

PHD DAY

HEALTH

PROGRAMME & ABSTRACTS

24 JANUARY 2014



AARHUS
UNIVERSITY

PHD DAY 2014

PROGRAMME

8.30 Welcome by Allan Flyvbjerg

Dean, Aarhus University, Faculty of Health Sciences

8.40 Welcome by Nis Pedersen Jørgensen

Chairman of the PhD-association

8.45 Fogh-Nielsen Prize Competition

Chaired by Professor Søren Moestrup, Chairman of the Fogh-Nielsen board

9.30 Coffee break, fruit is served

9.45 Oral presentations

11.15 Poster presentations

12.30 Lunch/poster viewing

13.15 Communication strategies at Health

Ulla Krag Jespersen, AU Communication

13.25 'Scientific Communication – Science/Science Fiction'

- speak and panel debate

Main Speaker:

- Peter Lund Madsen, MD, DMSc,

Panel participants:

- Leiv Sydnes, Professor, University of Bergen, member of International Council for Science
- Mette Davidsen-Nielsen, CEO, Dagbladet Information
- Lars Østergaard, MD, Clinical Professor, Aarhus University Hospital

Moderated by Ole Steen Nielsen

Vice-dean of Research, Aarhus University Faculty of Health Sciences



PHD DAY 2014

PROGRAMME

15.00 Coffee break

15.15 Skou Lecture

Understanding acid/base physiology a cornerstone in medical science and praxis
Professor Walter Boron, MD DMSc. Department of Physiology and Biophysics, Case Western
Reserve University. US.

16.00 Poster and oral awards

16.30 Closing remarks

Lise Wogensen Bach Vice-Dean, Head of Graduate School of Health

**18.30 Dinner & awards ceremony for JCD-price and The Fogh-Nielsen price at
'Centralværkstedet'**

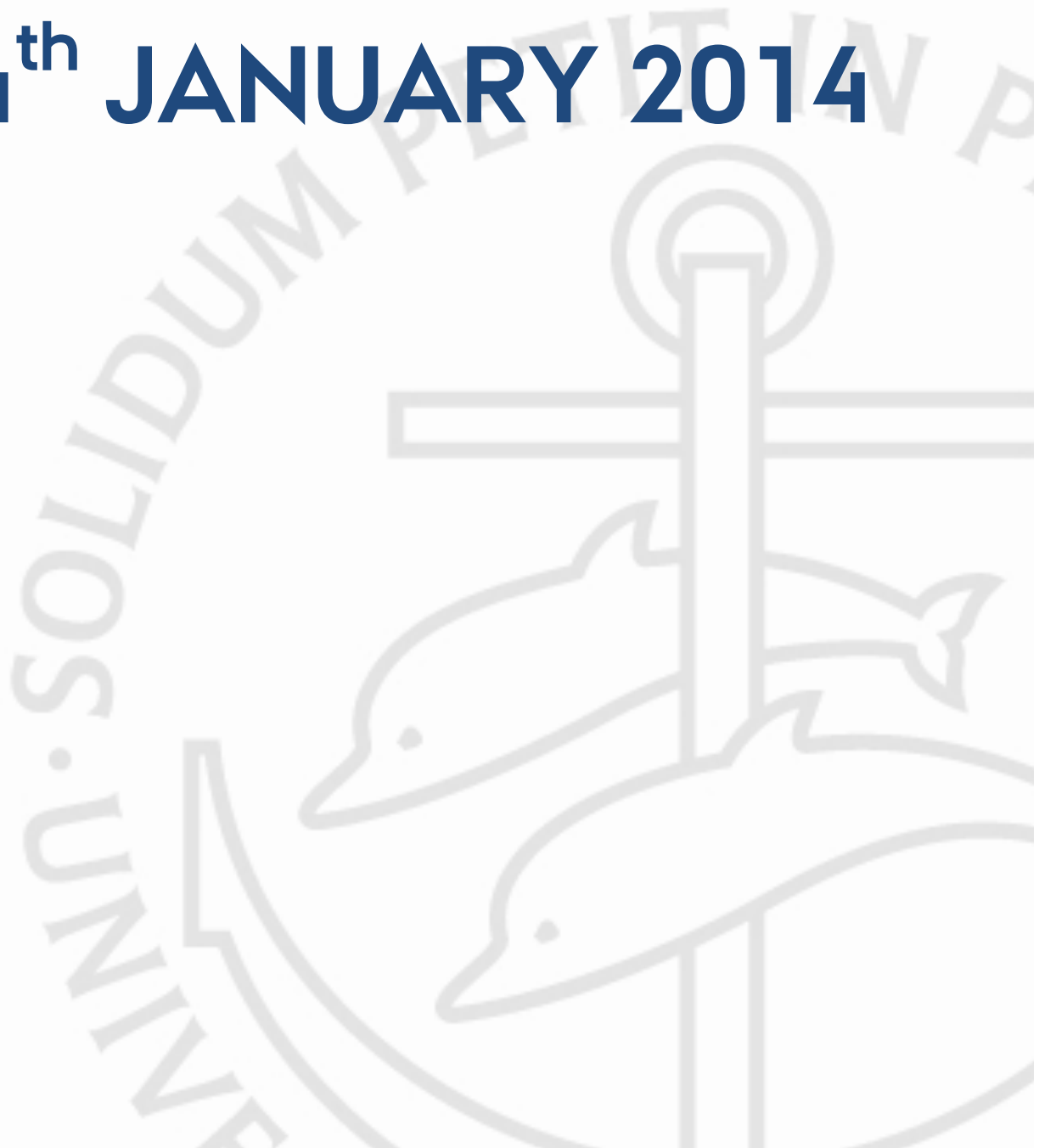
Festive speech by Niels Holmark Andersen, MD, Consultant

22.00 Band and dance



Aarhus University
Graduate School of Health

PHD DAY
24th JANUARY 2014



Practical Information

- Posters should be hung up between 4.30pm and 8pm on January 23rd or between 7.30am and 8am on January 24th. All posters must be taken down immediately after the closing of the conference.
- Oral presenters for sessions O1-O5 must meet in the auditorium concerned between 7.30am and 8:00am on January 24th to save their presentation onto the auditorium hard disk.
- Lunch packages will be handed out at the Lakeside Lecture Theatre and at the poster viewing areas in the Bartholin Building and at Anatomy.

- **Oral session 1:** Lakeside Lecture Theatres, Per Kirby Auditorium
- **Oral session 2:** Lakeside Lecture Theatres, Merethe Barker Auditorium
- **Oral session 3:** Lakeside Lecture Theatres, Eduard Biermann Auditorium
- **Oral session 4:** Lakeside Lecture Theatres, Jeppe Vontilius Auditorium
- **Oral session 5:** Bartholin building, Auditorium 1

- **Postersession 1-7 (Epidemiology):** Lakeside Lecture Theatres, William Scharff
- **Postersession 8-28 (Basic and Clinical Science):** Bartholin building, Auditorium 2, 3, 4, studyroom, gardenroom and Hall.
- **Postersession 29-38: (Clinical Science):** Anatomy (building 1230): Hall and Kollokvieroom 1

Organizing committee:

- Helle Prætorius, Professor mso, DrMedSc, Department of Biomedicine, Chairman
- Tine Gregersen, PhD student, Department of Clinical Medicine
- Martin Roelsgaard Jakobsen, Ass. Professor, Department of Biomedicin
- Jakob Østergaard, PhD student, Department of Clinical Medicine
- Sara Heebøll, PhD student, Department of Clinical Medicine
- Eugenio Gutierrez Jimenez, PhD student, Department of Clinical Medicine
- Alexander Juhl Andersen PhD student, Department of Clinical Medicine
- Betina Hansen, PhD student, Department of Clinical Medicine
- Kasper Pryds, PhD student, Department of Clinical Medicine
- Niels Jessen, Ass. Professor, Department of Clinical Medicine
- Trine Ji Holmgaard Jensen, PhD Administration
- Sidsel Lindberg Tefre, PhD Administration
- Emil Toft Brøndum, PhD Administration
- Birgitte Rosenvind Eriksen, PhD Administration

The Skou Lecture



Walter F. Boron M.D., Ph.D.

Dr. Boron is the David N. and Inez Myers/Antonio Scarpa Professor & Chairman of the Department of Physiology and Biophysics at Case Western Reserve University.

He earned his AB in chemistry at Saint Louis University, and his MD and PhD (Physiology & Biophysics with Albert Roos) at Washington University in St. Louis. Boron joined Yale University as a postdoctoral fellow with Emile Boulpaep in 1978, and remained there for the next 29 years, serving as

Chairman of the Department of Cellular & Molecular Physiology for three 3-year terms (1989-1998). In 2007 he returned to his hometown of Cleveland. Boron is the former President of the American Physiological Society (APS) and is currently Secretary-General of the International Union of Physiological Sciences (IUPS). He is the former editor-in-chief of the journals *Physiological Reviews* and *Physiology*. He and Emile Boulpaep co-edit the textbook *Medical Physiology*.

As a PhD student, Boron was the first to demonstrate the active regulation of intracellular pH (pH_i). He later discovered the sodium/bicarbonate cotransporter and cloned the gene that encodes it. Over his career, he developed many of the experimental paradigms for studying pH_i regulation. It was during experiments on pH_i regulation in cells from the stomach that he discovered the first gasimpermeable membrane, which led to his discovery of the first gas channel. Since then, his group discovered gas selectivity by channels and the blockade of gas channels by small-molecule inhibitors.

Among Boron's honors are a Young Investigator Award (American Society of Nephrology/American Heart Association, 1986), the Robert F. Pitts Award (IUPS, 1993), the Gottschalk Award (APS, 1998), an NIH MERIT Award (2002), the Homer Smith Award (ASN, 2005), the Sharpey-Schafer Award (The Physiological Society, 2008), and the Palade Gold Medal (shared with William Catterall and Richard Tsien, Wayne State University, 2010).

Scientific Communication - Science / Science Fiction



Peter Lund Madsen

This year's invited speaker on the theme "Scientific Communication – Science / Science Fiction" is MD PhD DrMed. Peter Lund Madsen

We are very pleased to welcome one of the absolute best scientific communicators, Peter Lund Madsen. Although Peter Lund Madsen is a renowned scientific entertainer, his main area of research is within brain activity during sleep, dream, stress and relaxation and he is the author and co-author of several scientific articles published in recognized international scientific journals.

Besides his work as a medical doctor and scientist, Peter Lund Madsen hosts his own radio programme "HjerneKassen" on P1 and has contributed to several TV-programs, such as "Hjerner i Spil", "Sjælen på vrangen", "Nedtur til Nytår", "Stuegang". Together with his brother, Anders Lund Madsen, Peter wrote and acted in the science/comedy-show "Mr. Nice Guy", which was seen by more than 60.000 persons.

Thus Peter Lund Madsen CV shows an impressive success within science and the art of communicating science and we can think of no better person to open this year's debate on the topic "Scientific Communication Science / Science Fiction".

Phdassociation.dk

All PhD students at HEALTH are members

- Including you!

The PhD association is working on improving your PhD education at HEALTH. We are always interested in any concerns and suggestions you have!

Some of our activities:

- **Collaboration with the Graduate School of Health to**
 - improve PhD courses
 - facilitate studying abroad
 - influence the structure of our PhD education
- **Organizing interesting meetings and workshops**
 - 2013's Researchers without Borders
 - 3 meetings each term with interesting speakers
- **Co-organizer of the PhD day.**

“Like” us on facebook – search for “The PhD Association”

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

Feel free to get in touch with us, whether you want to get involved or you have ideas that might improve the PhD education at Health, Aarhus University.

PHENOTYPING POSSIBILITIES AT AARHUS UNIVERSITY

Characterisation of living animals, phenotyping, is an important component of scientific and medical research. Exciting and ground breaking research involving animals take place at Aarhus University. The research areas span wide and are very diverse in nature.

FACILITIES

Research is carried out at the departments in the faculties of Health and Science and Technology in the Science Park and at Aarhus University Hospitals as well as other associated research facilities (e.g. Foulum and Påskehøjgård). Specific research facilities for laboratory animals available at all sites.

HOW MAY PHENOTYPING HELP YOUR RESEARCH PROJECT?

Researching complex reactions in living systems necessitates and requires the use of experimental animals. Animal research is one vital strand of medical research that together with *in vitro* experimentation ensures that research findings are more robust and reliable. Thus, phenotyping of live animals contribute greatly to the understanding of diseases, their development and mechanisms as well as the development of more specific and effective treatments of diseases and debilitating conditions. Phenotyping can be time consuming and resource-intensive and therefore a resource- and competency catalogue has been built.

RESOURCE AND COMPETENCE CATALOGUE

A dedicated website for phenotyping act as a resource- and competency catalogue for researchers at Aarhus University. It provides an overview of existing phenotyping possibilities and expertise that is available at Aarhus University. The website describes each phenotyping test in terms of measurable parameters, available equipment, location of equipment and provides contact information to a scientist who is a specialist in the specific research area. The website can be accessed at: (<http://biomed.au.dk/forskning/core-faciliteter/faenotyping/phenotyping/>)

For further information about phenotyping activities at Aarhus University contact Project Coordinator for Phenotyping, Ellen Villadsen: E-mail:evil@fi.au.dk or Tel: 21551544.





Working with diabetes

Danish Diabetes Academy – a research institution and a networking platform

In year 2020, almost 300 million people worldwide will be diagnosed with diabetes. This global disease is associated with serious health complications and will have devastating personal and socioeconomic consequences.

Are you interested in research and making a difference?

The Danish Diabetes Academy welcomes you as a member of a national and international research institution and networking platform.

We are a newly established research institution and networking platform which through the next five years will allocate funding to almost 150 researchers, such as post doc fellows, PhD students, professors and visiting professors/scientists.

We offer

- Membership of a national and international research institution and networking platform
- Participation in high class seminars & workshops
- Participation in high class PhD courses
- Information about available grants & career opportunities within diabetes research

Join us

Please visit our website www.danishdiabetesacademy.dk and register as a member.

Tore Christiansen
Managing Director
Danish Diabetes Academy

GERDA

AU ALUMNI COMMUNITY NAMED AFTER THE FIRST ALUM



GERDA WHO?

Gerda, our online community for alumni, is named in honor of the first alumn from AU who graduated in 1935.

Today, the alumni community is a central meeting point for alumni, students, faculty and staff, which sets the perfect scene for discovering old and new connections, staying up to date on events and other networking offers.

It's free to be a member – all you have to do is activate your profile at gerda.au.dk.

Research Support Office - So You can Focus on Research

(Forskningsstøtteenheden)

The Research Support Office at Aarhus University and Aarhus University Hospital is your point of entry to the world of fundraising. The Research Support Office is divided into Proposal Development, Project Administration and Strategy and Lobbying.

The Proposal Development - Health-Team provides support to all researchers within the health sciences. Knowing that different researchers have different requirements, The Research Support Office offers the assistance you need – for free!

For instance we offer:

- To help tailor your application to specific calls
- To provide input on non-scientific parts of your application
- To provide structure and clarity
- Workshops on how to write a good application
- www.ResearchFunding.Net – an extensive database of national and international funding opportunities.

In order for us to provide you with the best possible service, it is imperative you contact us early in the application process.

Health Team – Contact Information



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(Regional Hospitals Herning and Holstebro)



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International Academic Staff Services (IAS) at International Centre

In close collaboration with AU Human Resources, the International Academic Staff Services (IAS) helps foreign researchers (including PhD students) and their families overcome the practical challenges tied to their life in Denmark. As part of this, the unit operates a service desk and an extensive web-portal (www.ias.au.dk) for international and Danish PhD students admitted to AU.

The service desk, “International Student and Staff Services”, is open Monday – Friday 10am – 2pm and it is located at the International Centre, Høegh-Guldbergs Gade 4 (the Dale T. Mortensen Building).

IAS assists international staff and PhDs through counselling about practicalities when planning a period abroad, counselling about issues of relevance for the family, including job for spouses, international schools and kindergartens, etc.

IAS furthermore assists international staff and PhD students by providing guidance on paperwork and administrative issues during their stay in Denmark, including health insurance, extension of residence and work permits etc.

Twice a month the IAS invites newly arrived PhD students and researchers to the orientation and registration event “Getting Started in Denmark”. IAS will provide important on-arrival information and accompany newcomers to the International Citizen Service to be registered for residency. For further information, see www.ias.au.dk/gettingstarted .

Lastly, IAS organizes social and cultural activities for staff and their families through the University International Club (UIC) and in cooperation with the PhD House Activity Group. For further information, see www.au.dk/uic .

The PhD-House and the PhD House Activity Group

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

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

The PhD House contains:

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

For further information, see www.phd.au.dk/phdhouse





AU LIBRARY, HEALTH SCIENCES

The library is here to help

- Access to relevant literature
- Information about
 - Tips and tricks for PubMed, Scopus, Web of Science, and Cinahl
 - Citation searches in Scopus and Web of Science
 - Alerts from your favourite journals
 - Reference Tools – courses and support for EndNote and RefWorks
 - Bibliometrics and Research Evaluation; e.g. Bibliometric Research Indicator (BFI), Journal Impact Factor, and H-index
 - Copyright and Open Access
- Individual support and help for literature search designed for your specific project
- Regular PhD courses ‘Literature Search in Medical Databases’

Do you want to learn more about Aarhus University's PhD Association?

Q: Who are we?

A: AUPA is the coordinating body of all PhD associations at Aarhus University, and an independent political body on campus.

Q: What do we do?

A: AUPA works to improve talent development across the four main areas; Arts, Health, Science & Technology, and Business & Social Sciences

Q: How do you get involved?

A: Feel free to contact us if you have any topics or ideas that you want on AUPAs agenda, and join our mailing list at our site

Contact us : board@aupadk

Join our mailing list at our website: phd.au.dk/aupa



It's your **talent** – It's your **career** – It's your **choice!**

Do you know which career path to choose when finishing your PhD? Do you know which specific competences companies are interested in as regards PhD students from Health? Are you aware of your many opportunities?

If these are some of the questions you ask yourself, we may be able to guide you:

Get a mentor from the business community and increase your network outside of academia

Individual feedback on career paths, applications and CVs

AU Job & Project Bank

Information on career opportunities

Career events

Contact the AU Career Advisory Panel and get feedback from experts within your field

Best regards,
AU Career, Health

Jeanette Bach

Career Consultant - Health
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Vibeke Broe

PhD Career Consultant
Mobile: 2942 6029
Email: vibr@adm.au.dk

READ more about our services at phd.au.dk/au-career-health

Do not hesitate to contact us. We look very much forward to meeting you.

phd.au.dk/au-career-health

phd.au.dk/career

AU CAREER
HEALTH



AARHUS UNIVERSITY

Session Chairmen

Fogh-Nielsen	Søren Kragh-Moestrup (chairman), Lise Wogensen Bach, Ulf Simonsen, Anneli Sandbæk & Helle Prætorius
O1	Jeppe Prætorius, Jacob Johnsen & Søren Brandt Poulsen
O2	Hans Jürgen Hoffmann, Therese Koops Grønborg & Jeppe Skov
O3	Vibeke Hjortdal, Anto Praveen Rajkumar Rajamani & Lise Tornvig Erikstrup
O4	Bent Deleuran, Mohamed Ahmed Hassan & Kristine Rømer Thomsen
O5	Erling Falk, Lene Hee Christensen & Maj Høygaard Nicolaisen
P1	Reimar W. Thomsen & Gitte Susanne Rasmussen
P2	Per Fink, Lene Nyboe & Line Graversen
P3	Alma B. Pedersen, Bjørn Bay & Tue Kjølhede
P4	Cecilia Høst Ramlau-Hansen & Ioanna Milidou
P5	Henrik Kolstad & Helene Kirkegaard
P6	Ellen M. Mikkelsen & Ane Birgitte Telén Andersen
P7	Thomas Vorup-Jensen, Anne Fia Grahn & Jesper Padkær Petersen
P8	Karin Birkenkamp-Demtröder, Anne Brosbøl-Ravnborg & Thomas Nordstrøm Kjær
P9	Niels Gregersen & Marie Juul Ørnstrup
P10	Natalya Fedosova, Tine Kjærgaard & Ravikiran Mahadevappa
P11	Loni Ledderer, Christina Maar Andersen & Jean Farup
P12	Bent Deleuran & Marie Beck Iversen
P13	Tove Christensen & Troels Rønn Kjær
P14	Raben Rosenberg & Per Qvist
P15	Lise Lotte Hansen, Ming Sun & Jonatan Pallesen
P16	Per Höllsberg, Xiao Ma & Yujia Cai
P17	Jens Georg Leipziger, Jonas Jensen & Halldór Bjarki Einarsson
P18	Rikke Nørregaard & Paula Fernandez Guerra
P19	Karin Lykke-Hartmann & Priscila Corraini
P20	Christian Aalkjær, Janni Majgaard Jensen & Nikolaj Grøndal
P21	Ulf Simonsen, Karen Axelgaard Lorentzen & Jannik Bertelsen
P22	Ebba Nexø & Morten Christian Bay Grauballe
P23	Helle Prætorius & Morten Leif Stilund
P24	Poul Henning Jensen, Jay Rai & Marie Louise Schmitz
P25	Troels Krarup Hansen, Ann Mosegaard Bak & Gitte Bloch Rasmussen
P26	Jakob Udby Blicher, Mikkel Mylius Rasmussen & Jesper Jeppesen
P27	Donna Briggs Bødtkjer, Juan Manuel Shiquetomi Medina & Lotte Vinge
P28	Erisela Qerama Montvilas, Miao Wang & Lene Hjelle Tauris
P29	Irene Dige, Kresten Rickers & Sepp de Raedt
P30	Anneli Sandbæk, Stina Lou & Connie Timmermann
P31	Marianne Vámosi, Lotte Dahl Kristensen & Louise Mahncke
P32	Charlotte Guldborg Nyvold, Tinne Laurberg & Marie-Louise Feddern
P33	Anders Bonde Jensen, Sandy M. Ismail Mohamed & Helene Myrtue Nielsen
P34	Rikke K Andersen, David Christoffer Hansen & Marie Louise Bønnelykke-Behrndtz
P35	Jørgen Bjerggaard Jensen, Mette Julsgaard & Cathrine Bach
P36	Christoffer Sølling & Eva Sædder
P37	Klaus Krogh, Magnus Gottfredsson & Betina Hansen
P38	Holger Jon Møller & Birgit Sørensen Skoffer

Oral session overview

Fogh-Nielsen Price Competition

Morten Würtz. ASPIRIN IN CARDIOVASCULAR DISEASE – FUNCTIONS, LIMITATIONS AND CLINICAL OUTCOME

Søren Dinesen Østergaard. MEASURING PSYCHOTIC DEPRESSION

Morten Schmidt. CARDIOVASCULAR RISKS ASSOCIATED WITH NON-ASPIRIN NSAID USE

Oral session 1 GP 1, 6 & 7

Chairmen: Jeppe Prætorius, Jacob Johnsen (PhD student) & Søren Brandt Poulsen (PhD student)

- O01.01 Janus Hyldebrandt. NON-SUSTAINED EFFECT OF DOBUTAMINE DURING ACUTE RIGHT VENTRICULAR FAILURE IN THE NEWBORN PIGLET
- O01.02 Anette Tarp Hansen. COPEPTIN AS A NOVEL BIOMARKER FOR FETAL GROWTH RETARDATION: A CASE-CONTROL STUDY
- O01.03 Anders Jorsal. CARDIAC EFFECTS OF GLP-1 TREATMENT IN PATIENTS WITH CHRONIC HEART FAILURE
- O01.04 Vibeke Secher Nielsen. FUNCTIONAL CHARACTERISTICS OF PUTATIVE CA^{2+} -ACTIVATED CL^{-} CHANNELS - BESTROPHINS AND TMEM16A - IN RAT MESENTERIC SMALL ARTERIES
- O01.05 Mie Rostved Rasmussen. IDENTIFICATION OF SUBSTRATE SEQUENCE MOTIFS IMPORTANT FOR ADAM17-MEDIATED SHEDDING OF CD163 AND TNF-ALPHA
- O01.06 Pauline de Bruijn. THE THICK ASCENDING LIMB AS A MAJOR SITE FOR FUROSEMIDE-INDUCED URINARY ACIDIFICATION

Oral session 2 GP 2 & 3

Chairmen: Hans Jürgen Hoffmann, Therese Koops Grønberg (PhD student) & Jeppe Skov (PhD student)

- O02.01 Poul Frølund Vestergaard. GH SIGNALING IN SKELETAL MUSCLE IN HEALTHY HUMAN SUBJECTS: IMPACT OF GENDER AND AGE
- O02.02 Peter Hjertholm. VARIATION IN THE USE OF PROSTATE SPECIFIC ANTIGEN TESTING AND PROSTATE CANCER-RELATED OUTCOMES: A COHORT STUDY
- O02.03 Karen Fjeldborg. HUMAN ADIPOSE TISSUE MACROPHAGES ARE SKEWED IN AN ANTI-INFLAMMATORY DIRECTION IN OBESITY
- O02.04 Stine Klejs Rahbek. ACUTE EFFECTS OF RESISTANCE EXERCISE CONTRACTION MODE AND PROTEIN SUPPLEMENTATION ON MUSCLE PROTEIN SYNTHESIS AND HYPERTROPHY SIGNALLING
- O02.05 Annesofie Lunde Jensen. OSTEOPOROSIS GROUP EDUCATION - INTERPRETING AND INDIVIDUALISING A BONE FRIENDLY RECIPE
- O02.06 Tue Kjølhede. LONG-TERM PROGRESSIVE RESISTANCE TRAINING IMPROVES FUNCTIONAL CAPACITY FOR PEOPLE WITH MULTIPLE SCLEROSIS

Oral session 3 GP 5 & 10

Chairmen: Vibeke Hjortdal, Anto Praveen Rajkumar Rajamani (PhD student) & Lise Tornvig Erikstrup (PhD student)

- O03.01 Hanne Vinter. IMIQUIMOD INDUCED PSORIASIS-LIKE SKIN INFLAMMATION: A MODEL OF PSORIASIS
- O03.02 Henrik Lauridsen. HOW TO BUILD A HEART: COMPLETE REGENERATION AFTER MYOCARDIAL INFARCTION
- O03.03 Dennis Kjølhede Jeppesen. EXOSOME ISOLATION BY DIFFERENTIAL CENTRIFUGATION: ANALYSIS OF DISCRETE FRACTIONS
- O03.04 Tue Wenzel Kragstrup. DECREASED PLASMA LEVELS OF SOLUBLE CD18 LINK LEUKOCYTE MIGRATION WITH DISEASE ACTIVITY IN SPONDYLOARTHRITIS
- O03.05 Shivani Joshi. IDENTIFICATION OF DISEASE-RELATED GENES IN FAMILIAL STEROID SENSITIVE NEPHROTIC SYNDROME
- O03.06 Kristian Ravlo. EFFECT OF REMOTE ISCHEMIC CONDITIONING ON DENDRITIC CELLS AFTER KIDNEY TRANSPLANTATION FROM DECEASED DONORS

Oral session 4 GP 8 & 9

Chairmen: Bent Deleuran, Mohamed Ahmed Hassan (PhD student) & Kristine Rømer Thomsen (PhD student)

- O04.01 Lise Thorsen. IRRADIATION OF THE INTERNAL MAMMARY LYMPH NODES INCREASES OVERALL SURVIVAL IN NODE-POSITIVE BREAST CANCER
- O04.02 Peter Bondeven. EXTENT AND COMPLETENESS OF MESORECTAL EXCISION EVALUATED BY POSTOPERATIVE MRI
- O04.03 Tim van Hartevelt. TEMPORAL ASPECTS OF THE SENSE OF SMELL: A STUDY USING MAGNETOENCEPHALOGRAPHY
- O04.04 Thomas Lyhne Ravkilde. PREDICTING TREATMENT DELIVERY SUCCESS OF ADVANCED RADIOTHERAPY TREATMENTS OF CANCER
- O04.05 Henriette Bjerregaard. SUBSTRATE-INDUCED CONFORMATION OF THE HUMAN SEROTONIN TRANSPORTER
- O04.06 Anne Højland. INVESTIGATING SORLA MEDIATED TRAFFICKING IN POLARIZED CELLS

Oral session 5 GP 11 & 12

Chairmen: Erling Falk, Lene Hee Christensen (PhD student) & Maj Høygaard Nicolaisen (PhD student)

- O05.01 Michael Skovdal Rathleff. PATIENT EDUCATION WITH OR WITHOUT THE ADDITION OF MULTIMODAL PHYSIOTHERAPY FOR ADOLESCENT PATELLOFEMORAL PAIN; A CLUSTER RANDOMISED STUDY AMONG 121 ADOLESCENTS WITH 12 MONTHS FOLLOW-UP
- O05.02 Trine Eilenberg. ACCEPTANCE AND COMMITMENT GROUP THERAPY (ACT) FOR HEALTH ANXIETY. PRELIMINARY RESULTS FROM A RANDOMISED TRIAL
- O05.03 Eva Bjerre Ostenfeld. PREADMISSION USE OF GLUCOCORTICOIDS AND ANASTOMOTIC LEAKAGE FOLLOWING COLORECTAL CANCER RESECTION: A DANISH POPULATION-BASED COHORT STUDY
- O05.04 Dorthe Krogsgaard Bonnerup. PRESCRIBING ERRORS IN ACUTELY ADMITTED MEDICAL PATIENTS
- O05.05 Merete Gregersen. A LIBERAL BLOOD TRANSFUSION STRATEGY IMPROVES SURVIVAL IN NURSING HOME RESIDENTS WITH HIP FRACTURE
- O05.06 Mikkel Andreas Strømgaard Andersen. FIRST HOUR QUINTET 1-1-2 CALLERS AND COMORBIDITY

Poster session overview

Poster session 1 Research Year - Epidemiology

Chairmen: Reimar W. Thomsen & Gitte Susanne Rasmussen (PhD student)

- P01.01 Henrik Solli. OBESITY, SMOKING, DIABETES MELLITUS AND PHYSICAL EXERCISE AND RISK OF VENOUS THROMBOEMBOLISM: A DANISH COHORT STUDY
- P01.02 Lisbeth Lydiksen Christensen. IS IT POSSIBLE TO DEFINE AN OPTIMAL TIME FOR CHEMOTHERAPY AFTER SURGERY FOR OVARIAN CANCER?
- P01.03 Tine Jepsen Nielsen. USE OF GENERAL PRACTICE AFTER MYOCARDIAL INFARCTION ACCORDING TO DIFFERENT PATIENT CHARACTERISTICS
- P01.04 Karen Guldbrandsen. AGE OF MENARCHE AND TIME TO PREGNANCY - A STUDY WITHIN THE DANISH NATIONAL BIRTH COHORT
- P01.05 Jonas Lühje Munthe. MORTALITY AMONG PATIENTS HOSPITALIZED WITH PNEUMONIA - DESCRIBING THE 30-DAY MORTALITY AFTER ADMISSION WITH PNEUMONIA ON DANISH HOSPITALS
- P01.06 Imra Kulenovic. REALITY CHECK OF THE DANISH/EUROPEAN GUIDELINES ON CARDIOVASCULAR DISEASE PREVENTION IN CLINICAL PRACTICE (VERSION 2012)
- P01.07 Helga Lillian Guðmundsdóttir. ESTIMATING THE ORGAN DONOR POTENTIAL ON NON-INTENSIVE CARE UNITS IN DENMARK: A RETROSPECTIVE ANALYSIS OF POTENTIAL ORGAN DONORS IN REGION MIDTJYLLAND
- P01.08 Astrid Blicher Schelde. IMPACT OF COMORBIDITY ON THE RISK OF FIRST-TIME MYOCARDIAL INFARCTION, STROKE, OR DEATH AFTER SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY MYOCARDIAL PERFUSION IMAGING: A DANISH COHORT STUDY

Poster session 2 GP3->10: Epidemiology

Chairmen: Per Fink, Line Graversen (PhD student) & Lene Nyboe (PhD student)

- P02.01 Kristian Dahl Kragholm Sørensen. RETURN TO WORK IN OUT-OF-HOSPITAL CARDIAC ARREST SURVIVORS - A NATIONWIDE REGISTER BASED FOLLOW-UP STUDY
- P02.02 Lise Maria Lindahl. SECONDARY CANCERS, COMORBIDITIES AND MORTALITY ASSOCIATED WITH NITROGEN MUSTARD THERAPY IN PATIENTS WITH MYCOSIS FUNGOIDES: A 30-YEAR POPULATION-BASED COHORT STUDY
- P02.03 Jean-Christophe Philippe Debost. EFFECT OF BEREAVEMENT AND VARIATION IN THE GLUCOCORTICOID REGULATING ENZYME 11- β -HYDROXYSTEROID-DEHYDROGENASE TYPE 2 IN CHILDREN WHO LATER DEVELOP SCHIZOPHRENIA
- P02.04 Majbritt Mostrup Pedersen. EFFECTIVENESS OF AN EDUCATIONAL VIDEO FOLLOWING ACUTE WHIPLASH TRAUMA: A RANDOMIZED CONTROLLED TRIAL
- P02.05 Anne Bodilsen. NATIONAL VARIATION IN RE-OPERATION RATE AFTER BREAST CONSERVING SURGERY
- P02.06 Helene Tilma Vistisen. ASSESSMENT OF BREAST CANCER RISK BY USE OF THE DANISH WORKING HOUR DATABASE
- P02.07 Dinesh Neupane. COMMUNITY-BASED INTERVENTION FOR HYPERTENSION IN NEPAL
- P02.08 Janne Mortensen. IMPACT OF PRE-ADMISSION SELECTIVE SEROTONIN REUPTAKE INHIBITOR TREATMENT ON STROKE OUTCOME: A NATIONWIDE PROPENSITY SCORE-MATCHED FOLLOW-UP STUDY
- P02.09 Mette Lausten Hansen. PREDICTORS OF SICKNESS ABSENCE IN PREGNANCY - A DANISH COHORT STUDY

Poster session 3 GP3: Public Health - Epidemiology I

Chairmen: Alma B. Pedersen, Bjørn Bay (PhD student) & Tue Kjølhede (PhD student)

- P03.01 Kirstine Høj Obling. THE MILE STUDY: A MOTIVATIONAL, INDIVIDUAL AND LOCALLY ANCHORED EXERCISE INTERVENTION IN 30-49 YEAR OLDS. A RANDOMISED CONTROLLED STUDY IN PRIMARY CARE
- P03.02 Natalie Momen. MODE OF DELIVERY AND CHILDHOOD CANCER: A NATIONWIDE FOLLOW-UP STUDY IN THREE COUNTRIES
- P03.03 Martin Christensen. PREECLAMPSIA AND THE POSTPARTUM CARDIOVASCULAR RISK - A 10-YEAR FOLLOW-UP
- P03.04 Mette Sørensen Langfrits. SHARED CARE AND IMPLEMENTATION OF A PEDIATRIC CLINICAL PATHWAY
- P03.05 Henry Jensen. GENERAL PRACTITIONERS' SUSPICION OF CANCER AND USE OF STANDARDISED CANCER PATIENT PATHWAYS
- P03.06 Anette Riisgaard Ribe. LONG-TERM MORTALITY OF PERSONS WITH SEVERE MENTAL ILLNESS AND DIABETES
- P03.07 Xiaoqin Liu. BIRTH WEIGHT, GESTATIONAL AGE, FETAL GROWTH AND CHILDHOOD ASTHMA HOSPITALIZATION
- P03.08 Oleguer Plana Ripoll. PRENATAL MATERNAL BEREAVEMENT AND ADULT REPRODUCTIVE IMPAIRMENTS: A POPULATION-BASED COHORT STUDY

Poster session 4 GP3: Public Health - Epidemiology II

Chairmen: Cecilia Høst Ramlau-Hansen & Ioanna Milidou (PhD student)

- P04.01 Christina Marie Braüner. AN INVESTIGATION OF SMART PHONE APPLICATION IN EMERGENCY OBSTETRIC AND NEWBORN CARE IN GHANA
- P04.02 Cathrine Carlsen Bach. PERFLUORINATED CHEMICALS AND FETAL GROWTH - PRELIMINARY RESULTS
- P04.03 Pernille Pedersen. PSYCHOEDUCATION FOR SICK-LISTED INDIVIDUALS WITH MENTAL HEALTH PROBLEMS
- P04.04 Anne Mette Falstie-Jensen. ACCREDITATION IN THE DANISH HEALTHCARE SYSTEM: THE DANISH HEALTHCARE QUALITY PROGRAMME
- P04.05 Anna Budtz-Lilly. BODILY DISTRESS SYNDROME IN PRIMARY CARE: PREVALENCE AND PATIENT CHARACTERISTICS
- P04.06 Kirsten Høj. PREVALENCE AND CHARACTERISTICS OF DANISH ADULTS WITH POOR CARDIORESPIRATORY FITNESS: A CROSS-SECTIONAL STUDY
- P04.07 Lene Hellmund. RETURN TO WORK AND QUALITY OF LIFE AFTER SEVERE TRAUMATIC BRAIN INJURY. EFFECT OF DIFFERENT REHABILITATION SET-UPS
- P04.08 Anneli Clea Skjelmoose Bolund. FARMING EXPOSURE IMPAIRS LUNG FUNCTION IN YOUNG ADULTS - A 15 YEAR FOLLOW-UP STUDY

Poster session 5 GP3: Public Health - Epidemiology III

Chairmen: Henrik Kolstad & Helene Kirkegaard (PhD student)

- P05.01 Mette Skovgaard Christensen. EXPOSURE TO STYRENE AND RISK OF CANCER: A 40 YEAR FOLLOW-UP STUDY OF WORKERS IN THE DANISH REINFORCED PLASTICS INDUSTRY
- P05.02 Anita Eskildsen. THE DANISH VERSION OF THE 10-ITEM PERCEIVED STRESS SCALE: TOWARDS NATIONAL CONSENSUS
- P05.03 Maiken Ina Siegismund Kjærsgaard. EFFECT OF PSYCHOLOGICAL TREATMENT OF BEREAVED INDIVIDUALS ON SICK LEAVE: A POPULATION-BASED STUDY USING INSTRUMENTAL VARIABLE ANALYSIS

- P05.04 Maria Theresa Wimberley Böttger. PROGNOSTIC FACTORS FOR TREATMENT RESISTANCE IN SCHIZOPHRENIA
- P05.05 Kathrine Bang Laursen. GEOGRAPHIC VARIATION IN THE PREVALENCE OF ADHD
- P05.06 Susanne Hvolgaard Mikkelsen. MATERNAL AGE AND ADHD IN THE OFFSPRING
- P05.07 Line Hvidberg. CANCER AWARENESS AND ASSOCIATION WITH SOCIO-ECONOMIC POSITION: RESULTS FROM A POPULATION-BASED STUDY IN DENMARK
- P05.08 Ethel Mary Brinda Alexander. DECOMPOSITION OF SOCIOECONOMIC INEQUALITIES IN SELF-RATED HEALTH AND HEALTH SERVICE UTILIZATION AMONG OLDER PEOPLE IN INDIA: THE WHO STUDY ON GLOBAL AGEING AND ADULT HEALTH (SAGE)

Poster session 6 GP12: Clinical Medicine - Epidemiology

Chairmen: Ellen M. Mikkelsen & Ane Birgitte Telén Andersen (PhD student)

- P06.01 Cathrine Ladegaard Wildenschild Nielsen. GESTATIONAL AGE AT BIRTH AND SUBSEQUENT FECUNDABILITY
- P06.02 Henriette Holm Stabel. SUBARACHNOID HEMORRHAGE IN DENMARK: RISK AND PROGNOSIS
- P06.03 Holger Borup Wemmelund. PREADMISSION STATIN USE IS ASSOCIATED WITH LOWER MORTALITY AFTER RUPTURE OF ABDOMINAL AORTIC ANEURYSM
- P06.04 Peter Asdahl. LATE GASTROINTESTINAL MORBIDITY IN CHILDHOOD CANCER SURVIVORS: A NORDIC POPULATION BASED COHORT STUDY
- P06.05 Laura Ozer Kettner. ASSISTED REPRODUCTION TECHNOLOGY AND POST-NEONATAL SOMATIC MORBIDITY - A SYSTEMATIC REVIEW OF COHORT AND CASE-CONTROL STUDIES
- P06.06 Eva Natalia Glassou. RISK OF READMISSION, REOPERATION AND MORTALITY FOLLOWING TOTAL HIP AND KNEE ARTHROPLASTY IN FAST TRACK DEPARTMENTS IN DENMARK
- P06.07 Anne Birgitte Simonsen. CONTACT ALLERGY IN DANISH CHILDREN WITH ATOPIC DERMATITIS
- P06.08 Thomas Deleuran. ALCOHOLIC LIVER DISEASE IN DENMARK 2006-2011: A POPULATION-BASED DESCRIPTIVE STUDY

Poster session 7 GP12: Clinical Medicine - Epidemiology II

Chairmen: Thomas Vorup-Jensen, Anne Fia Grahn (PhD student) & Jesper Padkær Petersen (PhD student)

- P07.01 Lene Sofie Granfeldt Østgård. DELAYING CHEMOTHERAPY DOES AFFECT LONG-TERM SURVIVAL IN BOTH YOUNGER AND OLDER AML PATIENTS. A DANISH POPULATION-BASED COHORT STUDY OF 1388 AML PATIENTS
- P07.02 Rasmus Offersen. LATENCY-REVERSING AGENTS EFFECT ON HIV-1 TRANSCRIPTION IN A PHYSIOLOGICAL PBMC SET-UP
- P07.03 Mette Thorgaard. HEALTH ANXIETY AND ILLNESS BEHAVIOUR IN CHILDREN OF MOTHERS WITH SEVERE HEALTH ANXIETY
- P07.04 Kirstine Kobberøe Søgaard. PEPTIC ULCER AND SUBSEQUENT RISK OF GASTROINTESTINAL CANCER: A NATIONWIDE COHORT STUDY
- P07.05 Anne Hammer Lauridsen. SENSITIVITY OF THREE COMMERCIAL PCR-BASED ASSAYS FOR THE DETECTION OF HUMAN PAPILLOMA VIRUS IN A DILUTION STUDY
- P07.06 Jesper Smit. STAPHYLOCOCCUS AUREUS BACTEREMIA AND DIABETES MELLITUS: STUDIES OF RISK AND PROGNOSIS
- P07.07 Camilla Askov Mousing. PALLIATIVE CARE FOR COPD PATIENTS IN PRIMARY HEALTH CARE - AN INTEGRATIVE REVIEW
- P07.08 Charlotte Handberg. MALE CANCER SURVIVORS' BARRIERS TOWARDS PARTICIPATION IN CANCER REHABILITATION - A QUALITATIVE STUDY

Poster session 8 GP2+5: Mol Metab & Endo + Infl & Infec

Chairmen: Karin Birkenkamp-Demtröder, Anne Brosbøl-Ravnborg (PhD student) & Thomas Nordstrøm Kjær (PhD student)

- P08.01 Nis Pedersen Jørgensen. MBEC MEASUREMENT PREDICTS TREATMENT FAILURE IN MURINE BIOFILM INFECTION MODEL OF IMPLANT ASSOCIATED OSTEOMYELITIS
- P08.02 Hanne Mari Jørgensen. BONE MASS MEASUREMENTS IN RENAL FAILURE & NDASH; STUDY PROTOCOL
- P08.03 Jakob Dal. SOMATOSTATIN ANALOGUE TREATMENT OF ACROMEGALY: MOLECULARE ASPECTS
- P08.04 Line M. Underbjerg. CHARACTERIZATION OF PATIENTS WITH IDIOPATHIC HYPOPARATHYROIDISM, AUTOSOMAL DOMINANT HYPOCALCAEMIA AND PSEUDOHYPOPARATHYROIDISM
- P08.05 Nilani Ramshanker. GLUCOCORTICOI-INDUCED INHIBITION OF IGF-I ACTIVITY: EXPLORATION OF UNDERLYING MECHANISMS
- P08.06 Jesper Løkke Mehlsen. PROTEIN SUPPLEMENTATION HIGH IN KETOGENIC AMINOACIDS (E.G. LEUCINE) IN SARCOPENIC OSTEOPENIC PATIENTS. IMPLICATIONS FOR MUSCLE, BONE, METABOLISM, AND PHYSICAL FUNCTION
- P08.07 Christian Trolle. LONG QT INTERVAL IN TURNER SYNDROME & NDASH; A HIGH PREVALENCE OF LQTS GENE MUTATIONS
- P08.08 Emilie Glavind. ALCOHOLIC HEPATITIS DECREASES UREA SYNTHESIS

Poster session 9 GP2: Molecular Metabolism and Endocrinology

Chairmen: Niels Gregersen & Marie Juul Ørnstrup (PhD student)

- P09.01 Mette Ladefoged. IDENTIFICATION OF RETINAL VASCULAR MARKERS OF EARLY-STAGE DIABETIC RETINOPATHY
- P09.02 Sigrid Bjerger Gribsholt. PREVALENCE OF MEDICAL AND NUTRITIONAL COMPLICATIONS AFTER BARIATRIC SURGERY (GASTRIC BYPASS) BASED ON A COHORT STUDY AND A QUESTIONNAIRE SURVEY
- P09.03 Rakel Fuglsang Johansen. THE EFFECT OF ISOLATED HYPERGLYCEMIA ON VLDL KINETICS
- P09.04 Andreas Lodberg. IMMOBILIZATION INDUCED BONE LOSS IS STRAIN SPECIFIC IN MICE
- P09.05 Sine Knorr Sørensen. MORBIDITY AND MORTALITY IN OFFSPRING BORN TO MOTHERS WITH TYPE I DIABETES
- P09.06 Esben Axelgaard. THE PATTERN RECOGNITION MOLECULE, MANNAN-BINDING LECTIN (MBL), IN THE PATOPHYSIOLOGICAL MECHANISMS OF DIABETIC NEPHROPATHY AND IMMUNOMODULATORY THERAPY
- P09.07 Trine Maxel Juul. ZINC METABOLISM IN OBESITY: REGULATIONS OF AND ITS CONNECTION WITH LIPID- AND GLUCOSE PROFILE
- P09.08 Julie Støy. MARKEDLY ELEVATED 24-HOUR AMBULATORY BLOOD PRESSURE IN HEALTHY MALE CARRIERS OF ARG313CYS IN IDENTIFIES THE GENE AS A POSSIBLE NOVEL REGULATOR OF BLOOD PRESSURE

Poster session 10 GP1: Membrane, Transporters and Receptors

Chairmen: Natalya Fedosova, Tine Kjærgaard (PhD student) & Ravikiran Mahadevappa (PhD student)

- P10.01 Steen Fagerberg. &ALPHA;-HAEMOLYSIN FROM INDUCES $[Ca^{2+}]_i$ SIGNALLING AND CELL LYSIS OF THP-1 CELLS THROUGH ACTIVATION OF A DIFFERENTIAL SET OF ATP SENSITIVE P2 RECEPTORS
- P10.02 Nina Jensen. LOSS OF FUNCTION OF SLC20A2 ASSOCIATED WITH FAMILIAL IDIOPATHIC BASAL GANGLIA CALCIFICATION IN HUMANS CAUSES BRAIN CALCIFICATIONS IN MICE

- P10.03 Stine Mikkelsen. FUNCTIONAL IMPACTS OF THE DARIER DISEASE MUTATION E917/918K IN SERCA2B/SERCA1A AND ITS NETWORK OF BONDING PARTNERS
- P10.04 Ida Skødt Jensen. TOWARDS PURIFYING DNA-PROTEIN COMPLEXES
- P10.05 Henriette Lajgaard Christensen. SUBCELLULAR LOCALIZATION OF THE V-ATPASE IN THE CHOROID PLEXUS EPITHELIUM: PROSPECTS FOR REGULATION OF CEREBROSPINAL FLUID PH?
- P10.06 Inga Christensen. ATYPICAL LOCALIZATION OF CYTOSKELETAL AND MEMBRANE PROTEINS IN THE CHOROID PLEXUS
- P10.07 Åsa Lina Margaretha Jönsson. THE SLC34A2 GENE - CHARACTERISATION AND ROLE OF MUTATIONS IN PULMONARY ALVEOLAR MICROLITHIASIS AND EXTRA-PULMONARY CALCIFICATION SYNDROMES
- P10.08 Casper Kornbech Larsen. HYPERALDOSTERONISM IN $K_{CA1.1}$ CHANNEL BETA₂-SUBUNIT KO MICE

Poster session 11 GP3: Public Health - Basic Science

Chairmen: Loni Ledderer, Christina Maar Andersen (PhD student) & Jean Farup (PhD student)

- P11.01 Monica Milter Ehlers. A QUALITATIVE STUDY OF FUNCTIONING, DISABILITY, AND REHABILITATION OF PATIENTS AFTER HIP FRACTURE SURGERY
- P11.02 Seija Ylijoki-Sørensen. CODING UNKNOWN CAUSE OF DEATH IS 10 TIMES MORE FREQUENT IN DENMARK THAN FINLAND
- P11.03 Janne Brammer Damsgaard. ACKNOWLEDGING THE BACK PATIENT. A THEMATIC SYNTHESIS OF QUALITATIVE RESEARCH. A SYSTEMATIC LITERATURE REVIEW
- P11.04 Marie Mortensen. CONSTRUCT VALIDITY OF THE PERCEIVED STRESS SCALE AMONG ADULT DANES IN CENTRAL DENMARK REGION
- P11.05 Birthe Annamari Thomsen. SCREENING FOR CARDIOVASCULAR DISEASES AND DIABETES IN DANISH WOMEN; PREVALENCE, NON-ATTENDANCE AND COST-EFFECTIVENESS
- P11.06 Mette Munk Jensen. INCLUSION IN PHYSICAL EDUCATION IN THE DANISH PRIMARY SCHOOL
- P11.07 Marianne Eg. SIGNIFICANT FACTORS IN ACHIEVING SUSTAINED WEIGHT LOSS IN THE TREATMENT OF CHILDREN WITH OBESITY
- P11.08 Christian Bjerregaard Olesen. EXTRACTION AND FRACTIONATION OF PERFLUORINATED ALKYL ACIDS AND OTHER PERSISTENT ORGANIC POLLUTANTS FROM HUMAN SERUM

Poster session 12 GP5: Inflammation and Infection - Basic Science

Chairmen: Bent Deleuran & Marie Beck Iversen (PhD student)

- P12.01 Dorte Hansen. DIRECT PATHOGENIC EFFECTS OF HERV-ENCODED PROTEINS
- P12.02 Stine Hald. DIETARY INTERVENTION WITH A DIET RICH IN ARABINOXYLAN AND RESISTANT STARCH MODULATES T-CELL ACTIVATION ESTIMATED BY CD25 EXPRESSION IN METABOLIC SYNDROME
- P12.03 Signe Maria Nielsen. BIOFILM FORMATION IN ISOLATED FROM CYSTIC FIBROSIS PATIENTS
- P12.04 Maria Hønholt Christensen. INNATE IMMUNE EVASION BY THE HERPES SIMPLEX VIRUS - 1 PROTEIN ICP27
- P12.05 Kathrine Hansen. INDUCTION OF IFN-&BETA; EXPRESSION BY IN HUMAN MYELOID CELLS PROCEEDS THROUGH A PATHWAY DEPENDENT ON IFI16, CGAS AND STING
- P12.06 Uffe Nygaard. CYTOKINE IL-33 MAY DETERIORATE SKIN BARRIER FUNCTION IN ATOPIC

DERMATITIS

- P12.07 Annette Søndergaard. HORIZONTAL TRANSFER OF CHROMOSOMALLY-ENCODED RESISTANCE TO BETA-LACTAM ANTIBIOTICS BETWEEN AND
- P12.08 Chenglong Sun. NOVEL MECHANISMS IN IMMUNE RECOGNITION OF VIRUSES- DETECTION OF THE VIRAL CAPSID

Poster session 13 GP5: Inflammation and Infection - Basic Science II

Chairmen: Tove Christensen & Troels Rønn Kjær (PhD student)

- P13.01 Lars Skov Dalgaard. RISK OF BACTEREMIA IN PERSONS WITH CHRONIC RENAL FAILURE ON HEMODIALYSIS; AN OBSERVATIONAL COHORT STUDY
- P13.02 Christian Brink Scholz. CHARACTERIZATION OF PROPIONIBACTERIUM ACNES POPULATIONS
- P13.03 Rikke Fleron Leihof. INHIBITION OF INTRACELLULAR GROWTH OF UROPATHOGENIC IN AN BLADDER EPITHELIUM CELL MODEL
- P13.04 Kaja Zuwala. WHERE MEDICINE AND CHEMISTRY MEET: SCREENING OF ANTI-HIV MACROMOLECULAR PRODRUGS IN VITRO
- P13.05 Chalotte Willemann Stecher. THE GENITAL SCHISTOSOMIASIS AND HIV RESEARCH PROJECT (GENSHIV): EFFECT OF PRAZIQUANTEL TREATMENT ON GENITAL HIV-1 RNA SHEDDING IN SCHISTOSOMA HAEMATOBIIUM AND HIV CO-INFECTED SUBJECTS - A RANDOMIZED TRIAL
- P13.06 Thomas Andersen. INTERLEUKIN-23 LEVELS DOES NOT PREDICT DISEASE DEVELOPMENT IN EARLY RHEUMATOID ARTHRITIS PATIENTS
- P13.07 Ane Langkilde-Lauesen Nielsen. SUBCUTANEOUS ADIPOSE TISSUE UNDERNEATH PSORIATIC SKIN MAY RESEMBLE SUBCUTANEOUS ADIPOSE TISSUE FROM INSULIN RESISTANT PATIENTS
- P13.08 Julie Kristine Laustsen. OX40+ T CELLS AND OX40L+ B CELLS ACCUMULATE IN THE INFLAMED JOINTS

