACh or BK, respectively. Adding L-NAME (100µM) resulted in an almost complete abolishment of the ACh- and BK-induced relaxation, 2% and 1% respectively (n=2).
Summary
We have shown that NA, U46619 and ET- 1 can induce tonic and phasic contractions in the range corresponding to between 26 and 46 mmHg. Furthermore we have shown that NO is an important mediator of ACh and BK induced relaxations.

P01.10 Thala Marie Ørtoft Snerum

IRREGULAR MENSTRUAL CYCLE, OBESITY AND PRETERM BIRTH.
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Abstract
Background and aims: Obesity and pre-pregnancy irregular menstrual cycle may independently be associated with an increased risk of preterm birth. High body mass index (BMI) and irregular menstrual cycle are both symptoms of the polycystic ovary syndrome (PCOS). The aim of this study is to investigate the interaction between body mass index and irregular menstrual cycle on the risk of preterm birth.
Methods: A population of 53,462 women enrolled consecutively and followed during pregnancy through delivery. Self reported height and pre-pregnancy weight was used to define BMI <18.5, 18.5-24.9, 25-30 and >30 kg/m2. Irregular menstrual cycle (yes/no) was defined as a menstrual cycle >35 days. Odds ratios (OR) of preterm birth, i.e. birth before 37 completed weeks, determined by early ultrasonography, were estimated while adjusting for a variety of potential confounders using logistic regression.
Results: Compared to spontaneously-conceiving normal weight women (BMI 18.5-24.9) with regular menstrual cycle, the OR's of preterm birth for women with other BMI and menstrual cycle characteristics were: Regular menstrual cycle; BMI <18.5, 1.30 (95 % confidence interval (CI): 1.05; 1.61); BMI 25-30, 1.28 (CI 1.11; 1.48); BMI >30, 1.25 (CI 1.00; 1.58). Irregular menstrual cycle: BMI <18.5, 1.69 (CI 1.30; 2.21); BMI 18.5-24.9, 1.08 (CI 0.96-1.21); BMI 25-30, 1.09 (CI 0.88; 1.35); BMI >30, 1.94 (CI 1.49; 2.53).
Conclusion: Obese women with irregular menstrual cycle, who conceived spontaneously, had an increased risk of preterm birth. The prevalence of polycystic ovary syndrome is expected to be higher among these women.

P02.01 Louise Wamberg

1,25-OH-VITAMIN D HAS ANTI-INFLAMMATORY EFFECTS IN HUMAN ADIPOSE TISSUE IN VITRO
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Objective: Obesity is characterized by enhanced inflammatory activity in the adipose tissue which is related to health complications to the obese state. Moreover, circulating levels of vitamin D are generally low in the obese state. As vitamin D has shown to have anti-inflammatory properties in some cell systems, we aimed to study whether vitamin D may have anti-inflammatory activities in human adipose tissue in vitro.
Methods: Paired samples of human subcutaneous adipose tissue were obtained from 8 subjects (age: 31.0 years; BMI: 24.9 kg/m2) during aesthetic liposuction. Adipose tissue fragments were incubated for 24 hours with proinflammatory IL-1β

2 ng/ml in order to stimulate inflammation, or with IL-1β 2 ng/ml and 1,25-OH-vitamin-D 100 nM (vitD). Gene expression levels for MCP-1, IL-6 and IL-8 were measured by RT-PCR and was normalized to GADPH levels. Protein levels in media was measured by ELISA.
Results: Stimulation with IL-1β increased MCP-1 mRNA expression 6-fold ($p=0.009$). VitD reduced this MCP-1 expression by 48% ($p= 0.01$). IL-1β-stimulation increased the expression of IL-6 24-fold ($p<0.001$). This increase was reduced 32% by vitD ($p=0.002$). Expression of IL-8 increased 30-fold compared to controls ($p= 0.003$). Incubation with vitD reduced mean levels of IL-8 mRNA expression by 35% ($p=0.031$).
At the protein level vitD reduced IL1β-induced increased secretion of IL-8 protein by 18%($p=0,005$). The vitD-induced reduction in IL-6 and MCP-1 protein levels did not reach statistical significance.
Conclusion: VitD reduces the IL-1β mediated increased inflammation in human whole adipose tissue samples indicating anti-inflammatory effect of vitD in human adipose tissue.

P02.02 Zhulin Ma

A COMPARISON OF PHARMACODYNAMICS AND PHARMCOKINETICS OF INSULIN ASPART, BIPHASIC INSULIN 70 AND 50, AND FAST-ACTING HUMAN INSULIN IN PATIENTS WITH TYPE 1 DIABETES, A RANDOMISED, QUADRUPLE CROSS-OVER TRIAL

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Methods: Type 1 diabetes patients received individually identical doses of the four different insulin on 4 separate days in this randomized crossover study. Having achieved overnight stable blood glucose control by intravenous infusions of insulin and isotonic glucose, one of the trial insulin was injected subcutaneously and a standard meal was given in the morning. Plasma glucose and serum insulin were recorded the following 12 hr
Results: A total of 24 type 1 diabetic patients were screened and 23 patients were enrolled. One failed during screening. Nineteen patients (fifteen men and four women) completed all test visits. Three patients withdrawn due to personal reasons, and one withdrawn because of lack of compliance. Statistic analysis was based on the 19 completed patients. The average age was 40.7 (22-63) years old, duration of diabetes was 20.9 (3-47) years, baseline HbA1c was 8.2% (7.0-9.8), baseline insulin dose was 0.79 (0.49-1.28) U/kg/24 hr, and BMI was 25.5 kg/m2 (20.6-30.3). Twelve of the 19 patients experienced minor hypoglycaemic episodes. No major hypoglycaemic episodes occurred in this trial. Some patients experienced more than one event during a single visit. Average time to hypoglycaemia appeared to be fastest for Insulin Aspart (average 190 min) and slowest for Human insulin (average 266 min). Fourteen of the 19 patients had to discontinue the trial procedures because of the high glucose level. No serious adverse events were reported. Analyses of plasma glucose and serum insulin are ongoing; pharmacokinetic and pharmacodynamic comparisons are therefore incomplete.

P02.03 Esben Laugesen

ARTERIAL STIFFNESS AND ISCHEMIC CEREBRAL DISEASE IN PATIENTS WITH TYPE 2 DIABETES

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Background: Type 2 diabetes patients experience increased cardiovascular morbidity and mortality. Hence, identifying early markers of subclinical vascular pathology is crucial for efficient risk stratification and timely institution of individualized preventive measures. Stiffening of the arteries change the characteristics of the pulse waves in the conduit arteries during the cardiac cycle. However, it is unknown whether measuring the pulswave indices 1) pulse wave

velocity (PWV) in the aorta and 2) central systolic and diastolic blood pressure (BP), can enhance identification of diabetes patients with high risk of ischemic stroke, as indicated by cerebral white matter lesions (WML´s) identified by MRI, beyond and above traditional risk markers.
Hypothesis and aim: PWV and central BP can identify diabetes patients with high risk of macrovascular ischemic cerebral lesions with a higher sensitivity than conventional risk markers. To investigate if increased PWV and/or central BP is associated with a higher prevalence of cerebral WML´s in diabetes patients.
Methods: 100 type 2 diabetes patients with diabetes duration <5 years and 100 sex and age matched controls are included. Carotid-femoral PWV and central BP indices are measured non-invasively by applanation tonometry. Cerebral MRI is performed with a 1.5 Tesla scanner.
The association between white matter lesions and pulse wave indices will be analyzed with regression analysis adjusting for potential BP, biochemical and demographic confounders.
Status: 150 patients have been included as by September 2010, and the remaining patients are scheduled. Completion of data collection thus by February 2011.

P02.04 Thomas Svava Nielsen

DIFFERENTIAL REGULATION OF ADIPOSE TISSUE LIPOLYSIS IN HUMANS DURING FASTING AND EXERCISE - A POSSIBLE LINK TO INSULIN RESISTANCE

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Fasting and exercise are both characterized by a strong increase in lipolysis. However, in the fasting state insulin sensitivity decreases but during exercise it increases. The aim of this project is to determine how the gene expression, protein levels and activity of Adipose Triglyceride Lipase (ATGL) and Hormone Sensitive Lipase (HSL) and their co-regulators change in human adipose tissue in response to fasting and exercise.
Eight healthy men (25.5 ± 4.3 yr) were studied for 6 h (a 4 h basal and a 2 h clamp period) on 3 occasions: in the basal state and after 72 h fasting and 1-h ergometer cycling at 65% maximal oxygen uptake. Adipose tissue biopsies were taken at t = 0 and 270 min. Gene expression analysis was performed by RT-PCR, and proteins were analyzed by western blotting.
We found that circulating FFA levels were increased to similar levels (approximately 2-fold compared to control) by both fasting and exercise. During fasting insulin failed to suppress FFA levels, suggesting adipose tissue insulin resistance. Although most of the enzymes and co-regulators were unaffected at the protein level, ATGL protein was slightly increased after fasting. Furthermore, G(0)/G(1) Switch Gene 2 (G0S2) mRNA was decreased by fasting but was unaffected by exercise. Since G0S2 is an inhibitor of ATGL, this suggests that G0S2-mediated inhibition of ATGL could be decreased by fasting, resulting in an increased production and accumulation of diacylglycerol (DG). As DG accumulation is known to induce insulin resistance, this might explain part of the observed decrease in insulin sensitivity seen during fasting.

P02.05 Michael Gejl Jensen

DIFFERENCES AMONG LONG-ACTING INSULINS FOR THE TREATMENT OF TYPE 2 DIABETES (T2D)?

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Most guidelines suggest that failure of oral antidiabetic drugs should be followed by the addition of a basal insulin. In most countries NPH-insulin, glargine and detemir remain the only choices. Clinical trials show that the metabolism and metabolic outcomes after treatment with intermediate- or long-acting insulins differs little. Despite this, the hypoglycemic potential, the effect on body weight and adherence to

insulin treatment may affect the choice of basal insulin. Adherence seems to be negatively correlated to the prescribed dose and the number of injections. Further the choice of basal insulin might be influenced by the number of units necessary to achieve the goal for HbA1c.
By searching the literature we identified all RCTs comparing long-acting insulins for the treatment of T2D. We continued by reviewing only studies in which similar anti-hyperglycaemic potential of the treatments was achieved.
All drugs were efficacious regarding the main purpose of decreasing glycaemia. For an equal efficacy we were able to detect other differences among the treatments and furthermore an estimate on the number of units of insulin needed to achieve comparable glycaemic control. The analysis confirmed a favorable profile of both analogues regarding hypoglycaemia. For detemir, we additionally identified a favorable profile regarding weight gain and need for an increased number of units of insulin to achieve comparable HbA1c responses. We conclude that the efficacy of insulin treatment seems to vary little between the available products, however doses needed to achieve similar effects vary; units used per hba1c reduction could be a relevant parameter for the choice of insulin.

P02.06 Xiaoping Chen

DOES ISOSTEVIOL (ISO) HAVE A BENEFICIAL EFFECT ON GLUCAGON SECRETION AND TREATMENT OF TYPE 2 DIABETES (T2D)?

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Background: T2D is the result of an insulin deficiency and resistance along with an absolute or relative excess of glucagon. The increase in glucagon level contributes to the hyperglycaemic state seen in T2D subjects, by stimulating hepatic glucose mobilization. Our studies have shown that free fatty acids (FFAs) acutely stimulate glucagon secretion from the alpha cells. If Isosteviol (ISO) counteracts the α-cell hypersecretion caused by FFA and thereby possess a potential for prevention and treatment of T2D is unknown.
Methods: Long term incubation studies with alpha TC1-6 cells in the present of palmitate with/without different concentrations of ISO. We investigated the effect of ISO on glucagon secretion, glucagon content and proliferation in alpha TC1-6 cells.
Results: The cells were cultured for 72-h with ISO to detect glucagon secretion in the presence of 2 or 18 mM glucose with/without 0.5 mM palmitate. ISO per se (10-10 to 10-6M) had no effect on glucagon secretion. At 2 mM glucose, ISO (10-8 M) reduced palmitate-stimulated glucagon release by 12 %($p<0.05$). At 18 mM glucose, ISO (10-8,10-6M) reduced palmitate-stimulated glucagon release by 27 % ($p<0.05$) and 27% ($p<0.01$) respectively. At 18 mM glucose, palmitate with ISO reduced the proliferation rate of the TC1-6 cells with 25 % ($p < 0.05$). There was no significant change in glucagon content after 72-h culture with palmitate and/or ISO.
Conclusion: ISO counteracts the α-cell hypersecretion caused by long-term palmitate exposure. ISO seems to possess a putative role as a glucagonostatic drug, to be used as a new potential anti-diabetic drug in the treatment of T2D.

P02.07 Merete Lindberg Hartvigsen

EFFECTS OF BIOFUNCTIONAL CARBOHYDRATES ON THE METABOLIC SYNDROME

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Background: Sedentary lifestyles and inappropriate diets are causes of the global increase in the prevalence of the metabolic syndrome (Mets). People with Mets have among other hyperglycaemia and low-absorbable starch and dietary fibre can be used to regulate glucose uptake.
Objective: To study the effects of modified starch and whole grain on insulin sensitivity, satiety feeling, metabonomics and gene expression by ingestion of bread, which contain 1) enzymatic modified starch consisting of amylopectin with higher proportion of α-1.6 linkages 2) dietary fibre β-glucan 3) dietary fibre

arabinoxylans 4) bread with intact kernels 5) bread with milled kernels compared to 6) white bread.
Design: An in vivo parallel, randomized intervention study is going to be conducted in a pre diabetic animal model (Zucker Diabetic Fatty (ZDF) rats), where ZDF rats will be randomized to the six different diets. Determination of insulin sensitivity, lipids, gene expression and metabonomics will be performed. An acute, randomized crossover intervention study are planned to be conducted in subject with Mets. Blood samples will be collected over 4 hour after ingestion of test meals containing the six experimental breads together with water. Determination of glycemic, insulinaemic and incretin response, glycemic index (GI), glycemic load, ghrelin, PYY, stomach emptying rate, metabonomics and subjective satiety feeling with VAS technique will be performed.
Perspectives: This project will give us a greater understanding of the metabolic fingerprint, as seen after ingestion of low-GI foods and thereby improve opportunities for designing foods with low GI that is particularly suited to people with Mets.

P02.08 Ermina Bosnjak

ENDOTOXIN & CYTOKINES. DO PROTEIN LOSS AND METABOLIC EFFECTS DEPEND ON CNS ACTIVATION OF STRESS HORMONES OR ON LOCAL MECHANISMS IN MUSCLE AND FAT?

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Background: Endotoxin is a bacterial lipopolysacharide and generates cytokine release and inflammation. Cytokine TNF-α mediates protein loss, lipolysis and hyperglycemia, and generates stress hormone response with activation of the hypothalamo-pituitary axis and release of ACTH, growth hormone, glucagon and epinephrine. These hormones are in general catabolic and generate protein loss, lipolysis and hyperglycemia.
Objectives: We hypothesise that the metabolic effects of Endotoxin and TNF-α, including protein loss, fatty acid release and decreased glucose uptake, depend on two mechanisms: (i) direct local effects in muscle and fat tissue and (ii) activation of the hypothalamo-pituitary axis and a stress hormone response.
Methods: Study protocol 1: 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, under local anesthetics. TNF-α (6 ng/kg/h) vs. placebo were perfused into the femoral artery of the leg. Furthermore, catheters were inserted into the antebrachial veins for blood samples and infusion of isotope-labeled tracers. Femoral vein sampling allowed assessment of local metabolic events in the leg. Each study comprised a 3 h basal period and a 3 hour glucose clamp. Leg blood flow was measured using Doppler ultrasonography. Muscle biopsies were performed. Study protocol 2: Placebo, Endotoxin (0,1 ng/kg/h) and TNF-α (24 ng/kg/h) were given systemically (i.v.) in antebrachial vein in eight patients with hypopituitarism (to block stress hormone release) and in eight healthy subjects, all studied thrice. Every study comprises a 4 h basal period and a 2 h glucose clamp.

P02.09

P02.10 Mikkel Vendelbo

INSULIN RESISTANCE DURING PROLONGED FASTING IS ASSOCIATED WITH IMPAIRED AS160 PHOSPHORYLATION AND GLYCOGEN ACCUMULATION IN HUMAN SKELETAL MUSCLE

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During a prolonged fast human skeletal muscle is dependent on lipid oxidation for its energy substrate metabolism. This is associated with development of insulin resistance and a subsequent reduction of insulin stimulated glucose uptake. The mechanisms that control insulin sensitivity under these conditions are unresolved; insight into the regulation of insulin sensitivity can have important implications for pathological conditions as type 2 diabetes. Therefore, we investigated 8 healthy subjects after a 72 h. fast and during a control (overnight fast). Insulin action on skeletal muscle was assessed by a hyperinsulinemic-euglycemic clamp and by determination of insulin signaling to glucose transport. In addition, substrate oxidation, muscle lipid accumulation, regulation of glycogen synthesis, AMPK and Growth Hormone signaling were assessed. Insulin sensitivity was reduced during fasting and substrate oxidation shifted to predominantly lipid oxidation. This was associated with accumulation of lipid and glycogen in muscle. Insulin signaling to glucose transport was impaired at specific phosphorylation sites on AS160, a key regulator of glucose uptake. However, fasting did not affect the phosphorylation of the upstream kinases of AS160 (Akt and AMPK), or mRNA expression of SOCS3. These finding suggests that insulin resistance in muscles from healthy individuals can be induced by regulation of site specific phosphorylation of AS160 without affecting Akt. This indicates an important role for AS160 in the regulation of glucose uptake, not only in mediating the signal to glucose transport, but also as a point of regulation of insulin sensitivity under physiological conditions.

P03.01 Anne Sophie Ågård

AFTER INTENSIVE CARE &NDASH; THEN WHAT? PATIENT AND PARTNER PERSPECTIVES

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Introduction: In Denmark 15-25.000 patients are admitted to ICU annually. The number is increasing but survival is improving. Literature gives reason to believe that critical illness and admission to ICU radically affects patients and their relatives through hospitalisation and after discharge. We know very little about the long-term course after discharge and the ensuing concerns and coping strategies described from the perspective of patients and their partners. Particularly, the vital and extensive role of partners throughout recovery of patients requiring intensive care has not been adequately addressed.

Aim: 1) To study the trajectories of former ICU patients and their partners during the first year after discharge to develop a theoretical account of their situation, their concerns and ways of coping during convalescence.

2) To identify patients' and partners' use of health care and social services and long-term affiliation to the labour market.

Method and material: Design: Explorative interview study (grounded theory). Participants: 18 former ICU-patients intubated more than 96 hours with no appreciable chronic conditions prior to admission aged 25-70 years and their partners. Data: a) Semi-structured interviews with patients and partners at 3 and 12 months and group interviews, b) Data from public registers.

Findings: As data collection and analysis is incomplete, findings will be reported at the conference.

Conclusion: We expect our findings from this Danish 1-year follow-up study will add valuable knowledge to the on-going efforts of healthcare professionals to improve intensive care and prepare patients, their partners and family for discharge and convalescence.

P03.02 Morten Søndergaard Jensen

AGE AT CRYPTORCHIDISM DIAGNOSIS AND ORCHIOPEXY IN DENMARK: A POPULATION-BASED STUDY OF 508,964 BOYS BORN FROM 1995 TO 2009

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Background: Early treatment of cryptorchidism may be necessary to preserve fertility and international guidelines now recommend that congenital cryptorchidism be treated with orchiopexy before one year of age. Acquired cryptorchidism should be treated at presentation. The adherence to these guidelines during recent years is not known, and the aim of this study is to present data on age at cryptorchidism diagnosis and orchiopexy in recent Danish birth cohorts.
Methods: A population of 508,964 Danish boys, born alive from January 1, 1995 to December 31, 2009, was identified using The Danish Civil Registration System. Five birth cohorts were defined, 1995-1997, 1998-2000, 2001-2003, 2004-2006 and 2007-2009. The boys were followed in the Danish National Patient Registry for a diagnosis of cryptorchidism and for an orchiopexy procedure. Data was analyzed using the Kaplan-Meier estimator and Cox regression models.
Results: During follow-up, 10,094 boys were diagnosed with cryptorchidism and 5,473 of these underwent orchiopexy. The mean age (years) at diagnosis among boys followed for at least six years was: 1995-1997 cohort, 3.3 (95 % confidence interval: 3.3; 3.4); 1998-2000 cohort, 3.1 (3.1; 3.2); 2001-2003 cohort, 2.9 (2.8; 2.9). The corresponding mean age (years) at orchiopexy was: 1995-1997 cohort, 3.8 (3.7; 3.9); 1998-2000 cohort, 3.6 (3.5; 3.7); 2001-2003 cohort, 3.3 (3.2; 3.4).
Conclusion: In the more recent birth cohorts of 1995 to 2009 we found a shift towards younger age at cryptorchidism diagnosis and orchiopexy.

P03.03 Sofie Gry Pristed

ASSOCIATION BETWEEN ANTHROPOMETRIC MEASURES AND HEALTH RELATED QUALITY OF LIFE IN THE DANISH DIET, CANCER AND HEALTH STUDY

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Background: The association between anthropometric measures (AM) and health related quality of life (HRQoL) has predominantly been described in clinical studies of obese individuals seeking bariatric surgery. Less is known about the association at a population level; covering several BMI categories.
Aim: To examine associations between AM and HRQoL in a Danish population based study.
Hypotheses: A) AM are associated with HRQoL; thus, persons with AM outside the normal range are assumed to report a low HRQoL compared to individuals within the normal range. B) AM above the normal range is associated with a low physical HRQoL. C) AM below the normal range is associated with a low mental HRQoL.
Method: A cross-sectional study based on the Danish prospective study Diet, Cancer and Health. Men and women between 50 and 64 years of age, born in Denmark, living in Copenhagen or Aarhus County, with no former diagnosis of cancer registered in the Cancer Registry were invited to participate. After approximately five years of follow up questionnaires concerning diet, lifestyle, AM and HRQoL were mailed to the eligible persons.
Statistics: Associations between HRQoL and the two predictors, BMI and waist circumference, were investigated using multiple linear regression analysis. Separate analyses were performed for men and women. Age and co-morbidity were entered

as covariates. Graphical methods were used to ensure that the underlying assumptions for the regression analysis were not violated. HRQoL scores were calculated using QualityMetric Scoring Software.
Results: Analyses ongoing.
Conclusion: Analyses ongoing.

P03.04 Kirsten Krabek Frantzen

CARING FOR THE CAREGIVER - A QUALITATIVE STUDY OF PARENTS' PREFERENCES FOR TREATMENT OF THEIR CHILD WITH AUTISM

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Background: Autism Spectrum Disorder (ASD) is a severe neurodevelopmental disorder with childhood onset. The children have impairments in communication, social interaction and stereotyped repetitive behaviours, and the condition has pervasive impact on their families. Several studies conclude that parental and family aspects in various ways influence the parents' reason for treatment choice and the outcome for the ASD child. To optimize the conditions for intervention and development for ASD-children, it is necessary to investigate these parental and family aspects, which until now only has been sparsely studied.
Aim: The aim of this study is to investigate whether and how parent-related predictors are relevant as aspects to consider when one has to decide what autism-specific treatment is most optimal for the child and family. The aim of this PhD study is to explore and define factors that are important to parents in assessing whether they find the treatment optimal.
Method: In this research area sparsely investigated, an extensive qualitative design is chosen to gain varied insight and information about parameters important for parents in evaluating different treatment choices.
Data are collected through qualitative semi-structured interview with parents to children with ASD. The study is conducted at Aarhus University Hospital at department B, and includes 12 couple of parents of children now aged 7-11 years which previously have been diagnosed with ASD at the department. The 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.

P03.05 Jette Ahrensberg

CHILDHOOD MALIGNANCIES. SYMPTOMS AND DIAGNOSTIC INTERVAL.

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Background: Most children seen in primary care suffer from quite harmless conditions which makes it a diagnostic challenge to single out children with rare and life-threatening diseases such as cancer. Misinterpretation of cancer symptoms by patients, parents and physicians may delay diagnosis and treatment.
Methods: December 2009, we initiated a nationwide population-based study on childhood cancer in Denmark. We included all children (N=430) diagnosed with cancer from 1 January 2007 to 31 September 2009 by using information from the Danish Registry of Childhood Cancer. Data was obtained through questionnaires and register-based information.
Results: The time interval from symptom onset to initiation of treatment was divided into patient delay, doctor delay and system delay. Patient delay was defined as the time from symptom onset until first presentation to a primary care physician (PCP), doctor delay as the time from first presentation until initiation of a cancer-specific investigation and system delay as the time from start of a PCP-initiated investigation until start of treatment. Overall, the median total delay was 60 days (IQI 21-169 days). We found that delay varied considerably with cancer type and age at diagnosis. At first presentation, many children had few and uncharacteristic symptoms.

Conclusion: For all types of delay, a proportion of children experienced very long delays. Delay varied between diagnostic groups. Older children, in general, seem to wait longer from symptom onset until start of treatment than younger children.

P03.06 Dorthe Sørensen

COMMUNIKCATION AND COLLABORATION WITH COPD PATIENTS IN NON-INVASIVE VENTILATION

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Introduction: Although non-invasive ventilation (NIV) is an effective treatment for COPD patients with acute hypercapnic respiratory failure; achieving treatment success remains a challenge. Patients' inability to tolerate the mask is one of several indicators for treatment failure.
Aim: This nursing study aims to describe communicative and collaborative facilitators and barriers to promote success with the NIV treatment.
Methods: At present 10 hospitalised COPD patients with acute exacerbation treated with NIV have been recruited. Data was collected by participant observation of the COPD patients' treatment and care, followed by interviews with the patients after completed treatment and analysed according to the grounded theory methodology.
Results: Our preliminary results show a) that the patients' comfort is a main concern that covers mask tolerance and b) that the most important precondition for comfort is meeting the patients' basic needs. Some nurses are able to communicate and react to the patients' signs of unmet current needs, whereas others pay less or no attention to these signs. Once the patients feel comfortable with breathing, thirst, hunger, excretion, body temperature, sleep, communication and involvement, they tend to tolerate the mask.
Conclusion: The emerging grounded theory highlights the patients' comfort as a significant precondition for mask tolerance. Comfort should therefore be a primary goal in the communication and collaboration with patients in NIV. Further data collection and analysis are necessary to saturate this emerging grounded theory.

P03.07 Priscila Corraini

DEFINING AND DIAGNOSING CASES OF PERIODONTITIS

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The aim of this project is to contribute to the establishment of a scientific basis for the diagnosis and classification of cases of periodontitis, based on a nominalistic disease concept. The nominalistic approach dictates that subjects are classified based on well-defined operational criteria that link the diagnosis with the expected treatment outcome. We plan to recruit adults representing a broad spectrum of periodontal disease manifestations and treat them using standard non-surgical therapy including a one-year follow-up with regular supportive therapy. Unlike most studies on the effect of periodontal therapy, we plan to use explicit success criteria, allowing assessment to what extent goals for treatment have been reached. Using the treatment outcomes in relation to the defined success criteria we seek to classify the patients according to their baseline characteristics, using multilevel latent class modeling techniques. This approach allows us to define latent groups of patients with different treatment success probabilities, and we anticipate that we can predict group membership on the basis of the baseline characteristics of the latent groups. The baseline characteristics considered comprise standard clinical parameters; health-related behavioral parameters, such as smoking, and oral health-care habits; general health parameters, including conditions such as diabetes; and assessment of social and psychological stressors. The value and hence the validity of the classification model we hope to develop can then be subject to a more formal test using the randomized controlled clinical trial design.

P03.08 Kirsten Hansen

CONCERNING CHILDREN OF PARENTS WITH MAJOR DEPRESSION

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Numerous international studies have documented that a parent's depression increases the risk that the child experiences psycho-social impairment, psychiatric or somatic disease during childhood or as an adult. It remains an open question whether the potential consequences of parental depression are commonly known and acknowledged among general practitioners and professionals in municipal departments and in children's daycare in Denmark. International studies have reported positive results from intervention programmes and support targeting both children and their families; most of these studies have been conducted in psychiatric settings. In Denmark 96 % of patients with depression are treated in general practice. Previous project-experience suggests that an unknown, but large number of children receive little or no information or municipal support regardless of their parent having a depression.
The present study aims to answer the following questions:
Which support is given to 2-14-year-old children of parents with depression in Denmark?
How does the actual support match the children's needs?
Until May 2013 the investigation will be conducted in two phases.
Phase 1: Qualitative interviews in parts of municipalities – comprising a total of 175.000 citizens
Phase 2: A national questionnaires investigation.
Respondents: parents with depression, sick-listed for 8 weeks and their partners, general practitioners, municipalities.
The results will provide data that may be used for developing instruments for providing cross-sectional support to children of parents with depression in Denmark.

P03.09 Zhanna Tairova

DISRUPTION OF RETINOID AND CYP SYSTEMS AND EMBRYO DEVELOPMENT IN MARINE ORGANISMS &NDASH; A POTENTIAL MODEL FOR HUMANS.

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Some environmental persistent organic pollutants (POPs) can be highly toxic and pose risk for both natural fauna populations and humans. POPs can disrupt an array of molecular and cellular mechanisms causing endocrine disruptions, cancer and teratogenic effects. Potentially, POPs can interfere with embryo development and reproduction. At present, there is only limited knowledge of the potential effects of dioxin-like compounds and polycyclic aromatic hydrocarbons in the Danish environment. The Ph.D. project is expected to link exposure to POPs such as dioxin-like compounds and PAHs to effects in aquatic organisms and mammalian cell cultures by combining different in vivo and in vitro biomarkers in both laboratory and field studies. However, another perspective of this approach is exploring the potential of mammalian in vitro bioassays as screening tools for environmental samples and to contribute to a better integrated exposure assessment for aquatic organisms as well as for humans.

P03.10 Susanne Lemcke

EARLY SIGNS OF ADHD AND AUTISM IN TODDLERS.

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Background: Attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) are severe neuropsychiatric disorders appearing in childhood. The prevalence of ADHD and ASD is 30-70 and 6-7 per 1000 children, respectively. The average age of diagnosis for ADHD is 8-10 years and for ASD 4-6 years. Early identification and treatment of the disorders has shown to improve prognosis for the children. Studies have indicated that it is possible to identify early signs of ADHD and ASD in children in the first 2 years of life. However evidence leading to early detection on population basis is still lacking.
Objectives: 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 or ASD.
Methods: In the Danish National Birth Cohort (DNBC) approximately 70,000 women were interviewed about their child's development, behaviour and growth when the child was 6 and 18 months of age. In the study period, children in Denmark diagnosed with ADHD and ASD are registered in the Danish National Patient Register; thus, it is possible to identify children with ADHD and ASD in the DNBC. Analyses of the information about the diagnostic groups in DNBC will provide us with characteristics before the age of two years of children who later develop ADHD or ASD.
Perspective: In the future, the results from the project will help plan and implement an action to improve the early detection and care for children with ADHD and ASD to secure appropriate development.

P04.01 Eduardo Vázquez Garza

CHARACTERIZATION OF NK CELL SUBPOPULATIONS BY HCMV REACTIVATION IN IMMUNOCOMPROMISED PATIENTS, FOCUSING ON CD94/NKG2A- AND CD94/NKG2C POPULATIONS

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Background: Human cytomegalovirus in immunocompromised patients has increased morbidity and mortality. Natural killer cells are crucial controlling these infections. Assessing the response in groups with increased risk of HCMV disease (untreated/treated patients with chronic lymphocytic leukemia), and HCMV seropositive and negative healthy donors, will have an adequate surface marker comparison.
Hypothesis: The correlation of HCMV disease with relevant NK/T cell subpopulations and surface markers in immunosupressed patients may lead to a better understanding of how to diagnose patients with high risk of developing HCMV.
Purpose: To characterize NK and T cell subpopulations (NKG2A, NKG2C, CD56-) in patients with malignant hematological diseases in the course of cytoreductive treatment, which typically leads to immunosuppression, then comparing to normal gender-and age-matched controls.
Materials and Methods: We propose the use of an in-vitro system co-culturing HCMV (strain AD169) infected fibroblasts with mononuclear cells from 45 mL peripheral blood samples from patients and donors, infection will be assessed using the detection of HCMV Immediate Early Antigen. To characterize the effect of HCMV on NK cell subsets (expressing NKG2A and or NKG2C), multi-color flow cytometry will be performed to detect proliferation using CFSE, viability with 7-AAD as well as production of key cytokines.
Perspective: Improve the characterization of the immune system response focusing on NK cell changes against HCMV, being of importance for future infectious diseases control.
Status: Starting sample collection (2011-2012) and performing optimization of the above described methods.

P04.02 Maria Bro Kloster

DEREGULATED EXPRESSION OF PRDM1 ISOFORMS IN MALIGNANT B CELLS

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This study focuses on B-cell malignancies of non-Hodgkin´s lymphomas (NHL). The most frequent subgroup of NHL is diffuse large B-cell lymphoma (DLBCL) that initiates and progress through accumulation of genetic alterations and consequently changes in gene expression patterns.
The transcription factor, the positive regulatory zinc finger domain protein 1 (PRDM1), is the master regulator of the terminal B-cell differentiation. PRDM1 is deleted or mutated in a subset of DLBCL and is suggested to have an important role in development of DLBCL. In addition, two transcripts of PRDM1, namely PRDM1α and PRDM1β, are observed in DLBCL patients and cell lines, but not in normal tonsils, where only PRDM1α is expressed. PRDM1β is functionally impaired and differs from PRDM1α by having a disrupted PR domain. However, which role PRDM1β plays in DLBCL is unknown. Based on qPCR results from 24 DLBCL patients, PRDM1α and PRDM1β are differentially expressed with more than 2 fold in approximately 20% of the cases, but not in normal tonsils. In the same samples, the PRDM1 gene is deleted in approximately 15% of the cases based on a cytogenetic analysis.
A transcription repressor function of PRDM1β has been suggested due to its potential to compete with PRDM1α for DNA binding, thereby blocking for the function of PRDM1α. These isoforms are generated by use of two distinct promoters. Aberrant promoter usage is documented in various cancers but so far not in B-cell malignancies. Thus, the use and role of alternative promoters and resulting protein isoforms of PRDM1 in DLBCL will be pursued by analysis of DNA methylation and protein levels of PRDM1.

P04.03 Torben L. Andersson

PROTEIN PROFILES OG CHEMORESISTANCE IN B-CELL MALIGNANCIES STUDIED IN MYELOMA CELL LINES AND THE MYELOMA HIERARCHY BY PROTEIN ARRAY ANALYSIS

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Surface enhanced laser desorption/ionization time of flight mass spectrometry (SELDI TOF MS) combines matrix-assisted laser desorption/ionization (MALDI) and a variety of capture affinity techniques for protein purification and analysis. The SELDI TOF MS technique is a fast, robust and promising method for high throughput protein profiling.
The background for this project is to introduce a new protein identification array technology, which can be applied on clinical samples from patients with malignant B cell diseases. The idea is that a comparison of normal and malignant tissues could result in protein profiles identifying protein that can function as biomarkers for disease.
The objective of the current study is to optimise the method of protein isolation and analysis. To make SELDI reliable, there is still a need to optimize the mass spectral method and to identify and reduce the sources of technical and biological variation. The hypothesis is that optimizing the cell lysis buffer and addition of a protein pre-purification filtration step, will optimize the mass spike resolution and response and finally improve the reproducibility.
The aims are to establish and validate methods for protein purification To optimise fractionation, “chip array” purification and analysis of subcellular proteins. To establish a database of Mass spec array profiles, from B cell lines.

P04.04 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 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 control individuals.
Results: By combining an optimized panel of CD markers with RNA amplification we have to date performed global gene expression analysis on down to 5000 memory B-cells and 2800 plasmablasts from healthy individuals using the Affymetrix Exon array 1.0. Preliminary data from control samples show that 24 genes including the tumor suppressor gene FLCN are expressed at the same levels, however with marked differences in splice pattern between subpopulations in blood. 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
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P04.05 Niels Frost Andersen

THE IMPACT OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) GENE POLYMORPHISMS IN MULTIPLE MYELOMA PATIENTS TREATED WITH HIGH-DOSE THERAPY.

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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. Angiogenesis is a complex process in which new blood vessels grow from already existing vessels or develop from primitive stromal cells committed to endothelial differentiation. Angiogenesis is activated in different diseases, especially in malignant tumours where angiogenesis is important for the proliferation and metastatic process. In multiple myeloma, increased angiogenesis is associated with disease activity and survival. Vascular endothelial growth factor (VEGF) stimulates angiogenesis and thereby tumour growth and metastasis. VEGF is expressed by myeloma cell lines and bone marrow plasma cells and VEGF receptors (FLT-1 and KDR/FLK-2) are presented on endothelial cells, which on stimulation are able to produce various haematopoietic growth factors. Several single nucleotide polymorphisms (SNPs) in the VEGF gene with influence on VEGF expression have been described. In this study we investigated the impact of the SNPs -2578C>A (rs699947), -460C>T (rs833061), +405G>C (rs2010963) and +936C>T (rs3025039) in the VEGF gene in 348 patients with newly diagnosed multiple myeloma initially treated with high-dose melphalan and stem cell support. None of the examined geno- or haplotypes had impact on time to treatment failure after initial therapy.

P04.06 Anne Sørensen

BOLD MRI IN SHEEP FETUSES: A NON-INVASIVE METOD FOR MEASURING CHANGES IN TISSUE OXYGENATION.

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Objective. The purpose of this descriptive and experimental study was to correlate changes in the Blood Oxygen Level Dependent (BOLD) MRI signal with direct measurements of fetal tissue oxygenation.
Methods. Seven anesthetized ewes carrying singleton fetuses at gestation 125 days (term 145 days) underwent BOLD MRI, covering the entire fetus in a multi-slice approach. The fetuses were subjected to hypoxic, normoxic and hyperoxic

conditions by changing the O_2/N_2O ratio in the ventilated gas supply. The partial pressure of oxygen (pO_2) in the fetal liver was measured using an oxygen-sensitive optode. Maternal arterial blood samples were simultaneously withdrawn for blood gas analysis.
Results. We demonstrated a consistent increase in the BOLD signal with increasing tissue pO_2. For the fetal liver, spleen and kidney we observed a clear association between changes in maternal arterial blood pO_2 and changes in BOLD MRI signal. Interestingly, we found that the BOLD signal of the fetal brain remained unchanged during hypoxic, normoxic and hyperoxic conditions.
Conclusions. This study demonstrated that BOLD MRI is a reliable non-invasive method for measuring changes in tissue oxygenation in fetal sheep. The unchanged BOLD signal during altered maternal oxygen conditions is likely explained by the brain sparing mechanism.

P04.07 Michael Eriksen Benros

AUTOIMMUNE DISEASES COMBINED WITH SEVERE INFECTIONS AS RESK FACTORS FOR SCHIZOPRENIA: A 30-YEAR POPULATION-BASED
Abstract:
Background:
Autoimmune diseases have been associated with an increased risk of schizophrenia and it has been suggested that brain-reactive auto-antibodies may constitute part of the mechanisms behind this association. Further an increased permeability of the blood-brain-barrier (BBB) has been observed during periods with infection and inflammation. Therefore we investigate if autoimmune diseases combined with the exposures of severe infections can increase the risk of schizophrenia.
Methods:
We linked nationwide population-based registers including the Danish Psychiatric Central Register and the National Hospital Register. Data were analyzed as a cohort study using survival analysis techniques and 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 increases the risk of schizophrenia by 31% (IRR= 1.31, 95% CI, 1.20-1.43) and a history of hospitalization with infection increases the risk of schizophrenia by 59% (IRR=1.59, 95% CI, 1.56-1.63). If a person has both an autoimmune disease and an infection, the risk of schizophrenia is increased even more (IRR=2.25, 95% CI, 2.05-2.46). Three or more infections and an autoimmune disease increase the risk of schizophrenia with IRR of 3.42 (95% CI, 2.94-3.95). The results remained significant after adjusting for substance use disorders and psychiatric family history.
Conclusions:
Autoimmune disease and the number of severe infections requiring hospitalization are risk factors for the development of schizophrenia in a dose-response relationship. The increased risk is compatible with an immunological hypothesis for some cases of schizophrenia.

P04.08 Olga Kudryavtseva

THE ROLE OF L-TYPE CALCIUM CHANNELS IN VASCULAR REMODELING AND SMOOTH MUSCLE PHENOTYPIC EXPRESSIONS
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The voltage dependent L-type calcium channels (LTTC) are one of the key players in excitation-contraction and excitation-transcription coupling in vascular smooth muscle cells (SMC). Understanding LTTC physiology and function is essential for management of cardiovascular complications.
In vivo LTTC downregulation using transfection with small interference RNA (siRNA) is one of the approaches to tackle this issue. Preliminary findings in rat mesenteric vascular bed showed that the channel can be successfully downregulated by 75 % after 3 days of transfection. Functional consequences of LTTC downregulation include reduction of vascular tone and contractility, and

remodeling. There are also evidences that SMC could have switched phenotype from classical contractile to synthetic non-contractile.
In this project we aim to determine if change in expression of SMC marker genes, characteristic for both phenotypes, has occurred in LTTC down-regulated arteries. Moreover, we will investigate if other plasma membrane channels (store-operated calcium channels, T-type calcium channels) are compensatory upregulated, due to loss of LTTC, and if sarcoplasmic reticulum (SR) channels are functioning normally. Taking in notion the role of LTTC in excitation-transcription coupling, we will quantify of transcriptional factors CREAB and NFAT, which are activated by calcium influx through LTTC. Finally, blood flow and sheer stress will be assessed in order to distinguish between the primary effects of transfection and secondary effects of the blood flow disturbance in these arteries.
The genes of interest will be quantified with qPCR, the function of SR channels will be assessed by measuring agonist-induced calcium responses. NFAT and CREB will be assessed using immunohistochemistry. Stereology and BrDU immunostainig will be used to determine cellular background for the vascular remodeling observed in previous studies.

P05.01 Martin Skøtt

A NEW RODENT MODEL FOR STUDYING SUPERIMPOSED ACUTE KIDNEY INJURY ON CHRONIC KIDNEY DISEASE

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Objective: Pre-existing renal failure serves as a risk factor in the development of acute renal failure. Furthermore, superimposed acute on chronic renal failure is connected with an increased mortality and risk of progression to end stage renal failure.
Methods: A new two-stage rat model was developed, where 5/6 nephrectomy was performed, followed by intestinal ischemia and reperfusion. Wistar male rats were used, all initially undergoing either 5/6 nephrectomy or sham operation. Six weeks later half of each group were exposed to either clamping of the superior mesenteric artery for 45 min followed by 90 min of reperfusion or sham operation. Rats were placed in metabolic cages, i three periods of each three days, for collection of urine and measurment of water and food intake.
Results: During the six weeks of induction of renal failure, the nephrectomised rats develop polyuria, polydipsia, azotaemia and proteinuria. Furhermore, urinary excretion of neutrophil gelatinase-associated lipocalin (NGAL) was increased in the nephrectomised rats. Acute kidney injury induced by intestinal ischemia and reperfusion, was confirmed by a 60% increase in serum creatinine and 10% increase in serum urea. Conclusion: These results showes that in this two-stage rodent model, pre-existing as well as acute kidney injury were achieved.

P05.02 Johannes Martin Schmid

BASOPHIL SENSITIVITY DECREASES DURING THE UPDOSING PHASE OF SUBCUTANEOUS IMMUNOTHERAPY (SCIT) IN SUBJECTS ALLERGIC TO GRASS POLLEN

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Background: SCIT reduces the specific type-1 allergic response and is associated with significant relief of symptoms. Basophil sensitivity, defined as half maximum activation (LC50) after crosslinking of IgE by relevant allergen, is thought to reflect clinical intensity of allergic disease. We hypothesized that changes in basophil sensitivity can be used to evaluate the magnitude of the humoral component of these specific changes.
Methods: We measured the changes in basophil activation in 24 subjects (18 patients on standard SCIT, 6 patients in a control group) with rhinoconjunctivitis due to grass pollen allergy. Basophil activation was measured by flow cytometry as

the percentage of CD63 expression on the surface of CD193+ blood basophils activated by 8 $\log_{10}$ dilutions of grass pollen extract (0,00001-100 SQU/ml). This was done on washed cells and cells reconstituted with plasma from the baseline and present visit, respectively. Half maximum activation (LC50) was considered a measure of basophil sensitivity. The LC50 was used as the primary outcome measure.
Results: The LC50 in the samples reconstituted with present plasma changed from a median LC50 of -2,34 at baseline to a median LC50 of -1,10 after reaching maintenance dose (n=24. $p<0,001$). No significant changes were observed in the control group, the samples reconstituted with baseline plasma or the washed cells samples.
Conclusion: We found the LC50 a useful and accurate tool to follow the development of tolerance during SCIT. As sensitivity decreased 14-fold in samples reconstituted with present plasma, but not in the other groups, the main mechanism leading to allergen tolerance involves humoral factors.

P05.03 Frederik Hvid-Jensen

BARRETTS ESOPHAGUS AND ADENOCARCINOMA: A NATIONWIDE 17-YEAR FOLLOW-UP STUDY ON 15102 PATIENTS DIAGNOSED WITH BARRETTS ESOPHAGUS IN DENMARK.

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Dep of Gastrointestinal surgery L Research

Introduction: At present the risk among Barrett's Esophagus (BE)patients for developing esophageal adenocarcinoma (EAC) is believed to be around 0.5% per year which drives the decision for a widespread use of surveillance endoscopy. Though publication bias, small samples or restricted demography hampers many of the estimates making a large nationwide study necessary.
Material & Methods: Using the Danish Civil Registration System and the Danish Pathology Registry we identified all patients in Denmark, who between 1992 to 2009 had an endoscopy with biopsy and, following this, a histology diagnosis of Barrett' s esophagus. We assessed the incidence of EAC and High Grade Dysplasia (HGD) and compared with the expected number of cancer cases based on national age and sex specific incidence rates, calculating standardized incidence ratios (SIR) and 95% confidence intervals (CI).
Results: - 58 incident EACs and 98 HGDs in years 2-17.
- EAC incidence of $111/10^5$ years (Barrett's) and $2.5/10^5$ years(popul.). HGD incidence of $191/10^5$ years.
- 2372 EACs among age & sex adjusted nationwide background population in the same period.
- 2.8 times higher risk for EAC among male patients and only 2/58 (3.4%) EAC in the age-group of 18-49 years.
Conclusion: We believe this is the so far most well-founded and reliable estimate of the EAC risk among BE patients, and it is significantly lower than what has been published by the majority of studies within this area. The results further raises doubt about the cost-effectiveness of generalized BE surveillance.

P05.04 Hans Linde Nielsen

CLINICAL EPIDEMIOLOGY AND MANIFESTATIONS OF *CAMPYLOBACTER CONCISUS*

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Campylobacter jejuni/coli (95/5%) are currently the major causes of bacterial diarrhoea. After the acute gastroenteritis some patients have sequelae like irritable bowel syndrome, reactive arthritis, inflammatory bowel disease and Guillain Barré syndrome. For Campylobacter concisus the epidemiology and disease burden are not clarified. C. concisus has been proposed to cause diarrhoea among children and immunocompromised patients, and recently it has been proposed to be an etiologic factor for the development of Crohn's disease. In this study we will clarify the

epidemiology and clinical manifestations caused by C. concisus. We will describe the differences and similarities of the clinical presentations caused by C. jejuni/coli and C. concisus.
Methods: Patients with C. jejuni/coli and C. concisus in the faecal sample are included in the study. The study period will be two years and started January 2009. The patient's clinical data are reviewed by use of the patient's medical records as well as a questionnaire survey with a follow up for six months. From the first 18 months preliminary results show that C. concisus is very common. It is only surpassed by C. jejuni/coli and is more frequent than other enteric pathogens such as Salmonella spp. Early results show that patients with C. concisus present a more prolonged disease history more like chronic diarrhoea rather than acute enteritis. The study should provide a greater understanding of the clinical consequences of infection with the emerging C. concisus. It will provide information on whether the bacterium is a human pathogen of the gut causing diarrhoea and any sequelae as evidenced by infection with C. jejuni/coli.

P05.05 Anne Brosbøl-Ravnborg

CONTROL OF DENDRITIC CELL FUNCTION BY VITAMIN D_3

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Background: Dendritic cells (DCs) are antigen-presenting cells playing a major role during induction of immune responses by activating naïve T cells. The level of DC maturation is important for the development of regulatory T cells and thus the maintenance of tolerance and immunological homeostasis. 1,25-dihydroxyvitamin D_3 (vD_3) has immunomodulatory properties and affects the immune system through a number of mechanisms including the influence on DC differentiation. Low level of vD_3 is associated with various autoimmune diseases.
Hypothesis: We hypothesise that vD_3 is important in maintenance of periferal tolerance by influencing DC function.
Methods: DCs were generated from human monocytes and matured with LPS. DC differentiation and maturation were determined by changes in expression of surface molecules (HLA-DR, CD80, CD83, CD86, CD40 and CD14) by flow cytometry and morphology by microscopy. VD_3 was added in different concentrations and at different time-points during differentiation and maturation.
Results: The presence of vD_3 blocked both the differentiation and maturation of DC. Microscopic examination showed that vD_3 inhibited formation of dendrites on DCs consistent with immature DCs. In contrast to control DCs, maturation of DCs was repressed by vD_3 as judged by surface molecule expression. The effects of vD_3 were dependent on its concentration during differentiation.
Conclusions: The presence of vD_3 inhibited DC differentiation and maturation in a complex manner dependent on its concentration during the DC maturation process. Elucidating the mechanisms behind this may be of importance for understanding the role of vD_3 during induction of periferal tolerance.

P05.06 Kristian Ravlo

EFFECT OF REMOTE ISCHEMIC PRECONDITIONING ON DENDRITIC CELLS IN BLOOD AFTER RENAL TRANSPLANTATION - FLOW CYTOMETRY IN A PORCINE MODEL.

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Delayed graft function after transplantation is associated with an increased risk of rejection. Remote ischemic preconditioning (rIPC) is repetitive, brief, non-damaging periods of ischemia in a distant organ followed by reperfusion, which can induce a systemic protection against ischemia- reperfusion injuries. We speculate,

that the protective effect of rIPC involves myeloid (mDC) and plasmacytoid dendritic cells (pDC); cell-types that are attracted by ischemic endothelium and known to induce both tolerance and immunity. Specifically, we hypothesised that the number of circulating DCs is affected by rIPC.
Brain death was induced in seven 65-kg pigs that were subsequently nephrectomised. After 22 hours of cold ischemia, the kidneys were transplanted into fourteen 15-kg pigs. The recipients were randomised to either rIPC or non-rIPC before reperfusion and observed 10 hours after reperfusion. Blood samples were collected and the number of DCs were determined by flow cytometry. The DCs were identified on the basis of forward- and side-scatter characteristics of CD14 negative mononuclear cells with intermediate expression of Swine Workshop Cluster 3 (SWC3). DCs were further classified as either pDC ($SWC3^{dim}$, $CD4^{+}$, $CD14^{-}$) or mDC ($SWC3^{dim}$, $CD4^{-}$, $CD14^{-}$).
A significant development in the number of pDCs was found in both groups. No significant differences were found comparing rIPC and non-rIPC with respect to the number of mDC and pDC.
In Conclusion, DCs were quantified in the pig, and our study showed that rIPC did not affect levels of mDC and pDC in blood within the 10 hours after transplantation studied.

P05.07 Karen Leth Nielsen

EXPRESSION OF HUMAN &BETA;-DEFENSIN 1 IN CORRELATION TO URINARY TRACT INFECTION

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Background:Human β-defensin 1 (HBD-1) is an antimicrobial peptides of the urinary tract. The peptide production is up-regulated app. 3x during pyelonephritis. Additionally, KO defb-1 mice have 30% more bacteria in their urine than WT mice. In this study we asked, whether HBD-1 plays a role in predisposition to UTI.
Methods:This study aims for inclusion of 60 patients (E. coli infection of $\geq 10^4$ CFU and leucocyturia) and 60 controls (subjects who have never had UTI). All were women between 18 and menopause, and generally healthy. Patient samples were collected during and after infection and controls delivered 1 urine sample. HBD-1 was measured in urine by ELISA. The amount of HBD-1 was normalized to creatinine level (measured using an enzyme immunoassay) in the urine sample, i.e. expressed as ng HBD1/mg creatinine.
Results: Preliminary results based on 45 controls and 24 patients show a mean level of HBD-1 at 86.2ng/mg and 84.6ng/mg for patients after infection and for controls, respectively. The mean HBD-1 level for patients during infection was 90.7ng/mg. There was no significant difference between patients during and after infection, nor for controls compared to patients without infection (P=0.67, P=0.1, respectively). After infection 8 patients had lower HBD-1 level, 8 had similar level and 8 patients had higher HBD-1 contents in urine.
Conclusion: The results are only preliminary, however, they indicate that there is no significant difference in amount of HBD-1 produced between patients and controls, and the level of HBD-1 is not significantly up-regulated during cystitis or is poorly regulated in patient group. The latter will be investigated further.

P05.08 Srikanth Chiliveru

HERPES SIMPLEX VIRUS EXPLOITS IFI16 TO PROMOTE ITS REPLICATION

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Herpesviruses are important human pathogenic viruses that carry their genome in the form of double-stranded DNA. 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. Binding of type I Interferons (IFN) to their cognate cell surface receptors initiates a series of intracellular signaling cascades resulting in the activation of specific target genes, known as IFN inducible genes (Ifi genes). It is reported that Ifi204 gene, a member of the Ifi200 family is activated by Mouse Cytomegalovirus infection and is required for its replication instead of the antiviral activity. The function of Ifi204 on

regulation of viral replication is not known. Recent identification of Ifi16 (Ifi204 in mice) as a potential novel cytoplasmic DNA receptor for herpes simplex virus (HSV) from our laboratory encourages the project to investigate the involvement of Ifi16 in HSV replication.
In this project, preliminary information suggests that Ifi16 knockdown inhibits HSV replication and reduce IFN production. The future studies will investigate the involvement of Ifi16 in HSV replication using mutant HSV strains. Analysis of IFN activation and Ifi16 production in a time dependant manner explains the link between the Ifi16 and IFN production in relation to replication of the virus. The involvement of NF-κB pathway and recruitment of NF-κB and Ifi16 to immediate early promoters will also be addressed and also the specificity of Ifi16 to DNA viruses will be checked. Collectively, the project findings may address the relation between Ifi16 and HSV replication.

P05.09 Anders Kirch Dige

HIGH REGULATORY T CELL PERCENTAGE PREDICTS CLINICAL RESPONSE OF ADALIMUMAB TREATMENT IN CROHN'S DISEASE

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Background: Anti-tumor necrosis factor (TNF)-α antibodies modulates increased regulatory T cell (Treg) percentages in rheumatoid arthritis, but results from studies in Crohn's disease (CD) have sofar been conflicting. We investigated dynamic changes of peripheral Tregs in CD during treatment with the anti-TNF-α-antibody adalimumab (Humira®).
Methods: Blood samples from 26 CD patients were analysed by flow cytometry before and after initiation of adalimumab treatment at week 1 and 26 for the percentage of CD25+CD127-FoxP3+ Tregs among CD4+ T cells.
Results: High Treg percentages among CD4+ T cells predicted clinical response to adalimumab. Treg percentage was inversely related to disease activity, estimated by the Crohn's disease activity index (CDAI) (r=-0.41, p 0.040). Patients who did not respond to therapy had baseline Treg percentages which were significantly lower than those in responders (4.0% (95% CI) vs. 5.1%, p <0.007). During the 26 weeks treatment periode, we observed no changes in Treg percentages .
Conclusion: High Treg percentages among CD 4 T cells predicts clinical rsponse to adalimumab in CD. Treg percentage is inversely related to disease activity in Crohn's disease. There is no early modulation of Treg percentages among CD4+ T cells from adalimumab that could be mediators of the clinical effects.

P05.10 Christian Ammitzbøll

HUMORAL PATTERN RECOGNITION MOLECULES IN PLASMA AND SYNOVIAL FLUID IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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The innate immune system can contribute to the development of rheumatoid arthritis (RA). One potent contributor to such processes is the complement system, and evidence from animal and clinical studies show that the complement system contributes to the development of rheumatoid arthritis. The lectin pathway of the complement system is activated through the recognition of pathogens or altered self structures by mannan-binding lectin (MBL) or the three ficolins in collaboration with MBL-associated serine proteases (MASPs).
We assessed the lectin pathway by measuring MBL, MASP-2, MASP-3, M-ficolin and H-ficolin in paired samples of plasma and synovial fluid of 27 patients with RA and 30 patients with osteoarthritis.
The median concentration for each protein was significantly higher in plasma than in synovial fluid ($p<0.001$) and the concentration in paired plasma and SF concentrations correlated ($p\leq0.001$) for both osteoarthritis and rheumatoid arthritis. We found that the concentration of M-ficolin correlated to the neutrophil

granulocyte count in both plasma ($p=0.01$) and synovial fluid ($p<0.001$) of rheumatoid arthritis, and also in plasma of 78 controls ($p=0.03$). Our results indicate that the neutrophiles have an important physiological role in determining the M-ficolin concentration both locally and systemically. The role of monocytes for the level of M-ficolin was less obvious. Out of this finding entails the important knowledge, that it is critical in future clinical investigations of M-ficolin to include a WBC. We are planning further studies that will hopefully be able to elucidate if proteins of the lectin pathway play a role in the pathogenesis of rheumatoid arthritis

P05.11 Stine Maria Lund Andersen

VALRUBICIN ACTIVATES PKCA IN KERATINOCYTES

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Valrubicin is a cytostatic drug, a second generation anthracycline excelling from its predecessors by demonstrating preserved treatment efficiency combined with an improved safety profile, presenting no skin toxicity upon contact. It is currently approved for the treatment of bladder cancer, but the development of the new cream formulation paves the way for topical treatment of skin diseases. Recently, Valrubicin has shown a beneficial effect in animal models of psoriasis and non-melanoma skin cancer (NMSC): disorders both characterised by keratinocyte hyperproliferation.

The aim of the present study was to investigate the effect of valrubicin on intracellular signaling pathways. Signaling through protein kinase C (PKC) is suggested as valrubicin is localised in the cytosol and structurally resembles diacylglycerol (DAG), a natural PKC ligand.

Moreover, PKCa is located in the suprabasal layers of the epidermis and is important for the regulation of keratinocyte growth and differentiation.

The effect of valrubicin on activation of PKC was evaluated by its translocation from the cytosol to the plasma membrane.

The study was carried out in HaCaT cells and the effect of valrubicin visualized by western blotting and confocal microscopy.

Valrubicin stimulation significantly increased the levels of PKCa in the plasma membrane two fold, indicative of translocation and thus activation of PKCa.

The observed increase in PKCa activity may help explain valrubicin's mode of action in reducing proliferation and promoting apoptosis in keratinocytes, and may be responsible for the beneficial effect observed when treating psoriasis and NMSC.

P06.01 Camilla Nyboe

ATRIAL SEPTAL DEFECT IN THE ADULT

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Objective: Atrial Septal Defect (ASD) is an opening between the two atriums, which leads right ventricle over perfusion. Pulmonary infections, palpitations, fatigue and atrial fibrillation are common symptoms. Often symptoms do not appear until late adulthood and there is still no clear recommendation as whether to close an ASD in the elderly patients or how the natural progress of the disease evolves.

Hypothesis: Closure of an ASD will lessen symptoms and right ventricular dilation equally in patients over and under fifty years of age.

An untreated ASD will lead to increased use of antibiotics, more admissions to hospital and an increased incidence of atrial fibrillation compared to patients with a closed ASD and a control group.

Methods: Data from Dansk Register for Medfødte Hjertesygdomme will be used. Hospital records will be consulted for confirmation of diagnosis.

Study 1: 177 patients with an ASD closed surgically or by catheter in Skejby Hospital will be registered. Symptoms and pre- and post closure EKKO will be used to compare patients over and under fifty years of age.

Study 2 and 3: All Danish ASD patients above 18 years of age will be registered and divided into groups whether the ASD has been closed or not. The two groups will be compared to a control group matched in gender and age regarding number of pulmonary infections, use of antibiotics, occurrence of atrial fibrillation and pulmonary hypertension. Questionnaires will be sent to the patients questioning symptoms and NYHA class.
Perspectives: An increased number of patients born with an ASD reach adulthood and it is therefore relevant to investigate what treatment those patients should be recommended.

P06.02 Jo Bønding Andreasen

CAN ROTEM® ANALYSIS BE APPLIED FOR HEMOSTATIC MONITORING IN PEDIATRIC CONGENITAL HEART SURGERY?

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Successful management of bleeding disorders after congenital heart surgery requires detection of specific coagulation disturbances. Whole-blood rotation thromboelastometry (RoTEM®) provides continuous qualitative haemostatic profiles.
To compare the performance of RoTEM® with that of conventional coagulation tests in a paediatric population, we conducted a descriptive study in children undergoing congenital cardiac surgery. For that purpose 60 children were enrolled and had blood samples taken before, immediately after and 1 day after surgery. Conventional coagulation tests included: activated partial thromboplastin time, prothrombin time, fibrinogen, fibrin D-dimer, thrombin clotting time, factor XIII and platelet count.
Post-surgical haemostatic impairment was present to some degree in all children, as seen by pronounced changes in aPTT, prothrombin time, thrombin clotting time and platelet count as well as RoTEM® analysis. RoTEM® demonstrated marked changes in clotting time (prolonged by 7-18%), clot formation time (prolonged by 46-71%), maximum clot firmness (reduced by 10-19%) and maximum velocity (reduced by 29-39%).
Comparison of the two techniques showed that conventional coagulation tests and RoTEM® performed equally well with regard to negative predictive values for excessive postoperative drain production (>20 mL/kg/24 h) with an area under the curve of approximately 0.65.
RoTEM® can detect haemostatic impairments in children undergoing cardiac surgery and the method should be considered as a supplement in the peri-operative care of the paediatric population where targeted transfusion therapy is necessary to avoid volume overload.