Poster session 14 GP8: Neuroscience - Basic Science

Chairmen: Raben Rosenberg & Per Qvist (PhD student)

- P14.01 Mikkel Christoffer Vinding. THE DIFFERENCE BETWEEN DISTAL- AND PROXIMAL INTENTION FOR ACTION MEASURED WITH EEG
- P14.02 Sofie Christiansen. DISTURBANCES OF CIRCADIAN RHYTHM IN DEPRESSION
- P14.03 Christina Fischer. REPEATED INTERFERON-ALPHA ADMINISTRATION PRODUCES DEPRESSIVE-LIKE BEHAVIOR IN RATS
- P14.04 Sanne Bjørn Nygaard. GENOMIC PROFILING OF GLP-1 RECEPTOR AGONIST SENSITIVE CELLULAR PATHWAYS IN THE CNS
- P14.05 Esben Ahlburg Eickhardt. PATTERNS OF GENOMIC VARIABILITY IN THE INSERTIONS/DELETIONS OF PATIENTS WITH PSYCHIATRIC DISORDERS
- P14.06 Gitte Nikolajsen. NO EFFECT OF DHA ON SYNAPTIC TRANSMISSION AND PLASTICITY IN MICE
- P14.07 Desiree Del Carmen Leduc Galindo. THE MOLECULAR INTERACTIONS OF THE SCHIZOPHRENIA SUSCEPTIBILITY GENES AND IN NEURONAL CELLS
- P14.08 Signe Rode Andreasen. ELECTROPHYSIOLOGICAL ANALYSES OF SHORT-TERM PLASTICITY IN A MOUSE MODEL OF FAMILIAL HEMIPLEGIC MIGRAINE TYPE 2 WITH PERTURBED $\text{ALPHA}_2\text{NA}^+/\text{K}^+$ -ATPASE FUNCTION

Poster session 15 GP10: Translational Molecular Medicine - Basic Science

Chairmen: Lise Lotte Hansen, Ming Sun (PhD student) & Jonatan Pallesen (PhD student)

- P15.01 Veerle Paternoster. THE SCHIZOPHRENIA AND BIPOLAR DISORDER ASSOCIATED PROTEIN BRD1 INTERACTS WITH HISTONES AND INFLUENCES GLOBAL HISTONE MODIFICATION PATTERNS
- P15.02 Line Nilsson. INTRAPERITONEAL ADMINISTRATION OF CHITOSAN/SIRNA NANOPARTICLES TARGETING COX-2 PREVENTS INFLAMMATION AND OXIDATIVE STRESS IN RESPONSE TO UNILATERAL URETERAL OBSTRUCTION IN MICE
- P15.03 Iben Lyster Daugaard. MICRORNA AS REGULATORS OF LUNG ENDOTHELIAL PERMEABILITY AND CANCER PROGRESSION
- P15.04 Sigrid Salling Árnadóttir. CHARACTERIZATION OF INTRA-TUMOR HETEROGENEITY IN COLORECTAL CANCER
- P15.05 Malene Juul Rasmussen. DETECTION OF MUTATIONAL HOTSPOTS IN CANCER GENOMES
- P15.06 Anne Kruse Hollensen. MICRORNA INHIBITION BY DUAL-TARGETING AND CLUSTERED TOUGH DECOY INHIBITORS
- P15.07 Lise Bols Andersen. PATHOGENESIS OF AUTOSOMAL DOMINANT FAMILIAL NEUROHYPOPHYSEAL DIABETES INSIPIDUS- FROM PROTEIN MISFOLDING TO DEGENERATION OF MAGNOCELLULAR NEURONS
- P15.08 Natasja Leth Jørgensen. TOPOGRAPHICAL MICROSTRUCTURES INCREASE PROLIFERATION OF HUMAN PRIMARY CHONDROCYTES IN VITRO

Poster session 16 GP10: Translational Molecular Medicine - Basic Science II

Chairmen: Per Höllsberg, Xiao Ma (PhD student) & Yujia Cai (PhD student)

- P16.01 Mia Benedicte Lykke Roest Laursen. ISCHEMIC CONDITIONING; A METABONOMIC STUDY OF PLASMA
- P16.02 Moslem Ranjbar. MICROMANAGING BY LENTIVIRAL TRANSDUCTION-DEFINING ROLES OF MICRORNAS IN DIFFUSE LARGE B-CELL LYMPHOMA
- P16.03 Anders Laustsen. ROLE OF PLASMACYTOID DENDRITIC CELLS IN INNATE IMMUNE SENSING OF HIV
- P16.04 Nikolaj Worm Ørntoft. BILIARY EXCRETION OF CONJUGATED BILE ACIDS IN HUMANS MEASURED BY ¹¹C-CHOLYLSARCOSINE PET/CT
- P16.05 Anna Szyszka. DNA METHYLATION OF IN BIPOLAR DISORDER
- P16.06 Anne Sigaard Bie. THE HSP60 SUBSTRATE SPECTRUM
- P16.07 Gitte Brinch Andersen. DNA METHYLATION CHANGES IN OSTEOSARCOMA
- P16.08 Michal Switnicki. PROBABILISTIC METHOD FOR INTEGRATION OF CANCER GENOMICS DATA IMPROVES IDENTIFICATION OF PERTURBED GENES

Poster session 17 GP10: Translational Molecular Medicine - Basic Science III

Chairmen: Jens Georg Leipziger, Jonas Jensen (PhD student) & Halldór Bjarki Einarsson (PhD student)

- P17.01 Kang Ran. INTERFERING ENDPLATE NUTRITIONAL PATHWAY CAUSES INTERVERTEBRAL DISC DEGENERATION IN IMMATURE PORCINE MODEL
- P17.02 Anders Patrik Alexander Gunnarsson. STEM CELLS IN THE MURINE EPIDERMIS: INVESTIGATING THE RELATION BETWEEN GENE EXPRESSION, EPIGENETIC MARKS AND CELL POSITIONING
- P17.03 Morten Torvund-Jensen. STRUCTURAL CHARACTERIZATION OF THE INTERACTION

- BETWEEN HAPTOGLOBIN-HEMOGLOBIN AND MACROPHAGE RECEPTOR CD163
- P17.04 Maria do Nascimento Lopes Primo. ELUCIDATING ROLES OF MIRNAS IN DNA SENSING DURING AN INNATE IMMUNE RESPONSE
- P17.05 Kasper Hansen. EFFECT OF HYPERBARIC OXYGEN THERAPY IN A REGENERATIVE HEART MODEL
- P17.06 Jayaram Subramanian. EFFECTIVENESS OF GLYCINE POWDER AIR POLISHING (GPAP) DURING SUPPORTIVE PERIODONTAL THERAPY (SPT): A RANDOMISED CONTROLLED CLINICAL TRIAL
- P17.07 Trine Salomon Andreasen. CELL ASSAY FOR CONTROLLING ADVANCED GLYCATION ENDPRODUCT FORMATION
- P17.08 Akiko Shimada. EFFECTS OF REPETITIVE ORAL ADMINISTRATION OF MONOSODIUM GLUTAMATE ON PERICRANIAL MUSCLE SENSITIVITY

Poster session 18 Research Year - Basic Science

Chairmen: Rikke Nørregaard & Paula Fernandez Guerra (PhD student)

- P18.01 Thomas Ravn Lassen. EFFECT OF PAROXETINE ON LEFT VENTRICULAR REMODELING AFTER MYOCARDIAL INFARCTION
- P18.02 Marie Bek. VISUALIZATION OF THE SMOOTH MUSCLE CELL IN ATHEROSCLEROSIS: A MONOCLONAL POPULATION
- P18.03 Mette Christensen. $[Ca^{2+}]_i$ OSCILLATIONS IN RENAL EPITHELIA CAUSED BY ALPHA-HAEMOLYSIN FROM REQUIRE ATP RELEASE AND P2 RECEPTOR MEDIATED SIGNALLING
- P18.04 Eirild Espeseth. "SPOTTY" CALCIFICATION IN CORONARY ARTERIES: WHAT DOES IT REFLECT?
- P18.05 Tea Lund Laursen. LECTIN PATHWAY PROTEINS OF THE COMPLEMENT SYSTEM ARE ASSOCIATED WITH SURVIVAL IN PATIENTS WITH ACUTE LIVER FAILURE
- P18.06 Peter Kolind Brask-Thomsen. LIPOLYTIC EFFECTS OF GH: MOLECULAR MECHANISMS IN VIVO AND IN VITRO
- P18.07 Ole Kristian Møller-Helgestad. ORGAN BLOOD FLOW DURING MECHANICAL SUPPORT IN AN ANIMAL MODEL OF CARIOGENIC SHOCK
- P18.08 Morten Lykke Olesen. LEUKOCYTE-DEPLETION IN PLATELET-RICH PLASMA DECREASE THE PROLIFERATION EFFECTS OF HUMAN CHONDROCYTES – AN IN VITRO STUDY

Poster session 19 Research Year - Basic Science II

Chairmen: Karin Lykke-Hartmann & Priscila Corraini (PhD student)

- P19.01 Sofie Axelgaard. DIRECT EFFECTS OF CHRONIC ILOPROST AND TREPROSTINIL TREATMENT IN PRESSURE OVERLOAD INDUCED RIGHT HEART HYPERTROPHY AND FAILURE
- P19.02 Lilliana Beck. GENETIC DEFICIT IN KCA3.1 PREVENTS PULMONARY VASODILATION AND FATAL PULMONARY CIRCULATORY COLLAPSE INDUCED BY TRPV4 CHANNEL ACTIVATION
- P19.03 Rikke Viggers. REGULATION OF ANGPTL4 IN HUMAN MUSCLE- AND ADIPOSE TISSUE
- P19.04 Marie Rose Hjortbak. IS THERE AN ADDITIVE CARDIOPROTECTIVE EFFECT OF ISCHEMIC PRECONDITIONING AND MILD HYPOTHERMIA?
- P19.05 Rasha Salman. CARDIOPROTECTIVE AND ADDITIVE EFFECT OF ROTIGAPTIDE IN ISOLATED RABBIT HEARTS
- P19.06 Thomas Krarup Andersen. DIRECT EFFECTS OF CHRONIC LEVOSIMENDAN TREATMENT IN PRESSURE OVERLOAD INDUCED RIGHT HEART HYPERTROPHY AND FAILURE
- P19.07 Nanna Mørk. IDENTIFICATION OF INNATE IMMUNODEFICIENCIES BY WHOLE EXOME SEQUENCING
- P19.08 Rahul Prabha. A TOOTH FOR BONE

Poster session 20 GP6: Cardiovascular - Clinical Science

Chairmen: Christian Aalkjær, Janni Majgaard Jensen (PhD student) & Nikolaj Grøndal (PhD student)

- P20.01 Anders Sommer. FLUOROSCOPY IS INACCURATE FOR ASSESSMENT OF LEFT VENTRICULAR LEAD POSITION IN CARDIAC RESYNCHRONIZATION THERAPY
- P20.02 Rune Benjamin Borregaard. RADIOFREQUENCY ABLATION OF ACCESSORY PATHWAYS IN PATIENTS WITH THE WOLFF-PARKINSON-WHITE SYNDROME: THE POST ABLATION MORTALITY AND RISK OF ATRIAL FIBRILLATION
- P20.03 Sara Gaur. CORONARY CT-ANGIOGRAPHY AND NON-INVASIVE FRACTIONAL FLOW RESERVE MEASUREMENT FOR ASSESSMENT OF NON-CULPRIT CORONARY STENOSES AFTER ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION
- P20.04 Kasper Pryds. DISTINCT WINDOWS OF PROTECTION AGAINST ISCHEMIA-REPERFUSION INJURY FROM REMOTE ISCHEMIC CONDITIONING
- P20.05 Laura Sommer Hansen. THE CLINICAL IMPACT OF AN AGGRESSIVE APPROACH TOWARDS PLEURAL AND PERICARDIAL EFFUSIONS ON PHYSICAL AND RESPIRATORY PERFORMANCE FOLLOWING OPEN HEART-SURGERY - A STEP TOWARDS STANDARD GUIDELINES (THE IMAGING TRIAL)
- P20.06 Carsten Behr-Rasmussen. PATOPHYSIOLOGICAL AND POTENTIAL DIAGNOSTIC ASPECTS OF THE MURAL THROMBUS IN ABDOMINAL AORTIC ANEURYSMS
- P20.07 Søs Ann Christine Neergaard-Petersen. TYPE 2 DIABETES IS ASSOCIATED WITH COMPACT CLOT STRUCTURE AND PROLONGED LYSIS TIME IN PATIENTS WITH CORONARY ARTERY DISEASE
- P20.08 Eva Amalie Nielsen. ENDOTHELIN RECEPTOR BLOCKADE ABROGATE BIVENTRICULAR FIBROSIS AND RV REMODELING IN ISOLATED ELEVATED RIGHT VENTRICULAR AFTERLOAD

Poster session 21 GP6: Cardiovascular - Basic and Clinical Science

Chairmen: Ulf Simonsen, Karen Axelgaard Lorentzen (PhD student) & Jannik Bertelsen (PhD student)

- P21.01 Torbjørn Halle Brøgger. DECLINING SENSITIVITY TO U46619 WITH DECREASED SIZE IN ISOLATED HUMAN SMALL VILLUS ARTERIES
- P21.02 Peter Agger. MYOCARDIAL REMODELLING DUE TO RIGHT VENTRICULAR DILATATION IN CONGENITAL HEART DISEASE
- P21.03 Peter Skov Jensen. STUDIES OF THE DIAMETER RESPONSE OF SMALLER RETINAL VESSELS
- P21.04 Martin Grann. USE OF PHOTONIC FINGERPRINT AS DIAGNOSTIC TOOL AND MARKER FOR TREATMENT OF ENDOTHELIAL CELL DYSFUNCTION
- P21.05 Simon Gabriel Comerma Steffensen. ROLE OF SK₃ CHANNELS IN ERECTILE FUNCTION IN MICE
- P21.06 Nicolaj Christopher Hansson. MULTIDETECTOR COMPUTED TOMOGRAPHY VERSUS TRANSESOPHAGEAL ECHOCARDIOGRAPHY FOR ANNULAR SIZING IN TRANSCATHETER AORTIC VALVE REPLACEMENT
- P21.07 Astrid Drivsholm Sloth. NO APPARENT MODIFICATION BY CARDIOVASCULAR RISK FACTORS AND COMORBIDITY ON THE EFFICACY OF REMOTE ISCHEMIC CONDITIONING BEFORE PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION
- P21.08 Nikolai Hoffmann-Petersen. A COMPARISON OF OFFICE BLOOD PRESSURE, TELEMEDICAL HOME BLOOD PRESSURE AND AMBULATORY BLOOD PRESSURE MONITORING
- P21.09 Lisbeth Bonde. EXTRACELLULAR ACIDIFICATION INHIBITS NA⁺,HCO₃⁻ - COTRANSPORT ACTIVITY

Poster session 22 Research Year - Basic Science III

Chairmen: Ebba Nexø & Morten Christian Bay Grauballe (PhD student)

- P22.01 Jacob Reinholdt Jensen. Initiation of cancer investigations in general practice
- P22.02 Niels Peter Andersen. NON-INVASIVE REDUCTION IN NERVE CONDUCTIVITY IN CLOSE RELATION TO FLOW, USING MRI-GUIDED HIGH INTENSITY FOCUSED ULTRASOUND (HIFU)
- P22.03 Rasmus Hansen Olesen. BLOOD BRAIN GLUCOSE TRANSPORT IN RELATION TO INCREASING BMI EXPRESSION OF GLUT1 AND GLUT3 IN THE PREFRONTAL CORTEX
- P22.04 Kathrine Agergård Kaspersen. OBESITY AND RISK OF INFECTION
- P22.05 Julie Vendelbo Nielsen. NEUROINFLAMMATION IN DIABETES - A POSSIBLE LINK TO ALZHEIMER'S DISEASE? A MICROPET STUDY IN THE GK-RAT, AN ANIMAL MODEL OF TYPE 2 DIABETES
- P22.06 Rasha Abdelkadhem Al-Saaidi. THE MISSENSE MUTATION P.ARG471 HIS CAUSES DILATED CARDIOMYOPATHY THROUGH A DOMINANT NEGATIVE EFFECT
- P22.07 Mikkel Svankjær Thagaard. DOES METFORMIN TREATMENT CAUSE VITAMIN B12 DEFICIENCY?
- P22.08 Vincent Kalumire Cubaka. HEALTH EFFECTS OF CONTEXT-SENSITIVE, PHYSICIAN-ASSISTED, TRAINING-CENTERED SUPERVISION OF HEALTH CENTER PERSONNEL IN RWANDA

Poster session 23 GP7: Laboratory Medicine

Chairmen: Helle Prætorius & Morten Leif Stilund (PhD student)

- P23.01 Aisha Rafique. TARGETING BIOACTIVE NANOPARTICLE-ENCAPSULATED 1,25 VITAMIN D TO MACROPHAGES IN VITRO AND IN VIVO FOR ANTI-INFLAMMATORY THERAPY
- P23.02 Anne Winther Larsen. EGFR POLYMORPHISMS AS PREDICTORS OF CLINICAL OUTCOME IN ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH EGFR-TKI
- P23.03 Konstantin Kazankov. SOLUBLE CD163, A MACROPHAGE ACTIVATION MARKER, IS INDEPENDENTLY ASSOCIATED WITH FIBROSIS IN PATIENTS WITH CHRONIC VIRAL HEPATITIS B AND C
- P23.04 Christina Demuth. IDENTIFICATION OF NOVEL ERLOTINIB RESISTANCE MUTATIONS BY EXOME SEQUENCING OF PLASMA DNA
- P23.05 Johan Frederik Berg Arendt. CANCER PROGNOSIS IN PATIENTS WITH ELEVATED PLASMA VITAMIN B12
- P23.06 Peter Rubak. ASSESSING PLATELET FUNCTION: A NEW FLOW CYTOMETRY BASED ASSAY
- P23.07 Sidsel Rødgaard-Hansen. A SOLUBLE FORM OF THE MACROPHAGE-RELATED MANNOSE RECEPTOR (MR/CD206) IS PRESENT IN HUMAN SERUM AND ELEVATED IN CRITICAL ILLNESS
- P23.08 Omar Majed Abuyaman. THE SOLUBLE RECEPTOR FOR VITAMIN B₁₂ UPTAKE (SCD320) IS PRESENT IN EIGHT OUT OF TWELVE EXAMINED TYPES OF HUMAN BODY FLUIDS

Poster session 24 GP8: Neuroscience - Basic and Clinical Science

Chairmen: Poul Henning Jensen, Jay Rai (PhD student) & Marie Louise Schmitz (PhD student)

- P24.01 Mads Engel Hauberg. MICRO-RNAS IN THE AETIOLOGY OF SCHIZOPHRENIA
- P24.02 Michael Aagaard Andersen. PATHOPHYSIOLOGICAL INTERPLAY BETWEEN LRRK2 AND α -SYNUCLEIN IN THE MECHANISMS LEADING TO NEURONAL DYSFUNCTION AND NEURODEGENERATION IN PARKINSON'S DISEASE
- P24.03 Trine Gjerløff. [¹¹C]DONEPEZIL PET: A METHOD FOR ASSESSING AUTONOMOUS DYSFUNCTION I PARKINSONS' DISEASE?
- P24.04 Kristian Gaarn Du Jardin Nielsen. A SINGLE DOSE OF VORTIOXETINE OR KETAMINE, BUT

- NOT FLUOXETINE, INCREASES TRANSCRIPT LEVELS OF GENES INVOLVED IN NEUROPLASTICITY IN THE RAT PREFRONTAL CORTEX
- P24.05 Noemie Regine Virginie Tentillier. ANTI-INFLAMMATORY THERAPY VIA CD163-MACROPHAGES IN THE 6-OHDA PARKINSON'S DISEASE MODEL
- P24.06 Arnela Mehmedbasic. SORLA IN THE RETINA
- P24.07 Maryam Ardalan. STEREOLOGICAL STUDY OF NEURONAL AND SYNAPTIC PLASTICITY OF HIPPOCAMPUS
- P24.08 Ali H. Rafati. SPATIAL DISTRIBUTION OF NEURONS IN LAYER-III OF MEDIAL PREFRONTAL CORTEX OF FLINDERS RATS WITH MATERNAL SEPARATION

Poster session 25 GP2: Molecular Metabolism and Endocrinology - Clinical Science

Chairmen: Troels Krarup Hansen, Ann Mosegaard Bak (PhD student) & Gitte Bloch Rasmussen (PhD student)

- P25.01 Anne Kristine Amstrup. TREATMENT OF OSTEOPENIA WITH MELATONIN: EFFECT ON BONE MINERAL DENSITY, MUSCLE STRENGTH AND QUALITY OF LIFE
- P25.02 Nikolaj Rittig. METABOLIC CHANGES DURING ACUTE INFLAMMATION WITH AND WITHOUT AMINO ACID SUPPLEMENT
- P25.03 Joan Bach Nielsen. ETIOLOGY, ASSESSMENT AND TREATMENT OF POST-GASTRIC BYPASS SEVERE HYPOGLYCAEMIA
- P25.04 Sofie Hertz Rønn. INVESTIGATIONS OF THE EFFECT OF MK-7 ON BONE AND GLUCOSE METABOLISM AND ARTERIAL CALCIFICATION
- P25.05 Mette Bohl Larsen. WHEY, CASEIN, AND POST-PRANDIAL LIPAEMIA; A 12-WEEK, RANDOMIZED, PARALLEL-CONTROLLED, HUMAN INTERVENTION STUDY
- P25.06 Anke Elisabeth de Beijer. CLINICAL PATHWAY FOR THE DIAGNOSTIC AND TREATMENT OF TRIGGER FINGER AND CARPAL TUNNEL SYNDROME PATIENTS IN HOLSTEBRO REGIONAL HOSPITAL
- P25.07 Andreas Buch Møller. MOLECULAR MECHANISMS OF EXERCISE-INDUCED AUTOPHAGY IN HUMAN SKELETAL MUSCLE: EFFECT OF SUBSTRATE AVAILABILITY

Poster session 26 GP8: Neuroscience - Clinical Science

Chairmen: Jakob Udby Blicher, Mikkel Mylius Rasmussen (PhD student) & Jesper Jeppesen (PhD student)

- P26.01 Krystian Figlewski. TRANSCRANIAL DIRECT CURRENT STIMULATION AIDED REHABILITATION OF GAIT IN SUBACUTE STROKE. PILOT STUDY
- P26.02 Henrique Fernandes. SIGNIFICANT CHANGES IN LOCAL CONNECTIVITY IN EARLY-ONSET BIPOLAR DISORDER WITH PSYCHOSIS
- P26.03 Lene Duez. DETECTION OF INTERICTAL EPILEPTIC DISCHARGES BY MAGNETOENCEPHALOGRAPHY IN THE DANISH PRESURGICAL EPILEPSY EVALUATION
- P26.04 Lars Høj Markvardsen. LONG-TERM TREATMENT WITH SUBCUTANEOUS IMMUNOGLOBULIN IN HIGH DOSES IS EFFECTIVE IN PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY
- P26.05 Kristian Lundsgaard Kraglund. CITALOPRAM IN ACUTE STROKE
- P26.06 Gro Helen Dale. CAN EARLY TREATMENT WITH SOLU-MEDROL PREVENT VISUAL LOSS AFTER OPTIC NEURITIS?
- P26.07 Erhard Næss-Schmidt. PATHOLOGY IN THE BRAIN AFTER MTBI? A MULTIMODAL MAGNETIC RESONANCE IMAGING STUDY
- P26.08 Johanne Liv Agger. PHARMACOLOGICAL TREATMENT OF MULTI-ORGAN BODILY DISTRESS SYNDROME. A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF THE EFFECTS OF IMIPRAMINE (STRESS-3). CLINICALTRIALS.GOV, NCT01518634

Poster session 27 Clinical Science

Chairmen: Donna Briggs Bødtkjær, Juan Manuel Shiguetomi Medina (PhD student) & Lotte Vinge (PhD student)

- P27.01 Chris Amdisen. COMPARISON OF AN IMPLANTABLE ULTRASOUND PROBE AND MICRODIALYSIS FOR DETECTION OF GRADUAL RENAL VEIN OCCLUSION
- P27.02 Mette Tiedemann Skipper. OPTIMIZING WHOLE BLOOD IMPEDANCE AGGREGOMETRY IN SEVERE THROMBOCYTOPENIA
- P27.03 Rikke Hjortebjerg. METABOLIC FUNCTIONS OF THE IGF SYSTEM IN HUMAN ADIPOSE TISSUE
- P27.04 Julie Brogaard Larsen. COULD VON WILLEBRAND'S DISEASE BE OVERLOOKED IN WOMEN USING COMBINED ORAL CONTRACEPTIVES?
- P27.05 Andreas Engel Krag. ISCHEMIA-REPERFUSION INJURY IN EXPERIMENTAL MUSCLE FLAPS FOLLOWING HYPOTHERMIC OR NORMOTHERMIC ISCHEMIA
- P27.06 Abstract moved to session poster session 3
- P27.07 Heidi Kristine Støve Nielsen. EXTRAMEDULLARY LEUKAEMIA IN CHILDREN WITH ACUTE MYELOID LEUKAEMIA
- P27.08 Anders Gyldenkerne. GENERATION OF A MODEL DESCRIBING THE OPTICAL PROPERTIES OF THE CORNEA

Poster session 28 GP10: Translational Molecular Medicine - Clinical Science

Chairmen: Erisela Qerama Montvilas, Miao Wang (PhD student) & Lene Hjelle Tauris (PhD student)

- P28.01 Signe Væth. DIAGNOSTIC TIME TREND AND AGE AND SEX DISTRIBUTION OF CHARCOT-MARIE-TOOTH DISEASE
- P28.02 Luise Borch. THE EFFECT OF COMBINING TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) AND ANTICHOLINERGICS WHEN TREATING CHILDREN SUFFERING FROM URINARY INCONTINENCE AND AN OVERACTIVE BLADDER (OAB)
- P28.03 Steven Brantlov. BIOIMPEDANCE SPECTROSCOPY (BIS) PARAMETERS IN HEALTHY CHILDREN: RELATION TO AGE, WEIGHT, LENGTH AND BODY MASS INDEX (BMI)
- P28.04 Navid Sahebkhari. MITOCHONDRIAL PROTEOME CHANGES IN ETHE1 - DEFICIENT MICE: INDICATION OF METABOLIC IMBALANCE
- P28.05 Lilja Kristin Dagsdóttir. CHRONIC OROFACIAL PAIN PATIENTS EXPERIENCE PERCEPTUAL DISTORTIONS OF THE FACE
- P28.06 Tanni Kjær Borgbo. GENETIC VARIATIONS OF THE FOLLICLE STIMULATING HORMONE RECEPTOR AND THEIR IMPACTS ON FEMALE FERTILITY
- P28.07 Zahra Nochi. APPROACHES TO DECIPHERING THE BALANCE BETWEEN SURVIVAL AND DEATH MECHANISMS IN CELLS WITH MITOCHONDRIAL DYSFUNCTION
- P28.08 Lu Xing. RENAL AQP1&NDASH;3 EXPRESSION PATTERNS IN RESPONSE TO 1 WEEK CONGENITAL PARTIAL UNILATERAL URETERAL OBSTRUCTION IN RATS

Poster session 29 GP11: Tooth, Bone and Joint Diseases

Chairmen: Irene Dige, Kresten Rickers (PhD student) & Sepp de Raedt (PhD student)

- P29.01 Karen Toftdahl Bjørnholdt. DEXAMETHASONE FOR THE REDUCTION OF POSTOPERATIVE PAIN AFTER OUTPATIENT SHOULDER SURGERY: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL
- P29.02 Kristian Andersen. EFFECT OF MANDIBULAR DISTRACTION OSTEOGENESIS ON THE TEMPOROMANDIBULAR JOINT: A SYSTEMATIC REVIEW OF ANIMAL EXPERIMENTAL STUDIES
- P29.03 Jens Bay Vegger. ADDITIVE EFFECT OF PTH(1-34) AND ZOLEDRONATE IN THE PREVENTION OF DISUSE OSTEOGENESIS IN RATS

- P29.04 Mikkel Tøttrup. THE CONCENTRATION OF CEFUROXIME IN CORTICAL AND CANCELLOUS BONE CAN BE DETERMINED BY USE OF MICRODIALYSIS - A METHODOLOGICAL STUDY
- P29.05 Bahram Ranjkesh. APATITE FORMATION ON FAST-SETTING NOVEL MINERAL TRIOXIDE AGGREGATE AND DIAMETRICAL STRENGTH DEVELOPMENT IN VITRO
- P29.06 Polina Martinkevich. PRECISE AND FEASIBLE MEASUREMENTS OF LATERAL CALCANEAL LENGTHENING OSTEOTOMIES BY RADIOSTEREOMETRIC ANALYSIS (RSA)
- P29.07 Rubens Spin-Neto. VARIATION IN VOXEL VALUE DISTRIBUTION AND EFFECT OF TIME BETWEEN EXPOSURES IN SIX CBCT UNITS
- P29.08 Abhishek Kumar. EFFECTS OF EXPERIMENTAL PAIN ON FINE JAW MOTOR CONTROL - A PLACEBO CONTROLLED DOUBBLE BLINDED STUDY

Poster session 30 GP3: Public Health - Clinical Science

Chairmen: Anelli Sandbæk, Stina Lou (PhD student) & Connie Timmermann (PhD student)

- P30.01 Malene Beck. QUIET PLEASE! BETTER MEALTIMES AT THE NEUROLOGY WARD A PH.D. STUDY (IN PROGRESS)
- P30.02 Jette Pedersen. IS TRANSFER OF NUTRITIONAL RECOMMENDATIONS FROM SECONDARY SECTOR TO PRIMARY SECTOR AFFECTED BY THE PRESENCE OF A CLINICAL DIETICIAN IN HOSPITAL?
- P30.03 Anna Sundby. WHOLE GENOME SEQUENCING - NEW POSSIBILITIES, NEW DILEMMAS
- P30.04 Nanna Rolving Rasmussen. DOES A PREOPERATIVE COGNITIVE INTERVENTION AFFECT POSTSURGICAL PAIN, MOBILISATION AND LENGTH OF HOSPITALISATION IN LUMBAR SPINAL FUSION PATIENTS?
- P30.05 Rikke Aarhus. FAST-TRACK DIAGNOSTICS: EXPLORING HOW CANCER PATHWAYS FRAME CLINICAL ENCOUNTERS AND THE CONFIGURATION OF PATIENT AND HEALTH PROFESSIONAL IDENTITIES
- P30.06 Louise Møldrup Nielsen. THE EFFECT OF SYSTEMATIC ASSESSMENT OF FUNCTIONAL ABILITY, DEVELOPMENT OF REHABILITATION PLAN AND FOLLOW-UP AT HOME FOR ELDERLY MEDICAL PATIENTS
- P30.07 Janni Lisander Larsen. WOMENS EXPERIENCE OF LIVING WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A QUALITATIVE STUDY
- P30.08 Jette Lauritzen. THE MEANINGFULNESS OF PARTICIPATING IN SUPPORT GROUPS FOR INFORMAL CAREGIVERS OF OLDER ADULTS WITH DEMENTIA

Poster session 31 GP3: Public Health - Clinical Science II

Chairmen: Marianne Vámosi, Lotte Dahl Kristensen (PhD student) & Louise Mahncke (PhD student)

- P31.01 Sara Marie Hebsgaard. FROM BODILY SIGNS TO SYMPTOMS OF ILLNESS. AN ANTHROPOLOGICAL STUDY OF THE 'PATIENT INTERVAL'
- P31.02 Linda Christie Andrea. SUSPECTED IMPINGEMENT SYNDROME - PREDICTORS OF EARLY CLOSURE OF TREATMENT
- P31.03 Charlotte Simoný. ISCHAEMIC HEARTPATIENTS ARE ENCOURAGED TO ENJOY PHYSICAL EXERCISES IN THEIR REHABILITATION
- P31.04 Bettina Kjær Kristiansen. FOLLOW-UP OF ABNORMAL OR INADEQUATE TEST RESULTS IN THE DANISH CERVICAL CANCER SCREENING PROGRAMME: EFFECTS OF TWO INTERVENTIONS
- P31.05 Vita Ligaya Ponce Dalgaard. CHANGES IN SELF-REPORTED SLEEP AND COGNITIVE FAILURES: A RANDOMIZED CONTROLLED TRIAL OF A STRESS MANAGEMENT INTERVENTION
- P31.06 Christina Friis Jensen. DISCONTINUATION OF NASAL CPAP IN PRETERM INFANTS - A RANDOMIZED CONTROLLED MULTICENTER TRIAL
- P31.07 Mette Trads. QUALITY OF LIFE AMONG PATIENTS WITH CONSTIPATION

P31.08 Berit Skjødeberg Toftegaard. THE EFFECT OF CONTINUING MEDICAL EDUCATION (CME) ON GP CANCER RISK ASSESSMENT - PRELIMINARY RESULTS

Poster session 32 GP9: Oncology - Clinical Science

Chairmen: Charlotte Guldborg Nyvold, Tinne Laurberg (PhD student) & Marie-Louise Feddern (PhD student)

- P32.01 Maria Staub Ervandian. ANDROGEN DEPRIVATION THERAPY IMPROVES BIOCHEMICAL OUTCOMES IN PATIENTS TREATED WITH SALVAGE RADIOTHERAPY - A NATIONAL DANISH STUDY
- P32.02 Mai Lykkegaard Schmidt. DOSIMETRIC IMPACT OF INTRA- AND INTERFRACTION TUMOR MOTION AND ANATOMICAL CHANGES IN RADIOTHERAPY OF NSCLC
- P32.03 Nina Munk Lyhne. DHANCA 27; TRANSORAL LASER ASSISTED MICROSURGERY FOR T1A GLOTTIC CANCER
- P32.04 Sara Correia Marques. MICRORNAS AS BIOMARKERS FOR DOXORUBICIN RESISTANCE IN POST-GERMINAL B-CELL MALIGNANCIES
- P32.05 Marianne Hjorth Skorstengaard. TITLE: ADVANCE CARE PLANNING: A WAY TO IMPROVE END-OF-LIFE CARE
- P32.06 Anna Kirstine Winthereik. IMPROVING END-OF-LIFE CARE BY CONTINUING MEDICAL EDUCATION AND ELECTRONIC DECISION MAKING SUPPORT FOR GENERAL PRACTITIONERS IN DENMARK &NDASH; A RANDOMIZED CONTROLLED TRIAL
- P32.07 Jakob Kristian Jakobsen. PRE-TREATMENT DIAGNOSTIC CHARACTERISTICS OF 321 PENILE CANCER PATIENTS - A NATIONAL RETROSPECTIVE STUDY FROM DENMARK

Poster session 33 GP9: Oncology - Clinical Science II

Chairmen: Anders Bonde Jensen, Sandy Mohamed Ismail Mohamed (PhD student) & Helene Myrtue Nielsen (PhD student)

- P33.01 Maja Ølholm Vase. EBV AND HLA-TYPE IN POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)
- P33.02 Anne Vestergaard. CLINICAL EXPERIENCE WITH ADAPTIVE RADIOTHERAPY FOR MUSCLE INVASIVE BLADDER CANCER
- P33.03 Mette Marie Fode. TOWARDS BIOLOGY ADAPTED STEREOTACTIC BODY RADIATION THERAPY (SBRT) OF LIVER METASTASES
- P33.04 Alexander Juhl Andersen. MID-TERM EVALUATION OF DELAYED UNILATERAL BREAST RECONSTRUCTION AFTER MASTECTOMY
- P33.05 Mette Eline Brunbjerg. IMMEDIATE BREAST RECONSTRUCTION WITH ACELLULAR DERMAL MATRIX
- P33.06 Søren Haack. DIFFUSION WEIGHTED MRI ACQUISITION WITH HIGH ACCELERATION FACTOR FOR IMPROVING ACCURACY FOR USE IN RADIOTHERAPY PLANNING
- P33.07 Kennet Sønderstgaard Thorup. IMPROVING DIFFUSION WEIGHTED MRI FOR QUANTITATIVE BODY TUMOUR CHARACTERIZATION. PARTIAL VOLUME CORRECTION AND ISOTROPIC IMAGING STRATEGIES
- P33.08 Susanne Rylander. THE POSSIBILITY TO REDUCE RECTAL DOSE BY REMOVING THE ULTRASOUND PROBE PRIOR TO DELIVERY OF HIGH-DOSE-RATE BRACHYTHERAPY IN PROSTATE CANCER

Poster session 34 GP9: Oncology - Clinical Science III

Chairmen: Rikke Katrine Andersen, David Christoffer Hansen (PhD student) & Marie Louise Bønnelykke-Behrndtz (PhD student)

- P34.01 Morten Nørgaard Andersen. MACROPHAGES AND THERAPY RESISTANCE IN MULTIPLE MYELOMA - NOVEL TARGETS FOR TAILORED THERAPY
- P34.02 Maria Cathrine Corneliussen Vest Schmidt. HYPODONTIA AND OVARIAN CANCER - THE CONNECTION BETWEEN DENTAL AGENESIA AND EPITHELIAL CANCERS, ESPECIALLY OVARIAN CANCER
- P34.03 Jill Rachel Mains. DIFFUSION-WEIGHTED MRI (MR-DWI) AND DYNAMIC CONTRAST-ENHANCED CT (DCE-CT): A COMPARATIVE PILOT STUDY
- P34.04 Ninna Aggerholm-Pedersen. THE INFLUENCE OF HYPOXIA ON SARCOMA PATIENTS' RESISTANCE TO CHEMOTHERAPY AND IRRADIATION THERAPY
- P34.05 Mary Nguyen Nielsen. PROSTATE CANCER, COMORBIDITIES AND RISK OF VENOUS THROMBOEMBOLISM
- P34.06 Anne Wandler. THE BIOLOGICAL AND PROGNOSTIC SIGNIFICANCE OF MICRORNAS IN MELANOMA
- P34.07 Kristine Raaby Jakobsen. INVESTIGATING THE ROLE OF LUNG FIBROBLASTS IN NON-SMALL CELL LUNG CARCINOMAS

Poster session 35 GP12: Clinical Medicine - Clinical Science

Chairmen: Jørgen Bjerggaard Jensen, Mette Julsgaard (PhD student) & Cathrine Bach (PhD student)

- P35.01 Ditte Louise Egeskov Munkedal. LONGER DISTANCE TO THE ARTERIAL TIE FOR LAPAROSCOPIC SURGERY OF RIGHT AND LEFT SIDE TUMORS
- P35.02 Susanne Hass. CORTICAL EVOKED POTENTIALS IN RESPONSE TO RAPID BALLOON DISTENSION OF THE RECTUM AND ANAL CANAL
- P35.03 Lise Hald Nielsen. HYPERTENSION AND URINE PROTEASE ACTIVITY IN PREECLAMPSIA
- P35.04 Marie Krarup Schrøder. THE EFFECT OF GENDER ON ANTIDIURESIS
- P35.05 Jacob Gamst. ATRIAL FIBRILLATION AND RISK OF ARTERIAL THROMBOEMBOLISM FOLLOWING HOSPITALIZED PNEUMONIA: A POPULATION-BASED COHORT STUDY
- P35.06 Baris Isak. LASER EVOKED CUTANEOUS SILENT PERIODS IN PATIENTS WITH CHEMOTHERAPY INDUCED POLYNEUROPATHY
- P35.07 Line Pedersen. NO AND COX PRODUCTS ARE INVOLVED IN HYPOXIA-INDUCED DILATATION OF RETINAL VESSELS
- P35.08 Sanne Shiroma Harsløf. PAIN, QUALITY OF LIFE, ADHESIONS AND RECURRENCE AFTER LAPAROSCOPIC VENTRAL HERNIA REPAIR: A CLINICAL, RANDOMIZED, PROSPECTIVE, DOUBLE-BLINDED STUDY OF THREE TYPES OF MESH FIXATION

Poster session 36 GP12: Clinical Medicine - Clinical Science II

Chairmen: Christoffer Sølling & Eva Sædder (PhD student)

- P36.01 Christina Kjærgaard Rasmussen. INTER-OBSERVER VARIATION IN DIAGNOSING ADENOMYOSIS USING TWO- AND THREE-DIMENSIONAL TRANSVAGINAL ULTRASOUND
- P36.02 Ditte Lou Langhoff Gantriis. A CASE-CONTROL STUDY OF THE HOME ENVIRONMENT AMONG 7-YEAR OLD OFFSPRING OF PARENTS WITH SCHIZOPHRENIA OR BIPOLAR DISORDER
- P36.03 Jennie Maria Christin Strid. ULTRASOUND/MAGNETIC RESONANCE IMAGE FUSION GUIDED LUMBOSACRAL PLEXUS BLOCK
- P36.04 Rune Wilkens. INTESTINAL PERFUSION IMAGING IN CROHN DISEASE (CD)
- P36.05 Mads Skipper. THE LINKS BETWEEN ORGANIZATIONAL, GROUP, AND INDIVIDUAL MEDICAL POSTGRADUATE WORKPLACE LEARNING IN PEDIATRIC DEPARTMENTS

- P36.06 Katrine Fuglsang. HIGHLIGHTS ON RECURRENCE AFTER SURGERY DUE TO CERVICAL CANCER
- P36.07 Zhanyuan Kang. ABSTRACT TITLE (CLICK TO CHANGE ME) TNF&ALPHA; AND IL-17A-INDUCED S100A7 EXPRESSION IS REGULATED BY A P38 MAPK AND ERK1/2 DEPENDENT MECHANISM IN CULTURED HUMAN KERATINOCYTES
- P36.08 Anders Grejs. THE CARDIAC EFFECT IN PROLONGED HYPOTHERMIA AFTER CARDIAC ARREST

Poster session 37 GP12: Clinical Medicine - Clinical Science III

Chairmen: Klaus Krogh Magnus Gottfredsson & Betina Hansen (PhD student)

- P37.01 Esben Nielsen. FUCHS&RSQUO; ENDOTHELIAL DYSTROPHY: CLINICAL CHARACTERISTICS, TREATMENT OUTCOME, AND PATHOLOGY
- P37.02 Sidsel Hastrup. EFFECT OF CENTRALIZATION OF ACUTE STROKE; AND OPTIMIZATION OF THE PRE-HOSPITAL PHASE
- P37.03 Anne-Mette Haase. GASTROINTESTINAL MOTILITY AND SLEEP PATTERNS ASSESSED BY AMBULATORY TRACKING OF TELEMETRIC CAPSULES COMBINED WITH POLYSOMNOGRAPHY
- P37.04 Morten Thingemann Bøtker. PREHOSPITAL TRIAGE OF PATIENTS WITH SEVERE DYSPNEA USING POINT-OF-CARE N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE. THE PREBNP STUDY
- P37.05 Anders Rosendal Korshøj. INDIVIDUALIZED DEEP BRAIN STIMULATION TREATMENT OF CHONIC NEUROPATHIC PAIN
- P37.06 Tommy Kjærgaard Nielsen. CONTRAST ENHANCEMENT ON CT FOLLOWING RENAL CRYOABLATION - WHEN SHOULD TREATMENT FAILURE BE CONSIDERED?
- P37.07 Aja Neergaard Greve. A CASE-CONTROL STUDY OF ASSOCIATIONS BETWEEN SOCIAL COGNITION IN PARENTS WITH SCHIZOPHRENIA OR BIPOLAR DISORDER AND THEIR 7-YEAR OLD OFFSPRING
- P37.08 Mikkel Petersen. EVALUATION OF MR BASED FIBER TRACKING AS A TOOL IN DEEP BRAIN STIMULATION FOR MOVEMENT DISORDERS

Poster session 38 Research Year - Clinical Science II

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- P38.01 Pernille Libach Hansen. USE OF GENERAL PRACTICE, DIAGNOSTIC INVESTIGATIONS AND PRESCRIPTIONS IN THE YEAR PRECEDING COLORECTAL CANCER DIAGNOSIS
- P38.02 Wajd Abbas Hassan. IGFBP-2 AUTOANTIBODIES AS A SEROLOGICAL BIOMARKER IN THE DIAGNOSIS AND PROGNOSIS OF CANCER
- P38.03 Kristoffer Backman Nøhr. QUANTITATIVE EEG REACTIVITY IN COMATOSE NEUROSURGICAL PATIENTS
- P38.04 Anne Bank Boisen. LOW-GRADE SYSTEMIC INFLAMMATION IN ADOLESCENT OFFSPRING OF MOTHERS WITH TYPE 1 DIABETES
- P38.05 Khoa Manh Dinh. THE DANISH BLOOD DONOR STUDY: NASAL COLONISATION WITH AMONG HEALTHY DANES AND THE ASSOCIATION TO C-C CHEMOKINE RECEPTOR TYPE 5 &DELTA;32 DELETION
- P38.06 Tobias Pilgaard Ottosen. LACK OF IMPROVEMENT IN INCIDENCE AND CASE-FATALITY OF FIRST TIME HOSPITAL ADMISSION WITH INTRACEREBRAL HEMORRHAGE IN DENMARK 2004-2012
- P38.07 Pia Carstensen Simonsen. DEVELOPMENT OF A NEW CLASSIFICATION SYSTEM OF COMORBIDITY, TREATMENT COMPLEXITY, SEQUELAE AND COMPLICATIONS IN UROLOGICAL CANCER SURGERY
- P38.08 Christophe Henri Valdemar Duez. QUANTIFIED EEG REACTIVITY PREDICTS BOTH GOOD AND POOR OUTCOME. A PILOT STUDY ON CARDIAC ARREST PATIENTS

PhD Student Chairmen

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- CH.02 Søren Brandt Poulsen. SPECIFIC INACTIVATION OF THE EPITHELIAL SODIUM CHANNEL (ENAC) IN KIDNEY CONNECTING TUBULE: EFFECT ON SODIUM AND POTASSIUM HOMEOSTASIS
- CH.03 Jeppe Skov. EFFECT OF GLUCAGON-LIKE PEPTIDE-1 ON KIDNEY FUNCTION IN HEALTHY MALES
- CH.04 Therese Koops Grønberg. ESTIMATING HERITABILITY FOR TIME-TO-EVENT DATA USING TWINS AND PSEUDO-OBSERVATIONS
- CH.05 Anto Praveen Rajkumar Rajamani. THE IMPORTANCE OF BRD1 GENE IN AFFECTIVE BEHAVIOUR AND ITS RELATION TO DEPRESSION
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- CH.09 Lene Hee Christensen. QUANTITATIVE SONOELASTOGRAPHY OF THE UTERINE CERVIX BY INTERPOSITION OF A SYNTHETIC REFERENCE MATERIAL
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Abstracts the Fogh-Nielsen Price Competition

Morten Würtz THE ANTIPLATELET EFFECT OF ASPIRIN DECLINES THROUGH 24 HOURS IN PATIENTS WITH PREVIOUS STENT THROMBOSIS

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Background: Once-daily aspirin is considered to inhibit platelets for 24 hours, but recent studies suggest gradual attenuation of aspirin efficacy through this dosing interval. Stent thrombosis (ST) is a devastating complication of coronary interventions, and we have previously shown a reduced effect of aspirin in patients with ST.

Aim: We investigated if platelet inhibition by aspirin declines through 24 hours in patients with previous ST. Furthermore, we explored if platelet inhibition declines particularly rapid in patients with increased platelet turnover.

Methods: We included 50 patients with previous ST, 100 patients with stable coronary artery disease and 50 healthy volunteers all treated with aspirin 75 mg once daily. Platelet function was measured 1 and 24 hours after aspirin intake using platelet aggregometry (Multiplate[®] Analyzer). Furthermore, COX-1 activity, platelet turnover, platelet production, and platelet activation were measured.

Results: Platelet aggregation increased from 1 to 24 hours after aspirin intake ($p < 0.0001$) as did COX-1 activity ($p < 0.0001$) and platelet activation ($p < 0.0001$). Patients with previous ST displayed the highest levels of platelet aggregation ($p \leq 0.05$), platelet turnover ($p < 0.01$) and platelet production ($p < 0.0001$).

Conclusion: Platelet inhibition by aspirin declines significantly during the recommended 24-hour dosing interval. In particular, patients with previous ST have a prothrombotic phenotype involving increased production and turnover of platelets. Once-daily aspirin does not provide consistent platelet inhibition through 24 hours, and a twice-daily treatment regimen thus may better protect against thrombotic events.

Søren Dinesen MEASURING PSYCHOTIC DEPRESSION
Østergaard

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Objective: Psychotic depression (PD) is a highly debilitating psychiatric condition, which needs intensive monitoring and treatment. However, there is no established rating scale for evaluating the severity and treatment outcome in PD. Thus, the aim of this analysis was to assess the psychometric properties of established depression rating scales and a number of new composite rating scales, covering both depressive and psychotic symptoms, in relation to PD.

Method: The psychometric properties of the rating scales were evaluated based on analyses of data from the Study of Pharmacotherapy of Psychotic Depression.

Results: A rating scale consisting of the 6-item Hamilton melancholia subscale (HAM-D₆) plus five items from the Brief Psychiatric Rating Scale (BPRS), named the Psychotic Depression Assessment Scale (PDAS), displayed clinical validity (Spearman coefficient of correlation between PDAS and Clinical Global Impression - Severity (CGI-S) scores = 0.79 - 0.84), responsiveness (Spearman correlation coefficient between change in PDAS and Clinical Global Impression -Improvement (CGI-I) scores = -0.74 - -0.78) and unidimensionality (Loevinger coefficient of homogeneity = 0.41) in the evaluation of PD. The HAM-D₆ fulfilled the same criteria, whereas the full 17-item Hamilton depression scale failed to meet criteria for unidimensionality.

Conclusion: Our results suggest that the PDAS has higher psychometric and clinical validity than pure depression scales in the assessment of severity in psychotic depression.

Morten Schmidt **CARDIOVASCULAR RISKS ASSOCIATED WITH NON-ASPIRIN NSAID USE**

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The cardiovascular safety of non-steroidal anti-inflammatory drugs (NSAIDs) is controversial because COX-2 inhibitors have been found to increase the risk of myocardial infarction. We hypothesized that the cardiovascular risks of NSAIDs (1) are reduced in patients on dual antiplatelet therapy; (2) are not restricted to the arterial system, but also affect the venous system; (3) include an increased risk of atrial fibrillation through adverse renal effects including fluid retention and blood pressure destabilization; and (4) increase mortality following ischemic stroke.

We conducted population-based cohort and case-control studies to examine these hypotheses. We identified use of NSAIDs from prescription

registries and used the Danish National Patient Registry, the Western Denmark Heart Registry, the Civil Registration System, and the Danish Cause-of-death Registry to collect data on cardiovascular morbidity, comorbidity, and mortality.

We found that NSAID use was not associated with adverse arterial events in patients on dual antiplatelet therapy following coronary stent implantation (Schmidt et al. *Pharmacotherapy*, 2011). However, use of NSAIDs was associated with a two-fold increased risk of venous thromboembolism (Schmidt et al. *JTH*, 2011), a 40-70% increased risk of atrial fibrillation (Schmidt et al. *BMJ*, 2011), and a 30% increased short-term mortality following ischemic stroke (paper in preparation), especially when therapy was initiated with COX-2 inhibitors. Finally, in a methodology paper (submitted), we also described overall trends in use of NSAIDs in Denmark between 1999 and 2012 and how prescription registries provide a valuable source for identifying NSAID use.

Abstracts oral sessions

Oral session 1

O01.01 Janus
Hyldebrandt

NON-SUSTAINED EFFECT OF DOBUTAMINE DURING ACUTE RIGHT VENTRICULAR FAILURE IN THE NEWBORN PIGLET

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Objective: To investigate the effect of three commonly used inotropic treatment strategies in newborn piglets, with and without acute right ventricular failure.

Method: Sixty-three newborn piglets were treated with either 1: Adrenaline + Milrinone, 2: Dopamine + Milrinone, 3: Dobutamine, or 4: Saline, and observed for 180 minutes. Twenty-eight had acute right ventricular failure induced by 10 cycles of alternating 3- minute ischemia and reperfusion of the right coronary artery prior to treatment.

Measurements: Right and left ventricular systolic and diastolic parameters were measured using by conductance catheters. Arterial and central venous pressures and cardiac output were recorded continuously. Tissue oxygenation was evaluated by measuring pH and lactate in arterial blood samples.

Main results: In the normal piglets, all inotropes increased contractility, but we found no differences between any of the inotropic strategies. Dobutamine treated animals had a higher cardiac output and perfusion pressure compared to all other groups. In animals with acute right ventricular failure, both adrenaline and dopamine combined with milrinone increased contractility, whereas the effect of dobutamine was non-sustained and was indistinguishable from control after 3 hours. Dobutamine treated animals had lower right ventricular contractility, perfusion pressures and blood pH value compared to the other treatment groups.

Conclusions: In newborn piglets, dobutamine had a non-sustained effect on contractility during acute right ventricular failure, resulting in decreased contractility and impaired perfusion compared to both dopamine and adrenaline in combination with milrinone.

O01.02 Anette Tarp
Hansen

COPEPTIN AS A NOVEL BIOMARKER FOR FETAL GROWTH RETARDATION: A CASE-CONTROL STUDY

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Background: Maternal stress affects fetal development. Fetal growth retardation and pre-eclampsia share a common pathogenesis and copeptin, a novel stress marker, is found elevated in pre-eclampsia. The aim of our study was to establish reference intervals for serum-copeptin during pregnancy and to test our hypothesis that maternal serum-copeptin is elevated in women with fetal growth retardation.

Methods: A nested case-control study. Copeptin levels were determined in maternal serum at gestational weeks 12 and 19 by using a Copeptin ultra-sensitive Kryptor kit (BRAHMS). Cases were pregnancies later developing fetal growth retardation (N=39). Controls were normal pregnancies (N=119). Reference ranges were calculated as 95% prediction intervals and presented as anti-logarithm with 90% confidence intervals. Paired and unpaired t-test was performed to test the null-hypothesis of no difference in serum-copeptin levels within and between groups. Odds ratios were calculated for maternal characteristics and risk of fetal growth retardation.

Results: Reference intervals for copeptin in normal pregnancies were 1.24-5.51 pmol/L (90% confidence intervals on upper and lower limit 1.13-1.37 and 5.00-6.08 pmol/L) at gestational week 12, and 1.30-5.09 pmol/L (90% confidence intervals 1.19-1.42 and 4.65-5.57 pmol/L) at gestational week 19. Copeptin levels decreased from week 12 to 19 in cases (p=0.02), whereas no significant decrease was observed in controls (p=0.61). No difference was found in copeptin levels comparing cases with controls in gestational week 12 (p=0.10) and week 19 (p=0.81).

Conclusions: Copeptin did not add predictive information on fetal growth retardation.

O01.03 Anders Jorsal

CARDIAC EFFECTS OF GLP-1 TREATMENT IN PATIENTS WITH CHRONIC HEART FAILURE

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Background: Glucagon-like peptide 1 (GLP-1) is a naturally existing hormone, which is a part of the incretine system. GLP-1 stimulates insulin production and inhibits glucagon-excretion from the pancreas, thereby reducing blood sugar levels. Moreover, a beneficial effect of GLP-1 on cardiac function has been suggested in both diabetic and non-diabetic patients. Liraglutide (Victoza[®]) is a GLP-1-analogue developed for treatment of type 2 diabetes (T2D). The impact of liraglutide on cardiac function has not previously been investigated in patients with chronic heart failure (CHF).

Hypothesis: Liraglutide treatment for 24 weeks improves LVEF in CHF patients with and without T2D compared to placebo treatment.

Design and methods: An investigator initiated, multi-centre, randomised, double blind, parallel, placebo controlled intervention trial. In total, 240 CHF patients (patients with T2D and patients without diabetes 1:1) with left ventricular ejection fraction < 45% will be randomised to either subcutaneous injection of liraglutide 1.8 mg or matching placebo once daily for 24 weeks. The effect of liraglutide on left ventricular systolic function will be evaluated by advanced echocardiography, including 3-dimensional contrast echocardiography.

Status (1 September 2013):

Randomised: 134 (screened:255)

Ischemic heart disease: 68%

Diabetes: 33%

Adverse events: 168

Serious adverse events: 18

Perspectives: Potentially liraglutide can improve heart function substantially, thus changing the prognosis of CHF patients worldwide.

O01.04 Vibeke Secher
Nielsen FUNCTIONAL CHARACTERISTICS OF PUTATIVE Ca^{2+} -ACTIVATED Cl^{-} CHANNELS - BESTROPHINS AND TMEM16A - IN RAT MESENTERIC SMALL ARTERIES

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The presence of Ca^{2+} -activated Cl^{-} current ($I_{Cl(Ca)}$) in vascular smooth muscle cells (VSMCs) is well established and has been suggested to be important for synchronized rhythmic contraction, i.e. vasomotion. The molecular background for this membrane conductance is, however, elusive. Bestrophins (Best) and TMEM16 proteins are the most prominent candidates for this role. We have previously characterized two distinct $I_{Cl(Ca)}$ in VSMCs: the cGMP-dependent $I_{Cl(Ca)}$ current and the "classical" $I_{Cl(Ca)}$.

Best-3 or TMEM16A were knocked down in vivo in rat mesenteric small arteries using siRNA. Knockdown (KD) was confirmed at mRNA and protein levels. The $I_{Cl(Ca)}$ were measured by patch clamp. Arterial contraction in vitro was tested using isometric myography.

Best-3 KD induced secondary reduction of Best-1 and -2 expression, while TMEM16A expression was not affected. TMEM16A KD reduced the expression of Best. In contrast to Best-3 KD, which only suppressed the cGMP-dependent $I_{Cl(Ca)}$, TMEM16A KD suppressed both $I_{Cl(Ca)}$ currents. Co-immunoprecipitation revealed a physical interaction between TMEM16A and Best-3. Best-3 KD was without an effect on arterial contraction. TMEM16A KD reduced membrane depolarization, $[Ca^{2+}]_i$ and tension increase in response to agonist stimulation. This can be partially explained by secondary reduction in the expression of L-type Ca^{2+} channels. Vasomotion was significantly suppressed after both TMEM16A and Best KDs.

Bests and TMEM16A are both important for vasomotion in mesenteric small arteries, but only TMEM16A is involved in agonist-induced contraction. Regulatory interactions between these proteins occur at the expressional and functional levels.

O01.05 Mie Rostved Rasmussen IDENTIFICATION OF SUBSTRATE SEQUENCE MOTIFS IMPORTANT FOR ADAM17-MEDIATED SHEDDING OF CD163 AND TNF-ALPHA

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Upon inflammatory stimulation, the human macrophage membrane proteins CD163 and pro-tumor necrosis factor-alpha (proTNF- α) are subjected to ectodomain cleavage by the metalloprotease ADAM17. The resulting soluble fragment of proTNF- α is termed TNF- α , and it is a potent pro-inflammatory cytokine. The cleaved ectodomain of the haptoglobin-hemoglobin receptor CD163, termed sCD163, has an unknown function.

Inspection of the amino acid sequence of the juxtamembrane domain of human proTNF- α and CD163 revealed a similar palindromic motif (Arg-Ser-(Ser)-Ser-Arg). In the present study, site-directed mutagenesis experiments demonstrated that these sequences are essential for shedding of proTNF- α and CD163. Mouse CD163 lacks this palindromic sequence, and this protein was shown to be resistant to ADAM17-dependent ectodomain cleavage. Upon ADAM17-dependent stimulation, a soluble fragment resulting from mouse CD163 was, however, detected when the palindromic sequence was knocked in in the juxtamembrane domain of mouse CD163, thus further underscoring the importance of this sequence.

In conclusion, the present study identified a sequence essential for shedding of proTNF- α and CD163 by ADAM17. The study also demonstrated distinct differences in terms of regulation of CD163 in human and mouse. In humans, proinflammatory-induced shedding of the CD163 ectodomain leads to a down-regulation in surface-bound CD163 and, hence, the capacity for haptoglobin-hemoglobin complex internalization during inflammatory conditions is reduced.

O01.06 Pauline de Bruijn THE THICK ASCENDING LIMB AS A MAJOR SITE FOR FUROSEMIDE-INDUCED URINARY ACIDIFICATION

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Furosemide inhibits NaCl reabsorption in the thick ascending limb (TAL). In addition, furosemide causes urinary acidification and metabolic alkalosis. This is explained by an increased Na⁺ load to the distal tubule, which facilitates H⁺ secretion via the apical H⁺-ATPase in α -intercalated cells. The direct role of the TAL on the urinary acidification, however, has never been

investigated. Here we measured pH_i in single perfused mouse mTALs with BCECF-AM. Interestingly, luminal furosemide (100 μM) caused a major, stable and reversible intracellular alkalization both in HEPES (0.33 ± 0.04 , $n=7$) and $\text{CO}_2/\text{HCO}_3^-$ -buffered conditions (0.14 ± 0.03 , $n=5$). This alkalization likely indicates increased H^+ excretion from the mTAL cytosol. Intriguingly, the furosemide-induced alkalization was completely blocked by 1 mM luminal amiloride that fully inhibits the apical NHE3 antiporter. This was confirmed with the NHE3 specific inhibitor NHE#4167. Basolateral amiloride did not affect the alkalization. Thus, furosemide likely causes a NHE3-dependent secretion of H^+ to the lumen. To investigate this, we measured the pH_o of the tubular lumen with BCECF acid. Furosemide indeed caused a reversible luminal acidification from $\text{pH } 6.92 \pm 0.04$ to 6.46 ± 0.03 ($n=5$) providing direct evidence for this suggested mechanism. In contrast, luminal amiloride alkalinized the lumen. The increased NHE3 activity induced by furosemide is likely caused by a decrease of $[\text{Na}^+]_i$. Indeed, mTALs loaded with CoroNa Green showed furosemide-induced drop in $[\text{Na}^+]_i$. These results revise the mechanistic understanding of furosemide-induced urinary acidification and prove that furosemide stimulates H^+ secretion in the TAL.

Oral session 2

O02.01 Poul Frølund
Vestergaard

GH SIGNALING IN SKELETAL MUSCLE IN HEALTHY HUMAN SUBJECTS:
IMPACT OF GENDER AND AGE

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Background: Endogenous GH secretion declines with age, whereas elderly people are highly responsive to exogenous GH as judged by IGF-I generation and side-effects. By contrast, endogenous GH secretion is amplified in females as compared to males, whereas females are relatively GH resistant as judged by IGF-I generation. The underlying mechanisms at the level of GH signaling in peripheral target tissues are unknown.

Design: Twenty healthy non-obese (BMI < 30 kg/m²) adults ['young group' < 40 yrs (5F/5M) and 'elderly group' > 60 yrs (5F/5M)] were each studied twice: 1) after iv. injection of a GH bolus (0.5 mg) and 2) iv. saline injection. Muscle biopsies were obtained after 30 and 120 min. Total and phosphorylated STAT5b were measured by WB and IGF-I and SOCS and CIS gene expression at t = 120 min. measured by RT-PCR. Body composition (DEXA) and VO₂-max (bicycle) were also measured.

Results: The serum pharmacokinetic GH profile did not differ between groups. Phosphorylated STAT5b (pSTAT5b) was significantly increased in all subjects after injection of GH. The mean ±SE pSTAT5b (AU) response to GH was more pronounced in women as compared to men [203.1±28 vs. 108.2±14.3 (P = 0.01)]. In addition, old women had a higher response as compared to young women and men of both ages (p=0.046). IGF-I mRNA expression increased after 120 min. SOCS I-III and CIS mRNA expression increased significantly after 120 min.

Conclusion: 1) The relative GH resistance in females is located downstream of STAT5 and 2) Old age is associated with a relative increase in GH responsiveness at the level of STAT5 activation.

O02.02 Peter Hjertholm

VARIATION IN THE USE OF PROSTATE SPECIFIC ANTIGEN TESTING AND PROSTATE CANCER-RELATED OUTCOMES: A COHORT STUDY

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Importance: Variation exists between family practices in the use of prostate specific antigen (PSA), but the possible consequences regarding prostate cancer (PC) incidence and outcomes are unknown.

Objective: To examine associations between the use of PSA tests in family practice and the use of diagnostic procedures, PC incidence and

outcomes.

Design, setting and population: Population-based study of all men aged 40 years or older in the Central Denmark Region from 2004 to 2009. National registers were used to divide family practices in four groups based on their adjusted PSA test rate. We analyzed associations between PSA test rate and PC related outcomes.

Results: 368 practices and 303,117 men were included. 3942 incident PCs were diagnosed. IRR comparing the highest testing group (group 4) with the least testing group (group 1) were 1.17 (95%CI, 0.93-1.47) for trans-rectal ultrasound of the prostate, 1.77 (1.54-2.02) for biopsy, 1.36 (1.21-1.53) for PC diagnosis, 1.59 (1.35-1.87) for local stage disease and no differences regarding regional or distant disease stages. The IRR was 2.30 (1.76-3.01) for prostatectomy and 1.30 (1.04-1.64) for radiotherapy. PC-specific and overall mortality showed no differences between the groups. The 5-year relative survival was 74.0% (67.9%-79.6%) in group 1 and 79.6% (74.6%-84.3%) in group 4.

Conclusions and relevance: Variation in PSA test rates between family practices was significantly associated with the incidence of PC, the use of diagnostic and surgical procedures and relative survival, but had no association with mortality. This is important new knowledge concerning consequences of practice-level variations in PSA testing.

O02.03 Karen Fjeldborg HUMAN ADIPOSE TISSUE MACROPHAGES ARE SKEWED IN AN ANTI-INFLAMMATORY DIRECTION IN OBESITY

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Background: Macrophages in adipose tissue (AT) are increased in obesity and associated with low grade inflammation. In rodents, the phenotype of macrophages is changed to a pro-inflammatory (M1) profile by obesity.

Objective: We aimed to characterize the phenotype of macrophages in AT in humans in relation to obesity and insulin resistance.

Design: In subcutaneous AT samples from lean and obese subjects, the gene-expression levels of the general macrophage markers (CD68 and CD14), M1/pro-inflammatory markers (TNF- α , MCP-1, and IL-6) and the M2/anti-inflammatory markers (CD163, CD206, and IL-10) were determined by RT-PCR. Insulin resistance was determined by HOMA-IR.

Results: All macrophage markers were elevated in AT from obese compared to lean subjects ($p < 0.001$). To determine the phenotype of the macrophages we used the level of CD14 to adjust for the total number of macrophages. The relative expression of CD163 and IL-10 were elevated, and TNF- α and IL-6 were reduced in macrophages from obese lean subjects (all $p < 0.05$). HOMA-IR was positively associated with CD14 expression

($r: 0.37, P < 0.001$), and in a multivariate regression analysis CD163 was the

only macrophage marker significantly associated with HOMA-IR (β :0.57, $p<0.05$).

Conclusion: There is an increased expression of macrophage markers in obesity and, contrary to rodents, we found a preponderance of M2 and a decrement of M1 markers in AT from obese subjects. Moreover, CD163 was the only macrophage marker associated with HOMA-IR after multiple adjustments.

O02.04

ACUTE EFFECTS OF RESISTANCE EXERCISE CONTRACTION MODE AND PROTEIN SUPPLEMENTATION ON MUSCLE PROTEIN SYNTHESIS AND HYPERTROPHY SIGNALLING

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Introduction: The purpose was to comparatively investigate how eccentric (ECC) versus concentric (CON) muscle contraction mode with and without whey protein hydrolysate (WPH) versus carbohydrate (PLA) affect the protein synthesis and Akt-mTORC1 signalling.

Method: 24 subjects were allocated into either the WPH or the PLA group. Subjects were infused with ¹³C₆-phenylalanine tracer for measurement of muscular fractional synthesis rate (FSR). Subjects completed a single bout of maximal knee extensor exercise with isolated unilateral knee extension performed as ECC versus CON contraction. Muscle biopsies were taken from both legs prior to 1, 3 and 5 hours after the exercise. Western blot analysis was used to assess changes in phosphorylation of muscle Akt, mTORC1 and p70S6K.

Results: A contraction mode \times time interaction was observed at the phosphorylation level of mTORC1 ($p<0.001$). Accordingly, at 3 and 5 hours post exercise, ECC lead to a greater increase of the phosphorylation level than CON. There was no effect of contraction mode on phosphorylation levels of Akt and p70S6K, but a time effect was observed at 1 and 3 hours post exercise ($p<0.001$). There was no effect of supplementation on protein signalling. Muscular FSR analysis showed no differences between neither supplement type nor contraction mode interventions.

Conclusion: Resistance exercise and supplementation combined provided an acute stimulation of the muscular FSR and the Akt-mTORC1 signalling pathway. A contraction mode specific, but not supplement specific, effect was observed for mTORC1 phosphorylation. Muscular FSR analysis showed no differences between supplement and contraction mode interventions.

O02.05

Annesofie
Lunde Jensen

OSTEOPOROSIS GROUP EDUCATION - INTERPRETING AND INDIVIDUALISING A BONE FRIENDLY RECIPE

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Introduction: Osteoporosis group education is recommended as part of disease prevention and management. Characteristic for studies of osteoporosis group education is a lack of report on the interaction between patients and health professionals.

Aim: To analyse the practice of multidisciplinary group education for patients with osteoporosis, and to identify and interpret important characteristic of what is at stake when patients and teachers interact during group education.

Methods: An interpretive description design was utilized with 17 women and men diagnosed with osteoporosis. Data consisted of ethnographic field studies in five classes, sessions of the everyday life of the patients and semi-structured interviews before and 6-9 months after group education.

Results: The practice of group education revealed individual ways of interpreting disease specific recommendations. Two patterns formed the characteristics of group education: 1) "Interpreting a bone friendly recipe" outlined that interaction between patients and teachers concerned understanding and interpreting how to follow recommendations; 2) "Personal counselling" described how an inevitable part of the interaction concerned patients' personal perspective and entailed personalised advice given by the teachers directed at one patient.

Conclusion: Articulating and interpreting teachers' and patients' experience, knowledge and skills seemed essential if patients were to gain competences and transfer "a bone friendly recipe" into daily life. Group education involved personal counselling and individual consultations. Hence, group education may be of specific value to the unified treatment for patients with osteoporosis.

O02.06 Tue Kjølhedede

LONG-TERM PROGRESSIVE RESISTANCE TRAINING IMPROVES FUNCTIONAL CAPACITY FOR PEOPLE WITH MULTIPLE SCLEROSIS

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Introduction: Exercise therapy has become an important part of rehabilitation for people with Multiple Sclerosis (PwMS), with progressive resistance training (PRT) proving to be a safe and effective way of improving maximal muscle strength (MMS). However, most conducted studies are of relatively short duration and conflicting results exist regarding the effects of PRT on functional capacity (FC). Thus, one purpose of this

study was to elucidate the effects of long-term PRT on FC in PwMS.

Methods: 35 PwMS were randomized to perform either 24 weeks of supervised PRT (n=18) or constitute a non-training control group (n=17). Measures of FC included; timed 25ft walk test, 2min walk test, 5-time sit-stand and stair climb test. Additionally, the 12-item MS Walking Scale (MSWS12) was completed. MMS was measured as peak torque of the knee extensors and flexors. Baseline values, within and between groups changes (post-pre) was compared between groups using Student's t-test.

Results: 32 of 35 PwMS completed the study. For all patient characteristics, MMS and FC, training and control group were similar at baseline. After 24 weeks of supervised PRT, the improvements in MMS and all measures of FC were higher for training than for control group. Within the control group no changes were observed in any measures, while the training group improved in all measures of MMS and FC ($p<0.05$). No difference in changes between groups was observed for MSWS12, however within training group a tendency to improvement was observed ($p=0.06$).

Conclusions: This long-term study supports earlier short-term findings and further strengthens the contention that PRT is capable of improving MMS and FC for PwMS.

Oral session 3

O03.01 Hanne Vinter IMIQUIMOD INDUCED PSORIASIS-LIKE SKIN INFLAMMATION:
A MODEL OF PSORIASIS

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Recently, a new mice model of psoriasis-like skin inflammation induced by topical application of imiquimod has been introduced. Our aim is to study the imiquimod-induced skin inflammation in TNF α KO mice and WT mice in order to elucidate the role of TNF α in psoriasis. TNF α KO mice and WT mice, divided into comparable groups, are treated on a daily basis with cream Aldara containing 5% imiquimod or cream vehicle. Groups of animals are sacrificed on day 1, 3 and 5 and skin biopsies are taken for RT-qPCR-, myeloperoxidase- and histochemical-analysis. Visually, evaluated by topical sign score, we demonstrated that the TNF α KO mice developed a lesser and more delayed skin-inflammation compared with the WT mice. HE-stained tissue sections of skin biopsies supported this finding. WT mice showed a more pronounced hyperplasia of epidermis, parakeratosis and superficial perivascular inflammatory infiltrate in the dermis, compared with TNF α KO mice. mRNA analysis revealed the same pattern with a significantly higher expression of the pro-inflammatory cytokines: IL17a and IL22 on day 3 and 5 and IL17c and IL12p40 on day 3 in the WT mice compared with the TNF α KO mice. Similar results were obtained with the antimicrobial peptide S100A8 which on day 3 and 5 was significantly downregulated in the TNF α KO mice compared with WT mice. Clearly, TNF α plays a significant role in this imiquimod-induced psoriasis-like skin inflammation model. The results can contribute to our understanding of the early mechanisms in the pathogenesis of psoriasis and facilitate the identification of new targets in the treatment of psoriasis and other inflammatory diseases.

O03.02 Henrik Lauridsen HOW TO BUILD A HEART: COMPLETE REGENERATION AFTER MYOCARDIAL INFARCTION

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Introduction: Cardiac failure resulting from cardiac hypertrophy in response to myocardial infarction is a leading cause of death. This is the fatal result of the lack of regenerative capacity of the mammalian heart. Salamanders, such as the axolotl, possess unmatched regenerative capacity within the vertebrate subphylum, mastering the ability to regenerate internal organs in addition to whole limbs. To draw basic information about mechanisms in unscarred cardiac repair, we have established and validated a myocardial infarction model in the axolotl.

Materials and methods: Myocardial infarction in the axolotl heart devoid of coronary arteries was induced by applying a cryoprobe at the ventricular apex. Anatomical regeneration was described histologically using Masson's

Trichrome staining of heart sections 4, 7, 14, 31, 40 and 94 days post infarction and 4 days post sham. Concurrently, functional restoration of cardiac output was monitored using echocardiography and MRI. Protein profiles of myocardial tissue 4, 14 and 30 days post infarction and 4 days post sham was produced using LC-MS/MS.

Results and discussion: The axolotl restores complete myocardial structure and functionality within 2-3 months after a 25% myocardial infarction. Interestingly, the initial response to injury is fibrosis forming a scar as found in mammals. However, this response is replaced within a few weeks when cardiomyocytes are deposited in the fibrotic scaffold aiding a gradual recovery of cardiac output.

This infarction model has the potential to improve our understanding of regeneration in the heart, and we hope to be able to identify signalling events at the protein level using the proteomics data.

O03.03 Dennis Kjølhede EXOSOME ISOLATION BY DIFFERENTIAL CENTRIFUGATION: ANALYSIS OF
Jeppesen DISCRETE FRACTIONS

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Cells release a mixture of extracellular vesicles (EV) that differ in size, composition and cellular origin. Exosomes, the most studied of the EVs, are small membrane vesicles (40-120 nm) of endocytic origin. The most basic and standard method for obtaining samples of exosomes from fluid samples is ultracentrifugation at 100,000 × g. The rapidly expanding field of exosome research necessitates a better understanding of the proper steps needed to ensure efficient generation of pure exosome samples. Here we have used the recently developed Nanoparticle Tracking Analysis (NTA) technique to examine the size and concentration of EVs present in samples from FL3 bladder cancer cells as well as HEK293 cells before and after centrifugation at a range of speeds from 33,000 × g to 200,000 × g. Analyses revealed that efficient sedimentation of extracellular material occurs at lower speeds for HEK293 cell compared to FL3 cells. Western Blot analysis for the exosomal marker proteins CD81, Syntenin and TSG101 revealed that exosomes can be sedimented already at 33,000 × g and confirmed that HEK293 exosomes are rapidly purified at lower speeds compared to FL3 exosomes. Mitochondrial contamination of samples could be removed by a pre-clearing centrifugation step at 2,000 × g while contaminating microsomes persisted even after pre-clearing at 15,000 × g. NTA analysis indicated that there is significant, persistent aggregation of exosomes after pelleting by ultracentrifugation. In conclusion, our results indicate and highlight the need to examine and analyze each cell type or biofluid individually to determine the optimal preparations of exosome samples free from contaminants.

O03.04 Tue Wenzel DECREASED PLASMA LEVELS OF SOLUBLE CD18 LINK LEUKOCYTE
Kragstrup MIGRATION WITH DISEASE ACTIVITY IN SPONDYLOARTHRITIS

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Introduction: Spondyloarthritis (SpA) is an autoimmune disease characterized by spinal joint inflammation causing pain and disability. The inflammatory process in SpA is poorly understood, and tools for monitoring and treating the disease are needed. The CD18 integrins on leukocytes are pivotal for the generation of inflammatory responses. Recently, we demonstrated a soluble form of CD18 (sCD18) in the blood with the potential to attenuate inflammation. Here, we study the role of sCD18 in SpA.

Methods: Plasma levels of sCD18 in a study population with 84 SpA patients and matched healthy controls were analyzed with a time resolved immunofluorescence assay (TRIFMA). Binding of sCD18 to endothelial cells was studied with confocal microscopy and shedding of CD18 from peripheral blood mononuclear cells (PBMC) was studied with flow cytometry and TRIFMA.

Results: Plasma levels of sCD18 were decreased in SpA patients compared with healthy volunteers and exhibited an inverse correlation with clinical scores of disease activity in a multiple regression model. The mechanisms for these changes could be simulated in vitro. First, sCD18 in plasma adhered to endothelial cells, indicating increased consumption. Second, CD18 shedding from SpA PBMC correlated inversely with disease activity, suggesting insufficient generation.

Conclusions: Taken together, SpA patients fail to maintain normal sCD18 levels in the blood, and this facilitates leukocyte migration to the spinal joints and aggregates disease activity. In the future, our findings could be utilized by using the level of sCD18 as a marker of inflammatory activity or a compound resembling sCD18 as a therapeutic drug.

O03.05 Shivani Joshi

IDENTIFICATION OF DISEASE-RELATED GENES IN FAMILIAL STEROID SENSITIVE NEPHROTIC SYNDROME

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Nephrotic syndrome (NS) is defined by heavy proteinuria, edema and hypoalbuminemia. Most pediatric patients respond well to steroid therapy and have good prognosis. These patients have steroid sensitive NS (SSNS). Familial aggregates and kindred have been described in patients with SSNS, suggesting a potential genetic origin. However, very little data on molecular genetics of familial SSNS is available in literature. Fuchshuber et al reported in 2001 that familial SSNS was found to be genetically different from changes in NPHS2 gene. Till date, only one locus for SSNS has been mapped on chromosome 2p12-13.212, but no gene(s) have been ascertained for SSNS. Family studies could help to further identify genes that are altered in this patient group and will contribute to a better understanding of underlying molecular mechanism in familial SSNS. The purpose of this study is to identify new candidate genes in 9 families with siblings with SSNS, using SNP 6.0 microarray whole genome linkage analysis in all participants, followed by whole exome sequencing in selected patients. Our findings of whole genome linkage analysis and exome sequencing will be discussed.

Key words: nephrotic syndrome, SNP 6.0 microarray whole genome linkage analysis, whole exome sequencing

O03.06 Kristian Ravlo

EFFECT OF REMOTE ISCHEMIC CONDITIONING ON DENDRITIC CELLS AFTER KIDNEY TRANSPLANTATION FROM DECEASED DONORS

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In kidney transplantation, remote ischemic conditioning (rIC) protects the graft against ischemia-reperfusion injury and reduces the risk of rejection. In essence, rIC consists of repeated, brief, non-damaging periods of ischemia in a limb. But why this procedure protects against rejection is unknown. During graft rejection, the main antigen-presenting cells are probably dendritic cells (DCs). Because dendritic cells are attracted to ischemic endothelium, we hypothesise that rIC protects the organ by 'trapping' circulating DCs in the ischemic limb. As a result, fewer DCs are available to infiltrate the graft and present foreign antigens. To test this hypothesis, we shall measure the quantity of dendritic cells in circulation before and after rIC.

The CONTEXT study is a randomised, controlled clinical study of 200 patients, who are randomised to rIC or non-rIC. Blood samples will be obtained at baseline, day 1, day 3, and day 5; and 1 month and 3 months after transplantation. In these samples, myeloid and plasmacytoid DCs will be identified and quantified by flow cytometry after staining with antibodies against CD3, CD14, CD19, CD56, ILT3, HLA-DR, CD123, CD11c, and CD86.

Preliminary data are presented.

Oral session 4

O04.01 Lise Thorsen

IRRADIATION OF THE INTERNAL MAMMARY LYMPH NODES INCREASES OVERALL SURVIVAL IN NODE-POSITIVE BREAST CANCER

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Background: In 2003, as there was no evidence of the effect of adjuvant radiotherapy (RT) to the internal mammary lymph nodes (IMNs), the Danish Breast Cancer Cooperative Group (DBCG) discontinued IMN-RT in patients with left-sided breast cancer (BC) due to risk of radiation induced heart disease. Patients with right-sided BC continued to receive adjuvant IMN-RT. This national prospective cohort study investigates whether IMN-RT affects survival in node (LN) positive BC. Materials and methods: 3085 patients with operable unilateral BC, one or more involved axillary LNs, no prior cancer and age<70 received adjuvant RT+/- IMN-RT depending on BC laterality (right-/left-side n = 1492 / 1593). All patients were allocated to chemotherapy and/or antiestrogens. The primary endpoint was overall survival (OS). Secondary endpoints were disease free survival (DFS) and metastasis free survival (MFS). Results: At median follow up 7 years, 794 patients have died. A moderate increase in OS was observed in the group receiving IMN-RT: 78 % vs. 0.74 % (HR=0.86 (95 % CI: 0.75; 0.99) p=0.04). Seven year DFS displayed a similar tendency: 75 % vs. 73 % (HR=0.93 (95 % CI: 0.81; 1.06) p=0.28), as did seven year MFS: 79 % vs. 77 % (HR=0.91 (95 % CI: 0.79; 1.06) p=0.25). The number of deaths from cardiac disease was comparable in the two groups (no IMN-RT n=9 vs. IMN-RT n= 8), whereas death from BC was more frequent in the no IMN-RT group (n=368 vs. n=310). Conclusions: OS increased with IMN-RT at 7 years. With longer follow-up, DFS and MFS may increase significantly as well, indicating that IMN-RT does contribute to the effect of adjuvant RT in early BC

O04.02 Peter Bondeven

EXTENT AND COMPLETENESS OF MESORECTAL EXCISION EVALUATED BY POSTOPERATIVE MRI

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Aim: To determine the prevalence and localisation of residual mesorectum detected on magnetic resonance imaging (MRI) following rectal cancer surgery.

Methods: Postoperative T2-weighted MRI of the pelvis was performed on patients following mesorectal excision. A multidisciplinary team radiologist evaluated the images with regard to residual mesorectum and distal margin. Only mesorectum above the level of the anastomosis perpendicular to the bowel was regarded as inadvertent residual mesorectum following partial mesorectal excision (PME). Histopathological photos and clinical records were assessed. The pathology and MRI findings

were evaluated independently in a blinded fashion.

Results: Evidence of MRI-detected residual mesorectum was identified in 54 of 136 patients (39.7%). There was agreement with the pathology findings in 88 of 136 patients (64.7%). Residual mesorectum was more frequent in patients treated with PME (63%) than after total mesorectal excision (TME) (33%) or abdominoperineal resection (13%) ($P < 0.001$). Localisation of residual mesorectum was peri-anastomotic in all cases following PME, while being distal to the anastomosis in 21% after TME. Pathology and MRI concurred that the distal resection margin after PME was less than 3 cm in more than one third.

Conclusion: Inadvertent residual mesorectum was commonly found on postoperative MRI, especially following PME.

O04.03 Tim van
Hartevelt

TEMPORAL ASPECTS OF THE SENSE OF SMELL: A STUDY USING MAGNETOENCEPHALOGRAPHY

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The sense of smell is of great importance for food selection and reproduction, especially in animals. Furthermore, the loss of sense of smell has been shown to be a common symptom in neurological or psychiatric disorders, such as Parkinson's disease. Although the sense of smell has been under-investigated in humans compared to other sensory modalities, neuroimaging studies in recent years have started to elucidate some of the mechanisms involved in human olfaction, including the differential spatial distribution of activity to positive and negative odours. Yet, neuroimaging studies have not yet started to investigate the temporal aspects of olfaction in humans.

In the current study, we used magnetoencephalography (MEG) to measure the spatial and temporal aspects of brain activity whilst odours were delivered to the participant's nose. Six different odours (two pleasant, two unpleasant and two food related odours) were delivered using a purpose-built, computer-controlled, continuous air flow olfactometer, embedded in a continuous airflow of 6 litres per minute.

Negative odours are more likely to signal potentially dangerous substances such as spoiled food. We hypothesized that negative odours are processed not only in different areas of the brain, but are also processed faster than other types of odours including those perceived to be pleasant and food related.

The preliminary results show localised activity within the first 1000 milliseconds in the alpha band in the lateral orbitofrontal cortex and the

anterior cingulate cortex for negative odours, while positive odours gave rise to activity in the mid-anterior orbitofrontal cortex and the insular cortex.

O04.04 Thomas Lyhne
Ravkilde PREDICTING TREATMENT DELIVERY SUCCESS OF ADVANCED
RADIOTHERAPY TREATMENTS OF CANCER

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In current radiotherapy treatments of moving tumors, the underlying assumptions of regular motion are not necessarily met. Moreover, the past has presented examples of treatment errors leading to severe complications and lethal outcome, making it clear that dosimetric errors during treatment must be monitored. The aim of this study was to develop a method for reconstruction of the time-resolved delivery of dose during volumetric modulated arc therapy (VMAT) of moving tumors with and without dynamic multi-leaf collimator (DMLC) tracking.

Experiments were performed on a linear accelerator connected to prototype DMLC tracking software. A three-axis motion stage reproduced eight clinical tumor trajectories. For each trajectory, two VMAT treatment plans (low and high modulation) were delivered with and without DMLC tracking. Dose distributions were measured at 72 Hz using a biplanar dosimeter. Offline, the time-resolved doses were reconstructed by a novel simplified dose algorithm and compared to the measured doses by absolute dose differences.

The reconstructed doses were in good agreement with the measured doses of transient (2.5% mean absolute dose difference), cumulative (2.8%) and final accumulated doses (4.7%). The mean computation time for the dose calculation was 42.9 ms, making the algorithm feasible for online use.

Ongoing work focuses on online implementation of the developed algorithm, which may be used for treatment intervention in case of erroneous dose evolution during both tracking and non-tracking treatments, or even on-the-fly dose repair if dose errors exist. The method described is applicable to standard therapeutic linear accelerators available worldwide.

O04.05 Henriette
Bjerregaard SUBSTRATE-INDUCED CONFORMATION OF THE HUMAN SEROTONIN
TRANSPORTER

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The human serotonin transporter (hSERT) regulates serotonergic signaling in the brain by actively regulating the concentration of serotonin in the synaptic cleft. hSERT mediates reuptake of serotonin into the pre-synaptic neurons. hSERT is a molecular target for antidepressant drugs and psychostimulants that act by altering the serotonin concentration in the

synapses.

Conformational changes of hSERT occur during substrate and ligand binding and during translocation of serotonin. Overall, during the transport cycle, hSERT shifts from an extracellular-facing conformation through an occluded state ending in a cytoplasmic-facing conformation.

A bound ligand in a fixed concentration induces a given conformation of hSERT. It has previously been shown that the substrate serotonin and the hallucinogenic alkaloid ibogaine both bind to hSERT and stabilize an inward-facing conformation of hSERT. However, the interplay between ligand binding, substrate transport, and hSERT conformation is not fully understood.

We have analyzed binding characteristics of the substrate serotonin and its effect on conformation of hSERT using the Substituted Cysteine Accessibility Method. Surprisingly, in a high-affinity state for serotonin binding, the substrate induces an outward-facing conformation of hSERT, which is found to be ion-dependent. This novel dualistic nature of substrate and the resulting conformational state might represent a hitherto undescribed step of the transport cycle.

O04.06 Anne Højland INVESTIGATING SORLA MEDIATED TRAFFICKING IN POLARIZED CELLS

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SorLA belongs to the vps10p domain receptor family. This receptor family is multifunctional and highly expressed in the nervous system, where they have been implicated in Alzheimer's disease and injury-related neuronal cell death.

It has been shown that sorLA is involved in regulating the level of lipoprotein-lipase (LPL) in transfected fibroblast and in primary neurons. Therefore, it is likely that this mechanism is important for the release of the vps10p receptor family ligands, among others, LPL.

Recent studies indicate that sorLA is involved in asymmetrical transport in polarized cell lines and may be a key factor in the transcytosis across different types of epithelial and endothelial cells, among these, the Blood-Brain-Barrier and the endothelial cells of the arteries.

Thus, sorLA is likely to be of physical importance in regulating the level of LPL in the brain and systemic circulation.

Using the polarized kidney-epithelial derived cell line MDCK, the cellular localization and trafficking of sorLA has been further investigated. The motifs involved in the localization are also explored by use of chimera and mutated sorLA constructs. The methods used in these investigations are primarily immunocytochemistry and confocal imaging.

The study will also include identification of adaptor proteins involved in the transport as well as an investigation of sorLA-mediated transcytosis.

Oral session 5

- O05.01 Michael Skovdal PATIENT EDUCATION WITH OR WITHOUT THE ADDITION OF MULTIMODAL
Rathleff PHYSIOTHERAPY FOR ADOLESCENT PATELLOFEMORAL PAIN; A CLUSTER
RANDOMISED STUDY AMONG 121 ADOLESCENTS WITH 12-MONTH
FOLLOW-UP

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Introduction: The prevalence of Patellofemoral Pain (PFP) among adolescents is 7% and the long-term prognosis is poor. Multimodal physiotherapy is an evidence-based treatment of PFP. However, no randomised trials have specifically been conducted among adolescents with PFP, and the effect is unknown. The purpose of this study was to investigate the effectiveness of patient education with or without the addition of multimodal physiotherapy among adolescents with PFP.

Methods: Adolescents, aged 15-19 years of age, were recruited from a population-based cohort of 2953 adolescents attending 4 different high schools. Adolescents with PFP were cluster-randomized (on school-level) to either patient education or patient education and multimodal physiotherapy. Primary outcome was the proportion of adolescents recovered at 12 months. Adolescents were categorized as recovered if they rated themselves "completely recovered" or "strongly recovered" on the 7- point Likert scale going from "completely recovered" to "worse than ever".

Results: A higher proportion of adolescents randomised to patient education and multimodal physiotherapy were recovered at 12 months (OR: 1.75, 95%CI: 1.02-2.93). The same result was observed at 3 and 6 months. At 12 months, 29% were recovered in the group randomised to patient education and 38% were recovered in the group randomised to patient education and multimodal physiotherapy.

Conclusion: Multimodal physiotherapy and patient education were more effective compared with patient education on self-reported recovery. However, the proportion of adolescents recovered was low. This underlines the need to study long-term recovery and consequences of adolescent PFP.

- O05.02 Trine Eilenberg ACCEPTANCE AND COMMITMENT GROUP THERAPY (ACT) FOR HEALTH
ANXIETY. PRELIMINARY RESULTS FROM A RANDOMISED TRIAL

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Background: Health anxiety (Hypochondriasis) is prevalent, but rarely diagnosed and treated. The essential features of health anxiety are exaggerated rumination with intrusive worries about harbouring a serious illness. Severe health anxiety might be persistent and associated with severe psychological and physiological impairment. Treatment of health anxiety is sparsely investigated. Acceptance and Commitment Therapy (ACT) is a new third-wave behavioural cognitive therapy that has shown a positive effect in the treatment of mood and anxiety disorders.

Objective: To examine the effect of ACT in groups for patients with severe health anxiety.

Methods: 126 patients consecutively referred from primary care physicians or hospital departments, meeting research criteria for severe health anxiety, were block-randomised to either; a) ACT in groups or b) a ten-month waiting list. Primary outcome was self-rated improvement in illness worry on the Whiteley-7 Index (WI) 10 months after randomisation. Secondary outcomes were improvement in emotional distress (SCL-8) and physical symptoms (SCL-somatisation subscale) at ten months after randomisation.

Preliminary results: The intention-to-treat analysis showed that patients in the ACT group improved 22.1 score points on the WI at the primary end point, which were significantly better than the waiting list control group (unadjusted mean difference 21.3, 95% CI 12.6 to 30, $p < 0.001$) and effect sizes were large ($d = 0.89$, 95% CI 0.50 to 1.29). The ACT group also improved significantly more than the control group on most secondary outcomes.

Conclusion: ACT group therapy seems feasible, acceptable and effective in treatment of severe health anxiety.

O05.03 Eva Bjerre
Ostenfeld

PREADMISSION USE OF GLUCOCORTICOIDS AND ANASTOMOTIC LEAKAGE FOLLOWING COLORECTAL CANCER RESECTION: A DANISH POPULATION-BASED COHORT STUDY

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Background: It is controversial whether glucocorticoid use affects of anastomotic failure.

Methods: We conducted a population-based cohort study using Danish medical registries to examine the association between preadmission glucocorticoid use and anastomotic leakage following colorectal cancer (CRC) surgery. All patients treated with a primary anastomosis (2001-2011) following a CRC resection were included. Subjects who filled their most recent glucocorticoid prescription ≤ 90 , 91-365, and > 365 days before their surgery date were characterized as current, recent, and former users, respectively. We computed absolute risk of anastomotic leakage within 30

days after CRC resection and odds ratios (ORs), using logistic regression models and adjusting for potential confounders.

Results: Of the 24 043 CRC patients included, 2679 (11.1%) filled at least one prescription of glucocorticoids in the year preceding their surgery date. Overall, 1779 (7.4%) anastomotic leakages occurred. Absolute risk of leakage among current users of oral glucocorticoids was 9.0% versus 7.3% among non-users (OR = 1.50, 95% CI: 1.05-2.13). Risk estimates for recent and former use of oral glucocorticoids were slightly lower, yet statistically imprecise, as were estimates for current use of inhaled glucocorticoids and use of intestinal-acting glucocorticoids.

Conclusion: Current use of glucocorticoids was associated with an increased relative risk of anastomotic leakage following CRC resection. However, the increase in absolute risk was small.

O05.04 Dorthe
Krogsgaard
Bonnerup

PRESCRIBING ERRORS IN ACUTELY ADMITTED MEDICAL PATIENTS

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Background: An algorithm that can stratify patients according to risk of medication errors have been developed. In order to test the algorithm in a randomised controlled trial, the number of prescribing errors is vital to know. We define prescribing errors as errors in prescribing causing harm or implying a risk of harming the patients.

Aim: The aim of the study was to assess the number of prescribing errors in acutely admitted adult patients at the Emergency Department at Aarhus University Hospital, Denmark.

Methods: Patients were included prospectively on admission to the Emergency Department at Aarhus University Hospital. Patients aged 18 years or older who received at least one drug prior to admission were eligible for inclusion. Suicidal and intoxicated patients were excluded. A pharmacist and a clinical pharmacologist assessed medical records after discharge for prescribing errors during the hospitalization. These assessments were finally validated independently by two clinical pharmacologists. Chi square tests were used to assess factors related to risk of prescribing errors.

Results: 103 patients were included of which 51 patients (49.5%) experienced one or more prescribing errors (1-6). 86 prescribing errors were found in 748 prescriptions, corresponding to 9.5 percent of prescriptions. Drug-drug interactions (N=19) and dose-related errors (N=18) were the most frequent prescribing errors seen. Age above 65 years (p=0.013) and reduced kidney function (p=0.03) were factors related to increased risk of prescribing errors.

Conclusion: Prescribing errors were found in 9.5 % of prescriptions (86 errors in 748 prescriptions).

O05.05 Merete Gregersen

A LIBERAL BLOOD TRANSFUSION STRATEGY IMPROVES SURVIVAL IN NURSING HOME RESIDENTS WITH HIP FRACTURE

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Introduction: Surgery blood loss leading to anemia is common in elderly hip fracture (HF) patients. Nursing home residents are frail elderly with high mortality risk after HF. The most optimal transfusion threshold in the frail elderly HF patients has not yet been examined. Our aim was to test the hypothesis that a more liberal transfusion strategy would improve survival in the frail anemic elderly who had undergone surgery for HF.

Material and methods: In a randomized controlled trial, we included 65+ years old nursing home residents hospitalised with HF at the Department of Orthopaedic Surgery, Aarhus University Hospital. After surgery, we randomly assigned the residents to either a liberal transfusion strategy (a hemoglobin threshold of 7 mmol/L [11.3 g/dL]) or a restrictive blood transfusion strategy (a hemoglobin threshold of 6 mmol/L [9.7 g/dL]). Within the first week after surgery, hemoglobin was measured 4-6 times, and at least once a week during the following three weeks. When a blood test indicated blood transfusion, it was administered within 24 hours, and only one blood unit before a new measurement. Outcome was time to death within 90 days and was analysed in a Cox proportional hazard model.

Results: Hundred and sixty nursing home residents were enrolled. The intention-to-treat analysis showed that the 90-day mortality rate was 20% in the residents treated by the liberal strategy versus 35% in the residents treated by the restrictive strategy (p-value=0.03). Hazard ratio was 0.53 (95% CI: 0.29; 0.98).

Conclusion: Survival is improved by complying with a liberal transfusion strategy in the anaemic nursing home residents with hip fracture.

O05.06 Mikkel Andreas Strømgaard Andersen

FIRST HOUR QUINTET 1-1-2 CALLERS AND COMORBIDITY

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Introduction: First Hour Quintet (FHQ) consists of cardiac arrest, angina pectoris, stroke, severe breathing difficulties and severe trauma - all patients for whom the first hour after debut of symptoms is important. The task for the new nurse, paramedic and doctor staffed emergency medical communication centers (EMCC) in Denmark is to dispatch high priority ambulances to high-risk patients. We aimed to study the impact of co-

morbidity on the risk of ICU treatment and death among FHQ 1-1-2 callers.

Methods: We did a register-based follow-up study on 1-1-2 callers in a six-month period. The patients were included if they belonged to the FHQ groups in the dispatch protocol. The Charlson Comorbidity Index was used to categorize comorbidity and constructed for each patient using hospital discharge diagnoses. Logistic regression was used to analyze the association between comorbidity and risk of ICU treatment or death on same or the following day after a 1-1-2 call.

Results: A total of 20,500 patients were included. Of these, 11,006 patients had comorbidity. In total 1,818 patients received ICU treatment or died. Odds ratio (OR) for ICU treatment or death for patients with mild liver disease was 1.59 (95 % CI: 1.18-2.13 $P < 0.01$), distal vascular disease 1.33 (95 % CI: 1.13-1.56 $P < 0.01$), heart failure 1.32 (95 % CI: 1.14-1.53 $P < 0.01$), Chronic Obstructive Pulmonary Disease 1.29 (95 % CI: 1.14-1.46. $P < 0.01$), any tumor 1.18 (95 % CI: 1.01-1.38. $P = 0.04$). No other comorbidities were associated with risk of ICU treatment or death for FHQ patients.

Conclusion: Comorbidity seems to have a significant impact on the risk of an adverse outcome for first-hour quintet 1-1-2 callers.

Abstracts Poster sessions

- P01.01 Henrik Solli OBESITY, SMOKING, DIABETES MELLITUS AND PHYSICAL EXERCISE AND RISK OF VENOUS THROMBOEMBOLISM: A DANISH COHORT STUDY
- H. Solli¹, M. Schmidt¹, M. Olsen¹, L. Pedersen¹, M. Brimacombe², F.B. Larsen³, H.T. Sørensen¹*
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- Background: Acquired risk factors for myocardial infarction and stroke have been thoroughly assessed, but the same risk factors are not as well examined with regards to venous thromboembolism (VTE).
- Aim: To assess whether obesity, smoking, diabetes mellitus, and lack of regular physical exercise are associated with an elevated risk of VTE.
- Methods: We performed a cohort study (n=21,439) based on self-reported questionnaire data from the Danish survey "How Are You?". Using the Danish National Registry of Patients, we identified all inpatient and outpatient diagnoses of VTE. We subdivided VTE into provoked VTE (predating occult cancer or secondary to fracture, surgery, trauma, pregnancy or prevalent cancer) and unprovoked VTE (remaining cases). We followed participants from return of questionnaire in spring 2006 until VTE, emigration, death, or 31 December 2011, whichever came first. Cox regression with person age as the time-scale was used to compute hazard ratios (HRs), adjusting for sex.
- Results: During the follow-up period, 165 VTE events were recorded. The adjusted HR with 95% confidence interval for overall VTE was 1.99 (1.33-3.00) for obese compared with persons of normal weight, 1.47 (1.01-2.16) for current smokers compared with never smokers, 1.76 (1.03-3.00) for diabetics compared with non-diabetics and 1.60 (1.14-2.25) for physically inactive compared with active. All hazard ratios were increased for both provoked and unprovoked VTE.
- Conclusions: Our results indicate that obesity, current smoking, diabetes mellitus and lack of physical exercise are associated with VTE.
- P01.02 Lisbeth Lydiksen IS IT POSSIBLE TO DEFINE AN OPTIMAL TIME FOR CHEMOTHERAPY AFTER SURGERY FOR OVARIAN CANCER?
Christensen
- L. Lydiksen¹, S. Jensen-Fangel², J. Blaakær¹*
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- Objective: The current Danish Guidelines from 2012 recommend a time from primary surgery to initiation of adjuvant chemotherapy (TI) of a maximum of 11 days for ovarian cancer (OC) patients (15). This limit of 11 days is not based on evidence. We wanted to investigate the actual TI among Danish OC patients who underwent primary surgery in 2005-2006 and to compare the survival between groups with early and late initiation

of chemotherapy.

Methods: All Danish women who underwent surgery for OC in the period 2005-2006 recorded in the Danish Gynaecological Cancer Database were included. The five-year survival was estimated overall and by the exposure: TI. The Cox proportional hazard regression analysis was used to compute adjusted hazard ratio (HR).

Results: The median TI was 32 days (25-75% quartile: 24 days; 41 days). The overall five-year survival was 42.8%, (95% CI: 38.9%; 46.5%). The strongest prognostic factors for death were residual tumour and the International Federation of Obstetrics and Gynecology (FIGO) stage.

The unadjusted HR for death in patients with TI > 32 days compared with the reference TI ≤ 32 days was 0.85 (95% CI: 0.70; 1.04), p-value 0.12. When adjusted for residual tumour and FIGO-stage, the HR was 1.13 (95% CI: 0.92; 1.39), p-value 0.26, i.e. a non-significant increased risk of death for patients with TI > 32 days.

Conclusion: This nationwide population-based cohort study revealed a non-significant increased risk of death for patients with TI > 32 days compared with the reference TI ≤ 32 days. The strongest prognostic factors were residual tumour after surgery and FIGO-stage. The overall five-year survival was 42.8% (95% CI: 38.9%; 46.5%).

P01.03 Tine Jepsen
Nielsen

USE OF GENERAL PRACTICE AFTER MYOCARDIAL INFARCTION ACCORDING TO DIFFERENT PATIENT CHARACTERISTICS

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Background: Some myocardial infarction (MI) patients have a higher risk of recurrent events and premature death, e.g. patients with short education or depression. The mechanisms underlying this are not thoroughly understood, but part of the explanation may be that high-risk patients have an unmet need of more long-term chronic care. In Denmark, the long-term chronic care management primarily takes place in general practice (GP).

Objective: To examine the use of GP during two years after a first-time MI according to different patient characteristics. Hospital contacts were included to examine if differences in contacts to GP could be explained by differences in hospital contacts.

Design: Population-based cohort study based on questionnaires and registers.

Participants: All patients discharged with first-time MI from 1 January 2009 through 31 December 2009 in the Central Denmark Region.

Main outcome measure: Standardised mean number of contacts to GP per three months according to sex, age, education, cohabitation status, dyspnoea score, comorbidity, depressive symptoms, and anxiety symptoms

during two years after the MI.

Results and conclusion: In general, high-risk patients such as older patients and patients with comorbidity had more GP contacts after the MI compared to their counterparts. However, this did not apply to high-risk patients with low education, depressive symptoms and patients living alone; they had the same number of GP contacts as patients without these risk factors. Use of hospital services did not seem to compensate for this. Some groups of high-risk MI patients may have an unmet need of long-term chronic care.

P01.04 Karen Guldbrandsen AGE OF MENARCHE AND TIME TO PREGNANCY - A STUDY WITHIN THE DANISH NATIONAL BIRTH COHORT

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Background: The onset of menarche is a risk factor for several diseases later in life. Whether early or late age of menarche (AOM) is associated with increased risk of subsequent infertility has only been addressed in a few studies with conflicting results.

Methods: Between 1996 and 2002, 73,107 pregnant women with planned or partly planned pregnancies were enrolled in the Danish National Birth Cohort and gave retrospective information on AOM and time to pregnancy (TTP).