P06.03 Jakob Stegger

BODY COMPOSITION AND BODY FAT DISTRIBUTION IN RELATION TO LATER RISK OF ACUTE MYOCARDIAL INFARCTION: A DANISH FOLLOW-UP STUDY

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Introduction: Obesity is a modifiable risk factor for acute myocardial infarction (MI), but lean body mass (LBM) may also be an important factor. Low LBM may increase the risk of MI in lean persons, and furthermore LBM may modify the effect of obesity on MI. Thus, the inability of the classical anthropometric measures to evaluate LBM may lead to misclassification of MI risk in both lean and obese.
We investigated the associations between incident MI and bioelectrical impedance analyses (BIA) of body composition in combination with body mass index (BMI)

and anthropometric measures of body fat distribution.
Methods and Results: From 1993 to 1997, 27 148 men and 29 863 women, aged 50 to 64 year, were recruited into the Danish prospective study Diet, Cancer and Health. During 11.9 years of follow-up we identified 2 028 cases of incident MI (1 487 men and 541 women). BMI, waist circumference (WC), hip circumference (HC) and BIA of body composition including body fat mass (BFM) and LBM were measured at baseline. We used Cox proportional hazard models with age as time axis and performed extensive control for confounding.
Weight, BMI and classical as well as BIA estimates of abdominal obesity showed significantly positive associations with MI. However, BFM adjusted for WC showed no association. Low LBM was associated with a higher risk of incident MI in both gender, and high LBM was associated with a higher risk in men.
Conclusion: Obesity were positively associated MI, but estimates of obesity achieved by BIA seemed not to provide additional information to classical anthropometric estimates. Both high and low LBM may be positively associated with MI.

P06.04 Sidse Kringelholt

CARBONIC ANHYDRASE INHIBITORS INDUCE VASORELAXATION IN ISOLATED INTRAOCULAR PORCINE CILIARY ARTERIES.

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Purpose: Carbonic anhydrase inhibitors (CAIs) are widely used to reduce the intraocular pressure in glaucoma. However, CAIs have also been shown to have vasorelaxing properties and consequently beneficial effects on ocular perfusion. The purpose of the present study was to investigate whether CAIs have the same effect on the tone of intraocular ciliary arteries as on retinal arterioles, and if so to determine the mechanism of action of this effect.
Methods: Isolated intraocular porcine ciliary arteries were mounted in a myograph for isometric tension recordings. After precontraction with the prostaglandin analogue U46619, concentration-response experiments were performed with the CAIs acetazolamide and dorzolamide. The experiments were performed at normal pH and acidosis, each combined with normocapnia or hypercapnia, as well as the absence of CO2 and $HCO3^-$.
Results: Preliminary experiments showed that the examined CAIs induced a significant vasorelaxation of ciliary arteries. Dorzolamide induced relaxation at the seven highest concentrations ($p<0.05$, paired t-test), whereas acetazolamide only induced relaxation at the two highest concentrations ($3*10^{-3}$ M - 10^{-2} M, $p<0.05$).
Conclusions: Carbonic anhydrase inhibitors have a vasorelaxing effect on intraocular porcine arteries in vitro. The mechanism of action of CAIs in the treatment of glaucoma may involve several mechanims, including changes in aqueous humor production and changes in the blood flow to the ciliary body.

P06.05 Sophie Constantin Lütken

CARDIAC AND RENAL PARAMETERS IN LOW SODIUM DIET VERSUS STANDARD SODIUM DIET IN RATS WITH EXPERIMENTALLY INDUCED HEART FAILURE

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Heart failure (HF) is a common complication to myocardial infarction (MI) and is associated with increased plasma vasopressin levels and renal aquaporin-2 (AQP2) protein abundance as well as sodium and water retention. Thus reduced sodium intake is often recommended to patients with HF. However, the physiological and subcellular mechanisms in the heart and kidneys are not well understood.

Furthermore, extensive low sodium diet in rats is also a common way to elevate plasma aldosterone levels. Aldosterone acts on mineralocorticoid receptors mainly in the renal collecting ducts where it induces sodium retention. But there is also good evidence that aldosterone can act in concert with elevated vasopressin levels to increase the effect of the latter. This would lead to further increased water and salt retention than seen with vasopressin alone through activation of salt transporters throughout the nephron, as well as AQP2 in the collecting ducts. To further examine these hypotheses, male Wistar rats were subjected to ligation of the left anterior descending artery or sham operation. The following MI and HF were confirmed with echocardiography at day 10 and again at day16 to investigate the cardiac effects on seven days feeding with low sodium diet with or without co-treatment with dDAVP (0.5 ng/h s.c.) or vehicle. This is the first study to investigate the role of sodium restriction on renal and cardiac effects in HF rats versus sham rats.

P06.06 Jonas Agerlund Povlsen

CARDIOPROTECTION IN TYPE 2 DIABETES MELLITUS - SIGNIFICANCE OF THE MALATE-ASPARTATE SHUTTLE

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Background: The diabetic heart has a deficient ability to activate endogenous cardioprotection. Citrin, aralar and EAAT1 function as carrier proteins in the malate-aspartate shuttle (MAS) that couples glycolysis with mitochondrial ATP production. Preischemic MAS inhibition with aminooxyacetate (AOA) mediates cardioprotection. EAAT1 is downregulated in type 2 diabetic hearts.
We hypothesize that MAS transporter proteins are gradually downregulated in type 2 diabetic hearts with progression of disease, with resultant decreased ability to benefit from metabolic cardioprotection, i.e. preischemic MAS inhibition with AOA.
Materials and methods: The hearts of homozygote Zucker diabetic fatty rats (6 (prediabetic), 12 (onset of diabetes) and 24 (late diabetes) wks old) and age-matched heterozygote controls are studied in an isolated perfused rat heart model (KH-buffer containing 11 mM glucose) and subjected to 40 minutes ischemia and 120 minutes reperfusion. Each group is divided into two subgroups: (i) control and (ii) preischemic AOA (0.1 mM). Expression of MAS transporters citrin, aralar and EAAT1 is measured by qPCR and immunoblotting on tissue biopsies from the left ventricle. Differences between groups are determined from changes in infarct size, postischemic hemodynamic recovery and tracer estimated glucose metabolism. Additional measures include changes in concentrations of Krebs Cycle intermediates in interstitial microdialysis samples and lactate, pyruvate and glutamate in coronary effluent samples.
Research plan/perspectives: Data collection for the outlined project is performed in the autumn of 2010. Preliminary results are ready to present at the PhD Day 2011.

P06.07 Christian Daugaard Peters

CARDIOVASCULAR EFFECT OF IRBESARTAN IN NEWLY STARTED HEMODIALYSIS PATIENTS: A SUBSTUDY WITHIN THE SAFIR-STUDY

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Background: Cardiovascular disease (CVD) and high mortality associated with CVD are major concerns in patients with chronic renal failure. Several studies suggest that Angiotensin II receptor blockers (ARBs) have a favourable effect on CVD which can not be explained solely by the well-known blood pressure lowering effect of these drugs. Hence, ARBs might reduce arterial stiffness through inhibition of fibrosis and inflammation. Presently, fear of elevated potassium and hypotension during dialysis often results in the abandoning of ARB-treatment, when patients begin dialysis.
Hypotheses: ARB has a beneficial effect on the cardiovascular system in newly started hemodialysis patients (HD-pt.) causing:
- Stable or less cardiac hypertrophy
- Less arterial stiffening

- Improvement of intradialysis hemodynamics
Methods: SAFIR is a multicenter study begun in April 2009. 80 HD-pt. are recruited from 8 different dialysis centres in Denmark. Patients are randomized double-blind for treatment with either irbesartan or placebo and followed for 1 year. Blood pressure (BP) is closely monitored and a systolic BP of 140 mmHg is the target among all patients. Blood and urine samples are collected 6 times during the study period. A panel of biomarkers involved in inflammation, fibrosis and vascular calcification are studied in order to determine the effect of ARB-treatment. Cardiac status is evaluated by echocardiography at entry and at the end of the study. The degree of arterial stiffness is measured noninvasively by applanation tonometry. Hemodynamic parameters during dialysis are obtained using ultrasound flow devices connected to the HD-machines.
Perspectives: Reduction of CVD-burden in HD-pt.

P06.08 Niels Ramsing Holm

COMPARISON OF TWO-STENT TECHNIQUES FOR CORONARY BIFURCATION LESIONS. POOLED ANALYSIS OF THE BBC ONE STUDY AND THE NORDIC BIFURCATION STUDIES

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Background: There is limited data comparing clinical outcome after two-stent techniques for treatment of coronary bifurcation lesions. Although the simple one-stent strategy is prefered for most bifurcation lesions, the optimal two-stent technique(s) for complete lesion coverage has to be sorted out.
Methods: This patient level meta-analysis compares the culotte and the classical crush two-stent techniques performed in the British Bifurcation Coronary Old New and Evolving strategies study (BBC ONE), the Nordic Bifurcation Study and the Nordic Bifurcation Stent Technique Study by intention to treat.
Results: Clinical follow-up was available for a total of 811 patients treated by either culotte (n=332) or crush (n=479) two-stent techniques after 9 months. Major Adverse Cardiac Events (MACE) rate was 9.3% vs. 9.6% (ns). MACE included rates of total death (0.6% vs. 1.1%, ns), non-procedural myocardial infarction (2.7% vs. 2.3%, ns) and target vessel revascularization which was performed (8.1% vs. 8.2%, ns) in culotte and crush treatment respectively. Rate of stent thrombosis were 2.1% in culotte and 1.4% (ns) in crush treated patients.
Conclusion: The culotte and classical crush two-stent techniques were associated with similar and low rates of 9-months MACE after treatment of coronary bifurcation lesions.

P06.09 Rikke Esberg Kirkfeldt

COMPLICATIONS AND ASSOCIATED RISK FACTORS FOLLOWING PRIMARY PERMANENT PACEMAKER OR CARDIAC RESYNCHRONIZATION THERAPY IMPLANTATION. A POPULATION-BASED COHORT STUDY OF 28,860 DANISH PATIENTS

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BACKGROUND: During the past decades the indication for permanent pacemaker

(PM) implantation has expanded, and new principles of treatment has emerged, namely cardiac resynchronization therapy (CRT-P). Many studies have focused on device infections and associated risk factors, and studies have found reoperations to be a strong predictor of later device infections. However, few studies have examined the risk factors associated with complications in general and lead problems in particular, although lead problems are the predominant reason for early reoperations following de novo PM or CRT-P implantations.
AIMS: To determine the incidence of complications after device implantation and associated risk factors in a nationwide population-based cohort.
METHODS: A population-based historic cohort study was performed based on data in the Danish Pacemaker Register. We indentified all Danish patients undergoing primary permanent PM or CRT-P implantation from January 1997 to December 2008. Details regarding implantation procedure, technical specifications, patient related factors, and in-hospital complications after de novo PM or CRT-P implantations were prospectively reported to the DPR from the implanting centres. Furthermore, complication status and complication type (e.g lead problems requiring a reoperation, pneumothorax, and infection) were reported after the first outpatient visit after three to four months.
The incidence of complications is reported as absolute frequencies. Risk factors for complications following device implantation were assessed using unconditional logistic regression. Odds ratios with 95 % confidence intervals are reported.

P06.10 Maria Skytte Tørring

DIFFERENTIAL CONTRACTILE RESPONSE OF SMALLER AND LARGER PORCINE RETINAL ARTERIOLES IN VITRO

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Introduction: Disturbances in the diameter regulation of retinal arterioles are involved in the pathogenesis of retinal vascular disease. Hitherto, studies of diameter regulation have largely been performed on larger retinal arterioles, but recent evidence suggests that the smaller retinal arterioles are also involved in flow regulation and that mechanisms responsible for diameter regulation in these arterioles differ from those of the larger arterioles. Therefore, a method is needed for studying the diameter regulation of smaller retinal arterioles.
Methods: A special tissue chamber was designed for mounting and perfusing a spherical segment of the porcine retina. A camera was connected to an inverted microscope for video recording of changes in the diameter of mounted 1st, 2nd, 3rd and 4th order arterioles, followed by measurements of the vascular diameter on the digital images. Experiments were conducted to study the contracting effect of the prostaglandin analogue U46619, Endothelin 1 or PSS with high potassium (KPSS) on arterioles with different baseline diameter.
Results: All three compounds showed a significant decrease in the contractile properties from the larger to the smaller retinal arterioles ($p = 0.047$). The response was most pronounced for KPSS, was less pronounced for Endothelin 1, and least pronounced for U46619.
Conclusions: Compounds known to contract larger retinal vessels have less contractile power on smaller retinal arterioles. Further studies are needed in order to elucidate the mechanisms responsible for the diameter regulation of smaller retinal arterioles.

P06.11 Frank Holden Christensen

THE EFFECT OF ATORVASTATIN ON THE NO-SYSTEM IN PATIENTS WITH TYPE II DIABETIC NEPHROPATHY, NEPHROPATHY AND HEALTHY PERSONS

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Statins are used to lower serum cholesterol levels in primary and secondary prevention of cardiovascular disease. Statin therapy has led to a significant reduction in mortality and morbidity from cardiac adverse events, stroke and peripheral arterial disease. This is partly explained by a serum-cholesterol lowering

effect of statins. The beneficial effects of statins seem to extend beyond the cholesterol-lowering effects, the so-called pleiotropic effects. These pleiotropic effects may be due to an increase in Nitric Oxide (NO) bioavailability. NO-deficiency is seen in chronic diseases such as hypertension, diabetes and nephropathy
The purpose of this project is to investigate if statin treatment increases the bioavailability of NO.
This hypothesis will be investigated in three randomised, double blinded, placebo-controlled, cross over studies with three different patient groups
Healthy subjects Patients with non-diabetic nephropathy Patients with type II diabetes with nephropathy In the three studies patients will attend to two examination days. 4 days prior to each examination day subjects are treated with either atorvastatin or placebo. During treatment periods subject are given a standardized diet.
On the examination days subject are given L-NMMA, a NO inhibitor, and renal function, central hemodynamic and vasoactive hormones are evaluated.
This study is expected to contribute to increasing knowledge about the mechanisms in play in the development and progression of cardiovascular disease.

P06.12 Vibeke Secher Dam

MOLECULAR CHARACTERIZATION OF CA^{2+} ACTIVATED CL^- CHANNELS IN VASCULAR SMOOTH MUSCLE CELLS

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The presence of a Ca^{2+}-activated Cl^- current in the vascular smooth muscle cells (VSMCs) is well established. This Cl^- current has been suggested to be important for synchronized rhythmic contraction of VSMCs, i.e. vasomotion. We have previously identified two distinct Ca^{2+}-activated Cl^- conductances in the VSMCs. In spite of its obvious functional significance the molecular identity of the Ca^{2+}-activated Cl^- channels (CaCCs) is uncertain. Recently, the bestrophin family and TMEM16A were suggested as candidates for the CaCCs. Using siRNA approach we have previously shown that bestrophin-3 expression was associated with the cGMP-dependent Ca^{2+}-activated Cl^-conductance, while another niflumic-acid (NFA) sensitive Cl^- current was not affected. Her we have found expression of TMEM16A in the vascular wall. In vivo transfection, of rat mesenteric small arteries with siRNA, significantly downregulated TMEM16A. Surprisingly, downregulation of TMEM16A reduced both types of Ca^{2+}activated Cl^- conductance detectable in VSMCs: the cGMP-dependent and the classical Ca^{2+}-activated Cl^- currents. The observation that the cGMP-dependent current is affected by downregulation of both bestrophin-3 and TMEM16A suggests close interaction of these two proteins. Isometric force recordings of the TMEM16A downregulated arteries demonstrate a significant reduction of the amplitude of vasomotion (2 % vs.16% of maximal tension). The frequency of oscillation is not affected (0.20 vs. 0.23 Hz). In conclusion, TMEM16A is expressed in VSMCs and is essential for both Ca^{2+} -activated Cl^- currents. TMEM16a is important for VSMCs synchronization in rat mesenteric small arteries.

P07.01 Philipp Harbig

ADHERENCE IN TREATMENT WITH FUROSEMIDE IN OLDER ADULTS

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Introduction: Nonadherence with medicine intake is a major problem in medicine treatment. The aim of the project 'Methods for Improving Compliance with Medicine Intake (MICMI)' is to compare different compliance registration and intervention methods among elderly living in their own homes. The golden standard of the compliance registration methods in our project is pill count. We assessed adherence of the participants taking Furosemide and compared the adherence rate with the number of all prescriptions, number of changing doses in the observation period, gender and age of the participants. Methods: Among a total of 577 patients and 2728 pill counts and prescriptions, all participants in Furosemide treatment were detected (n=112) and adherence was calculated. Adherence in pill counts was

defined as >80% of the prescribed pills taken in the observed period of one year. Results: Fifteen percent of the participants took less than 80% of expected doses. There was no significant correlation between the number of the prescriptions of Furosemide and adherence (p=0.14), number of changing dose and adherence (p=0.66) and gender and adherence (p=0.9). There was a measurable effect of age on adherent Furosemide intake (p=0.005). Mean adherence rates were higher among older (100-91 year [n=6], 84% and 90-81 year [n=32], 89%) than 'younger' (80-71 year [n=55], 85%, and 70-65 year old participants [n=17], 79%). Conclusion: Adherence to treatment with Furosemide based on pill count among elderly living in their own homes appeared good. There is a trend for better compliance among the oldest compared to the 'younger' participants.

P07.02 Casper Foldager

ADAPTION TO HYPOXIA IN MESENCHYMAL STEM CELLS IS ONLY PARTIALLY IMPROVED BY CHONDROGENIC STIMULATION

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Introduction: Hypoxic environment is essential for maintaining the chondrogenic phenotype and the normal cartilage function. Mesenchymal stem cells (MSC's) from the bone marrow are currently used for the treatment of cartilage defects, but with dissapointing results. The aim of this study is to investigate the response of hypoxia on normal and differentiating MSC's compared to native chondrocytes.
Materials and Methods: Three cell cultures were used: 1. Human chondrocytes; 2. Immortalized (TERT-) MSC's in chondrogenic differentiation medium (diff); 3. TERT-MSC's in standard medium(std). The three groups were divided into three oxygen tensions: 21%, 15%, and 5%. They were cultured in groups for 1, 2, 7, and 14 days. Quantitative gene expression analysis was obtained using qRT-PCR (sox9, collagen type 1, 2 and 10, HIF-1α and 2α) and measurements of proteoglycans, VEGF and HIF-1 synthesis were performed. Data was analyzed using three-way ANOVA.
Results: MSC-diff. produced more proteoglycan than MSC-std. in 21% and 15% oxygen ($p<0.05$) with no difference in 5% oxygen. Expression of HIF-1α increased with lowering oxygen in MSC's while it decreased in chondrocytes. Chondrogenic stimulation of the MSC's resulted in lower VEGF synthesis compared to unstimulated MSC's in 21% and 15% oxygen, but both cultures had higher synthesis than in chondrocytes ($p<0.05$).
Conclusion: This is the first study to show a difference in synthesis of VEGF and HIF-1α in chondrocytes, MSC's and MSC's in chondrogenic differentiation. Our study suggests that a key factor to the lack of cartilage regeneration using MSC's might be an unfortunate response to hypoxia with subsequent angiogenesis.

P07.03 Anders Peter Søndergaard

CORNEAL HYDRATION AND SWELLING PROPERTIES FOLLOWING UVA RIBOFLAVIN COLLAGEN CROSS-LINKING

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Purpose: To evaluate the effect of UVA riboflavin collagen cross-linking on hydration and swelling properties of porcine corneas.
Methods: In porcine eyes, the central corneal thickness (CCT) was determined by ultrasound pachymetry. The treatment group was treated using the standard UVA riboflavin cross-linking procedure (CXL). The central 8 mm cornea was the trephined and the weight measured. In the control group no UVA light was applied. The swelling of the corneal buttons in a saline bath were measured in a custom engineered biomechanical setup. The force exerted by the corneas during swelling in the anterior-posterior direction was measured at different thicknesses (-5%, +10% and +20% of initial CCT). Finally, corneas were freeze-dried to determine dry weight and calculate changes in hydration.
Results: No significant difference in mean dry weight was observed between groups. No significant reduction of central corneal thickness after treatment was observed, and hydration in the CXL group was not significantly different compared to the

control group. The swelling force in all phases was not significantly different in the treatment group compared to the control group. Comparing linear regressions of CCT and swelling force in the groups showed no significant difference.
Conclusions: No changes in hydration or swelling force were observed after the CXL procedure. From previous studies, the CXL procedure primarily affects the anterior 200-µm stroma. In the current setup the full 800 µm thickness is tested and the changes in the anterior 200-µm stroma may not be detectable. Further studies comparing anterior vs. posterior stromal parts are currently being investigated.

P07.04 Trine Østergaard Nielsen

DIRECTING THE ALTERNATIVE SPLICING OF HER4 DECREASES CANCER CELL GROWTH

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The onset of cancer is often associated with a switch in alternative splicing of RNA. We have studied the implications of alternative splicing of human epidermal growth factor (EGF) receptor 4 (HER4), a member of the EGF family of receptors and ligands involved in development and growth of many cancers. In some cases, however, overexpression of HER4 can inhibit cell growth and be beneficial for the survival of cancer patients.
HER4 has two isoforms: CYT1 and CYT2. Skipping of exon 26 results in a receptor lacking 16 amino acids (CYT2) compared to the full-length receptor (CYT1). The skipped exon encodes a protein fragment that comprises a binding site for, among others, PI3K. Experiments in our lab suggest that the CYT2 isoform is associated with decreased cell growth as compared to CYT1 (unpublished data).
On this background we hypothesized that antisense oligonucleotides targeting the splice signals of exon 26, also termed splice switching oligonucleotides (SSOs), will switch the splicing of HER4 to generate CYT2 and lead to reduced proliferation.
We have designed a LNA modified SSO antisense to the 5' splice site of HER4 exon 26 (SSOe26) and demonstrated the ability of SSOe26 to shift the splicing of HER4 towards the CYT2 isoform in cell assays. We show that treatment of two human cancer cell lines expressing HER4 (lung (NCI358) and breast (MDA-MB-231) cancer cells) with SSOe26 results in a decrease in cell proliferation. A SSO with a scrambled sequence, showed no effect on splicing of HER4 pre-mRNA or cell growth.
We anticipate this oligo to have potential as a specific drug which can be used to treat cancer patients with tumors that express the CYT1 isoform of HER4.

P07.05 Eva Greibe

DEVELOPMENT OF A VITAMIN B12 FOOD ABSORPTION TEST BY USE OF RAINBOW TROUT PROTEIN

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Intro: Vitamin B12 (B12) deficiency is associated with anaemia, nerve damage and cognitive decline and is a common condition among the elderly. We have developed and launched an absorption test for free B12, named CobaSorb. In order to employ this test to study the uptake of food bound B12 there is a need for a standardized preparation of protein bound B12 to be used as proxy for food bound B12. The challenge is to find a suitable B12 binding protein. Our approach was to investigate food items eaten unprepared.
Methods: The supernatants of homogenized eggs from different fish were incubated with 57Co-labelled B12. For measurement of B12 binding capacity, affinity- and pH-sensitivity experiments; charcoal precipitation was used to remove excess labelled B12. For characterization of B12 binders, gelfiltration was performed, and glycosylation status was estimated by ConA sepharose precipitation. Protein was purified by affinity chromatography on B12-coupled sepharose followed by gelfiltration.
Results: From an initial screening, rainbow trout eggs were selected for further analysis based on a high content of B12 binding protein. The structural and

functional characteristics of the protein was compared to the human B12 binders; TC, HC and IF. The protein was found to be comparable to HC suggesting that it will be suitable for use in test. The egg fluid was shown to contain a larger content of protein, than did spawn, and the protein was purified from this source.
Conclusions: The findings suggest that the B12 binder from rainbow trout eggs could be used in the development of a B12 food absorption test. Clinical studies are needed to clarify its potential in diagnostics tests.

P07.06 Solveig Klok Matthesen

EFFECT OF DIETARY POTASSIUM SUPPLEMENT ON BLOOD PRESSURE, AUGMENTATION INDEX AND THE RENIN-ALDOSTERONE SYSTEM IN HEALTHY HUMANS.

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Purpose: Animal experiments and studies in humans have shown that potassium treatment can reduce blood pressure due to a reduced contraction of vascular smooth muscle cells. We wanted to test the hypothesis that potassium supplement would decrease peripheral and central blood pressure(CBP), pulse wave velocity (PWV) and augmentation index (AI).
Methods: The effect of potassium 100 mmol /day was measured in a randomized, placebo-controlled, cross-over study of 22 healthy humans. The treatment periods were 4 weeks separated by a 2 week wash-out period. The participants received a standardized diet during the last four days of each treatment period. We measured 24-hour-BP using Kiwex 2430, CBP, PWV and AI using Sphygmocor, GFR using the constant infusion technique with 51-Cr-EDTA, plasma concentrations of renin (PRC) and aldosterone (PAC) using RIAs, and fractional excretion of potassium (FEK) and sodium (FENa).
Results: Urinary potassium excretion increased during the intervention (placebo: 75± 22 mmol/24 hour versus potassium supplement: 168 ±37 mmol/24 hour, $p< 0.05$, means±SD). FEK increased (13±4 to 29±7, $p< 0.05$). FENa , 24-hours BP, PWV, CBP, AI and GFR were not significantly changed. During potassium supplementation, an increase was measured in PRC (7±4 to 10±8 mIU/ l, $P<0.05$) and PAC (378±217 to563±362 pmol/l, $P<0.05$)
Conclusions: Urinary potassium excretion was significantly increased during the intervention indicating that the compliance. Neither 24-hours-BP, CBP nor AI changed significantly during intervention. The lack of decrease in blood pressure might be attributed to an antagonizing effect induced by the increase in the activity of the renin-aldosterone system.

P07.07 Kristina Bennet Emdal

HER4 IN ESTROGEN-RESPONSIVE AND ANTIESTROGEN-RESISTANT BREAST CANCER

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Resistance to endocrine therapy, e.g. antiestrogens (AEs) and aromatase inhibitors, is one of the main challenges to overcome in the treatment of hormone-sensitive breast cancer (BC). HER4 is one of four members of the human epidermal growth factor receptor (EGFR/HER) family, which has essential roles in tumorigenic processes including BC. HER4 exists in four isoforms that exert biologically distinct activities. Two of these isoforms can be proteolytically processed to generate a HER4 intracellular domain (4ICD) which appears to exert different biological functions dependent on the subcellular localization. In order to study AE-resistance, we have developed several AE-resistant BC cell lines. HER4 expression is reduced in the majority of these AE-resistant cell lines compared to parental AE-sensitive MCF-7 cells, making loss of HER4 expression a potential marker for AE-resistance. The aim of this study is to disclose the role of the HER4 isoforms in estrogen-responsive and AE-resistant human BC cells through a combination of cell culture based studies and clinical studies. In AE-resistant cell lines each individual HER4 isoform will be re-expressed using a tetracycline-inducible expression system to

examine whether AE-sensitivity can be regained and to establish the specific roles of the HER4 isoforms. In tumor samples from 1323 Danish BC patients who have received adjuvant endocrine therapy, HER4 expression and intracellular localization of 4ICD will be examined by immunohistochemistry to evaluate the association with disease-free and overall survival. Taken together these studies will help define the role of HER4 for BC cell growth and AE-resistance.

P08.01 Caspar Skau Madsen

A DELTA AND C FIBER COMPONENTS OF CONTACT HEAT EVOKED POTENTIALS (CHEPS) IN CAPSAICIN INDUCED HEAT HYPERALGESIA

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Introduction: There is limited knowledge about the contribution of C and A delta fibers in capsaicin induced heat hyperalgesia. We wanted to examine whether 1) contact heat can evoke reproducible C fiber responses following selective A fiber nerve blockade alone or in combination with application of topical capsaicin and 2) the effect of capsaicin on the A delta response.

Methods: Twenty heat stimuli of 51°C were delivered using the contact heat evoked potential stimulator (CHEPS), and heat hyperalgesia was induced by topical application of 200 µl capsaicin (5%) on the dorsum of both hands. At the left wrist, a selective A delta nerve fiber block was performed by superficial radial nerve compression before capsaicin application, and on the right arm evoked potentials were recorded with and without capsaicin.

Results: On the right arm, capsaicin yielded a decrease in N2 latency from mean 345.2 (37.2) ms 310.5 (38.5) ms recorded from the vertex (Cz) position ($p=0.003$, paired t-test). On the left arm, when only the sensations of warmth remained unaffected of the pressure blockade (after 89.5 ± 5.9 min), 3 subjects showed ultra-late responses 1014-1242 ms (1111 ± 117.7 ms). After the subsequent capsaicin application, ultra-late responses were recorded in 11 subjects (N2 latency 1222.2 ± 75.2 ms).

Conclusions: Our findings suggest that capsaicin facilitates both A delta and C fiber mediated responses to heat.

Contact heat evoked ultra-late responses corresponding to C fiber activity were seen in a few subjects during the compression blockade, with increasing responses following capsaicin application.

P08.02 Anna Tietze

ADVANCED MAGNETIC RESONANCE IMAGING TECHNIQUES; A TOOL TO PREDICT BRAIN TUMOUR TYPES AND GRADES AND TO ASSESS THERAPY RESPONSE

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To date, conventional Magnetic Resonance Imaging (MRI) is the radiological cornerstone of brain tumour evaluation. However, in the past years advanced MRI techniques have been developed and have yielded considerable improvements in tumour assessment.

The objective of this study is to investigate the diagnostic accuracy of Perfusion-weighted Imaging (PWI) in the evaluation of sixty patients with primary brain tumours. We want to calculate tumour blood volume and vessel permeability, important indicators of malignancy. Moreover, we intend to assess basic physiological parameters from PWI data such as the vascular capacacity for oxygen delivery and vessel sizes. We want to investigate if these metrics can describe tumour biology even more precise allowing a more specific pre-surgical diagnosis regarding tumour type, tumour grade and extend of white matter infiltration. We want to combine PWI with Diffusion-weighted Imaging (DWI), a technique that

permits estimation of cellularity.
PWI might improve delineation of targets in tissue sampling in order to achieve the most representative biopsies. It is also very likely that PWI and the aforementioned physiological parameters allow more detailed treatment evaluation, a fact that may allow more specific and individual therapy adjustment in the future.
All patients will undergo pre-surgical MRI including PWI and DWI. The diagnostic accuracy for PWI and DWI regarding tumour type and grade will be assessed. Treatment response and treatment induced changes will be assessed longitudinally for two years comparing advanced and conventional MRI techniques.

P08.03 Tina Birgitte Carstensen

ARE THERE GENDER DIFFERENCES IN COPING WITH NECK PAIN FOLLOWING ACUTE WHIPLASH TRAUMA? A 12-MONTH FOLLOW-UP STUDY

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Background: Little is known about gender differences in coping after whiplash, and to date possible interaction of gender and coping on recovery has not been investigated.
Aims: To examine if gender differences in coping are associated with long-lasting neck pain after acute whiplash.
Methods: 740 participants referred from emergency departments or general practitioners after car accidents in Denmark. Within a median of five days post-collision participants completed questionnaires on collision characteristics, psychological distress, and socio-demographics. After three months they completed the Coping Strategies Questionnaire, and after 12 months a VAS scale on neck pain intensity.
Results: The odds for long-lasting neck pain were more than twice as high for women than for men (OR = 2.17 (95% CI: 1.40; 3.37). However, no gender difference in coping and no interaction between gender and any of the five coping subscales on neck pain after 12 months were found. 'Distraction' increased the odds for considerable neck pain for both men and women (OR = 1.03 (95% CI: 1.01; 1.05), 'reinterpreting pain sensations' (OR = 1.03 (95% CI: 1.01; 1.06), 'catastrophizing' (OR = 1.14 (95% CI: 1.10; 1.18), and 'praying and hoping' (OR = 1.10 (95% CI: 1.05; 1.13) for each point on these scales.
Concluions: No interaction between coping and gender on neck pain was found, thus different coping strategies did not explain the different prognosis observed in men and women. Clinically relevant influence of 'catastrophizing' and 'praying and hoping' to prognosis was found, therefore we should identify patients predominantly using these strategies.

P08.04 Emilia Horjales

BRAIN IMAGING STUDIES ON THE RELATIONSHIP BETWEEN PAIN AND EMOTIONS

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Everyone will experience acute pain at some point in their life: stubbing a toe, burning a finger, or cutting themselves. Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage, or described in terms of such damage". Acute pain functions are important as a warning system, however in cases of chronic pain conditions this state has become permanent, even in absence of any evident tissue damage.Emotions form an important component in the perception and manifestations of chronic pain conditions. Recent studies have focused on the effect of negative emotions on the perception of pain. Tang and colleagues analyzed how unpleasant emotions generated by music can increase the perception of pain and decrease tolerance to pain. The same has been observed in

models in which emotion is generated with odors or images. Important knowledge which still is to be determined is the relationship between positive emotions and pain perception.The overall aim of this Ph.D.-project is to study the relationship between positive emotions and pain. To achieve this we have divided the project into three sub-projects:
Study 1) Establish an experimental model where the interaction between standardized painful stimuli and positive vs. negative emotions can be tested.
Study 2) Analyze with the use of functional brain imaging which areas of the brain are involved in the pain-emotions relationship?
Study 3) Test in chronic pain patients if positive vs. negative emotions can influence the clinical levels of pain and which brain mechanisms may be involved in such interactions.

P08.05 Simon Hjerrild

CEREBRAL INVOLVMENT IN CHRONIC HEPATITIS C VIRUS INFECTION ASSESSED BY MRI

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Objectives: Patients with chronic HCV infection have a high prevalence of depressive disorders, cognitive disturbances, reduced quality of life and fatigue. The majority of HCV patients in Europe have a history of drug abuse and psychosocial stress, making the causal relationship between HCV infection and psychiatric symptoms complex. HCV have been isolated in brain tissue in HCV patients and cerebral magnetic resonance spectroscopy has revealed metabolic abnormalities indicating chronic inflammation. We aim to correlate neuropsychological performance and psychiatric symptoms with viral characteristics (HCV genomic sequencing from peripheral blood and cerebrospinal fluid) and magnetic resonance imaging (MRI). First, we wish to elucidate the causal relationship between chronic HCV infection, cognitive disturbances and psychiatric symptoms. Second, we would like to identify MRI markers for the development of interferon-induced depression.
Methods: An extensive MRI protocol using a 3 Tesla MRI scanner, including diffusion tensor imaging, magnetization transfer sequences, regional cerebral blood flow, FLAIR sequences, hippocampal volumetry and H MR Spectroscopy performed before and after antiviral treatment of 60 HCV patients. 40 HCV patients without pending antiviral treatment and 20 healthy subjects will serve as controls. HCV patients receiving antiviral therapy will be examined for the development of depression after 8 weeks of treatment. Neuropsychological testing, psychiatric assessment will be performed concomitant to the MRI in another study.
Results: Preliminary results will be presented at the Ph.d. day.

P08.06 Dariusz Orlowski

CHRONIC RESTRAINT STRESS CHANGES RAT HIPPOCAMPAL BRANCHING PATTERN AND SPINE DENSITY

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Stress conditions may change cerebral connectivity pattern. To study the effect of chronic stress on hippocampal neuron morphology and spine density a rat model of chronic restraint stress (CRS) was used in accordance with the guidelines issued by the Danish National Committee for Ethics in Animal Experimentation. Adult male Wistar rats were divided into two groups - control rats and rats subjected to 21 days of 6 hr/day restraint stress. The brains were collected and one hemisphere from each brain was fixated by immersion in 4% PFA for 14 days followed by 21 days of Golgi-Cox impregnation. 100 µm thick coronal vibratome sections were obtained and AMG developed. The sections were microphotographed and the morphology of 30-40 neurons from the CA1, CA3b, CA3c, and DG area, respectively were reconstructed (2D) and subjected to Sholl analysis. In addition, in all those areas, manual spine counting was done to estimate spine density. From the other halves of the brains hippocampi were free dissected and used for real-time qPCR analysis of

genes associated with postsynaptic density (spinophilin, homer1-3, and shank1-3). The branching pattern was changed only in the CA3c area where the number of apical dendrites and their total length significantly decreased. In contrast, total CA3 spine density (CA3b + CA3c) remained unchanged, whilst CA1 and DG spine density were significantly increased. Spinophilin, homer1, shank1, and shank2 were significantly up-regulated in the CRS group compared to the control group. In conclusion we find histological and molecular biological evidence that CRS influences hippocampal neuroplasticity by modulation of dendrite branching pattern and spine density.

P08.07 Mohit Kothari

COMPLEX TONGUE TRAINING- A NOVEL APPROACH IN REHABILITATION OF ORAL FUNCTION.

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Objectives: The human tongue is involved in many essential and complex functions. Many stroke patients suffer from potentially life threatening dysphagia. This study aimed to investigate the degree of improvement in performance with a complex tongue training paradigm, the Tongue drive system (TDS).
Methods: 16 healthy subjects participated in 1 hour complex tongue training (session1). With TDS, the subjects were instructed to play a computer game having control of the computer cursor through a magnet attached to the tongue. Data on the magnet position was transferred wirelessly from magnetic sensors on a headgear to a computer. After 1-2 weeks 6/16 subjects participated in a second session as experienced (EXP) subjects. Six naive (NAI) subjects were included as controls. Session 2 involved 2 times 5 min training separated by 30 min rest. Degree of motor learning (number of game points) was compared between sessions and groups. Data were analyzed with ANOVA/T-tests.
Results: The mean (±SEM) TDS performance increased from 21,487±4,089 to 72,620±10,931 points during session 1, $P<0.001$. In session 2, the EXP group showed a baseline (BL) TDS performance (56,423±9,635) similar to the level they had achieved in session 1 (56,861±3,105), $P= 0.966$. In the NAI group, BL performance was similar to session 1 BL, $P=0.521$ and there was a 64.72±17.52 % increase from first to last 5 min, $P=0.003$.
Conclusion: Tongue training with TDS is associated with increase in performance score during consecutive learning. Former experience with TDS influences BL success, indicating a degree of skill retention. The influence of this paradigm on tongue motor cortical plasticity needs further study.

P08.08 René Ernst Nielsen

COMPARING THE EFFECTS OF SERTINDOLE AND OLANZAPINE ON COGNITION (SEROLA)

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Cognitive deficits are considered as a core symptom of schizophrenia, and cognitive symptoms are correlated to functional outcome, partly independent of positive and negative symptoms. The effect of antipsychotics on cognition is not sufficiently examined, but side effects of antipsychotics can worsen cognitive function, e.g. extra pyramidal side effects (EPS), sedation and anticholinergic side effects. Sertindole is an effective and well tolerated atypical antipsychotic. There was no significant difference in EPS in patients treated with sertindole or placebo. Olanzapine is also an effective and well tolerated atypical antipsychotic. Sertindole has, compared to olanzapine, a low affinity for the muscarinergic and histaminergic receptors. Particularly the antagonistic effect on the muscarinergic receptor is believed to diminish cognition, but the theoretical difference has not been shown in clinical studies. Theoretically, sertindole should cause fewer cognitive side effects compared to olanzapine, but no double-blinded randomized studies comparing sertindole with other atypical antipsychotics, with cognition as primary outcome measure, have not

been conducted. In general the quality of previous pharmacological studies on patients with schizophrenia with cognition as outcome is heterogeneous; non-suitable comparator drugs, short study period, lack of double blinding, small study populations and no correlation analysis between cognitive improvements and changes in psychopathology. Further studies on antipsychotics effect on cognition are needed.

P08.09 Leslie Foldager

CONDITIONAL LOGIC REGRESSION: IDENTIFYING SNP INTERACTIONS FROM INDIVIDUALLY TIME-MATCHED CASE-CONTROL DATA

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Gene-gene and gene-environment interactions are likely to be involved in the aetiology of schizophrenia. In an individually time-matched (nested) case-control candidate-gene study of schizophrenia on subjects obtained from the Danish Newborn Screening Biobank[1], genetic markers were genotyped using whole genome amplified DNA from neonatal dried blood spot samples[2]. A number of environmental factors were also included.

Logic regression has been proposed as a classification method for prediction of a response by use of Boolean combinations of binary covariates[3]. A subset-based logic regression approach was recently proposed for identifying and quantifying importance of single nucleotide polymorphism (SNP) interactions in case-control studies[4]. Identification of gene-environment interactions is possible if the environmental measure can be formulated as a Boolean combination of binary variables. We aim at extending logic regression to individually time-matched case-control studies which we will term “conditional logic regression”.

Logic regression has been implemented as libraries in R (www.R-project.org): LogicReg and logicFS. The problem of missing genotypes can be solved by use of imputation as a pre-processing step[5], e.g. using the BEAGLE software package[6]. The documentation of LogicReg gives conditional logistic regression as an example of how to implement new models. Thus, implementation of conditional logic regression is expected to be fairly straightforward.

References: 1. J Inherit Metab Dis 30: 530-536; 2. Genet Test 11: 65-71; 3. J Comput Graph Stat 12: 475-511; 4. Biostatistics 9: 187-198; 5. J Toxicol Environ Health A 71: 803-815; 6. Am J Hum Genet 84: 210-223

P08.10 Karina Bendixen

DOUBLE-STRESS ALTERS EXPERIMENTAL MASSETER MUSCLE PAIN AND AUTONOMIC RESPONSE

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Objectives: The aim of this randomized controlled trial was to investigate the effect of simultaneous application of two stressors, hypertonic saline (HS) evoked pain together with either mental arithmetic test (paced auditory serial addition task, PASAT) or cold pressor test (CPT), on pain and on blood pressure (sBP, dBP).

Methods: 16 healthy women participated in three sessions. They received two 5% HS-injections (five minutes each, 30 minutes apart) per session in their right masseter muscle, to induce pain. First HS-injection was given as an internal control.

At the second HS-injection PASAT, CPT or control (HS alone) was performed. HS-evoked pain intensity was scored on a 0-10 numeric rating scale (NRS). SBP and dBP were recorded by Task Force Monitor (TFM). Correlations were tested with Spearman`s rank correlation test.
Results: PASAT and CPT significantly reduced the HS-pain (ANOVA:$P < 0.001$) compared with control and to a similar extent. SBP and dBP were significantly elevated from baseline during HS-injections ($P < 0.001$). Pain reduction from PASAT was inversely correlated to both sBP and dBP ($\rho = -0.6$, $P = 0.014$; $\rho = -0.8$, $P = 0.001$). No correlation was found between CPT and sBP/dBP ($\rho = 0.2$, $P = 0.620$; $\rho = -0.1$, $P = 0.826$). Control session demonstrated a significant correlation in rise in sBP/dBP and pain ($\rho = 0.6$, $P = 0.013$; $\rho = 0.6$, $P = 0.024$).
Conclusion: Application of a second stressor reduces significantly HS-evoked masseter muscle pain in women and alters the autonomic response. The rise in sBP/dBP from PASAT could be due to baroreceptor activation. CPT-induced stress probably activates other mechanisms, e.g. endogenous pain modulatory systems.

P09.01 Johanne Lade Keller

ANALYSIS OF GENETIC CHANGES AND PROTEIN EXPRESSION PROFILES IN MELANOMA

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Purpose: Melanoma arises from accumulated genetic and epigenetic alterations. Previous melanoma studies have identified various mutations and epigenetic changes. However, these studies have mainly focused on either single or a small range of biomarkers in modestly sized patient cohorts.
We now aim to examine multiple interconnected biomarkers in a large melanoma cohort.
Materials and methods: A total of 40 tissue microarray (TMA) blocks have been constructed from tissues excised at Aarhus University Hospital during the years 2001-2006 including benign naevi (n=60), naevi with dysplasia (n=45), melanoma in situ (n=22), melanoma (n=521) and melanoma metastases (n=19).
Expression of adhesion proteins (N-cadherin, E-cadherin, MCAM, β-catenin), cell-signaling proteins (CD117, PTEN, p-ERK1,2, MITF, p-AKT), and proteins involved in senescence (p16, p53, p14) has been or will be assessed using immunohistochemistry on the TMA slides.
Based on the results of an ongoing pilot study, DNA will be extracted from paraffin-embedded tissue from tumors with sufficient material (n≈150 melanomas) and analyzed for alterations in NRAS, BRAF and KIT.
Finally the results from both the immunohistochemical and the DNA analyses will be correlated with clinical data to identify potential prognostic biomarkers.
Perspectives: We believe ours is the largest melanoma TMA cohort in the world. Analysis of the molecular changes present in key cellular pathways in these melanoma cases, in combination with high-quality clinical data will lead to new insights in melanoma initiation and progression and will give us optimal conditions to identify novel prognostic biomarkers.

P09.02 Jesper Kallehauge

APPARENT DIFFUSION COEFFICIENT (ADC) AS A QUANTITATIVE PARAMETER IN DIFFUSION WEIGHTED MR IMAGING IN CERVICAL CANCER. DEPENDENCE ON B-VALUES USED.

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Background: Diffusion weighted imaging (DWI) has gained interest as an imaging

modality for assessment of tumor extension and response to cancer treatment. The purpose of this study is to assess the impact of the choice of b-values on the calculation of the Apparent Diffusion Coefficient (ADC) for locally advanced gynecological cancer and to estimate a stable interval of diffusion gradients that allows for best comparison of the ADC between patients and institutions.
Materials and methods: Six patients underwent a high resolution single shot EPI based DWI scan with 16 different diffusion gradients on a 3 Tesla Philips Achieva MR-scanner. Data analysis was performed by applying a monoexponential and a biexponential model to the acquired data. The biexponential function models the effect of both perfusion and diffusion.
Results and conclusion: ADC changes of up to 40% were seen with the use of different b-values. Using a lower b-value ≥ 150 s/mm^2 and an upper b-value ≥ 700 s/mm^{2}limited the variation to less that 10% from the reference ADC value. By eliminating the contribution of perfusion the uncertainty of quantitative ADC values were significantly reduced.

P09.03 Sidse Bregendahl

BOWEL DYSFUNCTION AFTER NEOADJUVANT THERAPY FOR RECTAL CANCER - PATHOPHYSIOLOGICAL MECHANISMS

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Background: Many patients experience severe disturbances in bowel function after treatment for rectal cancer. Both surgery and neoadjuvant therapy (NT) are known to have major effects on bowel function and may cause increased stool frequency, loose/liquid stool, flatus/faecal incontinence, urgency and insufficient evacuation of stool (Low Anterior Resection Syndrome (LARS)). The contribution of each treatment component to the development of functional disabilities and the underlying pathophysiological mechanism are poorly understood.
Aim: To examine the pathophysiology behind LARS in patients treated with NT followed by a low anterior resection (LAR) with anastomosis.
Material and methods: The study is based on the Danish National Colorectal Cancer Database, from which a retrospective cohort including all patients operated for rectal cancer from May 2001 to April 2007 was retrieved. Patients meeting specific inclusion and exclusion criteria were asked to fill out a validated questionnaire regarding bowel function. Among responders, 178 patients have been treated with NT in combination with LAR with anastomosis and are eligible for this study. 20 patients (+ LARS) will be compared to a control group of 20 patients (- LARS). All included patients will have their functional capacity of the bowel examined by three dimensional endoanal ultrasonography and anal manometry, segmental colonic transit time, rectal impedance planimetry and defecation scintigraphy.
Perspectives: Knowledge of the pathophysiological mechanisms behind LARS is essential in the effort for an improved treatment balancing optimal tumour control and minimal long-term side effects on bowel function.

P09.04 Anja Bille Bohn

CHANGES IN WATER AND SALT BALANCE IN RATS INDUCED BY COMBRETASTATIN

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Aim: The studied the effect of the anti tumour drug Combretastatin A-4 phosphate (CA4P) on blood water and salt balance as well as on changes in urination volume, urine parametres and kidney tissue aquaporins.
Background: CA4P is a vascular disrupting agent exerting its effect primarily on the immature tumor blood vessels. The side effect of this drug in clinical tumor teraphy is headache, hypertension, and occasionnaly cardiovascular incompensation.
Methods: CA4P was injected i.p and blood samples were withdrawn at various time points following treatment. Hematocrit and a range of plasma parameters were measured. The urination volume in the 20 hour following CA4P administration and different urine parameters ($Na^+$and K^+ concentration, osmolality, creatinin- and

carbamide) were determined. Kidneys were exanguiated 3 hours after CA4P treatment and the effect of CA4P on aquaporin and NKCC2 protein levels was determined.
Results: The mean hematocrit increased significantly and blood Na^+ and Ca^{2+} decreased significantly at all timepoints. Urine production increased significantly in CA4P treated rats. Additionally, significant changes in urine $Na^+$and K^+ concentration, osmolality, creatinin- and carbamide were observed. The protein level of aquaporins and NKCC2 did not change significantly following CA4P administration.
Conclusion: CA4P induced significant changes the water and salt balance in blood as well as changes in urine volume and urine parameters. These changes may be the source of some of the side effects occuring in patients.
Supported by a grant from the Danish Cancer Society

P09.05 Andreas Carus

CHRONIC INFLAMMATION AND CANCER - FOCUSING ON NEUTROPHILE LEUKOCYTES, MONOCYTES AND MACROPHAGES IN SOLID TUMORS
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Background: The observation that tumor cells have the ability to attract and educate tumor-infiltrating leukocytes, especially polarized macrophages and neutrophils, to serve as active collaborators, has gained considerable interest. The implication is that the immune system has a “dark side”, helping the tumor to grow.
Several papers have been published showing monocytes/macrophages and neutrophils to be “bad guys” for the clinical outcome in patients with localized and metastatic kidney cancer as well as localized and metastatic melanoma.
We plan to assess patients with breast, lung and cervical cancer for the prognostic impact of blood and intratumoral monocytes/macrophages and neutrophils.
If macrophages and neutrophils in general has a detrimental impact on survival, then these cells may represent an important drug-target for cancer treatment, with the aim of reducing the number or modifying the function of these immune cells.
Aim: To correlate blood as well as intratumoral neutrophils, monocytes and macrophages with outcome in patients with lung, breast and cervical cancer.
Materials: 1. Clinical databases, patient files and blood differential counts from approximately 5000 patients with breast cancer and lung cancer registered in the databases of DBCG and DLCR.
2. Immunohistochemical staining with CD66b, Cd34 and CD163 of patient tissue from the following patients
a) 3-400 consecutive patients with stadium I - IIIA non-small cell lung cancer, operated at Skejby Hospital, Aarhus, between 2000 and 2005
b)144 patients with T2 and T3 breast cancers treated in the scandinavian NICE-protocol.
c)102 patients operated for cervical cancer st. I and IIA.
Results: Study is ongoing

P09.06 Søren Haack

COMPARING MICROSTRUCTURAL INFORMATION USING DIFFUSION WEIGHTED MRI TO GEC ESTRO TARGETS USED FOR BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER
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Background: T2 weighted MRI is recommended for image guided adaptive brachytherapy (IGABT) in cervical cancer. Diffusion weighted imaging (DWI) and the derived apparent diffusion coeffecient (ADC) may add information on tumour cell density. We evaluate the distribution of the ADC within target volumes as recommended by GEC-ESTRO: Gross Tumour Volume, GTV_{BT}, High-Risk Clinical Tumour Volume, HR-CTV and Intermediate-Risk Clinical Target Volume, IR-CTV

and the change of diffusion between fractions of IGABT.
Materials: 15 patients with cervical cancer were examined by MRI before their first, BT1 and second, BT2 fraction of IGABT. ADC maps were calculated and fused with target contours and mean ADC was calculated. Volumes of low diffusion (ADC_{low}) were defined based on an ADC threshold of $1.2x10^{-3}mm^2/s$, and overlap with target volumes was evaluated. Change of ADC level in target volumes and of ADC_{low} volume from BT1 to BT2 was evaluated.
Results: Mean ADC was significantly lower in GTV_{BT} than in HR-CTV ($p<0.001$) which again was significantly lower than in IR-CTV ($p<0.001$). There was no significant change of the ADC_{low} volume or ADC level within each target structure between BT1 and BT2 ($P = 0.242$). All three GEC-ESTRO volumes contained volumes with low diffusion.
Conclusion: With DWI we were able to find a significant difference in ADC-values for the three different GEC ESTRO targets, supporting the assumption that target volumes contain tissues with different characteristics, with the tumour (GTV_{BT}) being the volume with the lowest diffusion. No significant changes were found from BT1 to BT2 indicating that changes of ADC level and volumes are stable at the time of BT.

P09.07 Kasper Jarlhelt Andersen

CLINICAL AND ECONOMIC CONSEQUENCES OF WORK-UP WITHOUT LAPAROSCOPY IN PATIENTS WITH CRC LIVER METASTASES

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Background and aims: Multi-detector computed tomography (MDCT) has dramatically improved in recent years. In a previous study we suggested that diagnostic laparoscopy (DL) and laparoscopic ultrasonography (LUS) no longer should be mandatory in the work-up of patients with colorectal (CRC) liver metastases. The aim of the present study was to evaluate the clinical and economic consequences of such a strategy.
Material end Methods: Seventy consecutive patients considered to have resectable liver metastases after MDCT were analysed. A pre-operative treatment strategy was in each case planned according to the result of the MDCT-scan. Patients considered to have incurable disease during operation were recorded, as were cases where the operative strategy had to be altered. For evaluating the economic and clinical consequences of adding a preoperative LUS, procedural and marginal cost effectiveness was calculated.
Results: Seventy patients underwent laparotomy. Three patients (4%) were considered incurable peroperatively and in 15 cases (21%) the strategy had to be altered. The average cost for a successful LUS was EUR 2 394 and the marginal costs for supplementing every MDCT with a LUS were EUR 59 849.
Conclusion: MDCT is sufficient and cost effective as the only preoperative work-up in patients with colorectal liver metastases.

P09.08 Thomas Reinert

COMPREHENSIVE GENOME METHYLATION ANALYSIS IN BLADDER CANCER; IDENTIFICATION AND VALIDATION OF NOVEL METHYLATED GENES AND APPLICATION OF THESE AS URINARY TUMOR MARKERS

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Purpose: Epigenetic alterations are common and can now be addressed in a global fashion. We investigated the methylation in bladder cancer with respect to location in genome, consistency, variation in metachronous tumors, impact on transcripts, chromosomal location, and usefulness as urinary markers. Experimental Design: A microarray assay with 27.000 CpG sites was utilized to analyze methylation in 56 samples. Independent validations were performed in 63 samples by a PCR based

method and bisulfite sequencing. Transcript levels were analyzed using expression microarrays, and pathways using dedicated software. Results: Global methylation patterns were established within and outside CpG-islands. We validated methylation of eight genes, the tumor markers ZNF154 ($p<0.0001$), HOXA9 ($p<0.0001$), and POU4F2 ($p<0.0001$) and progression marker TBX4 ($p<0.002$). The methylation of metachronous tumors was in general relatively stable, and was targeted to certain pathways. The correlation to expression was not stringent. Chromosome 21 showed most differential methylation ($p<0.0001$) and specifically hypomethylation of keratins, that together with keratin like proteins were found epigenetically regulated. In DNA from voided urine we detected differential methylation of ZNF154 ($p<0.0001$), POU4F2 ($p<0.0001$), and HOXA9 ($p<0.0044$), achieving 94% sensitivity and 100% specificity. Conclusions: Both hypo- and hyper methylation are stage dependent, over-represented at chromosome 21, and has a restricted influence on transcript levels in general, but clearly on keratins. The methylated genes are highly promising urinary cancer markers.

P09.09 Bente Thoft Jensen

EFFICACY OF A MULTI PROFESSIONAL REHABILITATION PROGRAMME IN BLADDER CANCER

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Background: The incidence of bladder cancer is increasing. Denmark have approximately 1600 incidence per year. The disease is most frequently in males above the age of 70 years. In invasive bladdercancer cystectomy is the first line treatment However the procedure is followed by a high morbidity and long convalescence. Extended surgical procedure cause pain, stress-induced metabolism and impaired organ function resulting in postoperative complications impacting on rehabilitation. The combination of the extended surgery and the increasing numbers of eldrly co-morbid patients with invasive bladder cancer challenge professional treatment and care.
Aim: to investigate the efficacy of a multi professional rehabilitation-programme for patients with invasive bladder cancer referred to surgery
Material and Methods: The study is a randomized controlled trial. All patients >18 years referred to radical cystectomy will be eligble for this study. The efficacy is expressed by the difference in length of stay(LOS), complications, health related Quality of life (HeQoL) and patient reported quality of care during hospitalization. The intervention includes precise instructions and education in nutritional support, intensive exercises and stoma care, supported by the multidisciplinary team.
Perspective: It is a national goal to improve rehabilitation in cancer care. This study is of critical importance and places great emphasis on the participant's perspective and involvement in a successful outcome for patients undergoing such complex surgery. This study proposes to demonstrate the hypothesis that early enhanced multidisciplinary support can lead to enhanced recovery, reduce LOS and increase HeQoL.

P09.10 Martin Skovmos Nielsen

IMAGE GUIDED RESPIRATORY GATED RADIOTHERAPY FOR LUNG CANCER PATIENTS: PRE CLINICAL EXPERIENCE ON GOTTINGEN MINIPIGS.

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Radiotherapy for lung cancer is complicated by the respiratory motion of the lung during both treatment preparation and the treatment delivery.
Lung motion results in image artefact on diagnostic image modalities (CT) which makes tumour definitions unclear. To compensate for lung motion during treatment, additional margin is needed for the treatment volume. These margins result in larger volume for treatment and consequently an increase in normal tissue complication.
With treatment preparation on retrospective 4D CT (time dependence 3D CT),

radiotherapy can be delivered in a predefined phase relative to the respiratory cycle. Even on time dependent 4D CT motion distortions happens. This is especially pronounced in the mid ventilated phases between deep inhale and exhale. Radiotherapy in these respiratory phases may be associated with large uncertainties in volume definition and consequently detection during treatment.
Repeated 4D CT shows deviation of the respiratory motion pattern between internal and external motions up to 10 mm. This despites lung volumes and respirations cycles are kept constant with respirator during the 4D CT scans.
This implies care must be taken for external gated treatment. Evaluation of motion errors for margin definitions can not be trusted based on a single 4D CT. As well as gated radiotherapy with no image guidance can lead to treatment off position.

P10.01 Torsten Bloch Rasmussen

A NOVEL RECESSIVE MUTATION IN DESMOPLAKIN CAUSING DILATED CARDIOMYOPATHY WITH SKIN AND HAIR ABNORMALITIES: NEW INSIGHTS INTO DISEASE MECHANISMS IN CAVAJAL SYNDROME

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Introduction: Desmoplakin gene (DSP) mutations are associated with arrhythmogenic right ventricular cardiomyopathy or Carvajal syndrome (CS) characterized by dilated cardiomyopathy, palmoplantar keratoderma and wooly hair. We report the results of genetic and protein investigations of the CS phenotype.
Methods: Mutation analysis of the DSP gene by sequencing. Protein investigations by western blotting (WB) and immunohistochemistry (IHC) using myocardium, skin biopsies and primary keratinocyte cultures from mutation carriers and controls.
Results: A homozygous frameshift mutation (c.7779_7780delT) in the last exon of DSP predicted to introduce a premature termination of translation (fs.S2594:2602X) was detected in the index patient. Healthy relatives were heterozygous carriers. WB confirmed that the homozygous patient expressed truncated DSP protein only. Heterozygous gene carriers expressed less amounts of wildtype DSP but truncated DSP protein could not be detected. IHC of DSP protein in myocardial- and epidermal- tissue from wildtype and mutation carriers was indistinguishable with normal localization.
Discussion: The results suggest that the mutant DSP protein is stable in homozygous mutation carriers with Carvajal syndrome. Surprisingly, heterozygous individuals express wildtype DSP only indicating that mutant DSP protein is degraded in the presence of normal DSP protein. We speculate that this may be explained by a faster and more efficient posttranslational folding of wildtype protein thereby hampering folding and processing of the mutated protein. Thus, it is likely that heterozygous gene carriers remain healthy due to efficient degradation of the mutant protein.

P10.02 Maria Jakobsen

AAV MEDIATED SHRNA EXPRESSION IN HUMAN SKIN

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shRNA delivery by recombinant adeno-associated viral (rAAV) vectors has succesfully been applied to several tissues in vivo. However, RNAi in human skin by rAAV-delivered shRNAs has never been reported. In a previous study using lentiviral vector delivery, we demonstrated that TNF-a can be downregulated in inflammatory psoriatic skin in the xenograft transplantation model by RNA interference with resulting clinically and histologically improvements (Mol Ther 2009; 17: 1743-1753).
We are now using the same model for comparisons between rAAV vectors and

lentiviral vectors for shRNA delivery into human skin in vivo. This is done using a highly potent TNF-a-directed shRNA (shTNFa3) which we designed and used in our previous study.
Currently, we are testing the efficiency of TNF-a knockdown in vitro by shTNFa3 when delivered by rAAV vectors with different designs and comparing these results to results obtained with shTNFa3 delivered by lentiviral vectors. Additionally, we are comparing different AAV serotypes in human skin grafted onto mice to determine the optimal serotype. This is done using luciferase as an in vivo marker.

P10.03 Charlotte Uggerhøj Andersen

BIOMARKERS IN PULMONARY HYPERTENSION ASSOCIATED TO INTERSTITIAL LUNG DISEASE

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Pulmonary hypertension (PH) (a mean pulmonary arterial pressure (MPAP) 25 mmHg) worsens the prognosis of interstitial lung disease (ILD). This study evaluates NT-proBNP, D-dimer and uric acid, troponin-t and exhaled NO as biomarkers in diagnosis of PH in patients with ILD. 96 patients with ILD were screened for PH by echocardiography. A tricuspid pressure gradient (TG) > 40 mmHg indicated PH and led to right heart catheterization (RHC). ROC analyses for the biomarkers to detect PH on echocardiography were performed.
Results (mean±SEM): 17 patients had PH on echocardiography (TG = 55 ± 4 mmHg). Of those, 11 had PH on RHC (MPAP = 40 ± 5 mmHg), while 5 were not eligible. One patient did not have PH on RHC. NT-proBNP levels were higher in patients with PH on echocardiography (1853±787 vs 167±27 ng/l ($p<0.001$). With a cut-off value of 200 ng/l, sensitivity of NT-proBNP was 94 % and specificity 78 % for detection of PH on echocardiography (Positive predicitive value = 47 %, negative predictive value = 98 %). Levels of uric acid, troponin-t, fibrin D-dimer and exhaled NO were equal in patients with and without PH on echocardiography.
Conclusion: In screening for PH in ILD, a value of NT-pro-BNP below 200 ng/l may be effective for exclusion of the diagnosis.

P10.04 Trine Dalsgaard

DEVELOPMENT OF GENE THERAPY OF PKU

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Phenylketonuria (PKU) is an inherited disease resulting in elevated levels of phenylalanine. In most patients this is due to defects in the enzyme phenylalanine hydroxylase (PAH). PKU positive children are treated with a lifelong diet with low concentrations of phenylalanine preventing the development of neurological and psychological changes especially intellectual impairment. The main goal of the project is to improve the current techniques in gene therapy and to target the PKU-disease.
We have constructed lentiviral vectors containing the functional PAH gene and a secreted reporter gene. These are injected in PKU mice to develop in vivo selection of PAH expressing cells. The mice are treated with carbon tetrachloride (CCl_4), which induce apoptosis in the hepatocytes it is metabolised in. The mice are afterwards treated with a phenylalanine and tyrosine free diet. We believe that the diet will give and advantage for the cells containing a functional PAH gene and thereby when the lever regenerates the amount of these cells are increased.
We are testing site-specific zinc finger nucleases (ZFN) targeted against the PAH gene (adjacent to the disease causing mutation found in more than 50% of the Danish PKU patients). The ZFN leads to specific double stranded breaks stimulating homologous recombination. The ZFN´s are cotransfected with a donor plasmid containing the functional PAH gene. So far we have used the ZFNs to insert a selection marker gene in the PAH gene by non-homology end joining in the doublestranded break in tissue cultured mouse cells. We are currently using H2AX antibodies to measure the amount of double stranded breaks in ZFN transfected cells.

P10.05 Yonglun Luo

GENERATION OF A BRCA1 KNOCKOUT PIG MODEL BY RECOMBINANT ADENO-ASSOCIATED VIRUS-MEDIATED GENE TARGETING

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Germline mutations of the breast cancer associated gene (BRCA1) account for approximately half of familial breast cancer cases and over 80% of familial breast and ovarian cancer cases, but the genomic alterations that lead to the onset of breast cancer in BRCA1 mutation carriers are poorly known. We developed a BCRA1 knockout (KO) pig model by targeting exon 11 using recombinant adeno-associated virus (rAAV) and Handmade cloning (HMC), based on somatic cell nuclear transfer (SCNT), to elucidate the pathogenesis of BRCA1 associated breast cancer. Fetal Yucatan minipig fibroblasts were subjected to BRCA1 homologous recombination by transduction with an rAAV serotype 1 vector, which would replace 55 bp in exon 11 of the BRCA1 gene with a cassette providing G418 resistance. PCR screening of G418 resistant clones revealed a very high targeting rate (~35%) of the resistant clones. One BRCA1 KO fibroblast clone (5D1), without any random integrations, was used as nuclear donor for SCNT. Reconstructed embryos were transferred to three recipient sows which gave birth to 6 piglets in total. Genotyping of the piglets indentified five of the piglets as pure BRCA1 heterozygotes ($BRCA1^{+/-}$) and one as wild type. Lower BRCA1 mRNA expression was found in fibroblasts from the $BCRA1^{+/-}$ pigs. Unexpectedly, all the $BRCA1^{+/-}$ piglets died within 20 days after birth except the WT one. We are presently investigating if the perinatal lethality is due to a combination of the BRCA1 haploinsufficiency and problems with epigenetic reprogramming or the particular Yucatan genetic background.

P10.06 Maiken Kudahl Larsen

GENETIC ASPECTS OF FAMILIAL HYPERCHOLESTEROLEMIA AND ABUSE OF ANABOLIC ANDROGENIC STEROIDS AS AN ENVIRONMENTAL RISK FACTOR IN YOUNG ADULTS

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Aim: Several cases of sudden death on basis of genetic heart disease have inspired to a retrospective study performed at the Department of Forensic Medicine, Faculty of Health Sciences, Aarhus University. The aim of the study is to examine inherited heart disease from selected forensic autopsies.

Material and Methods: The LDLR gene and the ligand binding region of the APOB gene were screened in 52 cases of sudden cardiac death (SCD). The deceased were younger than 40 years and under suspicion of familial hypercholesterolemia based on autopsy findings of moderate or severe atherosclerosis in the coronary arteries.

Results: 7.7 % had a rare sequence variant in the LDLR gene, of which 5.7 % is suspected of being a pathogenic mutation. In addition two of the four deceased were or had been using anabolic androgenic steroids (AAS).

Discussion: There are several risk factors for premature coronary heart disease (CHD). Premature CHD may be the final result of the concomitant effects of the rare sequence variants and environmental risk factors such as abuse of AAS. Postmortem examination of AAS can be analyzed in urine and may contribute to the investigation of SCD, as several cases of myocardial infarction and SCD have been argued as cardiovascular side-effects of AAS.

P10.07 Terese K. Jeppesen

GENDER-DEPENDENT EXPRESSION OF MATRIX METALLOPROTEASES AND THEIR INHIBITORS IN THE KIDNEY

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Introduction: The development of end-stage renal disease (ESRD) is a major health problem. The long-term goal is to find a cure for ESRD. To fulfill this goal elucidation of the involved signaling pathways in vivo is pivotal. The development of ESRD shows gender-specific variations. But still research on gender-specific molecular pathways is limited. Therefore, our research group focuses on the interaction between gender and different regulators of extracellular matrix (ECM) metabolism. The aim was to analyze the renal RNA and protein expression of MMP-2, MMP-9, and their inhibitors in female and male mice with and without TGF-beta1-induced kidney disease.
Methods: We used 4-month-old male and female TGF-beta1 transgenic (Tg) mice (Balb/cA). Non-transgenic (WT) littermates of both gender served as controls. The RNA expression of MMP-2, MMP-9, TIMP-1 and TIMP-2 was quantified by real-time PCR with GAPDH as reference. Matrix metalloproteinase activity was determined by gelatine zymography and protein localization by immunohistochemistry.
Results: Gender differences are present in all tested factors during normal conditions (WT). Gender differences are present in MMP-2 and -9 and TIMP-1 RNA expression during TGF-beta1-induced kidney disease, whereas the TIMP-2 RNA expression and MMP-2 activity is similar.
Conclusion: Gender differences in factors pivotal to ECM metabolism are present during normal conditions and during development of TGF-beta1-induced ESRD. This may contribute to gender-specific variation in the pathogenesis of ESRD.

P10.08 Raffaella Mangnoni

HETEROZYGOUS HSP60 KNOCK-OUT MICE REPRESENT A MODEL OF HEREDITARY SPASTIC PARAPLEGIA TYPE13

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Mitochondria are the primary energy-generating system in the cell and they are involved in many catabolic and anabolic metabolisms. Neuronal health relies strongly on mitochondrial functionality and integrity. Alteration of mitochondrial physiology induces several neurodegenerative disorders and aging.
The mitochondrial protein quality control chaperone Hsp60 assists folding and maintenance of mitochondrial proteins. Its role is necessary for cell survival in yeast (1) and mice (2). Mutations in Hsp60 are associated with a dominantly inherited form of spastic paraplegia (3,4) and a recessively inherited fatal hypomyelinating leucodystrophy (5). Heterozygous Hsp60 knock-out mice ($Hspd1^{+/-}$) (2) have a normal embryonic developments and postnatal survival rate; however, they show motor impairment and signs of neurodegeneration. Motor impairment becomes evident at 12 months of age using the rotarod test. This is associated with abnormal extension reflex of the hindlimbs and a clasping tendency.
Preliminary molecular analysis shows an increase of carbonylated proteins in mitochondria isolated from brain cortex. In addition, Sod2 expression is dowregulated. These findings point out that oxidative stress may play a key a role in the disease pathogenesis.
A mass spectrometry approach could provide us knowledge of HSP60 complex interactors and faulty processed polypeptides revealing information on molecular pathways in which they are involved. Decreased abundance of substrate proteins of Hsp60 may interfere with various mitochondrial metabolic pathways, leading to mitochondria dysfunctions specifically in neurons.

P10.09 Jonas Jensen

IN VIVO TESTING OF STRUCTURAL GRADED POLYCAPROLACTONE SCAFFOLDS IN A PORCINE CALVARIA MODEL

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In this study we investigated the osteogenic potential of a new scaffold produced by rapid prototype bioplotting.
The scaffolds were comprised of polycaprolactone (PCL). The pure bioplotted scaffolds were cylinder-shaped (10 mm diameter x 10 mm height). Scaffolds were infused with a homogenous mixture of PCL, water and 1,4-dioxane and underwent a thermal induced phase separation (TIPS) followed by lyophilization to manufacture a structurally graded scaffold (SGS) with micro- and nanopore PCL formation within the gaps of the bioplotted scaffold. 16 Danish landrace pigs were used with termination of eight pigs after 8 and 12 weeks. A total of six non-penetrating critical size defects were drilled in the calvaria. The following scaffolds were placed in the bottom of each drill hole by random: 1.) Autograft (1,12 g harvested from the drill holes) 2.) Empty hole, 3.) Bioplotted scaffold, 4.) SGS scaffold, 5.) SGS scaffold + autologous bone marrow stem cells, 6.) SGS scaffold + BMP-2 (1 mg / scaffold). Bone volume to total volume (BV/TV) was analyzed using µCT.
The µCT data showed significant less bone formation in the SGS scaffolds in all three variations after both eight and twelve weeks. Due to lack of discrimination between intertrabecular tissue and non-degraded scaffold on µCT, we were unable to quantify the cause. The bioplotted scaffold showed same bone volume to total volume as the empty defect without taking the existing volume of bioplotted scaffold into account. The lack of new bone formation could be due to too small pore size within the lyophilized PCL. Moreover, initial results suggest a slower degradation rate of the PCL than expected.

P10.10 Steffen Møller-Larsen

IN-DEPTH ANALYSIS OF TOLL-LIKE RECEPTOR ASSOCIATION WITH ASTHMA AND RELATED ATOPIC DISORDERS

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Toll-like receptors (TLRs) are pathogen sensing receptors responsible for initiating innate and adaptive immune responses against a range of pathogens. The atopic phenotype is frequently associated with a TH2 type of T helper cells whereas TLRs are strong inducers of the TH1 type highlighting these receptors as interesting targets for therapy and general research aimed at describing the pathophysiology related to atopy and allergy.
We have previously reported replicated association in two independently ascertained Danish cohorts of two viral sensing receptors, TLR7 and TLR8, to asthma and related atopic disorders.
In this study we report an in-depth association analysis of TLR1, 3, 6, 7, 8, 9, and 10 in two additional Danish cohorts. By adopting a tag-SNP approach we have attempted to cover the majority of the genetic variation in the general population. In these new cohorts, we - once again - find association of TLR7 and TLR8 with asthma and related atopic phenotypes, thus adding additional strength to the proposed importance of these genes in the etiology of asthma and atopy. We also find significant associations in the other analyzed TLRs, which highlights the general importance of these receptors in the etiology of atopy.

P11.01 Louise Hauge Matzen

ACCURACY OF SCANOGRAPHY USING STORAGE PHOSPHOR PLATE SYSTEMS AND FILM FOR ASSESSMENT OF MANDIBULAR THIRD MOLARS

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Objectives: The aim of this study was to compare the diagnostic accuracy of two digital PSP systems and film for assessment of mandibular third molars before

surgery.
Methods: 110 patients were referred to have both their mandibular third molars removed. Each patient underwent a radiographic examination with scanography using either Digora and film or VistaScan and film in a randomized paired design. Two observers examined the following variables on the scanograms: bone coverage, angulation of the tooth in the bone, number of roots, root morphology and the relationship to the mandibular canal. In 75 of the pairs (Digora/film pair=38 and Vista/film pair=37), both third molars were eventually removed. During and after surgery the same variables were assessed, which served as reference standard for the radiographic assessments. The Wilcoxon matched pairs signed rank test tested differences in accuracy (radiographic compared to surgical findings) between Digora/film and between Vista/film.
Results: There was no statistical significant difference between the diagnostic accuracy of film and either of the two digital receptors for assessment of mandibular third molars before surgery (P>0.05), although Digora obtained a higher accuracy than film.
Conclusions: Scanography is a valuable method for examination of mandibular third molars before removal, and the PSP digital receptors in this study were equal to film for this purpose.

P11.02 Charlotte Hartig Andreasen

ASSEMENT OF FACTORS INFLUENCING THE SURGICAL OUTCOME OF PERIACETABULAR OSTEOTOMI IN ADULTS

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Background: Hip dysplasia is a cause of hip pain, functional disability and osteoarthritis (OA) in 20 to 40 year old adults. The periacetabular osteotomy (PAO) is a joint preserving surgical treatment known to relieve pain, increase functionality and prevent early OA.
Hypotheses: PAO is the preferred treatment, but several issues remain unclear. These include 1) the exact indication for surgery and risk factors for early failure of the procedure; 2) the matter of surgical intervention on a torn acetabular labrum in addition to PAO, and 3) the outcome of total hip arthroplasty (THA) subsequent to PAO.
Methods and material: The material is approximating 450 PAOs of the Database of PAOs (study 1), the operative production through one year; approximating 100 PAOs (study 2), and approximating 40 patients having a THA following PAO constitutes study 3.
Study 1: A retrospective cohort study assessing pre- and postoperative radiographic indices of hip dysplasia in order to identify factors predicting failure following PAO. Failure is defined by a WOMAC pain score > 10 or a THA.
Study 2: A prospective case-control study of the clinical and radiographic outcome of PAO in patients with and without acetabular labral tears. The aim is to assess whether the outcome of PAO are equally good in patients with a torn labrum compared to patients having an intact labrum.
Study 3: A case-series study with a medium term clinical and radiographic follow-up of patients who had a THA subsequent to a PAO. The aim is to detect whether the number of complications or revisions is excessive or if a THA is a safe and lasting solution.
Results: No data to present yet.

P11.03 Maj Høygaard Nicolaisen

CLINICAL PERFORMANCE OF ZIRCONIA-CERAMIC AND METAL-CERAMIC POSTERIOR THREE-UNIT FIXED PARTIAL DENTURES: A RANDOMIZED CONTROLLED TRIAL

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Introduction: One method to replace lost teeth is with fixed partial dentures (FPDs).

FPDs are ordinarily manufactured with a metal framework and a ceramic veneer in order to obtain both strength and aesthetics. Zirconia-ceramic (ZC) FPDs have become popular in recent years, because the zirconia framework is believed to improve aesthetics and to be strong enough to resist mastication forces. In vitro studies indicate that the lifetime of ZC FPDs is as long as metal-ceramic (MC) FPDs. There is, however, a lack of clinical studies to confirm this.
Objective: The purpose of this study was to assess the performance of tooth supported ZC and MC FPDs. The aim was to identify differences between the two materials regarding aesthetics, patient's satisfaction and the longevity of the treatment when replacing a missing 2nd premolar or 1st molar with a three-unit FPD.
Method: 40 three-unit FPDs, 20 ZC and 20 MC, were placed in 40 patients, each in need of a three-unit FPD replacing a missing 2nd premolar or 1st molar. Excluding criteria were periodontal disease, apical lesions and parafunctions. Patient's satisfaction and discomfort was recorded on Oral Health Impact Profile (OHIP-14) and on 100 mm visual analogue scales (VAS) with extreme end points for the level of perceived satisfaction/dissatisfaction. Bleeding on probing, pocket probing depth and plaque accumulation were recorded before treatment, at placement of the FPDs, 3 months, 6 months, 1, 2 and 3 years after placement. Two examiners evaluated the FPDs individually using The CDA Quality Evaluation System. The results will be statistically analyzed.
Hypothesis: We expect to find no differences between the two materials

P11.04 Pernille Endrup Jacobsen

DENTAL ABNORMALITIES IN CHILDREN, EXPOSED TO ANTICONVULSANTS PRENATALLY

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Background
Every year, 200 women with epilepsy give birth in Denmark, and previous studies have shown, that their children have 2-3 time higher risk of congenital abnormalities. Some of the most frequent defects are: neural tube defects, limb defects, cleft lip and cardiovascular defects.
Dental aspects: Genetic as well as exogenous factors have been shown to be associated with dental hypomineralization. Prenatal exposure to drugs such as dioxin or tetracycline can induce dental hypomineralization in the child. It is there for likely that anti-epileptic medication can have the same effect.
Dental agenesis is known to have a genetic background. 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 registry, the birth cohort from Aarhus and the prescription database.
Study 1: 1) Children 6-10 years of age 2) 80 exposed children and 250 non exposed children will be enrolled in the study 3) Outcome measurement (hypomineralization) will be a clinical examination of permanent as well as primary teeth 4) Questionnaire survey of the medical condition, lifestyle habits and breast feeding habits, of the mother under the pregnancy 5) Ethical approval has been obtained from the The Scientific Ethical Committee.
Study 2: 1) Children 12-18 years of age 2) 200 exposed children and 250 non exposed children will be enrolled in the study 3) Outcome measurement (dental agenesis) will be collected from the children's dental chart 4) Correlation between agenesis and other congenital abnormalities will be explored

P11.05 Hans Gjørup

CRANIOFACIAL MORPHOLOGY OF PATIENTS WITH HYPOPHOSPHATEMIC RICKETS COMPARED TO HEALTHY CONTROLS

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[new institution (click to change me)]

X-linked Hypophosphatemic rickets (XHR) is a rare, inherited disease characterized by deficient mineralisation of the bones due to abnormal renal wasting of phosphate. Deformation of bony structures of cartilaginous origin is a major

symptom in patients with XHR.
The aim. To describe the osseous morphology of the craniofacial structures in patients with XHR compared to healthy individuals. We aimed to investigate the impact on bone of different origin.
The material. Patients with verified XHR. Healthy individuals served as controls.
Methods. Profile radiographs were obtained for cephalometric analysis. The cephalometric measurements of XHR-patients were compared to controls adjusted for gender, age and clustering.
Results. Fifty-three XHR-patients were included. The control group included 79 healthy individuals. XHR was associated with the following significant changes in craniofacial structures: increased cranial base angle, reduced depth of posterior cranial fossa; neurocranium with increased distances sella-frontale, sella-bregma, sella lambda, reduced distance basion-lambda, increased angle nasion-sella-frontale, increased theca-thickness frontal, parietal and occipital; reduced nasal bone length. Intermaxillary relations were unaffected.
Significant interaction (p-value>0.05) of gender upon effect of rickets was seen in 3 variables (angles ba-s-n, ar-s-n, parietal thickness).
Conclusion. Craniofacial structures of both cartilaginous and intramembraneous origin were affected in patients with XHR: cranial base has flattened, the size of neurocranium has increased, the neurocranial shape has changed and theca has thickened. Further, the nasal bone has shortened.

P11.06 Michael Skovdal Rathleff

EARLY INTERVENTION FOR ADOLESCENTS WITH PATELLOFEMORAL PAIN SYNDROME (THE EIAP-STUDY)

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Introduction: Patellofemoral Pain Syndrome (PFPS) is a prevalent condition[1] and less than 50 % of patients diagnosed with PFPS are pain free 12 month after initiation of treatment[2]. Younger patients with a shorter duration of symptoms have better odds for treatment success[3]. The purpose of this study is to 1) establish the prevalence of PFPS in adolescents 12-19 years of age, and 2) examine the short and long-term effectiveness and cost-effectiveness of a best-practice treatment compared to standard wait-and-see treatment.
Methods: Questionnaires regarding knee pain and general musculoskeletal pain will be forwarded to 2.000 randomly chosen students aged 12 to 19. Students who report knee pain will be offered a clinical examination to secure the diagnosis and establish the prevalence of PFPS. 104 students diagnosed with PFPS will be randomized into two groups. One group will receive standard wait-and-see treatment. The other group will receive best-practice treatment consisting of supervised physiotherapy and home training for a period of three months. The primary outcome measure is perception of recovery after 1 year.
Discussion: This study has been designed after reviewing the literature on exercise therapy for PFPS. It was concluded that a possible way to address the poor long term results is to apply intervention at an early state of the disease. The research will address both effectiveness and cost effectiveness of supervised exercise therapy in patients with PFPS.
1: Mølgaard, C.M; Rathleff, M.S, et al. JAPMA [In press]. 2010
2: Rathleff, M.S; et al. Ugeskrift for Læger [Submitted] 2010
3: Natri A, Kannus P, Järvinen M. Med Sci Sports Exerc. 1998 30(11):1572-7.

P11.07 Jan Rölfing

EPO'S EFFECT ON MSC IN VITRO

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Erythropoietin (EPO) is 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. Both angiogenesis and ossification are

essential for fracture healing and new bone formation. We aim to investigate EPO's effect on mesenchymal stem cells (MSC).
Hypothesis: EPO enhances MSC's proliferation and osteogenic differentiation.
Methods: Human MSC – TERT cells will be seeded on 96 well plates. Standard and osteogenic medium will be used. After one day four different concentrations of Epoetin alpha and beta will be added. The following assays will be used to evaluate cell viability, cell number and osteogenic activity: MTT, SYBR Green and alkaline phosphatase activity. After this pilot study, EPO's effect on osteoblasts and EPO's optimal concentration will be tested in porcine MSC in vitro.

P11.08 Lone Ramer Nygaard Mikkelsen

FEASABILITY OF EARLY PROGRESSIVE RESISTANCE TRAINING AFTER TOTAL HIP REPLACEMENT

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Purpose: The purpose of this pilot study was to evaluate the feasibility of early progressive resistance training after THR.
Participants: A convenience sample of 6 THR patients has been recruited.
Methods: A follow up study was conducted. The progressive resistance training was initiated 3-7 days after surgery and performed twice a week for 3 weeks with supervision by physiotherapists. After warm up, exercises were performed with the operated leg in 4 training machines (hip extension, leg press, hip flexion, hip abduction) at 10 RM (repetition maximum). Weight load and pain was measured at each session. Isometric muscle strength and patient reported function was measured preoperative and again after 3 weeks of training.
Results: One patient did not complete the training program due to hypertension problems. Pain during the 4 exercise and resting pain before and after training was unchanged or decreased during the 3 weeks of training. Below is shown some of the results concerning strength and weight load. Isometric strength i hip abduction preoperative, mean (sd): 90.65 (40.7), after 3 weeks training: 94.4 (36.5), P value (diff): 0.72. The preoperative strength level is regained during 3 weeks of resistance training. Weigth load, example 1st, 3rd and 6th session of training: Hip abduction, mean (sd): 12.83 (8.5) 22.50 (13.6) 30.50 (9.4). The weight load is steadily increasing during the 3 weeks of training.
Conclusions: It is feasible to apply progressive resistance training within the first week after THR with a continually increasing weight load, no increase in pain and the preoperative isometric strength of hip flexors and hip abductors is restored within the 3 weeks.

P11.09 Rubens Neto

BONE ALLOGRAFTS IN HUMANS: IMMUNOLOGIC, TOMOGRAPHIC, HISTOLOGICAL AND HISTOMETRICAL EVALUATION OF ITS INCORPORATION AND CAPACITY OF OSSEOINTEGRATING DENTAL IMPLANTS

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Fresh frozen bone allografts are indicated in the absence of autologous bone for captation, or in cases where the patient resists the necessity of creating a second (donor) surgical site. The aim of this study is to evaluate in humans, the remodeling of bone allografts and their capacity of osseointegrating titanium implants using histological, histometrical and tomographic evaluation, allied to a systemic immunologic evaluation and to assess a foreign body reaction towards the grafts. Thirty patients with an alveolar bone width of < 4 mm in sites, where dental implants were planned, were scheduled to onlay bone grafting procedures. Fifteen were randomized to be treated with autologous bone grafts and the other 15 with human fresh-frozen bone allografts. The patients went through computer

tomography examination (before, right after and 6 months after the graft procedure), blood tests (before, 14, 30, 90 and 180 days the graft procedure) allowing the calculation of serum TNF-α, IFN-γ, IL-1β and IL-10. Bone tissue biopsies were also taken, both of the grafted area alone (7 months after the graft procedure) and with a mini-implant (13 months after the graft procedure), inserted for evaluation of osseointegration in the grafted area, at the same time of implant placement. All patients have been through the grafting procedures, computer tomography examination, blood testing and bone-biopsy harvesting, and they are in the implant osseointegration period, after which the last biopsy (bone/implant) and the mini-implant with surrounding bone will be collected. So far, there were no clinical complications related to the surgeries, and also no patient drop-outs.

P12.01 Holger Borup Wemmelund

ASSOCIATION OF ACE INHIBITOR AND STATIN TREATMENT WITH SMALL ABDOMINAL AORTIC ANEURYSM PROGRESSION

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Background: The prevalence of diagnosed small infrarenal abdominal aortic aneurysms (AAA) is expected to increase in the future due to i.e. the extended use of diagnostic imaging in daily clinical practice. Currently there is no well-established medical treatment to slow the growth of AAA in respect to avoid surgical interventions and their potentially lethal complications. Recent studies indicate that drugs usually used in prevention of cardiovascular disease, angiotensin converting enzyme (ACE) inhibitors and statins, might alter the expansion rate of AAA independently of their cardioprotective effect.
Objectives: To evaluate whether either angiotensin converting enzyme (ACE) inhibitors or statins affect expansion rates and size of AAA.
Design: Historical population-based follow-up study using data from the Danish national health databases registries and medical records.
Subjects: Cases diagnosed with AAA in Jutland, Denmark from 1996-2008 (estimated 1000-1500 with available data on expansion (2 or more measurements) and about 4000-6000 with only one measurement.
Methods: Expansion data defined as 2 or more measurements from diagnostic images (ultrasonographies, computer topographies (CT) or magnetic resonance imaging (MRI)) will be sampled from medical records to compute rate of expansion and define the max. AAA diameter. Data on diagnose, medical history (co-morbidity), medication, smoking status, age, gender and socio-economic status will be sampled to adjust for confounding factors.
Main outcome measures: Analysis of average AAA expansion rate and max. AAA diameter in users of ACE inhibitors and statins respectively versus non-users.

P12.02 Yu Wang

DISTAL ADDING-ON PHENOMENON IN LENKE 1A SCOLIOSIS : RISK FACTOR IDENTIFICATION AND TREATMENT STRATEGY COMPARISON

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Background. Distal adding-on is often accompanied by unsatisfactory clinical outcome and high risk of reoperation. However, few studies have focused on distal adding-on and its attendant risk factors and optimal treatment strategies remain controversial.
Methods. All surgically treated AIS patients were retrieved from a single institutional database. Wilcoxon rank-sum test, Fisher's exact test and Spearman's correlation test were used to identify the risk factors for adding-on. A multiple logistic regression model was built to identify independent predictive factor(s).Five methods for determining lowest instrumented vertebra(LIV) were compared in both the Adding-on group and No adding-on group.
Results. Out of 278 patients reviewed, 45 met the inclusion criteria; 23 of these met the definition for distal adding-on, and were included in the Adding-on group. Multiple logistic regression results indicated that preoperative LIV+1 deviation from

CSVL was an independent predictive factor. Among the five methods, choosing EV as LIV was nearly unable to prevent distal adding-on; choosing EV+1 as LIV resulted in fusing many more segments than necessary; only choosing DV as LIV showed satisfactory outcome from both perspectives.
Conclusion. In Lenke 1A type scoliosis, the selection of LIV is highly correlated with the presence of adding-on; incidence increases dramatically when the preoperative LIV+1 deviation from CSVL is more than10 mm. Choosing DV (the first vertebra in cephalad direction from sacrum with deviation from CSVL of more than 10 mm) as LIV may provide the best outcome as it not only prevents adding-on but also conserves more lumbar motion.

P12.03 Morten Charles

EFFECTS OF EARLY DETECTION AND INTENSIVE TREATMENT ON PERIPHERAL ARTERIAL DISEASE &NDASH; ADDITION DENMARK

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Background: Our aim was to study the effect of intensive multifactorial treatment and routine care on PAD in persons with screen detected diabetes in a cluster randomized controlled study.
Methods: 466 individuals with screen-detected diabetes identified in 87 general practices. Practices were randomized to intensive treatment (IT) or routine care (RC). Individuals in the IT practices (45 practices) received a multi-factorial intensive treatment program. The RC group (42 practices) were offered treatment according to national guidelines. At follow-up ABI was measured according to a standardized protocol. An ABI of <0.9 in either leg was considered “abnormal”.
Results: The IT group had a prevalence of abnormal ABI in either leg of 7% (4; 10) compared to 9% (4; 13) in the RC group (p=0.43). The odds ratio of ABI<0.9 in IT compared to RC was 0.76 (0.38; 1.52), p=0.43.
Conclusion: The prevalence of PAD 5 years after a screen-detected diagnosis of diabetes was lower in our trial compared to cohorts of people with known diabetes. There was no significant difference between trial arms.

P12.04 Rune Erichsen

LONG-TERM STATIN USE REDUCES THE RISK OF GALLSTONE DISEASE - A POPULATION-BASED CASE-CONTROL STUDY

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Background: Most gallstones originate from cholesterol-supersaturated bile. Statins inhibit hepatic cholesterol biosynthesis, so may reduce the risk of gallstone disease. Population-based evidence is, however, sparse.
Objectives: To determine the risk of gallstone disease after treatment with statins and other lipid-lowering drugs.
Methods: We conducted a population-based case-control study using medical databases from Northern Denmark (1.7 million inhabitants) to identify 32,494 gallstone cases occurring between 1996 and 2008 and to identify ten age, sex, and county matched population controls to each case. Cases and their matched controls exposed to lipid-lowering drugs were categorized as current users if their last prescription was ≤90 days before the case’s diagnosis date, or otherwise as former users. Conditional logistic regression was used to estimate adjusted odds ratios (AOR) and 95% confidence intervals (CI) of gallstone disease in patients treated with lipid-lowering drugs.
Results: In current users, the AORs associating statins use with the occurrence of gallstone disease were 1.17 (95% CI: 1.06, 1.30) for 1-4 prescriptions, 0.89 (95% CI 0.80, 0.97) for 5-19 prescriptions, and 0.76 (95% CI: 0.69, 0.84) for 20 or more prescriptions. In former users the corresponding AORs were 1.24 (95% CI: 1.11, 1.39), 0.97 (95% CI: 0.86, 1.10), and 0.79 (95% CI: 0.64, 0.97), respectively. The use of other lipid-lowering drugs showed no similar association.

Conclusion: Long-term statin use reduces the risk of gallstone disease.

P12.05 Morten Schmidt

NONSTEROIDAL ANTI-INFLAMMATORY DRUG USE AND RISK OF VENOUS THROMBOEMBOLISM: A POPULATION-BASED CASE-CONTROL STUDY

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Background: The risk of venous thromboembolism (VTE) associated with use of nonselective (ns) NSAIDs or cyclooxygenase-2-selective inhibitors (COX2Is) remains unclear. We examined this association.

Methods: This population-based case-control study was conducted in northern Denmark (population 1.7 million). Using the National Patient Registry, we identified all patients with a first hospital VTE diagnosis during 1999-2006 and their comorbidities. For each case, we selected 10 controls matched by age and gender. From a prescription database, we ascertained use of NSAIDs at the time of admission (current use) or before (former use) and use of comedications. We used unconditional logistic regression to compute odds ratios (ORs) with 95% confidence intervals (CIs), controlling for potential confounders.

Results: Among 8,368 cases, 794 (9.5%) used nsNSAIDs and 709 (8.5%) used COX2Is. Among 82,218 controls, 2,971 (3.6%) used nsNSAIDs and 2,760 (3.4%) used COX2Is. Compared with never use, the adjusted OR associating current drug use with VTE was 2.51 (95% CI: 2.29-2.76) for nsNSAIDs and 2.19 (95% CI: 1.99-2.41) for COX2Is. Former users had substantially lower increased risks than current users. Among new users, the adjusted OR was 4.56 for nsNSAIDs (95% CI: 3.85-5.40) and 3.23 for COX2Is (95% CI: 2.69-3.89). Among long-term users, the adjusted OR was 2.06 for nsNSAIDs (95% CI: 1.85-2.29) and 1.92 for COX2Is (95% CI: 1.72-2.15). Similarly increased risks were observed for unprovoked VTE, deep venous thrombosis, pulmonary embolism, and for individual NSAIDs.

Conclusion: Use of nsNSAIDs and COX2Is was associated with increased short- and long-term risk of venous thromboembolism.

P12.06 Mette Julsgaard Nielsen

POSTPARTUM ADHERENCE TO MEDICAL TREATMENT AMONG WOMEN WITH CROHN'S DISEASE

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Aim: Adherence to medical treatment of Crohn's disease (CD) is important for induction and maintenance of remission. Predictors and prevalence rates of non-adherence to medical treatment among CD patients in the postpartum period have not previously been investigated.

Methods: Women with CD, who had given birth between 2000 - 2005 among a population of 1.6 million. Diagnoses and birth outcome were confirmed by the national registries. Predictors for, and extent of non-adherence were investigated by questionnaires.

Results: Of 132 women, 105 (80%) fulfilled the questionnaire. Overall 59 (56%)were in medical treatment in the postpartum period, of whom 48 had fulfilled a prescription on relevant medication according to the prescription database yielding a Positive Predictive Value of self-reported use of medication on 81.4%. 66% were adherent. Counselling regarding medical treatment decreased non-adherence (POR 0.50, 95% CI 0.1-2.2). Fear of medicine in breast milk was a reason for non-adherence. Among 34 (32%) women who reported to be smokers, 70% were in medical treatment while 49% were in medical treatment among non-smokers. 15% of smokers reported to be non-adherent compared with 24% among non-smoking women. Non-adherence was thus higher among non-smokers than among smokers (POR 0.55, 95% CI 0.1-2.5)Conclusion: Adherence to medical treatment in the post-

partum period was high and we found a high PPV for self-reported medical treatment. Fear of medicine in breast milk was most commonly stated as a reason for non-adherence, whereas counselling regarding medical treatment increased adherence. Smokers were more likely to be adherent to medical treatment than non-smokers.

P12.07 Niels Henrik Krarup

QUALITY OF CARDIOPULMONARY RESUSCITATION IN OUT-OF-HOSPITAL CARDIAC ARREST IS HAMPERED BY INTERRUPTIONS IN CHEST COMPRESSIONS - A NATIONWIDE PROSPECTIVE STUDY

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Background: Quality of cardiopulmonary resuscitation (CPR) is a critical determinant of outcome following out-of-hospital cardiac arrest. The aim of our study was to evaluate the quality of CPR provided by emergency medical service providers (Basic Life Support (BLS) capability) and emergency medical service providers assisted by paramedics, nurse anesthetists or physician-manned ambulances (Advanced Cardiac Life Support (ACLS) capability) in a nationwide, unselected cohort of out-of-hospital cardiac arrest cases.

Methods: We conducted a prospective, observational study of out-of-hospital cardiac arrest (> 18 years of age) occurring from the 1st to the 31st of January 2009 and treated by the primary Danish emergency medical service operator, covering approximately 85 % of the population. One hundred and ninety-one cases were eligible for analysis. Follow-up was up to one year or death. Quality of CPR was evaluated using measurements of transthoracic impedance.

Results: The majority of patients were treated by ambulances with ACLS capability (54 %). Interruptions in CPR related to loading of the patient into the emergency medical service vehicle were substantial, but independent of whether patients were managed by ACLS or BLS capable units (222 versus 224 seconds, P = 0.76) as were duration of interruptions during rhythm analysis alone (20 versus 22 seconds, P = 0.33) and defibrillation (24 versus 26 seconds, P = 0.07).

Conclusions: Nationwide, routine monitoring of transthoracic impedance is feasible. CPR is hampered by extended interruptions, particularly during loading of the patient into the emergency medical service vehicle, rhythm analysis and defibrillation.

P12.08 Karin Biering

RETURN-TO-WORK (RTW) AFTER PERCUTAN CORONARY INTERVENTION (PCI)

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Background: Coronary Heart Disease is prevalent in the workforce, in Denmark 2500 PCIs are performed among patients <65 years annually. There has been a large interest in work-related risk-factors of Coronary Heart Disease, but implications in working life are not as well known.

We aimed to describe patterns and predictors of RTW after PCI.

Methods: 1584 patients <67 years treated with PCI in 2006-2008 at Aarhus University Hospital, Skejby were enrolled. Clinical information was provided from West Denmark Heart Registry and 4 weeks after PCI we mailed questionnaires regarding self-rated health (responserate= 78.4%). RTW was defined on basis of public transfer payments from a public interdepartmental database. Data was analysed as time to event data with pseudovalue methods with competing risk.

Results: 4 weeks before PCI 50% patients were able to work, and 4 weeks after the PCI 25%, while after 1 year 43%. Risk factors for difficulties in RTW after 12 weeks were female gender and an acute indication for the procedure (AMI), and after 1 year female gender was still a risk factor. Left ventricular ejection fraction (LVEF) and the self-rated health were predictors of difficulties in RTW at both 12 weeks and 1 year. Patients own perception is important as their prediction on self-rated health shortly after the procedure was stronger than degree of disease measured by LVEF. The study has complete follow-up for all patients and the cohort is well-defined. However, there may be some selection bias as non-respondents were younger and with sligthly lower LVEF. Also self-rated health may be influenced by the patient's knowledge of LVEF and indication.

P12.09 Efe Levent Aras

SURGICAL TREATMENT OF VERTEBRAL COMPRESSION FRACTURES VERSUS CONSERVATIVE TREATMENT. EVALUATION OF LONG-TERM OUTCOMES AND COST-EFFECTIVENESS.

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Background and purpose: The thoracolumbar region, which comprises from the 11th thoracic to the 2nd lumbar vertebrae, is a common site of spine fractures. Majority (60-70%) of these fractures are AO type A (compression) injuries. Ethiology varies from high energy trauma to low energy trauma either in non-osteoporotic or osteoporotic patients. Despite the fact that these types of fractures are common, ideal management remains controversial, especially in patients without an associated neurologic deficit. Several surgical techniques, ranging from minimal invasive percutaneous cementing to open pedicle screw fixation, and conservative brace treatment are proposed in literature for the treatment; however the clinical evidence is still lacking. In this Ph.D. thesis, we aim to evaluate the outcomes not only with a clinical perspective but also with a health economic perspective.

Materials and Methods: Ph.D thesis is formed as two randomized controlled trials of non-osteoporotic and osteoporotic fractures, which patients will be randomized either surgical or conservative treatment. Follow-ups will be done in different time intervals during two years, regarding functional outcomes and radiological outcomes. These outcomes will be evaluated with different questionnaires such as VAS, ODI, SF-36 and EQ-5D. Cost-effective analysis will be applied after completion of these two randomized controlled trials.

Current Status:Both of the trials have been approved by local ethics committee and initiated patient inclusion.

P12.10 Palle Bager

WHAT'S CHEAPEST, INTRAVENOUS IRON SUCROSE- OR INTRAVENOUS IRON CARBOXYMALTOSE TREATMENT?

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Aim: To evaluate the health care cost for intravenous iron sucrose (IS) vs. intravenous iron carboxymaltose (IC) to outpatients with Inflammatory Bowel Disease (IBD).

Background: Intravenous IS can be given as a max of 200 mg Fe^{++} vs. intravenous IC max. of 1000 mg Fe^{++}. The drug-cost per mg iron is for IC is double the cost of IS.

Patients and Methods: Data related to 111 IBD-patients treated with intravenous iron at Aarhus University Hospital was used.

Analysis was: Budget Impact Analysis (BIA), Cost Effective Analysis (CEA) and Willingness to Pay Analysis (WTP). BIA and CEA was based on total infusion-doses from 500 mg till 1600 mg and WTP only 1400 mg.

Results: The BIA including: price for drug, utensils & nursetime; showed approximately 150€ extra cost per 1000 mg administrated, if IC was chosen. In contrast the CEA including both BIA-values and patient-related costs (transportation and lost income) showed IC to be more cost-effective than IS, due to

fewer outpatient setting visits. As IBD-patients could have less income as the average of the background population due to disease activity, sensitivity analysis using a 50% income level were done, showing the same tendency but less marked. The average patients WTP for a total of iron-dose was to 233€ to reduce the numbers of infusion from 7 till 2.
Conclusion: The cost of choosing IC rather than IS in treatment of iron deficiency in IBD differs depending of the economic perspective chosen. Only the BIA showed IS to be the cheapest. If the patients' perspective was included in the economic evaluation IC was the most cost-effective.

P13.01 Rasmus Foldbjerg

SILVER NANOPARTICLES INDUCE OXIDATIVE STRESS IN A549 CELLS

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The study aims at investigating the mode of action of nanoparticles (NPs) and evaluating the cytotoxicity of nanoparticles (NPs) in in vitro systems. Methods: The toxicity of two kinds of silver was studied (1) Ag NPs (PVP coated, length 81 nm; aspect ratio 1.2) and (2) Ag ions (AgNO3). The toxicity was examined by MTT reduction and annexin v/propidium iodide staining after 24 h exposure. The generation of intracellular reactive oxygen species (ROS) was monitored by oxidized dichlorofluoroscein diacetate (DCF-DA) by fluorescence spectrophotometry. The effect of NPs and ions on intracellular communication (ICC) was investigated by the scrape-dye assay and expression of the gap junctional protein, connexin 43 (Cx43). Results: Exposure of the A549 cells to Ag NPs at 1-10 µg/ml for 24 h, decreased cell viability, increased apoptosis and necrosis and induced ROS levels in a dose dependent manner. The cytotoxic effect could be prevented by pretreatment with the antioxidant, N-acetylcysteine. Increase in ICC was observed both at the level of expression of Cx43 and by the functional assay after 24 h exposure to 2 µg/ml Ag NP. Conclusion: Our results suggest that Ag NPs and Ag ions induce toxicity and change the ICC in vitro. The toxic effect is likely to be caused by elevated levels of reactive oxygen species which could be prevented by antioxidant treatment.

P13.02 Malene Outzen

SELENIUM STATUS MEASURED IN BLOOD AFTER A HIGHER INTAKE OF FISH AND SHELLFISH - A RANDOMIZED DIETARY INTERVENTION STUDY

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Background: Selenium is an essential trace element that is incorporated into proteins in the human body and it hereby plays a major role in several important cellular processes. Previous studies have indicated that the selenium status of the Danish population is below the levels required to optimize the suggested protective effects of selenium towards major diseases including cancer. In Denmark, important natural sources of selenium are fish and shellfish.
Aim: The primary aim of this study is to investigate, whether higher intake of selenium rich food items such as fish and shellfish, is associated with higher selenium blood levels, when compared to subjects having a habitual diet. The secondary aim is to investigate the uptake of selenium from fish and shellfish and the incorporation of selenium from those foods into proteins in the human body. Furthermore, the impact of the natural variation in the genes that are responsible for the accumulation of selenium in the proteins will be investigated.
Methods: The study includes 102 non-smoking men and women aged 50-74 years. The subjects were randomized into the intervention group (n=51) or the control group (n=51). The intervention group receives 200 grams of fish and shellfish five days a week for six months. Blood samples were collected at baseline and will be drawn after 3 and 6 month intervention period. In blood samples levels of selenium, selenoprotein P, genetic polymorphisms in the selenoprotein P gene, and heavy metals (lead, cadmium, and mercury) will be determined.
Perspective: This study is expected to provide knowledge on how to optimize the intake of selenium in the Danish diet.

P13.03 Mona Lisa Idriss Kise

SOCIOECONOMIC AND DEMOGRAPHIC CHARACTERISTICS OF CANCER PATIENTS AS A PREDICTOR OF THE SEVERITY OF FIRST PRESENTED SYMPTOMS

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Introduction: It is well-documented that there is a social gradient in cancer survival. Some studies also indicate that there is a social gradient in delay in cancer diagnosis. Since a social gradient in delay in cancer diagnosis and in cancer survival exists, it could be hypothesised that socioeconomic and demographic characteristics are associated with the severity of the first presented symptoms to the general practitioner (GP). Therefore, we explore the following hypotheses: 1) Patients with a high socioeconomic position (SEP) less frequently present with alarm symptoms due to an earlier health care-seeking behaviour. 2) Patients with a high SEP are more frequently categorised with alarm symptoms due to better doctor-patient communication.

Aim: To analyse if a patient's socioeconomic and demographic characteristics are associated with the GP's categorisation of symptoms as alarm, serious or uncharacteristic symptoms.

Methods: Data on symptom presentation (categorised as alarm, serious and uncharacteristic symptoms) of 2,212 incident cancer patients are linked to register data using the unique civil registration number allocated to all residents in Denmark. Associations between socioeconomic and demographic variables and symptom presentation are analysed using multiple regression analyses.

Results: Data analyses are ongoing. Final results will be presented. Preliminary results indicate that e.g. marital status, age and wealth may be associated with symptom presentation.

Conclusions: The study will contribute to new knowledge of the mechanisms behind social inequality in delay in cancer diagnosis.

P13.04 Susanne Lund Kristensen

THE ASSOCIATION BETWEEN ANTI-MULLERIAN HORMONE AND FEATURES OF POLYCYSTIC OVARY SYNDROME IN YOUNG WOMEN

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Introduction: Anti-Mullerian hormone (AMH) is produced in the ovary and is a good indicator of ovarian capacity. AMH is often elevated in women with polycystic ovary syndrome (PCOS), which is characterised by hyperandrogenism, increased number of follicles, and long menstrual cycles.

The aim of this population-based study was to investigate the association between AMH and features of PCOS in young women.

Material and Methods: The study population consisted of 256 (59%) adult daughters from a Danish pregnancy cohort established in 1988-89. In the present study, a blood sample was drawn to measure AMH and testosterone, a questionnaire provided information on menstrual pattern, and ovarian follicles were counted by ultrasound.

Results: Median (range) AMH and age was 2.6 (0.1-9.6) ng/ml and 20.1 (19.5-21.0) years. When performing multiple regression analysis controlling for use of hormonal contraceptives and BMI, the number of follicles (95% CI) was 13.4 (11.7-15.0), 16.1 (14.4-17.8) and 18.9 (17.4-20.4) in groups having low, medium and high AMH, respectively. AMH was also associated with testosterone: median (range) was 1.6 (1.4-1.8), 1.7 (1.5-1.9) and 1.9 (1.8-2.1) nmol/l in groups having low, medium and high AMH, respectively. In multiple regression analysis, AMH was not statistically significantly associated with length of menstrual cycle. When performing trend test, AMH was associated with all three outcome variables.

Conclusions: In these young women, trend tests showed statistically significant association between AMH and number of follicles, level of testosterone, and length of menstrual cycle. This study supports, that AMH could be an alternative tool in diagnosing PCOS.

P13.05 Peter Agergaard

THE DANISH NATIONAL PATIENT REGISTRY: A VALID DATA SOURCE REGARDING CONGENITAL HEART DISEASE

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Introduction: The present study was conducted to establish the validity of congenital heart disease (CHD) diagnoses in the Danish National Patient Registry (NPR), thereby exploring whether NPR can serve as a valid tool for epidemiologic studies of CHD.
Materials and methods: The study population comprised every individual born in 2000-2008, who was registered in NPR with a CHD diagnosis and treated at one of the two national departments of pediatric cardiology. Validity was calculated at two levels measuring the accuracy of NPR information as compared to the clinical record of each individual.
Results: 2,952 patients with a total of 3,536 diagnoses were eligible for validation. Review of their clinical records did not unveil any patient without CHD. In 98% [98-99%] of the cases, the NPR diagnosis could be found as the discharge diagnosis in the patient's clinical record, and in 90% [89-91%] of the cases the NPR diagnosis was considered a true reflection of the patient's actual malformation.
Conclusions: This study verifies that NPR is a valuable and valid tool for epidemiological research within the topic of CHD. Hence, it comprises an excellent sampling frame for longitudinal population-based and clinical research. Precautions should be made regarding cardiac malformations characterized by low prevalence.

P13.06 Lene Søndergård Larsen

THE SIGNIFICANCE OF FELLOW PATIENTS DURING HOSPITALISATION; A RESOURCE OR A LIABILITY?

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The objective of this project is to understand the social interaction between cancer patients during admission in a hospital.
The literature shows that patients spend approximately 90 % of the time with fellow patients which concludes that less than 10 % of the time is spent with the health personnel. The nurse regards the 90%, when she is not with the patient, as "empty time" where the patients keep themselves occupied with "trivialities not worth mentioning". In opposition to the nurses´ view, the patients regard the time spent with fellow patients as a rewarding fellowship where you can learn about your own disease. By talking about their disease, the patients construct meaning and increase their ability to cope with the disease (Album 1996).
The aim of the project is to study the significance of fellow patients when it comes to:
1) learning how to get on as a cancer patient,
2) retrieving information about the disease and course of the disease, and
3) psycho-social support and caring.
The project is carried out as a qualitative fieldwork inspired study with a combination of participant observation and semi-structured interviews with 15-20 participants.
Only a few studies are carried out worldwide and they all address the need for further exploration in this field. The literature shows that patients use each other when seeking information about their illness and support each other psychosocially. It is therefore relevant to seek an understanding of the patients´ social interactions during admission as this relationship may be of great importance to the quality of

life, the care and the course of admission to the cancer patients.

P13.07 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 movement disorder characterized by abrupt onset of dystonia, usually with signs of Parkinsonism. RDP is caused by missense mutations in the a3-isoform (ATP1A3 gene) 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 (haploinsufficiency), 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 of the mutations have been found to reduce the Na^+ affinity of the Na^+,K^+-ATPase, which might lead to an increase in the intracellular Na^+ concentration. It is a goal to establish a transgenic mini pig overexpressing Na^+,K^+-ATPase a3 with an RDP mutation causing reduced Na^+ affinity, thus allowing us to test the negative dominance hypothesis. The promoter that will be used is the porcine promoter of ATP1A3, which has been cloned. The function of the ATP1A3-promoter has been tested in two different cell lines, and its specificity will further be analysed. 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.

P13.08 Hanne Mainz

THE RELATIONSHIP BETWEEN NURSE STAFFING AND PATIENT OUTCOMES

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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, 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 instrument for measuring nurse staffing containing the elements: nursing resources (number and skills), nurse intensity and contextual factors. In Denmark no instrument has been validated to assess nurse staffing. The object of this study is to identify and validate an instrument for assessing nurse staffing in Danish somatic wards, and subsequently evaluate the relationship between nurse staffing and outcome for patients with hip fractures.
Methods: Instruments to assess nurse staffing will be identified in a systematic literature review, and selected methods to measure number, skills, nurse intensity, and context factors will be tested and validated in four Danish somatic hospital wards. The validated instrument will be used in a multicenter study, designed as a prospective cohort study. For a period of one year nurse staffing will be estimated in ten orthopaedic surgical wards, which annually receive a total of 2,500 patients with hip fracture. Outcome data will be obtained from The National Indicator Project and data on patient satisfaction will be collected from the nationwide patient satisfaction survey.
Expected results: An instrument for assessing nurse staffing can be used to achieve a better use and distribution of the existing nursing resources in order to optimize patient outcome.

P13.09 Jens Christian Jensen

WORK-RELATED PREDICTORS FOR MEDICAL CARE-SEEKING WITH UPPER EXTREMITY PAIN AND BACK PAIN IN A COHORT OF THE GENERAL WORKING POPULATION.

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Background: in western countries like Denmark, legislation has been promoted to secure a safe working environment. Furthermore, a lot of the manual labour tasks have been moved out of the country. Despite these changes at the labour market, no decrease in the occurrence of musculoskeletal pain has been observed.
Aim: to examine work-related physical and psychosocial risk factors for first time care-seeking with upper extremity or back pain during 18 months 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 men and women participated. 445 (10.3%) paid a first time visit with upper extremity pain and 498 (11.5%) showed up with back pain. Cox proportional hazard regression analyses of time to first visit was performed, yielding crude, partly adjusted and fully adjusted hazard ratios. Results were stratified on gender.
Results: There were no work related factors that predicted care-seeking with back pain. Heavy work predicted care-seeking with upper extremity pain for both genders. Repetitive work was associated with care-seeking with upper extremity pain among women. Computer work was related to care-seeking among men in an irregular pattern. Psychosocial work place factors were not associated with care-seeking.

P13.10 Emma Tina Bisgaard Olesen

VASOPRESSIN INDEPENDENT PHOSPHORYLATION AND TRAFFICKING OF AQUAPORIN-2 BY SELECTIVE E-PROSTANOID RECEPTOR AGONISTS
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Vasopressin increases the water permeability of the collecting duct (CD) acutely by targeting of aquaporin-2 (AQP2) to the apical plasma membrane of principal cells through activation of the Gs protein coupled receptor V2R. This involves phosphorylation of AQP2 at serine residues (pS256, pS264 and pS269). E-prostanoid receptor types 2 (EP2r) and 4 (EP4r) are alternative Gs protein coupled receptors expressed in the CD. We performed ex vivo studies in cortical CD suspensions (CCDS) and in vitro studies on MDCK cells stably transfected with AQP2 and we stimulated with either prostaglandin E2 (PGE2), an agonist for the EP2r (butaprost) or the EP4r (CAY10580). The effects on AQP2 phosphorylation were assessed by immunoblotting and apical plasma membrane abundance of AQP2 was assessed by cell surface biotinylation.
In MDCK cells, Butaprost caused a concentration-dependent (10^{-8}M to 10^{-6}M) increase in AQP2 phosphorylation and apical membrane abundance. Stimulation with either butaprost or PGE2 (both 10^{-7}M, 40 minutes) had similar effects on targeting, pS264 and pS269 abundance. Similarly, CAY10580 concentration dependently (10^{-8}M to 10^{-5}M) mimicked the effect of PGE2 on AQP2 targeting and also increased S264 phosphorylation without affecting pS269.
In CCDS, all three agonists increased AQP2 phosphorylation (pS256).
In conclusion, PGE2 and butaprost increase targeting of AQP2 and phosphorylation at S256, S264 and S269 whereas CAY10580 increases targeting, pS256 and pS264 without affecting pS269 phosphorylation. These results provide further understanding of the concentrating mechanisms of the kidney CD and could have implications for the treatment of nephrogenic diabetes insipidus.

P13.11 Annett Andersen

WORK RELATED SHOULDER LOADS: ESTABLISHMENT OF A JOB EXPOSURE MATRIX
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Aim: The aim is to construct a general Job Exposure Matrix (JEM) for mechanical shoulder loads in Denmark.
Methods: The two dimensions of the JEM will be occupations and mechanical shoulder exposure variables. The occupational dimension will include 2227 job titles from the Danish version of The International Standard Classification of Occupations. All job titles will be subdivided into approxomately 120 occupational groups with expected homogeneous exposure patterns. The exposure variables will comprise mechanical shoulder loads such as working with elevated arms, repetitive arm movements, forceful exertions and vibration.
The exposure assessment will be based on expert judgements and technical measurements. The expert judgements will be performed by 5 specialists in occupational medicine. The technical measurements will include whole day inclinometer recordings performed at the workplace. We anticipate obtaining a total of 400 measurement days.
Results: The exposures will be assessed on continuous scales, and mean exposure will be estimated. If possible expert judgement and technical measurements will be combined.
Discussion: The JEM can be applied as a general shoulder exposure information system for risk quantification. In further studies the JEM will be employed for exposure assessment in a Danish population-based register study of surgery treated shoulder disorders, where exposure-response relationships will be established. The JEM will also be employed in a case-referent study to investigate the risk of surgery treated shoulder disorders in relation to mechanical shoulder exposures.

P14.01 Ulrick Espelund

INTERSTITIAL FLUID COLLECTED BY THE SUCTION BLISTER TECHNIQUE CONTAINS A HIGHER IN VITRO BIOACTIVITY THAN SERUM.
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Background. The concentrations of Insulin-like Growth Factor 1 (IGF-1), IGF-2 and IGF binding proteins (IGFBP) in the blood have been extensively described, whereas data on the IGF system outside blood vessels are sparse. Current methods include microdialysis and nylon-wick methodology, both suffering from poor recovery rates and limited sample volumes.
Aim. To evaluate the suction blister technique for detection of IGFs and IGFBPs at the tissue level.
Design. Serum and interstitial fluid was collected from 6 healthy men at the end of a 20 hour fasting period and following food intake. Application of vacuum on the abdominal skin raised vesicles containing dermal interstitial fluid. Suction for 90-120 minutes yielded 1.5 mL of suction blister fluid (SBF). Blood samples were drawn before and after each of the two vacuum periods.
Results. Given as mean±SEM in the format (before meal vs. after meal, Student's t-test of ratio=1). In SBF, IGFs and IGFBPs were all detectable by immunoassay with values of 30-60% of the corresponding serum (all $P<0.001$). In spite of lower concentrations of IGF-1 and IGF-2, the IGF-1 bioactivity of SBF (1.69±0.23 vs. 1.70±0.28 µg/L, P=NS) was higher than the corresponding serum IGF-1 bioactivity measured by KIRA (1.23±0.24 vs. 1.30±0.23 µg/L, P=NS) (SBF vs. serum: P=0.01 and P=0.025). IGFBP-3 proteolysis was elevated in SBF (P=0.01).
Conclusion. The components of the IGF system were present in interstitial fluid at lower concentrations than in serum. We found higher levels of IGF-1 biological activity, whereas total concentrations were lower. This novel finding may be explained by an altered binding protein composition of SBF compared to serum.

P14.02 Jakob Østergaard

MANNOSE-BINDING LECTIN AND ACTIVATION OF COMPLEMENT SYSTEM IN TYPE 1 DIABETES
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Backgound: Clinical studies report increased blood levels of mannan-binding lectin (MBL) in patients with type 1 diabetes. This finding is not explained by MBL-genotype differences. Likewise, in wild-type mice streptozotocin (STZ) diabetes, a model of type 1 diabetes, is associated with an elevated MBL compared with wild-type mice without diabetes. Furthermore, in patients with diabetes a strong predictive value of MBL level for future deterioration of kidney function is seen. In mice, we have found causality between MBL and degree of functional and structural diabetic kidney alternations.

Hypotheses: 1) MBL level increases because of the diabetes. 2 Serum proteins are subject to glycosylation in the diabetic milieu. 3) These protein-glycasylations lead to activation of the complement system.

Aim and methods: Measurement of MBL before, during, and after the induction of multiple low-dose STZ-diabetes in female C57BL/6 mice. Test of inhibitory capacities of diabetic vs. normal serum to inhibite the binding of MBL to mannan-coated microtiter plates. Comparison of complement activation in diabetic vs. normal mice. Determination of MBL half-life in diabetes vs. non-diabetes by intravenous injection of recombinant human MBL.

P14.03 Louise Jung Nørgaard Jensen

PLASMA CALPROTECTIN IN PATIENTS WITH CHRONIC HEART FAILURE

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Aims: Low grade inflammation has been associated with the development of cardiovascular disease (CVD) and chronic heart failure (CHF). Recently, the inflammatory protein calprotectin was found elevated in plasma in patients with coronary heart disease (CHD) and furthermore was useful as a prognostic biomarker of mortality. The aim of the present study was to investigate the potential usefulness of calprotectin as a biomarker in CHF.

Methods and results: Plasma calprotectin was measured in 193 patients with CHF and 100 healthy controls at baseline. The level of plasma calprotectin was significantly increased in CHF patients compared to the control group 318 μg/L vs. 272 μg/L ($P<0.01$). In addition, calprotectin was significantly associated with hsCRP in CHF patients $\beta=0.40$ ($P<0.0001$). Patients with CHF were followed for a median period of 2.5 years according to mortality. After the follow-up period 46 patients had died. Plasma calprotectin levels did not predict mortality in CHF patients.

Conclusion: Plasma calprotectin is increased in CHF patients, indicating that inflammatory activity is upregulated.

P14.04 Morten Møller Poulsen

RESVERATROL PREVENTS DEVELOPMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE BY A COMPENSATORY UPREGULATION OF MITOCHONDRIA NUMBER AND IN PARTICULAR UCP2.

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Objective: In animal studies the polyphenol resveratrol has shown promising tendencies in ameliorating the development of metabolic disease, improving health and overall mortality. However, only little is known on how these beneficial effects are mediated.

Aim: With emphasis on NAFLD we wanted to investigate the metabolic effects of resveratrol in diet induced obese rats, aiming on describing the underlying mechanistic basis.

Design: 36 wistar rats were randomized to 1: Control feed, 2: High Fat feed (60 % fat) or 3: High Fat feed + 100 mg Resveratrol daily. After 8 weeks of treatment the rats were sacrificed.

Results: By semi-quantitatively microscopical grading no substantial hepatic steatosis in was found the C group. In HF the steatosis grade was 2-3, and in HFR interestingly these changes were reversed. Furthermore the liver triglyceride content was directly quantified, and in the HF group the content was significantly higher ($P<0,001$) than in the C and HFR groups which were alike. We found the expression of UCP2 significantly increased in HF as compared to C ($P<0,001$) and further significantly increased in HFR as compared to HF ($P<0,001$). Finally the mitochondria content in the livers from resveratrol treated rats was significantly higher as compared to both C and HF ($P<0,001$ and $P=0,004$ respectively).
Conclusion: Resveratrol possesses the potential to counteract the development of NAFLD in high fat fed wistar rats. Our data suggest that these effects could be caused by a compensatory increase in the mitochondria number and an increased expression of UCP2 – dissipating the excess energy as heat at the expense of ATP synthesis and oxidative phosphorylation.

P14.05 Karina Bech Cullberg

RESVERATROL INHIBITS THE HYPOXIA-INDUCED INFLAMMATION AND ANGIOGENESIS IN HUMAN ADIPOSE TISSUE *IN VITRO*.

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In obesity adipose tissue is thought to become hypoxic due to the inability of the vasculature to keep pace with adipocyte expansion and adipose tissue growth. Hypoxic conditions cause an increase in proteins involved in e.g. angiogenesis, glucose utilization and inflammation. Resveratrol is a natural polyphenolic compound synthesized in a large number of plant species. Resveratrol has powerful anti-inflammatory effects and beneficial effects on several metabolic disturbances. In the present study we investigated the effect of resveratrol on hypoxia-induced inflammation in human adipose tissue.
The effect of hypoxia, induced by incubation at low oxygen tension (1% O_2), was examined on the expression and secretion of inflammation and angiogenesis-related adipokines in whole human adipose tissue cultures - with and without addition of resveratrol (50 μM).
Exposure of adipose tissue to hypoxia for up to 24 hours resulted in increases in glucose transporter-1 (GLUT-1) (19-fold), vascular endothelial growth factor (VEGF) (10-fold), interleukin-8 (IL8) (8-fold) and interleukin-6 (IL6) (5-fold) mRNA levels and VEGF protein levels (8-fold) compared to normoxia. Resveratrol completely inhibited (by about 100%) the hypoxic response in GLUT-1, VEGF, IL8 and IL6 mRNA levels and protein levels. On the other hand, hypoxia and resveratrol had no effects on several other proteins such as leptin.
These results demonstrate that hypoxia induce extensive changes in human adipose tissue in the expression of inflammation-related adipokines. In addition, the inhibition of hypoxia mediated inflammation may represent a novel mechanism of resveratrol in preventing obesity-related pathologies.

P14.06 Lars Rolighed

STERNOTOMY IN THYROID OPERATIONS: RETROSPECTIVE STUDY OF 48 OPERATIONS.