The association between AOM and TTP was analyzed using multivariate logistic regression with TTP categorized into subfecundity (TTP ≥ 6 months) and infertility (TTP > 12 months) in two different models. We adjusted for pre-pregnancy BMI, occupational status as well as eating disorders and metabolic diseases in childhood.

Results: The mean (SD) AOM was 13.3 (1.4) years, 31.7% were subfecund (TTP ≥ 6 months) and 16.4% were infertile (TTP > 12 months).

Using 13 years as a starting point, later AOM was associated with higher odds for subfecundity (OR: 1.05 (95% CI: 1.03-1.06)) and infertility (OR: 1.04 (95% CI: 1.02-1.07)).

Compared to AOM at 13 years, the odds for subfecundity were higher among women with AOM at 15 or older than 15 years: OR: 1.09 (95% CI: 1.03-1.15) and OR 1.17 (95% CI: 1.09-1.25), respectively. Also, the odds for infertility (OR: 1.18 (95% CI: 1.08-1.29)) were higher among women with AOM later than 15 years compared to AOM at 13 years.

Women with AOM before the age of 11 had lower odds for subfecundity (OR: 0.86 (95% CI: 0.77-0.97)) compared to AOM at 13 years.

Conclusion: This study on pregnant women suggests that later AOM is associated with increased risk of subfecundity and infertility.

P01.05 Jonas Lüthje MORTALITY AMONG PATIENTS HOSPITALIZED WITH PNEUMONIA -
Munthe DESCRIBING THE 30-DAY MORTALITY AFTER ADMISSION WITH
PNEUMONIA ON DANISH HOSPITALS

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Background: Hospital standardized mortality rates (HSMR) are commonly used to assess quality of care in hospitals. Pneumonia is the diagnosis leading to most deaths within 30 days of admission in Danish hospitals, thus having a high influence on this quality measure. It is known that the standardized mortality ratios (SMR) for pneumonia vary between the hospitals. It is, however, unknown if this variation reflects real differences in quality or if it is due to variation in coding and unadjusted case mix.

Aim: To describe the incidence, distribution and (SMR) of admissions with the pneumonia diagnose codes J12.x-J18x in the different regions.

Method: Nationwide cohort study of all patients hospitalized from 1 January 2010 to 30 December 2011. SMRs were calculated using indirect standardization, with the number of expected deaths predicted from a logistic regression model, fitted on all observations and adjusting for case mix.

Results: 52,712 patients were admitted with pneumonia leading to 4817 deaths (9.1%) within 30 days of admission. On a regional level, the proportion of patients admitted with a pneumonia diagnosis specifying the causal pathogen ranged from 6.9% to 16.4%. The overall national SMR for the different pneumonia diagnoses ranged from 64.2(95%CI 48.3-84.0) for the diagnoses with specified pathogen to 108.3(95%CI 102.7-114.2) for the unspecified bacterial pneumonias.

Conclusion: Pneumonia is consistently related to many deaths in all regions. The ratio between pathogen specific and unspecific pneumonia codes vary substantially between regions. SMR for the different pneumonia diagnoses vary. But it is unclear what causes this variation.

P01.06 Imra Kulenovic REALITY CHECK OF THE DANISH/EUROPEAN GUIDELINES ON
CARDIOVASCULAR DISEASE PREVENTION IN CLINICAL PRACTICE
(VERSION 2012)

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Background: Cardiovascular disease (CVD) is a leading cause of mortality worldwide, despite that causal risk factors are well-known and effective, safe and inexpensive risk reducing medications are easily available. In Europe, the European Society of Cardiology (ESC) recommends that decision on risk reducing pharmacological prevention is based on the absolute 10-year risk of fatal CVD calculated using the Systematic Coronary Evaluation System (SCORE). However, we have recently conducted a pilot study which seriously questions the effectiveness of these guidelines as a mean to prevent atherosclerotic CVD suggesting that less than 8% of adults

without pre-existing CVD or diabetes hospitalized for a first AMI qualify for preventive pharmacotherapy. These results need to be validated in a larger study.

Hypotheses: (1) Very few (<10%) apparently healthy individuals destined for a near-term AMI use statin, (2) Very few (<10%) non-diabetic individuals without CVD, including women, destined for a near-term AMI qualifies for preventive pharmacotherapy, (3) Far from all (<75%) diabetic patients without CVD destined for a near-term AMI are treated with statin.

Materials and methods: To evaluate the performance of SCORE in the primary prevention of CVD, we plan to review the medical records of all patients admitted for an AMI during 2010-2012 to the following hospitals in Denmark: Aarhus University Hospital THG/Skejby and the Regional Hospitals in Randers, Herning, Silkeborg, Viborg and Horsens. Information on traditional risk factors (e.g. age, blood pressure and total cholesterol) for diabetes and statin use is extracted from the records, and SCORE risk is calculated for each patient.

P01.07 Helga Lillian Guðmundsdóttir ESTIMATING THE ORGAN DONOR POTENTIAL ON NON-INTENSIVE CARE UNITS IN DENMARK: A RETROSPECTIVE ANALYSIS OF POTENTIAL ORGAN DONORS IN THE CENTRAL DENMARK REGION

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Introduction: The aim of this study is to assess unexploited organ donor potential consisting of patients dying in non-intensive care units (ICU), of cerebral catastrophes, and without medical contraindications for organ donation.

Methods: Data were collected on patients who died within 48 hours from admission, by a catastrophic brain damage, in non-ICU wards in the Central Denmark Region, from January 2008 till December 2010. Incidence of conditions compatible with brain death was assessed by a medical records review of patients who had had a computed tomography scan of the cerebrum (CTC).

Results: After retrospectively reviewing a total of 287 medical records, excluding cases not consistent with imminent brain death, and with absolute contraindications for donation, the pool of possible DBDs (donors after brain death) consisted of 66 persons. The mean age of the possible DBDs was 77.16 years, 73% were older than 70 years, and 50% older than 80 years. According to the CTC, 70.1% of the deaths were due to cerebral hemorrhage, 20.9% died of subarachnoid hemorrhage, 7.5% of cerebral infarction and 1.5% due to a benign cerebral neoplasm. The main comorbidities of the possible DBDs were hypertension (67%), heart diseases (42%), lung diseases (15%), diabetes (15%) and kidney diseases (3%). Further results on the suitability for donation of each case are currently being reviewed by an experienced transplant coordinator.

Conclusions: A DBD donor potential of about 20 cases per year was

identified outside ICUs in a region with a population of about 1.3 million. A focus area for increasing the donor pool may allow for improvement in conferring possible DBDs with a transplant coordinator.

P01.08 Astrid Blicher
Schelde

IMPACT OF COMORBIDITY ON THE RISK OF FIRST-TIME MYOCARDIAL INFARCTION, STROKE, OR DEATH AFTER SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY MYOCARDIAL PERFUSION IMAGING: A DANISH COHORT STUDY

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Objectives: To examine the association between a normal vs. abnormal single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI) scan on 10-year risk of first-time myocardial infarction (MI), stroke, and all-cause death, overall and according to comorbidity level.

Background: The impact of comorbidity on the risk after SPECT MPI remains unclear.

Methods: We identified all patients with a SPECT MPI performed at Aarhus University Hospital in Skejby during 1999-2011. We categorized the SPECT MPI as normal (no defects) or abnormal (reversible and/or fixed defects). Using nationwide medical registries, we obtained information on comorbidity level (using Charlson Comorbidity Index) and outcomes. We used Cox regression to compute hazard ratios (HRs) adjusting for sex, age, and comorbidity level.

Results: Among 7,040 patients, 4,962 (70%) had normal scans and 2,078 (30%) abnormal scans. Patients with a normal vs. abnormal scan had a 10-year risk of 5.7% vs. 10.9% for MI, 6.0% vs. 7.8% for stroke, and 16.5% vs. 29.0% for all-cause death. Compared with a normal scan, an abnormal scan increased the risk of MI (adjusted HR=1.73, 95% CI: 1.37 to 2.18) and all-cause death (1.42, 95% CI: 1.23 to 1.65), but not stroke (1.12, 95% CI: 0.86 to 1.45). Comorbidity level did not substantially affect the association between the scan result and the outcomes.

Conclusions: Independently of comorbidity level, an abnormal SPECT MPI was associated with an increased 10-year risk of MI and all-cause death, but not stroke.

P02.01 Kristian Dahl
Kragholm
Sørensen

RETURN TO WORK IN OUT-OF-HOSPITAL CARDIAC ARREST SURVIVORS - A NATIONWIDE REGISTER-BASED FOLLOW-UP STUDY

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Introduction: Survival after out-of-hospital cardiac arrest (OHCA) has increased in Denmark. Neurological and functional outcome parameters are important. Therefore, we assessed return to work in OHCA survivors.

Methods: A total of 32,883 OHCA patients in whom resuscitation was attempted were identified through the nationwide Danish Cardiac Arrest Register (2001 - 2011), and 12,332 patients were of working age between 18 and 65 years. Cardiac arrest data were linked to data from other nationwide registries, including employment data from the DREAM registry. Of 1,434 patients, who were alive 30 days after arrest, 810 were at work until arrest.

Results: Of 810 patients, 81% were males and median age was 53 (46-59), 465 patients returned to work within one year while 22 died. The proportion returning to work between 2006 and 2011 was 58% compared to 53% in 2001-2005. When adjusting for pre-hospital factors in a multivariate logistic regression analysis, predictors were: (1) male sex (OR: 2.1, 95% CI: 1.2-3.7); (2) witnessed arrest (OR: 3.6, 95% CI: 1.7-7.5); (3) bystander cardiopulmonary resuscitation (OR: 1.7, 95% CI: 1.06-2.8); (4) survival at hospital arrival (OR: 8.3, 95% CI: 2.5-28); (5) low score on charlson comorbidity index (OR: 1.8, 95% CI: 1.02-3.2); and (6) arrest between 2006-2011 vs. 2001-2005 (OR: 2.4, 95% CI: 1.5-3.9).

Conclusion: More than half (57%) of 30-day survivors of out-of-hospital cardiac arrest returned to work within one year. Return to work was, in a multivariate adjusted regression modelling, significantly associated with having arrest between 2006 and 2011 compared to arrest in 2001-2005.

P02.02 Lise Maria Lindahl

SECONDARY CANCERS, COMORBIDITIES AND MORTALITY ASSOCIATED WITH NITROGEN MUSTARD THERAPY IN PATIENTS WITH MYCOSIS FUNGOIDES: A 30-YEAR POPULATION-BASED COHORT STUDY

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Background: Topical nitrogen mustard is a widely used therapy in patients with mycosis fungoides (MF). However, it remains controversial whether nitrogen mustard therapy is associated with increased risk of secondary cancers and chronic pulmonary diseases in patients with MF.

Objectives: To assess the risk of secondary cancers, comorbidities and mortality in MF patients treated with nitrogen mustard compared with MF

patients not receiving this treatment.

Methods: Linking the Danish nationwide registries in a 30-year population-based cohort study, we compared 110 MF patients from a regional Danish center using nitrogen mustard treatment with 193 patients from Danish centers not using nitrogen mustard. The two cohorts were compared by Cox regression analysis.

Results: Overall secondary cancers were not significantly increased (hazard ratio (HR) 0.84, 95% confidence interval (CI) 0.46-1.56), and subanalyses showed no increased risk of non-melanoma skin cancers, malignant melanomas and cancers in the respiratory organs in the nitrogen mustard treated cohort. Furthermore, we found no increased risk of any category of comorbidity, including chronic pulmonary diseases (HR 0.93, 95% CI 0.48-1.81), in patients treated with nitrogen mustard. Moreover, mortality did not significantly differ between the two cohorts.

Conclusions: This study does not support any previous suspicion of increased risk of secondary cancers and chronic pulmonary diseases among MF patients treated with nitrogen mustard. Furthermore, mortality and cause-specific mortality was not influenced by nitrogen mustard treatment. Thus, our findings indicate that topical nitrogen mustard is a safe therapy in patients with MF.

P02.03 Jean-Christophe EFFECT OF BEREAVEMENT AND VARIATION IN THE GLUCOCORTICOID
Philippe Debost REGULATING ENZYME 11-BETA;-HYDROXYSTEROID-DEHYDROGENASE
TYPE 2 IN CHILDREN WHO LATER DEVELOP SCHIZOPHRENIA

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Introduction: Maternal stress during pregnancy has been associated with schizophrenia. It has been speculated that stressful life events enhance production of glucocorticoids that adversely affect neurodevelopment in the immature brain, increasing the risk of mental illness. The authors hypothesized that the effect of bereavement was mediated via cortisol, and in part could be explained by variation in the gene HSD11B2 encoding the glucocorticoid regulating enzyme 11- β -hydroxysteroid-dehydrogenase type 2.

Method: A matched case-control study with 739 schizophrenia cases and 739 controls, matched on sex, exact date of birth, born in Denmark, alive and with no history of schizophrenia on the date of first diagnosis of schizophrenia of the matched case, and also including all their first-degree relatives. We used information from national registers and GWAS data from the Danish neonatal biobank to determine whether the effect of bereavement could be explained by variation in HSD11B2. Single nucleotide polymorphisms (SNPs) were imputed in the locus of HSD11B2, and data were analyzed with conditional logistic regression.

Results: We found a main effect of bereavement after pregnancy and each of the SNPs. For some of the SNPs, we also found an interaction with bereavement, independent of psychiatric family history and place of birth.

Conclusions: Our results suggest that there is an interaction between bereavement during fetal or early life and SNPs in HSD11B2 in offspring who later develop schizophrenia. This might suggest involvement of abnormal glucocorticoid metabolism as a mediating factor between maternal stress and offspring mental disorders.

P02.04 Majbritt Mostrup Pedersen EFFECTIVENESS OF AN EDUCATIONAL VIDEO FOLLOWING ACUTE WHIPLASH TRAUMA: A RANDOMIZED CONTROLLED TRIAL

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Background: Whiplash injuries affect 1-3 per 1000 inhabitants each year. Most patients only experience transitory neck complaints and recover within weeks. However, an estimated 10% will develop severe persistent pain seriously affecting long term well-being and work ability. The exact mechanisms behind this variation in recovery remain elusive, and our knowledge on how to prevent the transition from acute to chronic neck pain is sparse. Guidelines for management of acute whiplash emphasize the importance of patient information, but there is limited evidence as to how information should be provided in order to improve recovery. However, recent studies indicate that patient education by video may be a beneficial method to improve early pain management.

Aim: To examine the effect of an educational video on intensity of neck pain, illness perceptions and work ability following acute whiplash trauma caused by motor vehicle accidents.

Methods: 300 consecutive patients recruited at Danish Emergency Departments. Following usual care, participants are randomized to either intervention (educational video) or control (relaxation video). The educational video provides a biopsychosocial model for pain incorporating both physiological and cognitive-behavioural aspects, reassurance and advice on pain relief. Self-report data are obtained from questionnaires at 1 week, 3 and 12 months of follow-up. Data on health care use and work ability will be retrieved from public registers.

Perspective: The development of cost-effective interventions to aid recovery in the early stages of whiplash associated disorders may potentially reduce suffering for patients and financial costs for society.

P02.05 Anne Bodilsen NATIONAL VARIATION IN RE-OPERATION RATE AFTER BREAST CONSERVING SURGERY

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Introduction: With breast conserving surgery being standard procedure for

treating invasive breast cancer, approximately 2800 women are having lumpectomies yearly in Denmark. Some of these will need re-excisions to obtain a sufficient margin. However, the number of re-excision performed is currently unknown. Results from abroad are very diverse ranging from 10.6% to 72.7%.

Aim: To determine and compare re-operation rates nationwide.

Method: From a cohort of all women with invasive breast cancer having breast conserving surgery between 1996 and 2009 in Denmark, we identified patients with re-excisions. Re-excision was defined as one or more additional surgical procedures within two months of primary lumpectomy to achieve sufficient margin. Data was collected from the Danish Breast Cancer Cooperative Group, National Health registry, Pathology Registry, and hospital records.

Results: A total of 16,781 patients underwent breast conserving surgery. 2,131 patients had one re-excision (12.70%), 76 (0.45%) had two and 2 (0.01%) had three re-excisions. 266 (1.59%) women proceeded to mastectomy within 60 days of primary surgery. Hospitals with less than 20 breast conserving surgeries per year had a significantly higher rate of re-excision (OR=1) compared with hospitals performing 20-50 operations (OR=0.58, 95% CI 0.49-0.68), 50-100 procedures (OR=0.53, 95% CI 0.45-0.62), and more than 100 operations a year (OR=0.51, 95% CI 0.44-0.59).

Conclusion: Re-operation rates in different hospitals vary between 6.89% and 37.50% with a national average of 13.16%. The risk of re-operations is significantly higher in hospitals performing few breast-conserving surgeries.

P02.06 Helene Tilma
Vistisen

ASSESSMENT OF BREAST CANCER RISK BY USE OF THE DANISH WORKING HOUR DATABASE

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Background: In 2007, the International Agency for Research on Cancer classified nightshift work that involves circadian disruption as probably carcinogenic to humans, based partly on an increased risk of breast cancer among long-term nightshifts workers. Since then, several epidemiologic studies have examined this relation. Despite these efforts, inadequate information on nightshift work is an Achilles heel in the studies leading to persisting uncertainty regarding causality, and there is a need for prospectively collected, objective, and detailed data that allow analyses based on exposure metrics that reflect relevant effects on the circadian rhythm.

Aim: To study the association between night-work and risk of breast cancer by use of the newly established Danish Working Hour Database (DWHD). DWHD is a large national cohort of public health care professionals with a

high prevalence of night shift work.

Methods: Many of the Danish health care professionals are employed by the Danish Regions. For every employee, the Danish Regions keep information regarding the personal identification number, sex, date of birth, position, absence and reasons therefore, e.g. vacation, sickness and maternity leave, and seniority, in addition to date, hour, and minute for the beginning and end of every work duty. DWHD was established in 2012 and encompasses data as of 2007. The data are updated on an annual basis. Data from DWHD will be linked with national cancer registers. The database encompasses for 2007 102.487 female employees of which 36.419 work nightshifts. During the follow-up period in 2007-2012, we expect a total of 300 breast cancer cases among women working nightshifts.

P02.07 Dinesh
Neupane

COMMUNITY-BASED INTERVENTION FOR HYPERTENSION IN NEPAL

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Background: Hypertension confers the highest attributable risk to mortality and morbidity from cardiovascular diseases. An approach that decreases blood pressure level in the general population by even modest amounts has the potential to substantially reduce morbidity and mortality, or at least delay onset of hypertension. However, we lack evidence on such approaches from developing countries. Nepal has been a pioneer in the successful implementation of community-based public health initiatives through mobilizing Female Community Health Volunteers (FCHVs) particularly related to maternal and child health over the past 20 years. However, no effort has been made on what type and which level of services they can provide particularly related to non-communicable diseases (NCDs).

Objective: The general objective is to test whether existing community-based FCHVs of the Ministry of Health and Population can perform a set of activities that will result in controlling blood pressure among the general population.

Method: The study is a community-based cluster-randomised controlled trial with the community as the unit of randomization. After receiving 5 days intensive training, the FCHVs will deliver health promotion messages as well as measure the blood pressure for one year in the intervention area. Baseline and follow-up surveys will be used to compare the control and intervention areas.

Perspective: Many developing countries are struggling to combat NCDs, and there is a need for an appropriate and sustainable approach. Thus, the research output has the potential to bring immediate benefits to address hypertension in Nepal and possibly other resource-poor countries.

P02.08 Janne

IMPACT OF PRE-ADMISSION SELECTIVE SEROTONIN REUPTAKE INHIBITOR TREATMENT ON STROKE OUTCOME: A NATIONWIDE PROPENSITY SCORE-

Mortensen

MATCHED FOLLOW-UP STUDY

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Background and aim: Selective Serotonin Reuptake Inhibitors (SSRIs) appear to have antithrombotic effects that may increase the risk of bleeding. Evidence further suggests a neuroprotective effect in stroke, however, clinical data are sparse. We aimed to examine the implications of pre-admission SSRI use in ischemic and hemorrhagic stroke patients.

Methods: We did a nationwide registry-based follow-up study among ischemic and hemorrhagic stroke patients in Denmark between 2003 and 2011. We identified 3797 pre-admission SSRI users with ischemic stroke and 550 with hemorrhagic stroke and propensity score matched each group with non-users (1:1). Multiple conditional logistic regression was used to compute odds ratios (OR) of severe stroke (as measured on the Scandinavian Stroke Scale) and death within 30 days.

Results: There was no statistically significant difference in risk of severe stroke between pre-admission SSRI users and non-users (ischemic stroke adjusted OR, 1.02; 0.92-1.12 and hemorrhagic stroke adjusted OR, 1.17; 0.89-1.54) and no statistically significant difference in risk of death within 30 days (ischemic stroke adjusted OR: 1.15; 0.98-1.35 and hemorrhagic stroke adjusted OR: 1.19; 0.86-1.63) in either stroke group.

Conclusion: Pre-admission SSRI use did not impact the risk of severe stroke or the risk of death within 30 days in this cohort, although there was a signal indicating a slight increase in the risk of severe stroke among SSRI users with hemorrhagic stroke and a slight increase in case-fatality among SSRI users overall. Further studies are warranted to explore the possible neuroprotective and hemorrhagic effects of SSRI treatment in acute stroke.

P02.09

Mette Lausten
Hansen

PREDICTORS OF SICKNESS ABSENCE IN PREGNANCY - A DANISH COHORT STUDY

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Background: Increasing sickness absence among employed people is of rising concern in several European countries. Some studies indicate that the incidence proportion of sickness absence in pregnancy is increasing, although there are no well-established medical grounds for this increase. Research in pregnancy-related sickness absence, its consequences and related risk factors is very sparse.

Objective: To investigate if the following factors are risk factors for sickness absence during pregnancy until pregnancy week 30; parity, age, fertility

treatment, body mass index (BMI), time to pregnancy (TTP) and engagement in physical exercise.

Methods: We use data from the Danish National Birth Cohort (DNBC) and the Danish Register for Evaluation of Marginalisation (DREAM - a Danish acronym). DNBC contains information on 100,418 pregnancies; inclusion took place from 1997 until 2002. The women were telephone interviewed around pregnancy week 12-16 and 30, providing information on the potential risk factors as well as information on occupational exposures, lifestyle factors and health. We excluded women who were not employed at first interview, who were no longer pregnant at first interview and women with multiple pregnancies, leaving a study population of 66,682 women. Outcome data is retrieved from the DREAM register, which contains information on sickness absence on a weekly basis. Data will be analysed using a Cox regression model and adjusting for covariates. We will use multiple imputation methods to account for missing values on covariates.

Conclusions: Data analyses are in progress, and results will be presented at the PhD day.

P03.01 Kirstine Høj
Obling

THE MILE STUDY: A MOTIVATIONAL, INDIVIDUAL AND LOCALLY ANCHORED EXERCISE INTERVENTION IN 30-49 YEAR-OLDS. A RANDOMISED CONTROLLED STUDY IN PRIMARY CARE

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Background: Cardiorespiratory fitness (CRF) is inversely associated with non-communicable diseases and all-cause mortality. Physical activity level is the primary determinant of CRF in adults. However, knowledge on how to motivate people to engage persistently in physical activity is deficient.

Objective: To investigate the effect of a motivational, individual, and locally anchored exercise intervention in primary care on CRF in 30-49 year-olds with low levels of CRF.

Methods: Two-armed randomised controlled trial with 6 and 12 months follow-up. The primary outcome is CRF estimated via a maximal incremental exercise test. Secondary outcomes include physical activity level and sedentary behavior (objectively measured), biochemical parameters (HbA1c, HDL- and LDL-cholesterol, and triglyceride), self-reported physical activity, anthropometric parameters and health-related quality of life. A total of 236 participants with low levels of CRF classified at a local health check programme will be randomised. The intervention consists of four motivational interviews, a six-month membership to a local sport club, and a global positioning watch to upload training activity to Endomondo.com. The comparison group will receive standard care: a one-hour motivational interview. Effects will be estimated by evaluating the differences in mean changes in CRF between the two groups.

Results: Recruitment was initiated in the summer of 2013. Final results will

be available in 2015.

P03.02 Natalie Momen MODE OF DELIVERY AND CHILDHOOD CANCER: A NATIONWIDE FOLLOW-UP STUDY IN THREE COUNTRIES

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Mode of delivery has been suggested to affect the immune system's development and function. Epidemiological studies have found increased risks of diseases like asthma and type I diabetes mellitus in children born by Caesarean section (CS). Some have suggested the risk of childhood cancer may be increased. Different mechanisms have been postulated which make distinction between elective and unplanned CSs potentially important.

A population-based follow-up study was carried out using register data, including children born in Denmark (1968-2007), Sweden (1973-2006) and a randomly selected sample of 90% of children born in Finland (1987-2007) (N=7,029,843). Follow-up started at birth and ended at the first of the following: date of cancer diagnosis, death, emigration, end of 15th year or end of follow-up. Cox regression was used to obtain hazard ratios.

Altogether, 882,907 (12.6%) children were delivered by CS; 30.3% CSs were elective, 35.9% unplanned and 33.8% had no information as to whether planned or not. There were 11,181 children who received a cancer diagnosis. Exposed children had a 5% increased risk of childhood cancer (hazard ratio: 1.05; 95% confidence interval 0.99, 1.11). A significant association was not seen for elective or unplanned CSs, or for any type of childhood cancer.

Although positive associations were seen, mode of delivery does not appear to be an important risk factor for childhood cancer in general or possibly not for any specific types of childhood cancer. The CS rates in the Nordic countries are among the lowest in Europe, but high and increasing elsewhere. Even a very small increase in risk for individuals could have a great public health impact.

P03.03 Martin Christensen PRE-ECLAMPSIA AND THE POSTPARTUM CARDIOVASCULAR RISK - A 10-YEAR FOLLOW-UP

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Introduction: Pre-eclampsia (PE), defined as hypertension and proteinuria arising after 20 weeks of gestation, complicates 3-5 % of all pregnancies and is associated with significant fetal and maternal morbidity and mortality. Several studies have demonstrated an association between PE and premature development of cardiovascular disease (CVD) later in life. The association is incompletely understood, but may be linked to a postpartum persistence of endothelial dysfunction and angiogenic imbalance. At this point no recommendations on preventive interventions or screening for CVD risk in women with a history of PE have been established. A remaining step is to elucidate whether an increased CVD risk can be identified already 10 years postpartum, before the appearance of clinical symptoms.

Objectives: To assess markers of CVD risk, atherosclerosis and endothelial dysfunction as well as levels of angiogenic factors in women with previous PE compared to women with previous uncomplicated pregnancies.

Design: A 10-year follow-up study comparing 52 exposed women (pregnancy complicated by PE) and 104 unexposed women (uncomplicated pregnancy). Participants will be recruited from a well-characterised cohort, previously assembled at the Department of Obstetrics at Randers Regional Hospital in 2001-2004. Blood and urine samples are stored in a biobank, thus rendering the possibility of longitudinal assessment.

Perspectives: We hope to contribute new knowledge on assessment of increased CVD risk in women with a history of PE, and thereby to help clarify the possible need for screening and/or preventive interventions 10 years postpartum.

P03.04 Mette Sørensen SHARED CARE AND IMPLEMENTATION OF A PEDIATRIC CLINICAL
Langfrits PATHWAY

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Background: Asthma is the most common chronic disease among Danish children. Successful asthma management involves guideline-based treatment and regular follow-up. In the present population-based intervention study, we have implemented the international guidelines from "Global Initiative for Asthma" as a clinical pathway at a large Danish hospital and at affiliated general practitioners (GPs). Our hypothesis is that it can improve intersectional collaboration between physicians treating children with asthma based on a shared responsibility called Shared Care.

Aim: In 4 observational studies, we aim to examine whether implementation of clinical pathways and shared care lead to improvement of the following outcomes: Study 1) An increased proportion of asthmatic children followed at the right place. Study 2) An increased overall proportion of children with well-controlled asthma. Study 3) Favorable changes in the use of asthma medication. Study 4) Self-reported higher quality of life

among children with asthma.

Methods: Observational follow-up study from April 2011 to April 2014 to study the effect of implementation of a clinical pathway for the treatment of children with asthma. We have included 1540 children aged 0-15 years with a physician-validated asthma diagnosis who are followed either at a hospital specialist out-patient clinic or at one of 100 GPs. At baseline, the involved physicians participated in an introduction to the clinical pathway and treatment guide.

Perspectives: This project may provide documentation for an effective asthma quality improvement intervention, which could be used in the future organization of childhood asthma diagnosis, treatment and control.

P03.05 Henry Jensen GENERAL PRACTITIONERS' SUSPICION OF CANCER AND USE OF STANDARDISED CANCER PATIENT PATHWAYS

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Background: The decision to initiate a standardised cancer patient pathway (CPP) for a particular patient is a key issue in CPP standardisation. The GP's decision is assumed to be influenced by his or her suspicion of cancer based upon the interpretation of the patient's symptoms. We aimed to estimate how often GPs suspect cancer among incident cancer patients presenting symptoms in general practice and to analyse to what extent the GP's interpretation of symptoms may predict the choice of referral.

Materials and methods: In total, 3,829 newly diagnosed cancer patients were included in a cross-sectional study. We grouped patients according to the GP's symptom interpretation at the first consultation in primary care and estimated the prevalence ratios (PR) of initiating a CPP as a function of the GP's symptom interpretation using Poisson regression.

Results: Preliminary results show that 1,848 out of 3,829 (48%) patients presented with alarm symptoms suggestive of cancer. Overall, standardised CPPs were initiated in 37% of all cases and in 52% of the 1,848 cases where the GP suspected cancer. Patients were less likely to be referred to a CPP if they presented with symptoms suggestive of other serious illnesses (PR= 0.40 (95%CI: 0.34;0.48)) or with vague symptoms (PR= 0.53 (0.48;0.60)) compared to patients with alarm symptoms suggestive of cancer.

Conclusion: The results show that GPs suspect cancer more often than they initiate a CPP. However, the GPs also initiate CPP without specifically suspecting cancer. The data call for further analysis of decisions prompting CPP initiation and further investigation of how to best support the GP in referring patients who might have cancer.

P03.06 Anette Riisgaard LONG-TERM MORTALITY OF PERSONS WITH SEVERE MENTAL ILLNESS AND
Ribe DIABETES

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Background: Persons with severe mental illness (SMI) have an excess mortality, which may partly be explained by the high prevalence of diabetes among these persons. The aim was to assess the overall and cause-specific mortality of persons with SMI and diabetes in a large population-based cohort.

Methods: We compared the overall and cause-specific mortality in persons with SMI and diabetes with that of the general Danish population between 1997 and 2009 by linking data from Danish National Registries.

Results: The cohort counted 4,734,703 persons of whom 37,389 had SMI, 248,176 had diabetes, and 4,284 had SMI and diabetes. During follow-up, 651,080 persons died of whom 1,083 persons had SMI and diabetes. The overall mortality rate ratios (MRRs) for persons with SMI and diabetes were 4.14 (95% confidence interval (CI) 3.81-4.51) for men and 3.13 (95% CI 2.88-3.40) for women as compared with the background population. The cause-specific MRRs were lowest for malignant neoplasms (women: MRR=1.98, 95% CI 1.64-2.39; men: MRR=2.08, 95% CI 1.69-2.56) and highest for suicide among women (MRR=12.31, 95% CI 6.80-22.28) and accidents among men (MRR=7.89, 95% CI 5.51-11.29). The cumulative risks of death within seven years of diabetes diagnosis were 15.0% (95% CI 12.4-17.6) for those younger than 50 years, 30.7% (CI:27.8-33.4) for those aged 50-69 years, and 63.8% (95% CI 58.9-68.2) for those aged 70 years or older.

Conclusions: The long-term mortality is high for persons with SMI and diabetes. This calls for effective intervention from a coordinated and collaborating healthcare system.

P03.07 Xiaoqin Liu BIRTH WEIGHT, GESTATIONAL AGE, FETAL GROWTH AND CHILDHOOD
ASTHMA HOSPITALIZATION

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Background: Childhood asthma may have a fetal origin through factors affecting fetal development.

Objective: We examined to which extent short gestational age, low birth weight and fetal growth restriction were associated with increased risks of asthma hospitalization in childhood.

Methods: We undertook a cohort study based on several national registers in Denmark, Sweden and Finland. We included all live singleton children born in Denmark during 1979-2005 (N=1,538,093), in Sweden during 1973-2004 (N=3,067,670), and a 90% random sample of singleton children born in Finland during 1987-2004 (N=1,050,744). The children were followed from birth to first hospitalization for asthma, emigration, death, their 18th birthday, or the end of study (the end of 2008 in Denmark, and the end of 2007 in Sweden or Finland), whichever came first. We computed the pseudo-values for each observation and used them in the generalized estimating equation to estimate relative risks (RR) for asthma hospitalization.

Results: A total of 131,783 children were hospitalized for asthma during follow-up. The risk for asthma hospitalization consistently increased with decreasing birth weight and gestational age. A 1000-g decrease in birth weight corresponded to a RR of 1.19 (95% confidence interval (CI): 1.18-1.20). A one-week decrease in gestational age corresponded to a RR of 1.05 (95% CI: 1.04-1.06). Small for gestational age was associated with a moderately increased risk of asthma hospitalization (RR=1.23, 95% CI: 1.20-1.27).

Conclusions: Fetal growth and gestational age may play a direct or indirect role in the development of childhood asthma.

P03.08 Oleguer Plana Ripoll PRENATAL MATERNAL BEREAVEMENT AND ADULT REPRODUCTIVE IMPAIRMENTS: A POPULATION-BASED COHORT STUDY

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Introduction: Decline in fertility rates is partially explained by changes in family planning and in fecundity derived from socio-economic factors, psychosocial stress and unhealthy lifestyle among others. Recent research proposed that intrauterine environment also determines fertility in the offspring, and it could be associated with maternal stress through hormonal disturbance in fetal life. There is evidence from animal studies that prenatal exposure to glucocorticoids is related to fertility impairments in the

offspring. We hypothesized that prenatal stress due to maternal bereavement has a programming effect on adult reproductive impairments.

Methods: This population-based cohort study considered all subjects born in Denmark after 1968 and Sweden after 1973 and older of 12 years at the end of follow-up (N=4,128,761). They were exposed if their mothers lost a close relative during pregnancy or the year before and unexposed otherwise. The outcome was the age of each subject when having the first child. Data were analyzed using Cox model stratifying by country and gender and adjusting for different covariates.

Results: 93,635 subjects (2.3%) were exposed and 983,977 (23.8%) had a child during the follow-up time. For Danish subjects, the hazard ratio [95% CI] of having the first child for exposed compared to unexposed was 1.03 [0.97-1.09] for males and 1.02 [0.97-1.06] for females. For Swedish subjects, it was 0.98 [0.95-1.02] for males and 1.01 [0.98-1.04] for females.

Conclusions: We did not observe any substantial difference between exposed to prenatal stress due to maternal bereavement and unexposed when studying age of having their first child, but longer follow-up is needed.

P04.01 Christina Marie Braüner AN INVESTIGATION OF SMARTPHONE APPLICATION IN EMERGENCY OBSTETRIC AND NEWBORN CARE IN GHANA

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Introduction: Around the globe, more than a quarter of a million women die every year in relation to pregnancy and childbirth. The main cause of maternal death is post partum haemorrhage (PPH). Training of delivery staff can halve the incidence of PPH. Most training programs, however, do not reach birth attendants in the rural parts of the developing world where the majority of deliveries take place, and there is a need to assess alternative ways of providing training to delivery staff.

Objectives: This PhD aims to evaluate the impact of a smartphone application with animated clinical instruction videos (developed by Maternity Worldwide Denmark and Copenhagen University) as an alternative tool to train midwives in Ghana on how to prevent and manage PPH. The study will assess the impact on the midwives' knowledge and skills, along with the impact of the application on the incidence of PPH. Finally, the midwives' consumption patterns of the smartphone application and the cost effectiveness of using the app, compared to normal practice, will be assessed.

Methods: The impact of the application will be assessed in a cluster-randomized trial in rural health facilities in Ghana. Sixteen health facilities will be assigned to receive the smartphone intervention, or no intervention. Approximately 160 birth assistants will be observed while conducting about 3,200 deliveries. The outcome measures will be midwives' test scores from

knowledge and skills tests, and the incidence of PPH will be measured in millilitres.

Perspectives: A successful evaluation will provide the evidence that smartphone training is a low-cost solution to improve midwife skills and reduce PPH.

P04.02 Cathrine
Carlsen Bach

PERFLUORINATED CHEMICALS AND FETAL GROWTH - PRELIMINARY RESULTS

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Background: Perfluorinated chemicals (PFCs) are widespread environmental toxicants. They cross the placenta, and fetal exposure is suspected to disturb fetal growth. However, previous studies have shown conflicting results and have included few PFCs. The objective of this study was to investigate the association between PFC exposure and fetal growth.

Methods: 1350 participants (250 per year in 2008 to 2010 and 200 per year in 2011 to 2013) were randomly selected from a cohort of pregnant women who gave blood before 14 weeks of gestation, were nulliparous, provided a time to pregnancy if the pregnancy was planned, and gave birth to a liveborn child.

16 PFCs were measured in maternal serum by high performance liquid chromatography - tandem mass spectrometry. Multiple linear regression analyses were used to investigate the association between PFCs detected in more than 85% of samples and proxy estimates of fetal growth (birth weight, length and head circumference) while adjusting for covariates chosen a priori.

Results: Preliminary results from 499 mother-child pairs are presented. No significant associations were observed between PFOS, PFOA, PFHxS, PFNA, PFHpS or PFUnA and birth weight. However, increasing PFDA was associated with higher birth weight. PFC levels and birth length or head circumference were not associated.

Conclusion: There was no statistically significant association between levels of all, except one, investigated PFC and fetal growth. The increase in birth weight with PFDA could be a chance finding. Levels of PFCs were lower than in many previous studies. This may explain our lack of association. However, the sample is small, and results are only preliminary.

P04.03 Pernille
Pedersen

PSYCHOEDUCATION FOR SICK-LISTED INDIVIDUALS WITH MENTAL HEALTH PROBLEMS

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Background: In Denmark, it is estimated that 35-45% of all sick leave registered citizens are on sick leave due to psychiatric sufferings. Mental health conditions are of great consequence, not only to the sick-listed individual, but also to his/her family and to society in general.

Aim: The aim of the study is to systematically compare psychoeducation with the various standard offers to sick listed individuals with mental health conditions.

Methods: The study is designed as an RCT in which 400 sick-listed individuals are offered either 1) psychoeducation as well as the standard offer (intervention group) or 2) solely the standard offer (control group).

The applied psychoeducation focuses on stress and work life, and its purpose is to impart knowledge about psychiatric conditions in order to provide the sick-listed individuals with qualifications to understand and, thereby, improve their own situation.

The target group consists of recently sick-listed individuals with mental health issues - whether diagnosed or not. The individuals must be inhabitants of the municipalities of Struer, Lemvig, Skive, or Holstebro. The recruitment to the study began in September 2012 and is expected to end in January 2014.

The outcome measure is determined as the duration of the sickness absence, the severity of the psychiatric condition, self-evaluated health, and 'locus of control'. These outcome measurements are assessed at baseline and after 3 and 6 months.

P04.04 Anne Mette Falstie-Jensen ACCREDITATION IN THE DANISH HEALTHCARE SYSTEM: THE DANISH HEALTHCARE QUALITY PROGRAMME

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Introduction: The Institute for Quality and Accreditation in Healthcare was founded in 2005 to develop and manage the Danish Healthcare Quality Programme (DDKM). The first version was launched in 2009.

Objective: To describe the content of the DDKM and present the accreditation results from 2010 to 2012.

Setting: All public hospitals (39) and pre-hospital services (15) participated together with 36 private hospitals, 208 pharmacies and two municipalities.

Methods: The DDKM is developed in collaboration with stakeholders and consists of standards divided in measurable elements using the Plan-Do-Check-Act circle. Trained surveyors conduct on-site surveys to assess compliance using published rating principles and, based on these findings,

the Accreditation Award Committee awards the accreditation status.

Main outcome measures: Accreditation results and experiences with the on-site surveys.

Results: From 2010 to 2012, the majority of the hospitals were "accredited with comments" after the first proceeding while the majority of the pharmacies and the pre-hospital services were "accredited". In the final proceeding, all but eight organisations were awarded "accredited" status and only one organisation was "not accredited". The surveyed organisations and the surveyors in general reported positive experiences with the on-site survey. The organisations believed that the DDKM contributed more to organisational quality than to clinical or patient-experienced quality, however, the surveys primarily revealed previously known issues.

Conclusion: The vast majority of surveyed organisations were accredited in the first round of DDKM, and the overall experience with the on-site survey was considered positive.

P04.05 Anna Budtz-Lilly BODILY DISTRESS SYNDROME IN PRIMARY CARE: PREVALENCE AND PATIENT CHARACTERISTICS

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Objective: Medically unexplained, or functional, symptoms and disorders are common in primary care. Empirical research has proposed specific criteria for a new unifying diagnosis for functional disorders and syndromes: Bodily Distress Syndrome (BDS). The objective of this study was to estimate the prevalence of BDS and describe the characteristics of patients with BDS in primary care.

Method: A population-based cross-sectional study of primary care patients. Data were obtained from patient questionnaires, one-page general practitioner (GP) registration forms and national registers. Individuals with BDS were compared to individuals not fulfilling the criteria for BDS.

Results: We will present data on the prevalence of BDS in a primary care population and characteristics of patients with BDS, e.g. age, gender, self-evaluated health, health anxiety and mental health and sociodemographics.

Conclusion: Results from this study will contribute to the development of a clinically useful diagnostic classification for primary care patients with functional symptoms. These patients are currently poorly described in the classification systems. Improved diagnostic classification in primary care will provide the basis for future management strategies and enhanced patient care.

P04.06 Kirsten Høj PREVALENCE AND CHARACTERISTICS OF DANISH ADULTS WITH POOR

CARDIORESPIRATORY FITNESS: A CROSS-SECTIONAL STUDY

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Background: Improving cardiorespiratory fitness (CRF) increases health state and reduces mortality, especially at the lowest end of the fitness spectrum. Our aim was to assess the prevalence of Danish adults with low and very low CRF and to describe clinical and lifestyle characteristics of these groups.

Methods: A cross-sectional study of 2,650 Danish adults aged 30-49 years included in the community-based health promotion program "CORE". CRF (ml O₂/min/kg) was measured by submaximal cycle ergometer testing. Clinical and lifestyle measures were assessed using clinical examinations and questionnaires, incl. Short Form-12, version 2, Health Survey.

Results: The prevalence of low and very low CRF was 23% and 41%. Differences between the low and very low CRF groups were observed for: BMI \geq 30 kg/m² (women 15% vs. 38%, men 8% vs. 33%), waist circumference $>$ 80/94 cm (women 62% vs. 83%, men 39% vs. 67%), total cholesterol $>$ 5 mmol/L (women 30% vs. 61%, men 43% vs. 57%), poor self-rated health (women 10% vs. 17%, men 4% vs. 12%) and reporting of "No physical activity" (women 11% vs. 17%, men 5% vs. 16%) (all p-values $<$ 0.05). The prevalence of elevated diastolic ($>$ 90 mmHg), but not systolic ($>$ 140 mmHg), blood pressure was significantly higher in the very low CRF group. Age, tobacco and alcohol did not differ between groups.

Conclusion: The prevalence of low or very low CRF is high in Danish adults. Individuals with very low CRF differ significantly from those with low CRF by having the highest prevalence of adverse clinical measures, poor self-rated health and physical inactivity.

P04.07 Lene Hellmund RETURN TO WORK AND QUALITY OF LIFE AFTER SEVERE TRAUMATIC BRAIN INJURY. EFFECT OF DIFFERENT REHABILITATION SET-UPS

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Background: In 2004, the Danish Head Trauma Database (DHD) was established. It is assumed that the database covers the national population of patients with severe traumatic brain injury (TBI). The database has not been used for research yet. High quality of life (QOL) may be associated with labor market attachment. However, studies reveal ambiguous prognostic factors for return to work after TBI, and the reported proportions of patients that return to work are inconclusive. This uncertainty may be due to complex interactions of many factors, including rehabilitation services. In Denmark, the rehabilitation services partly depend on the residence of the patient.

Aims:

1. To validate DHD as data basis for the following studies.
2. To describe return to work and QOL after severe TBI compared to a background population.
3. To examine the effect of centralized vs. decentralized hospital-based neurorehabilitation on return to work and QOL.
4. To examine the effect of rehabilitation in large municipalities vs. small municipalities on return to work and QOL.

Design: Register-based cohort study.

Method: Data from medical charts and Danish nationwide registers are used to assess national completeness and the validity of selected parameters from DHD. After validation, patients injured between 2004 and 2012 are identified from DHD and matched with a background population through Statistics Denmark. Data on return to work is obtained from a nationwide register on public transfer payments and will be analysed as time-to-event data. QOL is obtained through a questionnaire and will be analysed with logistic regression.

P04.08 Anneli Clea
Skjelmose
Bolund

FARMING EXPOSURE IMPAIRS LUNG FUNCTION IN YOUNG ADULTS - A 15-YEAR FOLLOW-UP STUDY

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Background: Organic dust exposure in farming has a negative effect on lung function in older adults. Longitudinal studies on lung function in young farmers are few.

Aim: Our aim was to explore if farming exposure suppresses lung function in young adults.

Methods: We studied 1,964 farming students and 407 controls in 1992-1994, and 963 and 172 of these again at follow-up in 2007-2008. Spirometry, skin prick test, bronchial hyper-responsiveness (BHR), height, and weight were measured, and questionnaires collected. Cumulative dust and endotoxin exposures were estimated based on personal dust measurements. Lung function effect was expressed as change in z-score during follow-up compared to a reference population (Global Lung Initiative 2012).

Results: Longitudinal data were available for 1134 subjects with age <25 years at baseline. Adjusted multivariate linear regression analyses showed that current farming adversely affected $\Delta zFEV_1$ versus never farming with mean (95%CI) of 0.13 (0.25 to 0.02), and on $\Delta zFVC$ of 0.18 (0.30 to 0.06). For a male current farmer and a male control, standardized to age=25 years and height=175 cm, the z-score differences are equivalent to -67 mL

in FEV1 and -112 mL in FVC during follow-up. Only Δ zFVC for the 3rd quartile of endotoxin exposure differed from the 1st quartile by 0.16 (0.26 to 0.06), with similar results for dust exposure. There was no effect modification by smoking or sex. Farm upbringing attenuated the negative effect of baseline BHR on lung function.

Conclusion: We conclude that farming exposure negatively affects lung function in young adults. Those most heavily exposed were not affected, possibly reflecting healthy worker selection.

P05.01 Mette Skovgaard Christensen

EXPOSURE TO STYRENE AND RISK OF CANCER: A 40-YEAR FOLLOW-UP STUDY OF WORKERS IN THE DANISH REINFORCED PLASTICS INDUSTRY

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Background: Styrene is an economically important chemical used in the production of reinforced plastics among other things. In the past decades, studies of workers exposed to styrene have shown diverse results according to the risk of cancer. In 2002, IARC classified styrene as possibly carcinogenic to humans. In 2011, styrene was included in the 12th Report on Carcinogens. However, it is still widely discussed if this classification is correct.

Aim: The aim of this study is to investigate whether exposure to styrene increases the risk of cancer among workers in the Danish reinforced plastics industry.

Materials and methods: The study is based on a list of 481 companies ever producing reinforced plastics with the use of styrene in Denmark (1964-2009). Workers are identified with help from the Danish Supplementary Pension Fund Register. The study population consists of approx. 75,000 workers, expected to accumulate approx. 1,800,000 person years. 15,000 living subjects are invited to participate in an individual survey about work and confounder information. The exposure assessment is based on a matrix consisting of styrene measurements collected from the companies and company information (process, product, calendar year). The matrix is going to classify each worker with an estimate of exposure probability and level of exposure. Outcome information is found in the registries (Danish Cancer Registry, National Pathology Registry, and National Patient Registry) along with confounder information (Statistics Denmark and self-reported data). As reference group, we will use the whole Danish work force born after year 1900 and defined by payments to the Danish Supplementary Pension Fund.

P05.02 Anita Eskildsen

THE DANISH VERSION OF THE 10-ITEM PERCEIVED STRESS SCALE: TOWARDS NATIONAL CONSENSUS

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Background: The 10-item Perceived Stress Scale (PSS-10) is a global stress measure developed to assess the extent to which individuals find their lives to be unpredictable, uncontrollable, and overloaded. At least three different Danish translations of the PSS-10 have been used in different research projects. However, none of these have been formally validated in a Danish-speaking population.

Aim: The aim of the present ongoing study was twofold: First to develop and cross-culturally adapt a Danish consensus version of the PSS-10 and, second, to examine face validity.

Methods: The three researchers who had previously translated the PSS-10 into Danish, agreed to participate in a consensus building process. A new Danish consensus version was formulated based on the previous Danish translations and the original English version. The consensus version was back-translated into English according to international standards. Interviews with 6 patients with work-related stress complaints were conducted to examine face validity.

Results: The interviews showed that all items of the PSS-10 were well understood and patients found it easy to complete.

Perspectives: Further validation of the consensus version, in terms of minimum detectable change, responsiveness and minimal clinically important change, is on-going in a sample of 120 individuals: 60 patients with work-related stress complaints seen at the Dept. of Occupational Medicine, the Regional Hospital Herning, and 60 healthy matched controls.

P05.03 Maiken Ina
Siegismund
Kjærsgaard

EFFECT OF PSYCHOLOGICAL TREATMENT OF BEREAVED INDIVIDUALS ON SICK LEAVE: A POPULATION-BASED STUDY USING INSTRUMENTAL VARIABLE ANALYSIS

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Background: Randomized control trial (RCT) is the gold standard among research designs. However, treatment choice cannot always be based on RCTs. When evidence-based treatment is lacking, general practitioners (GPs) may develop different treatment preferences. Using a specific statistical model, this particular variation may be deployed in order to attain results that resemble those from RCTs. In Denmark, GPs can refer bereaved people to subsidized treatment with a psychologist. The effect of psychological treatment of bereaved people on sick leave is poorly understood as it is difficult to separate the effect of psychological treatment

from the effect of the underlying mental condition on sick leave.

Aim: Evaluate the effect of psychological treatment on sick leave in a cohort of individuals who lost a spouse or a first-degree relative using the instrumental variable method. In particular, evaluate if treatment prevents sick leave, and evaluate if treatment reduces the duration of sick leave among those sick-listed.

Materials and method: A patient listed with a GP who frequently refers patients to psychologists is more likely to get referred than if listed with a GP who rarely refers patients to psychologists. The instrumental variable method can be used to study the effect of this natural experiment to provide better evidence on psychological treatment in bereaved people. Data will be extracted from national Danish registers.

Perspectives: Evaluation of psychological treatment in bereaved people can inform treatment choices for GPs' referral practices.

P05.04 Maria Theresa Wimberley
Böttger

PROGNOSTIC FACTORS FOR TREATMENT RESISTANCE IN SCHIZOPHRENIA
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Background: Treatment-resistant schizophrenia (TRS) affects approximately 30% of patients with schizophrenia (SZ). Clozapine (CLZ) is recommended in TRS, but is considered to be underused.

Objective: To determine baseline factors predictive of TRS.

Methods: Danish population-based cohort study on patients with incident SZ between 1996 and 2006 and followed until 2010. We analyzed the following definitions of TRS. TRS A: CLZ initiation, TRS B: TRS A or eligibility for clozapine, and TRS C: TRS B or antipsychotic polypharmacy. Cox proportional hazards regression analysis was conducted on a set of candidate prognostic factors.

Results: Among 8,632 patients with SZ, percentages with TRS during follow-up (median 9.1 years, IQR: 6.3-11.9) were 13.2% (TRS A), 31.8% (TRS B) and 44.5% (TRS C). In the multivariable model including patient- and disease-related factors at first SZ diagnosis, rural living, age at onset, psychiatric hospitalization, antipsychotics, benzodiazepines, suicide attempt, diagnosis of personality disorder, and paranoid subtype were significantly associated with increased rate of TRS, regardless of definition of TRS: Female sex was associated with increased rates of TRS B and C.

Conclusions: Several disease-related factors were associated with increased TRS incidence. Overall, associations were similar for TRS A, B and C, but were in general stronger for TRS A. The patient-related factors lower age at onset, female sex and rural living were associated with increased TRS incidence. The factors identified in this study could potentially be

included in a prognostic model to detect TRS early after diagnosis.

P05.05 Kathrine Bang
Laursen GEOGRAPHIC VARIATION IN THE PREVALENCE OF ADHD

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Background: In Denmark as well as in several other countries, the incidence of ADHD has been increasing for the last decades. By mapping the geographic variation in the occurrence of ADHD, we expect to detect patterns that develop our understanding of this disorder.

Objective: We aim to explore the use of GIS in displaying geographic patterns of the distribution of different indicators of ADHD.