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Introduction: Surgical treatment of substernal goiter occasionally involves sternotomy. Classification and handling of these operations are widely discussed. This is a study of the surgical results after thyroid operations including median sternotomy in Aarhus University Hospital, Department of Surgery P, Brest and Endocrine Section.
Materials: All 1573 thyroid operations in the department from 01.01.95 to 31.12.08 were included. Median sternotomy was performed in 48 operations (3%).
Results: Mean operation time was 4 hours and 8 minutes (n=43). Mean estimated blood loss was 433 ml (n=42). In 5 operations (10%) blood transfusion was given. Median duration of postoperative hospitalization was 7 days (range 4 to 27 days).
Complications: Mortality: One patient with an anaplastic carcinoma and severe tracheal compression. Radical resection was not possible and this patient died

postoperatively. Mild pulmonary complications in 11 patients (23%). Permanent hypocalcaemia observed 2 patients (4%). Recurrent laryngeal nerve injury was not observed (0%).
Discussion: Postoperative hypoparathyroidism and recurrent laryngeal nerve injury after surgery for substernal goiter are reported in up to 5.8% and 14.3% respectively in 24 series. We did not observe recurrent laryngeal nerve injury during 14 consecutive years. The most frequent complication was minor pulmonary and did significantly elongate hospitalization (p=0.04).
Conclusions: Thyroid operations with sternotomy are complicated procedures accompanied with considerable pulmonary complications, but in experienced hands the risk is not increased of the specific complications hypoparathyroidism and recurrent laryngeal nerve injury.

P14.07 Jesper Fleischer

TESTING FOR CARDIAC AUTONOMIC NEUROPATHY: HEART RATE VARIABILITY IS SIGNIFICANTLY HIGHER IN HOME SELF-MONITORING COMPARED TO HOSPITAL TESTING.

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Background: The association between the finding of low Heart Rate Variability (HRV) and the presence of symptomatic as well as asymptomatic Cardiovascular Autonomic Neuropathy (CAN) in diabetic patients is well described in the literature, and the finding of CAN may be helpful in the detection of early signs of diabetic late complications. More recently a clear relationship between (undiagnosed) hypertension and CAN has been shown. Because of the technical setups available today, testing for CAN is only recommended at the point-of-care office or in a clinical laboratory setting.
Objectives: The primary objective was to assess any differences in measures at hospital and in the home testing. The secondary objective of this study was to evaluate reproducibility of self-monitoring at home vs. hospital testing.
Method: 10 type 1 diabetic all showing signs of CAN and 10 healthy volunteers were recruited. All subjects underwent thorough clinical examinations. Participants underwent in-hospital testing for CAN before and after home monitoring. For 6 consecutive home self-monitoring was performed every morning including: E:I ratio, 30:15 ratio, Valsalva ratio and SDNN(5 min). The intra- and inter-individual reproducibility was determined by coefficient of variation and the reproducibility coefficient.
Conclusions: Home testing of CAN is feasible. There was no significant difference between laboratory testing and self-monitoring when using autonomic reflex tests: E:I, 30:15 and valsalva manoeuvre. The SDNN (5 min) was, however, significantly higher in both groups indicating the presence of “White-Coat effect” in laboratory testing of Heart Rate variability.

P14.08 Birgitte Nellemann Sørensen

THE EFFECTS OF PHARMACOLOGICAL ANTILIPOLYSIS ON THE METABOLIC EFFECTS OF GHRELIN

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Ghrelin is a relatively new hormone, which is produced in the stomach and partly in the hypothalamus. The effects are diverse and include release of growth hormone (GH) and ACTH from the pituitary gland. We have previously shown that ghrelin stimulates metabolism of FFA and induces insulin resistance in skeletal muscle. These effects have we documented in GH-deficient subjects; a setting that makes it possible to investigate effects of ghrelin that are independent of GH and ACTH. The present study is a continuation of these experiments. We wish to investigate whether the effects on insulin sensitivity are dependent of stimulation of lipolysis. This can be done by reversible suppression of lipolysis with Acipimox, an experimental principle that have been successful in other contexts.
The present study involves 8 male volunteers with GH-deficiency in stabile

treatment regarding GH and hydrocortisone. All subjects participate in 4 study days in a 2x2 randomised design; 1) ghrelin infusion, Acipimox tablets, 2) ghrelin infusion, placebo tablets, 3) placebo infusion, Acipimox tablets, 4) placebo infusion, placebo tablets. Each study day is performed after a 12 hour fast and consists of 2 hours basal period and 3 hours hyperinsulinemic (insulin 0.6 mU/kg/min) euglycemic (p-glucose ~ 5,0 mM) clamp with muscle- and fat biopsies in each period. Additional methods involve tracer methodology with palmitate and glucose as well as determination of signal proteins for GH and insulin from adipose tissue- and muscle biopsies.
Knowledge of effects of ghrelin in general can be important for the understanding of growth disturbances such as overweight, type 2 diabetes and malnutrition.

P14.09 Lea Brader

HEALTHY NORDIC DIET IN THE PREVENTION OF METABOLIC SYNDROME; THE AARHUS UNIVERSITY PART OF A MULTI-CENTRE STUDY (NORDKOST)
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Background: Sedentary lifestyle and the obesity epidemic have produced an alarming rise in metabolic syndrome (MeS). MeS is a clustering of risk factors increasing the risk of diabetes and cardiovascular disease. The traditional Nordic diet contains many food items each capable of favourably affecting MeS. However, no studies have established if a “healthy Nordic diet” can, indeed, reduce the main metabolic abnormalities of MeS.
Aim: to determine if a “healthy Nordic diet” being in accordance with Nordic Nutrition Recommendations improves insulin sensitivity and other risk factors associated with MeS.
Method: A Nordic multi-centre, randomized, controlled, dietary intervention study is being conducted in 2009-2010 in 6 centers of SYSDIET consortium in MeS subjects. The subjects were stratified and randomized to a “healthy Nordic diet” or a control diet habitually consumed in Nordic countries for 18 weeks. Key food items were weekly provided to the subjects. Diet compliance was recorded daily using a FFQ. The subjects were instructed not to change body weight, physical activity level, medicine, and alcohol habits during the intervention.
The subjects visited the study clinic at screening, 0, 2, 4, 8, 12, 16 and 18 weeks. At the major visits (0, 12, 18 weeks) they completed a food diary and underwent clinical examination including diurnal blood pressure, diurnal urine sample, lipid profile, body composition, adipose tissue biopsy, fasting blood samples and OGTT.
Results: The dietary intervention has been successfully completed in Lund (n=42), Kuopio (n=32), Oulu (n=36), and Aarhus (n=32). In Uppsala and Reykjavik the intervention is still ongoing, and is completed November 2010.

P14.10 Pernille Høyem

Pernille Høyem[1], Esben Laugesen[1], Britt Christensen[1], Ulla Kampmann Opstrup[1], Samuel Alberg Thrysøe[2], Won Yong Kim[2], Jens Sandahl Christiansen[1] og Troels Krarup Hansen[1]. [1]Department of Endocrinology and Internal Medicine MEA, NBG, Aarhus University Hospital and [2]MR-Research Center, Skejby Hospital, Aarhus University Hospital.
Aim: To describe the prevalence of atherosclerosis in carotid arteries and the prevalence of cerebral infarctions and white matter lesions assessed by MRI-scans in patients with relatively newly-diagnosed type 2 diabetes versus healthy control subjects.
Methods: 98 patients with type 2 diabetes and 54 gender- and age-matched control subjects underwent a cross-sectional study, including an MRI part consisting of carotid arteries MRI-scan bilateral and cerebral MRI-scan. Carotid artery MRI was performed with 5 different contrast weights by which advanced characteristic of atherosclerosis is possible. The scans were subsequently visually rated for degree of atherosclerosis (degree 1-4 (no-severe)). Cerebral MRI was performed with 3 different contrast weights, thus were both cerebral infarctions and white matter lesions visualized.
Results: Mean age for patients vs. control subjects was 57.8 vs. 58.1 years. Mean body mass index was 30.1 vs. 26.2 kg/m^2. Degree of atherosclerosis was

significantly higher (p=0.043) for patients vs. control subjects. 10.5% of patients vs. 7.6% of control subjects (p=0.77) had cerebral infarctions. 24.4% of patients and 24.5% of control subjects (p=1.00) had more white matter lesions than expected according to age.
Conclusion: Degree of atherosclerosis in carotid arteries was significantly higher in patients than in control subjects. It is expected that diabetic patients have an accelerated atherosclerosis compared to healthy subjects, but this study shows that this process takes place already in an early stage of disease. No significant difference between the part of patients vs. control subjects with cerebral infarctions or increased

P15.01 Christian Wulff

EFFECT OF CASE MANAGEMENT IN COMPLEX CANCER PATHWAYS: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Case managers are increasingly engaged to improve continuity of cancer care pathways. Continuity of care through provision of patient-specific information and optimum shared care is the main purpose. However evidence of the effect of case managers is limited and methodologically rigorous research is needed.
Aim: To analyze effect of nurse case managers in complicated cancer care.
Methods: A two-arm randomized controlled trial (RCT) including approximately 280 colorectal cancer patients.
Intervention group patients are offered usual medical treatment plus supportive intervention from a case manager. Control group patients receive usual medical and supportive treatment.
The intervention: The case managers, registered nurses possessing thorough knowledge of cancer treatment and pathways, undertakes: planned and ad hoc personal and telephone patient contacts, surveillance of care pathways, coordination and dissemination of care plan (including transfer of patient-specific information to other departments and general practice).
Results: Primary outcomes: Patient evaluations of care pathways and 'Quality of Life' (questionnaires).
Secondary outcomes: Use of health care services and care process measures (The National Health Insurance Service Registry and The National Patient Registry; and GPs' evaluations of continuity of care (questionnaire).
I plan to present preliminary results of patient evaluations and 'Quality of Life' at the PhD day 2011.
Schedule: The RCT began in March 2009. Inclusion until mid December 2010. Case management-follow-up until June 2011. Last patient questionnaire-data December 2011. We anticipate that all results are publicised by spring 2012.

P15.02 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 ubiquitous, persistent, and suspected to act as endocrine disrupters. The compounds are able to cross the placental barrier, thus, in utero exposure is inevitable. In this study, we hypothesise that in utero exposure to PFOA and PFOS is negatively associated with semen quality and hormone profile.

Material and methods. Participants (n=176) were sons of a pregnancy cohort from 1988-89. They submitted semen and blood samples, which were analysed for the traditional semen parameters and reproductive hormone profile, respectively. Maternal blood samples from pregnancy week 30 were analysed for PFOA and PFOS levels and participants were grouped into three groups according to maternal levels of PFOA and PFOS (low, medium, and high) based on tertiles of exposure.
Results. Crude results show that of the traditional semen parameters, only the progressive sperm cells (A+B) appeared to be associated with prenatal exposure to PFOA. The proportion of progressive cells in the medium PFOA-group was significantly smaller than in the low PFOA-group (p=0.01). FSH level was significantly higher in the high PFOA-group compared to the low PFOA-group (p=0.03) and the trend was statistically significant (p=0.03). SHBG level in the medium PFOS-group was significantly lower than the high PFOS-group (p=0.04). Maternal levels of PFOS and PFOA were not associated with any of the remaining reproductive hormones.
Conclusions. The crude results do not indicate that in utero exposure to PFOA and PFOS is a risk factor for poor semen quality or altered reproductive hormone profile; however, results indicated small effects.

P15.03 Grethe Elholm FARMING EXPOSURE LEADS TO LESS ALLERGIC SENSITISATION

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Objectives: Farmers are exposed to a wide range of allergens and supposedly run the risk of developing allergy and asthma. However the prevalence of atopic sensitization and atopic asthma has been reported to be low in farmers.
Aim: We aim to describe the changes of allergen sensitization over time in The Danish Farming Cohort (SUS).
Methods: The SUS cohort consists of 1964 young farmers and 407 non-farming male controls. The participants were skin prick tested twice for sensitization to 15 different allergens, first during the SUS study (1992-1994) and subsequently 52% were re-investigated during the follow-up SUS12 study (2006-2008).
Results: We found an overall lower sensitisation rate among farmers compared to controls at both baseline (farmers 18% and controls 26%, p=0.012) and follow-up (farmers 30% and controls 41%, p=0.004). The low sensitisation rate among farmers compared to the controls was only seen in subjects born and raised on a farm regardless of smoking and asthma status. Furthermore we saw a tendency of an accelerated loss of sensitisation among farmers compared to the controls (farmers 18% and controls 9%, p=0.12). Additionally a tendency of smaller increase in sensitisation was seen among farmers compared to the controls (farmers 18% and controls 23%, p=0.22).
Conclusion: The analyses show that farmers born and raised on a farm with continued farming exposure maintain a low sensitisation rate and we observed a tendency to an increased loss of sensitisation in farmers compared to the non-exposed controls.
This supports the theory that farming exposure has a protective effect against development of allergy.

P15.04 Ioanna Milidou FIRST TRIMESTER NICOTINE EXPOSURE AND THE RISK OF INFANTILE COLIC

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Background: Although prenatal exposure to maternal smoking has been associated with infantile colic (IC), to date no published studies have reported on the relationship between the prenatal use of nicotine replacement therapy (NRT) and IC.
Aim: We aimed to assess the relationship between fetal exposure to nicotine, coming from both cigarette smoking and use of NRT early in pregnancy, and IC.
Methods: The study population consisted of 63,883 pregnancies that resulted in live born singletons enrolled in the Danish National Birth Cohort between 1997 and 2002. Mother's smoking habits and use of NRT during the first trimester was assessed through a computer-assisted telephone interview around gestational week 12. Positive exposure was defined as mother's report of any use of tobacco or NRT during this pregnancy.
Information on colic symptoms in the child was obtained by a computer-assisted interview of the mother at six months post partum. IC was defined using modified Wessel's criteria.
Crude ORs for IC were estimated with 95% confidence intervals (CI).
Results:A total of 5,259 (8.33 %) children fulfilled criteria for IC. Exposure to maternal smoking was associated with an increased risk of IC (OR = 1.34 [95% CI: 1.26 - 1.42]). We furthermore observed an association between use of NRT during early pregnancy and IC (OR = 1.44 [95% CI: 1.22 - 1.70]). A subgroup of infants (n=208) exposed to NRT but not to tobacco smoking in utero had an increased OR for IC of 1.55 [95% CI: 1.02-2.40].
Conclusion: The results indicate that prenatal exposure to nicotine from any source during the first trimester of the pregnancy increases the risk of infantile colic.

P15.05 Simon Grandjean Bamberger

GLOBALIZATION, ORGANIZATIONAL CHANGE AND PSYCHOSOCIAL WORK ENVIRONMENT: THE IMPACT ON MENTAL HEALTH

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Background: Companies implement organizational changes (OC) to compete on the world market and mediate the pressure of globalization, which has intensified due to advancements in information and communication technologies, free trade agreements and the opening of new markets. Continuously, mental health issues in the workplace have become an increasing problem affecting 22% of workers in the EU. Little research has been published on possible associations between OC and mental health.
Aim: To analyse the association between global competition, organizational change and mental health summed up in the following hypotheses:
Global competition pressure alters work conditions and may lead to job insecurity and psychosocial distress Different types of organizational change have different impacts on working conditions and mental health High individual resilience will modulate the effect of competition pressure and organizational change on mental health. Design: A multilevel study with longitudinal enterprise data and cross-sectional employee survey data.
Materials: Roughly 650 companies and 2,500 randomly selected employees assessed by questionnaire and registry based information.
Analysis: Exposure is measured by a matrix on competition pressure versus OC created by latent class analysis. The outcome variable mental health is measured by subjective health symptoms, use of psycho-pharmaceuticals, alcohol problems and sick leave.
Results: The unique study design enables exposure and outcome to be analysed on

multiple levels ensuring higher reliability and validity than previous studies that solely rely on self-reported data.

P15.06 Janne Fassov

FUNCTIONAL RESULTS OF SACRAL NERVE STIMULATION FOR IRRITABLE BOWEL SYNDROME

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Background:Irritable bowel syndrome (IBS) affects 10-20% of the general population.Currently, there is a paucity of treatments with long-term effect on symptoms.At present,sacral nerve stimulation (SNS) is a well-established treatment for faecal incontinence and constipation.Our pilot study of 6 IBS patients performed in 2006 significantly reduced IBS-specific symptoms during a three week percutaneous sacral nerve stimulation evaluation (PNE) test,thus indicating the relevance of a more detailed description of the treatment effect.
Aim:To determine the effect of SNS in patients with IBS.
Methods:IBS-specific symptom and quality of life (QoL) scores were determined a) at base line,b) during a three week PNE test,and c) after one year of SNS.
Population:Twenty-nine patients (25 women,age 19-69 (mean=36)) with IBS according to the ROME III criteria underwent a three-week PNE test.Based on positive results from the PNE test (at least 30% reduction in IBS symptom score),24 (83%) qualified for implantation of a permanent stimulator for SNS.Seventeen have now been implanted eleven among whom have had it for at least one year.
Results:During the three-week PNE test,mean IBS symptom score decreased from 60 to 35 ($p<0.001$),and mean IBS QoL score improved from 125 to 72 ($p<0.001$).There was significant improvement in all of the IBS-specific symptoms.At one year follow-up,mean IBS symptom score was 35 (vs 63 at base line ($p<0.001$)) and mean IBS QoL score was 78 (vs 133 at baseline ($p<0.001$)).
Conclusion:In highly selected IBS patients,SNS provides a significant reduction in IBS-specific symptoms.Furthermore,the present study indicates that the effect is maintained for at least one year.

P15.07 Henriette Vind Thaysen

HEALTH RELATED QUALITY OF LIFE AFTER SURGERY FOR LOCALLY ADVANCED PRIMARY RECTAL CANCER OR RECURRENCE OF RECTAL CANCER

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Background: Through the last 15 years improved surgical techniques and oncological treatment render many advanced rectal tumours amenable to curative resection. Treatment of locally advanced primary or recurrence of rectal cancer is extensive with a high postoperative morbidity but decreasing mortality. There is little information about the impact of the treatment on the patient's health related quality of life (HRQL).
Aim: To assess HRQL in patients treated with extensive surgical resection for locally advanced primary or recurrence of rectal cancer
Methods and material: Between 2001 and 2008 165 patients with locally advanced primary rectal cancer or recurrence of rectal cancer had surgery at Aarhus University Hospital. The patients were followed prospectively in the clinic 3, 6, 12, 18, 24, 36 and 48 months postoperatively. At every visit the patient were asked to complete the following HRQL questionnaires: SF- 36 (generic questionnaire), EORTC QLQ-30 (cancer specific) and EORTC-CR38 (colorectal cancer specific). The results will be compared with a reference group of patients with a primarily respectable rectal cancer having mesorectal excision alone.
Perspective: The results may be useful in the preoperative counselling and postoperative support of these patients.

P15.08 Mette Vinther

HBA_{1C} AS PREDICTOR OF ALL-CAUSE MORTALITY IN INDIVIDUALS AT HIGH

Skriver

RISK OF DIABETES WITH NORMAL GLUCOSE TOLERANCE, IDENTIFIED BY SCREENING: A FOLLOW-UP STUDY OF ADDITION, DENMARK

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Background: Stepwise screening for type 2 diabetes will not only identify people with the disease or some other form of dysglycaemia (impaired fasting glucose or impaired glucose tolerance), but also many individuals who are phenotypically at high risk of developing diabetes, but currently have normal glucose tolerance (NGT). We therefore sought to assess whether HbA_{1c} adds prognostic information in relation to all-cause mortality in people who have NGT and a high risk of type 2 diabetes mellitus.
Methods: In a Danish population-based stepwise screening programme for type 2 diabetes mellitus in general practice, we identified 15,634 persons at high risk of type 2 diabetes, who had NGT and a recorded HbA_{1c} measurement. As comparison groups we included 1,401 people identified as having type 2 diabetes mellitus and 8,149 individuals characterised as being at low risk of diabetes. All individuals were followed from time of screening (April 2001 to December 2006) until death or 31 October 2009. Excess mortality were estimated using Cox proportional hazard models with all-cause mortality as the outcome measure.
Results: Compared with individuals with NGT and HbA_{1c} below 6.0%, adjusted hazard ratios were: 1.21 (95% CI 0.94-1.55) for individuals with NGT and HbA_{1c} between 6.0% and 6.5%; 2.48 (95% CI 1.23-4.99) for individuals with NGT and HbA_{1c} 6.5% or above (in this group there were eight deaths among 68 individuals); 1.73 (95% CI 1.40-2.13) for individuals with type 2 diabetes mellitus.
Conclusions: HbA_{1c} level in people with NGT and at high risk of diabetes was clearly associated with increased all-cause mortality .

P15.09 Kristina Grønborg Laut

HEALTH TECHNOLOGY DIFFUSION: THE EXAMPLE OF PRIMARY ANGIOPLASTY IN THE EU15 COUNTRIES

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Background: Primary Percutaneous Coronary Intervention (PPCI) is the recommended treatment for patients with acute ST-segment elevation myocardial infarction (STEMI). Despite substantial evidence of its effectiveness, only 40 to 45 % of European STEMI-patients are presently treated with PPCI. This study seeks to identify important predictors of diffusion of PPCI in the EU15 countries.
Methods: An ecological study using aggregated country level data collected from international registers in 2006. Based on published literature, four factors possibly explaining the usage of PPCI were identified. These factors were used as covariates in a linear regression model with PPCI usage as the outcome variable. The estimation of PPCI usage was based on preliminary results combined with earlier published results. The outcome variable was available for 13 countries.
Results: Linear regression analyses did not reveal any significant correlations with usage of PPCI: number of acute care beds per 1.000 (coef. 0.1, 95 % CI= -0.1-0.3), publich health expenditure per capita (coef. -1.5, 95 % CI= -9.0-6.0), gross domestic product (coef. 0.6, 95 % CI= -0.5, 1.6) and population density per km^2 (coef. -13.0, 95 % CI=-41.5-15.5). Although the estimates were individually imprecise, the final model explained 61% of the variation in PPCI usage.
Conclusions: The preliminary analyses explained a substantial proportion of the variation in the usage of PPCI in the EU15 countries. Additional factors, such as organisational structure of the health care system, geographical aspects, and cultural differences are hypotheized to influence PPCI usage, and will be examined in the future process of this project.

P15.10 Margrethe

IDENTIFICATION OF PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY

Smidth

DISEASE (COPD) FROM ADMINISTRATIVE DATA

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Background: COPD is an irreversible life-threatening condition; secondary prevention, treatment and rehabilitation help control symptoms, increase patients' quality of life and delay disease progression. To accomplish this all segments of the healthsystem need a framework like the Chronic Care Model to provide organized care. To provide the evidence based proactive care to get improved results for the whole population; it is necessary to be able to identify patients with COPD.
Aim: To develop and test a method to identify people with COPD in a GP population.
Method: Seven general practices listed their COPD-patients and algorithms were derived from combinations of hospital admissions, use of medication and spirometries. The algorithm which found most patients and had most usable criteria was then used to identify patients in five different practices and in two municipalities. The GPs validated the lists and convergence was analyzed. In the municipalities 3000 people identified received a questionnaire.
Results: Using the algorithm which identified 72.2% of listed COPD patients from the initial seven practices, the GPs in the five practices validated that 62.2% of the identified patients had COPD. GPs using longest time to validate the lists of possible COPD-patients had higher similarity with the findings of the algorithm.
Assuming a prevalence of COPD of 9% the positive predictive value (PPV) was 65.0% (60.8-69.0%). For patients aged 65+ PPV was 89.0% (81.1-93.9%).
72.8% of the 1998 who returned the questionnaire had COPD.
Conclusion: The algorithm though not perfect can be used to identify a large proportion of people with known COPD which benefit the whole population and their care.

P16.01 Kaare Meier

SEGMENTAL INNERVATION OF THE GOTTINGEN MINIPIG HIND LIMB

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Background: The Gottingen minipig is used increasingly in biomedical research as an attractive alternative to other animal models.
Our lab has contributed to the accumulating knowledge of the central nervous system of the minipig, but so far the peripheral nervous system has been insufficiently characterized.
A few descriptions of the peripheral nerve supply exist in the veterinary literature; they are, however, all based purely on anatomical dissection studies.
We aimed to characterize the medullar segmental innervations of the hind limb region in the minipig.
Materials and Methods: Lumbosacral laminectomy was performed on anesthetized Gottingen minipigs, exposing the nerve roots. By direct recording from the nerve roots, detailed neurophysiological data were obtained from the skin. This procedure was supplemented with recording of action potentials from selected muscles.
Results: In our setting it was possible to obtain reproducible results from the neurophysiological examinations, thus enabling us to create an adapted dermatome map. Combining this with data from muscular activation we could correlate our results with our knowledge of human segmental innervations.
Conclusions: We were able to contribute to the increasing knowledge of the minipig nervous system. Our results can support the use of the Gottingen minipig as a model for experiments in medullar disorders and spinal cord-related treatment modalities.

P16.02 Vibeke Fuglsang

SOCIAL COGNITION IN FIRST-EPISODE SCHIZOPHRENIA: THEORY OF MIND AND SOCIAL PERCEPTION

Bliksted

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There is growing evidence that aspects of social cognition, primarily social perception, may serve as a mediator between neurocognition and functional outcome in schizophrenia.
This PhD project focuses on theory of mind (the ability to represent human mental states and/or make inferences about other's intentions) and social perception (the ability to process nonverbal, paraverbal, and/or verbal cues to make inferences about complex or ambiguous social situations).
Theory of mind was measured by The Hinting Tasks and Animated Triangles. Social perception was measured by a new Danish translation of small filmclips (TASIT part 2A) showing scenes from everyday life in either a sincere or a sarcastic version. TASIT (The Awareness of Social Inference Test) is thought to be a more ecologically valid and realistic reflection of the complexity of everyday social cognition than formerly used tests.
Neurocognitive deficits were measured by BACS and symptoms were rated by SANS and SAPS.
All the 36 patients in this study had just received a diagnosis of first-episode schizophrenia and were included from OPUS, Clinic for young people with schizophrenia, Aarhus University Hospital Risskov, Denmark.
Healthy controls were matched 1:1 to the schizophrenia patients regarding age, gender, race/ethnicity, education level (based on the quality of the last commenced educational level + parental educational level)), and community of residence.
Results will be presented regarding relationship between schizophrenic symptoms, neurocognitive deficits and specific social cognitive deficits.

P16.03 Mette Richner

SORTILIN IN NEUROPATHIC PAIN

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The molecular mechanisms underlying neuropathic pain are incompletely understood, but recent data suggests that down-regulation of the potassium-chloride co-transporter KCC2 in neurons of lamina I in the dorsal horn of the spinal cord by brain-derived neurotrophic factor (BDNF) is critical. Following peripheral neuronal injury, activated microglia release BDNF in the spinal cord, which stimulates TrkB to reduce KCC2-levels. As a consequence, chloride anions accumulate inside the neurons thereby reversing the action of the GABA-receptors in favour of chloride export and hence increasing the probability of depolarization. As sortilin modulates neurotrophin signalling, we speculated that receptor deficiency might influence development of neuropathic pain. Hence, we subjected wild-type and sortilin knockout mice (Sort1-/-) to two paradigms of peripheral neuronal lesion: the spared nerve injury (SNI) and spinal nerve ligation (SNL) models, respectively. The mice were then tested by Hargreaves test (thermal hyperalgesia) and von Frey's test (mechanical allodynia) to score neuropathic pain. While wild-type animals developed a profound hypersensitivity towards heat and tactile stimulation, mice lacking sortilin expression were fully protected. In agreement, western blotting suggests that expression levels of KCC2 remain unchanged in lesioned Sort1-/- mice as opposed to wild-type mice.

Current studies will examine 1) whether reduced BDNF-signalling is responsible for the observed phenotype, 2) if similar phenotypes may be observed in mice lacking other Vps10p-domain receptor family members, and 3) if a direct interaction between sortilin and KCC2 might (also) be involved.

P16.04 Kim Henningsen

THE ADULT RAT RESPONSE TO STRESS IS AFFECTED BY EARLY MATERNAL CARE QUALITY

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Maternal care is a vital factor in early life development and studies indicate that poor maternal care in early life is associated with an increased risk of getting life-style-associated diseases and for developing psychiatric disorders in adulthood. The focus of the present study was to investigate whether the level of maternal care in early life could affect how rats would respond to exposure to chronic mild stress in adulthood.

Methods: A standard method to evaluate maternal care was used to characterize rats as receivers of either good or poor maternal care. Adult, maternal care characterized, rats were exposed to a validated chronic mild stress regime and stress response was measured by monitoring sucrose intake, corticosterone levels and weight gain for a period of eight weeks.

Results: Rats that received good maternal care showed a significantly better ability to cope with stress compared to rats that received poor maternal care, expressed by almost complete resilience to developing an anhedonia-like symptom. Poor maternal care was associated with a symptom profile indicating endogenous stressed state, with both lower weight gain and sucrose intake levels, even in unstressed controls. Exposure to chronic mild stress was associated with an increased corticosterone level per se with no additive effect of maternal care state.

Conclusion: The results indicate that good maternal care in early life could be related to stress-resilience in adulthood. Poor maternal care, however, could be associated with a reduced ability to cope with stress.

P16.05 Annemette Bondo Lind

THE INFLUENCE OF MINDFULNESS-BASED COGNITIVE THERAPY FOR PEOPLE WITH SEVERE FUNCTIONAL DISORDER: A QUALITATIVE STUDY

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Background: Studies show that people with severe functional disorders are vulnerable to stressors and have difficulties coping with stress. We aimed to investigate how patients experienced and coped with stress in everyday life, before and after treatment with mindfulness-based cognitive therapy (MBCT), and how patients had experienced and coped with stress during their life history.

Methods: A qualitative grounded theory methodology was used in order to capture the patients' individual experiences well their social processes. 24 consecutively referred patients aged 20-45 years diagnosed with functional disorder participated in MBCT in two groups. They were all interviewed in-depth by a semi-structured interview-guide 1-2 months before and 4-6 months after treatment.

Preliminary findings: Patients narrated to be very sensible towards stress in daily life. They experienced their body to react highly on stressors with muscle tension, fatigue and pain. They expressed that they tried to ignore their bodily sensations and often used avoidance as coping strategy. During life they had tried to avoid difficult feelings of sadness and anger and were not trained in mastering these feelings. After treatment, patients experienced to be in better contact with their bodily sensations.

Conclusion: Patients with severe functional disorders often use avoidance as coping strategy in order not to experience difficult feelings of sorrow, sadness, anger and pain. MBCT seems to help people to connect to their bodily sensations, and thereby to connect to their feelings. This may cause ambiguity as they are confronted with difficult feelings.

P16.06 Louise Ørum Olesen

THE NEURAL BASIS OF COGNITIVE DEFICITS IN A MOUSE MODEL OF DEMENTIA

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Aim. To provide new insights into the neural basis of dementia, and at the same time to elucidate upon the co-morbidity between dementia and depression, both diseases causing severely cognitive deficits. Since the hippocampus plays a central part in the cognitive functions affected, focus will be on the dentate gyrus and the CA regions of the hippocampus; areas known to be affected in depression.
Background. Traditionally, AD has been considered a neurodegenerative disorder, caused by accumulation of amyloid plaques and neurofibrillary tangles, as well as loss of synapses and neurons, including loss of cholinergic (ACh'ergic) neurons. Recently, the early onset of behavioural symptoms, such as depression and aggression have become recognized as early signs of the cognitive decline in AD patients. This indicates a possible role of the monoamines, serotonin (5-HT) and norepinephrine (NE), in the pathogenesis of AD. Hypothesis. Manipulating the level of serotonin (5-HT) by treatment with antidepressants (SSRI) or by 5-HT depletion by stereotaxic lesioning of the median raphe nucleus will affect neurogenesis in the dentate gyrus in our APPxPS1 TG mouse model of dementia that develops amyloid plaques within 6-9 months. Said manipulation will also affect neuronal loss, dendritic arborisation, synaptic density as well as behavioural changes. Workplan. Using our APPxPS1 TG mouse model, neurogenesis, total neuron number, dendritic number and branching as well as synaptic number in the hippocampus will be assessed by histochemical studies. Behavioural changes are studied by testing at 9, 12, 15 and 18 months of age; the tests will a.o. be measuring emotional level and cognition.

P16.07 Louise Brøndt Hartlev

A NEW UNBIASED STEREOLOGICAL APPROACH FOR ESTIMATING CHANGES IN ARTICULAR CARTILAGE AND SUBCHONDRAL BONE IN HUMAN OSTEOARTHRITIC FEMORAL HEADS

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Background: Osteoarthritis (OA) involves all components of the affected joints, but special interest is focused on changes in the articular cartilage and the subchondral bone. The interplay between these tissues has been discussed for years, but quantitative histological studies, that include not only the most severe regions, but the entire joint, are still missing. We expect these findings to add new information to the many histological studies that already exists on OA.
Methods: A cross-sectional study with two cohorts (ten OA patients undergoing hip replacement due to severe primary OA, ten reference persons without OA), from where femoral heads were excised. They were then rotated around a vertical axis and sawn into 7-mm-thick slices a.m. Cavalieri. The slices were halved, embedded in methylmethacrylate, and cut into 7-µm-thick sections and stained with Masson Goldner trichome. The sections were analyzed using a microscope equipped with a motorized stage and controlled by the stereological software package NewCAST. Point- and line- grids were used for estimating either volumes of articular cartilage and subchondral bone or for estimating surfaces of articular cartilage, the tidemark and the border between calcified cartilage and subchondral bone.
Results: The application of the unbiased stereological approach will be presented. Furthermore, differences between OA patients and reference persons with respect to cartilage and subchondral bone parameters will be shown.
Conclusion: We have successfully applied an unbiased stereological approach that allows 3D quantification of volumes and surfaces of articular cartilage and subchondral bone in human OA femoral heads.

P16.08 Micah Allen

TRAINING THE BRAIN AT REST: MENTAL TRAINING AND PLASTICITY OF RESTING STATE NETWORKS

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In my project, I investigate the role of introspective meta-cognition in mediating the positive impact of mental training (meditation) on emotion and attention. To do this, I utilize subjective self-reports, longitudinal mental training, and resting state fmri.

Previously, irregular connectivity within the default-mode network (DMN) during cognitive tasks has been implicated in ADHD [1,2], OCD [3], depression [4], and anxiety [5]. These illnesses all disrupt meta-cognitive awareness and show improvement following mindfulness training [6]. Inability to suppress DMN activity in these pathologies has been postulated as a possible mechanism for ruminative thoughts [7,8]. An explicit goal of MT training is to reduce adherence to the stream of ruminative thought, or the production of greater experiential and mental stability [9]. DMN activity correlates with the onset of mind wandering and meta-awareness [10] and is intrinsically anti-correlated in it's activity with that of the the central-executive network (CEN).

Further supporting this theory is the finding that meditation training appears to partially decouple these networks [13]. If the reflective introspection-related DMN is consistently coupled to extrinsic stimulus, as it is without mindfulness training, then it is automatically reacting to the stimulus. This project seeks to test this theory by demonstrating that task-induced brain activations and error-aware performance are mediated by alterations in resting state DMN variability, which are further reflected by reduced self reports of mind-wandering activity.

P17.01 Kristian Kjær Andersen

HYPOTHERMIA DURING OPERATION ON THE ASCENDING AORTA: COMPARISON OF TO METHODS

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BACKGROUND: Cooling to 18o C using extracorporeal circulation (ECC) allows for circulatory arrest during operation on the ascending aorta. Two different methods are used either cooling the returning blood by 10o C, gradient cooling, or cooling as fast as possible, crash cooling. The operation and cooling elicit a stress response and the coagulation is influenced. There can be adverse effects on the cognitive skills due to the procedure. Cooling affects the colloid osmotic pressure which affects the fluid balance, and there is a theoretical risk of microbubbles formation in the blood using ECC and crash cooling. Both methods are used in the clinic but have never been subjected to comparison.

PURPOSE OF STUDY: To compare crash cooling versus gradient cooling and to investigate the physiological and cognitive changes during the procedure.

METHODS: Twenty patients between 18 and 80 yrs are randomized to either crash cooling or gradient cooling. Patients with severe comorbidity or known coagulapathy are excluded. Anesthesia and operation follow clinical standards. The primary endpoint is the length of cooling, secondary endpoints include coagulation parameters (thromboelastography, clot stability), stress response parameters (circulating adhesion molecules, oxidative stress analysis, inflammatory markers), cognitive tests, MRI of the cerebrum, and ultrasound imaging of the great vessels for detection of microbubbles. Patients are neurologically tested and MRI done at baseline and after the procedure, bloodsamples for analysis are obtained at baseline, under and after the procedure.

P17.02 Hanne Vinter

IMIQUIMOD INDUCED SKIN INFLAMMATION: A HUMAN MODEL OF PSORIASIS

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The study of psoriasis is limited by the fact that psoriasis only affects human beings . Animal models only partially reflect the mechanisms of the disease, but recently a new mice model of psoriasis-like skin inflammation induced by topical application of imiquimod has been introduced. Additionally, in casuistic reports the use of imiquimod have worsened or even triggered psoriasis. Our aim is to describe a human model of psoriasis-like skin inflammation by applying imiquimod on non-lesional skin in psoriasis patients.

Untreated psoriasis patients and matched healthy controls are treated with imiquimod and vehicle occluded by Finn Chambers for 48 hours. Prior to the treatment the skin is tape stripped to ensure sufficient imiquimod/vehicle absorption. On day 2, 4, 7 and 10, a clinical assessment of the skin inflammation is made by using the PASI-score. Biopsies are taken for PCR, Western blotting and immunohistochemical analyses.

So far 6 patients have been included in the study. 2 patients (10-fold tape stripped) showed clinical and histological psoriasis-like skin inflammation in the imiquimod-treated areas. HE-stained tissue sections of skin biopsies showed hyperplasia of epidermis, parakeratosis and a superficial perivascular infiltrate in the dermis. 3 patients (20-fold tape stripped) showed acute contact dermatitis-like skin inflammation with spongiosis in HE tissue sections. One patient showed a non-specific reaction.

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.

P17.03 Tue Kruse Rasmussen

INCREASED IL-21 AND IL-23 ARE ASSOCIATED WITH INCREASED DISEASE ACTIVITY AND WITH RADIOGRAPHIC STATUS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: RA is a chronic disease characterized by inflammatory reactions involving Th cells. The Th17 associated cytokines IL-21 and IL-23 have been proposed to have central roles in these processes.

Objective: To investigate the levels of IL-17A, IL-21, and IL-23 and their correlation with disease markers in RA.

Methods: In a longitudinal sample set from early RA patients (n=40) we measured plasma levels of IL-17A, IL-21, and IL-23 at baseline and after 3 and 12 months of treatment and investigated these for correlation with disease activity (DAS28), CRP, ESR, and Total Sharp Score (TSS). In a transverse sample set of chronic RA patients with paired PBMCs and SFMCs we investigated the cellular expression of IL-17A, IL-21, and IL-23R.

Results: Early stage RA patients have significantly increased plasma levels of IL-21 and IL-23, but not of IL-17A, compared with both chronic RA patients (all $p<0.05$) and controls (all $p<0.01$). After 12 months of treatment plasma levels of IL-21 and IL-23 correlated with DAS28 and ESR, but not to TSS. Changes in IL-23 plasma levels from time of diagnosis to month 12 correlated with change in DAS28 and with TSS at 2 years. Furthermore, numbers of CD4+ T cells producing IL-21, but not the ones producing IL-17A, were significantly increased in the synovial fluid compared to peripheral blood in chronic RA patients.

Conclusion: Our results show increased plasma levels of IL-21 and IL-23 in early RA and that these were significantly associated with disease activity, supporting that IL-21 and IL-23 are important pathogenic factors of this disease.

P17.04 Rikke Fleron Leihof

INHIBITION OF INTRACELLULAR GROWTH OF UROPATHOGENIC E. COLI

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Urinary tract infection (UTI) is considered to be one of the most common bacterial diseases worldwide. Uropathogenic E. coli (UPEC) is the primary cause of UTIs, accounting for 70-95% of the reported cases. UPEC can bind to, invade, and replicate within the bladder, forming intracellular bacterial communities (IBCs), representing a bacterial reservoir that can evade immune defences and antibiotic therapy. These intracellular bacteria mature into a biofilm-like state, creating pod-like bulges on the bladder surface that can burst into the bladder lumen and cause a re-infection of the bladder.

The aim of this study is to confirm the presence of IBCs and establish therapeutic methods to treat UPEC bladder infection by evaluating intervention of UPECs intracellular growth and biofilm formation.

The study will be conducted by mouse UTI experiments and electron microscopy to confirm the presence of IBCs as well as the establishment of an in vitro cellular model, using human bladder cell line 5637. In this model several treatment regimens, such as antibiotics, carbohydrates, antiserum against FimH and berberine amongst others will be investigated. The most successful therapeutic strategies will be further tested in the mouse UTI model for subsequent clinical treatment trials.

At this point, no results are available.

P17.06 René Østgård

INTESTINAL INFLAMMATION IN ANKYLOSING SPONDYLITIS ASSESSED BY FECAL CALPROTECTIN, CAPSULAR ENDOSCOPY AND COLONOSCOPY AND THE EFFECTS OF ADALIMUMAB ON MUCOSAL HEALING

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Intestinal Inflammation in Ankylosing Spondylitis assessed by Fecal Calprotectin, Capsular Endoscopy and Colonoscopy and the effects of Adalimumab on Mucosal healing

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.

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: 25 patients with active SpA and elevated feces calprotectin despite discontinuation of NSAID 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.

Status: Inclusion begins autumn 2010.

P17.05 Christine Lodberg Hvas

INTRACRANIAL HEMORRHAGE - A NEW LARGE ANIMAL MODEL OF BRAIN DEATH

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Objective: To develop a new brain death model where brain death is induced by intracranial hemorrhage and validated by CT angiography (CTA).
Background: Brain death impairs the function of organs in the potential donor and has a negative impact on organ retrieval. The underlying mechanisms are not clarified. In this study we established a model of brain death, with contact between blood and brain parenchyma. This creates a clinically relevant model mirroring patients suffering from brain death due to spontaneous intracranial hemorrhage.
Methods: Eleven Danish landrace pigs were anesthetized, intubated and their heads were fixated in a stereotaxic localizer box. A needle was inserted in the capsula interna at the level of the lateral ventricle. Intracranial pressure (ICP) was measured continuously and brain stem reflexes were tested before and after induction of brain death. Autologous blood was infused through the needle. At the speed of 40 ml/h coning was obtained at 30 min. The infusion continued for another 60 min to maintain an ICP sufficient to ensure brain death. CTA was performed 150 min after brain death. Atropine 3 mg was given and the heart rate observed for 1 min.
Results: Tachycardia, hypertension and diabetes insipidus developed as a response to increased ICP and intracranial bleeding. A second phase was recognized by a significant reduction in blood pressure. Atropine had no effect on the heart rate. Brain stem reflexes disappeared and CTA confirmed brain death by the absence of contrast material in and above the circle of Willis.
Conclusion: This is the first large animal model mimicking intracranial hemorrhage with subsequent brain death validated by CTA.

P17.07 Lone Schmidt Sørensen

OMEGA-3 FATTY ACIDS AND COMPLICATIONS AFTER COLORECTAL SURGERY

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Rationale: Several studies indicate that peri-operative supplementation with omega-3 fatty acids may reduce the risk of postoperative complications after surgery through an immune modulating effect. Omega-3 fatty acids are incorporated into cell membranes and thereby influence immune function. The purpose of this randomized placebo controlled trial was to discover whether an omega-3 fatty acid enriched oral nutritional supplement (ONS) given for 7 days before surgery and 7 days after surgery would be sufficient to reduce the risk of postoperative complications, and see the extent of incorporation of omega-3 fatty acids into cell membranes of granulocytes. Methods: 148 patients, who were referred for colorectal cancer surgery, were randomized to receive an omega-3 fatty acid enriched ONS (Supportan® Fresenius Kabi; 200 ml twice daily) or placebo for 7 days before surgery and 7 days after surgery. Blood samples were taken at day 0 and were analysed for incorporation of omega-3 fatty acid into neutrofile granulocyte cell membranes. Results: We found, that there was a statistically significant difference between the 2 groups with regard to incorporation of omega-3 fatty acid into neutrofile granulocyte cell membranes. (Students t-test P = 0,000).EPA was incorporated into cell membranes within one week.

P17.08 Ditte Andreasen Søborg

OCCURRENCE OF VIRULENCE GENES AMONGST NATURALLY OCCURRING ENVIRONMENTAL BACTERIA

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Background. Bacterial pathogenicity typically involves a combination of different virulence factors such as toxins, adhesins, invasins, secretion systems etc. Bacteria outside the human host might be able to acquire such pathogenic traits through horizontal gene transfer of virulence genes located on plasmids and pathogenicity islands. If survival and adaptation of bacteria in humans are similar to survival and

adaptation in the outer environment, then genes we typically associate with pathogenicity will be present in non-pathogens from the environment.
Materials and methods. To obtain knowledge of the presence of virulence genes in naturally occurring environmental bacteria, 22 selected genes associated with human disease were targeted by nested PCR in DNA extracted from four natural environments. Occurrence of the virulence genes was related to factors such as physical/chemical properties of the environments as well as to the prevalence of plasmids.
Key Results. Of the 22 selected virulence genes, 16 different were found to be present in a beech wood mulch soil, while 14 different genes were detected in an organic agricultural and a roadside soil. 11 genes were identified in biofilms on stones in a lake. Occurrence of the virulence genes differed between the environments and can possibly be related to selective pressures from land management practices and contaminant levels etc.
Conclusion. Natural environments were found to be a source of bacterial virulence genes. The presence of the virulence genes seemed not to be related to pathogenic bacteria in the environments but was expected to be used by non-pathogens to survive and adapt to different environmental conditions.

P17.09 Julie Prahl

PHARMACOKINETICS AND PHARMACODYNAMICS OF FIRST LINE TUBERCULOSIS DRUGS IN HUMANS AND MICE WITH TYPE 2 DIABETES.

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Background: Patients with diabetes are at increased risk of tuberculosis (TB). In developing countries where TB is endemic the prevalence of type 2 diabetes (type 2 DM) is increasing. One can therefore expect a growing number of TB patients with concurrent type 2 DM. The influence of concurrent type 2 DM on treatment response in patients with TB is not clear. Possibly type 2 DM may have an unfavourable influence on the pharmacokinetics of first line TB drugs thereby reducing the effect of standard treatment and increasing the risk of drug-resistance development.
Aim: The purpose of the Ph.D project is to investigate the influence of concurrent type 2 DM on the pharmacokinetics of first line TB drugs and on the treatment response.
Materials and methods: The Ph.D project comprises three studies:
1) Development of a new HPLC-MS-MS method for measurement of plasma concentrations of first line TB drugs in humans and mice.
2) Effect of type 2 DM on pharmacokinetics of first line TB drugs and on treatment response in mice with TB.
3)Pharmacokinetics of isoniazid, ethambutol and pyrazinamide in patients with type 2 DM with or without autonomic neuropathy and in healthy subjects
Perspectives: The project is expected to contribute to our understanding of how type 2 DM may affect the treatment of TB. This may in turn lead to improved management of patients with concurrent TB and type 2 DM. Measurement of plasma concentrations of TB drugs can also be used in other patients in whom altered phamacokinetics is suspected in order to optimize treatment.

P17.10 Line Reinert

THE ROLE FOR TYPE I IFN AND TOL LIKE RECEPTOR INDUCED ANTIVIRAL ACTIVITY AGAINST HSV

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The herpes simplex virus (HSV) is a common sexually transmitted virus causing genital ulcers, cold sores, infection of cornea, and encephalitis. HSV encephalitis is

rare, nevertheless it is the most common fatal sporadic encephalitis in humans. Around 80% of adults in industrialized countries are seropositive to one of the two types of HSV, HSV-1 or HSV-2.
In order to eliminate viral infections, the host immune response initiates with a rapid and less specific innate response. The virus is recognized by its pathogen-associated molecular patterns (PAMPs), which interacts with receptors on cells of the innate immune system, called pattern recognition receptors (PRRs). The virus recognition activates the cells of the innate immune system to produce interferons and chemokines, which recruits leucocytes to the infected area. Previous studies have shown that synergistic activation of antiviral activity by TLR2 and TLR9 during HSV infection in the brain.
In this study we focus on the mechanisms behind type I IFN induced antiviral activity against vaginal HSV infection in C57bl/6 mice. We are examining a subset of interferons and chemokines produced in the CNS of the Type I IFN receptor knock out mice. We also want explore the viral infections route to the brain by investigating the amount of virus and which cells are recruited to the vagina and the CNS.

P17.11 Frauke Rudolf

VALIDATION OF THE BANDIM TUBERCULOSIS-SCORE: RELIABILITY AND ABILITY TO PREDICT OUTCOME

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Setting: The study was carried out in Guinea-Bissau´s capital Bissau. Data were collected on both in- and outpatients from the six suburban districts constituting the Bandim Health Project´s study area.
Objective: Assessment of the variability between two physicians performing the Bandim Tuberculosis-score (TBscore), a clinical severity score for pulmonary TB patients, and to compare the Karnofsky Performance Score (KPS) with the TBscore.
Design: From August 2008 to July 2009 we assessed the TBscore of 141 included TB patients at one or more follow-up visits, resulting in 295 double assessments. Furthermore, we achieved 190 double assessments of both the TBscore and the KPS.
Results: The differentiation of TB patients being in the high severity class (TBscore>6) showed moderate agreement for both the TBscore (kappa= 0.57) and KPS (kappa = 0.48). While TBscore was able to differentiate between three risk groups, the KPS distinguished only two.
Conclusion: The Bandim TBscore had an acceptable inter-observer variability and performed better than the KPS. We found that individual TBscores obtained at treatment start carried prognostic information regarding a treatment outcome. However the variability of the individual parameters accumulates and a simplified score, based on comprehensive statistical analysis and consisting only of the most stabile variables, may be warranted.

P18.01 Anna Sellmer Sørensen

DUCTUS ARTERIOSUS IS OPEN ON DAY FOUR IN HALF OF ALL NEONATES BORN BEFORE 32 WEEKS OF GA

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Objectives: To investigate in an unselected population what proportion of neonates born before 32 weeks of gestation that has an open Ductus Arteriosus (DA) on day four. Furthermore, to characterize the DA ekkocardiographically if present.
Methods: All children born with gestational age (GA) < 32 weeks at Aarhus University Hospital, Skejby, were recruited consecutively (January - September 2010). Echocardiography was performed on day four after birth. Diameter of DA, the left pulmonary artery (LPA), peak systolic velocity in the DA (v_{max}), and left atrial-aorta ratio (LAAo) were measured. Flow in the LPA was evaluated.
Results: Forty six children were included. Median GA was 28.3 range (24-31) and median birth weight 984 g (470-2160 g). DA was open in 22 (48 %), of all and in 13 (62 %) of children with GA < 28 weeks. Median DA diameter was 2.0 mm (0.9-3.2 mm) and v_{max} 2.1 m/s (0.5-3.0 m/s). In children with an open DA median LAAo was 1.48 (1.07-2.14) compared to 1.24 (0.87-1.53) in children with a closed DA ($p < 0.001$). Median DA-LPA diameter ratio was 0.69 (0.29-1.06). Continuous blood flow in the LPA was observed in 17 (77 %) children with an open DA.
Conclusion: With a systematic echocardiographic evaluation we found that half of all neonates born with GA < 32 weeks have an open DA on day four. Further analyses are carried out in order to investigate whether the degree of clinical illness is associated with the presence and characteristics of the DA in this subgroup of neonates.

P18.02 Helle Damgaard Zacho

DOES TC99M-MEBROFENIN GET METABOLISED IN THE INTESTINES?

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Background: Measurement of the hepatic blood flow(HBF) is useful when investigating drug-metabolism in the liver and investigating for chronic intestinal ischaemia. The HBF can be measured using the Fick principle with infusion of a tracer e.g. Tc99m-mebrofenin(Tc-MBF). When the infusion rate of the tracer, the concentration of tracer in the portal and the hepatic vein is known the flow can be calculated. In patients it is not possible to obtain blood samples from the portal vein instead arterial blood samples are used. This part of the study aims at determines the difference in Tc-MBF between an arterial and portal vein plasma in a porcine model.
M and M: In 15 pigs catheters were placed in the portal vein, abdominal aorta for collecting blood samples, and a peripheral vein for infusion of tracer. Blood samples were taken from the aorta and the portal vein every 10 min. 5 times during fasting and 7 times after ingestion of a meal in order to see if the alterations in the hepatic haemodynamics would have any impact on the metabolism of Tc-MBF in the intestines.
Results: The mean difference between the arterial and portal concentration of Tc-MBF expressed in percentage of the arterial concentration is 0.21 % (95% c.i.: -0.12 to 0.54%) and no significant inference with time ($p = 0.48$).
Discussion: No net metabolism of Tc-MBF in the intestines was found. The content in arterial and portal vein plasma did not differ and most importantly the ingestion of a standard meal did not change this. An arterial sample can be used to calculate the HBF. This is assumed to be correct for humans too, although this requires further studies of the kinetics of Tc-MBF in man.

P18.03 Asger Andersen

EFFECTS OF PHOSPHODIESTERASE-5 INHIBITION BY SILDENAFIL IN THE PRESSURE OVERLOADED RIGHT HEART

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Background: Sustained pressure overload of the right ventricle (RV) causes RV hypertrophy and failure. Cyclic-GMP has previously been shown to modulate left ventricular hypertrophy. Aim: To evaluate the effects of sildenafil, a

phosphodiesterase-5 (PDE5) inhibitor elevating c-GMP, on myocardial hypertrophy and function in rats with RV hypertrophy.
Methods: Rats were pulmonary trunk banded (PTB) and randomized to receive sildenafil (SIL) or vehicle (VEC) for three (n = 14) and nine weeks (n=18). In addition, rats with established RV hypertrophy were randomized to SIL or VEC (n=17) three weeks after PTB. Right ventricular function was evaluated by echocardiography and RV hypertrophy by histology and RV weight. Results: Sildenafil failed to inhibit the development of RV hypertrophy when given for both 3 and 9 weeks. On the contrary, sildenafil increased RV hypertrophy after 3 weeks (RV/bodyweight: SIL 0.099 ± 0.016 vs. VEC 0.081 ± 0.011; p b 0.05) and total heart weight after 9 weeks (SIL 1.05 ±
0.10 vs. VEC 0.93±0.08 g; pb0.05). Sildenafil also failed to reverse established RV hypertrophy, but significantly improved RV myocardial function as measured by Tricuspid Annular Plane Systolic Excursion (TAPSE: SIL 1.85±0.027 vs. VEC 1.39±0.037 mm; pb0.05). Conclusion: PDE5 inhibition by sildenafil failed to prevent or reverse RV hypertrophy in rats operated by pulmonary trunk banding. It actually increased RV hypertrophy and improved RV contractile function when given to rats with established RV hypertrophy.

P18.04 Thomas Andersen Rix

FISH, MARINE N-3 POLYUNSATURATED FATTY ACIDS, AND THE DEVELOPMENT OF ATRIAL FIBRILLATION

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Some studies have shown a beneficial effect of fish intake with respect to the development of atrial fibrillation, but reports from different studies are inconsistent. The cohort Diet, Cancer, and Health included 57.055 Danish citizens aged 50 to 64 years enrolled between 1993 and 1997. During follow-up a total of 3425 incident cases of atrial fibrillation have been recorded in the National Patient Registry. The diagnosis will be validated in a random sample of 300 patients. There is evidence of a beneficial effect of marine n-3 polyunsaturated fatty acids (PUFA) on malignant ventricular arrhythmias. The objective of the present project is to investigate the possible association between fish intake, intake of total marine n-3 PUFA and the individual marine n-3 PUFA, eicosapentanoic acid, docosapentanoic acid, and docosahexanoic acid separately, in relation to development of atrial fibrillation. In addition, adipose tissue samples from baseline will be analysed for the content of marine n-3 PUFA as a long term (objective) measure of the intake of fish and n-3 PUFA. Adipose tissue samples have not been collected in other large epidemiological studies and with more than 3400 cases of atrial fibrillation, the study is expected to contribute valuable information on fish consumption, intake of n-3 PUFA and the risk of development of atrial fibrillation.

P18.05 Charlotte Strandhave

HAPTOGLOBIN PHENOTYPE IS ASSOCIATED WITH ELEVATED LEVELS OF HIGH SENSITIVITY CRP AND INTERLEUKIN-6 IN PATIENTS WITH STAGE 3-5 CHRONIC KIDNEY DISEASE

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Introduction: Three major phenotypes for the haptoglobin (Hp) gene have been identified: Hp 1-1, Hp 2-2 and Hp 2-1. Due to lower phenotype-dependent antioxidant capacity, Hp 2-2 acts as a weaker innate antioxidant. High sensitivity CRP (hsCRP) and Interleukin-6 (IL-6) are markers of low-grade inflammation and have been implicated as independent predictors of cardiovascular mortality among chronic kidney disease (CKD) patients.
Aim: To examine whether Hp phenotyping in patients with CKD could identify patients with a pro-inflammatory profile with high levels of hsCRP and IL-6.
Methods: Patients (n = 64) with stage 3-5 CKD were included from our outpatient clinic. The Hp phenotype was determined using a high-performance liquid chromatography, HsCRP using an immunoturbidimetric assay and Il-6 using

Luminex multiplex liquid array.
Results: The CKD patients were divided in two groups according to haptoglobin phenotypes: Hp 1-1 and 2-1 (n=45) and Hp 2-2 (n=19). The median hsCRP was 5.9 mg/L CI 95% (3.4;10.2) among Hp2-2 patients compared to 2.6 mg/L CI95%(1.9;3.5) in Hp1-1 and Hp 1-2 patients ($p < 0.01$). The median IL-6 was 5.8 pg/mL CI95%(4.2;8.1) in the Hp 2-2 patients compared to 4.2 pg/mL CI95%(3.5;5.2) in the group with Hp1-1 and 2-1, showing a non-significant trend ($p=0.08$).
Conclusion: Haptoglobin phenotyping in patients with CKD revealed that Hp 2-2 patients had significantly higher levels of hsCRP compared to Hp 1-1 and Hp 2-1 patients. Also, a trend towards higher levels of IL-6 was seen. Thus, this phenotype may identify a group of CKD patients with a pro-inflammatory profile potentially predicting a higher risk of cardiovascular disease and mortality.

P18.06 Rebekka Jensen

HUMAN DIABETICS RELEASE A CARDIOPROTECTIVE FACTOR.
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Introduction: Cardioprotective mediators released by remote ischemic preconditioning (rIPC) are dialyzable and cross-species transferable from humans to animal hearts. Diabetics are known to have a higher threshold for cardioprotection. It is unknown whether the underlying mechanism is impaired release of a mediating cardioprotective factor or a reduced tissue sensibility.
Objective: To investigate whether human diabetics can release a mediating cardioprotective factor.
Methods: Blood samples were drawn from 10 diabetic and 9 non-diabetic subjects before and after two intensities of rIPC stimuli. After dialyzing blood samples against Krebs-Henseleit buffer, the cardioprotective effect of the dialysate was tested on New Zealand White rabbit hearts mounted in a Langendorff-model subjected to 30 minutes stabilization, 25 minutes perfusion with either control or rIPC dialysates, 5 minutes wash-out perfusion, 30 minutes global no-flow ischemia and 120 minutes reperfusion. Hemodynamics were recorded and infarct size was determined by triphenyltetrazoliumchloride staining.
Results: In healthy subjects rIPC dialysate after both intensities of rIPC stimulus reduced infarct size and improved left ventricular develop pressure recovery. In diabetic subjects the rIPC1 stimulus resulted in induction of cardioprotection, whereas the intensified rIPC2 stimulus did not yield cardioprotective effect. There was no difference in infarct size between diabetic and non-diabetic control groups.
Conclusion: Plasma from human diabetics exposed to rIPC mediates cardioprotection in animal hearts. This suggests preserved release of rIPC mediating factor in human diabetics.

P18.07 Peter Juhl-Olsen

HYPOXIC CARDIAC ARREST RESEMBLES ECHOCARDIOGRAPHIC INDICES OF PULMONARY EMBOLISM IN A PORCINE MODEL
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Introduction: Acute pulmonary embolism (PE) is a common cause of hemodynamic insufficiency and echocardiographically characterized by acute dilatation of the right ventricle (RV) and change in left ventricular (LV) shape and filling. These findings will, in clinical settings, prompt immediate intervention. This study's aim was to evaluate the echocardiographic signs of prolonged hypoxia.
Methods: 16 female pigs were enrolled. Hypoxia was induced by expiratory apnoea. 2 dimensional echocardiography was performed continually and loops were analysed at the time of respiratory cessation (RC) (own control) and at the time of maximal septal impression of the LV.
The following measurements were performed at end systole and at end diastole: 1) short axis diameter of the LV, 2) short axis diameter of the LV perpendicular to 1), 3) maximal short axis diameter of the RV and 4) area of LV. The ratio between 2) and 1) is the eccentricity index (EI).
Results: RC facilitates enlargement of the RV and D-shaping of the LV in both

systole and diastole as expressed by the EI. LV area was reduced (all p<0,05).
Discussion: This porcine study shows that respiratory apnoea induces echocardiographic signs of RV pressure overload. Furthermore, the area of the LV diminishes which may be explained by reduced preload to the LV and impaired compliance due to impression of the interventricular septum. All changes mirror those of PE. As this study was performed in pigs, results are not readily interpretable in a human context, however, the obvious implications for acute diagnostics merit further attention to this subject.
Conclusion: In a porcine model, respiratory apnoea induced echocardiographic signs of PE.

P18.08 June Anita Ejlersen

IMPACT OF ULTRASOUND MICRO BUPPLE CONTRAST ON 2D-STRAIN ECHOCARDIOGRAPHY

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2Dstrain (EchoPac, GE) is based on speckle tracking in the echocardiographic grey tone images. The method allows semiautomatic quantification of myocardial deformation (strain). Ultrasound micro bubble contrast agents alter the speckle pattern. Only one study focused on the influence of contrast on strain (VVI, Siemens). The purpose of this study was to evaluate if 2Dstrain is affected by contrast.
Materials and methods: 20 patients with chest pain scheduled for echocardiography (Vivid 7) were included. Before, during, 3 and 7 minutes after contrast infusion (Sonovue) three standard apical loops (APLAX, 4CH and 2CH) were obtained for off-line analysis. Peak systolic longitudinal strain (S) and strain rate (SR) values were compared with paired t-tests. Reproducibility was assessed with the Bland Altman method and expressed as coefficient of repeatability (COR) which represents the 95% CI.
Preliminary results (9 patients): No-one had structural heart disease. All loops were analysed twice and the mean values used for paired t-test analysis. 1296 myocardial segments (78%) could be tracked by the 2Dstrain software. 568 segments (44%) were tracked in all 8 analysis and were used in the tests. Tracking was insignificantly poorer with contrast. No significant differences were found between readings at baseline, during or after contrast for S or SR. The reproducibility of S and SR were significantly poorer during and 3 minutes after, but not 7 minutes after contrast. Results from all 20 patients are presented in the poster.
Conclusion: Strain and strain rate are not influenced by contrast infusion, but the reproducibility of both is compromised up to 7 minutes after the infusion.