Methods: Our study population include all children born in Denmark between 1 January 1990 and 31 December 2005. We combine the use of register data from the Medical Birth Registry, the National Patient Registry on ICD-10 diagnosis of Hyperkinetic disorder (HKD) and the National Prescription Database on ADHD medication. Also psychometric data from the National Birth Cohort (DNBC) were used to show the prevalence of children with an abnormal hyperactivity score at the age of 7 measured with the Strenght and Difficulties Questionnaire (SDQ).

Results: The preliminary results show an overall prevalence of 1.4% (95% CI: 1.395; 1.440) children diagnosed with HKD while 5.2% (95% CI: 4.996; 5.366) children from the DNBC had an abnormal SDQ hyperactivity score. There were no associations between the diagnostic prevalence and the prevalence of children with an abnormal SDQ score in the municipalities. We will present GIS maps showing the geographic variation.

Conclusion: A large regional variation is seen in the diagnostic prevalence of ADHD while no obvious pattern is emerging from the SDQ data from DNBC. These differences may indicate that the geographic variation in the diagnostic prevalence may be due to differences in the diagnostic practices or access to diagnostic facilities.

P05.06 Susanne
Hvolgaard
Mikkelsen MATERNAL AGE AND ADHD IN THE OFFSPRING

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Background: One of the most common childhoods psychiatric disorder is attention-deficit/hyperactivity disorder [ADHD] with an estimated prevalence of 3-5 % in a general population. ADHD frequently co-occurs with other emotional and developmental problems such as conduct disorder, depression and anxiety.

Twin and adoption studies suggest that genetic influences contribute substantially to its etiology, but environmental factors may also play a

substantial role.

A few previous studies have reported that parents of children with ADHD are younger than other parents, but to our knowledge no studies have attempted to explore the cause of this difference.

Objectives: The aim of this study was to explore the association between maternal age and ADHD in the offspring.

Methods: A study cohort of 1.061.207 children was identified in the Danish Medical Birth Registry as all children born in the period January, 1990 through December, 2005. Children with ADHD were identified by using a combination of the ICD-10 Hyperkinetic Disorder [HKD] diagnosis and prescription of ADHD medicine.

Results: A total of 14,265 children (1,3%) had the HKD diagnoses. The risk of ADHD in the offspring increased with decreased maternal age: RR=3.36(3.11-3.63); 2.15(2.03-2.28); 1.36(1.29-1.44) and 1.03(0.97-1.09) in the maternal age categories: <21; 21-25; 26-30; 31-35, respectively when compared to the oldest category of maternal age >36 years.

The risk of ADHD increased further with decreased paternal age.

Conclusions: Decreasing parental age is associated with increasing risk of ADHD in the offspring. We plan to do sibling analysis, to study if this association can be accounted for by genetic factors.

P05.07 Line Hvidberg CANCER AWARENESS AND ASSOCIATION WITH SOCIO-ECONOMIC POSITION: RESULTS FROM A POPULATION-BASED STUDY IN DENMARK

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Background: There are large variations in cancer survival between countries. Also within Denmark, there are marked variations in survival between patients with the same cancer disease, often disproportionately affecting people with lower socio-economic position (SEP). The factors that contribute to these variations are complex, but in recent years, there has been a focus on differences in cancer awareness as a potential contributor due to its possible association with health-care seeking, which may ultimately affect cancer stage and survival.

Aim: To determine the awareness of cancer symptoms, risk factors and survivability in a Danish population sample and to analyse the association with SEP.

Methods: A population-based telephone survey was carried out among 1,000 respondents aged 30-49 and 2,000 respondents aged 50+ using the Awareness and Beliefs about Cancer measure. Data on SEP were obtained from Statistics Denmark. Prevalence ratios were used to determine the association between SEP and cancer awareness.

Results: A strong socio-economic gradient was found for cancer awareness.

Thus, people with a lower educational level and lower household income were more likely to have lower awareness of possible cancer symptoms and of the factors that can influence the risk of cancer. Also respondents with a low household income were more likely than people with a high household income to underestimate or overestimate the 5-year survival for three out of four cancer types.

Perspectives: Cancer awareness will often be a first step in the sequence that leads to e.g. health-care seeking. Thus, interventions to increase cancer awareness should be targeted people with lower SEP.

P05.08 Ethel Mary
Brinda
Alexander

DECOMPOSITION OF SOCIOECONOMIC INEQUALITIES IN SELF-RATED HEALTH AND HEALTH SERVICE UTILIZATION AMONG OLDER PEOPLE IN INDIA: THE WHO STUDY ON GLOBAL AGEING AND ADULT HEALTH (SAGE)

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Background: Growing socioeconomic inequities is a global concern, which affects health and healthcare in developing countries. Measurement of inequity aids to identify their contributors for specific targeted interventions. We aimed to measure and quantify the contribution of determinants of poor self-rated health (SRH) as well as health service utilization to socioeconomic inequity among older people in India.

Methods: We accessed a nationally representative multistage, stratified random sample of 2414 older people aged above 65 years from WHO-SAGE Indian survey. Socioeconomic status was constructed using principle component analysis. We estimated concentration index to measure socioeconomic inequity. Regression-based decomposition analysis was employed to identify contribution of observed determinants of poor SRH and health service utilization to socioeconomic inequity.

Results: The concentration indices of socioeconomic inequity in poor SRH and health service utilization were -0.118 (95%CI -0.10, -0.13) and 0.123 (95%CI 0.11, 0.14), respectively. The decomposition analysis revealed that economic status (32%) and disability (23.6%) contributed to the socioeconomic inequity in health service utilization. Economic status (60.2%), pension support (14.4%) and illiteracy (10.2%) were the main contributors of inequity in poor SRH among older Indians.

Conclusion: Achievement of health equity is valuable in its own right. Unequal distribution of health and healthcare are infiltrated by social determinants. Attention to social welfare policies can overcome the existing health and healthcare inequities among economically disadvantaged people.

P06.01 Cathrine
Ladegaard
Wildenschild
Nielsen

GESTATIONAL AGE AT BIRTH AND SUBSEQUENT FECUNDABILITY

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Background: Women born preterm may have decreased fertility, but there are little data on the cycle-specific probability of conception (fecundability). Furthermore, the impact of family history of preterm birth on fecundability has not been studied.

Materials and methods: We included 2,814 pregnancy planners participating in a prospective cohort study. Self-reported data on time to pregnancy were linked to data on the women's gestational age from the Danish Medical Birth Registry. Using proportional probabilities regression models, we estimated fecundability ratios (FR) and 95% confidence intervals (CI) for women born early preterm.

P06.02 Henriette Holm SUBARACHNOID HEMORRHAGE IN DENMARK: RISK AND PROGNOSIS
 Stabel

H.H. Stabel

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In Denmark, approximately 500 people experience a subarachnoid hemorrhage (SAH) each year; the average age is 50 years. SAH is a life threatening bleeding in the brain's system of arteries, which tends to strike down suddenly and mostly without warning. Even if treatment procedures and outcome have improved over the last decades, it still carries a high mortality rate as 50% of all patients die within the first 6 months. Those who survive are often left with physical, psychological, cognitive and social impairments which have major consequences for daily living and the lives of relatives. Also people's health-related quality-of-life and possibility to carry on an employment are affected.

The aim of this study is to contribute to the knowledge of non-traumatic SAH in Denmark and its consequences concerning patient survival, return-to-work, and functional outcome at hospital discharge. Also predictors for outcome at hospital discharge and long-term outcome in relation to activities-of-daily-living, base income, social status and health-related quality-of-life are examined. The study consists of a national population-based cohort study and a historical cohort study among patients who have received specialized interdisciplinary neurorehabilitation at Regionshospitalet Hammel Neurocenter. Data are collected from national registries, a local neurodatabase and a self-administrated questionnaire survey.

Study results will contribute to the existing knowledge of consequences of SAH and may also contribute to development of new as well as existing rehabilitation initiatives. Results can also form part of the priority of available health care resources in both regional and community settings.

P06.03 Holger Borup PREAMISSION STATIN USE IS ASSOCIATED WITH LOWER MORTALITY
 Wemmelund AFTER RUPTURE OF ABDOMINAL AORTIC ANEURYSM

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Objective: Rupture of abdominal aortic aneurysms (rAAA) is associated with high mortality. Statins reduce risk of cardiovascular events and death. Research suggests that statins may improve rAAA outcomes. We examined the association between preadmission statin use and 30-day mortality after rAAA in a large nationwide, population-based study.

Methods: We conducted a follow-up study among all patients with an incident diagnosis of rAAA in Denmark from 1996 through 2008 using Danish population-based registries. We obtained data on all filled statin prescriptions prior to admission with rAAA. We estimated 30-day mortality rate ratios (MRRs) with 95% confidence intervals (CI) associated with current statin use, using Cox proportional hazards regression analysis. Results were adjusted for age, sex, comorbidity, concomitant drug use, calendar year and socioeconomic factors.

Results: We identified 3,691 rAAA patients, 428 (11.6%) of whom were current statin users. Statin users had substantially more comorbidity, in particular cardiovascular diseases. The overall 30-day mortality rate among rAAA patients was 46.1% in current statin users compared with 59.3% in never users (adjusted MRR 0.80, 95% CI: 0.68 to 0.95). Patients who had formerly used statins, but had no current statin use, did not have reduced mortality (adjusted MRR 0.98, 95% CI: 0.78 to 1.22).

Conclusion: Preadmission statin use is associated with lower mortality after rAAA. These results provide support for current guidelines that recommend the initiation of prophylactic statin treatment in asymptomatic patients diagnosed with AAA.

P06.04 Peter Asdahl

LATE GASTROINTESTINAL MORBIDITY IN CHILDHOOD CANCER SURVIVORS: A NORDIC POPULATION BASED COHORT STUDY

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Background: Today, four out of five childhood cancer patients can expect to become long-term survivors. Among this growing population, many late-onset treatment-related health consequences have been documented. Late effects within the gastrointestinal system have only been sparsely described.

Aim: To investigate late gastrointestinal morbidity among childhood cancer survivors.

Methods: Adult Life After Childhood Cancer in Scandinavia (ALiCCS.org) is an inter-Nordic collaboration investigating late effects of childhood cancer therapy. We identified all patients diagnosed with cancer under the age of

20 in the Nordic countries in the last six decades. We used population-based registries to find information on hospital admissions and deaths. For each one-year survivor, we randomly selected five comparisons of same age and country of origin.

Results: The 31 132 one-year survivors had a total of 4 916 first time hospital contacts for gastrointestinal disease. The overall standardized hospitalization rate ratio (SHRR) was 1.5 (95% Confidence Interval (CI): 1.5 to 1.6) and the overall absolute excess risk (AER) was 419 (95% CI: 385 to 454) extra hospital contacts per 100 000 person years. Of six main diagnostic groups, liver diseases had the highest SHRR (2.8 (95% CI: 2.5 to 3.1)) and intestinal diseases had the highest AER (216 per 100 000 person years (95% CI: 191 to 240)). The strongest association to gastrointestinal morbidity was seen among survivors of hepatic tumors, neuroblastoma and leukemia.

Conclusion: Survivors of childhood cancer are at an increased risk of gastrointestinal diseases. The risk varies according to the childhood cancer diagnosis.

P06.05 Laura Ozer
Kettner

ASSISTED REPRODUCTION TECHNOLOGY AND POST-NEONATAL SOMATIC MORBIDITY - A SYSTEMATIC REVIEW OF COHORT AND CASE-CONTROL STUDIES

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Background: Ten percent of all deliveries in Denmark result from fertility treatment, and it is, therefore, crucial to consider the safety aspects.

Objective: To assess if children conceived by assisted reproduction technology (ART) are at increased risk of post-neonatal somatic morbidity compared with spontaneously conceived children.

Methods: Medline/Pubmed, Embase and The Cochrane Library were searched on May 20, 2013. Studies were included in the review if the main outcome was a somatic disease/disease category, which can arise beyond the neonatal period. Furthermore, health care contacts, chronic illnesses, surgery, medication use and mortality were considered. Only cohort and case-control studies were included.

To assess the risk of bias in the individual studies, all studies were scored independently by two of the authors, using the Newcastle-Ottawa Scale.

Results: Thirty-eight studies were included. Results indicate that children conceived by ART are at increased risk of leukemia and retinoblastoma, asthma and obstructive bronchitis, genitourinary diseases, and epilepsy or convulsions when compared with spontaneously conceived children. Furthermore, it appears that families with a child conceived by ART seek different primary health care providers than families with a spontaneously conceived child and that children conceived by ART are hospitalized

longer per admission, compared with spontaneously conceived children.

Conclusion: Children conceived by ART may be at increased risk of specific post-neonatal somatic diseases compared to spontaneously conceived children.

P06.06 Eva Natalia
Glassou

RISK OF READMISSION, REOPERATION AND MORTALITY FOLLOWING TOTAL HIP AND KNEE ARTHROPLASTY IN FAST-TRACK DEPARTMENTS IN DENMARK

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Objective: To examine if orthopedic departments with well documented fast-track arthroplasty programs had lower rates of readmission, reoperation and mortality 90 days postoperatively in patients treated with total hip or knee arthroplasty compared to all other orthopedic departments from 2005 to 2011.

Method: The Danish Hip and Knee Arthroplasty Registers were used to identify patients with primary total hip and knee arthroplasty from 2005 to 2011. Information about adverse events was obtained from the Danish National Patient Registry and the Civil Registration Registry. The fast-track cohort was defined by participation in the Lundbeck Foundation Centre for Fast Track Hip and Knee Replacement. Regression methods were used to calculate relative risk (RR) for the adverse events adjusting for age, gender, type of fixation and co-morbidity measured with the Charlson Co-morbidity Index.

Results: RR of readmission due to infection was increased in the fast-track cohort in 2005-2007 (1.32, ci 1.10-1.58). This may be explained by a shorter length of stay at index procedure in the fast-track cohort (4 vs. 6 days). An infection leading to readmission would in this cohort be recorded, while an analog infection in the control cohort, while still in hospital, might not be. RR of readmission due to thrombotic event was reduced in the fast-track cohort in 2010-2011 (0.73, ci 0.58-0.94). This can be explained by the early mobilization - 2 to 4 hours postoperatively - in the fast-track cohort.

Conclusion: The quality of treatment in orthopedic departments with documented fast-track arthroplasty programs was comparable to the general treatment of total hip and knee arthroplasty in Denmark.

P06.07 Anne Birgitte
Simonsen

CONTACT ALLERGY IN DANISH CHILDREN WITH ATOPIC DERMATITIS

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Background: Although previously considered rare, recent studies indicate that allergic contact dermatitis (ACD) is a highly relevant diagnosis in children. Contact allergy could be an aggravating factor contributing to the disease burden of atopic dermatitis, and several authors have stressed the risk of overlooking ACD in this patient group.

Objectives: To describe the demographic characteristics of Danish children referred for patch testing, and to examine the frequency of contact allergy among children with concurrent AD.

Methods: We performed a retrospective analysis based on data from The Danish National Database for Contact Allergy. From 1 January 2003 to 31 December 2011, a total of 2594 patients aged 1-17 were patch tested in 12 dermatological clinics throughout Denmark. All patients either suffered from recalcitrant eczema or had a suspected diagnosis of allergic contact dermatitis.

Results: 1710 girls and 884 boys were suspected of having ACD. Contact allergy to at least one allergen was found in 25.1% (n=651). Of all children, 44.8% (n=1161) had concurrent atopic dermatitis and the sensitization rate among these patients was 21.2% (n=246). The most common allergens overall were metals, fragrance, rubber chemicals, hair dyes, and preservatives.

Conclusions: ACD is a relevant diagnosis in both children with and without atopic dermatitis, and it should always be considered when encountering children with recalcitrant eczema. Children with atopic dermatitis were less likely to have contact allergy compared to children without atopic dermatitis, which calls for further elucidation.

P06.08 Thomas
Deleuran

ALCOHOLIC LIVER DISEASE IN DENMARK IN 2006-2011:
A POPULATION-BASED DESCRIPTIVE STUDY

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Background: The alcohol consumption per capita in Denmark is among the highest in Northern Europe, but the epidemiology of alcoholic liver disease in recent years is unknown. We describe incidence, prevalence, hospitalization rates, and patient survival for alcoholic liver disease in Denmark in 2006-2011.

Methods: We identified all Danish citizens with a hospital discharge diagnosis of alcoholic liver disease in the Danish National Patient Registry and computed age-specific incidence for the 1930-1970 birth cohorts and age- and gender-standardized incidence, prevalence, and hospitalization rates for the calendar years 2006-2011. The Kaplan-Meier method was used to estimate 1- and 5- year survival from ALD diagnosis.

Results: Persons born in 1945-1959 had higher age-specific incidence rates of alcoholic liver disease than earlier and later birth cohorts. Therefore, the incidence rate increased during 2006-2011 among persons aged 65 years or older and decreased among younger persons. Between 2006 and 2011, the overall incidence rate decreased from 343 (95% CI: 325-375) to 312 (95% CI: 297-326) per 1,000,000 population per year. The prevalence (0.2% of the Danish population) and hospitalization rate (1.2 per ALD patient per year) did not change. The overall 1- and 5- year survival probabilities were

70.2% (95% CI: 69.3-71.1%) and 43.5% (95% CI: 42.1-44.8%).

Conclusion: The incidence of alcoholic liver disease in Denmark decreased in 2006-2011. We expect the incidence to decrease further in the future owing to the declining incidence rate in younger citizens.

P07.01 Lene Sofie
Granfeldt
Østgård

DELAYING CHEMOTHERAPY DOES AFFECT LONG-TERM SURVIVAL IN BOTH YOUNGER AND OLDER AML PATIENTS. A DANISH POPULATION-BASED COHORT STUDY OF 1388 AML PATIENTS

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Acute myeloid leukemia (AML) in younger patients is generally accepted as a hematological emergency, and rapid initiation of chemotherapy is essential to avoid acute complications. Whether delay of chemotherapy affects the chance of complete remission (CR) and long-term mortality is not sufficiently examined.

We, therefore, examined the effect of time from diagnosis to treatment initiation (TTT) on CR rates, short- and long-term in a national population-based cohort study of 1388 AML patients who were allocated to intensive chemotherapy and diagnosed in Denmark during 2000-2012. Information on patient, disease and treatment characteristics was obtained from the DNLR and comorbidity from the Danish National Registry of Patients.

We did not find TTT beyond day 5 to be adversely related to achievement of CR. Neither did we find the 30-day adjusted mortality ratios (aMR) to increase with longer TTT. For patients younger than 60 years, long-term mortality (30-days to 3-years MRs, reference TTT=day 3-4) increased for TTT beyond 10 days (1.57 95% CI (1.05-2.35)). In patients 60 years and older, especially with secondary/treatment-related AML (sAML/tAML), aMRs increased with TTT as early as from day 5 (age \geq 60 years: TTT=day 5-10: 1.50 95% CI (1.07-2.12), TTT> 10 days: 2.03 95% CI (1.41; 2.92), age \geq 60 years and sAML/tAML: TTT=day 5-10: 3.41 95% CI (1.32; 8.76), TTT>10 days: 4.91 95% CI (1.81; 13.34)).

In conclusion, delaying treatment beyond day 5 in older patients and patients with sAML/tAML may adversely affect survival. If necessary for optimizing therapy, a delay up to day 10 in younger patients and older de novo patients does not seem to affect prognosis.

P07.02 Rasmus
Offersen

LATENCY-REVERSING AGENTS EFFECT ON HIV-1 TRANSCRIPTION IN A PHYSIOLOGICAL PBMC SET-UP

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Background: In the pursuit of an HIV cure, various in vitro models of HIV latency are being used to evaluate Latency-Reversing Agents (LRA). These models, however, do not reflect the heterogeneity in vivo. Thus, possible indirect effects of LRA may be overlooked. TLR9 agonists have been suggested as LRA, but cannot reactivate latently infected primary CD4⁺ T cells (which lack TLR9 receptors) in vitro. However, clinical studies have suggested that TLR9 agonists may impact the HIV reservoir.

To reflect the in vivo complexity and to evaluate the utility of TLR9 agonist based therapy, we have developed a novel physiological in vitro setup based on stimulated PBMCs from HIV patients.

Methodology: PBMCs from HIV-infected donors were stimulated with a TLR9-agonist, the HDAC-inhibitor panobinostat, CD3/CD28 as positive control or media (9×10^6 /stimuli). Subsequently, RNA was extracted from 1×10^6 purified CD4⁺ T cells/stimuli. Unspliced (US) HIV RNA was measured using a semi-nested RT-qPCR. 18S was used as reference gene.

Results: The observed fold-increase (median, [range]) in HIV-transcription was: CpG2006 2 ug/ml: 1.96 [0.8-4.1]; CpG2006 5 ug/ml: 3.33 [0.75-4.18]; panobinostat 7.5 nM: 3.93 [1.75-5.66]; positive control CD3/CD28: 2.62 [1.33-7.78] ($p < 0.001$ for each stimuli by Wilcoxon signed rank test). High-dose panobinostat (50 nM) induced the largest increase in US HIV RNA of all tested compounds (9.98 [6.75-62.5]).

Conclusions: This novel PBMC-based HIV latency set-up allows for studies of the single and combinatorial effects of agents acting on different cell types. Further, our findings support the results from clinical studies of TLR9 agonist based therapy acting as a LRA.

P07.03 Mette Thorgaard HEALTH ANXIETY AND ILLNESS BEHAVIOUR IN CHILDREN OF MOTHERS WITH SEVERE HEALTH ANXIETY

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Background: The current knowledge about health anxiety (HA) is limited in children and adolescents. Retrospective studies suggest that HA may originate in childhood and that intergenerational transmission could be an important mechanism for the occurrence of HA early in life.

Objective: To examine 1. The syndrome construct and symptoms of HA in three groups of children and 2. If children of mothers with severe HA compared to children of mothers with a well defined chronic physical disease and children of healthy mothers are more worried about health and illness, display more illness behaviour and experience more symptoms of other emotional mental disorders.

Methods: 150 children aged 8-17 years and their parents will be included.

Group 1: 50 children of mothers with severe HA.

Group 2: 50 children of mothers with rheumatoid arthritis.
Group 3: 50 children of healthy mothers.

The children and mothers will fill out standardized questionnaires about physical symptoms, health anxiety, general psychopathology and life quality. Furthermore, the children will undergo a physical examination. The fathers will be asked to fill out standardized questionnaires regarding their physical and mental health.

Finally, data on the child's contacts to the doctor and absence from school due to illness will be collected.

Results: Preliminary data will be presented.

Perspectives: This study will be one of the first steps to provide data on whether HA can be identified as a distinct disorder in childhood. In addition, the results will contribute with knowledge on the putative risk of intergenerational transmission of HA.

P07.04 Kirstine
Kobberøe
Søgaard

PEPTIC ULCER AND SUBSEQUENT RISK OF GASTROINTESTINAL CANCER: A NATIONWIDE COHORT STUDY

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Background: *Helicobacter pylori* play a key role in the pathogenesis of both peptic ulcer disease and gastric cancer. *Helicobacter pylori* infections also increase the risk of colorectal cancer, whereas it possibly decreases the risk of esophageal cancer, though the evidence is less clear. We examined the gastrointestinal cancer risk after admission with peptic ulcer disease.

Methods: We conducted a nationwide population-based cohort study of all Danes with a first inpatient or outpatient diagnosis of peptic ulcer from 1994-2011. Follow-up for cancer began at the admission during which ulcer was diagnosed and ended on December 2011. We quantified the excess risk of gastrointestinal cancers among peptic ulcer patients compared to the expected risk in the general population, using standardized incidence ratios (SIRs).

Results: We identified 126,759 patients with a first-time ulcer diagnosis. During the first 6 months, the SIRs for cancers of the stomach and small intestine were 54.6 (51.0-58.4) and 40.7 (31.7-51.4), respectively. We also observed a notable increased risk for esophageal (9.6 [7.8-11.7]), colon (7.4 [6.8-8.1]), liver (17.8 [14.9-21.1]), and gallbladder or biliary tract (13.7 [10.8-17.2]) cancers. The risk of cancer was attenuated during the 6-12 months following the ulcer diagnosis. Still, an increased risk persisted for most gastrointestinal cancers beyond one year after the admission with ulcer disease; the SIRs for colon, esophageal, and liver cancer were 1.1 (1.1-1.2), 1.5 (1.2-1.7), and 3.2 (2.8-3.6), respectively.

Conclusions: Peptic ulcer is a marker of undiagnosed gastrointestinal cancer, but also predicts an increased risk beyond 1 year of follow-up.

P07.05 Anne Hammer SENSITIVITY OF THREE COMMERCIAL PCR-BASED ASSAYS FOR THE

Lauridsen

DETECTION OF HUMAN PAPILLOMA VIRUS IN A DILUTION STUDY

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Objective: The objective of this study is to evaluate the sensitivity of three commercial assays for the detection and genotyping of Human Papilloma-virus (HPV). Previously, the assays have been compared through HPV genotyping on formalin- fixed, paraffin-embedded tissue or cytological material. The ability of PCR-based assays to detect an HPV infection in samples of only few infected cells in a larger sample of non-infected cells has been unclear until now.

Material and methods: A dilution study was conducted by mixing DNA extracted from HeLa and SiHa cells with DNA extracted from HEK 293 cells in a 10-fold dilutionseries ranging from 1:1000 to 1:10.000.000. Additionally, we diluted HeLa and SiHa cells with HEK 293 cells in a 10-fold dilutionseries. Prior to DNA extraction, all cells were fixed in formalin and embedded in paraffin. Five sections of 10 µm x 1 cm were sliced from each block. The DNA was extracted using QIA-symphony DSP DNA Mini Kit. The extracted DNA was tested for HPV using three commercial assays; HPV sign genotyping test kit (Qiagen), LINEAR ARRAY HPV Genotyping test (Roche), and INNO LiPA Genotyping extra (Innogenetics).

Conclusion: HPV Sign was more sensitive than Inno Lipa and Linear array in detecting HPV 18. It allowed detection of HPV 18 in the cell-dilution and in the DNA-dilution 1:1.000.000. The three assays were equally sensitive in detecting HPV 16 in the DNA-dilution. However, in the cell-dilution, HPV Sign tended to be more sensitive. Thus, it may be possible to detect HPV in a latent phase in epithelial cells of the human cervix. More analyses are needed to verify these results.

P07.06 Jesper Smit

STAPHYLOCOCCUS AUREUS BACTEREMIA AND DIABETES MELLITUS: STUDIES OF RISK AND PROGNOSIS

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Background: Staphylococcus aureus is the 2nd leading cause of bacteremia with a 2:1 proportion of community- vs. hospital-onset cases. SAB is associated with considerable morbidity, mortality and health care expenditure. However, limited data exist on how diabetes mellitus (DM) and other underlying disorders may impact the risk and prognosis of SAB.

Objectives: To ascertain the incidence, risk factors and prognostic factors in patients with community- and hospital-onset SAB with special emphasis on

diabetes mellitus.

Material and methods: Incident cases of SAB are identified in clinical microbiology databases in the North and Central Denmark Regions. The civil registration number allows linkage with administrative and health registries. Patients with DM are identified through an algorithm using registry data. The cohort is expected to include 5,700 patients with SAB. Three epidemiological studies are planned: Study 1 ascertains the incidence of hospital-onset SAB according to primary diagnosis and comorbidity. Study 2 has a matched case-control design and examines whether DM is associated with an increased risk of community-onset SAB. Study 3 evaluates 30-day and 1-year SAB mortality in patients with DM compared to patients without DM and assesses also duration of hospitalization and rate of readmission among the two groups.

Perspectives: This project will extend existing knowledge on incidence and risk factors for community- and hospital-onset SAB as well as the prognosis in these patients with focus on DM. We aim to identify modifiable risk factors in order to improve current prophylactic measures and hence improve the prognosis for this growing patient group.

P07.07 Camilla Askov Mousing PALLIATIVE CARE FOR COPD PATIENTS IN PRIMARY HEALTH CARE - AN INTEGRATIVE REVIEW

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Introduction: The literature suggests that patients with COPD are underserved in the primary sector and receive less palliative care than patients with other diseases with comparable symptoms and prognoses.

Aim: To identify, integrate and interpret the existing body of knowledge on the role and function of the health care professional in their work with palliative care in the primary sector.

Methods: An integrative review of existing literature was conducted. The systematic review included: problem identification, literature search, data evaluation, data analysis and synthesis, and presentation. 332 original papers addressed the health care professionals' experience of palliative approaches to patients with COPD. After detailed review of the abstracts, 11 papers were selected for in depth quality assessment and analysis. All selected papers address, in different ways, the health care professionals' experience of palliative approaches.

Results: Professionals in primary care experience multiple obstacles to palliative approaches, including vague definition of palliative care, unpredictability of the disease, insecurity about their professional role, lack of knowledge and access to advice from COPD specialists, fear of patients'

response and limited time to talk with patients.

Conclusion: A strong association between palliative care and death may be a barrier to having a palliative approach to care. Lack of knowledge and lack of communication skills may affect the role and function of the health professional, as these barriers affect the ability to identify, initiate and evaluate palliative needs and interventions.

P07.08 Charlotte Handberg

MALE CANCER SURVIVORS' BARRIERS TOWARDS PARTICIPATION IN CANCER REHABILITATION - A QUALITATIVE STUDY

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Objective: To describe male cancer survivors' perspectives on their lack of participation in cancer rehabilitation and to establish a specific research-based strategy for male cancer survivors in rehabilitation.

Background: Epidemiological studies indicate that men develop and die sooner from cancer than women. Men have rehabilitation needs, but are underrepresented in cancer rehabilitation where only approximately 16-25% of the participants are male.

Methodology: The study was designed as a qualitative ethnographic field study. Data were generated in three oncology departments and three municipalities in Denmark and include semi-structured and ad hoc individual interviews, participant observation and documents. The theoretical frame is Symbolic Interactionism, and data were analysed by means of Interpretive Description. The informants are 43 male cancer survivors with an average age of 64 and representing nine various types of cancer.

Results: The analysis revealed two overarching categories: 1. fear of losing control and 2. striving for normality.

We identified six themes relating to the overarching categories.

Symbolizes what rehabilitation would enforce:

'Isolation and independence'

'Affected manliness'

'Confrontation with death'

Represents what rehabilitation would hinder:

'Responsibility and usefulness'

'Solidarity and fellowship by choice'

'Forget and move on'

Perspective: To develop a research-based strategy for development of rehabilitation for male cancer survivors.

P08.01 Nis Pedersen Jørgensen

MBEC MEASUREMENT PREDICTS TREATMENT FAILURE IN MURINE BIOFILM INFECTION MODEL OF IMPLANT ASSOCIATED OSTEOMYELITIS

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Background: Biofilms are characterized by reduced susceptibility to antibiotics. Since MIC is evaluated on planktonic growing bacteria, this method is of questionable use in biofilm infections. We investigated the ability of a Minimal Biofilm Eradication Concentration (MBEC) assay to predict antibiotic treatment outcome in a murine model of implant associated osteomyelitis caused by *S. aureus* biofilm formation.

Methods: We used a modified Calgary Biofilm Device to assess MBEC of Vancomycin (Van), Linezolid (Lin) and Daptomycin (Dap) against *S. aureus*. MIC was measured with E-test. We used a murine model to investigate the efficiency of Van, Dap, and Lin as either monotherapy or combination therapy. C57Bl/6 mice received a tibia implant colonized with *Staphylococcus aureus*. 7 groups of 7 animals were used; 3 monotherapy, 3 combination therapy: Van+Dap, Dap+Lin, Lin+Van, and a control group (NaCl). Treatment duration was 14 days.

Results: MIC values: Van 2 µg/ml, Lin 1 µg/ml and Dap 0.38 µg/ml. MBEC values: Van >2048 µg/ml, Lin >1024 µg/ml and Dap > 1024 µg/ml. Dap+Lin and Van+Lin therapy resulted in a greater CFU reduction than other antibiotics (Mann-Whitney test). No significant reduction in CFU for any antibiotic against the biofilm was observed.

Conclusion: This study shows that MIC measurement cannot be used to predict treatment outcome in biofilm associated infections and MBEC measurements better reflect the susceptibility of the bacteria in the biofilm. In addition, the study underlines the difficulties associated with treating mature biofilm infections.

P08.02 Hanne Mari Jørgensen

BONE MASS MEASUREMENTS IN RENAL FAILURE: STUDY PROTOCOL

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Chronic kidney disease (CKD) is associated with a 2-4 fold increase risk of fracture, but there is no consensus on how to identify patients at risk. Bone mineral density (BMD) by dual X-ray absorptiometry (DXA) is not recommended in late stages of CKD as the association with fractures is weak. In CKD, there is both a loss of bone quantity and bone quality. Computed tomography (CT) provides three-dimensional images of high resolution and can provide a volumetric BMD (vBMD) separate for cortical and cancellous bone. This may be more accurate measurement of BMD

and may correlate better with fractures in CKD.

Goal: To determine vBMD of spine and hip from clinical CT scans and to investigate the relationship of vBMD with fracture status and disturbances of endocrine axes in patients with CKD.

Methods: A prospective longitudinal study of 150 patients with late stage CKD to be examined by angiographic CT scan at baseline and 3-year follow-up. Fracture status will be determined by previous clinical fracture or prevalent vertebral fracture. Aims are: 1) To investigate the ability of vBMD in discriminating fracture status and 2) To correlate vBMD with disturbances of calcium-phosphate-metabolism, the sex-hormone-axis and the insulin-like-growth-hormone I-system.

Discussion: Establishing a method of concomitant measurement of vBMD from clinical CT scans will enable a continuous collection of information on bone quantity from a wide range of diagnostic procedures with no extra burden of radiation. This method may form the basis of future intervention studies. Ultimately, we hope our research may contribute to reducing the burden of disease due to fractures among patients with CKD.

P08.03 Jakob Dal

SOMATOSTATIN ANALOGUE TREATMENT OF ACROMEGALY: MOLECULAR ASPECTS

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Background: Acromegaly is a rare disease usually caused by a benign growth hormone (GH) producing pituitary adenoma. In case of inadequate disease control, the condition is associated with significant morbidity and approximately a doubling of mortality compared to the background population. Treatment options include transsphenoidal resection (50-60%) and medical treatment with somatostatin analogues (60% responsive) and with a specific GH antagonist.

Hypotheses: Treatment of acromegaly with SA versus surgery alone is associated with: 1) glucose intolerance despite normalized insulin sensitivity, 2) evaluation of disease activity by measuring circulating levels of GH, and total IGF-I is not reliable enough, and 3) modified peripheral GH activity in peripheral target organs assessed on molecular endpoints.

Purpose and design: To deliver new and clinically relevant information on acromegaly and its treatment by a cross-sectional of thirty patients with well-controlled acromegaly for at least 6 months assessed on normalized serum IGF-I or (IGF-I SDS \leq 2) after surgery alone (n = 15) vs. SA treatment (n = 15).

Primary endpoints: 1) glucose tolerance, including AUC_{insulin}, 2) concentration of interstitial bioactive IGF-I as well as total IGF-I, IGFBP and insulin, 3) GH and insulin signal transduction in muscle biopsies measured by western blotting and qRT-PCR: pSTAT5, SOCS 1-3 and CIS, ANGPTL4, pAKT, pAS160.

- P08.04 Line M. Underbjerg CHARACTORIZATION OF PATIENTS WITH IDIOPATHIC HYPOPARATHYROIDISM, AUTOSOMAL DOMINANT HYPOCALCAEMIA AND PSEUDOHYPOPARATHYROIDISM
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- Background: Hypoparathyroidism (HypoPT) and pseudohypoparathyroidism (Ps-HypoPT) are rare diseases, characterized by low levels of parathyroid hormone [PTH] and plasma calcium or high PTH and low plasma calcium, respectively. A recent study by our group identified 123 living persons with idiopathic HypoPT and 62 living persons with Ps-HypoPT, only few of these have been genetically tested.
- Aim: The aim of the study is to perform a detailed clinical and genetic characterization of Danish patients with idiopathic HypoPT and Ps-HypoPT. Patients will be examined by questionnaires, biochemistry, DXA-, QCT-, and HRpQCT-scans, bone biopsies and genetic tests. Furthermore, we aim to perform family tracing for the hereditary forms. The prevalence of magnesium depletion will be assessed as well.
- Perspectives: In addition to providing new information on symptoms, comorbidity and prognosis for this group of patients, we presume that the study may improve our understanding on calcium homeostasis and bone metabolism in general.
- P08.05 Nilani Ramshanker GLUCOCORTICOID-INDUCED INHIBITION OF IGF-I ACTIVITY: EXPLORATION OF UNDERLYING MECHANISMS
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- Background: Long-term treatment with GC induces a general state of catabolism and increases insulin resistance. The underlying mechanisms are insufficiently characterized. However, GC induced changes of the Insulin-like growth factor I (IGF-I) and the IGF binding proteins (IGFBP's) appear to be of utmost importance.
- Aim: To investigate the mechanism behind GC-induced catabolism and insulin resistance.
- More specifically, we wish to investigate: 1) whether GC induces circulating IGF-I inhibitors in serum or interstitial fluid that block the ability of IGF-I to activate its receptor in vitro, 2) whether GC inhibits intracellular IGF-I and insulin signaling in vitro and in vivo. The mechanisms by which growth

hormone (GH) counteracts the CG-mediated inhibition of IGF-I action.

Study design and methods: Randomized, double-blinded, placebo-controlled, cross-over study with 20 healthy subjects. 10 subjects will receive 37½ mg of prednisolone for 5 days, then wash-out for 4 weeks, whereafter they will receive placebo for 5 days. The remaining 10 subjects will be investigated in the opposite order. Overnight fasting serum and whole blood will be collected day 1, 3 and 5. A hyperinsulinemic euglycemic (H.E.) clamp with glucose and urea tracers will be performed on day 5. Related muscle and adipose tissue biopsies will be collected before and during the H.E. clamp. On half of these subjects, an IV bolus injection of GH (0.5 mg) will be administered after the first batch of tissue samples. On the remaining half of the subjects, a suction blister technique will be performed before and during H.E. clamp. The suction blister fluid is comparable to the interstitial fluid.

P08.06 Jesper Løkke
Mehlsen

PROTEIN SUPPLEMENTATION HIGH IN KETOGENIC AMINOACIDS (E.G. LEUCINE) IN SARCOPENIC OSTEOPENIC PATIENTS. IMPLICATIONS FOR MUSCLE, BONE, METABOLISM, AND PHYSICAL FUNCTION

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Background: The age-related disorders sarcopenia (muscle wasting) and osteoporosis are associated with a reduction in functional capacity as well as increased risk of fractures and disability. This muscle-skeletal fragility may be caused by many factors.

Several studies, however, most in animal models, but also human, suggest that a relatively high intake of protein, especially high-quality proteins high in leucine content, can have a positive effect in the prevention and treatment of these conditions in the elderly.

Purpose: The aim of this study is to investigate the effect of protein supplementations high in the aminoacid, leucine (whey protein) as compared to a relatively low leucine content (soy protein). An isocaloric placebo group without proteins is also included in the study. The intervention will be performed in elderly patients with sarcopenia and osteopenia to demonstrate any possible differences in physical function, body composition and metabolism.

Methods: 70 volunteers will be randomized in three groups to supplementation with 1) whey protein, 2) soy protein, and 3) placebo in a 4- month intervention. All three groups will also perform resistance training in order to enhance the effect of the protein supplement. The inclusion criteria are age between 60 and 85 years, BMI below 30, and DXA scan showing osteopenia and sarcopenia. The outcomes of the trial will be changes in metabolism, bone/muscle mass and strength; measured with DXA (muscle, fat and bone mass), physical function tests and computer-monitored strength and coordination of muscles, as well as blood samples and muscle biopsies to study the muscle-protein metabolism.

P08.07 Christian Trolle LONG QT INTERVAL IN TURNER SYNDROME - A HIGH PREVALENCE OF LQTS GENE MUTATIONS

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Objectives: QT-interval prolongation of unknown aetiology is common in Turner syndrome. This study set out to explore the presence of known long QT mutations in Turner syndrome and to examine the corrected QT-interval (QTc) over time and relate the findings to the Turner syndrome phenotype.

Methods: Adult women with Turner syndrome (n = 88) were examined thrice and 68 age-matched healthy controls were examined once. QTc was measured by one blinded reader (intra-reader variability: 0.7%) and adjusted for influence of heart rate by Bazett's (bQTc) and Hodges' formula (hQTc). The prevalence of mutations in genes related to Long QT syndrome was determined in women with Turner syndrome and a QTc >432.0 milliseconds (ms). Echocardiographic assessment of aortic valve morphology, 24-hour blood pressures and blood samples were done.

Results: The mean hQTc in women with Turner syndrome (414.0±25.5 ms) compared to controls (390.4±17.8 ms) was prolonged (p = 0.001) and did not change over time (416.9±22.6 vs. 415.6±25.5 ms; p = 0.4). 45,X karyotype was associated with increased hQTc prolongation compared to other Turner syndrome karyotypes (418.2±24.8 vs. 407.6±25.5 ms; p = 0.055). In women with Turner syndrome and a bQTc >432 ms, 7 had mutations in major Long QT syndrome genes (SCN5A and KCNH2) and one in a minor Long QT syndrome gene (KCNE2).

Conclusion: There is a high prevalence of mutations in the major LQTS genes in women with TS and prolonged QTc. It remains to be settled whether these findings are related to the unexplained excess mortality in Turner women.

P08.08 Emilie Glavind ALCOHOLIC HEPATITIS DECREASES UREA SYNTHESIS

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Background: Urea synthesis is related to the functional liver mass and is decreased in patients with cirrhosis. In contrast, urea synthesis is increased in patients with inflammatory disease. Alcoholic hepatitis (AH) involves both compromised liver function and severe hepatic inflammation induced by alcohol, but how this affects ureagenesis is unknown.

Aim: To investigate how AH affects urea synthesis.

Methods: The study is ongoing. We included nineteen patients (m/f, 16:3; age 39-59 years) with clinically diagnosed AH. The severity of AH was assessed by the Glasgow alcoholic hepatitis score (GAHS). Severe AH (GAHS \geq 9) was observed in 11/19 patients. We measured blood α -amino-N levels and urea-N synthesis rate (UNSR) before, during, and after a 4-h constant infusion of alanine (2mmol/kg/h). Urea synthesis was quantified by the functional hepatic nitrogen clearance (FHNC), i.e., the slope of the linear relationship between UNSR and blood α -amino-N concentration.

Results: FHNC was 7.0 ± 4.5 l/h (mean \pm SD) (normal range 15-30 l/h) overall. FHNC was 5.5 ± 3.9 l/h in patients with severe AH and 9.0 ± 4.7 l/h in patients with non-severe AH (P=0.09). A trend for an association between FHNC and liver function by MELD score was observed ($\rho = -0.40$, P=0.09).

Conclusion: Urea synthesis is markedly decreased in patients with AH to a level comparable to previously demonstrated values for patients with acute liver failure. This decrease in metabolic liver function seems to be associated with increasing disease severity. The results imply that AH-induced inflammation decreases liver function rather than inducing increased ureagenesis.

P09.01 Mette
Ladefoged

IDENTIFICATION OF RETINAL VASCULAR MARKERS OF EARLY-STAGE
DIABETIC RETINOPATHY

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Background and objective: Diabetic retinopathy is the leading cause of vision loss among the working age population in the Western World. The pathogenesis involves changes in metabolic parameters affecting the retinal vascular supply. Due to ethical reasons, studying the roles of such changes in the retina is difficult in humans. Furthermore, there are no optimal animal models of diabetic retinopathy. Therefore, there is a need for the development of simple experimental systems to study the effect of pharmacological intervention on the changes that are exerted by the disturbed metabolism in the diabetic retina. The purpose of the present project is to identify vascular markers in the retina that are altered in diabetes mellitus.

Methods: Retinal vessels are isolated from the retina of diabetic and healthy mice. Differences in the expression level of markers of early-stage diabetic retinopathy are evaluated on gene level from extracted total RNA of the retinal vessels subjected to qPCR.

Results: A method has been developed to isolate the vessels from mouse retinas, which constitute approximately 1-2 % of the cells in the retina. Using this method, the RNA extracted from the isolated vessels has a quality and yield suitable for qPCR analysis.

Conclusions: The preliminary data show that it is possible to obtain RNA

from isolated mouse retinal vessels that can be used to study gene expression by qPCR. The next step will be to identify retinal vascular markers of early-stage diabetic retinopathy. Subsequently, the model will serve as a system to study diabetic retinopathy in rodent animal models.

P09.02 Sigrid Bjerge
Gribsholt

PREVALENCE OF MEDICAL AND NUTRITIONAL COMPLICATIONS AFTER BARIATRIC SURGERY (GASTRIC BYPASS) BASED ON A COHORT STUDY AND A QUESTIONNAIRE SURVEY

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As compared to conventional treatment, bariatric surgery, particularly gastric bypass (RYGB), has been shown to give larger and more permanent weight loss. RYGB and the following weight loss have shown to reduce and maybe even eliminate many obesity-related health complications (diabetes, sleep apnea, et cetera).

RYGB is, however, also associated with medical and nutritional complications. After RYGB, the food bypasses the entire ventricle and 100-150 cm of the upper part of the small intestine. Consequently, problems with uptake of vitamins and minerals are expected.

Moreover, many develop medical complications such as anemia, hypoglycemia and dumping, which may lead to readmissions and possibly decreased quality of life. Nevertheless, there has never been conducted a comprehensive inventory of the occurrence of nutritional and medical complications after bariatric surgery neither in Denmark nor in an international context. An overview of the occurrence of these problems will be important for determining the indications for bariatric surgery as well as to optimize the prevention of complications.

To get this information, a cohort study of complications will be conducted to investigate readmissions, mortality and other complications after RYGB, and also medication use before and after RYGB. All patients who have had bariatric surgery performed in Northern Denmark in the period of 2006-2011 will be included (about 5000 patients).

Since not all complications after bariatric surgery can be obtained through registry studies, a questionnaire survey will also be conducted concerning complications such as pain, quality of life, dumping and hypoglycemia after RYGB on 3500 patients.

P09.03 Raket Fuglsang
Johansen

THE EFFECT OF ISOLATED HYPERGLYCEMIA ON VLDL KINETICS

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An increased production of very low density lipoprotein-triglyceride (VLDL-TG) plays a key role in diabetic dyslipidemia. The reason for such an

increase is not fully understood, but insulin and glucose levels, insulin resistance, and free fatty acid (FFA) availability are believed to play a role in VLDL regulation. The aim of this study was to determine the isolated effect of hyperglycaemia on VLDL kinetics.

VLDL-TG kinetics was examined in 8 type 1 diabetic men (no endogenous insulin production). A 2.5-hour basal period (glucose 5 mmol/l) was followed by a 4-hour hyperglycaemic period (glucose 16 mmol/l). An initial insulin infusion ("pre-infusion" 1.0 mU/kg/min) was administered to normalize plasma glucose prior to the study period, followed by a replacement dose of 0.15 mU/kg/min during the rest of the study day. Steady state VLDL-TG kinetics (VLDL-TG secretion, clearance and oxidation rates) were assessed by the isotope dilution technique using an intravenous primed-constant infusion of ex-vivo labeled [^{14}C]VLDL-TG in combination with frequent blood sampling and sampling of expired air.

In the basal and hyperglycaemic period, stable insulin and FFA levels were observed. VLDLsecretion rate was unaltered comparing the basal and hyperglycemic period (36.0 ± 9.6 vs. 30.8 ± 6.1 $\mu\text{mol}/\text{min}$, $P = 0.53$), and VLDL-TG clearance rate was also unchanged (209 ± 30.4 vs. 197 ± 41.7 , $P = 0.48$). Likewise, VLDL-TG concentration stayed the same comparing levels the last hour of the basal and hyperglycemic period (0.25 ± 0.11 $\mu\text{mol}/\text{l}$ vs. 0.28 ± 0.10 $\mu\text{mol}/\text{l}$, $P=0.56$).

We conclude that VLDL-TG kinetics is unaltered by 4 hours of acute hyperglycaemia (16 mmol/l) in type 1 diabetic subjects.

P09.04 Andreas
Lodberg

IMMOBILIZATION INDUCED BONE LOSS IS STRAIN SPECIFIC IN MICE

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Introduction: Immobilization causes significant bone loss. At present, however, it is not known whether this bone loss is modulated by genetic factors.

Aim: To investigate immobilization induced bone loss in four genetically different mice strains.

Materials and methods: Four strains (BALB/cJ, C57BL/6J, DBA/2J, and C3H/HeN) of sixteen weeks old mice were divided into eight groups (one control (n=10) and one immobilized group (n=10) per strain). Immobilization was induced by injecting 2 IU Botulinum toxin A (BTX) in the right hind limb musculature. The mice were sacrificed after 21 days and were investigated using μCT , DEXA, and biomechanics.

Results: BTX resulted in significant loss of tibial trabecular bone volume fraction (BV/TV) and trabecular thickness (Tb.Th) in all strains. The loss of BV/TV was significantly smaller in BALB/cJ (-45%) and C3H/HeN (-34%) than in C57BL/6J (-57%) and DBA/2J (-60%) mice. The loss of Tb.Th was significantly smaller in C3H/HeN (-14%) than in BALB/cJ (-26%), C57BL/6J (-29%), and DBA/2J (-30%) mice. The loss of femoral mid-cortical bone strength (Fmax) was significant for BALB/cJ, C57BL/6J, and DBA/2J only, and this loss was significantly smaller in C3H/HeN (-1%) than in BALB/cJ (-

9%), C57BL/6J (-17%), and DBA/2J (-12%) mice. The loss of femoral area bone mineral density was significant for BALB/cJ and C57BL/6J only, and this loss was significantly smaller in C3H/HeN (-1%) than in BALB/cJ (-9%), C57BL/6J (-10%), and DBA/2J (-6%) mice.

Conclusion: The immobilization-induced loss of bone density, strength, and micro-architecture is highly strain specific in mice suggesting that genetics play a role in disuse osteoporosis.

P09.05 Sine Knorr
Sørensen

MORBIDITY AND MORTALITY IN OFFSPRING BORN TO MOTHERS WITH TYPE I DIABETES

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Background: Maternal type 1 diabetes (T1DM) in pregnancy is associated with an increased risk of stillbirth, perinatal mortality and congenital malformations. The current study aims at determining the long-term consequences of T1DM in pregnancy on offspring mortality, morbidity and use of medication.

Methods: During 1992-1999 pregnant women with T1DM were reported to the Danish Diabetes Association. We used this registry to identify the children of women with pregestational T1DM (index children n=1300) as well as 100 controls (n=128.594) for each index child through Statistics Denmark.

Results:

Mortality: Overall mortality was significantly increased for index children (HR=2.07, CI=1.34-3.22; P=0.001). When excluding deaths occurring the first year of life, the overall mortality was still increased (HR=1.57, CI=0.65-3.79; P=0.31), however, not significantly.

Morbidity: For index children, total morbidity after 1 month of age was increased (HR=1.19 CI=1.12-1.28; P<0.0001). When excluding admissions before the age of one, the total morbidity was still significantly increased with a HR of 1.10 (CI=1.03-1.17, P=0.003).

Medication: The overall use of medication was increased for index children (HR 1.086 CI=1.02-1.16; P=0.011) and use of medication in seven out of 14 ATC-groups was significantly increased.

Conclusion: T1DM during pregnancy have long-term implications on offspring health with an increased risk of mortality, morbidity and use of medication.

P09.06 Esben
Axelgaard

THE PATTERN RECOGNITION MOLECULE, MANNAN-BINDING LECTIN (MBL), IN THE PATOPHYSIOLOGICAL MECHANISMS OF DIABETIC NEPHROPATHY AND IMMUNOMODULATORY THERAPY

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The complement system is part of the innate immune system and is an important part of the first line of defense against pathogens. Mannan-binding lectin (MBL) is one of the pattern recognition molecules that may initiate of the lectin pathway of complement activation. As opposed to obvious evolutionary beneficial effects of the complement system, MBL may be associated with adverse effects in several diseases including diabetes. Evidence links MBL to poor prognosis for the kidney in diabetes. High serum levels of MBL have been reported in type 1 diabetic patients with nephropathy as compared to type 1 diabetic patients without nephropathy. A very clear predictive value of serum MBL levels for the risk of development of microalbuminuria has been reported. Furthermore, it has been identified that there is a clear causality between MBL and development of diabetic kidney disease in mice. The precise mechanism of linkage between complement system and diabetes is poorly elucidated. Two mechanisms are proposed: 1) The formation of neoepitopes for MBL pattern recognition on host cells would enable lectin pathway activation and 2) Inactivation of complement regulatory proteins by glycation that may initiate complement attack on host cells. It is our hypothesis that MBL does not bind to the body's own tissues and cells under normal conditions, but changes in glycation patterns of cell surfaces and/or complement regulatory proteins in conditions such as diabetes mellitus or following tissue ischemia may dramatically increase the autoreactivity of MBL. The aim is to unravel the functional influence of MBL binding to tissues/plasma proteins in type-1 diabetes inflammatory disease/injury.

P09.07 Trine Maxel Juul ZINC METABOLISM IN OBESITY: REGULATIONS OF AND ITS CONNECTION WITH LIPID- AND GLUCOSE PROFILE

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Background and aims: Obese individuals show signs of zinc deficiency; this is interesting as zinc assists in both pancreatic and peripheral functions of insulin. The zinc homeostasis is controlled by zinc transporters. We have previously been able to link the zinc transporter ZIP14 with adipogenesis. The aim of the present study was to investigate the gene expression of ZIP14 in human adipose tissue from obese individuals and to look at the effects induced by a weight loss.

Materials and methods: 14 healthy but obese patients and 14 lean controls were included. The obese individuals participated in a 10-week weight loss programme. Gene expressions of ZIP14 and PPAR γ from subcutaneous adipose tissue were investigated by quantitative real-time PCR. Indicators of lipid and glucose metabolism were measured in blood samples. Statistical analyses were done using t-test and pearson correlation.

Results: The average weight loss was 12.47 kg \pm 0.9. We found a significant down-regulation of ZIP14 in obese individuals compared with lean controls (4.4 fold, p=0.0002). ZIP14 was significantly up-regulated during the weight loss in the obese individuals (2.5 fold, p=0.0005). ZIP14 was positively correlated with the gene expression of PPAR γ (r=0.68, p<0.0001) and HDL (r=0.51, p=0.0008). Negative correlations were found in regard of triglyceride (r=-0.35, p=0.026), BMI (r=-0.53, p=0.0004), serum insulin (r=-0.40, p=0.01) and plasma glucose (r=-0.38, p=0.02).

Conclusion: We conclude that ZIP14 gene expression is down-regulated in obese subjects; this down-regulation is reversed by weight loss. Furthermore, high ZIP14 gene expression correlates with a beneficial lipid and glucose profile.

P09.08 Julie Støy

MARKEDLY ELEVATED 24-HOUR AMBULATORY BLOOD PRESSURE IN HEALTHY MALE CARRIERS OF ARG313CYS IN IDENTIFIES THE GENE AS A POSSIBLE NOVEL REGULATOR OF BLOOD PRESSURE

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Background: Hypertension, obesity, dyslipidemia, and glucose intolerance are metabolic disorders that often coexist in patients. Each of these disorders has been scrutinized in GWA studies with a large number of genetic variants identified that exert a subtle effect on disease susceptibility. The possibility that the metabolic disorders may share overlapping causative genes was recently explored in an exome sequencing project of 2000 Danes enriched for metabolic disorders. Three non-synonymous genetic variants were found to associate with type 2 diabetes (COBLL1 and MACF1), and HDL-cholesterol levels (CD300lg), respectively. In the present study, a cardiovascular phenotype characterization of carriers of the risk-allele in CD300lg was performed.

Methods: 20 healthy male carriers of the risk allele in CD300lg were matched with 20 healthy non-carriers. 24-hour ambulatory blood pressure, carotid intima-media thickness (CIMT), and fasting blood samples were evaluated.

Results: Risk-allele carriers had a higher mean 24-hour systolic blood pressure (122.2 mmHg (range 117.2-127.2) versus 114.7 (111.2-118.1); p=0.013) and a higher 24-hour diastolic blood pressure 76.6 mmHg (73.7-79.6) versus 71.8 (70.0-73.6); p=0.005) compared to the non-carriers. 24-hour mean arterial pressure was also higher for risk-allele carriers (p=0.007). Measures of CIMT showed a tendency to higher CIMT measures among risk-allele carriers, but none of the measures reached statistical significance.

Conclusion: Carriers of the risk-allele in CD300lg have substantially increased measures of 24-hour ambulatory blood pressure and points to

CD300lg as a potential novel regulator of blood pressure in healthy males.

P10.01 Steen
Fagerberg

ALPHA-HAEMOLYSIN FROM INDUCES $[Ca^{2+}]_i$ SIGNALLING AND CELL LYSIS OF THP-1 CELLS THROUGH ACTIVATION OF A DIFFERENTIAL SET OF ATP SENSITIVE P₂ RECEPTORS

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The extracellular signalling molecule, adenosine triphosphate (ATP), is shown to play an important role in the erythrocyte damage inflicted by α -haemolysin (HlyA). Moreover, extracellular ATP is important for the recognition of the damaged erythrocyte by the monocyte cell line THP-1. It is, however, uncertain how HlyA affects the monocytes themselves.

Here we show that HlyA triggers an immediate increase in intracellular $[Ca^{2+}]_i$, which is a combined signal from release from intracellular stores and from acute Ca^{2+} influx. The HlyA-induced $[Ca^{2+}]_i$ increase was markedly reduced by P₂ receptor antagonists and by inhibition of IP₃, and the inhibitor profile regarding P₂X and P₂Y antagonists was similar to the ATP induced $[Ca^{2+}]_i$ increase. Interestingly, prolonged exposure to HlyA causes lysis of the THP-1 cells via P₂X₇ despite that this receptor barely contributes to the HlyA- or ATP-induced Ca^{2+} response. We measured the amount of monocyte lysis produced by HlyA at both high and low extracellular concentrations of ATP, and during blockage of ATP signaling by oxATP. Our preliminary results show that receptor desensitization by preincubation with ATP increases the survival rate of HlyA-attacked THP-1 cells.

These data suggest that both the immediate and lytic effect of HlyA on THP-1 cells is mediated by ATP and P₂ receptor activation, and that this is an acute P₂Y mediated response followed by a P₂X mediated response. These findings will be further studied in monocytes isolated from transgenic mice defective of either of the P₂ receptors.

Perspectively, this may benefit patients clinically by improving monocyte survival rate during infections from HlyA producing E. coli.

P10.02 Nina Jensen

LOSS OF FUNCTION OF SLC20A2 ASSOCIATED WITH FAMILIAL IDIOPATHIC BASAL GANGLIA CALCIFICATION IN HUMANS CAUSES BRAIN CALCIFICATIONS IN MICE

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The type III sodium-dependent phosphate (Pi) symporters, PiT1 and PiT2, are involved in calcification of the medial layer of arteries and parts of the brain (Familial Idiopathic Basal Ganglia Calcification, FIBGC), respectively. FIBGC is characterized by symmetrical calcifications of the basal ganglia and other regions such as the thalamus. The neuropsychiatric and motor

symptoms are very heterogeneous, including dementia, psychosis, parkinsonism, and dystonia. Deleterious mutations in SLC20A2, encoding PiT2, were recently linked to FIBGC in almost 50% of the families reported worldwide. Several of the mutations found have been shown in our lab to impair the Pi uptake ability of PiT2, but it is unknown how deleterious mutations in SLC20A2 can lead to calcifications in distinct areas of the brain. To investigate the role of PiT2 in FIBGC, we established Slc20a2 homozygous knockout mice. We have found calcifications in 8-week-old and 19-week-old homozygous knockout mice, but not in wild type mice. These findings show that knockout of PiT2 is sufficient to cause calcifications in the brain, verifying the association found in FIBGC affected families. It is hypothesized that the calcifications in patients initiate in or around blood vessels, and PAS staining of paraffin-embedded brain slices from the 19-week-old knockout mice show that the calcifications are located very close to vessels. Electron microscopy will be performed to determine the location of the calcifications at an early stage of the disease in mice. This should show if the calcifications form in or around a specific cell type, and bring us closer to the mechanism of the disease.

P10.03 Stine Mikkelsen FUNCTIONAL IMPACTS OF THE DARIER DISEASE MUTATION E917/918K IN SERCA2B/SERCA1A AND ITS NETWORK OF BONDING PARTNERS

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Mutation E917K of the sarco(endo)plasmic reticulum Ca^{2+} -ATPase isoform 2b (SERCA2b) causes Darier disease, an autosomal dominantly inherited skin disease also denoted as Keratosis follicularis or Darier-White disease. The glutamate E917 is located in the cytoplasmic loop between transmembrane segments M8 and M9 (L8-9) and is involved in a major bonding network between residues in the transmembrane segments M5 and M7 and the cytoplasmic loops L6-7 and L8-9. In the fast skeletal muscle isoform SERCA1a, the residue corresponding to E917 is E918. In this study, the importance of the bonding network is examined by mutagenesis of the residues E917 of SERCA2b and E918 (L8-9), R819 (L6-7), R762 (M5) and R836 (M7) of SERCA1a in combination with functional analysis of the individual partial reaction steps in the pump cycle by steady-state and transient kinetic studies. These residues show to be highly important in the major conformational changes of the pump, $\text{E1P} \rightarrow \text{E2P}$ and $\text{E2} \rightarrow \text{E1Ca}^{2+}$. In addition, our measurement of the affinity for the phosphoryl transition state analog vanadate demonstrates the importance of the bonding network for the reaction $\text{E2P} \rightarrow \text{E2}$. Furthermore, four swap mutants were created to illuminate direct interaction patterns in this network. While each of the mutations E918R and R836E are disruptive, the combination of these two mutations leads to regain of wild type function in some parts of the pump cycle, indicating that E918 and R836 interact in the wild type. Based on these findings, it is reasonable to link the disturbances in Ca^{2+} homeostasis in the epidermal cells in Darier disease patients to disruption of the major bonding network caused by mutation of E917K.

P10.04 Ida Skødt
Jensen TOWARDS PURIFYING DNA-PROTEIN COMPLEXES

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Proteins, both alone and as part of higher-order macromolecular assemblies, are important for regulation of cell functions. Proteins are involved in all aspects of cell functions, and it is therefore important to have a basic knowledge of the functions of the proteins to elucidate the cellular role of the proteins and especially of the consequence of an alteration or complete lack of a given protein due to, for example, a genetic disease. The development of approaches to study macromolecular DNA-protein assemblies in their native form is currently a challenging field. The establishment of such an approach would be of high importance to the research community as DNA-protein assemblies are essential for cell function. The method could bring new information to all steps in the central dogma, where macromolecular assemblies are involved in both transcription and translation. New information could also shed light on the process of DNA replication and DNA repair, as well as to further our understanding of many human diseases. In many disorders, mutations of a gene lead to the expression of a mutant protein that is no longer able to interact with its natural binding partners. We wish to establish such an approach using the baker's yeast *Saccharomyces cerevisiae* as a model system. *S. cerevisiae* has the advantage that it resembles human cells very well as many genes and functions are conserved between the two species. Furthermore, *S. cerevisiae* is straightforward to work with, relatively cheap to culture, and methods to modify genes are well established.

P10.05 Henriette
 Lajgaard
 Christensen

SUBCELLULAR LOCALIZATION OF THE V-ATPASE IN THE CHOROID PLEXUS EPITHELIUM: PROSPECTS FOR REGULATION OF CEREBROSPINAL FLUID PH?

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Despite clinical importance, little is known about the molecular mechanisms behind cerebrospinal fluid (CSF) pH control. The CSF is produced by the choroid plexus epithelium (CPE) located in the ventricular system of the brain. The CSF communicates freely with the extracellular fluid of the brain, and a tight regulation of the CSF pH is a prerequisite for proper brain function. The general idea is that CSF pH is regulated by acid/base transport by the CPE. However, the mechanism is not yet understood.

The CPE expresses several acid/base transporting proteins. One of these is the vacuolar H⁺-ATPase (V-ATPase), which is found in nearly all cell types, where it acidifies intracellular organelles. However, in some cell types, the protein has been shown to acidify the extracellular milieu by translocation to the plasma membrane. In this study, we have investigated the sub-cellular localization of the V-ATPase in the CPE at normal and low levels of pCO₂.

Mice were subjected to acute hyperthermia, causing hyperventilation and

thereby a decrease in blood pCO₂. The mice were perfusion fixed, and immunohistochemical analysis of the CPE was carried out on paraffin embedded brain sections by fluorescence microscopy and electron microscopy.

Under control conditions, the V-ATPase-containing vesicles are evenly distributed across the cytoplasm. However, during hyperthermia, some of the vesicles seem to translocate towards the luminal plasma membrane. Electron microscopy revealed V-ATPase immunoreactivity corresponding to the luminal membrane as well as intracellular organelles. These findings indicate that the V-ATPase might be a part of the mechanism that guards the CSF against large changes in pH.

P10.06 Inga Christensen

ATYPICAL LOCALIZATION OF CYTOSKELETAL AND MEMBRANE PROTEINS IN THE CHOROID PLEXUS

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The choroid plexus epithelium (CPE) is a highly productive cell monolayer that plays a crucial role for cerebrospinal fluid production. The cellular distribution of membrane proteins in the CPE is known to differ from other transporting epithelia, and previous studies have shown luminal localization of the Na⁺,K⁺-ATPase, Na⁺/H⁺ exchanger 1 (NHE1) and Na⁺/K⁺/Cl⁻ cotransporter 1 (NKCC1) transporter proteins. Their luminal localizations are opposite to every other known epithelium, whereas other proteins, such as AE2, have a normal membrane distribution.

Previous studies have shown that the normal luminal membrane abundance of Na⁺,K⁺-ATPase, aquaporin-1 and NHE1 in the choroid plexus is severely affected by deletion of the *slc4a10* gene that encodes the bicarbonate transporting protein Ncbe/Nbcn2. In the current study, we explored the differences in the *slc4a10* wt and ko mice on the cellular localization and abundance of proteins expected to be involved in the polarization of CPE cells, with emphasis on selected transmembrane, anchoring, and cytoskeletal proteins.

We report that AE2 protein abundance is significantly increased in the *slc4a10* ko mice and that α -spectrin protein, which is present mainly in the basolateral membrane in the wt, is almost exclusively located in the apical membrane in the ko. Additionally, the protein abundance of α -spectrin is decreased in the *slc4a10* ko CPE. The causes for these deviations from normal epithelial polarization and redistribution following specific gene knockout are unknown, but may be significant for basic epithelial cell biology.

P10.07 Åsa Lina Margaretha Jönsson

THE SLC34A2 GENE - CHARACTERISATION AND ROLE OF MUTATIONS IN PULMONARY ALVEOLAR MICROLITHIASIS AND EXTRA-PULMONARY CALCIFICATION SYNDROMES

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Mutations in the SLC34A2 gene, which encodes the co-transporter NaPi-IIb, cause defect cell-uptake of phosphate, which leads to formation of calcium-phosphate concretions in the lungs as seen in Pulmonary Alveolar Microlithiasis (PAM). Calcific Aortic Valve Disease (CAVD) is characterised by calcification of the aortic valve leaflets. Deposition of calcium in the dermis is seen in the rare syndrome calcinosis cutis.

We have described a new mutation in SLC34A2 in two patients with PAM. One of the patients had severe arteriosclerosis, while the other had a significant aortic valve stenosis due to calcification¹. Moreover, we have identified SLC34A2 mRNA in a human aortic valve² and in the skin. These findings suggest that mutations in SLC34A2 may play a role in extra-pulmonary calcifications.

Hypothesis: Mutations in SLC34A2 are involved in the development of calcifications in different tissues and organs, as seen in CAVD and calcinosis cutis.

Study plan: Four studies will be performed to investigate: 1) the association between new mutations in SLC34A2 and the function and localisation of mutated NaPi-IIb, 2) a possible expression of SLC34A2 in extra-pulmonary tissues from patients with various calcification syndromes, and 3) if mutations in SLC34A2 are involved in these diseases.

Perspectives: This PhD project will provide important new knowledge about calcification syndromes. If mutations are involved in the pathogenesis, genetic screening may improve the prognosis in some patients. Furthermore, these studies may help to develop specific pharmacological treatment modalities in these diseases.

¹Jönsson et al., Eur Respir Rev 2012

²Jönsson et al., Am J Respir Crit Care Med 2012

P10.08 Casper
Kornbech
Larsen

HYPERALDOSTERONISM IN $K_{Ca}1.1$ CHANNEL BETA₂-SUBUNIT KO MICE

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Whole body K^+ homeostasis depends on matching K^+ excretion to daily K^+ intake. K^+ is excreted via the colon and the kidney, the latter handling the majority of the total K^+ excretion. Aldosterone is an important regulator of K^+ excretion in both the kidney and the colon. In the kidney, K^+ secretion depends on 2 apical K^+ channels, ROMK and $K_{Ca}1.1$, while $K_{Ca}1.1$ is the only apical K^+ channel involved in colonic K^+ secretion. We have acquired a novel global knockout mouse for the β_2 -subunit (KCNMB2) of the $K_{Ca}1.1$ channel, which is the only $K_{Ca}1.1$ β -subunit expressed in murine colonic epithelium.

The β_2 KO mice have increased plasma aldosterone. Primary hyperaldosteronism is characterized by low plasma K^+ , low renin and high blood pressure. β_2 KO mice present with normokalemia and low rennin, indicating

a secondary cause of hyperaldosteronism. The low renin in β_2 KO mice indicates that a K^+ handling deficiency, rather than hypotension, is causing the hyperaldosteronism.

Studying BK channel-dependent colonic K^+ secretion in the Ussing chamber showed normal function in β_2 KO mice. In contrast, urinary K^+ excretion, studied in metabolic cages, was reduced in β_2 KO mice ($P=0.06$, $n=5$). These data support that β_2 KO mice have a reduced capacity for renal K^+ secretion. mRNA expression of the β_2 subunit has previously been found in rabbit cortical collecting ducts, where the expression level is increased by K^+ loading and reduced by K^+ depletion. These data indicate an important function of the β_2 subunit of the $K_{Ca}1.1$ in renal K^+ excretion.

Our data support that hyperaldosteronism in β_2 KO mice is likely caused by deficient BK channel dependent K^+ secretion in the renal distal tubule.

P11.01 Monica Milter
Ehlers

A QUALITATIVE STUDY OF FUNCTIONING, DISABILITY, AND
REHABILITATION OF PATIENTS AFTER HIP FRACTURE SURGERY

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Introduction: The need for rehabilitation of patients older than 65 years after hip fracture surgery is increasing in Denmark. Rehabilitation consists primarily of muscle training and mobilisation, and the patients' functioning, disability and involvement in their rehabilitation process have not been investigated in scientific studies. This study investigates functioning, disability, and rehabilitation in order to optimise the rehabilitation efforts.

Aims: 1. To evaluate knowledge about functioning, disability, and rehabilitation of postoperative hip fracture in patients older than 65 years. 2. To investigate how health care professionals assess patients' functioning, disability, rehabilitation, and factors with an impact on functioning, disability, and rehabilitation. 3. To investigate how patients and their close relations have experienced patients' functioning, disability, rehabilitation, and factors with an impact on functioning, disability, and rehabilitation.

Material and method: The PhD project is based on the Model of the International Classification of Functioning, Disability, and Health, and White Paper of the Rehabilitation Concept. The method is qualitative, and the design used to answer the research questions is qualitative deductive content analysis. Data are generated by a systematic mixed-method review of literature, focus group interviews with health care professionals, and individual interviews with patients and their close relations.

Expected outcome: Acquired knowledge of the patients' health and health-related conditions is disseminated in three scientific articles. The knowledge can assess and optimise the rehabilitation efforts in Danish regions and municipalities.

P11.02 S. Ylijoki-
Sørensen

CODING UNKNOWN CAUSE OF DEATH IS 10 TIMES MORE FREQUENT IN
DENMARK THAN IN FINLAND

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The World Health Organization recommends avoiding the use of unknown causes of death (codes R96-R99) in the death certificate.

Aim: To investigate R96-R99 deaths in Finland (FI) and Denmark (DK).

Material and methods: A random sample of 90% of the Finnish data and 100% of the Danish data was extracted from the national mortality registries for 2000, 2005 and 2010. We calculated R96-99 code-specific mortality rates (MRs), frequency of autopsies and external examinations of the body.

Results: MRs were for 2000 1.7 (FI), 32.0 (DK); 2005: 2.5 (FI), 16.3 (DK); and 2010 2.4 (FI), 19.2 (DK). Forensic autopsy was performed in all Finnish cases. Only 5.7% (2000), 4.8% (2005) and 5.6% (2010) of Danish cases were autopsied, of which 25% were medical and 75% forensic autopsies. The Danish forensic autopsy frequency did not differ significantly between study years ($\chi^2 = 5.0$, $df = 2$, $p = 0.083$). External examination was overall performed in 94.5% of the Danish cases with no difference between the study years ($\chi^2 = 1.1$, $df = 2$, $p = 0.572$).

Discussion: Codes R96-R99 were little used in Finland, where forensic autopsy was performed in all cases. The codes were used ten times more frequently in Denmark. Only 5% of the R96-R99 coded cases were autopsied in Denmark. The implications hereof affect comparative studies of causes of deaths involving the R96-R99 codes. This may also affect the reliability of the cause of death statistics in Denmark.

Conclusion: Our data represent an argument for the use of autopsy to investigate deaths of unknown cause to improve death statistics accuracy in general and cause of death determination in the individual in particular.

P11.03 Janne Brammer ACKNOWLEDGING THE BACK PATIENT. A THEMATIC SYNTHESIS OF
Damsgaard QUALITATIVE RESEARCH. A SYSTEMATIC LITERATURE REVIEW

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Introduction: A thorough review of qualitative studies has revealed that telling about experiences and perceptions is important for back patients in order to feel accepted and acknowledged. Thus, it has been the aim of this qualitative literature review to investigate what it feels like to be a back patient and what back patients consider important when dealing with the healthcare system.

Methods: The method draws on James Thomas' and Angela Hardens approach in "Methods for the thematic synthesis of qualitative research in systematic reviews" (2008). The thematic synthesis aims to systematise and integrate findings of qualitative studies.

Results: The analysis reveals that many back patients feel that their experiences and perceptions are ignored by the health professionals, who are often concerned about identifying the cause. This can result in patients feeling mistrusted, marginalised and reluctant to speak out. Therefore, telling about experiences and perceptions is important for back patients in order to feel accepted and acknowledged. The health professionals must incorporate the patients' narratives as an integral part of the care and treatment.

Conclusions: In order to acknowledge the back patient, the narrative must be complemented by a different perspective that includes the issue of ethical responsibility. It is therefore also a question of adopting certain norms as binding; to be bound by obligation or loyalty. Thus, the literature review argues for a more process-oriented patient approach that incorporates patients' narratives as an integral and ethical part of the care and treatment.

P11.04 Marie Mortensen CONSTRUCT VALIDITY OF THE PERCEIVED STRESS SCALE AMONG ADULT DANES IN THE CENTRAL DENMARK REGION

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Background: Danish general practitioners (GPs) handle about 40 million patient contacts per year. Approximately 9% of these contacts seem to be caused by mental health problems, and 24% of these result from stress conditions.

Stress is a risk factor for depression and anxiety disorders. Nevertheless, incomplete acknowledgment and misclassification of mental disorders is a well-known problem in general practice. The Perceived Stress Scale (PSS) can be a possible instrument for measuring and diagnosing stress conditions in general practice. The PSS scale has previously been studied by using classic test theory. We want to investigate the underlying construct validity further by applying modern test theory.

Aim: The purpose of the study is to explore the construct validity of the PSS in measuring stress conditions and further to examine convergence validity of the PSS compared to the SF-12 Mental Health Summary Scale, from the Danish National Health Survey (DNHS) 2010 and 2013 "Hvordan har du det?/How are you?" of citizens in the Central Denmark Region.

Methods: The sample size is 30,000 (2010 and 2013) citizens who have completed both the PSS and SF-12 questionnaires. Possible ceiling and floor effects in PSS responses will be studied. A Rasch analysis will be used to examine item ranking and to test for local item dependence and uni-dimensionality. Rasch models will be used to study differential item

functioning for gender, age and ethnicity. In addition, quartiles of the SF-12 Mental Health Summary Scale will be compared to PSS scores.

Results: Data analysis is in progress. Results are expected to be presented in January.

P11.05 Birthe
Annemarie
Thomsen

SCREENING FOR CARDIOVASCULAR DISEASES AND DIABETES IN DANISH WOMEN; PREVALENCE, NON-ATTENDANCE AND COST-EFFECTIVENESS

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Cardiovascular diseases (CVD) are a major threat to the health of Danish women. CVD and stroke are causing death more frequently in Danish women compared to most other European countries. An increased effort is imperative to reduce the risk in women and the economic cost associated with CVD. A solution could be to offer a screening programme to women. The (cost-)effectiveness of screening programmes may be influenced by the participation rate, and a high participation rate is crucial to the validity of epidemiological studies.

The main objective is to evaluate whether systematic screening for CVD and diabetes (DM) in Danish women is attractive from a health care perspective. The project starts with a population-based cross-sectional screening study of approximately 2,000 women in order to generate prevalence estimates for abdominal aortic aneurysms, peripheral arterial disease, carotid artery disease, hypertension, atrial fibrillation, diabetes and dyslipidemia in Danish women aged 60, 65, 70 and 75. Information about lifestyle, anamnesis, walking-related pain, use of medicine and the EQ5D health questionnaire to obtain psychometric measures are gathered among the participants. Next, interviews with 10 non-participants are conducted. Finally, an analytic decision model for estimating the cost-effectiveness of the screening programme will be developed based on state-of-the-art methods. Incremental costs per gained quality-adjusted life year (QALY) will be calculated by dividing the difference in total costs between the two scenarios; screening versus non-screening.

P11.06 Mette Munk
Jensen

INCLUSION IN PHYSICAL EDUCATION IN THE DANISH PRIMARY SCHOOL

M. Munk

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Physical education (PE) is, due to the practical and bodily dimension of the subject, a special arena for inclusion. In this perspective, PE can be a unique player in efforts to develop social inclusion in and outside the context of PE. Unfortunately, national and international research indicates that not all students experience to be included in PE. Anyway, only little is known about how and why the processes of exclusion are going on and how an inclusive PE can be promoted. With the new Danish school reform enhancing the focus of physical activity, not only in PE, but in the school day in general, the importance of sociological and pedagogical knowledge about inclusion and exclusion processes in school sport is

enhanced. Therefore, the aim of this project is to gain a deeper understanding of the inclusion and exclusion processes in PE. Earlier studies indicate that the dynamic character of the inclusion and exclusion processes in PE is characterized by a complex interplay between a number of social, physical and cultural characteristics of the students as well as by contextual aspects. To take into account this complexity of the phenomenon, a single-case study is chosen. At a "typical" Danish school, the PE in grades 7-9 will be observed and students will be interviewed both individually and in focus groups. In the second phase of the study, an intervention aiming at facilitating inclusion will be tried out and evaluated through observations and student interviews. The inclusion and exclusion processes will be analysed with the theoretical perspective of Etienne Wenger's concept of legitimate peripheral participation and Pierre Bourdieu's concept of physical/symbolic capital.

P11.07 Marianne Eg

SIGNIFICANT FACTORS IN ACHIEVING SUSTAINED WEIGHT LOSS IN THE TREATMENT OF CHILDREN WITH OBESITY

M. Eg

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The number of obese and seriously obese children and young people has increased by 300% during the past 30 years in the Western World; and despite many efforts, the results of treating obesity are still disappointing.

One in five children in Denmark is obese, and 70 % of these children are also obese as adults.

The problem of obesity is a complex one; and it may result in social costs, physical complications and a shorter life for obese individuals.

The purpose of the PhD project is to develop a model for systematic, focused and individual treatment programmes for obese children and young people by: 1. identifying the current national treatment programmes for obese children and young people with the focus on long-term results in the form of sustained weight loss and 2. investigating the individual patient perspective by studying obese children and young people's experiences of and response to the treatment of obesity.

The project will be conducted in two phases using a mixed-method study design including both quantitative and qualitative data material. The first phase will consist of a quantitative identification of the existing national treatment programmes for obese children and young people at Danish children's wards. The second phase will study important factors regarding obese children and their response to the treatment of obesity by including the patient's perspective based on prospectively collected data material. These qualitative data will be obtained from family interviews. The main analysis will be done by collecting the results from the two phases.

P11.08 Christian
Bjerregaard
Olesen

EXTRACTION AND FRACTIONATION OF PERFLUORINATED ALKYL ACIDS AND OTHER PERSISTENT ORGANIC POLLUTANTS FROM HUMAN SERUM

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Human exposure to xenobiotic chemicals, such as persistent organic pollutants (POPs) including perfluorinated alkyl acids (PFAAs), is suspected to play a role in hormone-related diseases such as reproductive, neurological and immunological disorders and increased risk of cancer. The metabolism and excretion of lipophilic POPs (lipPOPs) and PFAAs in humans is slow with half-lives up to 4-10 years.

In the present study, we developed a method for extraction of PFAAs and lipPOPs from human serum in the same run. Following extraction, the PFAA and lipPOP fractions were analyzed for xenoestrogenicity using an estrogen receptor (ER) transactivation (tact) reporter gene assay.

The serum macromolecules were removed in a solid phase extraction (SPE) step. Upon SPE, the PFAAs and the lipPOPs were separated by solvent extraction using hexane/ethyl acetate (9:1); the lipPOPs were extracted to the hexane phase, whereas the PFAAs remained in the water phase. The hexane phase was further fractionated by HPLC to remove any potentially interfering endogenous hormones from the lipPOPs before ER-tact analysis. The water phase containing the PFAAs was further extracted using tetrahydrofuran: hexane (3:2) in a tetrahydrofuran extraction (TE) step that transferred the PFAAs to the supernatant. This supernatant was then fractionated by HPLC to remove potentially interfering endogenous hormones from the PFAAs. Furthermore, weak anion extraction (WAX) was needed before ER-tact analysis. ER-tact analysis of samples from pregnant women extracted by the SPE-TE-HPLC-WAX method showed that the PFAA fractions were free of ER-active endogenous hormones and ready for xenohormone activity measurements.

P12.01 Dorte Hansen DIRECT PATHOGENIC EFFECTS OF HERV-ENCODED PROTEINS

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Background: Multiple sclerosis (MS) is a demyelinating, inflammatory disease of the central nervous system (CNS). MS is mediated by the immune system, but the etiology of the disease remains unknown.

Retroviral envelope (Env) proteins, encoded by human endogenous retroviruses (HERVs), are expressed in increased amounts on B cells from MS patients. Furthermore, the amount of anti-HERV antibodies in serum and cerebrospinal fluid from patients with MS is increased when compared with healthy controls.

Aim: The overall aim of this project is to investigate the potential role of HERVs in the development of MS and the possible direct pathogenic effects of HERV-encoded Env proteins on the CNS.

Methods: Construction and characterization of a panel of recombinant Env-proteins is initiated and their pathogenic potential will be investigated:

Fusiogenic potential analyzed by flow cytometry and confocal microscopy. Analysis of Env-induced apoptosis/necrosis in CNS cells will be performed by both DNA fragmentation ELISA and qPCR. Furthermore, the cellular localization of HERV-antigens on cells from patients with MS will be determined by confocal microscopy. A flow cytometric/confocal method has been optimized for the detection of expression of HERV-antigens on cells.

Results: Preliminary results will be available in 2014.

Perspectives: Results will contribute new knowledge of MS pathogenesis and the possible involvement of HERVs herein. A more comprehensive understanding of HERVs in general will also be obtained.

P12.02 Stine Hald

DIETARY INTERVENTION WITH A DIET RICH IN ARABINOXYLAN AND RESISTANT STARCH MODULATES T-CELL ACTIVATION ESTIMATED BY CD25 EXPRESSION IN METABOLIC SYNDROME

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Background: Arabinoxylan and resistant starch are substrates known to stimulate colonic short-chain fatty acid production of which especially butyrate is suggested to exert an anti-inflammatory function in the colon. Metabolic syndrome is characterized by abdominal obesity, dyslipidaemia, hypertension and hyperglycaemia and is associated with a chronic low-grade inflammation.

Aims: To investigate the effect of a four-week dietary intervention rich in arabinoxylan and resistant starch on mucosal T-cell activation estimated by their CD25 and CD69 expression in subjects with metabolic syndrome.

Methods: Twenty subjects with metabolic syndrome were included in the study and followed the dietary intervention. Endoscopy was performed before and after the intervention. Lamina propriae were isolated using enzymatic digestion of mucosal specimens. Isolated cells were stained for CD3 (T-cell marker), CD4, CD25 and CD69 expression.

Results: T-cells showed decreased CD25 expression following a four-week intervention ($p=0.01$), but had unchanged CD69 expression. Also CD4+ T-cells and non-CD4+ T-cells showed decreased CD25 expression, but unchanged CD69 expression ($p=0.05$ and $p=0.009$, respectively).

Conclusion: Dietary intervention with arabinoxylan and resistant starch in subjects with metabolic syndrome seems to be associated with reduced activation in intestinal mucosal T- cells.

P12.03 Signe Maria Nielsen

BIOFILM FORMATION IN *ACHROMOBACTER XYLOSOXIDANS* ISOLATED FROM CYSTIC FIBROSIS PATIENTS

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Introduction: *A. xylosoxidans* is an emerging pathogen in cystic fibrosis (CF). It has the capacity to form biofilm, but little is known about how biofilm formation might contribute to its behavior during infections. The aim of this study is to investigate biofilm formation using the type strain and two clinical isolates of *A. xylosoxidans*.

Methods: Isolates of *A. xylosoxidans* were grown in microtiter plates and the amount of biofilm formed was quantified using a crystal violet micro titer assay. The biofilm matrix composition was investigated by differential staining for cells and matrix components: viable cells, extracellular DNA and polysaccharides and visualized using confocal microscopy. Extracellular biomolecules essential for biofilm formation was investigated by enzyme treatment of biofilms grown in the presence or absence of DNase, proteinase or alginate lyase. To determine if biofilm formation contribute to antibiotic resistance, MIC and MBEC was measured.

Results: Variation was seen in the amount of biofilm formed by the three isolates. Clinical isolate 1 produced more biofilm than clinical isolate 2 when grown in micro titer trays. We find that the isolates differ in biofilm composition and amount of eDNA and polysaccharides formed during growth in flow cells. Treatment with DNase prevented biofilm growth in isolate 1 (only), indicating that here eDNA plays a role in biofilm formation.

Conclusion: In an ongoing study, we investigate factors that might contribute to *A. xylosoxidans* biofilm matrix composition, formation, eradication and tolerance to antibiotics. We observe a difference in biofilm formation, structure and matrix composition between the two clinical isolates.

P12.04 Maria Hønholt Christensen INNATE IMMUNE EVASION BY THE HERPES SIMPLEX VIRUS -1 PROTEIN ICP27

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Herpes simplex virus 1 (HSV-1) is recognized by innate immune cells by multiple pathogen recognition receptors (PRRs). At the time of recognition, a potent innate antiviral response is induced to evoke antiviral responses against HSV-1 in the infected cell and protect bystander cells from infection. Type 1 interferon (IFN) is important to initiate the antiviral response and hence the expression of many antiviral proteins in infected as well as surrounding cells. To establish an efficient infection, specific HSV1 proteins, among others ICP0 and vhs, are evading the antiviral response. The HSV-1 immediate early (IE) protein ICP27 has multiply functions and HSV-1 mutants lacking this protein cannot replicate in human cells. ICP27 is induced in the nucleus 3 hours post infection and later in the cytoplasm. During infection, ICP27 shuttles between the nucleus and the cytoplasm and executes its functions in both compartments. It is thought that one

function of ICP27 is to inhibit the type 1 IFN response, but at which part of the IFN pathway and in which cellular compartment the inhibition occurs is not clear. My project will include infection studies on macrophage-like cells (THP-1) with a HSV-1 mutant lacking ICP27 and HSV-1 mutants, where ICP27 are predominantly expressed in either the nucleus or in the cytoplasm, and my results indicate that infection of THP-1 cells with an ICP27 deletion mutant induces higher amounts of type 1 IFN and CXCL10 on a protein level compared to infection with HSV-1 wt. Using the HSV-1 mutants, I am going to evaluate further how and where ICP27 executes the inhibition of the type 1 IFN response.

P12.05 Kathrine Hansen INDUCTION OF IFN-BETA; EXPRESSION BY *LISTERIA MONOCYTOGENESIS* IN HUMAN MYELOID CELLS PROCEEDS THROUGH A PATHWAY DEPENDENT ON IFI16, CGAS AND STING

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Cytosolic DNA and cyclic dinucleotides (CDN)s are potent inducers of type I IFN responses working by stimulating a pathway dependent on the signalling protein STING. Reported DNA sensors include IFI16, DDX41, and cGAS, and CDNs stimulate innate immunity by direct binding to STING and possibly also DDX41. Interestingly, the DNA sensor cGAS is a cyclase which catalyses synthesis of the noncanonical CDN 2'3'-cyclic-GMP-AMP upon DNA binding. *Listeria monocytogenes* is a facultative intracellular bacterium, which replicates in the cytoplasm of myeloid cells. The bacterium induces IFN responses in host cells. This has been proposed to play a deleterious role in the pathogenesis of listeriosis. Although recent studies in murine cells have proposed the CDN cyclic-di-AMP to be the key immunostimulatory bacterial molecule, the bacterial PAMP and host pathway responsible for IFN- β expression in human myeloid cells remain unknown. Here we report that, in human macrophages, induction of IFN- β expression does not correlate with overexpression of the multidrug efflux pump MdrT, which transports CDNs into the cytoplasm. By contrast, *Listeria* genomic DNA was found to be the major IFN-inducing pathogen-associated molecular pattern (PAMP) in *Listeria* extracts. Moreover, the IFN response to bacterial DNA and *L.monocytogenes* infection was dependent in IFI16, cGAS, and STING. Confocal microscopy revealed that *L. monocytogenes* DNA was present in the cytoplasm during infection and co-localized with IFI16 and STING. Thus, *Listeria* DNA is a major trigger of IFN β expression in human myeloid cells and engages a pathway dependent on IFI16, cGAS, and STING to induce innate immune responses.

P12.06 Uffe Nygaard CYTOKINE IL-33 MAY DETERIORATE SKIN BARRIER FUNCTION IN ATOPIC DERMATITIS

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Background: Atopic Dermatitis (AD) is a very common skin disease in affluent countries with 15-20% of children and 3-4% of adults being affected. However, only within the last decade, research has directed focus on the defective skin barrier as an early mediator of disease. Several papers have since presented data supporting an impaired stratum corneum as a primary event, leading to increased penetration of allergens and inflammation. IL-33, a newly described cytokine in the IL-1 family, has been of major interest in the pathogenesis of AD. We intend to investigate the role of IL-33 in the context of skin barrier dysfunction.

Objectives: To elucidate the actions of IL-33 on regulating transcription, translation and posttranslational modification of the pivotal barrier proteins filaggrin, involucrin and loricrin.

Methods: Cell cultures (primary keratinocytes) cultured with supplemented Ca^{2+} (1.3 mM) were stimulated for 96 hours with different concentrations of IL-33 (2, 20 and 100 ng/mL) using IL-25 (10 and 100 ng/mL) as positive control and vehicles as negative control. RT-PCR was used as primary method of analysis.

Results: IL-33 (100 ng/mL) significantly downregulates the expression of the filaggrin gene. IL-25 (100 ng/mL) significantly upregulates the expression of the loricrin gene. The involucrin gene shows a dose-dependent downregulation when stimulated with IL-33.

Conclusions: We hypothesize that IL-33 might play a major role in skin inflammation and hence could be a contributor to a functional skin barrier dysfunction in AD.

P12.07 Annette
Søndergaard

HORIZONTAL TRANSFER OF CHROMOSOMALLY-ENCODED RESISTANCE TO BETA-LACTAM ANTIBIOTICS BETWEEN *HAEMOPHILUS INFLUENZAE* AND *HAEMOPHILUS HAEMOLYTICUS*

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Objective: To document horizontal transfer of the *ftsI* gene between *Haemophilus influenzae* and *Haemophilus haemolyticus* in vitro.

Background: *Haemophilus influenzae* is the major human pathogen of the genus *Haemophilus* and a significant cause of respiratory tract infections, acute otitis media, and, in non-vaccinated populations, purulent meningitis. One of the resistance mechanisms to beta-lactam antibiotics found in *H. influenzae* is mutations in the chromosomally located *ftsI* gene. *FtsI* encodes the penicillin-binding protein 3 (PBP3), which is essential for cell wall formation during cell division.

The species *H. influenzae* is naturally competent for transformation.

Horizontal gene transfer of *ftsI* from the nonpathogenic species *Haemophilus haemolyticus* to *H. influenzae* has been suggested to occur based on the mosaic structures of *ftsI* found in some clinical strains of *H. influenzae*. However, this putative transfer has not been documented in vitro.

Results: We successfully transferred the *ftsI* gene between *H. influenzae* and *H. haemolyticus* in vitro by electroporation. Mutated *ftsI* from one *Haemophilus* species conferred a raise in MIC in the other species. Sequencing revealed that homologous recombination of almost the entire *ftsI* gene can occur between *H. influenzae* and *H. haemolyticus*.

Conclusion: This study documents interspecies and intraspecies transfer and homologous recombination of the *ftsI* gene in *H. influenzae* and *H. haemolyticus* in vitro. The *ftsI* transfer was able to confer a raise in MIC in recipient strains of both species. These results show that nonpathogenic species of *Haemophilus* could be potential reservoirs for antibiotic resistance genes.

P12.08 Chenglong Sun NOVEL MECHANISMS IN IMMUNE RECOGNITION OF VIRUSES-DETECTION OF THE VIRAL CAPSID

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In the infected cells, herpesvirus DNA can be exposed to the cytoplasm following proteasomal degradation of the viral capsid. Consequently, the exposed genome DNA will be detected as a pathogen-associated molecular pattern (PAMP) by intracellular germline-encoded pattern recognition receptors (PRRs) and induce IFN responses. About 10 intracellular DNA sensors have been identified at this stage. However, knowledge on how viral capsid is detected and targeted for degradation is still unclear. To address this question, we hypothesize that there are E3 ubiquitin ligases which can detect the invading herpesvirus capsid and catalyze ubiquitination and subsequent proteasomal degradation, which leads to release of genome DNA into cytoplasm. In this project, 11 E3 ligase candidates, which have been identified in a genome-wide siRNA screen to be involved in control of herpesvirus infection, are examined for involvement in innate immune responses to herpes simplex virus infection. To identify which one or several of the candidates that may be involved, we will knock down each candidate with siRNA in permissive (Hela) and nonpermissive (THP-1) cells and evaluate how this effects replication of HSV-1 and IFN- β production induced by HSV-1, respectively. In the first round KD including 4 candidates, MARCH8 has been identified as a potential candidate, based on reduced HSV-induced IFN- β expression. We are currently constructing THP1- and Hela-derived cell lines stably transfected with MARCH8 shRNA. These tools will be used to evaluate the role for MARCH8 in the early stages of immunological detection of herpesvirus infections.

P13.01 Lars Skov Dalggaard RISK OF BACTEREMIA IN PERSONS WITH CHRONIC RENAL FAILURE ON HEMODIALYSIS; AN OBSERVATIONAL COHORT STUDY

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Introduction: Bacteremia is a serious condition in the general population, but little is known about the epidemiology of bacteremia among patients with end-stage renal disease (ESRD). The aim of this project was to compare incidence and risk factors of bacteremia in patients on hemodialysis with an age and gender matched comparison cohort.

Methods: The Danish Nephrology Registry and the Danish Civil Registration System (CRS) were used to identify residents in Northern Jutland diagnosed with ESRD during 1995-2010. For each ESRD patient, 19 persons from the general population matched on age, gender, and county of residence were sampled from the CRS. Information on bacteremia was obtained from the North Denmark Region Bacteremia Research Database and the hospital laboratory system in the Central Denmark Region. Time at risk was calculated from the first day of hemodialysis to the first episode of bacteremia, death, emigration, end of hemodialysis therapy, or 31. December 2010, whichever came first. Incidence rates of first episode of bacteremia were computed and risk factors identified by Poisson regression.

Results: Among 1 847 ESRD patients initiating hemodialysis in 1995-2010 and 34 651 population controls, we identified 487 and 1 178 cases of first time bacteremia, respectively. Incidence rates of first episodes of bacteremia were 14.2 (95% CI; 13.0-15.5) per 100 person years among person on hemodialysis and 0.54 (95% CI; 0.51-0.57) per 100 person years among comparisons. ESRD patients had 26.5 (95% CI; 23.8-29.4) fold increased risk of bacteremia.

Conclusion: Among ESRD patients, the crude risk of bacteremia was 26-fold higher than among the matched comparisons.

P13.02 Christian Brink Scholz CHARACTERIZATION OF PROPIONIBACTERIUM ACNES POPULATIONS

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The Gram-positive microaerophilic anaerobe *Propionibacterium acnes* is one of the predominant members of the commensal skin microbiota. It is demonstrated to be involved in the pathogenesis of acne and is commonly involved in prosthetic surgery infections.

The *Propionibacterium acnes* population is divided into several phylogenetic clusters and only some of these are associated with disease. In order to distinguish between these, I will identify phylogenetic cluster- and/or lineage-specific marker sequences that can be exploited in PCR or blotting analyses as a substitute for expensive and time-consuming MLST

analysis.

I will also identify genes that are variably present and/or expressed in the *Propionibacterium acnes* population and identify those that are characteristic to the individual evolutionary lineages of *Propionibacterium acnes*. This may explain differences in their association with health and clinical infections. This is done using a database of almost 100 genome sequences.

P13.03 Rikke Fleron
Leihof

INHIBITION OF INTRACELLULAR GROWTH OF UROPATHOGENIC IN AN
BLADDER EPITHELIUM CELL MODEL

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Uropathogenic *E. coli*, the primary cause of UTI, can bind to, invade and replicate within the bladder cells, creating a reservoir that can evade the immune defence and antibiotic treatment leading to recurrent infections. The aim of this study was to evaluate different antimicrobial agents as well as non-antimicrobial agents on their effect on intracellular bacterial communities. An in vitro cellular model using bladder cells (HTB-9 5637) was infected with *E. coli* UTI89. Extracellular bacteria were removed with gentamicin (Gen). Ampicillin (A), fosfomycin (Fos), nitrofurantoin (Nit), ciprofloxacin (Cip) and gentamicin, all representing different functional classes of antimicrobial agents used for treatment of UTI, were added at drug concentrations simulating urine concentrations after standard clinical doses. Intracellular bacteria were enumerated by serial dilution colony counts. Experiments were done in triplicates and a plate without cells was used as a control. In non-treated controls, the intracellular bacterial counts reached 5.5×10^7 CFU/ml after 12 h. After treatment, the antibiotics eradicated all bacteria when no epithelial cells were present. Intracellular counts were reduced by all antibiotics (from log 7.7 to log 2.2 CFU/ml), but none were able to eradicate the intracellular *E. coli*. Gen showed least effect (reduction of log 3.5 CFU/ml), while Nit and Cip were the most effective at reducing the intracellular bacterial counts, i.e. a log-reduction in counts relative to non-treated controls of 5.4 and 5.5 CFU/ml after treatment, compared to 4.6 CFU/ml, 4.8 CFU/ml after treatment with Amp and Fos, respectively.

P13.04 Kaja Zuwala

WHERE MEDICINE AND CHEMISTRY MEET: SCREENING OF ANTI-HIV
MACROMOLECULAR PRODRUGS IN VITRO

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Approximately 34 mio people worldwide are infected with HIV requiring life-long treatment. HIV primarily infects CD4+ T cells, a vital component of cellular immune response, and destruction of these cells results in immunodeficiency. Combination antiretroviral treatment has dramatically

increased life expectancy of HIV-infected people, but if patients are non-compliant emergence of resistant viral strains rapidly occurs. Limited studies of macromolecular prodrugs in anti-HIV treatment are mainly based on natural polymers which properties cannot be controlled. In the present proof-of-concept work, we employed libraries of chemically synthesized polymers as carriers for AZT (retrovir). Well controlled polymer molecular weight and AZT content enable determination of structure-function relationship. Two different libraries were tested; one consists of negatively charged methacrylic acid (MA) based polymers, which themselves have antiviral activity, and a second consists of N-(2-hydroxypropyl)-methacrylamide (HPMA) based polymers already employed in bio-medicine. We screened polymer libraries for antiviral effects on TZM-bl model cell line and subsequently determined IC50 values of six specific polymers. In addition, bona fide antiviral activity of these polymers was verified in human primary CD4+ T cells. Both systems showed that HPMA polymers do not have antiviral activity, but delivering AZT in a macromolecular prodrug makes it a potent inhibitor of viral replication. Lastly, consistent observations in both settings verified that PMA polymers inhibit viral replication, yet again incorporating AZT into the macromolecular prodrug significantly increases viral inhibitory efficacy.

- P13.05 Charlotte Willemann Stecher THE GENITAL SCHISTOSOMIASIS AND HIV RESEARCH PROJECT (GENSHIV): EFFECT OF PRAZIQUANTEL TREATMENT ON GENITAL HIV-1 RNA SHEDDING IN SCHISTOSOMA HAEMATOBIMUM AND HIV CO-INFECTED SUBJECTS - A RANDOMIZED TRIAL

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- P13.06 Thomas Andersen INTERLEUKIN-23 LEVELS DO NOT PREDICT DISEASE DEVELOPMENT IN EARLY RHEUMATOID ARTHRITIS PATIENTS

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Introduction: Rheumatoid arthritis (RA) is a chronic disease characterized by inflammation in the peripheral joints. CD4+ T cells play a pivotal role in the establishment of the inflammation. In particular the Th17 subset has been shown to be fundamental for experimental joint diseases in mice. Recently, the Th17 cytokine interleukin (IL)-23 has been proposed as central in this process.

Methods: 151 early RA patients from an RCT study were included. Patients were randomized to methotrexate, intraarticular (i.a.) steroid injections and Adalimumab (n=76) (ADA) or Methotrexate, i.a. steroid injections and

placebo-Adalimumab (n=75) (MTX). Plasma samples were obtained at baseline 3, 6 and 12 months of treatment, together with disease activity parameters including CRP, DAS28CRP, CDAI, SDAI VAS-pain/fatigue/ doctors-global. IL-23 was measured at each time point using an optimized commercial sandwich ELISA system.

Results: IL-23 levels decreased significantly in the ADA group from 20.6 pg/ml (13.1-32.7) at baseline to 18 pg/ml (7.2-5.0) at 12 months ($p < 0.01$). No significant decrease in IL-23 was observed in the MTX group. No association between baseline IL-23 levels and measures of disease activity (DAS28CRP, CRP, CDAI or SDAI) at 12 or 24 months was present in either of the treatment groups. In the ADA group, an association between 12 months IL-23 and CRP levels and a tendency towards an association to DAS28CRP were found.

Conclusion: Our data show a significant but minor decrease in IL-23 levels in early RA patients treated with anti-TNF α , but no predictive value of IL-23 on disease activity after 12 months of disease, questioning the importance of IL-23 in RA development.

P13.07 Ane Langkilde- SUBCUTANEOUS ADIPOSE TISSUE UNDERNEATH PSORIATIC SKIN MAY
Lauesen Nielsen RESEMBLE SUBCUTANEOUS ADIPOSE TISSUE FROM INSULIN RESISTANT
PATIENTS

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Adipose tissue seems to play a role in the pathogenesis of psoriasis. A high Body Mass Index (BMI) is associated with severe psoriasis, and increased expression of resistin and leptin has been found in serum from psoriatic patients compared with healthy controls. Furthermore, adiposity and insulin resistance is increased in patients with severe psoriasis compared to controls.

The purpose of this study was to investigate the subcutaneous adipose tissue underneath areas with psoriasis compared with areas underneath non-psoriatic plaques in the same patient and with subcutaneous adipose tissue from normal healthy controls.

A microArray analysing 28,869 mRNAs was conducted on excision biopsies from 3 psoriatic patients (males, age: 25-45 years; Psoriasis Area and Severity Index (PASI): 17-23; BMI: 28.5-39.1). The biopsies were divided into subcutaneous fat and epidermal/dermal tissue. Expression of mRNAs was compared between the nonlesional and lesional tissue and between the subcutaneous fat and the epidermal/dermal tissue.

A top five listing of the most regulated pathways between subcutaneous fat underneath psoriasis and underneath non-psoriatic skin revealed the insulin pathway as being downregulated underneath psoriatic skin compared with tissue underneath non-psoriatic skin.

Preliminary histological results confirmed this finding. The subcutaneous fat underneath psoriatic skin showed more similarities with subcutaneous

adipose tissue from insulin resistant patients than tissue underneath healthy skin.

This study suggests that psoriatic subcutaneous fat may have an effect on the development of insulin resistance in psoriatic patients.

P13.08 Julie Kristine Laustsen

OX40+ T CELLS AND OX40L+ B CELLS ACCUMULATE IN THE INFLAMED JOINTS

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Background: RA is an autoimmune disease characterized by the presence of autoreactive T cells, leading to synovitis. OX40 and OX40L are crucial for the generation of memory T cells. Signals through the OX40 receptor lead to AKT phosphorylation, thereby leading to increase of anti-apoptotic signals and maintenance of the memory response.

Objectives: To investigate the cells expressing OX40 and OX40L and to examine the intracellular response after sOX40L stimulation.

Methods: Paired PBMCs and SFMCs from 12 RA patients were compared with PBMCs from 6 healthy volunteers (HV). Cells were stained with anti-OX40 and anti-OX40L and analysed by flow cytometry. To determine the intracellular response, cells were stimulated with sOX40L, followed by intracellular staining with anti-AKT antibody. Phosphorylation status was analysed by phosphoflow.