P18.09 Lau Brix

INCREASED TEMPORAL RESOLUTION IN CARDIAC MR IMAGING

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Background: Vendors of MRI scanners offer 'real-time imaging' protocols in which 4-5 frames are acquired and presented to the user each second. The purpose of the project was to implement a system that could increase this frame rate. Methods: A Philips Achieva 1.5T MRI system was programmed to acquire radial k-space profiles with a constant azimuthal profile spacing of 111.246° (the Golden Ratio). A time-resolved 2D balanced CINE sequence was applied to a healthy volunteer using a 5 channel cardiac coil. Radial k-space profiles were reconstructed by k-t SENSE using the parallel processing facilities of an Nvidia GTX 280 graphics card implemented with the CUDA programming language. Thereby, the images were also reconstructed and displayed in real time. For comparison the same MRI sequence

was applied using a standard cartesian read-out of k-space profiles. The quality of the radial images and the cartesian images was compared by visual evaluation by an experienced radiologist to ensure comparability of the two acquisition methods. Results: The standard Cartesian data acquisition yielded a frame rate of 3.9 frames per second (255 ms/frame) while the non-cartesian data acquisition yielded a frame rate of 8.6 frames per second (116 ms/frame) which gives an increase of 221% in frame rate. Conclusion: Real-time acquisition and reconstruction using radial k-space read-out based on the Golden Ratio increase the temporal resolution in cardiac imaging without compromising image quality in a healthy volunteer. This study is a step toward using MRI for imaging of moving objects and hereby overcoming some of the inherent problems with MRI being a time-consuming imaging modality.

P18.10 Martin Bødtker Mortensen

IN-VIVO CELLULARIZATION OF PCL SCAFFOLDS IN JUVENILE PIG AORTA: A STEP TOWARDS CREATING PCL VASCULAR PROSTHESES

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Background: Vascular disease is a major cause of morbidity and mortality in the western society. Because of the current lack of satisfactory small-diameter vascular grafts, there has been a rising interest in the creation of tissue engineered polymer substitutes for small-diameter revascularization. In this study we aimed to investigate cell growth, thrombogenecity and inflammation in polycaprolactone polymer scaffolds when implanted in porcine systemic circulation.
Material & Methods: Two different polymer scaffolds were designed. A singlelaminar and a trilaminar PCL scaffold, the last one containing layers of collagen, elastin and hyaluronic acid. The PCL scaffolds were implanted in the infrarenal part of abdominal aorta of 12 pigs for 4 weeks (n=6) and 8 weeks (n=6).
Results: All scaffolds were successfully implanted into the abdominal aorta. Gross anatomy examinations revealed various degree of tissue overgrow without thrombosis after 4 and 8 weeks. SEM evaluation confirmed the absence of platelet adhesion. Histological examination revealed fibrous sheath formation in various degrees in all explanted scaffolds. The inflammatory response towards the PCL scaffolds was limited except for two cases. Fibroblasts were observed growing inside the trilaminar scaffolds and the formation of neoangiogenesis could be seen in all explanted specimens.
Conclusion: Biodegradable PCL scaffolds demonstrate cell ingrowth, limited inflammatory response and the absence of thrombosis after 8 weeks. PCL polymer could therefore be considered a candidate for future vascular graft material with the addition of surface functionalization to facilitate in vivo cellularization.

P19.01 Line Brøndum

STIMULATION OF THE IMMUNE SYSTEM AND INHIBITION OF ANGIOGENESIS IN PATIENTS WITH RENAL CELL CARCINOMA: A RANDOMIZED PHASE II STUDY.

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Background: Interleukin-2 based immunotherapy is the only potentially curative modality of treatment for metastatic renal cell carcinoma (mRCC). However, only a minority of patients benefit from the treatment.
In this randomized, prospective study we will test the combination of immune stimulation and angiogenetic inhibition.
This project seeks to identify factors, which can identify patients that will benefit from the treatment.
In addition, we aim at obtaining a detailed knowledge on the biological basis of anti-cancer immune response and hereby improve the treatment of mRCC.
Materials and methods: We aim at randomizing 118 patients with mRCC. Treatment will consist of either immunotherapy alone or in combination with Bevacizumab (a

recombinant humanized monoclonal antibody targeting vascular endothelial growth factor). Translational studies will be performed on prospectively collected tissue biopsies and blood samples. The biopsies will be evaluated in regards to vasculature density, immune cell infiltration and genetic markers (selected biopsies). The blood samples will be evaluated using flowcytometry to determine the amount and combination of the circulating effector cells of the immune system. Biological assays will be correlated with dynamic imaging evaluating both tumor response and perfusion.
Results: So far 21 patients have been included. Up till now twelve baseline biopsies and eleven on-treatment biopsies have been collected. Blood samples have been obtained from all patients.
Conclusion: The study is ongoing. The perspectives are to contribute to the understanding of cellular, angiogenetic and immunologic mechanisms in mRCC and thereby improve the future treatment.

P19.02 Peter Sandegaard Skyt

THE THERMAL DEPENDENCE OF PRESAGE DOSE RESPONSE: EFFECT OF IRRADIATION AND STORAGE TEMPERATURES

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Along with the development of complex radiotherapy (RT) methods a need for three dimensional dosimetry has risen. This has lead to the development of dosimeters like the commercial available solid-state PRESAGE™ material. Due to radiation-induced chemical reactions the dose response of this dosimeter is likely to by thermally activated. In this study we have therefore investigated the temperature dependence of the PRESAGE™ dosimeter dose response, with respect to both irradiation as well as storage. The results of these measurements show a significant exponential temperature dependence on dose response both during irradiation and storage. Fit to Arrhenius equations revealed activation energies for the two series of data of respectively 1.4±0.2 eV and 1.7±0.2 eV. These results show that temperature stabilization is an important factor for correct dose readout and could potentially set a limit of the precision of this dosimeter when implemented into clinical use.

P19.03 Lotte Andreasen

THE PATHOGENIC FUNCTION OF MUTATIONS IN NLRP7 IN DIPLOID HYDATIDIFORM MOLES WITH BIPARENTAL GENOME

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Hydatidiform mole (HM) is a rare kind of human pregnancy characteristic by the absence of embryonic development and hydropic degeneration of chorionic villi. HMs are divided into two types, complete (CHM) and partial (PHM) hydatidiform mole, based on the extent of trophoblast proliferation and the absence or presence of embryonic tissue.
HM tissue most often contain two sets of DNA from the father and either none or one set from the mother. However sometimes the DNA composition can appear normal diploid, with genomic markers form both parents (“diploid biparental HMs”, “DiBiHMs”).
Some HMs are ensued by persistent trophoblastic disease (PTD). In PTD, the trophoblasts can spread to other parts of the body like cancer. The knowledge about the etiology behind HM and the development of PTD is very limited but a defect NLRP7 gene is suspected to be connected to development of HM. Mutations in NLRP7 have been found in women with familial recurrent HM (FRHM) which is often characterized as “DiBiHMs”.
We have screened a cohort of 11 women with “DiBiHMs” for NLRP7 mutations and only two women with DiBiHM have a mutation in the coding region (CDS) of NLRP7. Only in one of these women, the mutated gene is likely to have caused the

HM development. Thus we detect no connection between the presence of NLRP7 mutations and the occurrence of a molar pregnancy with biparental genome contribution in general.
As the only woman with pathogenic mutations in NLRP7 also is the only woman with FRHM in our cohorte, we next suspected NLRP7 mutations to be related to FRHMs rather than to "DiBiHMs". But preliminary results have suggested that this might not be the case.

P19.04 Martin Mørck Mortensen

THE MOLECULAR SIGNATURE OF CLINICAL LOCALIZED PROSTATE CANCER

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Background: The incidence of newly diagnosed prostate cancer (PC) has increased dramatically during the past decades. A distinct feature of PC is the high prevalence of latent cancer. Accurate prognostication is therefore a prerequisite for accurate therapeutics and management of PC because indolent tumours may require no intervention, whereas aggressive tumours lead to patient mortality. It has been shown that genome-wide gene expression profiling has the power to delineate clinically relevant sub-classes of PC's.
Objective: Our objective is to generate and validate prognostic markers for disease outcome in patients with localized prostate cancer.
Project description: Tissue will be collected from PC patients undergoing radical prostatectomy at Skejby hospital. A microdissection will be performed in order to procure pure cancer cells from the tumor specimens. Following, genome wide expression profiling will be done to delineate optimal markers for predicting tumour aggressiveness and disease outcome. Extracted miRNA will be profiled on Taqman LDA-cards containing PCR-probes for all known microRNAs. Promising markers will then be subjected to further analysis on independent test formalin-fixed paraffin embedded (FFPE) samples using immunohistochemisrty or in-situ hybridization. Validation cohorts are evaluated using tissue microarray and consist of a historical, no intervention cohort and a cohort of radical prostatectomized patients.

P19.05 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 a 40-60 % 5 year survival for high grade types. Approximately 200 cases are diagnosed 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. There is a need for larger, population based, detailed STS studies. Aarhus Sarcoma Registry 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 Aarhus Sarcoma Registry and trend in incidence. 2) Study the prognostic role of patient-, tumor- and treatment related 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, of approximately 1300 patients, consists of all STS patients treated at Aarhus Sarcoma Center in 1979-2008. Data sources: Aarhus Sarcoma Registry, Central Personal Registry (CPR), National Patients Registry (LPR), and the Cancer Registry. Data from Aarhus Sarcoma

Registry will be assessed by linking to CPR, LPR and the Cancer Registry. Comorbidity data will be assessed by Charlson Comorbidity Index. Cox-regression analysis with both unadjusted and adjusted Hazard Ratios will be used as well as Kaplan-Meier survival curves.

P19.06 Mette Bak Nielsen

TOTAL PELVIC EXENTERATION FOR PRIMARY ADVANCED AND RECURRENCE OF RECTAL CANCER

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Objective: Evaluation of sixty-six patient undergoing pelvic exenteration due to primary advanced rectal cancer and locally recurrent rectal cancer.
Materials and methods: All patients were registered in a prospective clinical database, evaluated with PET/CT, CT, and MR. There was no evidence of disseminated disease and the patients were discussed at a MDT conference.
Results: Pelvic exenteration was performed in sixty-six patients (30 with locally recurrent rectal cancer and 36 with primary advanced rectal cancer). The median age was 64(range 34-79). Eight women and fifty-eight men. Forty-six patients received a VRAM flap and four patients a gluteal flap. Thirty patients received brachytherapy postoperatively. R0 resection was possible in thirty-four, R1 in twenty-nine, and R2 in 3 patients. Twenty-eight were without any complications. Seventy-seven complications were registered – thirty-six minor and forty major complications. One patient died within thirty days (1.5%). Follow-up was 20.5 months (range 0.7-106.4). Five-year survival for primary advanced rectal cancer was 51.5% and for locally recurrent rectal cancer 18.5 %.
Conclusion: Pelvic exenteration is associated with considerably morbidity, but low mortality. Pelvic exenteration can achieve long-term survival especially for patients with primary advanced rectal cancer. However, pelvic exenteration is also justified for patients with locally recurrent rectal cancer.

P19.07 Anders Christian Larsen

VENOUS THROMBOEMBOLISM IN PATIENTS RECEIVING PREOPERATIVE CHEMOTHERAPHY FOR GASTRIC CANCER

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Background: Preoperative chemotherapy for adenocarcinoma of the stomach may increase survival but it is unknown how this new regime affects risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), collectively known as venous thromboembolism (VTE).
Material and Methods: All patients who had preoperative chemotherapy and scheduled for surgery for gastric cancer at Aalborg Hospital, Aarhus University Hospital, between May 2008 and August 2009 were included. Chemotherapy consisted of intravenous Epirubicin 50 mg/m2 and Oxaliplatin 130 mg/m2 and oral Capecitabine 500 mg/m2 twice daily in 14 days. Patients were scheduled for 3 series of chemotherapy. Screening for VTE before chemotherapy, preoperative after chemotherapy, and postoperative before discharge, included clinical examination, plasma D-dimer, flow-doppler ultrasonography of both legs, and thoracic CT or PET-CT scan modified also to diagnose PE. Patients received low molecular weight heparin (LMWH) per-operatively and until discharge.
Results: A total of 26 patients was included. None had VTE prior to chemotherapy. However, 2 patients (2/26 = 8%; 95%CI: 1% - 25%) had a VTE (1 DVT and 1 PE) after 3 series of chemotherapy but before surgery. Twenty-one (81%) patients completed surgery including the patient with a preoperative DVT. Of these, 1 patient had an asymptomatic VTE (both DVT and PE) before discharge despite

ongoing standard prophylaxis with LMWH. This patient had still no sign of recurrence 6 months postoperatively.
Conclusion: Our study shows VTE may develop during preoperative chemotherapy for gastric cancer. Whether this risk is due to delay before surgery or the chemotherapy per se needs further investigation.

P19.08 Kåre S. Ettrup

UNILATERAL DEEP BRAIN STIMULATION OF THE VENTROMEDIAL HYPOTHALAMUS CAUSE TRANSIENT AGGRESSIVE BEHAVIOR AND SUPPRESSION OF APPETITE, IN THE GOTTINGEN MINIPIG

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Objective: In this study, we assessed the feasibility of low frequency deep brain stimulation (DBS) in the ventromedial hypothalamus (VMH) as a potential treatment for obesity.
Background: Resent evidence suggests that VMH DBS might be a promising new treatment of severe adiposity. However, electrical stimulation of the VMH could also affect a number of closely related neural systems, thereby generating a mixture of adverse effects.
Methods: DBS leads were stereotaxically implanted, unilaterally, into the tuberal VMH of five Göttingen minipigs. The animals were kept under video surveillance throughout the experiment and programming of the pulse generator was performed while monitoring the heart rate.
Results: Low frequency VMH DBS elicited transient attack behavior and increased heart rate in all of the minipigs. Furthermore, continuous DBS lead to stimulation dependent suppression of appetite in three of the animals.
Conclusions: Unilateral low frequency VMH DBS resulted in behavioral changes, which may result from activation of closely related limbic and autonomic networks. Caution and further studies should be requested before this procedure is introduced in humans.

P19.09 Shallu Sharma

PROSPECTIVE DYNAMIC FUNCTIONAL EVALUATIONOF GAIT, BALANCE AND POSTURE FOLLOWING SPINAL RECONSTRUCTIVE SURGERY IN ADULT SCOILIOSIS AND CONTROLS

AUTHORS: Shallu Sharma, Cody E bunger, Ebbe S Hensen , Thomas Andersen

BACKGROUND: Spinal reconstructive surgery is the cornerstone in addressing physical symptoms and the deformity. Limited studies(2001-2008) are available investigating the biomechanics of gait and balance.
OBJECTIVES: To report and compare the pre and post operative (1 year) parameters of posture, balance gait in adult scoliosis and controls. And secondly To report and correlate the radiographic measures of deformity with respect to kinematic parameters from gait and balance assessment.
HYPOTHESIS: Adults with scoliosis will have significant difference in the pre, post operative parameters of posture, balance and gait compared to controls. There will be a positive correlation between radiographic measures of deformity (pre and post op) and kinematic parameters(pre& post op) from gait and balance assessments.
INCLUSION CRITERION: 40 patients with age between 30-70 yrs with diagnosis of degenerative or idiopathic scoliosis .Thoracic and or thoraco-lumbar and or lumbar scoliosis with cobb's angle greater than 20. Able to walk without any assistive aid
VARIABLES: Dependent variables:

1. Static balance and degree of sway on stance.
2. Maneuverability and timing with timed up and go test
3. Kinetic variables: speed, cadence, stance& swing time, and step &stride length.

PROCEDURE: The pre-procedural assement will be done. Patients will be asked to fill up the EQ5D, ODI and SF- 36 DPQ. Subsequent to which they will evaluated for gait and balance at Gait Lab. The dependent variables will be recorded and later used for analysis and comparison.The patients will now be put up for planned surgery by the independent group of surgeons at Aarhus university hospitals .The patients will undergo the same gait ,posture and balance assesment and information retreval from follow up radiographs at 6 month and 12 month follow up.

P20.01 Kathrine Just Andersen

ELECTROPHYSIOLOGICAL RECORDINGS IN SUBTHALAMIC NUCLEUS 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 (SN), which results in an imbalance between the two main pathways of the basal ganglia (BG), i.e. the direct and indirect pathways. Within the BG, the subthalamic nucleus (STN), assumed to play a pivotal role in the pathophysiology of PD, has been shown to be hyperactive in PD patients and in neurotoxin-based animal models. Interestingly, the presence of intracellular aggregated α-synuclein (α-syn) like the one found in Lewy Bodies in DA neurons in the SN 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 rats induces changes in STN firing activity.
Overexpression of α-syn in DA neurons of the SN in rats is induced by unilateral viral injections, which was shown to result in progressive cell loss and pathological accumulation of the protein resembling what is found in PD patients. Extracellular single unit recordings of STN neurons are conducted in anesthetized rats 5 and 12 weeks after viral injection. Both firing rate and firing pattern are analyzed for each recorded neuron and compared to findings in naïve rats.
Preliminary results show a trend for changes in firing pattern to a more bursty firing pattern 5 weeks after viral injection compared to naïve rats. Additional data will be presented. If confirmed, these data would further validate the viral-mediated overexpression of α-syn as a model of BG dysfunction, and strengthen the putative role of α-syn in the pathophysiology of PD.

P20.02 Cristine Betzer

FINDING LIGANDS FOR &ALPHA;-SYNUCLEIN OLIGOMERS

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The natively unfolded protein a-synuclein is the major protein in proteinous inclusions, called Lewy bodies, which is found in patients diagnosed with Parkinson's disease. a-Synuclein has the propensity to aggregate and on the pathway to form mature fibrils, several intermediate structures exist. A currently accepted hypothesis is that the cytotoxic form of a-synuclein is the oligomeric forms. Ligands binding to a-synuclein oligomers, and not or in less degree to the monomeric or fibrillary structure, may be responsible for this cytotoxicity. The oligomer binding ligands are isolated by immunoprecipitation and identified by gel electrophoresis followed by mass spectrophotometric analysis. Several ligands are identified including Parkinson's disease related proteins such as DJ-1.

P20.03 Morten Jønsson

FUNCTIONAL CONNECTIVITY IN DEPRESSION: A MEG STUDY

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Functional imaging using positron emission tomography (PET) and functional

magnetic resonance imaging (fMRI) have revealed increased functional connectivity in the subgenual cingulate, the thalamus, the orbitofrontal cortex, and the precuneus in adults with major depression compared to normal controls (Greicius, 2007). While the subgenual cingulate seems to be a key node in the depressed group network it is absent in the control group network (Greicius, 2007). This is in accordance with results from deep brain stimulation for treatment-resistant depression, where stimulation of subgenual cingulate gyrus lead to sustained remission of 4 of 6 patients (Mayberg, 2005).
With the use of magneto-encephalography (MEG) a group comparison between 20 healthy control and 20 adults with depression was carried out. The groups were matched for age, gender and handedness. Each subject was scanned for 5 minutes with eyes closed. The preliminary approach for analysis is to use Dynamic Imaging of Coherent Sources (DISC) for the beamforming (Gross, 2001) and make a graph theoretical comparison of the regions of interest based on various measures of causality, connectivity and synchronization.
We hypothesize that the paralimbic network is defective with respect to synchronization, power, and causality in depression and that the subgenual cingulate will be a key node in the neural network of the adults with depression. These MEG results are interesting because the much higher temporal resolution of the MEG method allow us to tract the interregional interactions in much greater detail than with fMRI/PET.

P20.04 Zita Dósa

INCREASED TONIC GABA-A RECEPTOR MEDIATED SIGNALING IN DENTATE GYRUS OF SSADH DEFICIENT MICE

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Excessive γ-aminobutyric acid (GABA) during brain development may lead to structural and functional changes in the brain tissue. This is the case in succinic semialdehyde dehydrogenase (SSADH) deficiency, which is an inherited neurometabolic disorder of GABA catabolism. Since SSADH participates in the breakdown of GABA, this condition leads to elevated GABA levels, but also increased γ-hydroxybutyric acid (GHB) in the brain, which also activates GABA receptors. SSADH deficient patients display neuropsychiatric symptoms, ataxia, and epileptic seizures, and SSADH knock-out mice were recently engineered to model the human disorder. The purpose of this study was to determine how the SSADH gene dosage impacts single-neuron physiology, since this might offer insight into how SSADH regulates the extracellular GABA levels in physiological and pathophysiological situations. To investigate the activation of $GABA_A$ receptors in SSADH deficiency, we performed whole-cell patch-clamp recordings in SSADH wild-type, heterozygous, and knock-out mice. Both in dentate gyrus granule cells and interneurons, we found an increase in extrasynaptic $GABA_A$ receptor-mediated tonic current. On the other hand, the frequency and waveform of spontaneous inhibitory postsynaptic currents (sIPSCs) arising from GABAergic activity showed no significant alteration in these cells. Decreases in the SSADH gene dosage led to non-linear increases in $GABA_A$ receptor mediated neurotransmission in these mice. We conclude that SSADH deficiency preferentially leads to increased tonic GABAergic inhibition in the dentate gyrus, which may play a role for the pathophysiological activity in cortical networks.

P20.05 Sanne Kjær Vandborg

IS TREATMENT OUTCOME ASSOCIATED WITH COGNITIVE FUNCTIONS IN OCD?

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Obsessive Compulsive Disorder (OCD) is a debilitating neuropsychiatric disorder

characterised by intrusive, recurrent and distressful thoughts (obsessions) and repetitive behaviours (compulsions). It is well documented that patients with OCD have cognitive dysfunctions, primarily in visuo-spatial memory and executive functions. First choice treatment of OCD is Cognitive Behavioural Therapy (CBT) and Selective Serotonin Reuptake Inhibitors (SSRI). Up to 50% of OCD-patients do not respond optimally to this treatment. A main object of this PhD project is to investigate whether treatment outcome is associated with cognitive functions in OCD. 40 adult patients with OCD will be assessed with neuropsychological tests to estimate cognitive functions and a semi-structured interview to establish treatment outcome pre- and post standard treatment at an outpatient clinic for OCD at Aarhus University Hospital Risskov. A comparison group of 40 healthy controls will be assessed with neuropsychological tests and re-assessed after 20 weeks. If cognitive dysfunctions are associated with poor treatment outcome, future treatments may need to take this aspects into account, either by compensating for or by focusing treatment directly at cognitive dysfunctions.

P20.06 Stephen Austin

METACOGNITION AND SCHIZOPHRENIA: AN INVESTIGATION OF METACOGNITIVE BELIEFS AND PSYCHOPATHOLOGY WITHIN THE OPUS COHORT AT 10 YEAR FOLLOW UP.

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Metacognition has been defined as beliefs and attitudes held about cognition or "cognition about cognition". Studies investigating metacognition within schizophrenia have found those with psychosis often experience elevated levels of metacognitive beliefs compared to healthy controls. Metacognitive beliefs can lie on a continuum and may be implicated in the vulnerability, transition or maintenance of psychotic symptoms. Disturbances in metacognition have also been linked to deficits in executive functioning. Researchers have shown that clinical interventions can modify metacognitive biases and reduce psychological and emotional distress. The OPUS study is a randomized clinical trial with previous multiple points of assessment (baseline, 1yr, 2yr & 5yr) and investigated the effect of standard versus assertive treatment in first episode psychosis. A total of 547 participants included in the original trial (1998-2000) will be invited to participate in the 10 year follow-up. Psychopathology, metacognitive beliefs and cognitive functioning will be systematically evaluated within the OPUS cohort.
Hypotheses
1. The OPUS cohort will show significantly elevated metacognitive beliefs compared to the general population.
2. Metacognitive beliefs will lie on a continuum and vary as a function of type/severity of psychopathology.
3. Deficits in cognitive functioning and elevated metacognitive beliefs will predict distress and psychopathology.
The study will help clarify the relationship between metacognitive beliefs, psychopathlogy and neurocognitive deficits and the results could have implications for clinical interventions that can modify metacognitions and reduce distress.

P20.07 Noomi Gregersen

MARKERS ON CHROMOSOME 19P13 ARE ASSOCIATED WITH PANIC DISORDER

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Intorduction: A genome wide scan conducted on 13 patients with panic disorder

(PD), from the isolated population of the Faroe Islands, showed significant association to markers within chromosome 19p13. The aim of the current study was to replicate these findings in a larger Faroese PD sample and in an outbred Danish sample of patients with PD and control individuals.
Methods: Four of the most significantly associated microsatellite markers from the genome wide scan were genotyped using a standard PCR procedure and the ABI PRISM® 3100 Genetic Analyzer (Applied Biosystems, Fostercity, USA). The Faroese sample consisted of 36 cases and 162 control individuals. The Danish sample consisted of 365 cases and 649 control individuals. All patients were diagnosed with PD according to the ICD-10 Diagnostic Criteria for Research. Allelic association tests (chi-squared) were performed. RUNGC was used to detect differences in haplotype frequencies between cases and controls.
Results: Three of four markers were significantly allelic associated with PD in the Faroese sample (D19S394, P=0.00014; D19S922, P=0.00064; D19S586, P=0.048). The haplotype association analysis showed one significantly associated two-marker haplotype in the Faroese sample (D19S922-D19S586; P=0.01). The two markers (D19S922 and D19S586) analysed in the Danish sample did not show any significant association with PD.
Conclusion: We were able to replicate and therefore confirm association between markers on chromosome 19q13 and PD in the Faroese population. We suggest that chromosome 19p13 harbors susceptibility genes for PD in the Faroese population.

P20.08 Martin Dietz

MISMATCH NEGATIVITY (MMN) AND NEGLECT SYNDROME

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The mismatch negativity (MMN) is a component of the auditory event-related potential observed in electroencephalography (EEG) as a negative inflection at fronto-central scalp locations to a violation of a regular auditory sequence (Näätänen et al 2007). The MMN can be interpreted as an index of how the brain predicts incoming sensory data based on a predictive model of how the data were caused. In this context, the MMN corresposponds to a prediction error signal. As causes in the environment (causes of sensory data) cannot be observed directly, they constitute hidden states that the brain tries to infer based on a probabilistic model of the most likely cause given the sampled sensory data. In the brain this is likely implemented in a Bayesian fashion where 'higher' areas provide priors for 'lower' sensory areas to yield the most likely interpretation of the environment given the sensory data and model (Friston 2005).
We present data from a MMN study in healthy volunteers using a oddball paradigm that combines perception of a simple vowel phoneme (the ‘standard’) with a left/right deviation in its sound location and a deviation in the frequency spectrum of the vowel pronounced by a human voice. The observed MMN is here interpreted as an error signal providing feedback to the ‘higher’ levels of the system to adjust its prediction concerning the environment.
We now propose to use this paradigm in neglect patients with damage to the right hemisphere, where we predict a normal MMN to frequency deviants, but an abnormal MMN to changes in spatial location given the dominance of the right temporo-parietal cortex in the processing of spatial information (Kaiser et al 2000).

P20.09 Line Gebauer Josefsen

MUSICAL EMOTIONS IN PEOPLE WITH AUTISM AND ASPERGER’S SYNDROME

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Background: Music is often described as the language of emotions, and the ability of music to communicate emotional states and create emotions in the listener is often proposed as an argument for why music has sustained such prominence in our life

during the past 100.000 or more years. Accordingly, music is used in a wide variety of situations to enhance, modulate or change the emotional atmosphere. However, not everybody is affected by emotions in the same way. Especially people with Autism Spectrum Disorders (ASDs) are characterized by difficulties in socio-emotional interaction and in identifying and describing their own emotional states. This has lead several music psychologists to suggest that people with ASD are not emotionally affected by music and do not find the same pleasure in music listening as typically developing people (TDs). However, recent research indicates that this is not at all the case. People with ASD seem to have a wide interest in music, show a higher prevalence of absolute pitch, and be able to identify emotions in music as well as TDs. Aim: The present study aim to investigate whether people with ASD experience emotional music in the same way as typically developing people (TDs) and whether they activate the same brain regions as TDs, while listening to emotional music. Methods: We intend to test 30 people with ASD and 30 TD people between 18 and 45 years of age. The participants will be tested on a variety of behavioral tasks related to emotion induction and emotion identification in music, and be fMRI scanned while listening to self-selected and experimenter-selected emotional music. Finally, they will complete a psychological test-battery.

P20.10 Katja Anna Hybel

NEURO AND METACOGNITIVE MARKERS AND PREDICTORS OF TREATMENT RESPONSE IN CHILDHOOD OCD

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Background: Obsessive Compulsive Disorder (OCD) is a debilitating disorder with a frequent occurrence in childhood. There is a growing consensus to view OCD as highly heterogeneous. Neuropsychological and metacognitive aspects has been put forward as core markers but studies pertaining to children and adolescents are scarce. As for treatment there is a need to identify key factors associated with response respectively non- or partial response to treatment.

Objective: The main study objectives are to pinpoint potential neuro- and metacognitive markers of childhood OCD and investigate these markers in relation to treatment response as potential moderators of change

Method: Population: 50 children 7-17 years old with OCD; 50 normally developing children matched for sex, age and length of parent education; 50 children 7-17 years old with other anxiety disorders

Design: Children are tested prior to and immediately after a manualized CBT intervention. The intervention is followed up by evaluation of symptom severity on the CY-BOCS IQ and Neuropsycological test battery: RIAS short IQ screening, CANTAB selection on speed, working memory, inhibition, set shifting, planning and decision making tasks; Emotional Dot Probe paradigme including positive, neutral and disorder specific visual stimuli

Physiological measure: Pulse rate as indicator of anxiety level during testing

Parent and self report measures of executive functions: BRIEF-SR 11-18, BRIEF 5-18

Parent and self report measures of metacognition: Self-report regarding expectation of own performance and anxiety level during testing, Metacognitions Questionnaire (MCQ-C-DK); Obsessive Beliefs Questionnaire (OBQ-44CV-DK)

The project is ongoing

P21.01 Christina Jespersen

P21.02 Franz-Joachim Kaiser

INITIAL RECOMBINATION IN THE TRACK OF HEAVY CHARGED PARTICLES

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Background: Ionization chambers (ICs) are widely used for dosimetry. Within the IC, electron hole pairs are generated by the energy deposition originating from incoming radiation. High-LET particles create a high charge carrier density in the particle track core. As a consequence an increased initial recombination takes place, besides of the general recombination.

A theory for a sub-type of initial recombination ("columnar" recombination) is the Jaffe theory. Here, a diffusion and recombination PDE is solved by applying several simplifications and approximations such as a Gaussian shaped track. These simplifications are leading to discrepancies between theory and experiments.

Material and Methods: We solved the fundamental PDE presented by Jaffe numerically, taking into account more realistic models of the initial charge carrier distribution developed by track structure theory for air filled and liqud filled a plane parallel ICs

Results: We compare the experimental results of the collection efficiency of air and liquid filled ICs to both the Jaffe theory and to our numerical solution of the PDE using more realistic and Jaffes initial charge carrier distribution. Applying Jaffe's theory the measured collection efficiency resulted in values comparable to the literature for air filled ICs. The results show a good agreement between measurements and our numerical solution using more realistic charge carrier distributions

Conclusion: Our numerical solution assuming a Gaussian track shape is well described by Jaffe's theory. Additionally, the results show that that the calculated response depends on the core radius of the assumed radial dose distribution as well as in Jaffe's theory.

P21.03 Lasse Sommer Kristensen

INCREASED SENSITIVITY OF *KRAS* MUTATION DETECTION BY HIGH-RESOLUTION MELTING ANALYSIS OF COLD-PCR PRODUCTS

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Considerable effort has been invested in the development of sophisticated technologies enabling detection of clinically significant low-level tumor specific KRAS mutations. Coamplification at lower denaturation temperature-PCR (COLD-PCR) is a new form of PCR that selectively amplifies mutation-containing templates based on the lower melting temperature of mutant homoduplexes versus wild type homoduplexes. We have developed a fast COLD-PCR and High-Resolution Melting (HRM) protocol to increase the sensitivity of KRAS mutation detection. The clinical applicability of COLD-PCR for KRAS mutation detection was assessed by analyzing 61 colorectal cancer specimens, for which KRAS mutation status has been evaluated by the FDA approved TheraScreen® KRAS mutation kit. The sensitivity was increased by 5 to 100 fold for melting temperature decreasing mutations when using COLD-PCR as compared to standard PCR. Mutations, undetectable by the TheraScreen® kit in clinical samples, were detected by COLD-PCR followed by HRM and verified by sequencing. Finally, we have observed a previously undescribed low prevalence synonymous mutation (KRAS c.39C>T, codon 13) in colorectal cancer specimens and in the peripheral blood from an unaffected individual. In conclusion, COLD-PCR combined with HRM is a simple way of increasing the sensitivity of KRAS mutation detection without adding to the complexity and cost of the experiments.

P21.04 Stine Elleberg Petersen

MORBIDITY IN PATIENTS WITH PROSTATE CANCER TREATED WITH RADIATION THERAPY

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Background: The rectum is a highly critical organ in prostatacancer patients treated with radiotherapy. However, the structural and functional changes caused by irradiation are poorly understood. The present study will focus on subjective, physiological and structural changes following RT.
Materials and methods: Project 1: A cross-sectional study of radiation induced morbidity in prostatecancer patients treated with radiotherapy based on questionnaires. Primary endpoints are the prevalence of bowel symptoms focusing on leakage, frequency and urgency.
Project 2: Fifty patients will be selected from project 1: 25 with moderate/severe toxicity scores and 25 without any reported toxicity. They will be asked to participate in ano-rectal examinations in which functional, structural and morphological changes will be investigated. Primary endpoints are changes in ano-physiology measures.
Project 3: Fifty patients treated with RT for PC will be followed in a longitudinal study on patient reported side effects and by ano-rectal physiology measures as defined in project 2.
Results: The study is ongoing.
Conclusion: The study is ongoing. With modern radiation techniques it will be possible to intensify the radiation dose to the prostate. Increased dose also increases the risk of radiation induced side effects. The scope of the study is to elucidate these side effects.

P21.05 Lotte Abildgaard

MINIMAL RESIDUAL DISEASE MONITORING IN CHILDHOOD ACUTE MYELOID LEUKAEMIA

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Background: The diagnostic evaluation and follow-up analyses of children with leukaemia have undergone major improvements. Molecular-based techniques are more sensitive than standard techniques as morphology and immunophenotyping and have established the concept of molecular complete remission and minimal residual disease (MRD). These new techniques render possible a much more individualised treatment based on risk stratification using MRD monitoring on specific time points.
A sizeable part of children with AML lack balanced translocations amenable to MRD detection.While not disease specific like fusion transcripts, genes with abnormally high expression in malignant cells compared to normal controls might be candidate MRD markers.Several genes are found to be over-expressed in childhood AML but the knowledge on their normal expression in children and thereby their applicability as MRD markers is sparse.
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 chemotherapy on these levels will be examined.
RNA is purified from mononuclear cells isolated from bone-marrow and blood samples and reverse transcribed before being analysed with RQ-PCR. For quantification purposes, serial dilutions of cDNA from reference cell lines are used to generate standard curves.The MRD markers are analysed in triplicate along with two internal control genes Abelson (ABL) and β-2-microglobulin (β2M). Gene levels are determined as ABL normalised levels.

P21.06 Maria Thor

RECTUM MOTION AND MORBIDITY PREDICTION: IMPROVING CORRELATION BETWEEN LATE MORBIDITY AND DVH PARAMETERS THROUGH USE OF RECTUM PLANNING ORGAN AT RISK VOLUMES

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Aim: In this study late rectal morbidity is investigated in relation to the internal motion of the rectum by applying the 'Planning organ at Risk Volume' (PRV) concept.
Materials and methods: Late rectal morbidity was analysed in 242 prostate cancer patients treated to 70 Gy with conformal RT to either the prostate, the prostate and seminal vesicles or the whole pelvis (initial 50 Gy only). Late rectal morbidity was classified as late gastro-intestinal (GI) toxicity. Dose-volume histograms (DVHs) were derived for the rectum OR and the OR expanded with six different margins (narrow/intermediate/wide in anterior direction or in both anterior and posterior direction). The difference in rectum dose-volume parameters between patients with Grade 0–1 vs. Grade 2 or higher morbidity was investigated by logistic regression and permutation tests.
Results: Late grade 2 or higher morbidity was observed in 25 of 242 (10%) patients. The logistic regression analysis and the permutation tests reached significance ($p \leq 0.05$) for only one dose level of the rectum OR (40 Gy). For the PRVs, several dose levels were found to be significant (p-value range: 0.01-0.046), most pronounced for the PRV with narrow margins of 6 mm anterior and 5 mm posterior with five intermediate (38–42 Gy) and ten high (62–71 Gy) dose levels.
Conclusions: The statistical methods displayed consistently a small though significant difference in DVH parameters between patients with vs. without Grade 2 or higher late rectal morbidity for intermediate and high dose levels. The difference became most evident when using a PRV with narrow margins.

P21.07 Hanna Rahbek Mortensen

REDUCTION OF DYSPHAGIA-RELATED MORBIDITY IN HEAD AND NECK RADIOTHERAPY

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There are 1000 new cases of head and neck cancer (HNC) in Denmark per year, primarily treated with radiotherapy and/or surgery. The results of radiotherapy for HNC has substantially improved, but a significant proportion of the patients still have major chronic side effects, of which dysphagia and swallowing problems are the most troublesome, leading to reduced quality of life, malnutrition and aspiration pneumonia. Studies have shown that both subjective and objective swallowing problems are frequent and severe and correlates with dose and volume parameters of the upper aero-digestive tract.
The aim is to identify prognostic factors for dysphagia, develop a new objective assay for measuring swallowing dysfunction, and to test interventional strategies to reduce dysphagia in the setting of intensity modulated radiotherapy (IMRT) and concomitant chemoradiotherapy.
Study 1: Clinical and radiobiological factors important for dysphagia in the DAHANCA 6&7 cohort with 1485 patients.
Study 2: Evaluation of cine-MRI as a potential tool for assessing damage to swallowing structures after IMRT including 70 patients.
Study 3: The clinical importance of long-term dysphagia in patients after parotid-sparing IMRT in a cohort of 300 patients treated in Aarhus between 2006-2008.
Study 4: Prevention of dysphagia through systematic swallowing exercises – a randomized prospective study of 50 patients.
Study 5: A mucosal protecting agent to reduce acute dysphagia and aspiration – a prospective clinical trial.

P21.08 Patricia Switten Nielsen

SIMPLE IMMUNOHISTOCHEMICAL DOUBLE STAINS WITH STRONG DIAGNOSTIC CAPABILITIES IN MELANOCYTIC LESIONS

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Distinction between benign and malignant melanocytic lesions may be difficult by today's methods and even skilled dermatopathologists may fail to diagnose melanoma on a skin biopsy. Improved diagnostic tools are thus highly needed. We have studied discriminative abilities of immunohistochemical (IHC) double stains

using the IHC markers Ki67 combined with MART1, and HMB45 combined with MITF. Paraffin-embedded tissue sections from 50 melanomas and 78 benign nevi were stained using a simple IHC double staining technique. Both semi-quantitative estimates of immunopositivity in the deepest one-third of the lesions and full-scale quantitative measurements of Ki67 and HMB45 indices were performed, and scores for melanomas and nevi were compared. The differences between melanomas and nevi were significant ($P<0.0001$) using either analysis or stain. The misclassification rates for melanomas and nevi were generally lower for Ki67/MART1 stains than for HMB45/MITF stains. In semi-quantitative Ki67/MART1 analyses the misclassification rates were 6% (2%-17%) for melanomas and 12% (6%-21%) for nevi. In full-scale quantitative analyses the corresponding rates were 4% (1%-14%) and 8% (4%-16%), respectively, and by combining the Ki67 and HMB45 indices the misclassification rates were 0% (0%-7%) for melanomas and 13% (7%-22%) for nevi. We conclude that both semi- and full-scale quantitative analyses of Ki67/MART1 stains are valuable diagnostic tools to distinguish melanomas and nevi that potentially may reduce the misinterpretations of melanomas. The HMB45/MITF stains may serve as adjuncts to predict malignancy and the diagnostic potential of combining HMB45 and Ki67 indices are promising.

P21.09 Esben Schjødt Worm

SETUP ERRORS IN STEREOTACTIC BODY RADIATION THERAPY: RELATION TO TREATMENT TIME, TUMOR POSITION, AND BODY MASS INDEX

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Introduction
Localisation errors in cone-beam CT (CBCT) guided stereotactic body radiation therapy (SBRT) were compared to positioning using the coordinates of a stereotactic body frame (SBF) alone. Possible correlations to factors such as patient body mass index (BMI), treatment delivery time, and distance between tumor and spinal cord were explored to determine whether they influenced on the benefit of image-guidance.
Methods
A total of 34 patients received SBRT (3 fractions) for tumors in the liver (n=15) or the lung (n=19). Positioning was obtained with a SBF. Pre- and post-treatment CBCT scans were registered with the bony anatomy of the planning CT to find inter- and intrafractional patient positioning errors (PPE). For lung tumor patients, matching was also performed on the tumors to find the tumor positioning errors (TPE) and baseline shifts relative to bony anatomy.
Results
The mean inter- and intrafractional 3D vector PPE was 4.5 ± 2.7 mm (average ± SD) and 1.5 ± 0.6 mm, respectively. For lung tumors, the interfractional misalignment was 5.6 ± 1.8 mm. The baseline shift was 3.9 ± 2.0 mm. Intrafractional TPE and baseline shifts were 2.1 ± 0.7 mm and 1.9 ± 0.6 mm, respectively. Statistical significant correlation was found between interfraction PPE and BMI. The magnitude of interfractional baseline shift showed significant correlation with the distance between the tumor and the spinal cord.
Conclusion
Image-guidance targeting the tumor itself reduced setup errors considerably, especially for obese patients. Protection of the spinal cord was facilitated by the correlation between the tumor position relative to the spinal cord and the magnitude of baseline shift.

P21.10 Sara Thörnqvist

SENSITIVITY TO TARGET MOTION IN SIMULATED INTEGRATED BOOST TREATMENTS OF PROSTATE AND LYMPH NODES FOR DIFFERENT SET-UP METHODS AND TREATMENT DELIVERY TECHNIQUES

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Aim: The aim is to evaluate the sensitivity towards target motion for two image guided radiotherapy (RT) set-up methods in patients (pts) with simultaneous irradiation of pelvic lymph nodes (LN) and prostate using intensity modulated RT (IMRT) or volumetric modulated arc therapy (VMAT).
Material and Methods: Eight previously treated pts with 8-10 CT-scans evenly distributed throughout the treatment were studied. An oncologist delineated bladder, rectum, LN and prostate in all CT-scans. Treatment plans for IMRT and VMAT were optimised on the plan-CT geometry. All CT-scans were rigidly registered to the plan-CT based on intensities (anatomy) and intra-prostatic fiducials.
Results: For prostate 5 pts received on average less than 95% of the prescribed dose (D95%) using set-up on fiducials for both IMRT and VMAT. The underdosage increased to 6 pts with set-up based on anatomy. For the LN-target no pts received a mean D95% of less than the planned D95% when positioned on anatomy. Set-up on fiducials resulted in 1 and 2 pts having a mean D95% of less than the planned D95% for IMRT and VMAT, respectively. The impact of set-up method on the summed generalized uniform dose (gEUD) to bladder and rectum was larger for IMRT than VMAT. Using IMRT the summed gEUD to rectum was higher in 5 pts and using VMAT 4 pts, with set-up on fiducials as compared to anatomy. The summed gEUD to bladder was higher when positioned on fiducials for 6 and 4 pts with IMRT and VMAT, respectively.
Conclusions: Positioning based on fiducials gave the best trade-off between coverage of the prostate and LN-target. However, this choice of set-up combined with IMRT lead to a higher summed gEUD to both bladder and rectum.

P22.01 Mette Konow Bøgebjerg Dolberg

MAGNESIUM IN ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE
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Aim: To assess the effect of a daily oral magnesium (Mg) supplement in the treatment of asthma and chronic obstructive pulmonary disease (COPD).
Background: Mg inhibits contraction and relaxes smooth muscles in airways owing to blocking of calcium-ion-flux across the cell membrane. Mg deficiency increases the intracellular concentration of calcium and the secretion of histamine and inflammatory cytokines. A high dietary intake of Mg seems to indicate a better lung function, reduced risk of airway hyperreactivity and wheezing. Chronic asthmatics with low Mg are more often hospitalized than chronic asthmatics with normal Mg. The use of Mg is well-established in the treatment of acute asthma attacks. Hence, it seems plausible that Mg may have a beneficial effect on chronic asthma and COPD.
Materials & methods: The study falls into five parts: 1) A review of the role of Mg in the human airway; 2) A pharmacokinetic study of oral and intravenous Mg supplementation; 3) Study of the effect of daily Mg supplementation in steroid-resistant, severe asthmatics 4) Study of the effect of daily Mg supplementation upon bronchial hyperreactivity in asthmatics; 5) Study of the effect of daily Mg supplementation in patients with moderate to severe COPD. Parts 3) to 5) are double-blinded and the participants are randomized to either 12 weeks with a daily magnesium-supplementation or placebo and cross-over after a 12-week wash-out period.
Results & conclusion: The study was commenced recently. Hence, data remain to be collected and analyzed.

P22.02 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-initiation and metastasis has been proposed. Which 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: Study1 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. Study2 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. Study3 Drug delivery system for treatment of breast cancer bone metastasis in vivo. study.

P22.03 Maja Ludvigsen OUTCOME-RELATED PROTEIN EXPRESSION PROFILE IN PATIENTS WITH CLASSICAL HODGKIN LYMPHOMA.

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Background: The treatment results in patients with relapsed/refractory classical Hodgkin lymphoma (cHL) are often still unfavorable. Thus, there is a need to identify prognostic markers that can identify cHL patients, who may benefit from an intensified upfront approach as compared to conventional therapy. In order to better characterize tumor features of potential prognostic significance, we investigated protein expression profiles of cHL tumor extracts.
Aim: To compare protein expression patterns in tumors of cHL patients with favorable and unfavourable outcome, respectively following first treatment.
Methods: Clinical data and frozen tissue from 14 patients with advanced stage cHL were identified; seven had chemosensitive disease and seven displayed relapsed/refractory disease. Tissues were subjected to high-resolution two-dimensional gel electrophoresis. Individual protein spots were visualised and the expression profile in the two groups were compared by computer analysis. Differentially expressed proteins were identified by liquid chromatography- tandem mass spectrometry and further studied by immunological methods.
Results: This study confirms the feasibility of using archival frozen tissues from cHL patients for proteomic analysis. The protein expression profiles of the two clinical groups analyzed showed significant and distinct differences. Specific protein expression was further verified by western blotting.
Conclusions: Significant differences between samples from patients experiencing favorable versus unfavorable treatment outcome were found. Further functional studies of these proteins may provide novel insight into the pathophysiology of the disease.

P22.04 Halldór Bjarki Einarsson OSTEOCLASTS IN BONE TISSUE ENGINEERED ALTERNATIVE

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Introduction: Recently, researchers have suggested polycaprolactone (PCL) as a promising template of choice for cartilage and bone tissue repairing. Immune cells recruitment to the site of implantation, should however be considered a biological process of interest. We hypothesized, that osteoclast (OC) pre-cursor cells can differentiate to OC and attach to PCL. We suggested that the differentiation is affected by the immune system.
Materials and methods: Peripheral blood mononuclear cells (PBMNC) were isolated from buffy coats, plated at fusiogenic density and cultivated in α-medium supplemented with OC inductive cytokines. Monocytes and T-cells were isolated using Dynabeads Untouched Human Monocyte and T-cell kit (Invitrogen), according to the manufacturer's instructions.
Results: Cell purity demonstrated 95.7% CD3 and 96.1% CD14 intensity, and we found a significant difference in OC genesis in T-cell co-culture. Active OC were scored as cells able to reabsorb dentin. OC-like cells on PCL were detected by Confocal microscopy. SEM imaging showed membrane fusion properties. The results were supported by quantitative RT PCR of OC mRNAs. Fluorescent microspheres were incorporated into PCL, and fluorescence within the cells detected. Phagocytic index was significantly increased upon OC inductive cytokine exposure.
Conclusion: OC pre-cursor cells can differentiate to OC and attach to PCL, and T-cells play an important role in the genesis of OC. The study indicates a cell mediated degradation of PCL in 2D culture. This should be considered of importance, for determination of bone formation success rate, at the implantation site for alternatives substituting allo- and autograft.

P22.05 Kasper Lynghøj Christensen

NOVEL CARBONYL SCAVENGER?

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The development of age-associated diseases, such as diabetes and Alzheimer´s disease, as well as biological ageing is probably caused by long term accumulation of damaged biopolymers due to reactive oxygen species (oxidative stress) and highly reactive carbonyl species (carbonyl stress). Oxidative stress and carbonyl stress is closely intertwined and both lead to undesirable modificantions and degradations of (vital) proteins (e.g. mitochodrial) via a range of non-enzymatic reactions. To slow down this ageing process much research is currently directed towards the understanding of the intiation and progresson of the deletious processes, in which depletion of carbonyl scavengers (antioxidants) seem to play a crucial role.
Recently, we discovered a fast reaction between the ketone body acetoacetate, which is generated as the body utilizes fat as ATP-source, and a highly reative carbonyl specie: methylglyoxal. Methylglyoxal is known to afford pathological changes e.g. by the formation of so-called advanced glycation end-products (AGEs). These findings suggests that acetoacetate may play a role as a hitherto unknown scavenger of the highly cytotoxic methylglyoxal in vivo and thus slows undesirabel AGE-formation.

P22.06 Miao Wang

PREDICTIVE VALUE OF THE TOKUHASHI SCORING SYSTEMS IN SPINAL METASTASES (EVALUATION OF 448 PATIENTS IN THE AARHUS SPINAL METASTASES DATABASE)

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Study design. A prospective cohort study of 448 patients with spinal metastases.

Objective. To compare the predictive value of the Tokuhashi scoring systems (T12 and T15) for life expectancy in the various primary tumor subgroups
Background. Tokuhashi formulated a point-addition-type scoring system (T12) in 1990 and revised it in 2005
Methods. This study included 448 patients with vertebral metastases, all of whom underwent surgical treatment at Aarhus University Hospital. Data was retrieved from the Aarhus Spinal Metastases Algorithm. Scores based on the T12- and T15 scoring systems were calculated prospectively for each patient.We use the Log-rank test to evaluate the predictive value, and McNemar's test to evaluate the accuracy rate.Survival curves were estimated using the Kaplan-Meier methods.
Result. Both of T12 and T15 have significant predictive value ($p<0.0001$) in the whole study group. T15 has a significant higher ($p<0.0001$)accuracy rate than T12. The further analyses by type of metastases showed that the predictive value of T12 and T15 was found in the prostate ($p=0.0003$), breast ($p=0.0385$), other tumor group ($p<0.001$) and lymphoma ($p<0.05$). The accuracy rate of prognosis in T15 was significantly higher in those groups with spinal metastases originating from prostate ($p=0.0032$), breast ($p<0.0001$) and lung ($p=0.0076$).
Conclusion. Both the T12 and T15 scoring systems have significant preoperative predictive value. The accuracy rate was significantly improved in T15 for the total study group and in the subgroups of prostate, breast, and lung tumor.

P22.07 Nanna Cornelius

RIBOFLAVIN-RESPONSIVE MULTIPLE ACYL-COA DEHYDROGENASE DEFICIENCY (RR-MADD); A SYNERGISTIC EFFECT OF RIBOFLAVIN AND TEMPERATURE

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Riboflavin-Responsive-Multiple-Acyl-CoA-Dehydrogenase-Deficiency (RR-MADD) is a rare neuromuscular disorder. Until recently it was thought to be caused by an inherited defect in the availability of riboflavin-derived flavin cofactors, thus causing dysfunction of cellular flavoproteins; many of which are acyl-CoA dehydrogenases. We and others have recently established that RR-MADD is caused mainly by mutations in the mitochondrial electron transfer protein, Electron-Transfer-Flavoprotein-Ubiquinone-Oxidoreductase (ETF-QO).
In our current study we have used transient overexpression of recombinant ETF-QO protein in HEK-293 cells to test the riboflavin sensitivity of variant ETF-QO proteins identified in riboflavin-responsive (RR-MADD) and non-responsive MADD patients. By incubating the cells at increasing concentrations of riboflavin we showed that the activity/amount of variant ETF-QO proteins associated with a RR-MADD phenotype can be rescued to >70% of that of wild-type, whereas the enzyme activity/amount of variant ETF-QO proteins associated with non-responsive MADD disease could not be rescued to more than 20% of that of wild-type. Further studying the protein thermal stability of the riboflavin-responsive variant proteins, showed that the riboflavin-responsive variant proteins are more unstable than the wild-type protein at high temperature, even when grown under high riboflavin concentration. Based on these results we suggest that ETF-QO variations associated with a RR-MADD phenotype only give rise to significant disease when expressed under low cellular riboflavin content and/or high temperature.

P22.08 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. The recent years' technological development has made large scale protein investigation possible, and yet to be applied, we see the techniques as obvious candidates for bringing proteomics into the cholesteatoma research field and take it to the next step.
Methods: Biopsies from cholesteatoma tissue, middle ear mucosa, tympanic membrane and external auditory canal skin 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 tissue for specific examination of the cytokine inflammation profile.
Objectives: To investigate the interrelation and discrepancies of cholesteatoma and surrounding tissue, to thereby indicate the origin of the tumor and to detect key proteins of the pathogenesis that might serve as targets for future treatment. Comparison of the cholesteatoma cytokine profile with that of known skin diseases might lead to the adoption of the treatment of these.

P22.09 Kirstine Kjær Kirkegaard

TIME-LAPSE IMAGING AND METABOLIC PROFILE OF HUMAN PRE-IMPLANTATION EMBRYOS AFTER BLASTOMERE REMOVAL

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Background: Preimplantation genetic diagnosis (PGD) is offered to couples whose potential offspring are at risk of an inherited single gene disease or a structural chromosomal disorder. PGD requires DNA from the embryo for either PCR or FISH. One or two cells for diagnosis are obtained by blastomere biopsy of the 6-10 cell embryo. It has been argued that blastomere removal does not affect embryonic development. Few studies have verified the safety. Time-lapse studies on mice have suggested, hovwever, that blastomere removal has a retarding effect on embryonic development.
Time-lapse is a novel method of evaluating the spatio-temporal patterns of embryo development using kinetic markers to assess embryo quality.
Near Infra Red spectroscopy is an analytic technique based on spectroscopy used for metabolic profiling of spent culture media. Metabolic profiling has been shown to correlate with embryo competence.
Purpose: To evaluate whether blastomere biopsy affects embryonic development using time-lapse analysis and metabolic profiling.
Materials and methods: Couples undergoing IVF treatment with and without PGD, respectively, are requested permission to include embryos in the project. The diagnosis healthy/diseased is made by PCR and FISH analysis of a blastomere biopsy on day 3. Until day 5 after oocyte retrieval the embryos are cultured in the EmbryoScope , a time-lapse incubator. Spent culture media are analysed with NIR. Time-lapse analysis and metabolic profile are used to compare biopsied embryos with non-biopsied embryos in order to evaluate the effect of blastomere biopsy on embryo development.
Results: preliminary results of the time-lapse analysis will be presented

P22.10 Nynne Sharma

TRANSCRIPTIONAL REPRESSION OF TRANSGENES DELIVERED BY SLEEPING BEAUTY, PIGGYBAC AND TOL2 DNA TRANSPOSON VECTORS

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DNA transposons have become important nonviral vectors for efficient genomic integration of transgenes. A potential obstacle, however, for integrating vectors is silencing of the element and its genetic cargo, and transcriptional repression of the Sleeping Beauty (SB) transposon is routinely observed in F9 murine teratocarcinoma cells and in human retinal pigment epithelial cells. In this study,

we extended our analysis of vector silencing to include also the piggyBac transposon and the Tol2 transposon. Transposon vectors encoding an eGFP-IRES-puro cassette driven by an RSV promoter were genomically inserted in F9 cells by transposition. Pools of stably transfected F9 cell clones were grown for 10 weeks under non-selective conditions, and eGFP expression was measured by flow cytometry and compared to the initial eGFP expression level. All three transposon systems showed reduced eGFP expression levels after 10 weeks. F9 pools containing the SB transposon inserted with the SB10 transposase had the highest decrease in eGFP expression (18 ± 8.2 fold), whereas SB pools constructed with the hyperactive SB100X transposase, and with an expected increased vector copy number, showed an 8 ± 6.5 fold decrease in eGFP expression. PB pools had the lowest decrease in eGFP expression (2 ± 0.9 fold), whereas Tol2 pools showed a 4 ± 0.9 fold decrease in eGFP expression. Next, we incorporated 1.2-kb 5'-HS4 chicken β-globin (cHS4) insulators into the vectors to test for possible protective effects. Future expression analyses will determine if insulator sequences can exhibit protection against long-term silencing effects.

P23.01 Jan Danz

GINGIVAL RECESSIONS AND TOOTH MOVEMENT

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Wether orthodontic arch expansion is an etiological factor of development of gingival recession (exposure of the root surface) is unclear. In a large epidemiological study, the prevalence of ≥1 mm recession in a population ≥ 30 years was 58%. The aim of the present study program is to evaluate parameters of possible importance for the prevalence and/or amount of gingival recession during arch expansion: a) the distance the roots of the teeth are moved beyond the skeletal envelope, b) the retention time after the tooth movement is stopped, c) the magnitude (high vs. low) of orthodontic forces, d) the type of movement (tip vs. bodily movement) e) gingival thickness. 15 male wistar rats were used in a pilot study to establish a model of buccal tooth movement. The results of the pilot experiment, based on clinical and micro-CT evaluation showed that a bodily movement of the teeth could be achieved with the following model: Direct bonding of two different transpalatal spring types (high force 0.016x0.022" TMA; low force 0.016" TMA single helix spring body welded to 0.016x0.022" TMA; both preactivated with 30° buccal root torque) with .018"x.025" tubes on the upper 2nd & 3rd molars was applied. A transpalatal bar served as prevention from opening of the midpalatal suture and as a landmark for measurements. Micro-CT scans to evaluate three-dimensional tooth movement, non-decalcified histological and histomorphometric analysis will be performed. In situ hybridization (ISH) to display activity of different genes will also be performed. Thus a model to move rat molars buccaly with different forces and types of movement was established.

P23.02 Line Kjeldgaard Pedersen

INTRA- AND INTERRATER RELIABILITY OF PRESSURE PAIN THRESHOLD IN CHILDREN WITH ORTHOPEDIC DISORDERS.

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Background: Children undergoing orthopedic surgery are often in pain. Assessment of pain in children can be difficult and alternative tools for assessing the threshold for pain in children would be an advantage. Pressure algometry is used to assess pressure pain threshold (PPT).

Children with a history of unspecific pain have lower PPT than healthy children. This study determines the intra/inter-rater agreement of PPT's in children with orthopedic disorders.

Materials and Methods: 50 children aged 4-12 years were included. 20 were

examined twice and 20 were examined by two different investigators. Ten children were only examined once. A Somedic®pressure algometer was used. PPT is defined as the minimum pressure applied that can induce pain. The child was instructed to say 'stop' when the sensation of pressure changed into a sensation of pain. The thenar of the dominant hand and the back of the calf were examined.
Results: The mean age was 8.2 years. The mean PPT was 183 kPa at the thenar and 179 kPa at the leg. Bland-Altman plots revealed very good intrarater reliability and good interrater reliability. PPT's were significantly lower both at the leg (difference: 41.4 kPa, SD: 57.5, $p < 0.01$) and at the thenar (difference: 29.4 kPa, SD: 42.7, $p<0.01$) for values obtained by reader 1 when compared with thresholds obtained by reader 2.
Conclusion: Pressure algometry has good intra-rater reliability and satisfactory inter-rater reliability and may be used as a supplemental tool for evaluating pain and pain thresholds in children with orthopedic disorders in relation to surgery. Furthermore preoperative algometry may help identify which children are at risk of severe postoperative pain.

P23.03 Merete Gregersen

MULTIDISCIPLINARY GERIATRIC INTERVENTION AMONG NURSING HOME RESIDENTS WITH HIP FRACTURE REDUCES MORTALITY

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Objectives: Nursing home residents represent a large proportion of patients hospitalised with hip fracture. Early discharge to nursing homes after surgery is common practice. A previous study indicates an increased risk of death immediately after discharge.
Method: A total of 236 residents, hospitalised for hip fracture surgery, were selected for a retrospective follow-up study. A multidisciplinary orthogeriatric team (GO-team) visited the residents no later than one day after discharge. The number of visits depended on the need for treatment and rehabilitation. Intervention in nursing home was, among others, focusing on: nutrition, fluid therapy and blood transfusion. The intervention group was compared to historical data on patients with traditional orthopaedic treatment discharged to nursing homes after 3 days of hospitalisation.
Results: Intervention reduced 30-day mortality from 28% to 8% (Adjusted Odds Ratio (OR^{adj}) = 0.18 [95% Confidence Interval (CI): 0.07; 0.45]) and reduced 3-month mortality from 36% to 19% (OR^{adj} = 0.37 [95% CI: 0.19; 0.76]). Acute readmissions were reduced from 24% to 14% (OR= 0.47 [95% CI: 0.23; 0.93]) concurrently the length of stay at hospital was shortened from 3 to 2 median days (β^{adj} = -0.42 [95% CI: -0.55; -0.29]).
Conclusions: Multidisciplinary geriatric intervention among residents in nursing homes has a positive effect. It improves survival and reduces non-elective readmissions within three months. Still, it is not obvious which part of the intervention that is most important.

P23.04 Martin Svoldgård Vesterby

REMOTE REHABILITATION SUPPORT

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Remote Rehabilitation Support
The RRS project is investigating the effect of "RRS" via a telemedicine solution for patients undergoing an fast-track orthopedic surgery procedure with the implementation of a total hip arthroplasty (THA). With the telemedicine solution, connected to the patients TV-set, we will support and try to motivate the patient to be discharged after only one day of hospitalization. The RRS Project will be the first of its kind for orthopedic patients. It will be one of few RCT studies evaluating the effect of telemedicine. By creating fast-track orthopaedic surgery procedures, we are moving some of the tasks and responsibility normally undertaken by the hospital to the patient's own home and thereby to the patient's relatives, referred to as support

persons. Consequently, we anticipate more anxiety in the patients undergoing a fast-track procedure as well as their support persons, which is why the optimized fast-track procedures increase the need for high quality pre- and postoperative information as well as the education and support of both the patient and his support person. It is believed that patients who receive information about surgery and recovery will be less anxious and better able to handle the stressful, emotional and physical impact of the procedure.
The study is designed as a RCT including 74 patients. It is the intention to gain knowledge about the possibilities of telemedicine solutions, aimed at patients undergoing accelerate or complex procedures for the future benefit of a majority of patients and relatives. The changes in ways of thinking hospitalization and treatment have made the RRS project interesting local and international.

P23.05 Dan Østergaard Pradsgaard

ULTRASONOGRAPHY IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is one of the most common chronic diseases in childhood. Fast intervention with relevant treatment is of great importance to avoid severe sequelae. Therefore we need sensitive methods to secure an early diagnosis and to monitor treatment effect. Joint cartilage destruction is an early outcome in arthritis, which can be monitored by biomarkers of cartilage synthesis and degradation. Ultrasound (US) measurements of joint-cartilage thickness have been shown to be reliable and reproducible, and it correlates well with MRI findings.
Hypothesis: Serum and urine markers of cartilage and bone synthesis and degradation, together with US measurements of cartilage thickness, are useful tools in the early evaluation of JIA patients, - as diagnostic, prognostic and monitoring methods.
Methods: Cross sectional study, 90 patients (30 Oligoarticular, 30 polyarticular, 15 systemic onset and 15 newly diagnosed (any subtype)) from the Pediatric Rheumatology Clinic, AUH, Skejby. Journal and questionnaire: Demographic data, treatment history, disease duration and physical activity. Examination: Clinical joint score, US examination 14 joints, plain radiography 5 joints, MRI (knee only). Previous investigations of joint cartilage thickness assessed by US in healthy children serve as reference values.
Biochemistry: Blood samples for routine markers of inflammation/arthritis. Serum and urine samples for markers of cartilage and bone turnover: COMP, RANKL/OPG, PYD, DPD, CTX-II.
Perspective: To improve the clinical examination of JIA patients, so early diagnosis and prompt relevant treatment can better the prognosis for these patients.

P24.01 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. This is especially true for persons diagnosed with schizophrenia who mainly suffer from heart disease and metabolic disorders. Antipsychotics are likely to cause weight gain and metabolic syndrome associated with a two- to threefold increase in cardiovascular mortality and a twofold increase in all-cause mortality. The quality of the general health care in patients with severe mental illness and the lack of consensus about the prevention of somatic illness in this group of vulnerable patients need to be improved. We need more knowledge about how to integrate the prevention and care of somatic illness to the group of patients with severe psychiatric illness. The present Danish study investigates ways of improving the psychical health of people with a psychiatric diagnosis.
Hypothesis: There is a correlation between the awareness of physical health and the physical health among patients as well as staff members.

Material and methods. Design: Randomised intervention study with follow-up after nine months. Study population: The study population (184 patients and 200 staff members) is from six facilities in the region of North Jutland for severe chronically mental ill patients. In the intervention facilities individual health promotion and guidance will be carried out.
Perspective: The study is part of the process of improving the physical health of people with a diagnosis of severe mental illness. The individual participants can benefit from the study and the health check and might discover early signs of illness and thereby possibilities for early intervention.

P24.02 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.
Objective: The aim of the study is to develop a program based on strategies to address poststroke fatigue and to test and evaluate the program.
Material and Methods: Intervention Mapping is the comprehensive approach of the study. It describes a protocol for the development of theory- and evidence-based health promotion programmes.
Step 1) The program is developed based on a needs assessment. Existing knowledge about physical, psychosocial and environmental factors associated with poststroke fatigue is mapped in a literature review.
Step 2) The program will be tested in a pilot study (clinical controlled trial). In addition to conventional treatment, the patients in the intervention group will participate in the program for a period of 12 weeks. The control group will receive conventional treatment only.
Step 3) Evaluation of the program: Primary outcome measure will be fatigue, measured on the Multidimensional Fatigue Inventory-20. Secondary outcome measures will be identified during the development of the program. Patients will be tested at baseline, after 3 months and after 6 months. The effect size in the pilot study will be assessed and will be used in order to estimate the required sample size for a large-scale randomized controlled trial on formally testing the efficacy of the program.

P24.03 Kasper Grosen

PREVALENCE AND CHARACTERISTICS OF CHRONIC PAIN FOLLOWING VIDEO-ASSISTED THORACIC SURGERY AND ANTERIOR THORACOTOMY IN PATIENTS WITH PULMONARY MALIGNANCIES

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Introduction: The prevalence of chronic pain following both video-assisted thoracic surgery (VATS) and anterior thoracotomy in patients with pulmonary malignancies is poorly characterized and the influence of this pain on patients' lives remains unclear.
Objectives: To investigate the prevalence and characteristics of chronic pain following video-assisted thoracic surgery (VATS) and anterior thoracotomy and to assess the influence of chronic pain on daily functioning
Materials and methods: Patients with pulmonary malignancies undergoing thoracic surgery by means of video-assisted thoracic surgery (VATS) or anterior thoracotomy between 2000 and 2009 (N=702) were invited to fill in a specifically developed

questionnaire consisting of 18 questions regarding present post-surgical pain.
Results: Of the 702 patients contacted, 626 (89.2%) filled in and returned the questionnaire. In all, 178 patients (28.4%) were excluded, leaving 448 patients (71.6%) to be included in the final analysis. Of the 448 respondents, 82 reported persistent post-surgical pain due to previous thoracic surgery. That is an overall prevalence of chronic pain of 18.3% (95% CI: 14.8 to 22.2%). The prevalence of chronic pain following anterior thoracotomy and video-assisted thoracic surgery (VATS) was 18.7% (95% CI: 15.1 to 22.8%) and 13.8% (95% CI: 3.9 to 31.7%), respectively.
Discussion: A higher prevalence of chronic pain reported in previous studies may be explained by a different surgical approach (anterior versus postero-latreral thoracotomy), by different inclusion and exclusion criteria and/or bias due to lower return rate of questionnaires.

P24.04 Rasmus Østergaard Nielsen

PROTOCOL FOR THE DANO-RUN STUDY: A 1-YEAR OBSERVATIONAL FOLLOW UP STUDY ON RUNNING RELATED INJURIES IN 1000 NOVICE RUNNERS.

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Background: There is a paucity of knowledge about the relation between running patterns and Running Related Injuries (RRIs). Thus, it is necessary to identify which running exposures increase the risk of injuries and which exposures might be considered safe.
Objective: The purpose of this study is to investigate the link between the running volume and the development of RRIs.
Methods: Observational prospective follow up study. Healthy individuals who have not been running the past one year are included. All participants receive a GPS watch (GFR 110) and are instructed to start running as much as they want, two times a week as a minimum. They must wear their GPS watch at each training session and upload data to an internet based database.
Assessment of Risk Factors: Running volume measured as absolute number of kilometres and the graduation in kilometres pr. week over a period of three weeks.
Main outcome measurement: RRI is defined as any musculoskeletal complaint of the lower extremity or back causing a restriction of running for at least one week.
Results: Time to RRI will be compared between groups with different absolute running volumes. In a similar way time to injury will be compared between individuals with different weekly training graduations.
Conclusion: This study may be the first study to adequately measure running patterns reliably in a large sample. The exposure is quantified by GPS. This method is not affected by subject recall bias. If absolute volume or running graduation over time seems to lead to injury, the study findings and methodology create a solid foundation for future randomised controlled trials in this field.

P24.05 Matias Grynderup

PSYCHOLOGICAL DEMANDS, DECISION LATITUDE AND THE RISK OF INCIDENT DEPRESSION

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Background: It is still unclear whether psychosocial factors at work are risk factors for depression.
Aim: The aim was to determine whether work-unit average and individual-level measures of psychological demands and decision latitude predict incident depression.
Methods: A total of 4,291 public employees within 378 different work-units participated in a baseline study in 2007. Two years later 3,224 (72%) were followed up. At baseline data on perceived psychological demands and decision latitude were obtained by established questionnaires and for each work unit we calculated the average levels. Participants reporting a high level of depressive symptoms at baseline or follow-up went through a psychiatric interview (SCAN). Hundred met the requirements for an ICD-10 depression diagnosis at baseline and were excluded. At follow-up, 68 incident cases were identified. Odds ratios of incident depression following work-unit and self-reported psychological demands and decision latitude at baseline were estimated by multivariate logistic regression adjusted for established risk factors.
Results: Odds ratio of depression increased significantly by higher levels of self-reported psychological demands and lower levels of decision latitude (tests for trend, p-values<0.05). The highest level of self-reported psychological demands and lowest level of decision latitude showed OR-values of 1.41 (95% CI 1.02-1.95) and 1.89 (95% CI 1.18-3.03), respectively. Work-unit average decision latitude also showed a statistical significant trend while this was not the case for psychological demands.
Conclusion: These data indicates that decision latitude predicts incident depression.

P24.06 Connie Berthelsen

RELATIVES PARTICIPATION IN OLDER PATIENTS ACCELERATED TREATMENT PROGRAMME DURING TOTAL HIP OR KNEE REPLACEMENT. CONSTRUCTING GROUNDED THEORY.

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In Denmark, there is annually performed (year 2007) 7691 hip- and 6740 knee arthroplastysurgeries, and 49 % of patients are over the age of 70. Indications for hip and knee arthroplasty areoften arthritis and excruciating pain, which can lead to loss of ability to function. Elderly are henceexpected to have some need for help and support in the daily living, by their relatives, both before,during and after hospital admission. Today, hip and knee surgery is performed through anaccelerated treatment programme, with admission for only three days and the demand for efficientinformation between patient, relatives and health professionals is important. The programmerequires responsibility from the patient to follow through daily regimes, but this will need a strengthand knowledge the elderly patient may not withhold. The relatives´ role in the accelerated treatmentprogramme is presumed to be important but has never before been examined. Knowledge is neededand the purpose is to construct grounded theory about the relatives` participation in elderly patientsaccelerated treatment programme during total hip or knee arthroplasty.Participants are relatives to elderly patients over the age of 70 years old, undergoing hip or kneearthroplasty. 15 relatives are estimated to participate or until it is assumed that theoretical saturationis reached. Through Grounded Theory, with a theoretical approach by Glaser & Strauss (1967),Glaser (1968) and Charmaz (2006), data is generated through non-participatory observations ofplanned meetings with patients, relatives and health professionals and subsequently conversationswith relatives afterwards. Additionally qualitative in-depth interviews with relatives are performedtwo weeks after discharge. The constant comparative method is used for data analysis andadvancing guides and theoretical sampling.The results are expected to develop into a substantial theory about relatives` participation inelderly patients accelerated treatment programme during hip or knee arthroplasty. The research willprovide 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 potentialresources in the accelerated treatment program as well as in clinical guidelines. The results willexpose a necessity for further theory about relatives´ participation and role and be an opportunityfor improvement of quality in clinical practice.

P24.07 Palle Larsen

REHABILITATION NURSING RESEARCH IN PATIENTS HEART REHABILITATION IN PHASE III .

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Background: Rehabilitation has been in focus for the last 15 years, within heart diseases. Focus has been on efficacy of treatment in relation to mortality, morbidity and health-related quality of life. Patients ADL functionality and self-care capacity, is less described/known.
Hypothesis: Systematic preparation of rehabilitation program of patients in Phase III based on identifikation of self-care behavior on patients with CHF in NYHA class II and III, leading to patients' self-care behavior strengthened, will improve health status and ADL level 6 months after discharge from hospital with heart failure.
Aim: 1. To develop evidence-based clinical guidelines for patient rehabilitation phase III. 2. To test the efficacy of individual rehabilitation plans based on clinical guidelines for patient rehabilitation in Phase III. Efficacy assessed in changes of self-care behavior, health status and ADL function.
Materials and Method: This study included patients undergoing cardiovascular programs. Patients who have followed rehabilitation program's Phase I and II and prints to fase III rehabilitation will bee included consecutively.
Inclusion: Patients aged 18 years or older and assessed as NYHA II and III.
Exclusion: Patients who do not want to participate. Patients who were not able to read Danish language and communication complicates a sufficient participation. Patients who do not understand information, and patients with diagnosed neurological outcome. The calculation of patient numbers are based on powercalculation
Prospects: The project may be contributing to evidence-based clinical practice, and thus been an essential element in development of evidencebased rehabilitative care

P24.08 Jakob Jakobsen

SACRAL NERVE STIMULATION FOR IDIOPATHIC FAECAL INCONTINENCE - EFFICACY AND PATIENT SATISFACTION -

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Background: Sacral Nerve Stimulation (SNS) is an established treatment for patients with faecal incontinence (FI) when conservative treatment has failed to restore continence.
Aim: To document the efficacy of SNS in patients with FI and to evaluate patient satisfaction with the treatment.
Method: Multicenter retrospective analysis of data collected prospectively from patients with idiopathic faecal incontinence (IFI) treated with SNS at Aarhus University Hospital, Denmark from September 2001 to August 2008 and at Masstricht University Center, The Nederlands from April 2000 to May 2009. A 49-item questionnaire describing bowel habits, quality of life and self reported satisfaction with current treatment response and a 3 week bowel diary were mailed to the patients. All presented data are median values. Paired t-test with two-tailed p-values was used.
Results: 130 patients were contacted. Response rate was 65.4%. 89% of the responders were actively stimulated. A decrease in FI episodes in three week from baseline 24.9 to 6.1 ($p<0.0001$) at latest follow up was shown. 57 (75%) of the patients were satisfied with the current treatment. They experienced better continence than the group that was not satisfied (19 patients) in terms of: FI episodes (0 versus 10 ($p<0.0001$)), days with soiling (2 versus 15 ($p<0.0001$)), days

with pad (2 versus 21 ($p<0.03$)). Overall satisfaction rate after 41 months follow-up were 61% when non-responders were excluded and non-actively stimulated and explanted SNS patients were deemed as failures.
Conclusions: SNS improves continence and 2/3 of the patients are satisfied with the treatment outcome at long-term follow-up.

P24.09 Mai-britt Guldin

RISK ASSESSMENT OF COMPLICATED GRIEF AMONG FAMILY CAREGIVERS OF DECEASED CANCER PATIENTS. A RANDOMIZED CONTROLLED STUDY.
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Objective: The aim of the study was to describe bereavement reactions among family caregivers of deceased cancer patients and implement a risk assessment tool in general practice to identify those at risk of complicated reactions to provide targeted support and prevent unnecessary prolonged suffering.
Methods: Newly bereaved caregivers were recruited at a number of palliative care units, hospital departments and hospices. Approximately 6 weeks post loss the bereaved caregivers received a baseline questionnaire battery by mail. Follow-up assessment was conducted at 6 and 13 months post loss. Assessment battery consisted of a screening instrument for early identification of complicated grief, Beck's Depression Inventory (BDI), self-reported health (SF-36), Impact of Events Scale (IES), anxiety subscale of SCL-90 and a number of demographic questions. Participants were assigned to either a control- or interventions group in a blinded cluster randomization based on their listed GP. Only the intervention group received information of the results of their bereavement risk assessment. The study is ongoing.
Results: At this point participation has been offered to 635 newly bereaved. Accept of participation has been given by 320 (50%). Results from the baseline questionnaire will be presented to describe parameters of the bereavement reaction of the caregivers. Furthermore, the study will yield information on the risk assessment on complicated grief within the study groups.
Conclusions: The study will provide data on whether early risk assessment of bereavement in general practice can help identify bereaved individuals in need of help and avoid preventable prolonged grief reactions.

P24.10 Helle Svenningsen

SEDATION - DELIRIUM - PTSD
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Background: Patients in intensive care that experience delirium have longer hospital stay, higher mortality and morbidity. Foreign studies indicate that post-traumatic stress disorder (PTSD), dementia or depression emerge after discharge from hospital. There is a link between delirium and sedation. In Denmark sedation is used frequently.
Hypotheses: 1. Patients, who are sedated minimal, remember staying in intensive care and experiences fewer episodes of delirium
2. Patients are more likely to develop post-traumatic stress syndrome after discharge if they have experienced delirium during hospital
3. Patients who have experienced delirium, have impaired health-related quality of life after discharge compared with patients without delirium
Methods: All adults admitted to Aarhus University Hospital intensive care ITA or 600 from September 2009 - September 2011 is in this cohort study with follow-up. Patients hospitalized less than 48 hours in intensive care, with head injury or less than 18 years is excluded. Approximately 1 week after discharge from ITA/600 the ICU Memory Tool is applied. Correlation between sedation level and memories will be calculated. Two and 6 months after discharge from the hospital the patient are contacted by telephone. Through a structured interview the ICU Memory Tool, and the Harvard Trauma Questionnaire for PTSD are applied. To screen for depression

the Major Depression Inventory is used. State-Trait Anxiety Inventory is used to assess the degree of anxiety. Quality of life is assessed by Short-form 36.

P25.01 Lise Graversen

IDENTIFICATION OF PRESCHOOL CHILDREN AT HIGH RISK OF FUTURE OVERWEIGHT

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Introduction: Overweight is augmenting globally. Given that overweight emerge at younger ages early intervention is vitally important, but presupposes an efficient identification of high risk children. The associations between overweight in adolescence/adulthood and smoking during pregnancy, high parental BMI, birthweight, short breastfeeding, different measures of infancy/early childhood weight gain and early adiposity rebound (AR) are strong. The aim of this study is to identify future overweight risk factors feasible for a risk estimation tool to be used among preschool children in general practice.
Methods: We use The Northern Finnish Birth Cohorts born 1966 (N=4000) and 1986 (N=5500) to test known risk factors' ability to predict future overweight. Cohort participants were followed from birth to the age of 31 and 16 years respectively. Weight and height data from routine child health examinations from the age of 0 to 13 years were collected and a end of follow-up clinical examination included BMI and waist circumference.
Results: The preliminary results show that smoking during pregnancy, parental BMI, growth patterns in infancy and early childhood (BMI at specific ages, BMI percentile crossing at specific ages, absolute weight gain between specific ages, BMI peak ect.), are strongly associated with overweight in adolescence/adulthood and candidates for the risk estimation tool.
Perspective: By combining various risk factors using statistical modeling we attempt to verify whether known risk factors offer sufficient ability to predict risk of future overweight among preschool children.

P25.02 Zara Ann Stokholm

LONG-TERM OCCUPATIONAL NOISE AND ANTIHYPERTENSIVE MEDICATION: A REGISTER-LINKED STUDY

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Aim: To establish whether exposure to occupational noise is a cause of chronic arterial hypertension.
Methods: All production workers of 800 companies within 10 noise exposed industrial trades will be identified and followed during 2001-2007. Cumulative noise exposure (dBA*years) will retrospectively be assed using logarithmic addition of noise intensity (LAeq mean) and the duration of employment in a given job. By register linkage, all redeemed prescriptions for antihypertensive drugs during follow-up will be identified.
Statistics: Data will be analyzed with logistic regression analyses. All analyses will be adjusted for relevant potential confounders.
Results: Preliminary results will be ready for poster presentation in January 2011.

P25.03 Christina Malmose Stapelfeldt

MEASURING SICK LEAVE AMONG ELDERCARE WORKERS: ARE DANISH ADMINISTRATIVE DATA ON SICKNESS BENEFIT AS VALID AS DATA ON SICK LEAVE FROM COMPANY RECORDS?

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Background: The DREAM database consists of information concerning all social

public transfer payments per week received by Danish citizens since July 1991, including sickness benefit. During the last decade approximately 90 studies have been conducted and published in the field of sick-leave and return to work in Denmark, of those 1/3 used DREAM, though this register has never been validated.
Aim: To study the agreement between data on sick leave from company records and Danish administrative data on sickness benefit related to sick leave spells of at least two weeks.
Methods: Municipal eldercare employees in Aarhus sick-listed for at least 2 consecutive weeks in the company records in 2006 and employed the entire year of 2006 were categorised as "sick". The remaining employees were categorised as "not sick". The same employees were identified in DREAM and those receiving sickness benefit were categorised as "sick".
Sick leave data from the 2 registers were compared using company records as reference. Sensitivity, specificity and predictive value were calculated. McNemar´s test was used as statistical test ($p<0.05$ was considered significant).
Results (preliminary): 3645 employees (females 95.1 %), mean age was 45.7 years (SD 10.1).
Sensitivity was 86.4, specificity was 96.2, 95% CI (95.4 ; 96.9) and positive predictive value was 88.3, 95% CI (86 ;90.4), $p=0.21$. Conclusion (tentative): The agreement between dichotomized sick-leave data from DREAM and the municipal elder care was acceptable when analysed on employees employed the entire 2006.

P25.04 Rikke Jørgensen

MEANINGFUL CHANGE WITH THE METHOD GUIDED SELF-DETERMINATION &NDASH; A RANDOMISED CONTROLLED STUDY FOR PATIENTS DIAGNOSED WITH SCHIZOPHRENIA.

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Background: Rehospitalisation and discontinued treatment are common among patients with schizophrenia and is often associated with lack of insight into the illness. Improving patients' insight has been attempted through psychoeducation and standard treatment but without any considerable change. The method, Guided Self-Determination (GSD) has been adjusted to patients with schizophrenia.
Aim and hypotheses: The aim of the study is to evaluate the effects of the method GSD in the care of patients with schizophrenia compared to treatment as usual. Following hypotheses will be tested:
The method GSD will improve: Cognitive and clinical insight in patients, various domains of self-management of schizophrenia, self-esteem, psychopathology and social functioning. Primary outcome is cognitive insight measured by the self-rating scale Beck Cognitive Insight Scale.
Material and method: The study design is a randomised controlled trial. The participants are diagnosed with schizophrenia, receiving treatment in 3 Assertive Outreach Teams and 3 Psychosis Teams in Region North. Participants complete four self-rating questionnaires, a demographic data sheet, an interview concerning psychopathology and an assessment of social functioning at baseline, and after 3, 6, and 12 month. Inclusion of 50 participants in each group is sufficient to detect an effect of 3 BCIS scale points. Intervention with the method GSD will be conducted by the community nurses.
Results: no preliminary results yet to be presented.
Perspectives: If the method GSD proves effective in the care of patients with schizophrenia, the method is ready for further research on implementation in mental health nursing practice.

P25.05 Anette Werner

MENTAL TRAINING AND CHILDBIRTH - THE EFFECT ON PAIN EXPERIENCE, LENGTH OF BIRTH AND OTHER BIRTH OUTCOMES

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Environment
Background: 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 a mental trainings method, self-hypnosis, has a positive impact on labour pain and several other birth outcomes.
Aim: The aim of this study is to examine the effect of a short antenatal course in self-hypnosis primary on the use of epidural analgesia during birth.
Secondary on Length of birth; Birth progression at admission to labour; Birth experience (pain, control, anxiety); Medical interventions during birth including mode of delivery; Hemorrhage during birth; Saliva cortisol profile at birth; Child's condition at birth.
Method: This interventional single center study is designed as a randomised, controlled, single blinded trial using a 3 arm group design.
The intervention group receives antenatal traning in hypnosis.
The active comparator group receives antenatal training in different relaxation methods and mindfulness.
The control group receives no additional interventions.
The data collection is based on questionnaires, register data, medical records and biological material.
We started including participants during July 2009 and plan to recruit in total 1210 participants.
Perspective: Antenatal mental training is a simple and inexpensive intervention. Personal as well as socio-economic costs can be reduced if this method turns out to be effective in relieving birth pain and reducing side effects from birth.

P25.06 Lene Jacobsen

METABOLIC SYNDROME IN PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA - PREDICTION AND PREVENTION
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Introduction
The metabolic syndrome (MetS) is a cluster of factors significantly increasing the risk of cardiovascular disease and MetS is highly prevalent in patients with schizophrenia. Several studies have investigated the metabolic side effects of antipsychotic medication. However, the question whether unhealthy lifestyle, comprising physical inactivity, smoking, unhealthy dieting, and sleeping disturbances adds to the metabolic risk of patients with schizophrenia remains unanswered.
The aim of this study is to investigate the prevalence of MetS in drug-naïve patients with first-episode schizophrenia before and after 1 year of treatment and to investigate the risk of physical inactivity and disturbed bodily experiences in developing MetS.
Methods and material: The study is a clinical, prospective, observational study. All patients consecutively assigned to The OPUS project in The Region of Midtjylland (Denmark) having an ICD-10 diagnosis of first−episode schizophrenia and aged between 18-40 years are 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 included. MetS is evaluated for all participants as well as levels of physical activity, aerobic fitness, sleeping disorders, disturbed bodily experiences, eating habits, socio-economic status, smoking and drug abuse and medication. Patient's view on interaction of disturbed bodily experiences and physical activity level are examined with in-depth qualitative interviews.
Results: The study's preliminary results will be presented. The aims and methods of this newly commenced study will be presented and discussed.

P25.07 Bjarne Rittig-Rasmussen

NECK PAIN, NECK TRAINING AND CORTICAL PLASTICITY
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By tradition musculoskeletal pain research has focused on peripheral tissues and

biomechanical factors. New research demonstrates, however, that pain may be accompanied by measurable cortical plastic changes. The hypothesis of this study is therefore that a difference can be demonstrated in transcranial magnetic stimulation induced neuronal plasticity measured by motor evoked potentials (MEPs) and latencies in healthy participants who perform neck training compared with participants who do not perform neck training.
We investigated corticomotor excitability in 40 healthy men and women aged 19-35 years on four subsequent times: before, immediate after, one hour after and one week after neck training. The subjects were randomized to neck training or no neck training. MEPs and latencies were measured from the unilateral trapezius muscle and from the thumb muscle which was used as a control, and if possible to ascertain specific effects at the cortical level.
With the related t-test we found an MEP amplitude increase in those who performed neck training equivalent to 247 μV ($p = 0.046$) compared to those who did not ($p= 0.29$). Latencies in neck MEPs were unchanged ($p = 0.1633$), MEPs and latencies from the thumb muscle were also unchanged ($p = 0.61$ and $p = 0.053$). Analysis of variance for repeated measurements did not disclose any statistical differences between those who performed neck training and those who did not.
The results from this study did not disclose any statistically significant increase in neuronal plasticity or excitability following neck training over time in this setup.

P25.08 Anne-Birgitte Vogelsang

PARTNERS TO ICD RECIPIENTS A DISREGARDED RESOURCE? A DESCRIPTIVE CROSS-SECTIONAL RETROSPECTIVE MULTI-CENTRE QUESTIONNAIRE STUDY OF THE PSYCHOLOGICAL PROFILE OF ICD PARTNERS, DETERMINANTS OF THEIR REHABILITATION NEEDS AND SATISFACTION WITH INDIVIDUAL INFORMATION AND SUPPORT OFFERED.

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BACKGROUND: In 2007, 3162 Danish individuals had an ICD. The typical ICD recipient was male (76%) with a median age of 62 years. Little is known about the impact of an ICD implantation on partners, their needs and concerns. In one Danish study (n=161) it was shown that more than 70% wanted better personal support. Over half of the partners worried when the ICD recipient was physically active, and not noing what to do if shock-therapy were set off.
AIM:To identify individual needs of personal information and support in partners associated to the support provided by health care professionals and family. To identify determinants of individual needs and ICD concerns of the partner. To evaluate the psychological influence of an ICD treatment on partners and recipients relative the general population. To conduct a program that makes it possible for the partner to be more secure and supportive in the rehabilitation process of the recipient.
METHOD: Multi-centre, cross-sectional, retrospective questionnaire study, carried out from December 2008 to February 2009. All adult ICD recipients, implanted for the first time in the period from the 1 of January 2005 to the 1 of January 2008 were included (n=1888). Recipients who had passed away, were under 20 years of age or had had heart transplantation were excluded, which left 1635 ICD-recipients and their possible partners. Responding recipients (n=1129 (70%)) 28% of those did not have a partner. Responding partners n=756.
RESULTS:Analysis is ongoing.
PERSPECTIVE: This study is meant to lead to a RCT were partners in are included in rehabilitation. The effect of the intervention will be evaluated in both partner and patient outcome.

P26.01 Anne Dorte Blankholm

MR ANGIOGRAPHY WITHOUT GADOLINIUM CONTRAST AGENTS

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Background: Nephrogenic Systemic Fibrosis is related to use of Gadolinium based contrast agents (GD) in Magnetic Resonance. Based on this the Danish National Board of Health developed guidelines for use of contrast agents. Candidates for kidney transplantation have been examined using MR-angiography (MRA) with GD (CE-MRA) or CT-angiography with iodine based contrast agent (CTA). According to the guidelines the first choice of examination is ultrasound (US), eventually followed by MRA and finally CE-MRA or CTA.

Possible kidney donors undergo examinations to exclude disease and clarify vascular anatomy. Currently the examination used is CTA. Since CT is based on x-rays it is desirable to replace the CTA with MRA.

Aim: To develop sufficient non-contrast MRI examinations.

Methods: 1. A study evaluating MRA versus US and CT without contrast agents as preoperative examination in kidney transplantation. The scanning results will be compared to each other and to surgery.

2. Different MRA sequences without GD will be evaluated with respect to image- and diagnostic-quality.

3. A comparative study on kidney donors. CTA with contrast agent will be compared to MRA without GD and to surgery. The methods will be compared on number and length of vessels, degree of stenoses and diagnostic quality.

Perspective: If US, MRA without GD, CT without contrast agent or a combination of two of these techniques is sufficient for preoperative planning of kidney transplantation the result will be a totally non-invasive examination.

If MRA without GD is sufficient for preoperative planning of kidney donation a totally non-invasive examination without ionising radiation or use of contrast agents can be offered.

P26.02 Steen Fjord Pedersen

MRI ASSESSMENT OF ENDOTHELIAL DAMAGE AND ANGIOGENESIS IN PORCINE CORONARY ARTERIES USING GADOFOSVESET

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Introduction: Endothelial damage and angiogenesis are essential in atherosclerotic plaque development and destabilization. Macromolecules in the blood may extravasate into the vessel wall through leaky neovessels or damaged endothelium. Gadofosveset is an MRI contrast agent that binds reversibly to albumin and may enter damaged tissue such as the atherosclerotic vessel wall together with albumin. We sought to examine whether contrast enhanced MRI using gadofosveset would enable the detection of endothelial damage and neovessels in balloon injured porcine coronary arteries.

Methods: Ten pigs underwent balloon injury of the LAD to induce endothelial damage and angiogenesis. After balloon injury, in-vivo and ex-vivo T1-weighted coronary MRI was performed after intravenous injection of gadofosveset. The ex-vivo MR images were matched with corresponding histological sections and correlated to endothelial damage and angiogenesis.

Results: Ex-vivo coronary vessel wall MRI contrast enhancement was in agreement with extravasated Evans blue as a marker of endothelial damage with a kappa value of 0.64 ($p<0.001$). Sixty minutes post contrast, MRI showed contrast enhancement of the injured LAD as compared to the non-injured circumflex artery that served as control with a significant increase in the diameter of the artery (30±19 % versus 4±8%; $P=0.01$). There was a linear correlation between coronary MRI contrast-enhancement and microvessel density ($r=0.78$, $p<0.001$).

Conclusion: Contrast enhanced coronary MRI using gadofosveset is a promising approach for the non-invasive detection of endothelial damage and angiogenesis in the coronary artery wall

P26.03 Christoffer Laustsen

NON-INVASIVE METABONOMICS ON DIABETIC RATS BY HYPERPOLARIZED 13C MRI

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Diabetes mellitus type 2 is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. According to WHO, an estimated 285 million people, corresponding to 6.4% of the world's adult population, will live with diabetes in 2010.

Hyperpolarized 13C metabolic MR is a novel imaging and spectroscopic technique that has recently demonstrated the ability to quantify metabolic rates after injection of endogenous agents into living organs.

This study will evaluate the feasibility of systemic and intrarenal pyruvate carboxylase measured by [1-13C]pyruvate hyperpolarized NMR. Pyruvate carboxylase (PC) has a high activity in gluconeogenic tissues, as the kidney. In type 2 diabetes, elevated glucose levels, will result in decreased PC enzyme activity, which will be observable as a decreased signal in oxaloacetate. Similarly the activity of LDH and PDH will be reflected in the metabolites lactate and bicarbonate.

In this experimental study, 5 adult Goto-Kakizaki (GK), type 2 diabetes model, rats are included for in-vivo characterization of the pyruvate carboxylase in the kidney, and 5 adult Wistar rats will be used as a control group. The rats will be sedated by isoflurane and placed in the MRI scanner, vital signs will be monitored.

Hyperpolarized pyruvate is transferred from the DNP to a storage syringe and injected iv. 13C-MRI spectroscopic images are obtained with a CSI sequence, or dynamic data is acquired with localized spectroscopy. Based on spectral analysis, mean signal intensities of pyruvate and its metabolites, lactate, oxaloacetate are calculated in both kidneys, pancreas and in the leg muscle.

P26.04 Anette Luther Christensen

POISSON REGRESSION MODELS OUTPERFORM THE GEOMETRICAL MODEL IN ESTIMATING THE INTENSITY OF SEASONAL VARIATION: A SIMULATION STUDY

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Edwards (1961) derived an estimator based on a geometrical model, which fits a single-cycled sinusoidal curve to equidistant frequencies spanning the calendar year. The model has been applied in epidemiological studies in seasonal variation. Several seasonal variation intensity estimators based on this geometrical model have been proposed by Brookhart and Rothman (2008), concluding that a second-order moment-based estimator is superior in comparison with Edwards' estimator. Alternatively seasonal variation may be modelled by the generalised linear models. These models provide flexibility in modelling the pattern of seasonal variation and adjustments for covariates.

Based on a simulation study, we evaluated the performance in estimating the intensity of seasonal variation of two models, the geometrical model, and log-linear Poisson regression model by estimating the bias of the peak-to-trough ratio. We evaluated one estimator based on the geometrical model and two estimators based on the log-linear Poisson regression model. All estimators are evaluated on data influenced by a secular trend and a seasonal variation characterised by several peaks and troughs during the calendar year.

The results show that the estimators of the Poisson regression model have smaller absolute biases, than the estimator of the geometrical model, when evaluated on data simulated according to the corresponding model assumptions.

This simulation study encourages the use of Poisson regression models in estimating the intensity of seasonal variation as opposed to the geometrical model.

P26.05 Christian Alcaraz Frederiksen

PREOPERATIVE ASSESSMENT OF CARDIAC FUNCTION BY SPECKLE TRACKING ULTRASOUND

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Introduction: The handling of patients with a failing heart during surgery and anesthesia requires extensive information about cardiovascular status. Point-of-care ultrasound protocols like focus assessed transthoracic echocardiography (FATE) provide the information, but are hampered by subjective measures of left ventricular (LV) function.
Speckle tracking ultrasound (STU) measurements of strain provides objective information on LV function, but normally requires measurements from three different cardiac views.
We hypothesized that preoperative global strain measurements from three different cardiac views were in good agreement with measurements from only the 4-chamber view.
Methods: 40 patients undergoing elective cardiac surgery were included. Ultrasound examination was carried out preoperatively using a Vivid E9 (GE Healthcare, Horten, Norway) ultrasound system equipped with a M5S transducer.
Results: The mean value of global strain measurements was 14.22% (±0.55) and mean value of 4-chamber strain measurements was 13.96% (±0.60). Blandt-Altmann analysis of the data showed good agreement when global strain was compared with strain from the 4-chamber view, p=0.34. Lower and upper limits of agreement of the differences were -3.17% and 3.69%.
Discussion: STU measurements of strain from the 4-chamber view are interchangeable with global strain measurements. The use of only one acoustic window makes it very simple to implement STU in point-of-care ultrasound protocols like FATE.
Further studies evaluating the agreement between STU and well established methods of assessing cardiac function are needed to further define the role of STU in the preoperative assessment of cardiac function.

P26.06 Sanne Bøjet Larsen

REDUCED PLATELET RESPONSE TO ASPIRIN IN PATIENTS WITH PREVIOUS MYOCARDIAL INFARCTION COMPARED WITH PATIENTS HAVING CORONARY ARTERY DISEASE WITHOUT PREVIOUS MYOCARDIAL INFARCTION

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Introduction: Aspirin reduces the risk of thrombotic events in patients with coronary artery disease (CAD). However, several studies report a variable platelet response to aspirin.
Aim: To investigate whether platelet response to aspirin differed between patients with previous myocardial infarction (MI) compared with CAD patients with no previous MI.
Methods: We included 230 patients in chronic aspirin therapy: 170 with previous MI and 60 with CAD and no previous MI. Patients receiving any other antiplatelet drug than aspirin were excluded. Platelet response to aspirin was assessed by determination of platelet aggregation using multiple electrode platelet aggregometry (MEA) using the agonists arachidonic acid and collagen. Furthermore, serum P-selectin was measured and compliance was determined by serum thromboxane B2.
Results: Patients with previous MI had a significant higher aggregation indicating lower platelet response to aspirin compared with CAD patients. This was statistical significant when using arachidonic acid (P<0.0001) but not with collagen (p=0.14).

P-selectin was increased in patients with MI compared with CAD patients, however, this was not statistical significant (p=0.18)
Conclusion: Platelet response to aspirin assessed by MEA using arachidonic acid as agonist was significantly lower in patients with previous MI compared with CAD patients. P-selectin was higher in patients with previous MI compared with CAD patients but this did not reach significance. Future studies to investigate whether causiality exists between low platelet response to aspirin and the risk of MI are needed.

P26.07 Lars Jakobsen

SEX- AND AGE-RELATED DIFFERENCES IN OUTCOME AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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Objectives: To compare the outcome after PPCI according to sex and age in unselected real-world patients, and to compare the survival after PPCI with the survival in the general population across sex- and age-groups as an indirect measure of effectiveness and safety of PPCI.
Design: Population based follow-up study
Patients: 6373 consecutive real-life patients treated with PPCI from 2002-2006 and 35885 sex, age and comorbidity matched controls.
Main outcome measures: Composite endpoint of mortality, reinfarction, and stroke at 30 days and at 1 and 2 years.
Results: Women were older and had overall higher baseline risk profile than men. The cumulative risk of the composite endpoint after 30 days, 1 year and 2 years were 10.7%, 17.2% and 20.6%, respectively, for women compared to 6.6%, 12.2% and 15.5% for men. (adjusted hazard ratio (HR)=1.13, 95% CI: 0.91-1.39, adjusted HR=1.09, 95% CI: 0.93-1.27 and adjusted HR=1.05, 95% CI: 0.92-1.21). When comparing patients treated with PPCI and matched general population controls we found a higher mortality among patients up to 90 days after admission with STEMI. This difference was present in both men and women of all ages. However, after 90 days the mortality in the study population was similar to the mortality in the general population.
Conclusion: Outcome after PPCI is comparable in men and women after controlling for differences in baseline risk profile. PPCI treated patients, independent of sex and age, have no excess mortality after 90 days compared to the general population. Thus, PPCI appear to be an efficient and safe treatment in both men and women of all ages.

P26.08 Bent Roni Ranghøj Nielsen

SHORT TERM HYPERGLYCEMIA IMPROVES LEFT VENTRICULAR SYSTOLIC FUNCTION AND INCREASES WALKING DISTANCE IN PATIENTS WITH TYPE 2 DIABETES AND HEART FAILURE.

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Objective: We investigated whether short term changes in circulating glucose levels affect cardiac function in patients with type 2 diabetes.
Methods: In a randomized, open label cross-over design patients with insulin treated type 2 diabetics without heart failure (DM-nonHF, n=8) (Mean ± SD, EF 61 ± 5%) and with heart failure (DM-HF=10) (NYHA 2-3 and Mean EF 36±6%) underwent hyper- and euglycemia for approximately 24 hours. Echocardiography, 6 minutes hall walk test, and treadmill exercise tests were performed after 24 hours in both study arms.
Results: Blood glucose levels differed between study arms in DM-nonHF (10,9 ± 2,1mM vs 6,3 ± 1mM, P<0.001) and in DM-HF (12,8 ± 2,5mM vs 6,3+-0,7mM, p<0.001) during a 5 hours period prior to the investigations. Levels of

catacholamines did not differ between study arms. During hyperglycemia global myocardial maximal systolic tissue velocity Vmax and longitudinal mitral annulus velocity Smax increased significantly (14% P=0,039 and 10% P<0,001 respectively in DM-HF; 11% P=0,017 and 11% P=0,006 respectively in DM-nonHF). In the total study population we found an increase in strain by 9% (P=0,047), increase in strain rate by 8% (P=0,019) and an increase in systolic longitudinal mitral annulus velocity by 7% post exercise (P=0,029). During hyperglycemia DM-HF improved 6 minutes hall walk distance by 7% (P=0,016).
Conclusion: Short term hyperglycemia in type-2 diabetics with and without heart failure increases myocardial systolic tissue velocity. In DM-HF patients 6 minutes hall walk test increased during hyperglycemia. Our findings suggest that short term hyperglycemia has beneficial cardiac effects in patients with DM2.

P26.09 Thomas Larsen

SUPPRESSION OF PLASMA RENIN CONCENTRATION AND ANGIOTENSIN II AFTER INHIBITION OF SYSTEMIC NITRIC OXIDE SYNTHESIS IN HEALTHY SUBJECTS. A DOSE-RESPONSE STUDY.

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Purpose: We wanted to test the hypothesis that systemic NO inhibition causes a dose-dependent suppression of the plasma renin concentration (PRC).
Methods: The effect of L-NMMA, an inhibitor of NO synthase, was investigated in a randomized, placebo-controlled, blinded, cross-over, dose-response study in healthy males (n=12; mean age 20). On four different occasions, subjects received either saline vehicle or one of three different doses of L-NMMA after an overnight fast. L-NMMA was administered as a 3 mg/kg bolus followed by a 2 mg/kg/hr infusion for 60 min, a 4.5 mg/kg bolus + 3 mg/kg/hr infusion, and a 6 mg/kg bolus + 4 mg/kg/hr infusion. Blood samples were obtained at baseline after three hours of supine rest, after 60 min of L-NMMA infusion, and 60 min after cessation of the infusion. PRC and angII were measured using RIAs. Data were analyzed using a general linear model with repeated measures.
Results: Mean baseline PRC and angII were 12±5 pg/ml and 11±5 pg/ml, respectively (means±SD). PRC decreased significantly from baseline during administration of all three L-NMMA doses (dose 1: -16%; dose 2: -31%; dose 3: -41%), but not during infusion of saline vehicle (3%). Likewise, L-NMMA suppressed angII (dose 1: -12%; dose 2: -28%; dose 3: -30%), whereas saline vehicle did not (2%). Mean arterial pressure (MAP) increased dose-dependently.
Conclusion: Systemic inhibition of NO synthesis caused a significant dose-dependent suppression of both PRC and angII in healthy males, which is in good agreement with the role of NO as a stimulator of renin secretion. This novel finding suggests that basal renin secretion is highly dependent on NO in healthy subjects.

P26.10 Torjus Skajaa

THE BIOLOGICAL PROPERTIES OF IRON OXIDE CORE HIGH-DENSITY LIPOPROTEIN IN EXPERIMENTAL ATHEROSCLEROSIS

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Introduction: Lipoproteins are endogenous nanoparticles and the primary vehicles of lipid transportation within the body. It is well recognized that high density lipoprotein (HDL) has an important role in cardiovascular disease. We recently reported a series of nanocrystal core, HDL-like nanoparticle, that allowed multimodality imaging of atherosclerosis. In the current study we exploit fluorescent and superparamagnetic iron oxide HDL to investigate the biological properties of iron oxide core high-density lipoprotein in experimental atherosclerosis.
Methods: The nanoparticle was synthesized and extensively characterized. The

uptake of FeO-HDL in various cell lines in vitro was analyzed with imaging techniques, while uptake mechanisms and metabolism were investigated at sub-cellular detail using TEM. In vivo experiments included high resolution MRI of the abdominal aorta of apoE-KO mice. Cholesterol efflux was measured and the dynamics of lipid exchange between HDL particles were investigated.
Results: Characterization of FeO-HDL revealed this platform to closely resemble native HDL, in terms of both physical properties and cholesterol efflux capacity. In vitro experiments showed that the particles were avidly taken up by macrophages. In vivo experiments on apoE-KO mice revealed a substantial signal decrease in the liver and lesioned vessel wall on T2*- weighted MR images. Ex vivo results confirmed the presence of FeO-HDL in atherosclerotic plaques using optical imaging and TEM.
Conclusion: HDL mimicking iron oxide nanoparticles enable the multimodality investigation of receptor mediated interactions and metabolism of high density lipoproteins in cardiovascular disease.

P26.11 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: Pre-hospital diagnosis of acute coronary syndrome (ACS) enables direct admission to a department optimally suited for treatment of the individual patient. Bypassing the emergency department or other in-hospital departments, saves time from symptom onset, to initiation of optimal and advanced treatment. However, in some cases the diagnosis of acute myocardial infarction (AMI) is difficult to establish based on the ECG alone. ECG changes are dynamic and also the importance of bundle branch block myocardial infarction (BBBMI) is very difficult to evaluate based on a single ECG. BBBMI constitutes approx. 10% of MI and carries a mortality rate twice that of a STEMI patient without bundle branch block. It has been shown that only 10% of patients with BBBMI receive acute reperfusion therapy at present.
Thus, clearly we need yet another tool to supplement the ECG to improve the diagnostics of patients with heart attacks. One potential modality is pre-hospital biomarker sampling
Methods: 1000 patients transported by ambulance suspected of ACS are included. A blood sample is drawn in the ambulance and Troponin T analysis is performed by the ambulance staff. The blood sample is collected at the admitting hospital and plasma is kept at -80°C. After full inclusion, plasma samples are analyzed using a Troponin T high sensitive assay.
Evaluation: Diagnostic accuracy of the two modalities is compared. Sensitivity, specificity, positive predictive value and negative predictive value are calculated. On site time consumption in relation to blood sampling is calculated. The fraction of patients with result of ambulance analysis before arrival to the hospital is calculated.

P26.12 Michael René Skjelbo Nielsen

THE EFFECT OF LOW-DOSE N-3 FATTY ACIDS ON LEUKOTRIENE BIOSYNTHESIS IN AN OVERWEIGHT POPULATION.

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Background: Long chain n-3 polyunsaturated fatty acids (n-3 PUFA) from fish have been shown to reduce the incidence of cardiovascular morbidity and mortality. However, optimal dosage and causal effects remain unclear. Some evidence suggests that anti-inflammatory properties, partly due to inhibition of proinflammatory leukotrienes (LT), could be an important causal factor. This study aimed to investigate the acute and short term effect of n-3 PUFA in a recommended

cardioprotective dosage on proinflammatory LT levels in an adipose population, which is known to be in a state of low grade inflammation.
Methods: 50 patients with abdominal obesity were randomly assigned to receive a daily supplement of either 1 g n-3 PUFA or placebo (olive oil). Blood and adipose tissue samples were collected at baseline, after 1 day and after 6 weeks of intervention.
Findings: Samples are collected, but data are not yet analysed. Using repeated measures ANOVA, the analysis will address the question, whether LT levels (1 day and 6 weeks, respectively) is affected by the supplement with n-3 PUFA. Secondly, we will investigate, whether the content of n-3 PUFA in cell membranes and in adipose tissue are associated with LT levels, using a linear regression model.

P27.01 Adjmal Nahimi

NEUROPROTECTIVE AND ANTIDYSKINETIC MECHANISMS OF NOREPINEPHRINE IN PARKINSON'S DISEASE

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The cardinal symptoms of Parkinson's disease are effectively treated with conventional dopamine agonist therapy with the precursor of dopamine, L-DOPA, direct dopamine agonists, or a combination. However, chronic treatment with conventional dopamine agonist therapy is complicated by the manifestation of motor fluctuations, dyskinesia, and psychiatric side effects. In addition, dopamine agonist therapy does not alter the progression of the disease, and its clinical efficacy is reduced in patients with advanced disease.
The beneficial effects of conventional dopamine agonist therapy normally are attributed to its ability to restore lost dopaminergic innervation. However, L-DOPA and dopamine also are precursors of norepinephrine. In addition to high affinity for dopamine receptors, some direct dopamine agonists also show high affinities for other catecholamine receptors and transporters. In this light, synergism between norepinephrine and dopamine may account for the therapeutic potential of direct dopamine agonists. In contrast to the possible beneficial effects of norepinephrine, non-physiological increases of norepinephrine can induce L-DOPA induced dyskinesia in a similar manner as L-DOPA.
In conclusion, norepinephrine seems to play crucial but complex roles in both the beneficial and the less beneficial effects of conventional dopamine agonist therapy. In this project we will identify the mechanisms through which norepinephrine conveys these effects in an attempt to suggest treatments that may be effective in Parkinson's disease.

P27.02 Signe Groth Renvillard

NEUROPSYCHOLOGICAL IMPAIRMENT AND HIGH PREVALENCE OF PSYCHIATRIC MORBIDITY IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS

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Objectives: WHO estimates that globally 170 million people are infected with chronic hepatitis C virus (HCV). App. 75% of these people have contracted the disease by intravenous substance abuse. Impaired cognitive function is commonly found in patients infected with HCV. This may be due to a toxic effect of the virus or by neuroinflammatory processes having a damaging cerebral effect. The cognitive deficits appear in the pre-cirrhotic stage of the disease and impair in combination with a high prevalence of depression, chronic fatigue and reduced quality of life the patient's level of functioning. Furthermore, the antiviral treatment with interferon induces depression in approximately 30% of the patients. Still very little is known about the causal relationship of HCV infection, psychiatric disorders and neuropsychological deficits, but evidence has shown that these symptoms cannot solely be accounted for by a history of substance abuse. In the present study we wish to thoroughly examine cognitive impairment and psychiatric symptomatology in HCV patients in order to understand the causal relationship.
Methods: 60 HCV patients about to commence antiviral treatment will be examined

with an extensive neuropsychological assessment battery and diagnosed according to the diagnostic interview Schedules for Clinical Assessment in Neuropsychiatry (SCAN). 40 HCV patients not about to commence treatment and 30 healthy participants will serve as controls. An extensive MRI protocol will be administered on the same study group in another study (S. Hjerrild).
Results: Preliminary results will be presented delineating the cognitive function and psychiatric symptomatology of HCV patients.

P27.03 Anne Hansen

PAIN FOLLOWING STROKE: A PROSPECTIVE STUDY

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Background: Chronic post-stroke pain is an often overlooked consequence of stroke.
Aims: The objective of this study was to determine the incidence, frequency and intensity of pain at stroke onset plus 3 and 6 months after stroke.
Methods: All consecutively eligible patients admitted to the Stroke Unit at Aarhus University Hospital within two time periods were included. They were interviewed about pain prior to and at stroke onset followed by a brief examination of sensory abnormalities. Follow-up was conducted 3 and 6 months after the stroke where the patients were contacted and interviewed by phone. The pain was grouped into headache, shoulder pain, other joint pain and other pain. Only pain with onset at or following the stroke is reported here.
Results: A total of 299 patients were found eligible and included in the study. The included patients were younger than the excluded patients (mean age: 65.9 vs 71.2 years ($p < 0.0001$)) with no difference in gender ($p=0.062$). The following results are based on the 275 patients who completed the 6-month follow-up. Pain following stroke was reported by 36.7% (101/275) at stroke onset and increased to 41.1% (113/275) and 44.4% (122/275) at the 3-and 6-month follow-up. More than one pain type was reported by 4.7% of the patients at stroke onset and by 20.0% and 13.5% at 3-and 6-month follow-up. The impact of pain following stroke on the daily life of the patients was moderate to severe in 37.0% and 35% at 3-and 6-month follow-up.
Conclusion: Pain following stroke is common and may have great impact on the daily life of the patients.

P27.04 Mette Buhl Callesen

PATHOLOGICAL GAMBLING IN PARKINSON'S DISEASE

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Parkinson's disease (PD) is a neurodegenerative disorder caused by progressive loss of dopamine-producing cells in the midbrain. One way of treating PD symptoms is using dopamine agonists, which bind to the dopamine receptors in the brain. Unfortunately, for a subgroup of PD patients (6-8%) a side effect to this specific kind of treatment is developing pathological gambling (PG) (Driver-Dunckley et al., 2003; Dodd et al., 2005; Grosset et al., 2006), which is an impulse control disorder characterized by persistent maladaptive gambling behavior associated with psychosocial consequences (DSM-IV-TR, 1994).

The objective of the project is to explain the pathogenesis of the particular complication to DA in PD. In a PET study we use [^{11}C]-raclopride to determine changes in dopamine occupancy in the striatum in a baseline and an active gambling situation in testing the hypothesis that PD patients with PG release more dopamine during gambling than patients without PG. 3 PD patients with and without PG have completed participation in the study so far. The preliminary results reveal non-significant changes in binding potential in striatum, though the change in the left ventral striatum approaches the level of significance ($p<0.08$) with PD patients with PG showing a larger decrease than patients without PG. Though very preliminary, this is in accordance with the findings reported by Steeves et al. (2009), who found that the binding potential for [^{11}C]-raclopride decreases in the

striatum during gambling in both patient groups, however the decrease was significantly larger in the ventral striatum in patients with PG.

P27.05 Kartheeban Nagenthiraja

PERFORMANCE OF LINEAR AND NON-LINEAR MODELS IN PREDICTING TISSUE OUTCOME IN ACUTE ISCHEMIC STROKE

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Introduction: The early identification of tissue at risk of infarction after acute ischemic stroke may aid clinical decision-making and potentially improve long-term patient outcome. In this study we compare the performance of logistic regression (LR) and projection pursuit regression (PPR). Methods: Acute (< 12 hours) diffusion- and perfusion-weighted images were acquired in 16 acute stroke patients. Maps of isotropic DWI, ADC, T2, CBF, CBV and MTT maps were calculated and co-registered. The PPR and LR models were trained according to two strategies; a single-subject model fitted to the data of each patients and an aggregate model based on pooled data from all patients. The aggregate model was tested by a boot-strapping method. Performance was quantified by means of AUC scores. Results: For the single-subject models, PPR AUC scores were significantly better than LR. The median difference, AUC_{PPR}-AUC_{LR} was 0.0448 (IQR: 0.0332 - 0.0647: $P<0.0001$). For the aggregate models, AUC scores were 0.8067 for PPR and 0.7792 for LR, respectively. Discussion: We have presented a flexible procedure for predicting final tissue outcome combining a dimension reduction method with efficient regression modeling of the resulting low-dimensional projections using smooth non-linear ridge functions. Increase in performance was observed for PPR notably in single-subject models, while performance in data pooled across patients was similar to LR, possibly owing to increased heterogeneity. We speculate that PPR in combination with techniques for identifying homogenous patient subgroups could further improve quantification of regional risk of infarct progression.

P27.06 Tue Hartmann

PRETREATMANT MR-SCANNING IN OCD

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Several brain imaging studies report differences between OCD patients and normal controls. Most often an increase has been reported in striatum, thalamus or orbito-frontal cortex. These differences have been ascribed to a “cortico-basal ganglia circuit”, which is associated with OCD. To further approach the understanding of the function of the cortico-basal ganglia circuit in OCD, important aspects await clarification:

a. Comparison of activity in areas of the cortico-basal ganglia circuit on different cognitive tests to clarify the significance of the circuit

b. Symptom provocation using visual stimuli to differentiate between anxiety related reactions in OCD and controls

Methods: Both Structural and functional MR-imaging will be combined to investigate the

Functional magnetic resonance imaging (FMRI)-scans and clinical measures are gathered before the first cognitive behavioural sessions as well as on completion of the treatment approximately 20 weeks later to clarify the influence of the short-term effects of cognitive behavioural therapy. Clinical measures are gathered in the clinic.

Results: Preliminary results will be presented at the PhD day.

Conclusions: These are investigated before and after cognitive behavioural treatment to clarify the influence of the short-term effects of treatment.

Opposite most studies the focus will be on neuronal circuits rather than simple anatomical localisation.

The location of white matter lesions will be analysed to examine whether the OCD patients differ from the controls with respect to number or location. Special interest will be given to lesions in fibres between striatum and cortical areas.

P27.07 Kari

RECONSTRUCTION OF HERV-F(C)1, ASSOCIATED WITH MULTIPLE

Konstantin Nissen

SCLEROSIS

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The complex and still obscure etiology of Multiple Sclerosis (MS) seems to involve hereditary and environmental, probably infectious, factors alike. Human endogenous retroviruses (HERVs), inherited as mendelian genes, could be the link between these factors.

A recent association study in our group investigated association between Multiple Sclerosis and all HERVs with potential for (or close to) protein expression. This analysis revealed association in a region of chromosome X, containing HERV-F(c)1. The HERV-F(c)1 sequence contains the general retrovirus structure of LTR-elements and the three genes Gag, Pol and Env. The Env gene seems intact with an open reading frame, whereas the Gag and Pol frames are interrupted by two premature stop-codons and a frameshift mutation. Thus, we suspect that only three point mutations keep this provirus remnant from having expression potential for all three viral proteins. In order to gain more knowledge about the capacity of the virus and particles derived from it, we decided to reconstruct the potential for Gag-Pol polyprotein expression of HERV-F(c)1 by means of site-directed mutagenesis. BLAST-search comparison with other viral sequences indicated the most probable nucleotides for substitution (point-mutation) or deletion (frameshift).

The sequences for HERV-F(c)1 Gag-Pol and Env were cloned into two different expression vectors respectively. This minimizes the risk of replication competent retrovirus (RPR) production upon concurrent expression and virion production. The expression vectors allow for various future studies revealing the nature of this virus upon reactivation.

P27.08 Kristina Dupont Hougaard

REMOTE ISCHEMIC PERCONDITIONERING IN ACUTE STROKE; AN ENDOGENEOUS MODEL TO GENERATE NEUROPROTECTION.

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Background: Intravenous trombolyses with atleptase (rtPa) is the only approved treatment for acute ischemic stroke. Preventing damage in the reperfusion phase may further improve outcome. Animal studies have proven several neuroprotective methods effective resulting in smaller brain infarcts. Experimental animal studies have shown reduction of final infarct size in the brain by the method of conditioning. Remote ischemic perconditioning (r-IPer) created by stopping the blood flow to an extremity temporarily by an inflated blood pressure cuff results in release of a substance to the blood that protect the neurons during ischemia.

Aim: To estimate the size of the effect of remote ischemic perconditioning as an ad on treatment to i.v. rtPa within the 4½ h window.

Methods: A blinded randomized study. 120 patients are needed. Randomization (1:1) and treatment with r-IPer as soon as possible underway to the hospital are undertaken in ambulance by paramedics after obtaining informed content. After the acute MRI scan the final inclusion can take place. As the size of the effect is unknown, we will use multiple MRI scans and predictive models to determine the size of a potential neuroprotective effect in human brain.

Results: Until September 1th. 2010 110 patients is included. The study terminates december 2010.

Perspective: A follow-up randomized Danish or international multicenter study is planned in which the clinical effects can be documented according to the estimated effect size based on imaging. If shown effective remote perconditioning is a simple new treatment possibility of low cost.

P27.09 Mikkel Mylius Rasmussen

SCINTIGRAPHIC ASSESSMENT OF COLORECTAL MOTILITY AND EMPTYING FOLLOWING XIAOS PROCEDURE IN SPINAL CORD INJURY PATIENTS

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Background: Nerve anastomosis as a possible treatment for neurogenic bladder dysfunction has had increased attention in recent years. Special interest has been given to Xiaos procedure, where the motoric branch of the 5th lumbar nerve is anastomosed to the autonomic branch of S2 or S3 allowing L5 fibers to reinnervate into the sacral nerve, creating an artificial reflex arch. The distal part of the colon is innervated by the same segment as the bladder (S2-S4), thus simultaneous reinnervation is plausible.

The aim of this study is to investigate the effect of Xiaos procedure on colorectal motility and emptying, in patients with supraconal motoric complete spinal cord injury.

Material and methods: Patients are recruited via file review. Xiaos procedure is done at the Neurosurgical department. Patients undergo scintigraphic assessment pre- and postoperatively. In this procedure patients swallow a small amount of radioactive substance (^{111}Indium). The radioactivity in each colonic segment is measured by a gamma counter, and data allow us the following three substudies:

1) Colorectal motility and emptying in patients with supraconal spinal cord injury

2) The effect of Xiaos procedure in colorectal motility following continuous cutaneous stimulation

3) Colorectal emptying following Xiaos procedure

Perspectives: The treatment possibilities of Xiaos procedure concerning neurogenic bowel dysfunction in spinal cord injury patients will be enhanced. Further, this will contribute to an ongoing debate of this procedures role in relation to the care for this and other patient groups with neurogenic bowel dysfunction, for example spina bifida patients.

P28.01 Jacob Mørup Schlütter

THE NUMBER OF FETAL CELLS IN MATERNAL BLOOD IS ASSOCIATED TO EXERCISE AND FETAL GENDER

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Introduction: We have established a robust method to specifically identify and isolate a placental fetal cell in maternal blood (fcmbs) at a gestational age of 12 weeks. The concentration of these cells, however, varies considerably among pregnant women (median 3 fcmbs/30 mL blood, range 0-18), which is a challenge for the implementation of the method for prenatal diagnostic purposes. We conducted a study to identify factors influencing the number of fcmbs at a gestational age of 11-14 weeks.

Methods: 59 pregnant women at weeks 11-14 were included, and information about lifestyle and daily activity was obtained by a questionnaire and a structured interview. The number of fcmbs was assessed in 30 mL blood processed by a proprietary method developed in-house. Fetal cells in the blood, binding to fetal cell specific antibodies, were initially isolated by magnetic cell sorting. The fetal cells were then stained with a cocktail of fetal cell-specific antibodies, identified and counted.

Results: Participants carrying male fetuses had higher median number of fcmbs per 30 mL blood than those carrying female fetuses (5 vs. 3, p=0.006). Exercise within 3 hours (1.5 vs. 4, p=0.02) and 24 hours (2 vs. 4, p=0.06) decreased the number of fcmbs, whereas coitus the evening before increased the number (4 vs. 3, p=0.11).

Conclusion: The number of fcmbs is affected by normal activities. This should be taken into account when planning collection of fetal cells in connection for prenatal diagnosis. The association of fetal gender might reflect yet unknown aspects of placentation.