Results: Memory T cells in PBMCs from RA patients had significantly elevated OX40 compared with HV ($p < 0.05$). Furthermore, OX40+ memory T cells accumulated in the SF of RA patients ($p < 0.01$). B cells from SFMC expressed significantly more OX40L compared with the PBMCs from RA patients and from HV (All $p < 0.05$). T cells from RA patients had significantly increased baseline levels of AKT phosphorylation in their T cells, but this was not metabolised differently from HV after stimulation with sOX40L.

Conclusions: Cells expressing OX40 and OX40L accumulate in the inflamed joints of RA patients. Further, CD4+ T cells from RA patients have significantly higher AKT phosphorylation compared with HV, and thus have up-regulated anti-apoptotic signals. However, the cells from RA patients did not respond differently after adding or removing sOX40L.

P14.01 Mikkel Christoffer Vinding

THE DIFFERENCE BETWEEN DISTAL AND PROXIMAL INTENTION FOR ACTION MEASURED WITH EEG

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The role of conscious intention in relation to motoric movements has become a major topic of investigation in neuroscience. Subjective reports of conscious intention have been compared to various features of the readiness-potential (RP) - an electrophysiological signal that appears before voluntary movements, often with the conclusion that conscious

intention has no causal relation to action. Experiments, however, tend to study intentions in immediate relation to movements (proximal intention), thus ignoring other aspects of intentions such as planning or deciding in advance of movement (distal intention). We examined the difference between proximal intention and distal intention, using electroencephalography (EEG). Participants formed an intention to move and then waited 2.5 sec before performing the actual movement. In this way, the electrophysiological activity related to forming a conscious intention was separated from any confounding activity related to automated motor activity. We found that late RP differed significantly depending on the type of intention. In addition, we found a slow negative electrophysiological "intention-potential" above the mid-frontal areas at the time participants formed a distal intention. This potential was only found when the distal intention was self-paced and not when the intention was formed in response to an external cue. A follow-up study showed that distal intentions enhanced the sense of agency compared to proximal intentions. This shows that how intention is defined is not trivial and implies different cognitive and physiological roles of different kinds of intention.

P14.02 Sofie
Christiansen

DISTURBANCES OF CIRCADIAN RHYTHM IN DEPRESSION

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Aim: The focus of this project is to identify biomarkers related to circadian disturbances in major depressive disorder.

Background: A large body of clinical data from depressed individuals showed that sleep, temperature, hormones, physiological states and mood changes are consistent with disturbances in circadian related processes. The suprachiasmatic nucleus (SCN) is well known for its function as the master clock and regulates several circadian systems by clock genes expression. In addition to central expression of clock genes, peripheral clock genes have been found.

Methods: The study is based on a highly validated animal model of depression, the chronic mild stress model (CMS). Depression-like rats and control rats were killed by decapitation during 24 h. Brain, trunk blood and liver were collected. The quantitative amount of plasma corticosterone was measured using an ELISA kit. Identification of specific clock genes in the liver was done by using the q-PCR method. Quantification and visualization of clock genes in the brain were established by the in situ hybridization method.

Results: We studied three of the most essential clock genes, PER1, PER2 and Bmal1, and found that depression-like animals showed an abnormal circadian rhythm in the liver and in subregions of the rat brain related to depression. However, the SCN was well protected against stress. We found an increase in the rodent cortisol analog, corticosterone, in the depression-like animals as well as a shifted circadian rhythm.

Conclusion: Abnormalities in circadian rhythms, both centrally and peripherally, are related to depression-like state in the CMS model.

P14.03 Christina Fischer REPEATED INTERFERON-ALPHA ADMINISTRATION PRODUCES DEPRESSIVE-LIKE BEHAVIOR IN RATS

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Background: Recent evidence suggests that the immune system plays a role in depression. Immunotherapy with interferon-alpha (IFN- α), commonly used in treatment of chronic hepatitis C, leads to depressive symptoms in 16-45% of patients (with no history of psychiatric illness) during the course of therapy. However, supplementary treatment with antidepressants is able to reverse the IFN- α induced symptoms of depression.

Aim: To further explore the association between the immune system and depression, the aim of this study was to investigate whether IFN- α could induce a depressive phenotype in rats. We further wished to study whether antidepressant (imipramine) or anti-inflammatory (celecoxib) drugs could reverse the IFN- α induced depressive-like behavior.

Methods: Rats received daily injections with IFN- α or vehicle for 7 days and were subsequently tested for depressive-like behavior using the Forced Swim test (FST). Additional groups of IFN- α injected rats were daily co-administered with imipramine or celecoxib for 7 days, and their behavior was then evaluated in the FST.

Results and discussion: IFN- α treated animals showed a significant increase in immobility in the FST compared to controls, indicating that IFN- α injections induce a depressive-like phenotype. Treatment with imipramine significantly reduced the IFN- α induced depressive-like behavior, while celecoxib induced a trend toward an antidepressant effect.

Conclusion: Given that IFN- α induces depressive-like behavior in rats, which furthermore respond to antidepressants improves the validity of the model, and suggests that repeated IFN- α injections in rats could serve as an immune-mediated model of depression.

P14.04 Sanne Bjørn Nygaard GENOMIC PROFILING OF GLP-1 RECEPTOR AGONIST SENSITIVE CELLULAR PATHWAYS IN THE CNS

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Background: There is no current treatment for the underlying neurodegeneration in Alzheimer's disease (AD). Abnormalities in cerebral blood flow, in microvascular structures and in the blood brain barrier are common findings in AD. The molecular mechanisms underlying these changes are not yet known, but recent reports indicate that amyloid beta can have deleterious actions on cerebrovascular function. Experiments in mouse

models of AD show that metabolically active hormones and drugs can improve and reverse some of the disease relevant phenotypes. GLP-1 (Glucagon like peptide 1) affects cerebral glucose metabolism and functional impairment. Recently, small molecule agonists of GLP-1 with oral bioavailability and the potential to enter the CNS have been reported. This provides molecular tools for the investigation of metabolic regulation and neuro-vascular diseases such as AD.

Hypothesis: Treatment with a GLP-1 receptor agonist will cause changes in the transcriptional control of central cellular pathways and processes regulating brain metabolism.

Design: Cortex and Hippocampal tissue is obtained from wildtype mice and rTg4510 (Tau model of AD) after chronic and acute treatment with GLP-1 receptor agonist, Liraglutide, to be examined for alterations transcriptional regulation of genes to identify the molecular pathways regulated by the central GLP-1 receptor.

Methods: The primary endpoint is to perform bioinformatics analysis of the data obtained from RNA sequencing of the isolated brain tissue. The secondary endpoint is to evaluate cognitive function, ketone body levels, immunohistochemical markers of aging and metabolism.

P14.05 Esben Ahlburg
Eickhardt PATTERNS OF GENOMIC VARIABILITY IN THE INSERTIONS/ DELETIONS OF PATIENTS WITH PSYCHIATRIC DISORDERS

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Background: Psychiatric disorders have been projected to account for as much as 14.7% of the total global burden of disease by 2020. Though several of the most common psychiatric disorders have been shown to have high heritabilities (40-80%), little is known about their exact genetic mechanisms. Numerous single nucleotide variants (SNVs) from several distinct loci have been identified, in particular for schizophrenia and bipolar disorder, but these only account for a minor fraction of the estimated heritability. While SNVs have been extensively investigated in sequencing data, rare SNVs and insertions/deletions (INDELs) remain insufficiently characterized.

Aim: In whole exome sequencing studies, we aim to elucidate if rare and potentially damaging INDELs account for a higher genomic variability and mutational load compared to that of relatively common SNVs, and if these may contribute to the susceptibility to the disabling disorders.

Methods: The study will build on deep (30x) exome sequencing data of cases and controls from national biobanks, and environmental/phenotype data obtained from the Danish register system. Initially the study will focus

on 344 exomes from the Faroe Islands, and then will be expanded to larger data collections of up to 30,000 exomes. The variant distribution will be characterized in terms of: a) Distribution in the genome (what regions, functional elements and genes do the variants affect), b) Allele frequencies, c) Positions in the coding sequences, d) Distribution across loss of function tolerant genes, e) Identification of clusters where the previously described characteristics may partition into.

Results: Pending

P14.06 Gitte Nikolajsen NO EFFECT OF DHA ON SYNAPTIC TRANSMISSION AND PLASTICITY IN MICE

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Epidemiological and clinical trials suggest that insufficient consumption of the omega-3 fatty acid docosahexaenoic acid (DHA) during pregnancy is associated with poor cognitive development. In this regard, it has been suggested that DHA deficiency may affect normal synaptic plasticity. Previous studies of the effects of DHA on synaptic functions have been performed in rat hippocampal slices, where rats kept on a DHA deficient diet had a significant lower level of long-term potentiation (LTP).

In this study, we investigated DHA's influence on synaptic transmission and plasticity in wild-type (Wt) mice and a transgenic (Tg) mouse model of Alzheimer Disease (AD).

Female Wt and APP^{swe}/PS1^{deltaE9} mice were given an enriched or DHA free diet during breeding. This Tg mouse shows an age-related increase in Abeta42 levels from 4 months of age, but no changes of synaptic transmission when fed a normal diet. Female offspring were used for this study, which were kept on the same diet as their parent through life. This resulted in 4 experimental groups at 7 months of age.

The synaptic transmission was evaluated by recording field excitatory postsynaptic potentials (f-EPSP) and input/output responses to Schaffer collateral stimulation. Synaptic plasticity was evaluated by LTP recordings induced by theta burst stimulation. The results showed that a DHA deficit or enriched diet from embryo stage had no significant effect on LTP in these female mice, regardless of genes. This suggests that DHA consumption in mice do not have the same impact on the synaptic plasticity as in rats. Moreover, the expression of amyloid does not seem make the mouse more responsive to a DHA deficient diet.

P14.07 Desiree Del Carmen Leduc Galindo THE MOLECULAR INTERACTIONS OF THE SCHIZOPHRENIA SUSCEPTIBILITY GENES AND IN NEURONAL CELLS

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Zinc finger E-box binding homeobox 1 (ZEB1) locus is found to be associated with schizophrenia (SZ) in region-wise genome wide association studies (GWAS) (Børglum et al. 2013). Genome wide significant association was also found for the zinc finger E-box binding homeobox 2 (ZEB2) locus in a large SZ GWAS meta-analysis (Ripke et al. 2013).

ZEB1 is part of the CtBP co-repressor core complex, important in neuro-development and neurodifferentiation. ZEB2 plays a role in cortical neurogenesis, hippocampal formation and myelination and mutations in ZEB2 cause Mowat-Wilson syndrome, which is associated with mental retardation and developmental phenotypes. ZEB2 mRNA is also a predicted target for MIR137, encoded by the SZ-associated gene MIR137.

We hypothesize that ZEB1 and ZEB2 participates in protein complexes as gene specific transcriptional repressor and that the interacting proteins and genomic targets accordingly represent candidate genes to be involved in neurodevelopment and SZ.

We have cloned the coding regions of ZEB1 and ZEB2 with N-terminal and C-terminal epitope tags and stably expressed these in HEK293T and working on SH-SY5Y cell lines, proteins that interact in complexes with (N- and C- terminal) epitope tagged ZEB1 and ZEB2 will be co-immunoprecipitated with anti-V5 and HA antibodies and identified by LTQ-Orbitrap mass spectrometry. Interaction partners will be validated by reciprocal immunoprecipitation, western blotting analysis and co-immunofluorescence staining in primary mouse neurons.

Genomic targets will be identified by chromatin immunoprecipitation (ChIP) followed by next generation sequencing.

P14.08 Signe Rode
Andreasen

ELECTROPHYSIOLOGICAL ANALYSES OF SHORT-TERM PLASTICITY IN A MOUSE MODEL OF FAMILIAL HEMIPLEGIC MIGRAINE TYPE 2 WITH PERTURBED $\alpha_2\text{Na}^+/\text{K}^+$ -ATPASE FUNCTION

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Background: Normal neuronal activity depends on the ability of the Na^+/K^+ -ATPase to generate an ion gradient across the mammalian plasma membrane essential for neuronal excitability and secondary transport. The $\alpha_2\text{Na}^+/\text{K}^+$ -ATPase is expressed mainly in astrocytes, and mutations in the α_2 -subunit are associated with development of Familial Hemiplegic

Migraine type 2 (FHM2), a severe hereditary form of migraine with aura and associating hemiparesis. Additionally epileptic seizures, coma and varying degrees of cognitive decline are observed.

Hypothesis: We speculate that FHM2 is a consequence of a dysfunctional astrocytes-neuron interaction, caused by an altered membrane potential, glutamate uptake and gliotransmitter release in turn affecting the astrocytes ability to modulate synaptic activity.

Method: To investigate the physiological consequences of perturbed $\alpha_2\text{Na}^+/\text{K}^+$ -ATPase function in hippocampus, we use extracellular field recording to determine possible alterations in the short-term synaptic plasticity. We employed a mouse model of FHM2 carrying a G301R knock-in (KI) mutation in the α_2 -subunit of the $\alpha_2\text{Na}^+/\text{K}^+$ -ATPase (Bøttger et al., in submission).

Results: To determine possible alterations in the short-term plasticity, we analyzed input-output curves, paired-pulses and trains of stimulation. We observed no significant effect of G301R KI mutation on basal single-pulse evoked neurotransmission or relative paired-pulse facilitation. From train stimulations, no statistically significant difference in fEPSP slopes was found, suggesting that presynaptic alterations are not the cause of FHM2 symptoms.

P15.01 Veerle Paternoster

THE SCHIZOPHRENIA AND BIPOLAR DISORDER ASSOCIATED PROTEIN BRD1 INTERACTS WITH HISTONES AND INFLUENCES GLOBAL HISTONE MODIFICATION PATTERNS

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Accumulating data from genetic, cell and animal studies form strong evidence that the Bromodomain-containing 1 (BRD1) gene is involved in the pathogenesis of schizophrenia (SZ) and bipolar disorder (BD). The BRD1 protein interacts with Histone Acetyl Transferases (HATs) HBO1 and TIP60 and binds to the transcription start sites of genes. BRD1 seems to be involved in Histone H3K14 acetylation and to a lesser extent Histone H3K9 acetylation. One aim of the PhD project is to examine the effect of Brd1 depletion in the mouse brain on global histone modification profile patterns using nanoLC-MS/MS.

Preliminary results show that conditional homozygous Brd1 knockout mice (Brd1^{-/-}) have a 66% reduction of H3K14 acetylation (p=0.0029) and a 23% reduction of H3K23 acetylation (p=0.0259) compared to conditional heterozygous Brd1 knockout mice (Brd1^{+/-}). Both of these histone

modifications are described to be involved in transcriptional activation. There is limited functional knowledge concerning H3K23 acetylation, but indirect evidence implies CREB binding protein (CBP) as a regulator of H3K23 acetylation. H3K14 is a known interaction site for the BRD1-HBO1 HATcomplex. Data for other BRD1 sensitive histone modifications will be presented on the PhD day.

Additional to the identified Brd1 depletion sensitive histone marks, a novel histone modification was detected: H3R49 methylation. Methylated Arginine (R) in histone tails was previously described to influence gene transcription, and therefore one could envisage a similar function of this novel histone mark.

Understanding the molecular mechanisms of BRD1 in brain gene regulation will help unraveling the role of BRD1 in the SZ and BD.

P15.02 Line Nilsson

INTRAPERITONEAL ADMINISTRATION OF CHITOSAN/SIRNA NANOPARTICLES TARGETING COX-2 PREVENTS INFLAMMATION AND OXIDATIVE STRESS IN RESPONSE TO UNILATERAL URETERAL OBSTRUCTION IN MICE

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Cyclooxygenase type 2 (COX-2) is induced in response to unilateral ureteral obstruction (UUO). We examined the role of COX-2 in the progression of inflammation and oxidative stress in response to UUO using COX-2 siRNA loaded chitosan nanoparticles targeted to macrophages.

Mice were subjected to 3 days UUO and COX-2 knockdown were mediated by intraperitoneal injection of chitosan/COX-2 siRNA nanoparticles. Sham-operations were performed in parallel. Localization of Cy5-labeled siRNA was determined by in vivo optical imaging for nanoparticle tracking. COX-2 mRNA and protein level was evaluated by QPCR and immunoblot, respectively. Expression of the inflammatory markers, TNF- α and IL-6, were investigated at the mRNA level and the oxidative stress marker, heme oxygenase-1 (HO-1) and antioxidant enzymes, superoxide dismutase 1 and 2 (SOD1 and -2) by immunoblot analysis. HE staining was performed to investigate tubular morphology.

Cy5-labeled siRNA were predominantly accumulated in the macrophages in the obstructed kidney accompanied with increased COX-2 mRNA and protein levels. The induced COX-2 expression was attenuated by COX-2 siRNA treatment. TNF- α , IL-6 and HO-1 were increased during UUO, and this increase was prevented in response to COX-2 siRNA treatment. SOD1 and SOD2 protein levels were downregulated in response to UUO and treatment with COX-2 siRNA attenuated the downregulation of SOD2. HE staining showed lesser tubular damage in COX-2 siRNA treated UUO mice compared to the siRNA control group.

This study demonstrates that nanoparticle-mediated COX-2 knockdown in mice may contribute to impaired development of inflammation and

oxidative stress in response to 3 days UUO.

P15.03 Iben Lyster
Daugaard

MICRORNA AS REGULATORS OF LUNG ENDOTHELIAL PERMEABILITY AND
CANCER PROGRESSION

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Lung cancer has been the leading cause of cancer deaths worldwide for several decades. Today, the 5-year survival rate remains at 5-15%, which is generally due to an advanced stage of disease at the time of diagnosis. Tight Junctions (TJs) are the most apical adhesion complexes in epithelial and endothelial cells. They form a selective barrier and regulate the paracellular permeability. TJ disruption is considered a common event in cancer, and endothelial TJs represent one of the first barriers that a tumor must overcome to metastasize. MicroRNAs (miRs) are small, non-coding RNAs that posttranscriptionally regulate gene expression. We have performed an anti-miR lentiviral library screen in human lung endothelial cells and identified two miRs as regulators of lung endothelial permeability; miR-A and B. We demonstrate that overexpression of both miRs is sufficient to cause a significant increase in permeability and conversely, knockdown result in a significant decrease. For miR-B, we show that this effect is mediated through regulation of the TJ protein Claudin-5. Moreover, we have investigated the effect of miR-A and B on the growth and metastatic potential of a lung cancer cell line, A549. We show that knockdown of these miRs inhibit the growth by approx. 90% and 50%, respectively, and we have preliminary data indicating that this is caused by induced apoptosis and G1 arrest. Furthermore, preliminary data show that these miRs are also capable of inhibiting A549 migratory potential and facilitate tumor transendothelial migration. This study demonstrates that miRs are capable of affecting several aspects of a complex pathological process such as lung cancer progression.

P15.04 Sigríð Salling
Árnadóttir

CHARACTERIZATION OF INTRA-TUMOR HETEROGENEITY IN COLORECTAL
CANCER

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Colorectal cancer (CRC) is the second leading cause of cancer-related death worldwide. So far, almost all translational molecular CRC studies have been based on a single biopsy from the tumor, followed by molecular analyses and correlation to outcome. However, we believe that this approach is often inadequate as the tumors are genetic, epigenetic and phenotypic heterogeneous and contain many cellular subpopulations with different properties. The prognosis and response to therapy will often be determined by a small number of cells in the tumor that possess the ability

to metastasize or avoid treatment. Obtaining a more detailed view of the tumor and information about these critical cell populations is therefore important. It is our hypothesis that the heterogeneity has attenuated CRC biomarker development, and we therefore seek to characterize the phenomenon in detail. Moreover, we expect that a greater insight into CRC tumor heterogeneity will lead to a better understanding of CRC evolution. It is our intention to disaggregate CRC tumors into single cells and separate these into subgroups by flow cytometry based on: 1) DNA ploidy and 2) expression of differentiation markers. Detailed genetic characterization of each subgroup will be performed by Next Generation Sequencing (NGS), and in parallel we will analyze the DNA methylome of each subgroup. Furthermore, matched lymph-node and distant metastases will be investigated in order to elucidate the characteristics of the subgroup of cells that had the ability to form metastases. The potential clinical utility of these characteristics as prognostic biomarkers will be investigated in large independent patient cohorts.

P15.05 Malene Juul
Rasmussen

DETECTION OF MUTATIONAL HOTSPOTS IN CANCER GENOMES

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Known methods exist for analyzing cancer SNV data sets to identify protein-coding genes with a higher mutation rate than expected by chance. Such a state-of-the-art method is MutSigCV [1]. However, methods for identifying significantly mutated non-coding elements are lacking.

NGS allows genome-wide data sets to be created routinely. In this work, we aim to use this increasing amount of data in developing a statistical method for detecting mutational hotspots in genome-wide SNV data sets, including non-coding regions.

Our focus is to analyze the mutation rate in highly conserved regions of the genome, suggesting regions of functional importance. Statistical tests will be implemented to assess whether a given mutation rate is higher than expected by a background model. The initial approach will be based on a sliding window scanning through the genome.

As in MutSigCV, our method will be able to take a number of covariates measured along the genome into account, such as expression level and replication time which correlate with the mutation rate. This information will be used to robustly estimate the background model.

The method development will be based on 507 whole-genome mutation data samples from ten different cancer types made publicly available from international consortia [2].

Significantly mutated non-coding regions detected will be analyzed experimentally by local collaborators for their role in cancer initiation and progression.

[1] Lawrence, M.S. et al. Mutational heterogeneity in cancer and the search for new cancer-associated genes. *Nature* 499-2013. p. 214-18.

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P15.06 Anne Kruse
Hollensen

MICRORNA INHIBITION BY DUAL-TARGETING AND CLUSTERED TOUGH
DECOY INHIBITORS

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MicroRNAs (miRNAs) are posttranscriptional gene regulators that play a role in almost any cellular process, and disturbed miRNA expression is associated with development of a wide range of diseases. In relation to diverse experimental and therapeutic applications, methods for managing miRNA activity are attracting increasing attention. In contrast to the often used synthetic and chemically modified miRNA inhibitors, vector-encoded miRNA inhibitors expressed from either plasmids or viral vectors allow persistent miRNA inhibition and tissue-specific expression. Currently, the hairpin-shaped "Tough Decoy" (TuD) miRNA inhibitor containing two miRNA binding sites is among the most efficient vector-encoded miRNA inhibitors. Here, we refine the design of the TuD miRNA inhibitor in order to increase the inhibitory potency and to obtain synchronized inhibition of two or more miRNAs. Using RNA polymerase II-transcribed inhibitors carrying clustered TuDs with up to a total of four TuDs in tandem, we demonstrate in luciferase-based assays enhanced miRNA inhibition compared to single TuDs. Additionally, we show potent co-suppression of pairs of unrelated miRNAs by RNA polymerase III-transcribed dual-targeting TuDs carrying two different miRNA binding sites. Finally, we demonstrate robust inhibition of six miRNAs by a single multi-targeting TuD expression cassette containing a cluster of three dual-targeting TuDs. These refined TuD miRNA inhibitors unveil a new efficient potential for inhibition of miRNA clusters or families and might by adaptation to a circularized design, similar to the recently discovered naturally occurring circular RNA sponges, be optimized even further.

P15.07 Lise Bols
Andersen

PATHOGENESIS OF AUTOSOMAL DOMINANT FAMILIAL
NEUROHYPOPHYSEAL DIABETES INSIPIDUS- FROM PROTEIN MISFOLDING
TO DEGENERATION OF MAGNOCELLULAR NEURONS

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Background: Autosomal dominant familial neurohypophyseal diabetes insipidus (adFNDI) is a rare disease characterized by severe low-solute polyuria and polydipsia. The condition manifests during childhood. The symptoms are caused by a gradual diminishing neurosecretion of the bioactive antidiuretic hormone, arginine vasopressin (AVP). The most widely accepted pathogenic hypothesis is "The misfolding-neurotoxicity hypothesis". This hypothesis proposes that variant AVP is retained in the

endoplasmatic reticulum by the protein quality control system leading to accumulation in the neurons, eventually causing degeneration.

Aim: To extract induced pluripotent stem cells (iPSCs) from adFNDI patients using fibroblasts and to describe a method for differentiating iPSCs to human neurons. If successful, it will be possible to compare WT neurons and neurons expressing variant AVP in regards to viability.

Methods: Skin biopsies will be obtained from patients suffering from adFNDI and healthy controls. Dermal fibroblasts will be grown in cell cultures. Cells will be plated onto a medium for primate embryonic stem cell cultures. Growth of iPSCs is possible through culture in stem cell media. qPCR analysis and fluorescence-activated cell sorting will be used to identify neurons. The amount of AVP immuno-reactivity will be determined using radioimmunoassay. Immuno-staining will be performed using specific antibodies. Confocal laser scanning microscopy will achieve visualization. A cell viability assay will be used to compare the two cell types. Furthermore, WT neurons and neurons expressing variant AVP will be exposed to oxidative stress, and subsequently the viability will be examined.

P15.08 Natasja Leth
Jørgensen

TOPOGRAPHICAL MICROSTRUCTURES INCREASE PROLIFERATION OF HUMAN PRIMARY CHONDROCYTES IN VITRO

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Aim: Chondrocyte-based cartilage repair techniques require control of autologous articular chondrocyte expansion and differentiation in vitro. Culture surface topography might be a tool to control the behavior of chondrocytes. In this study, we aimed at identifying topographical structures that stimulated the proliferation of human primary chondrocytes (HPCs) in vitro.

Methods: HPCs were isolated from healthy patients undergoing anterior cruciate ligament reconstruction. HPCs were isolated and 10,000 cells/cm² seeded upon the BioSurface Structure Assay (BSSA) library. Subsequently, the cells were stained with DRAQ5 for detection of proliferation using infrared imaging. The BSSA consisted of distinct topographical patterns organized in 10 different series (A-J) each series with 16 unique combinations of pillars with variable of dimension (X = pillar size and Y = inter-pillar gap size) and a non-structured control (SM). Interactions between the independent variables were investigated using two-way ANOVA. The level of significance was p < 0.01.

Results: The systematic screening of topographies identified that inter-pillar gap size Y, and to a smaller extent pillar size X, had a clear systematic effect on proliferation of HPCs. The structure dimensions (X=2, 4 µm) and (Y=1 µm) resulted in the most significant increase in proliferation

comparable to the unstructured control, while the dimension ($Y=6\ \mu\text{m}$) had the lowest proliferation effect.

Conclusions: Screening of different topographies identified structures with specific pillar size and inter-pillar gap size, which increased the proliferation capacity of HPCs compared to a planar structure.

- P16.01 Mia Benedicte Lykke Roest Laursen ISCHEMIC CONDITIONING &NDASH; A METABONOMIC STUDY OF PLASMA
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Ischemic conditioning is a protective phenomenon shown to reduce ischemia-reperfusion injuries in multiple organs. The intervention consists of brief alternating ischemia and reperfusion periods applied before, during or just after a longer and lethal ischemic event (ischemic pre-, per and postconditioning) and protects not only the organ in question, but also organs remote from this site. Additionally, plasma isolated from subjects undergoing ischemic conditioning can induce protection in untreated subjects, suggesting that the release of one or more blood borne mediators could be responsible for the protection. A number of metabolic pathways have been shown to be affected by ischemic conditioning, but the exact nature of such mediator(s) is not yet known. Using untargeted metabolomics, this study seeks to unravel the metabolic changes in plasma initiated by ischemic conditioning. Thus, a comparison between the metabolome of treated and control plasma samples is hypothesized to give insight into the mechanisms behind ischemic conditioning.

- P16.02 Moslem Ranjbar MICROMANAGING BY LENTIVIRAL TRANSDUCTION-DEFINING ROLES OF MICRORNAS IN DIFFUSE LARGE B-CELL LYMPHOMA

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MicroRNAs (miRNAs) are a subclass of non-coding RNAs that contribute to gene regulation through mRNA degradation or inhibition of translation. However, it is largely unknown how erroneous expression and inhibition of miRNAs may affect cancer development and progression. Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin Lymphoma in adults with low survival rate due to drug resistance. In this study, we address the role of miRNAs for drug resistance in cancerous B cells.

We studied the effects of lentiviral transduction on cancerous B cell lines to characterize molecular variations in vector-treated cells. Candidate miRNAs with potential involvement in drug sensitivity were identified by miRNA profiling analyses of drug-sensitive and/or -resistant cell lines. Our established lentiviral toolbox enabled us to manipulate the expression of different miRNAs in cancerous B cell lines for further investigation of their phenotypic roles. We evaluated the drug response and proliferation of transduced cells using BrdU Assay, whereas apoptosis rates were measured

based on detection of cleaved PARP.

We showed that lentiviral transduction significantly increases the resistance of the cancerous B cell lines to Rituximab. Interestingly, miR-9* decreases the proliferation in Ly-7 cells, and apoptosis rate in RIVA cells. On the contrary, miR-30a increases the proliferation in RIVA cells, whereas the miR-221-2 cluster increases the apoptosis rate in Ly-7 cells. We are currently analyzing the role of these miRNAs in the response to Rituximab. Our data demonstrate the applicability of lentiviral miRNA delivery for studies of miRNA roles in cancerous B-cell lines.

P16.03 Anders Laustsen ROLE OF PLASMACYTOID DENDRITIC CELLS IN INNATE IMMUNE SENSING OF HIV

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The level of the immune system during acute human immunodeficiency virus (HIV) infection determines whether virus is eliminated at mucosal sites or establishes expanding foci of infection and disseminates. What is often seen in acutely HIV infected individuals is a strong systemic induction of IFN- α that is believed to originate from plasmacytoid dendritic cells (pDCs). pDCs constitute one of the main components of the innate immune system against viruses. Furthermore, being a key source of IFN- α and pro-inflammatory cytokines, pDCs contribute to the induction of adaptive immunity. There are multiple indications that the activation of pDCs appears through interactions of cell-to-cell contact between pDCs and infected CD4⁺ T cells. This activation occurs through an endosomal pathway, where Toll-like Receptor 7 (TLR7) recognizes viral nucleotides. In this manner, pDCs mount an IFN- α response, without being productively infected by HIV. However, there are clear evidences for low levels of HIV-infections in pDCs and it has been shown that impairment of TLR7 may still lead to detectable IFN- α induction. These pieces of evidence indicate that pDCs may be activated through an unknown DNA sensor, detecting HIV viral DNA. The overall aim of this project will be to identify the DNA sensor involved in pDC endosomal-independent immune activation. Furthermore, we wish to address how HIV is transported from infected CD4+ T cells to uninfected pDCs.

P16.04 Nikolaj Worm BILIARY EXCRETION OF CONJUGATED BILE ACIDS IN HUMANS MEASURED BY ¹¹C-CHOLYLSARCOSINE PET/CT
Ørntoft

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Background: Hepatobiliary excretion is an internal function not accessible to conventional means of measurements. We aim to show that the radiolabelled bile acid tracer [N-methyl-¹¹C]Cholylsarcosine (¹¹C-CSar) PET/CT allows assessment of this function in healthy subjects and patients with cholestasis.

Methods: Seven healthy subjects and six patients with cholestasis underwent dynamic liver PET/CT using both bolus injection and continuous infusion of ^{11}C -CSar. The blood concentration of ^{11}C -CSar was measured from activity in samples from a radial artery and the hepatic vein. Tissue concentrations were generated from scan data. Hepatic blood flow was estimated using indocyanine green and Fick's principle. Steady-state extraction fraction and clearance of ^{11}C -CSar were estimated. Fractional biliary excretion was calculated as the ratio between ^{11}C -CSar excreted into bile and ^{11}C -CSar supplied to the liver.

Results: The estimated extraction fractions for healthy subjects were 0.89 and 0.58 for patients with cholestasis ($p < 0.0004$). For healthy subjects, the fractional biliary excretion was 89% and patients with cholestasis had a significant lower estimate of 63% ($p < 0.006$). Hepatic clearance of ^{11}C -CSar was not significantly different in the two groups (healthy 2.27 l/min, cholestatics 1.4 l/min, $p = 0.06$). The clinical degree of cholestasis (lab tests and biopsy) correlated with the results of the PET/CT scanning.

Conclusions: ^{11}C -CSar PET/CT enables assessment of hepatic uptake of bile and hepatobiliary excretory function. While kinetic analyses are still ongoing, these initial results show great potential for future noninvasive investigation of the hepatobiliary function.

P16.05 Anna Szyszka DNA METHYLATION OF CACNA1C IN BIPOLAR DISORDER

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CACNA1C encodes a subunit of the L-type voltage-gated calcium channel, which is important for proper function of the brain and other organs. A recent large genome-wide association study has identified a cluster of SNPs in the intron of CACNA1C to be highly associated with bipolar disorder and schizophrenia. However, the mechanism is unknown, and it has been suggested that it may involve epigenetic changes caused by unknown environmental factors. This study investigates differences in DNA methylation of CACNA1C between bipolar patients and healthy controls in their blood samples with the use of Sequenom technology (EpiTYPER and IPLEX). Investigation of single CpG sites in all CpG islands (CGIs) of CACNA1C by EpiTYPER showed strong similarity in methylation levels between most individuals in four of the five CGIs, which showed to be either fully methylated or fully unmethylated. One CGI and the CGI shore showed a moderate methylation level and a larger spread between individuals. Preliminary comparison of the two subject groups suggested few sites to be significantly differentially methylated, and confirmation of these findings will be performed in a larger population of cases and controls with the use of IPLEX technology. If methylation differences between cases and controls can be consistently identified in a larger sample, they will provide a mechanism in which environmental factors like medication may be used to impact calcium signaling and thereby disease.

P16.06 Anne Sigaard
Bie THE HSP60 SUBSTRATE SPECTRUM

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Hereditary spastic paraplegia and MitCHAP 60 are two rare neurodegenerative diseases caused by mutations in HSPD1, the gene encoding the mitochondrial chaperonin Hsp60. The molecular mechanisms underlying the diseases are unknown, but identifying the substrates of Hsp60 is the first step towards uncovering these mechanisms.

Hsp60 is a barrel-shaped chaperone residing in the mitochondrial matrix. Non-native proteins are folded in the cavity of the barrel in cooperation with Hsp10 which functions as a lid. Most of the approximately 1200 mitochondrial proteins are encoded in the nucleus and imported post-translationally. Upon entry into the mitochondrial matrix proteins are first folded by Hsp70 and further folding assistance is given by Hsp60 if needed. It is therefore only a subset of mitochondrial matrix proteins requiring Hsp60 for correct folding and maintenance of the native state.

We suspect that some of these proteins are part of pathways crucial for mitochondrial function, and that slight disturbances in mitochondrial functions due to misfolding or impaired folding of certain proteins are the cause of hereditary spastic paraplegia and MitCHAP60. We have investigated which proteins interact with Hsp60 in vivo. Using crosslinking, immunoprecipitation and mass spectrometry, we have identified interactors of Hsp60. Of the 332 proteins identified, 299 proteins are mitochondrial proteins representing a broad range of mitochondrial pathways.

P16.07 Gitte Brinch
Andersen DNA METHYLATION CHANGES IN OSTEOSARCOMA

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The main objective of the presented project is to obtain a better understanding of the epigenetic deregulation in osteosarcoma (OS) tumorigenesis based on genome-wide analysis of DNA methylation patterns.

Background: Osteosarcoma (OS) is the most common primary malignant bone tumor with a strong predilection for occurrence in children and young adults. The first indication of OS is pain, which is often misjudged with "growing pains," resulting in a late diagnosis. OS is characterized by a complex array of cytogenetic abnormalities with the consequence that only very few markers exist to help predict the prognosis and determine the best treatment of the patient. Therefore, there is a great necessity in understanding the biology of OS progression and metastasis.

Methods: To characterize the DNA methylation pattern of OS a methylation specific array screening for the identification of differential DNA

methylation patterns between osteosarcoma and non-malignant bone tissue was performed on DNA from 38 fresh frozen osteosarcoma samples, three non-malignant bone tissue samples, five OS cell lines and three osteoblast cell lines. The Infinium 450k Methylation BeadChip (Illumina) was used to obtain genome wide coverage as it allows the interrogation of >450.000 methylation sites per sample at single-nucleotide resolution and covers >96% of CpG islands.

Results: We have established the genome-wide epigenetic changes of OS and have found several genes displaying pronounced hypo- or hypermethylation.

Conclusions: We have substantiated the epigenetic features of OS, which contribute to a better understanding of the tumorigenesis and progression of this disease.

P16.08 Michal Switnicki PROBABILISTIC METHOD FOR INTEGRATION OF CANCER GENOMICS DATA IMPROVES IDENTIFICATION OF PERTURBED GENES

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Cancer development is driven by a complex pattern of genomic and epigenomic perturbations. Amongst these, especially important are changes in abundances of transcripts as they reflect altered regulation or mutations of underlying genes and relevant regulatory elements, and ultimately cause abnormal cell behaviour. Another convenient to look at element of cancer biology is the CpG methylation of DNA, a mark that serves as fingerprint of short-term epigenetic changes, and may have different implications based on function of the genomic element it occurs at. Most often independence is assumed when analysing multiple such data types, which is often not the case. For example, DNA methylation affects transcript abundance via promoting its elongation or insulating corresponding promoter region in case of hypermethylation. Here we develop and apply a method which allows dependencies between data types to be specified or learned from data. We used probabilistic graphical models for integration of global gene expression and CpG methylation profiles and demonstrate a significantly better detection of known cancer drivers (30% better recall than Fisher's method for panel of 18 genes) in a large dataset (n=75) of breast invasive carcinomas available from The Cancer Genome Atlas consortium. In short, our method evaluates likelihoods of cancer samples given posterior probability distribution of healthy control samples. This approach for data integration not only has the potential to improve discovery of relevant clinical biomarkers but also to reveal combined genetic and epigenetic perturbations in other diseases.

P17.01 Ran Kang INTERFERING ENDPLATE NUTRITIONAL PATHWAY CAUSES INTERVERTEBRAL DISC DEGENERATION IN IMMATURE PORCINE MODEL

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Purpose: Bone cement blocking endplate nutritional pathway did not result in obvious intervertebral disc degeneration (IDD) in mature animal models. However, less has been studied in immature animal model. As vertebroplasty now also used in young patient, down to 16 years old, not limited in old patients, it is important to investigate this cement blocking affect in immature animal model.

Methods: Two lumbar intervertebral discs in immature pigs were either blocked by cement in both endplate pathway, or stabbed by scalpel in annulus fibrosus (AF) as positive control, with an intact disc as normal control. Magnetic resonance imaging (MRI) including T1, T2-weighted, T2-weighted 3D, sagittal T2 mapping, was performed pre and 3 months post intervention. Serial post-contrast T1-weighted MRI and histology study also performed at the end.

Result: After 3 months, these cement blocked discs showed severe IDD, with the percentage of disc height index, Nucleus Pulposus (NP) area, and NP T2 value significantly lower than the normal controls. Post-contrast MRI showed diseased nutritional diffusion patterns in the cement blocked discs. Histology confirmed these IDD changes. Moreover, the degeneration changes of the cement blocked discs exceeded those of the positive controls by AF injury.

Conclusions: Endplate nutritional pathway was interfered and diseased after bone cement intervention in immature porcine model. Severely interfering endplate nutritional pathway in immature porcine model caused IDD. It might also be an issue that using large amount of cement in vertebroplasty or balloon kyphoplasty in immature or young patients will affect the health of adjacent discs.

P17.02 Anders Patrik
Alexander
Gunnarsson

STEM CELLS IN THE MURINE EPIDERMIS: INVESTIGATING THE RELATION BETWEEN GENE EXPRESSION, EPIGENETIC MARKS AND CELL POSITIONING

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Purpose: Degenerative diseases can be caused by the loss of specific cell types, and it is believed that such diseases can be treated using stem cell therapy. Due to the complexity of the stem cell compartments, a deeper knowledge of cellular reprogramming is crucial in order to select the best stem cell population to maximize efficiency and safety of the treatment. The murine epidermis contains a number of stem cells, residing at different locations. In addition, the absence of Sca-1 expression has been shown to identify follicle stem cells and will be further analyzed during the project.

Objectives: A) Examine how different keratinocyte stem cell populations can be described by their epigenetic- and gene expression profiles, B) Examine how epigenetic and gene expression profiles are altered after induced cellular reprogramming: Will an epigenetic profile reveal their

origin? and C) Examine the epigenetic and gene expression profiles in transgenic mice that overexpress Sca-1 and thus explain the role of Sca-1 in epidermal stem cell fate determination.

Methods: Transgenic mice in which Sca-1 has been activated at different levels in compartments that normally lack Sca-1 expression are used. K14 driven EGFP is used to facilitate isolation of pure epithelial cell populations. Cells are surface stained with several antibodies and isolated for subsequent RNA isolation and epigenetic analyzes. The epigenetic profiles will be mapped using chromatin immunoprecipitation (ChIP).

Transcriptome profiling will be made using next generation sequencing (NGS). Viral vectors expressing the Yamanaka factors Oct3/4, Sox2, Klf4 and c-Myc are used for cellular reprogramming.

P17.03 Morten Torvund- STRUCTURAL CHARACTERIZATION OF THE INTERACTION BETWEEN
Jensen HAPTOGLOBIN-HEMOGLOBIN AND MACROPHAGE RECEPTOR CD163

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Release of hemoglobin (Hb) into the circulation during intravascular hemolysis is a potential hazard because Hb is a toxic compound outside red blood cells. The toxicity of Hb is mainly due to the reactivity of the heme group that is able to generate free radicals, which may eventually cause severe oxidative damage to tissues. In mammals, Hb released into the circulation is immediately bound by the plasma glycoprotein haptoglobin (Hp) in one of the strongest non-covalent interactions observed in plasma. In the HpHb complex, Hb is protected from oxidative modification, thus the function of Hp may be to protect the structural integrity of Hb by preventing oxidative modifications. The endocytic SRCR domain-containing macrophage receptor CD163 internalizes the HpHb complex in a Ca²⁺-dependent manner and degrades heme into non-toxic metabolites.

Detailed determination of the interfaces between CD163 and HpHb could assist in development of cell-directed therapies targeting macrophage CD163, which is a highly attractive target candidate in many fatal diseases due to its restricted expression pattern and its ability to internalize ligands.

The main objective of my PhD studies will be to determine the structure of the macrophage receptor CD163. HpHb is purified from blood, whereas CD163 is expressed using a mammalian expression system. Crystallization of CD163 alone, as well as in complex with HpHb, will be attempted. As CD163 is expected to adopt a rather flexible, elongated fold a truncated version of the receptor will be used, as well as the full-length, to obtain crystallization.

P17.04 Maria do ELUCIDATING ROLES OF MIRNAS IN DNA SENSING DURING AN INNATE
Nascimento IMMUNE RESPONSE
Lopes Primo

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Numerous small RNA species have emerged as crucial regulators of RNA processing and translation. Among these, microRNAs (miRNAs) constitute a layer of posttranscriptional regulation that serves to buffer and balance gene expression. As important regulators of translation, miRNAs are believed to play a role in almost any cellular process. Emerging evidence suggests that virus infection is accompanied by a cellular miRNA response with potential implication for triggering and regulating innate immunity. Similarly, immune-regulatory miRNAs are deregulated during development of inflammatory diseases and may represent potential key players in underlying disease mechanisms. With focus on miRNA-directed regulation of the DNA sensing machinery and components of the downstream signalling pathways that shape an innate response, this PhD project plans to elucidate the roles of miRNAs during regulation of the innate immune response to HIV-1 infection. Given the uncertainties of the possible roles that miRNAs might play in HIV-1 infection, we have started by focusing our investigations on the deregulation of cellular miRNAs upon exposure of THP-1 cells to lentiviral vectors. We have been characterizing miRNA profiles in cells treated with HIV-1 and non-treated cells and preliminary data shows that the global miRNA pattern is affected during transduction of cells with HIV-based lentiviral vectors. Our upcoming goal is to identify and characterize which of these miRNAs play a key role in DNA sensing and signaling pathways triggered by foreign DNA, ultimately aiming at demonstrating how HIV-1 counteracts such protective mechanisms.

P17.05 Kasper Hansen EFFECT OF HYPERBARIC OXYGEN THERAPY IN A REGENERATIVE HEART MODEL

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Introduction: Hyperbaric oxygen treatment (HBOT) is clinically used as an adjuvant treatment in different critical disorders (e.g. are clostridial myositis and myonecrosis (gas gangrene), delayed radiation injury (soft tissue and bony necrosis), compromised grafts and flaps, and thermal burns). Possible signalling effects of HBOT are currently being investigated; however, the treatment ensures effective oxygenation of tissues through a highly elevated arterial blood plasma oxygen tension.

Objective: This study aims to evaluate if the elevated tissue oxygen tension during HBOT translates into increased myocardial regeneration-rate in a regenerating environment, namely the iconic Mexican axolotl (*Ambystoma mexicanum*). Axolotls are urodele amphibians, which in contrary to mammals are capable of remarkable regeneration of many inner organs as well as entire limbs.

Study design: A cryoprobe was used to induce an infarct on the exposed ventricle (approximately 25%) on 11 animals; 5 sham-animals (no HBOT) and 6 HBOT-animals receiving 46 HBO-treatments during a period of 11 weeks after cryo-infarction. Sham-animals were exposed to normobaric conditions in water, whereas HBOT-animals were pressurized to 3 ATA for

120 min in oxygenated water. The progression of ventricular regeneration was assessed through functional echocardiography; systolic- and diastolic total-ventricle vs. infarct-area, heart rate and cardiac output was measured at days 4, 7, 14, 21, 30, 40, 51 and 70 after infarction.

- P17.06 Jayaram Subramanian EFFECTIVENESS OF GLYCINE POWDER AIR POLISHING (GPAP) DURING SUPPORTIVE PERIODONTAL THERAPY (SPT): A RANDOMISED CONTROLLED CLINICAL TRIAL

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Aim: To investigate the short-term (3 months) differences between GPAP and traditional Scaling and Root Planing (SRP) during SPT on bleeding on probing; hypersensitivity, pain and discomfort, and safety; and subgingival bacterial counts for 15 selected putative periodontal pathogens.

To investigate the long-term (12 months) differences between GPAP and traditional SRP during SPT on bleeding on probing, plaque, probing depth and clinical attachment levels; hypersensitivity, pain and discomfort, and safety; morphology of root surfaces as assessed using an impression technique; and horizontal attachment level and bleeding in furcation defects.

Methods: This is a randomised, single-centre, two-arm, parallel group, examiner blinded and controlled clinical non-inferiority trial comparing the effect of traditional SPT with that of GPAP. All patients will undergo standard non-surgical active periodontal therapy carried out by Clinician I. Upon completion of the active therapy, patients will be randomly assigned to one of two groups for SPT, GPAP (intervention group) or Traditional SPT (control group). Clinician II will carry out SPT treatment for both groups. GPAP treatment consists of cleaning in pockets with the use of a low abrasive amino acid glycine powder (Air-Flow Perio Powder, EMS, Nyon, Switzerland) applied with Perio-Flow hand-piece connected to an airflow unit (Air-Flow Master, EMS). Traditional SPT will comprise SRP re-instrumentation using Gracey curettes and a piezoceramic ultrasonic device.

Significance: This project would set up the stage for better understanding of the clinical and microbiological efficacy of GPAP and its impact on the patient satisfaction.

- P17.07 Trine Salomon Andreasen CELL ASSAY FOR CONTROLLING ADVANCED GLYCATION ENDPRODUCT FORMATION

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Proteins can undergo glycation by reaction with α -oxoaldehydes such as methylglyoxal (MG). MG is highly reactive and capable of forming advanced glycation endproducts (AGEs) with e.g. arginine residues potentially causing functional impairment of the protein, and in extension

causing oxidative stress. It is generally acknowledged that AGEs play an important role in ageing and age-related diseases (diabetes, Alzheimers, Parkinson etc.).

The glyoxalase system is a natural cellular system which detoxifies α -oxoaldehydes. However, the system does not appear to be sufficient in aging and disease. We therefore turned our focus to the ketone body acetoacetate, which in preliminary studies has proven to react rapidly with MG under simulated physiological conditions forming a less reactive compound.

We are currently working on a cell assay, where the level of AGEs is increased by addition of a glyoxalase I inhibitor to the cell media. When this setup is fully established, we wish to increase the acetoacetate level, either by addition to the media or by triggering fatty acid degradation within the cell. The aim is to investigate whether acetoacetate decreases AGE levels.

The analytical approach is based on highly sensitive and selective LC-MS/MS method currently monitoring five of the most abundant advanced glycation endproducts. The work flow consist of 1) purification of protein from cell culture, 2) exhaustive hydrolysis of protein using four enzymes in sequence, resulting in free advanced glycation endproducts, 3) further purification of the AGEs by solid phase extraction using a polymeric cation exchanger and finally 4) quantitative LC-MS/MS analysis.

P17.08 Akiko Shimada EFFECTS OF REPETITIVE ORAL ADMINISTRATION OF MONOSODIUM GLUTAMATE ON PERICRANIAL MUSCLE SENSITIVITY

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Background: A randomized, double-blinded and placebo-controlled study was conducted to investigate the relationship between repetitive consumption of high-dose monosodium glutamate (MSG) and interstitial concentration of MSG in masseter muscles.

Materials and methods: Thirty-two healthy participants (23.6 \pm 3.3 years old) without any chronic craniofacial pain drank exclusively MSG (150 mg/kg) or NaCl (24 mg/kg) diluted with a 400 ml soda in five continuous experimental daily sessions. The concentrations of glutamate before and after the intervention were assessed in dialysate and plasma samples on first and last day. Moreover, saliva glutamate concentration was assessed every day. Pressure pain threshold, pressure pain tolerance, autonomic parameters (heart rate, systolic and diastolic blood pressure) and reported side effects were also assessed.

Results: The results of changes in the interstitial concentration of glutamate did not show statistical significant accumulation of MSG in masseter muscle in daily baselines, though the concentration peaks increased significantly.

A statistical significant increase of systolic and diastolic blood pressure after MSG intervention was observed. As well as a significantly higher frequency of reports of nausea and headache in MSG group. No robust effect of MSG on muscle pain sensitivity was shown.

Conclusion: This study indicated that the pain sensitivity and metabolism of MSG in masseter muscle are not highly perturbed by excessive repetitive intake of MSG in healthy participants.

P18.01 Thomas Ravn Lassen

EFFECT OF PAROXETINE ON LEFT VENTRICULAR REMODELING AFTER MYOCARDIAL INFARCTION

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Background: Remodelling of the heart is a process following a myocardial infarction (MI). The pathology includes myocyte hypertrophy, interstitial fibrosis and left ventricular dilatation leading to congestive heart failure. Formation of reactive oxygen species (ROS) is involved in the underlying mechanisms of remodelling. Paroxetine is a selective serotonin reuptake inhibitor that has recently been demonstrated to inhibit ROS formation.

Aim: To investigate the effect of Paroxetine on remodelling of the left ventricle, following an MI.

Method: We have established an in vivo model for MI in rats. This is accomplished by a 30-minute ligation of the left anterior descending artery followed by reperfusion. This ischemic insult induces an acute infarct size of approximately 40% of the area at risk.

The cardiac function and morphology will be evaluated during the respective follow-up periods of 7 and 28 days after MI, with dedicated high-frequency ultrasound and magnetic resonance imaging. At the end of the follow-up period, the susceptibility to arrhythmias will be evaluated by an in vivo electrophysiological study. Finally, the hearts will be excised and used for histological evaluation, including specific staining for fibrosis and ROS production.

Perspective: We expect to demonstrate that treatment with Paroxetine decrease ROS production and thereby possibly influence remodelling of the heart after a MI. Consequently, Paroxetine potentially represents a novel pharmacologic strategy to prevent the development of congestive heart failure, following MI.

P18.02 Marie Bek

VISUALIZATION OF THE SMOOTH MUSCLE CELL IN ATHEROSCLEROSIS: A MONOCLONAL POPULATION

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Introduction: Smooth muscle cells (SMC) in human atherosclerosis are arranged in relatively large monoclonal populations (patches). Monoclonality could arise because single cells proliferate vigorously during

plaque development or by migration from pre-existing developmental clones in the arterial media. In the present study, we will use two mouse models to describe the clonal architecture of SMCs in normal and atherosclerotic vessels, and determine whether SMC clonal expansion precedes atherosclerosis or occurs concomitantly with plaque growth.

Methods: First, chimeric mice were created by aggregating embryos from GFP-apoE^{-/-} mice and apoE^{-/-} mice. Second, mice transgenic for the Brainbow transgene were bred with mice expressing a tamoxifen-inducible Cre recombinase under the SMC-specific Myh11 promoter (Myh11-cre/ERT2⁺).

The Brainbow transgene uses Cre/lox recombination to express one of four fluorescent proteins (XFPs). After tamoxifen injections transient Cre expression is induced, and each SMC (and their daughter cells) in the combined transgenic strain express one of four XFPs.

By analyzing the arterial media and atherosclerotic plaques from chimeric mice, we can directly visualize and compare patch size and geometry in the arterial media and in the plaque. To determine whether clonal expansion occurs as part of the atherosclerotic process, we will analyze patch size and geometry of normal vessel and atherosclerotic plaques in Brainbow-Myh11-Cre/ERT2⁺ mice.