P28.02 Tina Rask

IS IMATINIB MESYLATE AN EFFECTIVE TREATMENT OF NEPHROGENIC

Elmholdt

SYSTEMIC FIBROSIS? AN OPEN-LABEL CLINICAL TRIAL

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Purpose: To investigate if patients with medium to severe nephrogenic systemic fibrosis (NSF) have a beneficial effect of imatinib mesylate (Glivec) treatment.
Methods and materials: We included patients diagnosed with NSF and with a modified Rodnan skin score => 20 or with a progression of disease either in the skin or in the inner organs. We excluded patients with elevated alanine aminotransferase (ALAT) and/or severe heart disease (NYHA class III or IV). Our primary endpoints were fibrosis in the skin and the mobility of the joints, evaluated by modified Rodnan skin score and extension/flexion degree. Secondary endpoints were histological changes in the skin biopsies and changes in Daily Life of Quality, evaluated by pathological examination and DLQI schema.
Results: 4 patients have until now been included in the project. 1 patient experienced neutropenia, 1 patient urticaria and 1 patient diarrhea and fever, and 1 dropped out because of a longer lasting hospitalization with vomiting and sub febrile. All 4 patients had a reduction in dosage from the initial 400 mg/day, 3 patients to half the dosage equalizing 200 mg/day and 1 patient to 100 mg/day. But even with a reduced dosage some improvement of joint movement and softening of the tethering of the skin as well as a reduction in pain was registered.
Conclusion: Imatinib mesylate may be an effective treatment for moderate to severe NSF. This is suggested in two former studies, where a beneficial effect of imatinib mesylate was observed. In these studies a recurrence of symptoms was registered shortly after imatinib mesylate had been discontinued. We will follow our patients to observe how long the effect lasts in our patients.

P28.03 Lise Juul

INVOLVEMENT OF NURSES IN TYPE 2 DIABETES CARE IN DANISH GENERAL PRACTICE

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Introduction
More tasks in Danish general practices are provided by nurses. To what extent nurses provide consultations to patients with type 2 diabetes, and whether it has consequences for the quality of diabetes-management are unknown. Accordingly, the aims of this study are
1) To describe the extent to which nurses in Danish general practices provide consultations to patients with type 2 diabetes, and
2) To assess the difference between a) the mean proportions of type 2 diabetes-patients with measurements performed according to guidelines and b) the mean values of HbA1c and cholesterol among the patients - dependent on different levels of nurse involvement in the practices.
Methods: In August 2009, 193 of 263 general practices from the former county of Aarhus completed a questionnaire encompassing the following questions: “Number of nurses employed in the general practice” and “Among patients with type 2 diabetes participating in a diabetes consultation during the last year, how many percentages participated in a consultation provided by a nurse?”
Patients with type 2 diabetes, registered with the practices, were identified in the “Aarhus Diabetes Database”.
We plan to estimate the proportions of patients with type 2 diabetes with at least - one measurement of HbA1c and - one measurement of cholesterol during the period of 90 days before and - after the practices completed the questionnaires.
Furthermore, we plan to estimate the mean values of HbA1c and cholesterol among the patients in the practices. The estimates will be compared between practices depending on different levels of nurse involvement in type 2 diabetes care.
Results: The results will be presented on PhD-day.

P28.04 Ole Halfdan Larsen

KAOLIN ACTIVATED THROMBOELASTOGRAPHY FAILS TO DISTINGUISH DILUTIONAL COAGULOPATHY FROM THROMBOCYTOPENIA

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Thromboelastography (TEG/ROTEM) is a commonly used guidance tool in the management of transfusion therapy. This study investigated the diagnostic capacity of kaolin activated whole blood (WB) vs. a panel of TEM-reagents distinguishing: Dilutional coagulopathy, thrombocytopenia, hyperfibrinolysis and heparin. Consequent treatment strategies were compared based on published algorithms. Blood samples were drawn from healthy volunteers (n=11). Dilutional coagulopathy was generated by 50% dilution with hydroxyethyl starch 130/0.4. WB thrombocytopenia (mean platelet count 20x109/L) was induced using a validated model. Hyperfibrinolysis and heparin contamination was generated by addition of t-PA 2 nM and unfractionated heparin 0.1 U/mL, respectively. Coagulation tests were run on ROTEM Delta using proprietary reagents. In kaolin activated WB there were no significant differences between dilutional coagulopathy and thrombocytopenia. Hyperfibrinolysis specifically disclosed an increased maximum lysis (ML, >38%), and heparin was distinctly different as evaluated by a prolonged clotting time (CT, all $p<0.02$). All coagulopathies were readily distinguishable using a panel of TEM-reagents. In particular, dilutional coagulopathy was separated from thrombocytopenia by fib-TEM (MCF, $p<0.001$). The algorithm using kaolin would suggest intervention with platelets in all cases of dilutional coagulopathy, while the algorithm based on a panel of reagents would conclude to use fibrinogen. In conclusion, the sole use of kaolin fails to distinguish dilutional coagulopathy from thrombocytopenia, and algorithms based on kaolin may lead to unnecessary transfusion with platelets.

P28.05 Chris Bath Søndergaard

STEM CELL THERAPY OF SEVERE CORNEAL DISORDERS: TRANSCRIPTOME ANALYSIS OF DISCRETE CORNEAL SUBPOPULATIONS AND DEVELOPMENT OF ANIMAL ORIGIN FREE (AOF) CULTURE SYSTEMS

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Background: Corneal blindness can be caused by limbal stem cell deficiency (LSCD), which is characterized by dysfunction or depletion of the limbal epithelial stem cells (LESCs) residing in limbus next to the cornea. Since 1997 experimental transplantation of ex vivo expanded LESCs has been performed on hundreds of patients suffering from LSCD worldwide.

Hypothesis: Laser Capture Microdissection and RNA-seq of discrete subpopulations of human corneal epithelial cells, niche cells, and conjunctival cells can reveal specific stem cell markers and increase knowledge about stem cell biology of the ocular surface. This knowledge enables development of new AOF culture systems, which will be safer and more efficient for transplantation than current techniques.

Materials and Methods: Human corneas will be flash-frozen. Serial cryosections (10mm) will be counterstained. Interactive 3D computer models will enable precise selection of individual cells to be captured by Laser Capture Microdissection. In parallel, 1 mm2 explants will be cultured on inactivated feeder cells, including 3T3 cells and human foreskin fibroblasts. Different substrates/carriers will be tested along with hypoxic growth conditions. Medium composition will be optimized for AOF cultures. RNA integrity will be assessed using the Agilent Bioanalyzer. Transcriptomes of individual LCM captured cells and culture systems will be compared using RNA-seq and bioinformatics.

Perspectives: This study will increase knowledge about the stem cell biology of ocular surface. It will directly procure cell material for future transplantation to Danish patients and will be a cornerstone for future bioengineering of cornea.

P28.06 Trine Borup

PREDICTION OF RENAL FUNCTION (GFR) FROM CYSTATIN C AND

Andersen

CREATININE IN CHILDREN: BODY CELL MASS INCREASES ACCURACY OF THE ESTIMATE.

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Aim: To derive an accurate prediction model for estimating glomerular filtration rate (GFR) in children based primarily on the endogenous renal function marker cystatin C (CysC) and body cell mass (BCM).

Theory: Cystatin C is produced at a constant rate in all cells of the body and is excreted by glomerular filtration followed by catabolization in the tubular cells. We hypothesized that production rate is proportional to body cell mass (BCM) and inferred GFR (mL/min) to be proportional to BCM/CysC.

Materilas and methods: GFR was determined with 51Cr-EDTA-clearance in 131 children (52 girls, 79 boys) aged 2-14 years. GFR was 14-147 mL/min/1.73m2. BCM was estimated using bioimpedance spectroscopy. Log-transformed data on BCM/CysC, serum creatinine (SCr), body-surface-area (BSA), height×BSA/SCr, CysC, weight, sex, age, height, serum urea and albumin were considered possible explanatory variables using regression in a forward, stepwise procedure. GFR (mL/min) was the dependent variable. The accuracy and precision of the prediction model were compared to other prediction models from the literature, using k-fold cross-validation. Local constants and coefficients were calculated for all models.

Results: New prediction equation GFR (mL/min) = 10.2×(BCM/CysC)^0.40×(heightxBSA/SCr)^0.65 could predict 99% within ±30% of reference GFR, and 67% within ±10%. This was higher than all other equations. The present equation also had the highest R2 (96%).

Conclusion: The new equation predicts GFR with higher accuracy than other equations. Endogenous methods are, however, still not accurate enough to replace exogenous markers when GFR must be determined with high accuracy.

P28.07 Mie Hessellund Samson

TREFOIL FACTOR FAMILY PEPTIDES IN HUMAN CYCLICAL CERVICAL MUCUS. METHOD EVALUATION AND RESULTS.

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Background: Trefoil peptides are 7-12 kDa molecules, secreted by a variety of mucin-producing epithelial cells from different tissues. The peptides are believed to be essential for protection and maintenance of gastrointestinal mucosa and may be able to influence the viscosity of secretions. Data on concentrations of trefoil peptides in secretions are limited.

Methods: We validated in-house ELISA assays, developed for measurements of trefoil peptide concentrations (TFF1, TFF2 and TFF3) in serum, for use with cervical mucus. Cervical mucus as well as blood collected three times during the menstrual cycle from healthy women (n=18), were subsequently analyzed.

Results: Recovery of all three trefoil peptides in the initial supernatants was 92 % or more. Recovery of exogenously added trefoil peptides was 95 % ore more. Western blotting showed that antibodies used in the TFF3 ELISA assay recognised one molecule of the same size as TFF3. Median (range) concentrations of TFF1, TFF2 and TFF3 were 2.7 (0.28-11), 0.58 (0.05-11) and 430 (58-1400) nmol/g protein with a significant decrease in concentrations after ovulation. Serum levels resembled previously measured values in blood donors and showed no cyclic change.

Conclusions: Cervical secretion contains the highest concentration of TFF3 ever recorded in biological fluids. Concentrations of all three peptides showed cyclic changes with peak values around the time of ovulation.

P29.01 Christian Dalgas

THE EFFECT OF FREE FATTY ACIDS ON AMINOOXYACETATE INDUCED CARDIOPROTECTION.

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Introduction: We have previously demonstrated that preischemic inhibition of the malate-aspartate shuttle (MA-shuttle) by aminooxyacetate induces cardioprotection in glucose only perfused rat hearts. The aim of this study is to investigate the effect of free fatty acids (FFA) on AOA-mediated cardioprotection.

Methods: Rat hearts are isolated and perfused with a modified Krebs-Henseleit buffer consisting of 11 mM glucose, 3% bovine serum albumine and FFA (palmitate) in various concentrations. AOA is administered 5 min prior to ischemia. Hearts are allocated into 5 groups (n=10 in each): 1) Control, 0 mM palmitate 2) 0.4 mM palmitate 3) 1.2 mM palmitate 4) 0.4 mM palmitate, 0.1 mM AOA 5) 1.2 mM palmitate, 0.1 mM AOA. Hearts are subjected to 30 min global no-flow ischemia followed by 120 min reperfusion. Infarct size and left ventricular function are evaluated. Concentrations of glutamate, lactate and pyruvate are measured in coronary effluent. Glucose oxidation is determined using radioactive tracers.

Preliminary results: Groups 2 and 3: 1.2 mM palmitate caused a significantly higher infarct size than 0.4 mM palmitate (80.6±3.2% vs. 62.7±4.6%, $p<0.005$). This was associated with an attenuated postischaemic hemodynamic recovery in terms of maximal left ventricular developed pressure (12.0±1.6 vs. 26.1±3.5 mmHg, $p<0.005$)

Conclusion: Preliminary data suggest that high concentration of FFA have a negative impact on both post-ischemic haemodynamic recovery and infarct size.

P29.02 Hjördis Osk Atladõttir

NEONATAL COMPLICATIONS AND AUTISM SPECTRUM DISORDERS

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Background and aims: Autism spectrum disorders (ASDs) are disorders of neural development characterized by impaired social interaction and communication, and by restricted and repetitive behavior. Only few previous studies have investigated neonatal factors and the risk for ASDs.
Methods: A Danish population based cohort study, including all children born in Denmark from 1994, through 2002, a total of 604,140 children. Diagnoses of neonatal complications were retrieved from the Danish National Hospital Register. Children diagnosed with ASDs were identified using the Danish Psychiatric Central Register. Data was analyzed using Cox proportional hazards regression.
Results: A total of 4,145 children were diagnosed with ASDs. We found an increased risk of ASDs after exposure to a variety of neonatal complications; respiratory distress: adjusted hazard ratio (aHR)=1.30 [95% confidence interval (CI): 1.13-1.49], intracranial bleeding, cerebral edema or seizures: aHR=2.33 [95% CI: 1.72-3.16], neonatal hypoglycemia: aHR=1.50 [95% CI: 1.27-1.77], and neonatal infection: aHR=1.47 [95% CI: 1.25-1.73].
Conclusions: Different neonatal complications are likely to cause neurological damage and alter brain development, and hence increase the risk of ASDs. This effect seems to be mediated through different pathways including lack of oxygen, glucose, and possibly through activated immune function during early neonatal life.

P29.03 Mirela Dzeko

IPSILATERAL VERSUS DIAGONAL ASSESSMENT OF PULSE WAVE VELOCITY IN THE LARGE ARTERIES: IS THE RESULT DIFFERENT?

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Background

Patients with end stage renal disease (ESRD) suffer from a high risk of cardio-vascular disease (CVD), and CVD mortality is markedly above what is seen in the general population. This is partly due to increased arterial stiffness, which is well-known among ESRD patients. Indices of central arterial stiffness, derived by use of applanation tonometry, have shown to be strong independent predictors of cardiovascular morbidity and mortality. Applanation tonometry is a non-invasive method for assessment of the cardio-vascular function based on pulse-wave analysis (PWA) and estimation of pulse-wave velocity (PWV). Current methodology in PWV assessment dictates ipsilateral measurements. Anatomically there is a small difference in the way the carotid arteries branch from the aorta between the right and left side of the neck, and theoretically this could lead to a different PWV value.

Aim

It is our aim to elucidate (1) if PWV results rely on which side of the neck is chosen for measurement in healthy individuals and (2) the inter-observer reproducibility in our laboratory concerning PWV, PWA and heart rate variability (HRV).

Methods

50 healthy individials without known cardio-vascular disease including hypertension or prescription of antihypertensive medications, aged 18-70 years, are enrolled and examined once by two different observers in a random order. PWA, PWV and HRV are measured using SphygmoCor© equipment. PWV will be performed both ipsilaterally and diagonally with use of the same femoral artery in both cases.

P29.04 Peter Bondeven Petersen

POST-OPERATIVE QUALITY ASSESSMENT IN PATIENTS WITH RECTAL CANCER BY MRI OF THE PELVIS

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BACKGROUND: Management of rectal cancer has changed significantly over the last 20 years and as a result improvements in outcome has been confirmed. Magnetic resonance imaging (MRI) has excellent soft tissue contrast enabling superior depiction of pelvis structures in rectal cancer and recurrent rectal cancer. This study aims to determine whether it is possible to use post-operative MRI of the pelvis as a tool in quality assessment of rectal cancer surgery to supplement the histopathological evaluation.

METHODS: MRI of the pelvis was performed in 56 patients identified from a population of 118 surgically treated with total mesorectal excision (TME) or partial mesorectal excision (PME) since August 2007. Two experienced multidisciplinary team (MDT) radiologists evaluated images with regard to residual mesorectal fatty tissue and height of anastomosis. Histopathological records, standardized photos and clinical records were assessed. Pathology and MRI were evaluated independently, blinded to the other and then compared.

RESULTS: Evidence of residual mesorectal fatty tissue was identified in 43% of patients. With PME a high 57% of cases, primarily owing to coning of the specimen. Insufficient distance from tumour to anastomosis was suggested in 79% of patients treated with PME. Pathological assessment documented absent mesorectal fatty tissue in 46% of cases and correlates well to those found by MRI.

CONCLUSION: Our data support earlier work by depicting residual mesorectal fat in 43% of patients by MRI. MRI is a useful tool in quality assessment of rectal cancer surgery and pathology by focusing on the tissue left behind as opposed to tissue taken out.

P29.05 Ninna Sønderby Lund

METALLOTHIONEINS AND BETA CELL FUNCTION DURING GLUCOSE OR PALMITATE STRESS

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Background and aims: Metallothioneins (MT) are metalloregulatory proteins partly controlling zinc metabolism. MT are important for the regulation of pathophysiological processes depending on zinc and the processes during which oxidative stress mobilizes zinc. ß-cells depend on zinc ions for insulin storage and secretion. The aim of this study was to investigate the effects of MT on insulin secretion, gene expression of the apoptosis-regulating genes Bax and Bcl-2 as well as the expression of the zinc transporting protein ZnT3.

Materials and methods: Glucose sensitive INS-1E cells were examined after exposure to varying doses of glucose or palmitate for 24h with or without MT. Gene expressions of Bax, Bcl-2 and ZnT3 were investigated by RT-PCR, ZnT3 protein level was investigated by Western Blotting and insulin secretion and content were determined by ELISA.

Results: During basal conditions MT decreased insulin secretion but MT increased the insulin secretion during stress. The Bax/Bcl-2 ratio was decreased by MT during glucose stress. ZnT3 gene expression was increased by MT after palmitate but decreased by MT at basal conditions and the ZnT3 protein density was partly decreased by palmitate.

Conclusion: Manipulating intracellular zinc metabolism by exogenous MT influence insulin secretion, the expression of zinc transporting proteins and genes related to apoptosis in a complex manner. Exogenous MT seem to favour an enhanced insulin secretion during stress and may affect the expression of apoptotic genes in a favourable direction. Induction of MT may favourably influence beta cell function and survival, a complex mechanism of action involving also ZnTs needs clarification.

P29.06 Janus Adler Hyldebrandt

RIGHT VENTRICLE PHYSIOLOGY, METABOLISM AND PHARMACOLOGICAL RESPONSE IN HEALTHY NEWBORN PIGS IN ASSOCIATION WITH RIGHT VENTRICULAR ISCHEMIA, HYPERTROPHY AND DILATATION

Synopsis of a ph.d. protocol.

Background: During birth and in the neonatal period the heart undergoes changes in terms of metabolism and physiology. Inotropic support to the failing newborn heart is therefore significantly different from adult cardiac failure. Further, newborns most often experience right ventricle failure in contrast to adults. Phosphodiesterase III (PDE III) inhibitors like milrinone are used in all age groups, but have not been specifically evaluated in the newborn. Investigations will be carried out to elucidate the response to milrinone in the failing dilated, hypertrophic and ischaemic right ventricle.

Hypotheses: 1) Haemodynamic responses to milrinone differs in potency and quality between the mature and immature myocardium, ischaemic and non-ischaemic myocardium, dilated and hypertrophic myocardium. 2) Expression and activity of PDE III in the myocardium is related to the hemodynamic response seen in milrinone treated animals. 3) Milrinone combined with catecholamines exerts different metabolic changes in the myocardium, dependent on age and type of heart failure.

Method and materials. A biventricular conductance catheter model, with simultaneous microdialysis of the myocardium will be used to study the hemodynamic and metabolic responses to milrinone and catecholamine treatment. Animal models for producing dilated and hypertrophic right ventricle failure exist. Expression and activity of PDE III in myocardium and vessel tissue will be analysed using western blot and colorimetric assay.

Perspectives: Knowledge from this study is mandatory in order to describe the unique features of the failing newborn heart, with due respect to physiology and

metabolism.

P29.07 Johan Frederik Berg Arendt

HOW TO EXPLAIN AN ELEVATED LEVEL OF PLASMA VITAMIN B12

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Introduction: Surprisingly around 15% of all samples analysed for plasma cobalamin (Cbl, Vitamin B12) show a value above the reference interval of 200-600 pmol/L.

Aim: We hypothesize that an unexpected 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 aim to include blood samples from 200 patients with plasma Cbl: <200, 200-600, 601-1000 and >1000 pmol/L. We exclude patients in Cbl supplementation therapy and non-hospital treated patients. In-house ELISAs are used for measurement of HC and TC. Clinical data is collected from the electronic systems of Region Midt (SUP/E-journal).

Results: Preliminary results show HC values above the interval of reference of 240-680 pmol/L in patients with high Cbl (>1000 pmol/L, n=51) (HC levels: Mean 1245 pmol/L 95% CI: 942-1548 pmol/L) and that both total TC and HC is significantly higher than in patients with both normal Cbl (200-600 pmol/L, n=120) and low Cbl levels (<200 pmol/L, n=120). Seventeen (33%) of the patients with Cbl>1000 pmol/L had chronic alcoholism and 8 (16 %) had diseases of the kidney.

Conclusions: Our preliminary results suggests an increased level of HC to be the major cause for an increased level of plasma Cbl and suggests the most common cause for such an elevation to be related to chronic alcoholism.

P29.08 Linn Berger Håkonsen

DOES WEIGHT LOSS IMPROVE SEMEN QUALITY AND REPRODUCTIVE HORMONES?RESULTSFROM A COHORT OF SEVERELY OBESE MEN

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Introduction: A high body mass index (BMI) has been associated with poor semen quality and altered reproductive hormones. Whether this is related to obesity itself or the underlying causes of obesity is unknown but weight loss studies may help disentangle these two hypotheses. The aim of this first prospective cohort study, is to see if weight loss improves semen characteristics.

Materials and methods: Men with BMI > 33 kg/m2 were included when they participated in a weight loss program lasting from 12 to 16 weeks. Semen samples were collected at baseline (n = 41) and after the weight loss program (n = 27). Semen samples were analyzed according to WHO criteria (1999), and sperm DNA integrity was analyzed by the sperm chromatin structure assay (SCSA).

Results: The mean age was 33.8 years (range:18-60 years). BMI was negatively associated with sperm concentration (p=0.02), total sperm count (p=0.02), normal sperm morphology (p=0.04) and sperm motility (p=0.005). The median weight loss

was 22 kg (range: 4-39 kg). The percentage weight loss correlated positively with an increase in total sperm count (p=0.02) and semen volume (p=0.04). The group with the largest weight loss had a statistically significant increase in total sperm count [193 millions (95% CI: 45, 342)] and normal sperm morphology [95% CI: 4% (1, 7)]. Conclusion: These results suggest that obesity have a negative effect on spermatogenesis, and it may be possible to diminish this effect by loosing weight. Whether this is due to a reduction in fat tissue or better nutrition and more exercise is, however, not known and in recognition of the limited power of the study, the findings should be replicated in larger cohorts.

P29.09 Majbritt Jeppesen

INTERNETBASED INTERACTIVE DECISION SUPPORT IN THE TREATMENT OF TYPE 2 DIABETES

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Background
The prevalence of type 2 diabetes is rapidly rising. Type 2 diabetes increases the risk of cardiovascular disease, nephropathy, neuropathy, retinopathy, amputation, and infections. However, high-quality treatment of type 2 diabetes can reduce the risk of these complications considerably. Interactive health communication has a positive effect on treatment outcome, patient satisfaction, and the health services' organisation and quality. There is, however, little evidence concerning the usage and effect of interactive IT systems in the treatment of chronic illnesses such as type 2 diabetes, all though large scale implementation is planned.
Aim
The aim of the study is to evaluate the present quality of treatment in a cohort of patients with type 2 diabetes in Region Midtjylland. Furthermore to identify patients in suboptimal treatment and evaluate their ability and motivation to participate in Internet based interactive diabetes decision support.
Method
The study is based on register data and questionnaire data collected from a cohort of 12,000 patients with type 2 diabetes between 40 and 70 years of age identified in the Aarhus Diabetes Database. Measurement frequency and levels of glycated haemoglobin and cholesterol are analysed. Standardized and validated instruments for measuring diabetes literacy, IT skills, patient motivation and activation are used.
Perspective
The study will document the quality of treatment of type 2 diabetes in a Danish cohort and will contribute with new knowledge to be used in the implementation of patient targeted IT systems.

P29.10 Pall Karlsson

DETERMINATION OF INTRAEPIDERMAL NERVE FIBER DENSITY AND SMALL FIBER FUNCTION IN HEALTHY MEN AND IN PATIENTS WITH NEUROPATHY

Malfunction of nerves in the peripheral nervous system is called peripheral neuropathy. Peripheral nerves process sensory information from small sensory nerve fibers in the epidermis and dermis of the skin to the central nervous system. Patients with peripheral nerve disorders often have allodynia associated with sensitization of damaged nociceptors. The relationship between the sensory profile as determined by Quantitative Sensory Testing (QST) and nerve fiber density is not known. Neuropathic patients can use 8% capsaicin dermal patch for pain relief with a risk for functional depletion of neurons in the epidermis.
The overall perspective of the study is to compare structure and function in the somatic sensory nervous system by comparing small fiber function with biopsies taken from the skin in normal subjects and in patients with small fiber neuropathy - a decrease of small fibers in the epidermis. 3 mm skin biopsies will be taken, fixed, frozen down and 50µm sections cut and stained against Protein-Gene-Product 9.5 using immunohistochemistry. Three ways of quantifying nerve fibre length with 3-D stereological sampling techniques will be tested. We will compare the length density of the nerve fibers between healthy individuals and neuropathy-patients. Finally, we

will subject healthy volunteers to one 60 min topical exposure to 8% Capsaicin on the thigh, using the contralateral thigh as a control. Sensation test using QST and skin biopsies will be carried out in the same area at week 1, 4 and 12 and the nerve fiber density determined and compared between time points and sites to investigate the time course of depletion of the fibers and sensibility.

30.01 Tanja Tvistholm Sikjær

REDUCED MUSCLE STRENGHT IN PATIENTS WITH LONG STANDING HYPOPARATHYROIDISM COMPARED TO HEALTHY CONTROLS.

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BACKGROUND: Hypoparathyroidism(HypoPT) is known to be associated with varies complains of muscle aches, fatigue and a reduced endurance despite standard treatment.
Receptors for both PTH and calcium have been identified in muscular tissue. Intracellular calcium plays an important role in muscle contraction.
AIM: To perform a cross-sectional study of patients with HypoPT compared with healthy controls focusing on muscle strength and balance.
METHODS: 39 patients with HypoPT were compared with 39 age- and gender-matched healthy controls randomly selected from CPR register.
Max. voluntary force was performed on the dominant leg using a dynamometer. Measurements were performed on the knee extensors and flexor of the dominant leg with the knee in 90° and 60° flexion. Maximal voluntary contraction (MVC) is estimated as the best of three measurements given in Newton (N). In addition, grip strength and strength at elbow extension and flexion was measured using the same equipment. Balance function was assessed by measuring dynamic stability using a stadiometer.
RESULTS: Patients and healthy controls were well matched by age (median 59, range 32-79 years) and gender (85 % females). MVC was significantly lower in HypoPT compared with healthy controls in both flexion and extension at 60°($P<0.005$). At 90° flexion, only extension MVC was decreased in patients compared with controls ($P<0.005$). However, MVC at elbow extension, flexion and hand grib did not differ between groups and neither did postural stability.
CONCLUSION: Our study showed a significantly lower MCV at both extension and flexion of the knee in patients with HypoPT compared with healthy controls.

30.02 Magdalena Julia Dabrowska

IMPACT OF GROWTH FACTOR INDEPENDENCE 1 IN HUMAN T-CELL LYMPHOMAS; PATHOGENIC POTENTIAL IDENTIFIED BY INSERTIONAL MUTAGENESIS IN A MURINE T-CELL LYMPHOMA MODEL

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The transcriptional repressor and oncogene Gfi1 has a major oncogenic potential and is aberrantly expressed in murine lymphomas and several human cancers. Gfi1 is a 55 kDa protein containing six C2H2 zink finger motifs and a SNAG domain, making Gfi1 a nuclear protein responsible for transcriptional repression. In a mouse model for T-cell lymphoblastic lymphoma, Gfi1 is frequently activated, indicating that it is essential in development of these tumors. In human cancers, Gfi1 protein expression has been observed in several cases but no knowledge exists on how Gfi1 contributes to initiating and maintaining human T-cell lymphomas.
Localization and expression patterns of the Gfi1 protein was determined in normal mouse tissue and mouse T-cell lymphomas by immunohistochemical staining with Gfi1 and with nuclear/cytoplasmic fractioning of the tissue and tumors with subsequent immunoblotting.
In normal mouse tissue, a 50 kDa Gfi1 protein was detected in the cytoplasm, whereas in the mouse T-cell tumors and T-cell lines, Gfi1 proteins of 35kDa, 50 kDa and 55kDa were observed in both cytoplasm and nucleus. Staining of normal

human tonsil tissue demonstrated a 50kDa and 55 kDa Gfi1 protein in the cytoplasm and a 50 kDa and 35 kDa Gfi1 protein in the nucleus. In human T-cell lines, Gfi1 was detected at 50 kDa in the cytoplasm whereas additional 35 kDa and 55kDa proteins were found in the nucleus.
Our data shows that more Gfi1 variants and nuclear Gfi1 expression are observed in malignant samples. We hypothesise that regulation by Gfi1 may include shuttling between cytoplasm and nucleus and that lymphomagenesis enables unlimited nuclear access of one or more protein variants.

30.03 Vivien Schack

A REDUCED PHOSPHORYLATION RATE ACCOUNTS FOR THE FUNCTIONAL DISTURBANCE OBSERVED FOR SEVEN NA+,K+-ATPASE MUTATIONS ASSOCIATED WITH THE NEUROLOGICAL DISORDER: FAMILIAL HEMIPLEGIC MIGRAINE TYPE-2 (FHM-2)
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The Na+,K+-ATPase was recently found to be associated with two neurological disorders: Rapid-Onset Dystonia Parkinsonism (RDP) and Familial Hemiplegic Migraine type-2 (FHM-2). So far, we know of 9 RDP-causing mutations in the α3 isoform of Na+,K+-ATPase, and >40 mutations in the α2 isoform that give rise to FHM-2. The pathophysiological mechanisms underlying the development of RDP and FHM-2 have remained elusive. Both α3 and α2 isoforms of Na+,K+-ATPase are localized in the brain, but they are expressed in separate cell types. While α3 is predominating in neurons, α2 is the abundant form in glia cells, where it is believed to contribute to clearance of extracellular K+. Here we present functional data for 9 FHM-causing mutations. All of the investigated mutants exhibit a decrease in the catalytic turnover of the pump. A major functional alteration of these mutations was a significant decrease in the rate of phosphorylation of the E1Na3 form as detected in rapid kinetic studies at 25 °C. The Na+ affinity of the FHM-associated mutants was on the other hand found to be wild type-like, which is in contrast to the severe decrease in Na+ affinity induced by the RDP-causing mutations studied so far. Because of the possibility that K+ clearance is reduced in FHM, the K+ affinity of the FHM-mutants was investigated in two different functional setups, demonstrating wild type-like affinities for most of the mutants. One mutant showed a slight reduction in the affinity for K+; nevertheless, this effect was not large enough to account for the development of FHM. Hence, the disease-causing enzymatic defect for the mutations studied is likely the reduced phosphorylation rate.

30.04 Jimmi Søndergaard

INTER- AND INTRA-FRACTION MOTION OF THE BLADDER TUMOR BASED ON PERITUMORAL LIPIODOL INJECTIONS IN THE BLADDER WALL.
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Purpose: We have tested a procedure of focal injection of the contrast medium Lipiodol as a fiducial marker for image-guided boost of the tumor in bladder cancer radiotherapy (RT).In this study, we have evaluated the feasibility and the safety of the method as well as the inter- and intra-fraction shift of the bladder tumor.
Materials and methods: Five patients with muscle invasive urinary bladder cancer were included in the study. Lipiodol was injected during flexible cystoscopy into the submucosa of the bladder wall at the periphery of the tumor or the tumor-bed after resection of the bladder. Cone-beam CT (CBCT) scans were acquired daily throughout the course of RT. Automated matches on the pelvic bones as well as the Lipiodol spots were preformed in Varian OBI software (OBI v.1.4, Varian Medical System, Palo Alto (CA)).
Results: Lipiodol demarcation of the bladder tumor was feasible and safe with only a minimum of side-effects related to the procedure. The Lipiodol spots were visible on CT and CBCT scans for the duration of the RT course. After match on the pelvic bones more than half of all the treatment fractions required a geometric shift of 5

mm or more to match on the Lipiodol spots. The mean intra-fraction shift (3D) of the tumor was 3 mm, largest in the anterior-posterior and cranial-caudal directions. Conclusion: This study demonstrates that Lipiodol can be injected into the bladder mucosa and subsequently visualised on CT and CBCT as a fiducial marker. The inter-fraction shifts in the positions of the Lipiodol spots indicates that image-guided RT based on radio-opaque markers is important for RT of the bladder cancer tumor.

30.06 Anders Jensen

MICROBIAL DIVERSITY OF INFECTED AND HEALTHY TONSILS

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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. Tonsillitis is a common infection of the palatine tonsils especially in children and adolescents and is caused by both viruses and bacteria. Bacterial tonsillitis is mainly caused by b-haemolytic streptococci, especially group A streptococci. In addition, anaerobic and yet uncultured bacteria also seem to cause tonsillitis. The reason why some individuals are more prone to tonsillitis is not fully understood. Exposure to pathogens and differences in the innate immune system may be a part of the explanation. Furthermore, variations in the normal microbial flora on the tonsils and especially in the tonsilar crypts may be an explanation. 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 using using 454 pyrosequencing. With this technique an almost complete characterization of the bacterial community can be made. Results will be presented at the phd-day. The results will give 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.

30.07 Ivana Konvalinka

NEURAL OSCILLATIONS OF INTERPERSONAL COORDINATION: DUAL EEG AND MEG STUDIES OF JOINT TAPPING

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Interpersonal coordination involves the coupling of perception and action from two or more individuals. However, the neural mechanisms underlying the coordination of these subsystems have mainly been studied in isolated brains (Sebanz et al., 2006). In order to investigate differences in oscillations when coordinating with another person who is responsive, compared to a non-responsive computer, we set up a dual EEG experiment, recording 32-channel EEG simultaneously from both members of a pair. 9 pairs of participants were recruited and asked to maintain a given beat while synchronizing with an auditory signal coming from either the other person or the computer, by tapping with their right index finger. They were informed prior to each trial which auditory feedback they would be receiving. Behaviourally, we found that the pair became a coupled mutually and continuously adaptive unit of two hyper-followers when they could hear each other, with their inter-tap intervals oscillating in opposite directions on a tap-to-tap basis (Konvalinka et al., 2010). Time-frequency analysis revealed a higher decrease in oscillatory power in the 10 Hz range during preparatory tempo setting and during tapping when coordinating with the other person compared to the computer. The

topography of this component was distinct from motor-related mu-suppression (Neuper et al., 2006) as well as the phi complex (Tognoli et al., 2007), with maxima in the left-frontal, right-medial frontal, and left motor electrodes. Preliminary results suggest that this component may be a marker of social attention, but further analysis is required to investigate this.

30.08 Stine Christensen

SORLA REGULATES LIPOPROTEIN LIPASE ACTIVITY BY INTRACELLULAR TRAFFICKING

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Many different tissues and cell types exhibit regulated secretion of Lipoprotein Lipase (LpL). However, the sorting of LpL in the trans-Golgi network is hitherto not understood in detail. Here we characterize the role of SorLA in the intracellular trafficking of LpL. LpL binds to SorLA under neutral and acidic conditions, a binding that in cells mainly takes places in vesicular structures. SorLA expression changes the subcellular distribution of LpL so it becomes more concentrated in endosomes. From the endosomes LpL is further routed to lysosomes which results in a degradation of newly synthesized LpL. Consequently, a fivefold reduction of LpL activity is observed in cells with SorLA expression. In analogy, SorLA regulates vesicle-like localization of LpL in primary neuronal cells. Thus, LpL binds to SorLA in the biosynthetic pathway and is subsequently transported to endosomes. As a result of this SorLA mediated-transport, newly synthesized LpL can be destined to specialized vesicles and eventually sent to degradation and its activity thereby regulated.

30.09 Jenny Blechingberg Friis

REGULATION OF GENE EXPRESSION BY THE FET-PROTEIN FAMILY

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The FUS, the EWS and the TAF15 proteins are RNA- and DNA-binding proteins which together are called the FET-protein family. They are structurally and functionally related and are found in a variety of cancer-associated fusion genes. The FET-proteins are also involved in neuronal diseases such as familiar Amyotrophic Lateral Sclerosis, Huntingdon's disease and frontotemporal dementia. The FET-proteins are expressed in the majority of human tissues. They localize mainly to the nucleus, but are also seen as a smaller amount in the cytoplasm. The wild-type FET-proteins associate with a number of factors involved in transcription and RNA processing, implying the FET-proteins are involved in transcriptional regulation. However, the functions of the RNA- and DNA-binding capacities of the FET-proteins are largely unknown.
This project aims to elucidate the roles of the FET-proteins in regulation of gene expression. These functions are analyzed by siRNA mediated gene knock-down of the FET-proteins in human Hek293 cells, and subsequent expression array analysis. We found that the TAF15, the EWS and the FUS proteins alter the expression of 307, 407, and 293 genes respectively, and that they regulate distinct different groups of genes. The mechanisms by which the FET-proteins regulate mRNA expression are analyzed by mRNA stability assays and chromatin immunoprecipitation.

30.10 Thais A.

Pedersen

LATE CARDIOVASCULAR MORBIDITY IN REPAIRED AORTIC COARCTATION: NO CURE FOR THE AORTIC COARCTATION SYNDROME

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Introduction: Coarctation of the aorta (CoA) is related to high long-term cardiovascular mortality and morbidity, but the prevalence of late complications and the mechanisms behind them are still unknown.

Methods: 133 patients operated for CoA (84 men, mean age 41Y) were examined with: exercise testing; neurohormonal assessment; 24-h blood pressure measurement; echocardiography; MRI; and compared to 39 sex and age-matched controls.

Results: 34 patients (27%) were hypertensive. Exercise performance was reduced in 37 (29%). Exercise-induced hypertension was present in 47 (37%). 66 (50%) had a bicuspid aortic valve (BAV). Recoarctation was found in 58 (46%) and aortic aneurysms in 28 (22%), mostly among those with BAV ($p=0.0028$). CoA patients had impaired systolic and diastolic function compared to controls, with higher left ventricular mass (200 vs. 167g, $p<0.001$), higher left atrial area (17 vs. 15 cm^2, $p=0.035$), higher E/E' (9.41 vs. 6.85, $p<0.001$) and lower STDI (8 vs. 7 cm/s, $p=0.005$). ANP and NT-pro-BNP were increased among patients (respectively 7.35 vs. 5.35 pmol/L, $p=0.033$ and 6.15 vs. 4.4 pmol/L, $p=0.006$), while AVP and aldosteron were suppressed (respectively 0.6 vs. 0.8 pg/ml, $p=0.005$ and 316 vs. 379 pmol/L, $p=0.019$). The presence of recoarctation did not influence neurohormones, blood pressure or ventricular function.

Conclusions: Patients operated for CoA are far from cured. The high prevalence of aneurysms and BAV reveal a disease generalised to a much larger portion of the vascular system than the coarctation site. Abnormal neurohormonal activation seems to be a marker and/or a mediator of the early stage of ventricular dysfunction among these patients.

30.11 Ruta Tuckuviene

PEDIATRIC THROMBOEMBOLISM IN DENMARK 1994-2006: A NATIONWIDE POPULATION-BASED STUDY

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Aim: To asses the incidence rates (IR), clinical characteristics, risk factors, treatment and outcome of pediatric venous and arterial thromboembolism (TE).

Methods: Patients aged 0-18 years with first-ever venous and/or arterial TE, in Denmark, between 1994 and 2006 were identified in the nationwide registry of patients, medical records were reviewed and all diagnoses validated.

Results: In total 623 cases of TE were confirmed during 15.8 millions person-years of observation. The distribution of cases was as follows: arterial ischemic stroke (n=211), cerebral sinovenous thrombosis (n=40), and venous and/or arterial TE (n=372) corresponding to IRs of 1.33, 0.25, and 2.35 per 100,000 person-years, respectively. The IRs peaked in infancy (<1year) for all types of thrombosis with an additional peak among adolescents (15-18 years) for venous TE and cerebral sinovenous thrombosis. Boys predominated in IR of venous TE in infancy, females in adolescence ($p<0.001$). The IR of arterial ischemic stroke increased 3.9% per year ($p=0.036$), whereas no changes of IRs over time were found for other types of

TE.
Possible risk factors were present in 72.3% of patients. Thrombophilia was diagnosed in 141 out of 436 cases investigated. 72.0% of patients received antithrombotic treatment without significant complications. A total of 46 patients died after median follow-up time of 8 years, corresponding to all-cause fatality of 7.4%. TE-related 30-days case fatality was 1.9%. Morbidity was reported in 57.0% of survived patients one year after thrombosis.
Conclusion: Our study provides important epidemiological and clinical data on pediatric TE in the Danish population.

30.12 Vibeke Bregnballe

PARENTING ADOLESCENTS WITH CYSTIC FIBROSIS: ADOLESCENTS' POINTS OF VIEW
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Aim: To find out what kind of parental support adolescents with cystic fibrosis want and find beneficial in preventing decrease in disease-related physiological and quality of life parameters.
Background: In adolescence many patients with cystic fibrosis experience declining lung function, stagnating growth, reduced compliance and quality of life as well as psycho-social and psychiatric problems, often irreversible continuing into adult life. Previous studies indicate that the adolescents are not prepared well enough for adulthood and that they need help concerning personal development in addition to help with coping with their disease. The parents may also need help to support their children.
Method: A qualitative study using interpretive description as the methodological approach. The participants were adolescents with cystic fibrosis aged 14 to 25 (N=16). Two focus group interviews were carried out, one for 14-18-year-olds and one for 19-25-year-olds and three individual interviews.
Results: The adolescents want their parents educated in adolescence. They want their parents to learn how to involve the chronically ill child in the medical treatment at an early age and they want their parents to learn how to gradually hand over the responsibility for the medical treatment.
Perspectives:
The findings of this study indicate that education of parents in handling children and adolescents with cystic fibrosis may be a task for health professionals in the future.

30.13 Gitte Dam

30.14 Thomas Greve

ACUTE EFFECTS OF INGESTION OF BRANCHED-CHAIN AMINO-ACIDS ON MUSCLE AMMONIA METABOLISM
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Branched-chain amino acids (BCAA) are used to prevent hepatic encephalopathy. Their effect is believed to take place in muscle. We studied the effects of BCAA on ammonia metabolism in thigh muscle by 13N-ammonia PET and measurements of arterial-venous differences and blood flow.
Seven patients with cirrhosis and 14 healthy subjects were studied. Net-balances and net-clearances of ammonia and amino acids across the leg muscle were studied by measurements of arterial and venous blood concentration and blood flow before and 1 and 3 hours after ingestion of an oral BCAA load. The net clearance and flux of arterial ammonia was also studied by 13N-ammonia PET before and at 2.5h. Applying these two methods enabled us to separate net-metabolism of ammonia across the leg including any production of ammonia by the leg itself from net uptake of exogenous blood ammonia presented to the leg.
Ingestion of BCAA led to an increased uptake of ammonia by muscle tissue in both the healthy subjects and the patients measured by both methods (all $P<0.05$). This was followed by glutamine release from the muscle. Ingestion of BCAA also caused an increase in blood ammonia in both groups. The net clearance of ammonia

measured as Flow (A-V)/A increased in both groups (both $P<0.05$) whereas the net clearance of exogenous ammonia was unaffected. This indicates that BCAA caused a diminished release of ammonia from the leg itself and not an increased removal of ammonia from the blood. The results thus indicate that the effect of BCAA on muscle ammonia metabolism mainly occurs through a beneficial effect on muscle metabolism itself and not through an increased removal of blood ammonia.

IS THE LYTA-GENE IN THE MITIS GROUP OF THE VIRIDANS STREPTOCOCCI IN GENERAL DIFFERENT IN EACH GROUP MEMBER?

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OBJECTIVE

Introduction of new molecular diagnostic tests for S. pneumoniae augments the necessity for a target that is unique for this microorganisme.

Our objective is supplementary validation of the lytA-gene as a suitable target for distinguishing S. pneumoniae from other streptococci.

METHODS

The practical work is based on the use of a PCR specific for the lytA-gene in S. pneumonia. Three panels of bacteria have been designed to test the primers and probes. The first one is 31 strains of bacteria that are not S. pneumoniae or within the mitis group. The second is 41 strains of S. pneumonia. The third is 22 strains within the mitis group, which were kindly provided by M. Kilian and blinded to us while working with them. All of these strains contained the lytA-gene.

The theoretical work consists of a phylogenetic analysis of the lytA-gene in most of the fully sequenced strains of streptococci within the mitis group.

RESULTS

The practical approach yielded a convincing result finding 45/46 S. pneumoniae strains; test sensitivity 97.9%. It found 0/48 of the “not S. pneumoniae” strains; test specificity 100%. The PPV was 100% and the NPV was 98%.

The phylogenic approach showed that the lytA-gene is present in most of the strains of the mitis group. The gene is different in general in each species visualized as separate clusters in the tree. A majority of the sequences that have a match are placed within the S. pneumoniae cluster.

CONCLUSION

The test is able to distinguish S. pneumoniae from other mitis group streptococci. This is due to minor differences in the gene. The test is therefore relatively specific for the S. pneumoniaes “version” of the lytA-gene.

30.15 Birgitte S. Kousholt

NATRIURETIC PEPTIDE INFUSION IN MYOCARDIAL ISCHEMIA/REPERFUSION IS ASSOCIATED WITH REDUCED MYOCARDIAL DAMAGE AND INVERSED ENDOGENOUS RELEASE OF NATRIURETIC PEPTIDE IN PIGS

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Introduction: Plasma measurement of cardiac natriuretic peptides has gained clinical use in diagnosis of heart disease. In cardiac disease, the peptides may possess cardioprotective properties by reducing local fibrosis.

Aims: We examined the acute cardiac effects of infusion of B-type natriuretic peptide (BNP) and a C-type natriuretic analogue (CD-NP) in a porcine model of myocardial ischemia/reperfusion.

Methods: Anaesthetized pigs were subjected to one hour of regional cardiac ischemia followed by three hours of reperfusion.The systemic response was monitored by hemodynamic measurements. Blood samples were collected every hour. Cardiac damage was assessed by biochemical measurements of myocardial damage by porcine-specific immunoassays and PCR. Infarct size was determined by tetrazolium staining.

Results: Pigs tolerated the BNP and CD-NP infusion well with a similar decrease in systemic blood pressure (~20 mmHg) and an increase in diuresis compared to

controls. BNP infusion selectively reduced the cardiac release of troponin T by 30%, suggesting a major cardioprotective effect. Moreover, the endogenous natriuretic peptide release was completely inversed by the BNP infusion with a decrease in plasma proANP concentrations compared to an increase in both control and CD-NP infused animals.
Discussion: For the first time, we show that BNP infusion in ischemia/reperfusion damage selectively reduces cardiac damage and inverses the cardiac response in endogenous release of natriuretic peptides. Taken together, our results advocate for pursuing natriuretic peptide treatment in cardioprotection in cardiac ischemia and myocardial infarction.

30.16 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, inflammatory mediators and cell surface molecules. Dysregulation of B-cell differentiation can result in 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 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 1000 B-NHL patients, 500 patients with Hodgkin's disease and 330 Myeloma patients, 308 RA patients and 605 healthy controls. DNA is extracted from whole blood or archival formalin-fixed, paraffin-embedded tissue. 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.

30.17 Asger Granfeldt

7.5% NACL WITH ADENOSINE, LIDOCAINE AND MG2+ REDUCES FLUID REQUIREMENT AND IMPROVES KIDNEY FUNCTION FOLLOWING 70% BLOOD LOSS IN A PIG MODEL OF SEVERE HEMORRHAGIC SHOCK
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Introduction: Re-establishment of circulation following hemorrhagic shock triggers ischemia-reperfusion(I/R) injury. Excessive fluid therapy in the pre-hospital setting further worsens outcomes. The combination of adenosine, lidocaine, and magnesium(ALM) stabilizes cardiovascular function and hemodynamics after I/R.
Hypothesis: Treatment with 7.5% NaCl ALM at resuscitation 1) reduces fluid requirements during permissive hypotension, and 2) restores kidney function after

re-infusion of shed blood.
Methods: Anesthetized pigs (38kg) were randomized to 2 groups: Hemorrhage + placebo(n=11) and Hemorrhage + ALM(n=9). Blood was withdrawn to a MAP of 30-35mmHg. After 90min Ringers Acetate and 20ml 7.5% NaCl±ALM was infused to achieve a MAP of 50mmHg. After 30min 75% of the drawn blood was re-infused±ALM and the pigs were observed for 6 hours. Glomerular filtration rate(GFR) was estimated by the renal clearance of 51Cr EDTA, and tissue bloodflow was quantified by microspheres.
Results: In the placebo group 46.7± 24 ml/kg of Ringers acetate were needed to maintain a MAP of 50-55mmHg for 30 min while the volume needed in the ALM group was 25.9± 9.0 ml/kg,(p=0.03). Two pigs in the placebo group could not be resuscitated with Ringers acetate. Despite an increase in fluid volume in the placebo group there was no difference in hematocrit , regional myocardial or renal bloodflow. In the ALM group GFR returned to 83% of baseline(baseline 66±20ml/min vs. end of experiment 51±15ml/min), whereas GFR in the placebo group returned to 54% of baseline (98±39ml/min vs. 51±19ml/min)(p=0.01)
Conclusion: 7.5% NaCl with ALM reduced fluid requirements and restored kidney function to near baseline levels.

30.18 Flemming Bandholm Jakobsen

THE LONG TERM IMPACT OF HEALTH PROFESSIONAL STUDENTS LEARNING IN AN INTERPROFESSIONAL TRAINING UNIT
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Background: The Interprofessional Training Unit (ITU) is a clinical learning environment for students from the professions: occupational therapy, physiotherapy, nursing, and medicine. The aim of this study was to examine the long term impact of a clinical placement in the ITU.
Methods: Data were collected on the students last day in the ITU where the students were asked for statements concerning the most important they had learned in the ITU. The former students were on a questionnaire asked the same question 1 – 4 years after graduation. Furthermore they were asked to answer a number of questions on a Likert scale. The answers in the questionnaires were counted up and the statements were transcribed and analysed on group level.
Medical students were not included in the study since none had graduated at the time of data collection.
Results: In the period from September 2006 to January 2008 428 students attended the ITU. We identified 392 of which 336 (86%) answered. A majority (82-91%) answered that they had learned about their own as well as about other professions. When students and graduates' statements concerning the most important learning outcomes were compared a significant increase in the rating of the learning environment and foundation of professional identity and significant decrease in the rating of uniprofessionalism were found in graduates. No difference in outcomes concerning interprofessionalism was identified.
Conclusion: Occupational therapists, physiotherapists and nurses all thought that the ITU lived up to its aims concerning learning environment, uniprofessionalism, interprofessionalism and foundation of professional identity in a 1 – 4 years follow up period.

30.19 Lene Bastrup Jørgensen

30.20 Nis Borbye Pedersen

TITLE: INNOVATIVE METHOD FOR INVESTIGATING COPD PATIENTS' STRATEGIES FOR COPING WITH BREATHLESSNESS
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Introduction: COPD patients' strategies for coping with breathlessness constitute a complex process including a variety of interacting physiological, cognitive, affective

and existential dimensions. Conventional methods have not succeeded to capture the complexity, thereby offering a theoretical understanding of the COPD patients' coping mechanisms.
Aim: To develop a novel research method to combine the individual dimensions in an explanatory model of how COPD patients cope with breathlessness.
Method: 12 patients with moderate to very severe COPD were recruited during hospitalization. Data were collected through "Videobased narratives"(VN) and recordings of various physiological parameters. VN encompassed video recordings of the patients combined with interviews conducted while the patients' watched themselves on the video
Results:The novel method was suitable to capture the patients' verbal and nonverbal behaviour as well as compromised physical condition, and made it possible to develop an explanatory model for how COPD patients deal with breathlessness.
Discussion: Striving to develop a method matching the multidimensional coping process, the innovative method became complex and might to some extent compromise the transparency of the method. Still, the method seems to initiate new knowledge and may therefore be a possible stride in the attempt to understand the complexity of coping with breathlessness.
Conclusion: The novel method seems to match the complexity of COPD patients' coping strategies. We suggest the method to be tested with regard to validity and reliability before concluding on to what extent the method contributes to the existing knowledge.

IDENTIFICATION OF REGULATORY PROTEINS OF THE KIDNEY SPECIFIC NA-CL COTRANSPORTER, NCC

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The thiazide-sensitive Na+-Cl- cotransporter (NCC), expressed in the distal convoluted tubule of the kidney, is important for renal electrolyte balance. Previously, we have demonstrated that the anti-diuretic hormone vasopressin regulates the phosphorylation status and thereby activity of NCC. Recently, angiotensin II has been demonstrated to increase phosphorylation of NCC. The regulatory proteins that mediate the effects of these hormones on NCC are to a large extent still unknown. To address this question, we performed a yeast two hybrid screen against a mouse kidney with the NH2-terminal cytoplasmic fragment of NCC as bait. Several physiologically interesting hits from this screen, such as the A-kinase anchoring protein 1 (AKAP1) and protein phosphatase 2 regulatory subunit B' alpha isoform (PPP2R5A), were found to be expressed in the distal convoluted tubule of rat kidney by immunohistochemistry. Biochemical methods and RNA interference studies are underway to confirm the interacting proteins and their relevance in regulation of NCC.
As a model system, we have created an MDCK cell line expressing NCC with an enzymic tag (SNAP-tag) under the control of tetracycline (a so-called 'TetOn' system). The SNAP-tag, being a modified DNA repair protein optimized to react with benzyl-guanine-conjugated substrates, enables the labeling of NCC with chemical molecules such as biotin or fluorescent dyes, including non-cell permeable substrates. Our preliminary data suggests that this cell line will be very useful for studies on NCC trafficking and localization in relation to the signaling processes mentioned above.

30.21 Malene Bek-Thomsen

EVOLUTION OF STREPTOCOCCUS PNEUMONIAE INTO FUNCTIONALLY DISTINCT SUBPOPULATIONS

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Background: Streptococcus pneumoniae is a leading cause of invasive disease and respiratory-tract infections worldwide. In addition to its function as a pathogen, S. pneumoniae is also carried asymptomatically in the nasopharynx, especially of

young children. In general, S. pneumoniae is characterized by extensive recombination resulting in blurring of distinct evolutionary lineages. Nevertheless, preliminary analyses based on comprehensive Multilocus Sequence Type (MLST) data sets of all recognized sequence types of S. pneumoniae demonstrate the existence of 3-4 distinct evolutionary clades. Aim: To investigate the existence of functionally and genetically distinct evolutionary lineages within S. pneumoniae with differences in virulence and disease potential. Methods: A reference population of 83 clinical strains was assigned to the respective subpopulations by MLST based phylogenetic analyses. Characterizations of subpopulations are performed by comparative genome hybridizations (CGH). At present, a pan-genome microarray covering all open reading frames of S. pneumoniae is under construction. It is based on 46 publicly available genome sequences and strain specific sequences identified by Novel Gene Discovery performed on 30 clinical S. pneumoniae strains by subtractive hybridization. Bioinformatic analyses are currently performed and unique features will be represented by 60-mer oligonucleotides (Agilent technologies). Perspectives: CGH analysis based on a pan-genome microarray will help to identify genetic features of S. pneumoniae with relevance to virulence and disease. In addition, new vaccine candidates, covering all variants of S. pneumoniae may be revealed.

30.22 Marie Bagger Bohn

30.23 Janne Lund Helverskov

THREE-DIMENSIONAL KINEMATIC ANALYSIS OF KNEE ROTATIONAL STABILITY IN ACL-DEFICIENT PATIENTS DURING PIVOTING.

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Background:During the last five years there has been a shift towards more anatomic anterior cruciate ligament (ACL) reconstruction principles with the purpose of restoring natural knee biomechanics. Rotational instability in the ACL deficient and ACL reconstructed knee has been associated with development of osteoarthritis.
Aim:The aim of the study was to measure the functional knee rotation of ACL deficient knees (ACLD) and to compare it with the contra-lateral healthy knee of the patients using 3-D motion analysis.
Methods:31 ACLD patients were included in the study. All subjects were tested using an 8-camera QTM system. A pivoting task was conducted, i.e., the patient was to descend a stairway and immediately pivot on the landing leg 90° and walk away from the stairway. Maximum tibial rotation was recorded during this task.
Results:On average the ACL-deficient knee had a range of motion (ROM) in the transverse plane (rotation) on 32,7° ± 6,3°. The average ROM for the healthy knee was 30,4° ± 6,1°. No statistically significant difference was found ($p=0.09$). Even though none of the patients reported discomfort at executing the task, 10 patients had a higher rotation (more than 1°) at their healthy leg indicating compensatory mechanisms. The 21 patients without this phenomenon rotated 34,2° ± 6,8° on the ACLD knee and 28,1° ± 5,8° on the healthy knee. This difference was statistically significant ($p<0.001$).
Conclusion:These preliminary results suggest that some ACLD patients have compensatory mechanism while performing a pivoting task. An average difference in rotation of 6 degrees between the ACLD and the healthy knee was measured in patients without compensatory mechanisms.

30.24 Lisbeth Venø Kruse

EMPIRICAL SUPPORT FOR A RECLASSIFICATION OF EATING DISORDERS NOT OTHERWISE SPECIFIED

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Background: Patients with eating disorders not otherwise specified (EDNOS)

represents 50-60 % of all patients with an eating disorder referred to specialised treatment. The approaching revision of the DSM-IV diagnostic criteria actualises the considerations on how to improve the classification of eating disorders, including how to reduce this residual group.
The objective of the present study was to explore the empirical support for a reclassification of the EDNOS category.
Methods: In a cross-sectional design eight specific subgroups of EDNOS were compared to anorexia nervosa (AN) and bulimia nervosa (BN) on interview-based data and questionnaire measures. The subgroups definitions were based on results from previous empirical studies. The results were compared to the revisions proposed for the DSM-5 by The Eating Disorders Work Group, American Psychiatric Association(APA) . The sample consisted of 965 patients in the age 13-54 years admitted to treatment for an eating disorder.
Results: According to the DSM-IV 176(18%) presented with AN, 290(30%) with BN and 499(52%) with EDNOS. Of all EDNOS cases 34% could be reclassified as AN or BN. Three specific subgroups emerged as separate diagnostic entities. A heterogeneous subgroup of 122 patients (13% of all) was proposed as “true” EDNOS. Thus this study supports a broader definition of AN and BN and suggest three subgroups of EDNOS as separate diagnostic entities. This results in a substantial reduction of the heterogeneous EDNOS group. Comparisons between the present results and the criteria proposed for the DSM-5 (APA) reveals differences in how to categorise patients in the borderline territory between AN and BN.

THE HERITABILITY OF ATOPIC DISEASE - ESPECIALLY ALLERGIC RHINITIS

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Background: Allergic rhinitis (AR) is a growing problem worldwide. Today 10 to 30% of adult and up to 40% of children suffers from this condition. It is a frequent cause of morbidity, medical treatment costs, lost workdays, and reduced school performance. Atopic diseases are complex disorders being multifactorial and polygenic. The genetic contribution to AR is substantial with a heritability of 71%.
Aim: To clarify whether earlier found susceptibility regions indeed are true findings and to identify new chromosome regions containing risk genes for AR by complete genome scanning.
Methods: We have included 125 Danish nuclear families in the study (Sample 1). All persons were clinically examined and questionnaire tested. Blood was drawn from all participants for DNA analysis and for measurements of total IgE and allergen-specific IgE antibody to 11 common allergens. Two earlier collected Danish sib-pair samples were included in the genotyping and analyses. Sample 2 comprises 130 families with at least two full sibs with atopic dermatitis. Sample 3 includes 100 families enrolled in the Danish allergy project ITA. Thus, a total of 432 AR children and 380 parents from 190 Danish nuclear families were analysed in the present study. A complete genome scanning has been performed on sample 1 and 2. A total of 415 chromosomal STR markers and 14 X-linked markers were genotyped in all individuals. Linkage analysis is being preformed by the affected sib-pair method. Multipoint non-parametric linkage analyses (no assumptions are made as for the mode of inheritance) are being performed using the programe Genehunter NPL
Results: Presently several potential susceptibility regions have been revealed.

30.25 Camilla Molich Hoff

THE IMPORTANCE OF HAEMOGLOBIN LEVEL AND EFFECT OF TRANSFUSION IN HNSCC PATIENTS TREATED WITH RADIOTHERAPY - EVALUATED IN THE RANDOMIZED DAHANCA 5 STUDY

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Patients with head and neck squamous cell carcinoma (HNSCC) and a low level of haemoglobin (Hb) often have a poor response to radiation which may be related to hypoxia induced radioresistance. The aim of the study was to evaluate the prognostic significance of low Hb level and its modification by transfusion in HNSCC patients treated with radiotherapy (RT) and performed as a subrandomization in the DAHANCA 5 trial.
Patients were randomized to treatment with the hypoxic radiosensitizer nimorazole, and in addition, patients with "low" pre-irradiation Hb values (F<13 g/dL; M<14.5 g/dL) were subrandomized to +/- transfusion. The treatment effect was evaluated using the endpoints of locoregional control (LRC), disease-specific survival (DSS) and overall survival (OS). Data were analysed according to 'the intention to treat' principle and 5-year results were obtained from uni- and multivariate analyses.
A total of 414 patients were included, 243 patients had high Hb levels. Of the low Hb patients, 82 were randomized to receive transfusion and 89 not to receive transfusion. In the majority of patients, transfusion resulted in increased Hb levels although this tended to decline throughout treatment. Patients with high Hb levels had a significantly better probability of LRC, DSS and OS. In the low Hb group, transfusion did not improve the outcome in LRC, DDS or OS. In multivariate analyses there was no significant influence of transfusion or Hb level on endpoints.
The prognostic importance of high Hb level was demonstrated in patients with HNSCC treated with RT; however, transfusion prior to and during treatment did not improve the outcome in patients with low Hb values.

30.26 Jeppe Grøndahl Rasmussen

TRYPSINIZATION AND PROLONGED HYPOXIC CULTURE INCREASES THE EXPRESSION OF GENES RELATED TO ANGIOGENESIS IN HUMAN ADIPOSE TISSUE-DERIVED STEM CELLS
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Purpose: Paracrine effects are believed to mediate the beneficial effects of mesenchymal stem cell transplantation in the treatment of ischemic disease, particularly vascular endothelial growth factor (VEGF) and insulin-like growth factor 1 (IGF-1) have anti-apoptotic and angiogenic effects. We hypothesized that hypoxic culture and trypsinization, used to detach adherent cells from culture surfaces, could upregulate the expression of angiogenic cytokines in human adipose tissue-derived stem cells (ASCs).
Methods: ASCs from three patients were cultured at 1%, 5%, and 21% oxygen for 13 days. Gene transcription was measured by using quantitative real-time RT-PCR. The effect of trypsin was evaluated by seeding ASCs after trypsinization and placing one half in hypoxia immediately and the other half in normoxia for 3 days before placement in hypoxia, after 24 hours in hypoxia cells were harvested for quantitative real-time RT-PCR analysis.
Results: Comparing gene expression levels between day 13 and day 1 only IGF-1 (21% oxygen, $p<0.01$) was significantly upregulated, whereas VEGF was not. Comparing day 13 and day 4 VEGF (1%, 5%, and 21% oxygen, all $p<0.05$) and IGF-1 (1% oxygen, $p<0.05$) were significantly upregulated. The effect of recent trypsin exposure was demonstrated as both VEGF (1%: $p<0.01$, 5%: $p<0.001$, and 21%: $p<0.001$) and IGF-1 (1%: $p<0.001$, 5%: $p<0.001$, and 21%: $p<0.05$) genes were significantly upregulated at day 1 compared to day 4 after trypsin exposure.
Conclusions: Prolonged hypoxic culture increased the expression of the VEGF and IGF-1 genes. Trypsin increased the expression of the VEGF and IGF-1 genes independent of the oxygen concentration.

30.27 Maria Luise Salskov-Iversen

THE CASPASE-5 EXPRESSION IS UPREGULATED IN PSORAISIS

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Caspase-5 belongs to the family of inflammatory caspases, which activates the pro-inflammatory cytokines IL-1b and IL-18. The purpose of this study was to: 1) characterise caspase-5 expression in psoriatic skin, 2) investigate caspase-5 mRNA induction in cell cultures, 3) investigate the signalling pathways involved in caspase-5 mRNA induction. RNA and protein was purified from paired biopsies from nonlesional and lesional psoriatic skin and used for RT-PCR and Western blotting. Normal human keratinocytes and PBMC´s were stimulated with IFN-g, IL-4, IL-17A, IL-22 or LPS. In other experiments, PBMC´s were pre-incubated 45 minutes with inhibitors of the p38 MAPK or NF-kB signalling-pathways before LPS stimulation. We found a 20.0 fold upregulation ($p<0.05$) of caspase-5 mRNA and a 1.4 fold increase in caspase-5 protein ($p<0.05$) in lesional psoriatic skin compared with nonlesional skin. In in vitro PBMC cultures, LPS induced a 20 fold ($p<0.05$) increase in caspase-5 mRNA after 12 hours stimulation, whereas IFN-g induced a 3.6 fold ($p<0.05$) increase in both keratinocyte and PBMC cultures. In PBMC´s, pre-incubation with a NF-kB-inhibitor significantly reduced the stimulatory effect of LPS. In conclusion, both caspase-5 mRNA and protein are significantly upregulated in lesional compared with nonlesional psoriatic skin. In vitro studies of keratinocytes and PBMC´s reveal that IFN-g induces caspase-5 mRNA in both cultures, and that caspase-5 mRNA can be induced through the NF-kB signalling pathway. Our data suggests that caspase-5 may play an important role in psoriatic skin inflammation.

30.28 Lotte Ørneborg Rodkjær

DISCLOSURE DECISIONS: A GROUNDED THEORY OF HIV-POSITIVE PERSONS COPING WITH DISEASE-RELATED STRESSORS

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The purpose of this grounded theory study was to investigate how HIV-positive persons live with their disease, focusing on HIV-related stressors. Textual data from in-depth interviews with 16 HIV-positive persons was analyzed using the Glaserian method. Decisions about disclosure appeared to be a major concern and a determining factor for HIV-related stress and we developed a substantive theory about disclosure decisions. According to this, three different strategies can be identified: (1) disclosing to everyone (being open); (2) restricting disclosure (being partly open); and (3) disclosing to no one (being closed). Disclosure was a continuum; none of the three strategies automatically relieved HIV-related stress. The theory describes the main determinants and consequences of each strategy. The study demonstrates the importance of recurrent individual considerations about disclosure choices and plans, and offers a theoretical basis for interventions designed to assist persons living with HIV in making the best possible individual decisions regarding disclosure and, thereby, reducing HIV-related stress.

30.29 Eduardo Adrian Garza Garza Villarreal

SONATA ANALGESICA: MUSIC, PAIN AND THE PLACEBO EFFECT

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Music reduces pain perception in humans. However, it is poorly understood why and how. It has been suggested that the mechanisms behind this effect are distraction and emotion. Nonetheless, personality type as well as placebo effects has not been taken into account. Our goal is to understand how music reduces pain

perception, determine its limitations and improve its therapeutic use. To study this effect, 48 healthy participants were recruited (24 male/24 female). The sample was divided into personality types using different questionnaires. The participants listened to different auditory stimuli (control, active distraction, sounds, and music) during which they received acute pain at different times, rating if using the Visual Analog Scale (VAS). To elicit a placebo effect, the participants were suggested that some of the sounds and musical pieces reduced pain more than others, and this was balanced by giving different suggestions to each participant. After the study, the participants rated the auditory stimuli for valence, arousal and liking, as well as for different emotions. Our preliminary results suggest that Distraction reduced pain perception significantly more than any other condition; however, Sounds and Music also significantly reduced pain perception more than the Control. There was no significant difference on pain perception depending on the personality of the participant. On the other hand, the emotional perception of the auditory stimuli, specifically valence and liking, were good predictors of pain reduction. There was an effect of suggestion which is still being investigated. Future studies aim to use fMRI and EEG to further investigate these questions.

30.30 Hans Henrik Møller Nielsen

SINGLE CENTRE TRANSCATHETER AORTIC VALVE IMPLANTATION USING THE EDWARDS SAPIEN VALVE

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Background: The use of transcatheter aortic valve implantation (TAVI) for high-risk patients was introduced in the early 00s for treatment of surgically non-amenable patients with aortic valve stenosis. There has recently been a dramatic increase in TAVI procedures. TAVI programmes have been or are being implemented in numerous cardiac centers. This paper describes a single center experience with the first 100 TAVI procedures.

Methods: The study included our first 100 patients who underwent either transfemoral (F-TAVI) or transapical (A-TAVI) aortic valve implantation at Aarhus University Hospital, Skejby, using the Edwards SAPIEN valve. The study was based on retrospective data collection. The indication for TAVI was inoperability by conventional surgery.

Results: The consecutive patients were treated between February 2006 and June 2010. Of those were 44 % male and 56 % female with an age of 83 [63-93]. Thirty-day mortality was 8% (n=8), and decreased from 12% among the first 50 patients to 4% in the last 50 patients. Successful implantation was achieved in 92% of patients. Major non-fatal complications were seen in 4 (5 %) out of 76 A-TAVI and in 1 (4 %) out of 24 F-TAVI patients. Mean EUROscore in the F-TAVI and A-TAVI groups was 15.9 and 21.5, respectively (p=0.06). Post-procedural leakage of cardiac biomarkers was significantly higher in the A-TAVI group. Mean NYHA class improved from 2.9 [2.8-3.0] to 1.8 [1.7-2]

Conclusion: In surgically non-amenable patients, TAVI can be performed with acceptable mortality and morbidity and results in marked functional improvement. A decrease in 30-day mortality over time indicated a learning curve in implementing this treatment.

30.31 Anders Knudsen

STEREOLOGICAL ASSESSMENT OF ISCHEMIA/REPERFUSION INJURIES IN THE RAT LIVER. EFFECTS OF ISCHEMIC PRE- AND POSTCONDITIONING

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Ischemia/reperfusion (I/R)-injuries is a known complication to liver resections. Ischemic pre- and post-conditioning (IPC and IPO), has been proven to protect the liver against I/R injuries judged by liver enzymes and conventional histological examination. The aim of the present study was to evaluate and compare the hepatoprotective properties of IPC and IPO using stereological methods for 3-dimensional assessment.
Methods: In a rat model 60 min of partial liver ischemia was used. 64 rats was divided between four groups; sham, IRI, IPC and IPO. At the end of the reperfusion period (either 4 or 24 hours), blood samples were taken before 10 min of in situ formalin perfusion of the liver. The paraffin embedded left median lobe was examined using the cavalieri´s principle on SURS sections. Total liver volume and total necrotic volume were estimated on HE-stained sections.
Immunohistochemical stained SURS sections with antibodies against apoptotic marker Caspase-3 and cellular proliferation marker KI-67, were used to estimate the number of these cells.
Results: ALAT showed a large increase in the intervention groups compared to sham operated controls. Surprisingly no differences were found in ALAT levels after 4 and 24 hours of reperfusion between the groups IRI, IPC and IPO. Stereological examination is currently being performed and will be ready for presentation at the phd-day.
Conclusion: Stereological assessment of the I/R induced lesions in the liver, seems to be an efficient method to estimate and characterise the degree of damage.

30.32 Jasna Furtula

TRIPLE STIMULATION TECHNIQUE APPLIED ON ALS PATIENTS AND CONTROL SUBJECTS
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Objective Triple stimulation technique (TST) is an electrophysiological method to study corticospinal conduction to a target muscle. TST gives an estimate of the fraction of conducting central motor neurons. We applied this quantitative method in assessment of upper motor neuron (UMN) function in ALS patients and controls.
Methods TST combines transcranial magnetic stimulation (TMS) with a peripheral collision technique. Bilateral recordings were obtained from the abductor digiti minimi muscle. Thirty healthy subjects (12 males, 18 females) - age 35-70 yrs - and 8 patients with clinical suspicion of ALS were examined. Clinical UMN signs were present in the upper limbs of 4 patients with probable ALS based on the El Escorial and Awaji criteria.
Results In healthy subjects, the TST amplitude- and area ratio demonstrated that nearly 100% of motor units could be excited by TST (left side): mean 1.02 (SD 0.05) and 1.04 (SD 0.07), respectively. Similar values were found on the right side. In the patient group, one parameter, TST area ratio on the left side, was decreased - mean 0.93 (SD 0.09). Three of 7 patients, all 3 with probable ALS, had decreased TST amplitude and/or area ratio. Two of those patients had clinical signs of severe lower motor neuron (LMN) involvement in the opposite limb. In one patient, recordings could not be obtained due to severe atrophy of the target muscle.
Conclusions Although TST has not yet gained widespread use for quantification of UMN lesion, the technique should be considered when assessing UMN involvement in order to increase diagnostic yield. The lack of concordance between LMN and UMN affection in ALS suggest that both sides should be examined.

30.33 Michael Winterdahl

TRACER INPUT FOR KINETIC MODELLING OF LIVER PHYSIOLOGY DETERMINED WITHOUT SAMPLING PORTAL VENOUS BLOOD IN PIGS
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Purpose: Quantification of hepatic tracer kinetics by PET requires measurement of

tracer input from the hepatic artery (HA) and portal vein (PV). We wished to develop a method for estimating dual tracer input without the necessity to sample PV blood.
Methods: 40-kg pigs were administered bolus doses of C15O (CO), 2-[18F]fluoro-2-deoxy-D-glucose (FDG), [11C]-methylglucose (MG), 2-[18F]fluoro-2-deoxy-D-galactose (FDGal) or H215O (H2O); tracer concentration 3-minute time courses were measured in the femoral artery and PV by blood sampling; blood flow was measured in the HA and PV by flowmeters. A model for transfer of tracer through the splanchnic circulation was used to estimate values of a tracer-specific model parameter β. Tracerspecific mean values of β were used to estimate tracer concentration time courses in the PV from the measured arterial concentration. A model-derived dual-input was calculated using the mean HA flow fraction (0.25) and validated by comparison of the use of the measured dual-input and a kinetic model with a fixed "true" K1(true) , i.e. clearance of tracer from blood to liver cells.
Results: The rank order of the means of BETA was CO < FDG ≈ MG < FDGal < H2O, reflecting their different splanchnic mean transit times. Estimated K1(est) was not significantly different from true K1(true).
Conclusion: The hepatic dual tracer input, which is of great importance for the assessment of processes such as transfer across the plasma-hepatocyte membrane or hepatic blood perfusion, can be well approximated in pigs without the necessity to sample PV blood and measure hepatic blood flow; only arterial blood sampling is needed.

30.34 Rikke Vestergaard

BONE HEALING AFTER MEDIAN STERNOTOMY: IS OSTENE® SUPERIOR TO BONE WAX?

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Background: Cardiac surgery is predominantly performed through a median sternotomy, a procedure which entails some serious complications; mainly bleeding and infections. To prevent bleeding, bone wax is traditionally applied to the spongiose bone marrow as an effective hemostatic device. Unfortunately it interferes with bone healing and increases the risk of infection in experimental studies. Recently, a water-soluble hemostatic wax (Ostene®) was introduced to reduce bone-marrow bleeding. Ostene® aims to diminish bone marrow bleeding while avoiding the drawbacks of bone wax. This study aims to compare sternal healing after application of either bone wax or Ostene®.
Methods: Twenty-four pigs were randomized into one of three treatment groups: Ostene®, bone wax or no hemostatic treatment. They were subjected to a midline sternotomy. Either Ostene® or bone wax was applied to spongiosa surfaces until local hemostasis. The control group received no hemostatic treatment. The area of the bone defect was determined with PQ-CT-scanning; bone healing was displayed with plain X-ray and chronic inflammation was histologically assessed.
Results: Both PQCT and X-ray showed that bone healing was significantly impaired in the bone wax group ($p<0.01$) compared with the other two groups, and the former group had significantly more chronic inflammation ($p<0.01$) than the two latter.
Conclusion: Bone wax inhibits bone healing and induces chronic inflammation in a porcine model. Animals in which Ostene® was used for hemostasis displayed bone healing characteristics and inflammatory reactions similar to those of the control group without application of a hemostatic agent.

30.35 Sine Nygaard Langerhuus

DIETARY FISH OIL REDUCES PLASMA PGE2 METABOLITE CONCENTRATION

AND WEIGHT-GAIN SUPPRESSION IN A PORCINE MODEL OF EARLY AORTIC VASCULAR PROSTHETIC GRAFT INFECTION

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Dietary long chain polyunsaturated fatty acids (LC-PUFA) were evaluated in a porcine model of early aortic vascular prosthetic graft infection (AVPGI). In total 84 pigs were randomised to a 35-day dietary treatment with 10% (w/w) fish oil (rich in n-3 LC-PUFA), sunflower oil (rich in n-6 LC-PUFA), or animal fat (rich in saturated and monounsaturated fatty acids). After 21 days of dietary treatment the pigs had an aortic vascular prosthetic graft inserted and inoculated with Staphylococcus aureus (106Colony-forming units) during surgical procedure. Plasma and erythrocyte n-3 and n-6 LC-PUFA concentrations, and plasma PGE2 metabolite concentration were measured in blood samples drawn prior to dietary assignment, prior to surgery, and on day 6 and day 12 post-surgery. Weight-gain in the pre- and post-surgical period was determined for each pig. The development in plasma and erythrocyte n-3 and n-6 LC-PUFA concentrations pre-surgery reflected the fatty acid composition in the dietary treatments. Within the dietary treatments the pre-surgical development was partly reversed in the post-surgical period. The plasma PGE2 metabolite concentration decreased in the pre-surgical period and remained at a lower level post-surgery in pigs receiving fish oil compared to sunflower oil and animal fat ($P<0{\cdot}015$). A higher weight-gain post-surgery was observed ($P=0{\cdot}038$) in the fish oil treated pigs (314(202;426)g/d) compared to the sunflower oil treated pigs (179(69;287)g/d). In conclusion, dietary enrichment with n-3 LC-PUFA compared to n-6 LC-PUFA reduced plasma PGE2 metabolite concentration and post-surgical weight-gain suppression in this porcine model of early AVPGI.

30.36 Iva Susanna vio Streym Thomsen

ASSESSING VARIABILITY OF PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY OF TIBIA IN 9 MONTH OLD INFANTS.

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Background: Vitamin D has an effect on bone health throughout life. In an ongoing study, the objective was to determine the association between maternal vitamin D status and their infants bone variables.

Aim: In this pilot study, we wanted to compare the precision of Peripheral Quantitative Computed Tomography (pQCT) as assessed by the coefficient of variation (CV %), with measurements in the tibial bone among nine months old infants.

Method: We performed two repeated pQCT scans on 10 infants, at the age of 9 months (±14 days). The scanner was adjusted at same fixed point when scanning the infants. The researcher supported the leg during the measurement. We measured 2 pictures at the same position of the bone. In-between the measurements we took the leg out of the scanner and repositioned it, to make the same procedure once again.

Results: CV for total, trabecular and cortical density were 1.8, 8.1 and 1.7% respectively. CV for cross-sectional area (CSA) was 14.6%. This would yield Least Significant Differences (LSD) in total, trabecular and cortical density of 5.1, 22.9 and 4.8%. LSD for CSA were 41.3%.The average measure for the Intraclass Correlation Coefficient (ICC) for total, trabecular, cortical density and CSA were 0.91, 0.72, 0.87, and 0.96%, respectively.

Conclusion: CV at the total, trabecular and cortical density, shows the reproducibility measurements ranged from 1.7 to 8.1%. In our measurements the CSA was 14.6%.The ICC of the total, trabecular and cortical density ranged from 0.72% to 0.91% and was 0.96% in the CSA. We therefore conclude that the pQCT-scans in the nine months old children are valid except for the CSA, which had a

higher variability.

30.38 Rune Thomsen

DEVELOPING THE BOYDEN CHAMBER ASSAY FOR PURIFICATION OF LOCALIZED RNAS IN ASTROCYTIC CELLS

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Localization of mRNA to the processes of polarized cells is a well described phenomenon, where for example in neurons beta-Actin mRNA localize to the distal parts of the neurites. Localized RNAs are important in cellular growth and migration, where they are translated locally as response to extracellular stimuli. Astrocytes are the most abundant cell type in the central nervous system, that like neurons grow long cellular processes. Yet, only a few studies have demonstrated RNA localization in the processes of astrocytes, where for example the mRNA of the intermediary filament protein GFAP, localize to the processes of cortical astrocytes isolated from a neonatal rat, and in Müller cell in the retina of the eye.The two chamber assay also known as the Boyden Chamber Assay, has been developed for various cell types, to investigate the RNA and protein content of cell processes. The Boyden Chamber Assay, is designed in such way that it allows only parts of a cell to grow through a porous membrane, thereby separating the cell soma from the cell processes. The cell processes can subsequently be purified and their content of RNA and protein can be analysed. To study the localization of RNA molecules in the processes of astrocytes, the development of new methods have been essential for this PhD project. I have developed the Boyden Chamber Assay, to allow growth of processes of the murine astrocyte cell line C8-S, and subsequently purification of RNA from such processes. This method provides an excellent way to screen for localized RNAs in the processes of cells of astrocytic origin.

30.39 Iben Blaabjerg Sundtoft

CERVICAL INSUFFICIENCY CAUSING PRETERM BIRTH DUE TO LOW CERVICAL COLLAGEN CONCENTRATION

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Cervical Insufficiency causing Preterm Birth due to Low Cervical Collagen Concentration

Objective: The aim of the study was to investigate the cervical collagen concentration in non-pregnant women with a history of cervical insufficiency.

Methods: The collagen concentration was determined in cervical biopsies obtained from 32 non-pregnant women with cervical insufficiency in their first pregnancy and a control group of 115 non-pregnant women.

Results: Women with cervical insufficiency had a significantly lower collagen concentration (65.8±4.8%) compared with the control group (69.0±4.7%) ($p=0.001$). The results remained statistically significant after adjusting for age and parity ($p=0.023$).

Conclusion: Cervical insufficiency causing preterm birth may be associated with a low cervical collagen concentration.

30.40 Pia Kirkegaard

DEVELOPMENT OF A COMPLEX INTERVENTION IN RISK COMMUNICATION USING ACTION RESEARCH AS METHODOLOGY

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Introduction and aim: In 2008, the Medical Research Counsil revised a five-step model for complex interventions in healthcare research, recommending attention to early phase development. It was argued that inadequate descriptions of the

interacting components in complex interventions in healthcare research have impeded replication in other contexts, hampering the scientific and practical value of effects. The aim of this study was to analyse the early phase development of a complex intervention in risk communication concerning development of a risk communication training programme. Method: Action Research (AR) was used to develop a training programme in risk communication. This included participant observation among medical researchers and interviews with general practitioners and patients at risk of cardiovascular disease. The AR approach initiated reflections on the research process, and called for a theoretical perspective to analyse the data produced during the development. A Science-and-Technology approach called SCOT was deemed appropriate for the analysis. SCOT has three key elements: interpretative flexibility, stabilisation of technology, and technological frames.Results: The SCOT perspective helped identify the following elements: Positions regarding purpose of risk communication (interpretative flexibility); rationales for the shape and content of the risk communication training (stabilisation of technology); and health risk discourses on medical disease prevention (technological frames). Discussion: Application of appropriate theoretical perspectives may prove necessary in order to produce knowledge about intervention developments applicable in other contexts.

30.41 Anna Pietraszek

POSTPRANDIAL DYSMETABOLISM - THE EFFECTS OF MONOUNSATURATED VS. SATURATED LIPIDS ON LIPID AND CARBOHYDRATE METABOLISM AND INFLAMMATION IN HEALTHY 1ST DEGREE RELATIVES OF PATIENTS WITH TYPE 2 DIABETES

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Type 2 diabetes (T2D) is a serious common disease and 1st degree relatives of patients with T2D have an increased risk of developing T2D themselves. This risk can be modified by the ingested diet. T2D is a part of the metabolic syndrome, the pathogenesis of which is partly explained by fasting dyslipidemia, postprandial dysmetabolism and impaired metabolic flexibility. This is established in patients with T2D, but sparsely studied in healthy relatives of patients with T2D.
In this project, we study postprandial dysmetabolism, inflammation, oxidative stress, adipocytokines, inkretines, appetite regulating hormones and the expression of the genes involved in above mentioned. We compare healthy 1st degree relatives of patients with T2D with healthy controls with no family history of T2D and look into differences in the response to meal stimulation with respectively saturated and monounsaturated fat. The subjects are examined with HOMA-IR and a DEXA scan (to establish their body fat percentage). Before and after the meal stimulation numerous blood samples and muscle (m. vastus lateralis) and fat tissue (abdominal subcutaneous) biopsies are taken. The biopsies will be used for studies of a vast number of genes.
The project will give us new knowledge about the interaction between the intermediate metabolism and the innate immune system and the early pre-diabetic changes in the 1stdegree relatives of patients with T2D. In the long run, the project will hopefully contribute to improving our guidance and treatment of persons at risk of developing T2D.

30.42 Filippo Peder D'Andrea

CANCER STEM CELLS INTRINSIC RADIOSENSITIVITY IN A MESENCHYMAL MOUSE MODEL FOR SOFT TISSUE SARCOMA

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Tumour resistance to irradiation is believed to be dependent on clonogenic cancer stem cells (SC), intrinsic radioresistance, and microenvironmental parameters. Recent studies show that various tumour SC are more resistant to radiation. So to what extent will radiation response of tumours be determined by radio-sensitivity of

cancer SCs relative to other in-vivo micro-environmental factors such as hypoxia? We have investigated this in a unique human sarcoma model derived from immortalized tumourogenic mesenchymal SC.
Mesenchymal SC were immortalized with retroviral insertion of human teleomerase (TERT20) and subclones (BB3 and CE8) were obtained. In-vitro radiation sensitivity was tested through estimation of Survival fraction at 2, 3 and 4Gy (SF2, SF3 and SF4). In-vivo sensitivity tested in NMRI nu/nu mice with tumour growth delay assay on xenografts irradiated with 5 or 10Gy when at a volume of 400mm3. Intra-tumoural oxygenation levels measured using Eppendorf pO2 probe.
In-vitro radiosensitivity could categorise cell lines into 3 groups: The most resistant cell line was the CE8 (SF2 0.40±0.01), the most sensitive was BB3 (SF2 0.23±0.02); the remaining cell lines showed intermediate response. In-vivo tumour growth delay curve confirmed that the most sensitive tumour was the BB3 and the most resistant one was CE8. At 400 mm3, there was no statistical difference in tumour oxygenation of the various cell lines.
In-vitro estimation of cancer SC radio-sensitivity prediced in-vivo radiation response better than measuring tumour oxygenation. These data suggests that intrinsic radio sensitivity of tumour cancer SC can be more detrimental for radiation response than hypoxia.

30.43 Nicklas Heine Staunstrup

30.44 Lene Sundahl Mortensen

A TRANSGENIC PORCINE MODEL FOR PSORIASIS AND A NOVEL SKIN-SENSOR SYSTEM

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The project consists of two legs, i) generating a psoriasis model based on over-expression of human integrin alpha2 and beta1 ii) a model harboring a sensitive sensor-receptor system allowing for evaluation of skin penetration of topical applied formulations and their potency.
Psoriasis involves dysregulation of keratinocyte proliferation and differentiation and inflammation caused by the cytokine release from skin-homing leukocytes. In the epidermis integrin alpha2 and beta1 expression is normally confined to the basal layer, however in psoriatic skin ascending post-mitotic keratinocytes also express these integrins thereby delaying differentiation and promoting proliferation.
We have constructed Sleeping Beauty (SB) transposons comprising expression-cassettes with one or both integrins under control of the human skin-specific involucrin promoter and have to date 6 transgenic animals.
The sensor-receptor model has a broad application potential, allowing for efficacy assessments of topical applied modalities interesting to the pharmaceutical industry. In the current context the Gal4 DNA binding domain is fused to the ligand binding domain of the human vitamin D receptor which is under control of the human stratum basale -specific K14 promoter. In formulations reaching the basal layer the ligand will induce hVDR activation which attaches to the UAS element by courtesy of the Gal4 domain where it acts as a transcription factor. Vitamin D analogs are employed in the treatment of psoriasis as they preserve homeostasis in the skin.
A SB transposon with the system in cis, is highly functional, however, all blastocyte transfers have lead to miscarriages.

EFFECTS OF DIFFERENT FRACTIONS OF WHEY PROTEIN ON POSTPRANDIAL LIPID AND HORMONE RESPONSES IN TYPE 2 DIABETES

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Background: Exacerbated postprandial lipid responses are associated with an increased cardiovascular risk. Dietary proteins influence postprandial lipemia differently, and whey protein has a preferential lipid lowering effect.
Objective: To compare the effects of different whey protein fractions on postprandial lipid and hormone responses added to a high-fat meal in type 2 diabetic subjects.
Design: Twelve type 2 diabetic subjects ingested 4 isocaloric test meals in randomized order. The test meals contained 100g of butter and 45g of carbohydrate in combination with either 45g of wheyisolate (iso-meal), wheyhydrolysate (hydro-meal), alpha-lactalbumin enhanced whey (lac-meal) or caseinoglycomacropeptide enhanced whey (CGMP-meal).Plasma concentrations of triglyceride, retinyl palmitate, free fatty acids, insulin, glucose, glucagon, GLP-1, GIP were measured at regular intervals until 8-h postprandially.
Results: The incremental area under the curve (iAUC) for triglyceride in plasma, the chylomicron-rich, and the chylomicron-poor fraction did not differ significantly between the 4 test-meals. The retinyl palmitate response was higher after the hydro-meal than after the iso- and lac-meal in the chylomicron-rich fraction ($P=0.008$) while no significant differences were found in the chylomicron-poor fraction. The hydro- and iso-meal produced a higher insulin response compared to the lac- and CGMP-meal ($P< 0.001$).Otherwise no significant differences in the hormone responses were found in iAUC over the 480 min period.
Conclusion: A supplement of four different whey protein fractions to a fat-rich meal had similar effects on postprandial triglyceride responses in type 2 diabetic subject

30.46 Kasper Toustrup

HYPOXIC GENE EXPRESSION CLASSIFICATION WITH PROGNOSTIC AND PREDICTIVE IMPACT IN HEAD AND NECK SQUAMOUS CELL CARCINOMAS (HNSCC)

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Aim: To develop a gene expression classifier for identification of hypoxic tumours in HNSCC.
Background: Hypoxic tumours are associated with increased resistance to radiation therapy. In HNSCC this resistance can be reduced by the additive use of hypoxic modifier. Gene expression classification is a promising strategy to identify hypoxic tumours and thereby candidate patients for such therapy.
Methods: We developed a hypoxic classifier based on in vivo validated hypoxia responsive genes and gene expressions from a training set of 58 HNSCC biopsies that had previously been ranked according to oxygen status. To evaluate the classifier, we classified 323 independent HNSCC's from the randomized, double blinded DAHANCA 5 study as "more" or "less" hypoxic. This study had previously proved beneficial effect on the locoregional tumour control at 5 years (LRC) by adding the hypoxic modifier Nimorazole to the radiation treatment.
Results: The final hypoxic classifier constituted 15 genes. Of the 323 HNSCC from the independent dataset 35% were classified as "more" hypoxic. The LRC was significantly improved in those classified as "more" hypoxic and receiving Nimorazole compared to those categorized as "more" hypoxic treated with placebo (49% vs 18%, $p=0.002$). We found a uniform LRC in the group categorized as "less" hypoxic, irrespective of additive treatment with placebo or Nimorazole (50% vs 44%, $p=0.42$).
Conclusion: The classification as a "more" hypoxic tumour based on the developed 15 gene hypoxic classifier is associated with a significantly poorer LRC in HNSCC, which can be improved and made equal to the "less" hypoxic tumours by adding Nimorazole to the radiation treatment.

30.48 Francesco

Trepiccione

ACUTE LITHIUM EFFECT ON INNER MEDULLARY COLLECTING DUCT

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Lithium treatment affects the urinary concentration ability. Here we used a mass spectrometry-based quantitative phospho-proteomics to examine the early molecular targets of Li action in principal cells. We treated 2 equal groups of rats with a gavage of either LiCl or NaCl (2.4 mmol/Kg BW). After 9 hours rats were killed and IMCD suspensions were made from the kidneys. IMCD suspension was digested by trypsin and phosphopetides enriched by immobilized-metal affinity chromatography (IMAC). Phopshopetides were submitted to an LTQ-Orbitrap LC-MS/MS system and label free relative quatification of MS1 peak integration was carried out. Three serarching algorithms (InsPect, OMSSA, SEQUEST) were used to analyse the data.

Serum Li level reached 0.81 ± 0.05 mmol/L while Li total excretion after 9 hours was 136,16 ± 11,78 μmol. Urine volume was larger in Li treated group 47.29 ± 6.74 μl/min/Kg ($p<0.01$). We identified 1224 unique phophopeptides. Motif analysis of 74 phopshopeptides with, at least, 1,5 fold increased abundance in the Li group shared a common predominant proline-directed motif. This is consistent with a Li-induced upregulation of mitogen activated kinases protein cluster. Proline directed motifs are target sequence for MAPK. Other proline directed phosphopeptides upregulated by Li belonging to tight-juncture cluster was identified.

Vasopressin downregulates MAPK and so phosphopeptides containing a proline directed motifs in mpkCCD cells. Our data suggest that MAPK pathways could be an early target of Li action in IMCD. By regulating in opposite direction of vasopressin the MAPK pathway Li could drive the aquaretic effect.

30.49 Kristian Havmand Mortensen

HAEMOSTATIC BALANCE IN TURNER SYNDROME

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Background: The haemostatic balance remains unknown in Turner syndrome (TS) even though case reports infer increased occurrence of thromboembolic disease on a backdrop of life-long elevated risk of premature myocardial infarction of unresolved etiology.

Objective: We aimed to assess the hemostatic balance in unselected adult Turner syndrome.

Methods: In 60 patients with TS we characterized the activities of the haemostatic system, elucidated by assessment of a panel of clotting factors and thrombosis risk factors. We related these findings to selected inflammatory and liver markers, and further compared them with normative data.

Results: Most (81%) patients received hormone replacement therapy. The medians of all measured factors and inflammatory parameters were not different from normative data, but many cases displayed values of CRP, fibrinogen, fibrin D-dimer, factor VIII, von Willebrand factor (vWF), cholesterol and liver parameters that were greater than normative limits. CRP, fibrinogen, vWF, factor VIII and liver parameters were highly and positively correlated. The Factor V Leiden G1691A gene polymorphism heterozygosity was detected in 12.5%.

Conclusion: We describe a significant proportion of individual TS females having high levels of vWF, factor VIII, fibrinogen and CRP and an increased frequency of the Leiden mutation. Our findings suggest that a subset of TS have an unfavourable

haemostatic balance that may contribute to the increased risk of premature ischemic heart disease and possibly increase the risk of deep venous and portal vein thrombosis.

30.50 Janne Lebeck

GENDER SPECIFIC REGULATION OF AQUAPORIN-9 AND GLYCEROL KINASE IN STARVED RATS

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Glycerol, a product of lipolysis, is an important precursor for hepatic gluconeogenesis. However, the regulation of hepatic glycerol metabolism is far from fully elucidated. Aquaporin-9 (AQP9) has been linked to the hepatic uptake of glycerol and once inside the cell glycerol kinase (GK) phosphorylates it into glycerol-3-phosphate. In order to investigate gender differences in regulation of the initial hepatic glycerol metabolism, we used Western blotting and immunohistochemistry to analyze the effect of starvation on hepatic protein expression in male and female rats. Furthermore, the effect of ovariectomy was analyzed. We here demonstrate that hepatic protein expression of AQP9 and GK is coordinately regulated in a gender dependent manner. Starved males had increased expression of both AQP9 and GK whereas no changes were observed in starved females. In addition, biophysical assessment of hepatocyte membrane glycerol transport in starved rats showed higher permeability in males when compared with females. Starvation was accompanied by increased plasma glycerol levels only in female rats. Furthermore, starvation of ovariectomized rats resulted in an increased expression of AQP9 similar to what was observed in starved males, whereas GK abundance remained unchanged. Like in starved males, no increase in plasma glycerol was observed in the starved ovariectomized females. Overall, these results demonstrate that sexual dimorphism exists in the initial hepatic handling of glycerol in starved rats. Moreover, our data suggest that ovary derived factors are crucial for the gender specific regulation of hepatic AQP9 expression.

30.51 Dorte Rytter

MATERNAL INTAKE OF FISH OIL DURING PREGNANCY AND BLOOD PRESSURE IN THE 19 YEAR OLD OFFSPRING

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Background: Studies in experimental animals and humans have suggested that changes in the peri- and early post-natal intake of n-3 fatty acids can affect CVD risk factors in adult life. This has lead to the hypothesis that n-3 fatty acid supplementation in pregnancy may have a beneficial effect on blood pressure in the offspring.

Specific aims: The aim of the present study was to investigate the effect of supplementation with 2.7 grams of long chain n-3 fatty acids during third trimester of uncomplicated pregnancies on blood pressure in the 19 year old offspring.

Design and methods: The study was based on long term follow-up of a randomised controlled trial from 1990, in which 533 pregnant women were randomised to fish-oil (2.7g n-3 fatty acids/day; n=266), olive-oil (4g/day; n=136) or no oil (n=131). In 2009, the offspring from the randomised controlled trial were invited to a physical examination including blood pressure measurements.

Intention to treat analysis was performed and a t-test was used to compare blood pressure between the fish-oil and olive-oil groups.

Results: A total of 243 of the offspring were studied (fish-oil n=108, olive-oil n=72 and no oil n=63). Blood pressure did not differ between the fish-oil and olive-oil groups. The unadjusted difference was -0.48 (-3.37; 2.4) mmHg in systolic blood pressure and 1.12 (-0.60; 2.84) mmHg in diastolic blood pressure.
Conclusion: We could detect no effect of fish-oil supplementation during pregnancy on offspring blood pressure in adolescence

30.52 Claus Tvedesøe

ENHANCEMENT OF ANTI-TUMOR ACTIVITY BY USING IL-2 IN COMBINATION WITH CANCER THERAPY

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Objective: The concept of activating the host immune mechanisms to destroy residual tumor cells after chemotherapy has long beenproposed. IL-2, used as a single agent, has shown activity both preclinically and clinically against a wide spectrum of tumors.
However, due to the rapid clearance of IL-2, high and frequent doses must be administered to achieve significant antitumor activity, leading to serious side effects, including capillary leakage, cardiac toxicity, and hypotension. Combined treatment with doxorubicin and non-toxic doses of IL-2 has been shown to be effective against a variety of murine tumors.
Our aim in this study is to compare the treatment effect of different combination regimes with IL-2 by adding radiation therapy and localized mild hyperthermia as treatment modalities.
Materials and Methods: The study will be performed using C3H mammary carcinoma grown in the right rear foot of female CDF1 mice.
On day 0 (tumours at 100 mm3) the mice will recieve their respective treatments and the mice recieving IL-2 as mono or combination will recieve recieve injections with 150,000 IU IL-2 on day 0-4. Mice in combination groups will be beside IL-2 be randomized to recieve a single treatment of either mild hyperthermia (42.5°C/60 min), radiation (10 gray) or liposomal doxorubicin 8mg/kg. Outcome will be tumor growth time to 1000mm3.

30.53 Marta Bauerek

30.54 Emil Kofod-Olsen

EFFECT OF DIETARY CHOLESTERYL ESTERS ON THE PLASMA LIPID LEVELS IN LDLR-DEFICIENT MICE

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Objective. A few older animal studies indicate that esterification reduces the absorption of cholesterol and lowers the plasma cholesterol level in animal models. We tested the effect of dietary cholesteryl esters (CLE) on plasma cholesterol levels in LDLR-/- mice. Methods. Male LDLR−/− mice were randomized into 5 dietary regiments: (1). Normal chow (NC), (2). NC+0.2% CLE, (3). Western type diet (WD) + 0.2% CL, (4). WD + 0.1% CL and 0.1% CLE, (5). WD + 0.1% and 0.1% CLE. Desired study length is 24 weeks. Serum lipoprotein profiles at the baseline and the end of week 10 of the intervention period were determined by means of fast-protein liquid chromatography (FPLC). Total cholesterol and triglycerides concentrations were measured in all fractions enzymatically using commercially available kits (CHOD/PAP and GPO/PAP, Roche). Results. After first 10 weeks of the study compared with those fed with NC, in mice fed with NC supplemented with 0.2% CLE cholesterol and triglycerides plasma concentrations were slightly increased. Compared with WTD, both interventions reduced plasma cholesterol levels. Supplementation with 0.1% CLE decreased total cholesterol by 42%, whereas mean plasma total cholesterol level in the 0.2% CLE group was 22% lower than that of the WTD group. Plasma triglycerides level in group with 0.2% showed no changes, but increased in the 0.1% CLE by 13%. As the study is on-going, the further results will be presented at the PhD day 2010. Conclusion. Dietary CLE lowered plasma cholesterol but not triglyceride levels in LDLR-/- mice.

HUMAN HERPESVIRUS-6B PROTEIN U20 IS A NOVEL INHIBITOR OF TNF

RECEPTOR SIGNALLING

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Human Herpesvirus-6B (HHV-6B) is a ubiquitous virus with a seroprevalence of >90% in the adult population. Primary infection leads to a mild childhood disease, after which the virus enters a latent stage and is tolerated by the immune system. HHV-6B expresses several cytoplasmic and membrane bound immune-regulating proteins. We here report a novel immune regulating function of the HHV-6B-encoded protein (U20). We identify U20 as a 75 kDa membrane protein that completely blocks signalling through the Tumour Necrosis Factor alpha Receptor 1 (TNFR1).. The block is at the receptor-level, since receptor proximal downstream signalling pathways are obstructed. Blocking of TNFa, the ligand for TNFR1, is a widely used anti-inflammatory treatment in a number of autoimmune diseases such as rheumatoid arthritis and Crohn's disease. U20 may therefore potentially be used as a drug in treatment of autoimmune diseases.

30.55 Krista Dybtved Kjærgaard

RELIABILITY OF 51CR-EDTA PLASMA AND URINARY CLEARANCE AS A MEASURE OF RESIDUAL RENAL FUNCTION IN DIALYSIS PATIENTS

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Background: Residual renal function is a topic discussed currently and randomized controlled trials are conducted to clarify how to preserve residual renal function. However, existing methods for measuring residual renal function are all subject to uncertainty and there is a need for establishing a standard for measurements for glomerular filtration rate in dialysis patients. As 51Cr-EDTA is a true renal filtration marker, 51Cr-EDTA is suitable for measuring glomerular filtration rate.
Methods: 11 peritoneal dialysis patients and 12 hemodialysis patients, all stable with urine output > 300 ml/24h underwent 2 separate and identical investigations approx. 1 week apart. 51Cr-EDTA was injected, and blood samples were drawn at 3, 3½, 4, 4½, 5 and 24 hours giving a plasma activity curve. Urine and peritoneal dialysate fluid were collected in the same period for measurement of 51Cr-EDTA activity.
Results: 51Cr-EDTA clearance in plasma was 2.2-15.8 ml/min/1.73m2 and in urine 0.7-10.8 ml/min/1.73m2. Week-to-week reproducibility expressed as coefficients of variation were below or equal to 10% for plasma clearances and 13% and 14% for urine clearances in hemodialysis and peritoneal dialysis patients, respectively.
Conclusions: Due to a simplified single sample technique, plasma clearance of 51Cr-EDTA can be used for clinical purposes when urine collection is impossible. Moreover, urine clearance of 51Cr-EDTA seems promising for estimations of residual renal function in a research setting. However, further studies are needed to consolidate the methods.

30.56 Stefan W. Harders

LIMITED VALUE OF 99MTC DEPREOTIDE SPECT COMPARED TO CT FOR THE EVALUATION OF PULMONARY LESIONS

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Purpose: Today a contrast enhanced Multi Detector CT scan is the first-choice examination when evaluating patients with suspected lung cancer. However, while

clinical focus is on CT, research focus has shifted to molecular biologic methods where radioactively marked substances are injected into subjects and home in on malignant lung tumors. We examined whether a contrast enhanced CT scan supplied with an additional non contrast enhanced HRCT scan, or a new and more costly 99mTc depreotide SPECT scan, was the best first-choice examination for the work-up of pulmonary lesions. Furthermore, whether a 99mTc depreotide SPECT scan was an appropriate second-choice examination for patients with indeterminate lesions.
Methods: 140 participants were included for analysis. CT images were given a malignancy potential rating of 3, 2, or 1 with higher rating being indicative of disease, and 99mTc depreotide SPECT images were graded either positive or negative. Histopathology and CT follow-up were used as reference standard. Sensitivity, specificity and diagnostic accuracy were calculated.
Results: Overall sensitivity, specificity and diagnostic accuracy of CT were 97%, 30% and 84%. Overall sensitivity, specificity and diagnostic accuracy of 99mTc depreotide SPECT were 94%, 58% and 76%. For indeterminate lesions sensitivity, specificity and diagnostic accuracy of 99mTc depreotide SPECT were 71%, 68% and 69%.
Conclusion: Both CT and 99mTc depreotide SPECT contributed valuably to the evaluation of pulmonary lesions. Although CT was matched by 99mTc depreotide SPECT, results were not superior and did not contribute further to the diagnostic work-up. For indeterminate lesions, sensitivity was too low.

30.57 Pernille Kure Vandborg

30.58 Casper Nielsen

RELATIONSHIP BETWEEN ACUTE INTERMEDIATE-ADVANCED BILIRUBIN ENCEPHALOPATHY, SERUM BILIRUBIN LEVELS AND CHRONIC BILIRUBIN ENCEPHALOPATHY IN LATE PRETERM AND TERM NEONATES

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Background: Jaundice occurs in the majority of newborn infants during the first week of life and is normally harmless. Occasionally the plasma bilirubin levels increase to very high and extreme levels and the infants develop early phase acute bilirubin encephalopathy characterized by lethargy, hypotonia and poor sucking. In rare cases this condition progress to intermediate and advanced phase characterized by opistotonus, alternating tonus, high pitched cry and ultimatively seizures, fever, coma and respiratory failure. The infants who progress to intermediate and advanced acute bilirubin encephalopathy most often suffer from chronic brain damage, kernicterus.
Aim: To describe the relationship between acute intermediate-advanced bilirubin encephalopathy, total serum bilirubin (TSB) levels and the risk of chronic bilirubin encephalopathy.
Materials and methods: All late preterm and term infants, i.e with a gestational age ≥ 35 weeks, born throughout the period of 1st of january 2000 to 31st of december 2007 in Denmark who had a TSB ≥ 450 umol/l in the neonatal period were identified by linking electronically stored laboratory data with the personal identification number. Through the Danish National Hospital Register all infants with a diagnosis of bilirubin encephlaopathy in the study period were identified.
Results: During the study period 502,766 infants were born alive with a gestational age ≥ 35 weeks and 242 developed a TSB ≥ 450 umol/l (incidence 48 per 100.000). Five infants had acute intermediate-advanced bilirubin encephalopathy with peak TSB varying from 544-986 umol/l. Three of those infants developed chronic bilirubin encephalopathy and two had no sequelae.

A NEW SAMPLE PREPARATION METHOD TO PREVENT INTERFERENCES FROM L-LACTATE DEHYDROGENASE IN THE QUANTITATIVE DETERMINATION OF D-LACTATE IN PLASMA.

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Background: Naturally occurring L-Lactate dehydrogenase (L-LDH) in plasma interferes with the chemical reaction in the quantitative determination of D-Lactate in plasma.

In the presence of NAD+, L-LDH converts naturally occurring L-Lactate in plasma to pyruvate and NADH. Sample deproteinization with perchloric acid (PCA) or ultrafiltration procedures are widely used in the preparation of plasma samples to prevent interference from L-LDH, but both procedures are time consuming. A simple sample preparation method was developed to prevent this interference.

Methods: D-Lactate was analyzed by using a D-Lactic Acid kit. In the reaction D-Lactate is oxidized to pyruvate by NAD+ in the presence of D-Lactate dehydrogenase (D-LDH). The amount of NADH formed in the coupled reaction, measured by the change in absorbance at 340 nm, is proportional to the concentration of D-Lactate. NaOH was added to the plasma samples, and pH, L-LDH, L-Lactate and D-Lactate was measured in the samples and compared to untreated plasma samples and plasma samples deproteinizated with PCA.

Results: By increasing the pH in plasma samples to 11.5, the L-LDH activity was totally inactivated. The chemical reaction in the D-Lactate determination was unaffected by the increased pH. There was no significant difference of D-Lactate or L-Lactate in plasma samples mixed with NaOH compared with plasma samples treated with PCA. In the untreated plasma samples D-lactate was increased due to the L-LDH and L-Lactate.

Conclusions: The developed sample preparation method to prevent interference from L-LDH in the quantitative determination of D-Lactate in plasma is a simple, cheap, and labour saving method.

30.59 Simon Rasmussen

INDUCTION OF AUTOPHAGY DURING HERPES SIMPLEX VIRUS INFECTION BY A POTENTIAL NOVEL MECHANISM

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Autophagy is a cellular degradation pathway known to be involved in toll like receptor (TLR)-mediated recognition, degradation, and antigen presentation of pathogens. During herpes simplex virus (HSV) infection of permissive cells dsRNA-dependent protein kinase (PKR) has been identified as an essential inducer of autophagy.

Our aim is to investigate the existents of PKR independent autophagy induction during HSV infection in non-permissive cells. The role of autophagy in delivery of HSV to endosome-located TLR9 is also studied.

We have found indications of PKR independent induction of autophagy in bone marrow derived dendritic cells (BM-DC)s. Entry defect glycoprotein (g)H- and gB-deficient HSV-1 as well as L particles, which are HSV-1 particles lacking capsid and DNA, all induced a low level of the autophagy marker, LC3 II. In addition uv-inactivated HSV-1, incapable of replicating and thus producing dsRNA, leads to formation of LC3 II, suggests a PKR independent induction of autophagy.

Preliminary results also indicate LC3 II formation in a macrophage like cell line expressing dn PKR. TLR9 mediated HSV-1 IFNβ induction is independent of viral replication but dependent on viral entry. In addition, inhibition by 3-methyladenine of PI3 kinase Class III, which is crucial in autophagosome formation, abrogates IFNβ induction.

Collectively, these findings indicate the existence of an entry and PKR independent induction of autophagy during HSV-1 infection. The results also indicate a role for autophagy in TLR9 mediated recognition of HSV-1. The precise mechanism, in which HSV mediated LC3 II up regulation, and thus autophagosome formation, is still to be established.

30.60 Tina Storm

NOVEL CUBN MUTATION REVEALS NO DETECTABLE RENAL CUBILIN AND SUGGESTS THAT IT IS NOT VITAL FOR HUMAN EMBRYONIC DEVELOPMENT

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Background: Cubilin is an important receptor involved in intestinal absorption of vitamin B12 and reabsorption of proteins from the glomerular ultrafiltrate. Murine studies furthermore suggest that both cubilin and the receptor partner amnionless are essential for normal embryonic development. Cubilin function is affected in Imerslund-Gräsbeck syndrome (IGS) patients. IGS is a rare, autosomal recessive disorder characterized by a selective, intestinal, intrinsic factor-vitamin B12 malabsorption and is often accompanied by an additional proteinuria. Aim: To investigate the role of cubilin in renal protein handling in a patient with cubilin deficiency. Results: We identified a novel homozygous guanine for thymine exchange in the conserved donor splice site of exon 23 of the cubilin encoding gene, CUBN in an IGS patient. No cubilin was detected in a renal biopsy suggesting an effective null mutation of the CUBN gene as well as an abnormal, cytoplasmic distribution of the receptor partner amnionless. Immunoblotting of patient urine accordingly showed selective tubular proteinuria with increased excretion of cubilin ligands such as vitamin D-binding protein, transferrin and α1 microglobulin. Conclusions: Correlations between immunohistochemical data and the urinary protein excretion pattern demonstrated a central role of cubilin in the handling of filtered proteins in the human kidney and demonstrated the interdependent relationship of cubilin and amnionless in man for the first time. This patient, however, presented with no additional developmental abnormalities or physical disabilities suggesting that cubilin is not essential for human embryonic development.

30.61 Michael Smærup Brandt

30.62 Thomas Maribo

IT-SUPPORT IN HOME REHABILITATION OF GERIATRIC PATIENTS WITH VESTIBULAR DYSFUNCTION

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Objectives: Elderly patients with vestibular dysfunction have a 8-fold increase in the odds of falling compared to other fall patients. Vestibular rehabilitation (VR) including home training may reduce this risk. However, several studies show, that the elderly persons have low compliance as to perform home exercise. A computer-training program "Move it To improve it" (MiTii) was successfully used for home exercise by patients with cerebral palsy. In cooperation with Center for Cerebral Palsy (Elsass Center) we have developed this program to be used by patients with vestibular dysfunction when training at home the aim of this pilot study was to test the acceptability by elderly patients.

Method: Two females aged 95 and 76 years participated. Peripheral vestibular dysfunction was diagnosed in one patient and mixed (peripheral and central) vestibular dysfunction in the other.

The patients were selected from the Fall Clinic, Department of Geriatrics, Aarhus University Hospital. Computers were installed in their homes by the author. Observation of the patients was used to determine whether the patients accept MiTii.

Results: MiTii seemed to motivate the elderly to exercise. This may be due to: MiTii is user-friendly. MiTii is adjusted and adapted to the individual user, who can perform exercise while being challenged. MiTii generate feedback to the therapist at the hospital. Conclusions

MITII seems to motivate at least these two elderly ladies to exercise at home. For further evaluation of the effect on VR a randomised study has just started.

POSTURAL STABILITY IN LOW BACK PAIN PATIENTS: RELIABILITY OF SWAY MEASURES ON A PORTABLE FORCE PLATFORM

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Low Back Pain (LBP) patients have poorer postural stability compared to healthy controls. Postural stability has been assessed by means of the force platform technique in clinical trials. A number of authors have reported that LBP patients are more dependent on vision compared to a healthy population, and the difference between tests with eyes open (EO) and eyes closed (EC) (EO/EC difference) might be of interest for rehabilitation.
The objective was to assess postural stability in LBP patients by analysing the intra-session reliability of the Portable Force Platform technique and further more analysing reliability of the differences in testing with eyes open and eyes closed.
49 LBP patients were tested using a portable force platform and were carried out with eyes open and eyes closed. There was a 10 minute break between tests and retests. The analysis calculated the intra-class correlation coefficient (ICC2.1), and the standard error of measurement (SEM).
Results: We found ICC=0.86 and a SEM of 11% using for trace length and velocity from the portable force platform technique. We found acceptable ICC of 0.85 in the EO/EC difference but a too high SEM.
Conclusions: The reliability of the portable force platform as a measure of postural stability in LBP patients is acceptable on a group level, while only trace length and velocity are reliable on a single-patient level. The reliability of the EO/EC difference was acceptable with regard to group-level reliability, but not on a single-patient level. The portable force platform technique is easy and time-efficient, and its reliability makes it relevant as outcome measure in clinical trials, but not on a single-patient level.

30.63 Martin Majlund Mikkelsen

INSULIN RESISTANCE, ADIPONECTIN AND ADVERSE OUTCOMES FOLLOWING ELECTIVE CARDIAC SURGERY: A PROSPECTIVE FOLLOW-UP STUDY

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Background: Insulin resistance and adiponectin are markers of cardio-metabolic disease and associated with adverse cardiovascular outcomes. This study examined whether preoperative insulin resistance or adiponectin were associated with short- and long-term adverse outcomes following cardiac surgery.
Methods: In a prospective study, we assessed insulin resistance and adiponectin levels from preoperative fasting blood samples in 836 nondiabetic patients undergoing elective cardiac surgery. Population-based medical registries were used for postoperative follow-up. Outcomes included all-cause death, myocardial infarction or percutaneous coronary intervention, stroke, reexploration, renal failure, and infections. The ability of insulin resistance and adiponectin to predict clinical adverse outcomes was examined using receiver operating characteristics.
Results: Insulin resistance and adiponectin were not statistically significantly associated with 30-day mortality, but adiponectin was associated with an increased 31-365-day mortality (adjusted odds ratio 2.9 [95%CI 1.3-6.4]) comparing the upper and three lower quartiles. Insulin resistance was a poor predictor of adverse outcomes. In contrast, the predictive accuracy of adiponectin (area under curve 0.75 [95%CI 0.65-0.85]) was similar to that of the EuroSCORE (area under curve 0.75 [95%CI 0.67-0.83]) and a model including adiponectin and the EuroSCORE had an area under curve of 0.78 [95%CI 0.68-0.88] concerning 31-365-day mortality.
Conclusions: Elevated adiponectin levels, but not insulin resistance, were associated with increased mortality and appear to be a strong predictor of long-term mortality

following cardiac surgery.

30.64 Jesper Brink Askov

NOVEL PAPILLARY MUSCLE FORCE TRANSDUCER: INITIAL TESTS AND RESULTS

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Background: Force transfer from the papillary muscle tip (PMT) through the chordae tendineae to the mitral valve is essential in maintaining proper valvular and left ventricular function; however, the exact PMT force which is a crucial element of valvular-ventricular interactions is still unknown as this has never been investigated in vivo.

Hypothesis/Aims: This study aimed at designing a device capable of measuring the force transferred from the chordae tendineae to the PMT with minimum interference with subvalvular geometries and papillary muscle contraction.

Materials & Methods: Using computer aided design the device was configured to be implanted in between the fibrous part of the PMT and the remaining papillary muscle, see figure 1. The active height of the device was only 2 mm in order to preserve native subvalvular geometries. A strain gauge was mounted at the connection point of the two plates and the device was calibrated with respect to a force acting perpendicular on the plates.

Results: A prototype of the transducer was implanted in between the posterior papillary muscle and PMT in a pig heart without visible distortion of the mitral valve apparatus verified by ultra sound. The peak systolic PMT force was 6.2 N at a left ventricular pressure of 90 mmHg.

Conclusions: Initial tests prove that it is possible to measure forces acting on the PMT in vivo with minimal interference of subvalvular geometries. These measurements are the first to describe the forces acting through the papillary muscle in vivo.

30.65 Anne-Cathrine Bareid Østby

30.66 Michael Kjeldager Tjørnild

MULTIPLEX PCR DIAGNOSTICS OF 12 COMMUNITY RESPIRATORY VIRUSES THROUGH FOUR YEARS

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Introduction: Community respiratory virus infections represent a significant burden to the society. PCR methods are increasingly used to diagnose respiratory viruses as they provide rapid and sensitive results, which is of importance in hospital settings. Few PCR-based studies of major respiratory viruses analyzed during multiple years have been published.

Objective: To show the results after 4 years of systematically testing all received respiratory samples with real-time multiplex PCR.

Methods: 7024 respiratory samples collected between 01.01.2005 and 31.12.2008 from 5653 outpatients and hospitalized patients were analyzed for: Influenza A and B, respiratory syncytial virus (RSV), human metapneumovirus (HMPV), adenovirus, parainfluenza viruses 1-3, coronaviruses 229E, NL-63 and OC43, and rhinovirus. For patients presenting several samples, only the first sample was included.

Results: 2546 samples were positive for one virus. 315 samples were positive for 2-4 viruses. The viruses showed seasonality, except from perennially detection of rhinovirus and adenovirus. Seasonality was similar between in- and outpatients. Children less than 3 years were mainly infected with RSV, rhinovirus and adenovirus. Influenza A and B were detected in youth and adults. HMPV, coronaviruses and parainfluenza viruses were detected in all age groups.

Conclusion: Introduction of multiplex PCR detecting all major respiratory viruses in

diagnostics can enhance the management of patients with respiratory infections, especially in hospital settings. Systematic PCR-based surveillance of respiratory viruses provides additional etiological knowledge of these infections.

REPEATABILITY AND DETECTION QUALITY IN DOUBLE DXA-SCANS - A CLINICAL COMPARISION OF 2 SOFTWARES

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Aim of this study was to compare knee-specific (K) to spine-mode software (S) for Dual X-ray Absorptiometry (DXA) knee-scans. We investigated the possible difference in 1) clinical precision of double examinations and 2) implant and tibial bone edge detection.

42 patients were double scanned with both K and S. We evaluated Bone Mineral Density measurements (g/cm2) in 3 regions of interest below the tibial plateau (Coefficient of Variation CV and Repeatability Standard deviation (Sr)). We also evaluated automatic detection ability of implant and tibial bone edges.

CV for K: 2.78-6.18%. CV for S: 2.19-5.59%. Sr: 0.015-0.047 for K and 0.032-0.043 for S ($p=0.54$). S implant detection was 100% in both AP and LA; for K implant detection was 10.7% AP ($p<0.01$) and 94% LA ($p=0.06$). S AP bone edge detection was 0% laterally and 70.2% medially. K AP resulted in 45.2% laterally ($p<0.01$) and 70.2% medially ($p=1.00$). S LA bone edge detection was 65.5% anteriorly and 2.4% posteriorly. K LA resulted in 48.9% anteriorly ($p<0.05$) and 2.4% ($p<0.01$).

Precision of repetitive scans was equal in both softwares. Implant detection was better with S in AP scans, which favors S, since manual detection is time-consuming and could result in incorrect point-typing. On the other hand K was significantly better in detecting the medial tibial limit in AP scans and both the anterior and posterior limit in LA scans. Whether DXA follow-up is carried out with either of the examined software types, one should not disregard the fact that in both cases much effort must be put into manual correction. More precise detection algorithms will be applauded by researchers and could lead to more accurate DXA measurements.

30.67 Chunsen Wu

RISK OF CANCERS AND CARDIOVASCULAR DISEASES IN OFFSPRING EXPOSED TO A DIABETIC ENVIRONMENT IN UTERI

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Aims:

We explored whether children exposed to diabetes mellitus (DM) in uteri have an associated with increased risk for childhood cancers and cardiovascular diseases.

Materials and Methods:

We used data from the Danish Medical Birth Registry, the Danish Civil Registration System, and the Danish National Hospital Register to identify 1,546,815 singletons from 1978 to 2004 in the final population.

Statistical Analyses

Children were followed from the day of birth until the first hospitalization or first outpatient visit for the disease under study, death, emigration, or December 31, 2006, whichever came first.

Hazard ratios (HRs) and 95% confidence intervals (95%CIs) for risks of outcomes of interest were estimated by using Cox regression. Subsequently, We adjusted the results for potential confounders.

Results

There were 2,386 (0.15%), 5,646 (0.37%), 578 (0.04%), and 5875 (0.38%) children exposed to type1 DM (T1DM), type2 DM (T2DM), Unspecified DM (UnDM), and gestational DM (GDM), respectively. The exposed children had an increased of birth weight in all categories. An increased risk for malignant neoplasm was only found among children exposed to T2DM (HR=2.19, 95%CI: 1.26;3.79). The risks for cardiovascular diseases increased regardless of which types of exposure. (HR=3.89,

95%CI: 2.34;6.48), (HR=1.82, 95%CI: 1.31;2.52), and (HR=1.51, 95%CI: 0.78;2.90) are risks for children exposed to T1DM, T2DM, GDM respectively.
Conclusion
Children exposed to T2DM in uteri have an increased risk of malignant neoplasm. While children exposed to DM in uteri have an increased risk of cardiovascular diseases regardless of exposure to which types of DM.

30.68 Morsi Abdallah

INTRAUTERINE INFLAMMATION AND AUTISM: MEASUREMENTS OF SELECTED NEUROTROPHINS AND CYTOKINES LEVELS IN AMNIOTIC FLUID SAMPLES FROM A DANISH HISTORIC BIRTH COHORT

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Background: Imbalanced immune response has an important role in the pathophysiology of autism. Many studies have examined patterns of inflammatory biomarkers in individuals with autism but results reported are inconsistent. However, to our knowledge, no investigations have been carried out using amniotic fluid samples.
Objectives: In this study, measurements of selected neurotrophins and cytokines in amniotic fluid samples of mothers of autistic offsprings, and their controls are performed.
Material and methods: A total of 414 cases and 843 controls were identified in a Danish historic birth cohort (HBC) created at Statens Serum Institute. Data of interest were retrieved from different Danish national registers using the unique number assigned to all citizens in Denmark (CPR). Selected inflammatory markers were measured using Luminex techniques. Data were analyzed in a case-cohort design. Relevant statistical methodologies including regression analyses, Cox proportional hazard models and mixed-model analysis of variance models will be used with correction for multiple testing.
Results and conclusion: Preliminary results performed on dried blood spots samples showed a significantly increased risk for Infantile Autism (IA) overall with elevated Interleukin 8(IL8), low Regulated upon Activation, normal T cell Expressed and presumably Secreted (RANTES) and low Brain-Derived Neurotrophic Factor (BDNF). There was a decreased risk from low Triggering Receptor Expressed on Myeloid cells (TREM-1) for IA in girls and from low C-reactive protein for IA in normal birth weight infants. Results from this study will contribute directly to the general understanding of the pathophysiology of autism.