Preliminary results: The first results indicate that patch size is larger in the plaque compared to media, and that the clonal population of cells in the plaque is located in layers under the endothelium.

P18.03 Mette Christensen

[Ca²⁺]_i OSCILLATIONS IN RENAL EPITHELIA CAUSED BY ALPHA-HAEMOLYSIN FROM REQUIRE ATP RELEASE AND P2 RECEPTOR MEDIATED SIGNALLING

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Urinary infections are commonly caused by α -haemolysin (HlyA)-producing *E. coli*. HlyA forms pores in cell membranes that renders the attacked cells permeable to ions and water. In erythrocytes, the effect of HlyA is strongly amplified by purinergic signalling. We hypothesize that HlyA-induced [Ca²⁺]_i oscillations in renal epithelia is mediated by ATP-dependent P2 receptor activation. Here we confirm that HlyA initiate marked [Ca²⁺]_i oscillatory activity in renal epithelia. This was quantified by live cell fluorescence microscopy in both MDCK cells and freshly isolated murine thick ascending limb (TAL). HlyA-induced oscillations were reversible and did not cause permanent cell-damage. [Ca²⁺]_i oscillations are completely prevented by non-selective P2-receptor antagonists (suramin/PPADS) and by ATP-degradation (apyrase). HlyA-induced [Ca²⁺]_i oscillations was significant lower in tubules from P2Y₂ receptor knock out mice compared to wild type controls. To confirm these results, we tested the effect of HlyA on ATP-biosensor cells. In native 132-1N1 that do not express P2 receptors, HlyA barely caused any changes in [Ca²⁺]_i. Transfection of the cells with a hP2Y₂ receptor resulted in an extensive increase in [Ca²⁺]_i oscillatory activity, which is also sensitive to P2 receptor antagonists. Moreover, we found that HlyA induces release of interleukin (Il)-6 and Il-8 from murine

kidney outer medulla and release of Il-6 but not Il-8 is dependent on ATP release and P2Y₂ receptor activation. These results suggest that HlyA triggers ATP-release from renal epithelia, which via P2 receptor activation is responsible for the HlyA-induced [Ca²⁺]_i oscillations and the release of Il-6.

P18.04 Eirild Espeseth "SPOTTY" CALCIFICATION IN CORONARY ARTERIES: WHAT DOES IT REFLECT?

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Objectives: The purpose of this study is to examine the relationship between radiological and morphological features of coronary atherosclerotic plaques in autopsy materials.

Background: Previous studies have documented that the presence of shown that "spotty" calcification of coronary plaques is associated with a higher likelihood of developing acute coronary syndrome (ACS). On the other hand, plaques responsible for stable angina are more calcified than plaques responsible for ACS. The risk of coronary heart disease and mortality increase with increasing total coronary artery calcium scores determined by non-contrast computed tomography (CT). However, the relationship between the pattern of calcification and the morphological features of the plaque (plaque type) has not been evaluated.

Methods: We collected 20 coronary arteries from forensic autopsies. The arteries were scanned using a cabinet x-ray system and 64-slice CT. Up to 12 sites in each artery, with and without calcification, were selected, and processed for plastic embedding and microscopic examination with preserved calcium.

Preliminary results: 16 out of 20 arteries have been collected. 7 arteries and 36 plaques have been analysed. 30 plaques contained sheet calcification and 28 plaques contained micro calcification. 4 plaques presented with fibrous cap atheroma, and these plaques where related to sheet calcification and micro calcification. Inflammatory cells were found in 8 of the plaques, osteocytes in 1 plaque and angiogenesis in 5 of the collected plaques.

P18.05 Tea Lund Laursen LECTIN PATHWAY PROTEINS OF THE COMPLEMENT SYSTEM ARE ASSOCIATED WITH SURVIVAL IN PATIENTS WITH ACUTE LIVER FAILURE

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Background: The complement system is activated in liver diseases, including acute liver failure (ALF). However, the lectin pathway of complement has scarcely been investigated in ALF. This pathway is initiated by soluble pattern recognition molecules: mannan-binding lectin (MBL), H-, L- and M-ficolin and collectin-liver-1 (CL-L1), which are predominantly synthesised in the liver. We aimed to study lectin levels in ALF patients and associations with clinical outcome.

Methods: Serum samples from 75 patients enrolled by the US ALF Study Group were collected on days 1 and 3. We included 20 stable cirrhosis patients and 75 healthy blood donors. Analyses were performed by sandwich-type immunoassays (ELISA, TRIFMA).

Results: At day 1, the MBL level in the ALF patients was 40% lower compared with healthy controls ((median $\mu\text{g/ml}$ (interquartile range) 0.72(0.91) vs. 1.15(1.92) ($p=0.02$)) and increased significantly by day 3 (0.83(0.94)($p=0.01$)). The M-ficolin level was 60% lower compared with healthy controls (0.54(0.50) vs. 1.48(1.01) ($p<0.0001$)). The CL-L1 level at day 1 was slightly higher in ALF patients than in healthy controls (3.20(2.37) vs. 2.64(0.72) ($p=0.11$)); this was significant at day 3 (3.35(1.84) ($p=0.006$)). H- and L-ficolin levels were similar to healthy controls. Spontaneous ALF survivors had higher levels of MBL at day 1 (0.96(1.15) vs. 0.60(0.60) ($p=0.02$)) and lower levels of L-ficolin by day 3 compared with patients who died or were transplanted (1.61(1.19) vs. 2.17(2.19) ($p=0.02$)).

Conclusion: We observed marked dynamics and differences in lectin levels, which may suggest involvement in ALF pathogenesis. High MBL and low L-ficolin levels are associated with survival.

P18.06 Peter Kolind LIPOLYTIC EFFECTS OF GH: MOLECULAR MECHANISMS IN VIVO AND IN
Brask-Thomsen VITRO

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Background: Growth hormone (GH) is known to stimulate lipolysis in adipose tissue both in vivo and in vitro, but the underlying molecular mechanism is still unknown. Recently, it has been shown that increased lipolysis during a 72-hour fast is accompanied by an increase in Adipose tissue triglyceride lipase (ATGL)-levels as well as a decrease in ATGL-inhibitor G(0)/G(1) Switch Gene 2 (GOS2) protein-levels.

GH is an important regulator of substrate metabolism during fasting, and we therefore hypothesized that the observed regulation of ATGL and GOS2 can be induced by GH-stimulation in humans in vivo and in vitro.

Methods: In vivo GH study: 10 healthy young men are included in a 2x2 factorial design ± 48 h fasting and \pm GH infusion. Adipose tissue biopsies are sampled at $t= 90$ and 270 min (in the basal state and during

hyperinsulinaemia, respectively).

In vitro experiment: Human adipocytes from adipose tissue are cultured in cell media and incubated as follows \pm GH in 4, 8, 24 and 48 hours. Protein extraction is performed by SDS-based homogenization and protein expression is measured by Western Blotting technique. Targets are ATGL, HSL, p-HSL, PLIN1, CGI-58, G0S2 and β -actin.

Results: In vivo: Basal serum FFA levels increased significantly with GH and Fasting as compared to the control day. This was associated with a decrease in G0S2 after fasting, but no change in ATGL expression.

Analysis of the in vitro experiments is still ongoing.

P18.07 Ole Kristian
Møller-
Helgestad

ORGAN BLOOD FLOW DURING MECHANICAL SUPPORT IN AN ANIMAL MODEL OF CARDIOGENIC SHOCK

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Introduction: Cardiogenic shock (CS) is the main cause of death after an acute myocardial infarction (AMI). International guidelines recommend mechanical support on top of pharmacological treatment, but there is currently no scientific evidence on the efficiency of any mechanical device available. The aim of our study was to compare blood flow to the brain, heart and kidneys obtained with two different support devices, namely the intra-aortic balloon pump (IABP), which is considered standard care, and the Impella2.5, which is a newer device.

Methods: Thirteen pigs were anesthetized and AMI was induced by inflating a balloon in the left anterior descending artery (LAD) for 45 min. The right carotid artery had a flow probe surmounted after surgical exposure. Blood flow velocity was measured in the LAD and the renal artery by means of two intravascular Doppler FloWires. The Impella2.5 and IABP were inserted via the left and right femoral artery, respectively. The two devices were tested individually and combined both before and after induction of an AMI.

Results: The IABP did not improve any parameters. The Impella2.5 significantly improved perfusion pressure and oxygen availability to the tissues. After AMI the Impella2.5 increased carotid blood flow from 307 ± 109 mL/min to 332 ± 109 mL/min ($p < 0.05$) and renal blood flow from 245 ± 104 mL/min to 303 ± 146 mL/min ($p < 0.05$). None of the devices, separately or combined, improved the coronary blood flow.

Conclusion: In this pig model, the Impella2.5 improved hemodynamics and blood flow to the brain and kidneys. However, the device should be tested in a proper clinical trial with patients in CS, before any firm conclusion can be made.

P18.08 Morten Lykke

LEUKOCYTE-DEPLETION IN PLATELET-RICH PLASMA DECREASE THE

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Background: Numerous preparation methods are available for platelet-rich plasma (PRP) generation, but evidence defining the optimum composition is lacking.

Aim: The purpose of this study was to investigate the effects of PRP containing low and high leukocyte concentrations on both proliferation and the chondrogenicity of human chondrocytes in vitro.

Materials and methods: Two PRP groups, low leukocyte PRP (lPRP) and standard PRP (sPRP), were generated from whole blood from 9 healthy donors (age 36-58 years) using a two-step centrifugation procedure. The PRP groups had similar platelet concentration but low and high leukocyte concentrations, respectively. Human chondrocytes were isolated from articular biopsies obtained from 3 patients with healthy cartilage (age 21-41 years), and cultured in monolayer for 7 days in either control media or control media with lPRP or sPRP of 1%, 5% or 10% v/v concentrations. Proliferation was assessed using an XTT assay. qRT-PCR was used to perform quantitative gene expression analyses using primers for collagen type 1 (Col1a1) and 2 (Col2a1) and Sox9. Data were collected on day 2 and 7, and evaluated using three-way ANOVA analysis.

Results: We observed a positive proliferative effect by both PRP groups compared with the control group ($p < 0.0001$). sPRP group showed an increased proliferation compared with the lPRP group ($p < 0.05$). Presence of leukocytes did not affect the relative mRNA expression of Sox9, Col2a1, or Col1a1 in any of the formulations.

Conclusion: We conclude that a high absolute leukocyte concentration in PRP increase chondrocyte proliferation. Inclusion of leukocytes in PRP showed no effect on chondrogenic gene expression.

P19.01 Sofie Axelgaard DIRECT EFFECTS OF CHRONIC ILOPROST AND TREPROSTINIL TREATMENT IN PRESSURE OVERLOAD INDUCED RIGHT HEART HYPERTROPHY AND FAILURE

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Background: Right ventricular (RV) failure is a critical complication to a broad spectrum of cardiopulmonary diseases. Prostacyclin analogues are used in the treatment of pulmonary hypertension. The most important mechanism of action is vasodilatation of the pulmonary vessels leading to improved haemodynamics. Several recently published data indicate that acute administration of prostacyclin causes increased inotropy in the dysfunctional and failing RV independent on the effects on the pulmonary circulation. The direct effect of chronic treatment with prostacyclin

analogues on RV hypertrophy and failure is, however, not clarified.

Aim: To investigate the direct effect of chronic treatment with prostacyclin analogues in pressure overload induced right heart hypertrophy and failure.

Methods: For the purpose of inducing RV hypertrophy and failure, rats are subjected to pulmonary artery banding. The rats will be randomized to 6 weeks of treatment with iloprost, treprostinil or placebo. At the end of treatment, RV evaluation will be performed using echocardiography, MRI and invasive pressure-volume measurements. RV tissue will be extracted for molecular analysis.

Perspectives: Pulmonary hypertension and RV failure are serious conditions causing significantly increased morbidity and mortality. An increased focus on the subject has led to a greater appreciation of the diseases and of the present possibilities of intervention. However, the prognosis is still extremely poor. This study will contribute with information about RV physiology and dysfunction in addition to giving further insight into prostacyclins and their possible new role in the treatment of RV failure.

P19.02 Lilliana Beck GENETIC DEFICIT IN KCA3.1 PREVENTS PULMONARY VASODILATATION AND FATAL PULMONARY CIRCULATORY COLLAPSE INDUCED BY TRPV4 CHANNEL ACTIVATION

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Background: The TRPV4 channel has been suggested to be involved in the endothelial dependant calcium signalling which leads to vasodilatation. We investigated involvement of TRPV4 and KCa3.1 channels in endothelium dependent relaxation of mouse pulmonary arteries. **Methods/results.** In wildtype and KCa3.1 channel knockout mice, the effects of GSK1016790A, a selective TRPV4 channel opener on right ventricular hemodynamic parameters using Millar catheter, isometric tension recordings in isolated pulmonary arteries using wire myographs, TRPV4 channel currents in isolated pulmonary arterial endothelial cells by whole cell patch clamp were investigated. In wt mice, 0.2mg/kg GSK induced pressure drop in mean and systolic pressure leading to circulatory collapse. While in KCa3.1^{-/-} mice, GSK had no effect on pressure. In wt isolated pulmonary arteries, 10nM GSK induced relaxations that were abolished by blocking KCa2/3.1, TRPV4 channels, eNOS-activity, and removal of endothelium. Similar results were found in the KCa3.1^{-/-}, but without an effect of blocking KCa3.1 channels. In PAEC from WT and KCa3.1^{-/-}, GSK increased membrane currents sensitive to TRPV4 channels block. Blocking KCa3.1 channels decreased coactivated KCa3.1 currents in wt mice. **Conclusion.** In mouse pulmonary arteries, activation of TRPV4 channels induces relaxation that required activation of both KCa3.1 channels and eNOS. Although deficiency of KCa3.1 abolishes TRPV4 induced right ventricular pressure drop and circulatory collapse. These results suggest that TRPV4 activation produces a significant calcium influx resulting in KCa3.1 activation as an essential step for endothelium-

dependent relaxation in pulmonary arteries.

P19.03 Rikke Viggers REGULATION OF ANGPTL4 IN HUMAN MUSCLE- AND ADIPOSE TISSUE

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Lipoprotein lipase (LPL) is the rate limiting step in plasma TG clearance. LPL hydrolyzes TG-rich lipoproteins thereby maintaining a supply of fatty acids (FAs) to tissue metabolism. Angiopoietin-like protein 4 (ANGPTL4) is the only known LPL inhibitor synthesized in the same tissue as LPL itself, e.g. myocytes and adipocytes. The transcription of ANGPTL4 is induced during fasting as a result of adipocyte lipolysis. It seems that ANGPTL4 provides a preferential alteration in the lipid homeostasis; circulating FFA rather than the lipoprotein TG-derived FAs as substrate for oxidation. The level of ANGPTL4 is altered in obesity and type 2 diabetes, contributing to impaired metabolic flexibility and insulin resistance. Data on ANGPTL4 in human tissue are scarce and mainly quantified on the level of mRNA, especially in liver and white adipose tissue.

The aim of this study is to examine ANGPTL4 protein in human skeletal muscle and adipose tissue biopsies as well as human plasma from already established cohorts consisting of obese non-diabetic and diabetic subjects, diabetic subjects during situations with strict and poor metabolic control respectively and subjects exposed to situations where adipocyte lipolysis is stimulated and inhibited. Tissue samples will be analyzed and quantified for ANGPTL4 by western blotting.

Greater insight into the mechanisms regulating the uptake of FAs in skeletal muscle is paramount to understand the development of metabolic dysfunctions. It is our hope to increase the knowledge of the effects and regulations of ANGPTL4 by detecting the protein under conditions and disorders in which the metabolic flexibility is altered and manipulated.

P19.04 Marie Rose Hjørtbak IS THERE AN ADDITIVE CARDIOPROTECTIVE EFFECT OF ISCHEMIC PRECONDITIONING AND MILD HYPOTHERMIA?

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Hypothesis: Both ischemic preconditioning (IPC) and mild hypothermia are known to reduce cardiac ischemia-reperfusion injury. The underlying mechanisms are not well documented, and the mechanistic interactions between the two treatment strategies need further investigation. The main purpose of this study was to investigate the effect of combining IPC and mild hypothermia in terms of optimal timing and mechanistic responses. Our main hypothesis was that IPC reduces reperfusion injury, while hypothermia

attenuates ischemic injury.

Methods: Hearts from male Wistar rats were mounted in an isolated perfused heart model (Langendorff) and exposed to 40min ischemia/120min reperfusion at 37 °C. IPC was induced before ischemia by two cycles of 5 min of global ischemia and 5 min of reperfusion. Hypothermia was induced at different time points during the protocol and the target temperature was 34 °C. The cardioprotective effect was evaluated by hemodynamic recovery and final infarct size (IS). Mechanistic responses were monitored by LDH release, glucose oxidation and microdialysis.

Results: Applying either IPC or mild hypothermia during ischemia, significantly reduced IS compared to normothermic controls. Hypothermia during reperfusion only did not reduce IS. Combining hypothermia during the last part of ischemia with IPC provided superior infarct reduction compared to IPC alone (p=0.02).

Conclusion: Both IPC and mild hypothermia have a strong infarct reducing effect, but hypothermia only when applied during ischemia. The additive cardioprotective effect of the two interventions suggests different underlying working mechanisms. Data on potential mechanism are pending.

P19.05 Rasha Salman CARDIOPROTECTIVE AND ADDITIVE EFFECT OF ROTIGAPTIDE IN ISOLATED RABBIT HEARTS

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Background: Remote ischemic conditioning (RIC) by short periods of limb ischemia induces protection against sustained myocardial ischemia. RIC has been successfully translated to the clinical setting showing reduced infarct size in patients admitted with ST-elevation myocardial infarction who were treated with RIC prior to acute coronary angioplasty.

Another potentially important concept of cardioprotection is pharmacological conditioning. Connexin modulation by rotigaptide (ZP123) has been shown to protect against ischemia-reperfusion damages in experimental models. The exact mechanism of action of rotigaptide remains to be fully clarified. However, connexin modulators, in contrast to most other pharmacological agents used for cardioprotection, are believed to act independently of the pathways involved in ischemic conditioning.

Hypothesis: The cardioprotective effects of RIC and connexin modulators are additive.

Method: The study will examine the additive effect of RIC and rotigaptide on isolated rabbit hearts. Rabbits undergo RIC in-vivo and the hearts are isolated and mounted on a Langendorff model and perfused with a Krebs-Henseleit buffer. Hearts will undergo 20 minutes of stabilization, subjected to 30 minutes of global no-flow ischemia and 120 minutes of reperfusion. A total of 48 rabbits will be randomized into 6 subgroups (control, rotigaptide before or after ischemia, RIC in-vivo, RIC in-vivo with rotigaptide before or

after ischemia).

Endpoints: Primary endpoints will be the infarct size and left ventricular developed pressure. TCA cycle intermediates, glucose oxidation and the effect of the RISK and SAFE pathways are secondary endpoints.

- P19.06 Thomas Krarup
Andersen DIRECT EFFECTS OF CHRONIC LEVOSIMENDAN TREATMENT IN PRESSURE OVERLOAD INDUCED RIGHT HEART HYPERTROPHY AND FAILURE

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Aim: To investigate the direct effects of long-term treatment with levosimendan in the hypertrophied and failing right heart of rats.

Methods: Male Wistar rat weanlings (N=30, 78g ± 5 g) were randomized to treatment with levosimendan 3mg/kg bw/day (LEVO) or vehicle (VEH) in their drinking water. Three days after treatment start, the rats were randomized to undergo sham operation or pulmonary trunk banding. Treatment was continued for 45 days after surgery and at the end of study, heart function was evaluated by echocardiography, magnetic resonance imaging, pressure volume relations and gross anatomy.

Results: Pulmonary trunk banding caused right heart hypertrophy with compensated heart failure. Levosimendan did not prevent the development of right ventricular hypertrophy normalized to tibia length (LEVO vs. VEH 10.94 ± 0.28 vs. 10.61 ± 0.43 kg/m, p = 0.53), but right heart function was normalized by levosimendan treatment evaluated by cardiac index (LEVO vs. VEH 362 ± 34 vs. 281 ± 17 mL/min/kg, p < 0.05), ejection fraction (LEVO vs. VEH 68% ± 3% vs. 57% ± 2%, p < 0.01) and by the load independent measure of systolic function: end systolic elastance (LEVO vs. VEH 667 ± 118 mm vs. 367 ± 57 mm Hg/mL, p < 0.05)

Conclusion: Chronic treatment with levosimendan normalizes RV function in rats with right ventricular hypertrophy and failure.

- P19.07 Nanna Mørk IDENTIFICATION OF INNATE IMMUNODEFICIENCIES BY WHOLE EXOME SEQUENCING

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Background: In recent years, it has been demonstrated that mutations in Toll-like receptor 3 and downstream signaling molecules may contribute to the development of herpes encephalitis (HSE). These genetic defects lead to reduced antiviral interferon (IFN) responses. In this study, whole exome sequencing (WES) was performed to identify mutations associated with

susceptibility to HSE or other herpes simplex virus (HSV) disease manifestations. The goal is to identify host factors in innate immunity which may explain the mechanism underlying differential susceptibility to HSV infections between individuals.

Methods: As part of a pilot study, we performed WES on 4 patients with HSE or mucocutaneous HSV infection. WES was performed with Illumina technology and analyzed PolyPhen-2 PhyloP and SIFT prediction software. Next in vitro studies to evaluate the functional consequences of identified mutations will be done.

Results: In this small number of patients, we identified several interesting mutations in molecules involved in antiviral IFN responses. In a 5 year-old girl with recurrent severe HSE, we identified a missense mutation in IKKe, a kinase involved in phosphorylation of the transcription factor IRF3 to induce IFN production in response to various viral replication intermediates.

Conclusion: Knowledge of the molecular and genetic mechanisms underlying innate immunodeficiencies is a prerequisite for understanding disease pathogenesis. Importantly, a better insight into these aspects may have an impact on clinical practice, including genetic testing, prophylactic antiviral treatment and, possibly, initiation of early treatment with both aciclovir and IFN in patients with HSE.

P19.08 Rahul Prabha A TOOTH FOR BONE

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Background: Management of critical size bone defects caused by surgical interventions, osteotomies and distraction osteogenesis continues to be a challenge, where healing of bone still remains a matter of concern. An approach that could contribute to a shortening of the healing period and enhance high-quality bone formation would reduce the risks of late complications, such as insufficient bone formation and the thereof derived resource loss.

Aim: The aim of this PhD project is to develop a clinical relevant protocol combining the classic techniques applied in the healing of bone defects in the craniofacial region with human adult dental pulp stem cells (DPCs) and scaffold-based tissue engineering therapy in order to achieve enhanced bone regeneration. In this study, DPCs are also compared with human bone marrow mesenchymal stem cells (BMSCs). The osteogenic differentiation and bone forming capacity of the two cell lines are tested on three distinct novel scaffolds, namely Bioceramic granules, Electrospun membrane, and Injectable hydrogel.

Material and methods: The study involves in vitro scaffold characterization with DPCs and BMSCs. The constructs would further be tested for efficient closure of critical sized bone defects in animal models.

Results: Our results showed attachment, viability, proliferation and

osteogenic differentiation of DPCs on Electrospun membrane scaffolds. Cell attachments were seen on Bioceramic granules and Injectable hydrogels. Further optimization of seeding protocols on Bioceramic granules and Injectable hydrogels are required to confirm osteogenic differentiation of cells in these scaffolds.

P20.01 Anders Sommer FLUOROSCOPY IS INACCURATE FOR ASSESSMENT OF LEFT VENTRICULAR LEAD POSITION IN CARDIAC RESYNCHRONIZATION THERAPY

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Aim: To analyze the accuracy of biplane fluoroscopy to determine LV lead position in a standard LV 16-segment model as compared to cardiac computed tomography (CT) in cardiac resynchronization therapy (CRT).

Methods: Fifty-nine patients undergoing transvenous CRT implantation were included (mean age 69 ± 9 years, 16 female, mean left ventricular (LV) ejection fraction 24 ± 5 %, and mean LV end-diastolic volume 256 ± 72 ml). Post-implant biplane fluoroscopy and contrast-enhanced cardiac CT were evaluated in all patients by two electrophysiologists and cardiologists, respectively. LV lead position was determined according to a standard LV 16-segment model, in the LV short-axis 360° circumference, and in the LV long-axis (basal 0 - 0.33; mid-LV .34 - 0.66; apical 0.67 - 1.00), respectively.

Results: Agreement between fluoroscopy and cardiac CT on segmental LV lead position was found in 20 (34%) patients. Fluoroscopy demonstrated a 1-segment and ≥ 2 -segment error in 32 (54%) and 7 (12%) patients, respectively. In the LV short-axis 360° circumference, the mean LV lead position was $114 \pm 27^\circ$ by fluoroscopy and $133 \pm 27^\circ$ by cardiac CT ($P=0.0003$). In the long-axis, the mean LV lead position was 0.48 ± 0.19 and 0.34 ± 0.21 by fluoroscopy and cardiac CT, respectively ($P=0.0001$).

Conclusions: The ability of fluoroscopy to correctly localize the LV lead in a standardized LV 16-segment model is poor. Fluoroscopy misclassified the LV lead positions anterior-lateral and apical as compared to cardiac CT. Cardiac CT should be applied to determine the exact pacing site in studies assessing the clinical impact of optimal LV lead positioning in CRT.

P20.02 Rune Benjamin Borregaard RADIOFREQUENCY ABLATION OF ACCESSORY PATHWAYS IN PATIENTS WITH THE WOLFF-PARKINSON-WHITE SYNDROME: THE POST ABLATION MORTALITY AND RISK OF ATRIAL FIBRILLATION

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The Wolff-Parkinson-White (WPW) syndrome is characterized by symptomatic supraventricular tachycardia and an ECG with pre-excitation

of the QRS complex. Individuals with the WPW syndrome have an orthodromic conducting accessory pathway (AP) that connects the atria and the ventricles. The prevailing treatment of the WPW syndrome is a radiofrequency ablation (RFA) of the AP.

Objective: To assess the mortality in patients undergoing RFA for the WPW syndrome and to identify independent risk factors for post-ablation mortality and atrial fibrillation (afib) after the RFA.

Methods: A retrospective case-control study of all patients (N=262) subjected to RFA of WPW at Aarhus University Hospital from 1990 to 2011. A control group was generated from the Danish national board of health cpr registry. Survival data was obtained from the Danish national board of Health "cause of death database". Data on post-ablation morbidity including post-ablation afib were obtained from the Danish National Patient Registry.

Results: We found no significant difference in all-cause mortality when comparing the WPW group with control group (HR 0.77 CI 0.47-1.25). A subgroup analysis on the WPW group showed that cardiac arrest prior to ablation was a significant risk factor for post-ablation mortality (HR 7.32 CI 1.33-40.39). When identifying risk factors for post-ablation afib within the WPW group, we found that afib prior to ablation (HR 3.36 CI 1.67-6.77) and pseudoventricular tachycardia (HR 2.98 CI 1.27-7.03) prior to ablation were independent risk factors.

Conclusion: Patients with RFA treated WPW syndrome have a post-ablation mortality that is similar to the background population.

P20.03 Sara Gaur

CORONARY CT-ANGIOGRAPHY AND NON-INVASIVE FRACTIONAL FLOW RESERVE MEASUREMENT FOR ASSESSMENT OF NON-CULPRIT CORONARY STENOSES AFTER ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Background: Non-invasive coronary computed tomography angiography (cCTA) is increasingly used as an anatomic test for exclusion or detection of coronary artery disease. Invasive fractional flow reserve (FFR) is the gold standard for assessment of lesion-specific myocardial ischemia. Recent advances in computational fluid dynamic techniques applied to standard cCTA images allow for computation of FFR (FFR_{CT}). The potential of FFR_{CT} to diagnose lesion-specific ischemia in patients with prior ST-elevation myocardial infarction (STEMI) and multivessel disease is not yet established.

Aim: To determine the ability of FFR_{CT} to diagnose lesion-specific ischemia in non-culprit vessels in patients with recent STEMI.

Methods: Prospective, observational design. The study population will comprise 65 patients with recent STEMI, scheduled to undergo clinically indicated invasive coronary angiography (ICA) with FFR of non-culprit stenoses. CCTA images obtained prior to the invasive assessment are sent

to a core laboratory for FFR_{CT} analysis.

The diagnostic performance of FFR_{CT} will be assessed by the area under the receiver operating characteristic curve for FFR_{CT} (≤ 0.80) versus cCTA (stenosis $\geq 50\%$) and versus ICA (stenosis $\geq 50\%$) for the diagnosis of at least one hemodynamically significant lesion.

The accuracy, sensitivity, specificity, positive and negative predictive value of FFR_{CT} will be determined. FFR is the reference standard in all analyses.

Perspectives: FFR_{CT} may be used as a non-invasive tool to determine the need for further revascularization in STEMI patients with multivessel disease. A non-invasive diagnostic approach may reduce the risk of complications as well as costs.

P20.04 Kasper Pryds

DISTINCT WINDOWS OF PROTECTION AGAINST ISCHEMIA-REPERFUSION INJURY FROM REMOTE ISCHEMIC CONDITIONING

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Background: Remote ischemic conditioning (RIC) by brief episodes of intermittently ischemia and reperfusion of the upper-arm results in distinct windows of protection against ischemia-reperfusion (I/R) injury: a first window of protection (First Window RIC), second window of protection (SWOP RIC), and persistent protection when applying repetitive daily RIC stimuli (Chronic RIC).

Aims: To compare protective effects from First Window RIC, SWOP RIC and Chronic RIC. Secondly, to compare systemic anti-inflammatory effects from these three distinct windows of protection.

Methods: Twenty young healthy volunteers will be included in a paired study design. Blood samples will be drawn at four occasions: at baseline, immediately after RIC stimulus, 24 hours following RIC stimulus, and following 14 days with daily RIC stimuli. RIC stimulus will consist of 4 x 5 minutes of upper-arm ischemia achieved by inflation of a blood pressure cuff and 5 minutes reperfusion between inflations.

Following preparation, blood samples will be tested in an isolated rabbit heart Langendorff model for investigation of myocardial I/R protective effects. Further, blood samples will be investigated for effects on inflammatory markers: selectins, interleukins, cellular adhesion molecules, interferon- γ and tumor necrosis factor- α .

Perspectives: This study will be the first to investigate the humoral effects of the distinct windows of RIC protection, and to compare myocardial I/R protective effects between these windows of protection. We find that the study can uncover some of the mechanisms behind RIC and potentially

optimize future treatment for patients suffering from ischemic heart disease.

- P20.05 Laura Sommer Hansen THE CLINICAL IMPACT OF AN AGGRESSIVE APPROACH TOWARDS PLEURAL AND PERICARDIAL EFFUSIONS ON PHYSICAL AND RESPIRATORY PERFORMANCE FOLLOWING OPEN HEART-SURGERY - A STEP TOWARDS STANDARD GUIDELINES (THE IMAGING TRIAL)

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Introduction: Pleural and pericardial effusions are common in the early postoperative period following open heart surgery. Chest sonography before patient discharge has revealed a far greater incidence of pleural and pericardial effusions than conventional X-ray imaging, owing to greater sensitivity. Consequently, a significant number of effusions are missed with the current regimen. It has been proposed that untreated effusions, regardless of size, can lead to impaired physical recovery. A more aggressive approach towards effusions has been suggested, but further studies are needed.

Design and methods: The study is a randomised controlled intervention trial. Patients admitted for open heart surgery (aortic valve surgery, coronary artery bypass graft surgery, or combinations) will be randomised into either an intervention group or a control group. The intervention group will be followed with physical tests and ultrasonic examination the month following surgery. Any pleural or pericardial effusion that causes symptoms or exceeds a certain size will be drained and effect measured. The control group will follow the current postoperative regimen.

Outcome and data analysis: The primary efficacy outcome parameter is the size of pleural and pericardial effusions that cause at least a 30% reduction of performance in the 6-minute walking test (decreased distance or increased heart-rate recovery time). The absolute values and adjusted mean change from baseline, the difference in adjusted mean change between the intervention group and the control group, and the 95% confidence interval will be presented.

- P20.06 Carsten Behr-Rasmussen PATOPHYSIOLOGICAL AND POTENTIAL DIAGNOSTIC ASPECTS OF THE MURAL THROMBUS IN ABDOMINAL AORTIC ANEURYSMS

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Background: Rupture of the abdominal aortic aneurysm (AAA) is the 10th most leading cause of death in men above 65 years of age and the prevalence ranges from 1-8.8%. Increased size is directly related to

increased annual risk of rupture. It has been and still is being discussed if the presence of an ILT decreases or increases the risk of a growth. It is thought that the porosity of the ILT negates biological active substances, such as proteases, to infiltrate the aortic wall destabilising the matrix. The active substances present at the luminal surface could be found in the peripheral blood stream. Presence of an ILT is, according to recent research, more likely to mean bigger risk of growth and rupture.

Aim: 1. To describe the possible association between the mural thrombus and growth of the AAA, 2. To identify components in the luminal part of the thrombus which are many-fold increased compared to the circulation and 3. To test the validity of these identified components together with key markers of coagulation as: a. Screening tool to detect AAA and b. Potential diagnostic tool for endoleak by comparing the change in the circulation after repair with size matched controls not having repair.

Planned studies: 1. Observational study of the role of the mural thrombus in the VIVA* AAA cohort, 2. Paired protein analysis of luminal mural thrombus and plasma and 3. Set up of ELISAs of identified potential clinical useful predictive proteins and testing on cases and controls.

* VIVA: Large screening trial to detect AAA in 65-74 year old men living in the Central Denmark Region.

P20.07 Søs Ann
Christine
Neergaard-
Petersen

TYPE 2 DIABETES IS ASSOCIATED WITH COMPACT CLOT STRUCTURE AND PROLONGED LYSIS TIME IN PATIENTS WITH CORONARY ARTERY DISEASE

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Background: Type 2 diabetes mellitus is associated with an increased risk of cardiovascular events and poor prognosis. Fibrin clot structure may influence predisposition to cardiovascular events.

Aims: To investigate the influence of type 2 diabetes on fibrin clot structure in patients with coronary artery disease (CAD) treated with 75 mg aspirin daily. Underlying mechanisms to altered clot structure including inflammation and glycaemia.

Methods: We studied fibrin clot structure and fibrinolysis in 581 CAD patients (148 with type 2 diabetes), using turbidimetric assays and confocal and scanning electron microscopy. Inflammatory markers were evaluated by ELISA and glycaemia by HbA1c.

Results: Diabetes patients had more compact clots with increased maximum absorbance compared with non-diabetes patients (0.36 ± 0.1 vs. 0.33 ± 0.1 au, $p=0.01$), associated with prolonged lysis time (804 (618; 1002) vs. 750 (624; 906) sec, $p=0.03$). These changes in fibrin networks were confirmed by confocal and electron microscopy. Fibrinogen levels were increased in diabetes patients ($p<0.001$), and using purified fibrinogen at 1

mg/mL differences in clot structure parameters were not detectable. Inflammatory markers including CRP and C3 were increased in diabetes patients and particularly C3 correlated with clot lysis time ($r=0.36$, $p<0.0001$). HbA1c did not correlate with clot structure.

Conclusions: CAD patients with type 2 diabetes had more compact clot structure with impaired fibrinolysis compared with CAD patients without diabetes despite aspirin. This may be related to an adverse effect of type 2 diabetes on the fibrin network, coupled with increased levels of fibrinogen and inflammatory proteins.

P20.08 Eva Amalie Nielsen

ENDOTHELIN RECEPTOR BLOCKADE ABROGATE BIVENTRICULAR FIBROSIS AND RV REMODELING IN ISOLATED ELEVATED RIGHT VENTRICULAR AFTERLOAD

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Background: Pulmonary arterial hypertension is usually fatal due to right ventricular (RV) failure. Endothelin receptor blockers are commonly used vasodilators in pulmonary arterial hypertension. Their effects on biventricular injury and remodeling, independent of RV afterload reduction is unknown. The objective of this study was to investigate effects of endothelin receptor blockade (ERB, Macitentan) on biventricular remodeling and function in a rabbit model of isolated RV afterload.

Methods and results: Increased RV afterload was induced by sequential pulmonary artery banding (PAB). 5 rabbits underwent PAB without ERB (positive controls); 5 received PAB + ERB; and 5 did not undergo PAB inflation (sham-operated controls (SOC)). RV and LV collagen content was increased with PAB compared to SOC and ameliorated by macitentan. LV collagen content increased in the PAB group 4.1 (1.7-6.1) vs SOC 2.9 (1.7-3.7), $p<0.0001$ and decreased with macitentan 3.1 (0.6-5.3) vs PAB $p<0.0001$. RV collagen content also increased with PAB 8.3 (1.3-38.1) compared to SOC 2.9 (2.4-3.6) $p<0.0001$ and reduced by macitentan to 4.5 (1.6-39.5), $p<0.0001$. RV fibrosis signaling (connective tissue growth factor (CTGF) and endothelin-1 protein levels); extra-cellular matrix (ECM) remodeling (matrix-metalloproteinases 2 and 9), apoptosis and apoptosis-related peptides (caspases 3 and 8), were increased with PAB compared with SOC and decreased with macitentan.

Conclusion: Isolated RV afterload cause biventricular fibrosis and apoptosis, this is mediated by up-regulation of ET-1, CTGF and ECM signaling. The adverse ventricular-ventricular interactions are ameliorated by the ERB, macitentan.

P21.01 Torbjørn Halle Brøgger

DECLINING SENSITIVITY TO U46619 WITH DECREASED SIZE IN ISOLATED HUMAN SMALL VILLUS ARTERIES

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Background: The placenta is the base for the exchange of nutrients, oxygen and waste products for the fetus. Thromboxane A₂ (TxA₂) is attributed a major role in control of fetal placental perfusion, which suggests potent effects in the resistance arteries. We compared the effects of the TxA₂ analogue U46619, endothelin-1 and PGF_{2α} in isolated fetal villus and maternal intramyometrial arteries of varying size.

Method: This study was approved by the Danish scientific ethical committee (j. nr 20100229). From fresh-born placentas stem villi arteries were carefully dissected, and uterine samples were harvested at caesarian section at term. Then, using wire myography, the arteries were investigated in terms of contractility and sensitivity to U46619, endothelin-1 and PGF_{2α} in relation to their inner diameter.

Results: Fetal stem villous arteries responses to U46619 showed a positive linear correlation between pD₂ and the inner diameter ($r^2=0.725$). In contrast, responses to PGF_{2α} and endothelin-1 showed unchanged pD₂ with increasing inner diameter.

Maternal arteries did not show any change in pD₂ with different diameter when stimulated with U46619, PGF_{2α} or endothelin-1.

Conclusion: The results suggest a selective decrease in sensitivity to TxA₂ receptor stimulation with decreased vascular size in human fetal villus arteries.

P21.02 Peter Agger

MYOCARDIAL REMODELLING DUE TO RIGHT VENTRICULAR DILATATION IN CONGENITAL HEART DISEASE

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Background: Right ventricular dilatation is a well known pathological consequence of congenital heart disease mainly caused by pulmonary regurgitation. Patients with this disease have an increased risk for severe arrhythmias, heart failure and sudden death and very little is known about the aetiology of these complications and how to predict them. Today the treatment is valve substitution whenever cardiac symptoms occur, but knowledge is sparse about the optimal window for surgery. We hypothesize that morphological changes in the myocardium is the keystone in understanding this disease.

Materials and methods: The changes in myocardial architecture due to right ventricular dilatation will be investigated using diffusion tensor magnetic resonance imaging. This technique measures the spontaneous self-diffusion of water in the tissue. Using this technique in fibrous tissue, such as the myocardium, the direction of water diffusion is a measure of

fibre direction. Initially, we will examine a group of piglets with induced pulmonary regurgitation and dilated right ventricle. This will be done using existing ex vivo high field 9.4T MRI protocols. Subsequently, we will attempt to establish a non-invasive in vivo setup, which can be used for clinical testing in humans.

Expected findings: We anticipate that significant changes in the right ventricular myocardial architecture will occur in the dilated right ventricle and that these changes can explain the complications in this disease. Furthermore, we hope to be able to measure disease progression in vivo using MRI technique.

P21.03 Peter Skov
Jensen

STUDIES OF THE DIAMETER RESPONSE OF SMALLER RETINAL VESSELS

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Background: Disturbances in retinal blood flow are involved in the most frequent causes of blindness in the Western world. The mechanisms underlying the tone regulation in larger arterioles have previously been studied extensively, but evidence suggests that disturbances in the regulation of the retinal microcirculation may also play a major role in the development of vision threatening retinal diseases. However, hitherto no satisfactory in vitro model has been available for studying regulation of blood flow in the smaller retinal vessels.

Aim: To establish a method for studying the regulation of blood flow in the smaller retinal vessels in vitro.

Methods: Freshly isolated porcine retinas are mounted in a newly developed experimental setup for studying diameter regulation of smaller retinal arterioles, followed by the study of calcium activity in the cells surrounding the vessels.

Results: Preliminary results have confirmed a different diameter regulation in larger and smaller retinal vessels, and the cellular basis for these differences will be investigated in the coming experiments.

P21.04 Martin Grann

USE OF PHOTONIC FINGERPRINT AS DIAGNOSTIC TOOL AND MARKER FOR TREATMENT OF ENDOTHELIAL CELL DYSFUNCTION

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Background: Endothelial cell dysfunction is associated with cardiovascular disease. While certain pharmacological interventions and life-style changes have been suggested to reverse endothelial cell function, early detection methods are necessary for successful implementation of such strategies. The present project is intended to aid in the development of such methods within the framework of the EU LIPHOS project in which the main concept is that of living photonics. This concept involves studying light

propagated through cells to determine their spectral pattern. For distinct cell types, their morphologies as well as their conditions this light pattern has been shown to be unique and has been thus named the photonic fingerprint (PIN).

Aim: To study the PIN and determine the living photonic patterns of healthy versus diseased cells.

Experimental methods: The PIN will be collected using a broadband light source and fiber optics from different models of cardiovascular disease. The known indicators and biomarkers of endothelial cell dysfunction will be benchmarked, using existing methods, and correlated to the changes in PIN between cell conditions and the resulting information used to create a diagnosis tool integrated with lab-on-a-chip technology.

Perspective: We aim to develop an inexpensive screening method for early detection of cardiovascular disease leading to enhanced prevention strategies.

P21.05 Simon Gabriel ROLE OF SK₃ CHANNELS IN ERECTILE FUNCTION IN MICE

Comerma
Steffensen

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Cardiovascular disease and erectile dysfunction are associated and share the same risk factors, and probably are linked by endothelial dysfunction. Modulation of endothelial calcium-activated K channels has been proposed as an approach to restore endothelial function (Simonsen et al., Pharmacol. Report 2009; 61, 105-115), but the role of these channels in erectile function has not been addressed. The present study hypothesized that calcium-activated K channels with small conductance (KCa_{2.3} or SK₃) contributes to erectile function. This was addressed in mice with either overexpression (SK₃^{+/+}) or downregulation (SK₃^{-/-}) of the SK₃ channels and in wild type (WT) C57Bl/6 mice. Mean arterial pressure (MAP) as well as intracavernosal pressure (ICP) were measured in anaesthetized animals, and corpus cavernosum strips were mounted for isometric tension recording and immunoblotting was performed. MAP was decreased in SK₃^{+/+} mice compared to WT and SK₃^{-/-} mice. Stimulation of the cavernous nerve caused frequency-dependent increases in erectile function measured as ICP/MAP, and these responses were markedly decreased in SK₃^{-/-} mice compared to WT and SK₃^{+/+} mice. An opener of SK_{Ca} and intermediate conductance calcium-activated K channels (IK or KCa_{3.1}) induced concentration-dependent relaxations which were enhanced in corpus cavernosum from SK₃^{+/+} versus SK₃^{-/-} mice, while responses to the NO donor sodium nitroprusside (SNP) were statistically unaltered. Our findings suggest that downregulation of SK₃ channels blunts erectile function, and that opening of these channels may restore erectile function in disease.

P21.06 Nicolaj
Christopher
Hansson MULTIDETECTOR COMPUTED TOMOGRAPHY VERSUS TRANSESOPHAGEAL
ECHOCARDIOGRAPHY FOR ANNULAR SIZING IN TRANSCATHETER AORTIC
VALVE REPLACEMENT

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Background: Paravalvular aortic regurgitation (PAR) remains a major limitation in transcatheter aortic valve replacement (TAVR). The influence of aortic annular assessment with either multidetector computed tomography (MDCT) or conventional transesophageal echocardiography (TEE) on the incidence of post-procedural PAR was evaluated.

Methods: In an observational study design, outcomes following TAVR with a balloon expandable THV were compared in two cohorts identified according to whether THV size selection was based on TEE (study group 1, n = 80) or MDCT (study group 2, n = 58).

Results: The two study groups were comparable with regard to baseline clinical risk score and echocardiographic characteristics. The incidence of moderate/severe PAR was lower in study group 2 than in group 1, 8.6% versus 28.8% ($p < 0.01$). Using receiver operating curves analysis, the difference between the THV nominal diameter and MDCT annular diameter was predictive of moderate/severe PAR (AUC 0.84; 95% CI: 0.72-0.92). Neither age, gender, body mass index, annular eccentricity index, aortic valve calcification nor the difference between the THV diameter and the TEE annular diameter predicted post-procedural PAR. Increased THV oversizing relative to the MDCT mean annular diameter was associated with reduced severity of PAR. No difference in per-procedural complications between two study groups was observed.

Conclusion: MDCT-based annular sizing in TAVR significantly reduces post-procedural PAR, and THV oversizing appears pivotal in this aspect. Further delineation of the optimal degree of THV oversizing is needed.

P21.07 Astrid Drivsholm
Sloth NO APPARENT MODIFICATION BY CARDIOVASCULAR RISK FACTORS AND
COMORBIDITY ON THE EFFICACY OF REMOTE ISCHEMIC CONDITIONING
BEFORE PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN
PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION

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Background: Remote ischemic conditioning (RIC) induces cardioprotection in patients undergoing primary percutaneous coronary intervention (pPCI)

for ST-elevation myocardial infarction (STEMI). However experimental studies of myocardial infarction have demonstrated that the effect of RIC may be attenuated by comorbidity. This study evaluates the potential effect modification by cardiovascular risk factors and comorbidity on RIC in pPCI treated patients with STEMI.

Methods: The present analysis was performed on a clinical trial involving 251 patients with STEMI randomized pre-hospitally to receive pPCI with (n = 126) or without (n = 125) RIC (intermittent arm ischemia through four cycles of 5-min inflation and 5-min deflation of a blood-pressure cuff). The primary endpoint of the parent trial was myocardial salvage index estimated by single photon emission computed tomography. We applied stratified analyses for myocardial salvage index according to the presence of cardiovascular risk factors and comorbidity to assess for effect modification.

Results: The presence of cardiovascular risk factors and comorbidity did not significantly modify the efficacy of RIC in patients with STEMI. The effect of RIC tended to be reduced in current smokers.

Conclusion: We did not identify specific cardiovascular risk factors or comorbidity that caused significant attenuation of the efficacy of RIC. The present analysis suggests that RIC may be an effective adjunctive treatment in all STEMI patients regardless of cardiovascular risk factors and comorbidity. Our findings need confirmation in large-scale randomized clinical trials.

P21.08 Nikolai Hoffmann-Petersen

A COMPARISON OF OFFICE BLOOD PRESSURE, TELEMEDICAL HOME BLOOD PRESSURE AND AMBULATORY BLOOD PRESSURE MONITORING

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Background: Telemonitoring of home blood pressure is a new advance in blood pressure monitoring (HBPM). The aim of this study was to compare the accuracy of office blood pressure and telemedical home blood pressure with 24-h ambulatory blood pressure (ABPM).

Methods: 102 patients were consecutively recruited from a Renal Out-patient Clinic. Office blood pressure was measured three times with HBPM equipment. Next patients used HBPM with telemonitoring three times daily for four consecutive days and finally ABPM on the following day.

Results: There was a significant difference between OBPM and ABPM (24-h and daytime) and between HBPM and daytime ABPM; HBPM was lower (-4.1 mmHg/-1.6 mmHg) than daytime ABPM (p<0.05). The strongest correlations were seen between all HBPM readings day 2-4 and ABPM (24-h and daytime). There was no significant difference between HBPM and 24-h ABPM.

Conclusion: The telemedical HBPM reflected more accurately 24-h ABPM than office readings.

P21.09 Lisbeth Bonde

EXTRACELLULAR ACIDIFICATION INHIBITS Na^+ , HCO_3^- -COTRANSPORT

ACTIVITY

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Background: In the vascular smooth muscle cells of resistance arteries, the net acid extrusion is primarily mediated by the Na⁺/H⁺-exchanger NHE1 and the electroneutral Na⁺,HCO₃⁻-cotransporter NBCn1. Both transporters are activated upon intracellular acidification and contribute to a rapid recovery of intracellular pH (pHi). Extracellular acidification has been demonstrated to inhibit Na⁺/H⁺-exchange but the effect of extracellular pH (pHo) on NBCn1 activity has not yet been clarified.

Aim: The present study aimed to investigate the effect of pHo on NBCn1.

Method: We used BCECF-based fluorescence microscopy to study pHi dynamics. Mesenteric arteries were isolated from male NMRI mice and kept in physiological saline solution. After intracellular acidification induced by addition of 20 mM NH₄Cl and subsequent washout, the pHi recovery was measured in the presence and absence of CO₂/HCO₃⁻ and 1 mM amiloride at pHo 7.4, 7.1 and 6.8. Groups were compared by one-way ANOVA.

Results: NHE1 transport rates in the pHi range 6.7-6.8 gradually decreased when pHo was reduced. The Na⁺/H⁺-exchange activity decreased by 26 ± 7% (means ± SEM, p<0.05, n=6) when pHo was changed from 7.4 to 7.1, and by 66 ± 14% (p<0.01, n=6) when pHo was reduced to 6.8. NBCn1 activity in the pHi range 6.7-6.8 was also significantly inhibited (59 ± 10%; p<0.01, n=6) by a pHo decrease from 7.4 to 6.8. Yet, the transporter was resistant to moderate changes in pHo as no change in Na⁺,HCO₃⁻-cotransport activity (9 ± 11%; p=0.43, n=6) was seen when pHo was changed from 7.4 to 7.1.

P22.01 Jacob Reinholdt INITIATION OF CANCER INVESTIGATIONS IN GENERAL PRACTICE Jensen

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Background: Close to 90% of all cancers are diagnosed because the patient presents symptoms and signs. Of these patients, 85% initiate the diagnostic pathway in general practice. Therefore, the initiation of a diagnostic pathway in general practice becomes extremely important. On average, a general practitioner (GP) is involved in 7500 consultations each year, and in the diagnostic process of 8-10 incident cancers.

One half of cancer patients consult their GP with either general symptoms, which are not indicative of cancer, or vague and non-specific symptoms. The other half present with what the GP assess as alarm symptoms. Three months prior to diagnosis, patients who are later diagnosed with cancer have twice as many GP consultations than a comparable reference

population. Thus the complex diagnostic process in general practice requires the GP to react on very different and vague symptoms to ensure early cancer diagnosis. To enable earlier cancer diagnosis, we need much more knowledge and a better understanding of the initiation of cancer-specific tests and investigations in general practice.

Aim: To investigate how, how often and on which background investigation for suspected cancer is initiated in general practice.

Methods: Participating Danish GPs will fill in an electronic questionnaire after random consultations. A total of 70,000 consultations will be included.

Perspectives: The results will show how often and why GPs suspect cancer, how they perform the initial investigations and whether this process can be supported and optimised. This insight is crucial in order to improve the diagnostic pathway.

P22.02 Niels Peter Andersen

NON-INVASIVE REDUCTION IN NERVE CONDUCTIVITY IN CLOSE RELATION TO FLOW, USING MRI-GUIDED HIGH INTENSITY FOCUSED ULTRASOUND (HIFU)

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Background: Resistant hypertension, a leading cause of death worldwide, is caused by hyperactivity of the sympathetic nerves in the walls of the renal artery. When orally administrated, antihypertensive drugs have no effect, and patients with resistant hypertension are subjected to renal denervation, using an invasive catheter-based (radiofrequency) ablation technique. We hypothesize that a non-invasive method of renal denervation could be performed using MRI-guided High Intensity Focused Ultrasound (HIFU). To address this, our first step was to demonstrate the usefulness of MRI-guided HIFU for nerve damage in close relation to major vessel flow.

Materials and methods: Danish landrace pigs (30 kg, n=6) were positioned in a Philips Sonalleve HIFU system with the neck area facing down towards a multielement HIFU transducer. HIFU treatments were made on one vagus nerve while the contra lateral side served as control. Neurophysiological conductivity tests of the nerves were after the Ultrasound treatments carried out, with a stepwise increase in voltage (0.2, 2.0 and 20 V).

Results: We were able to successfully target the vagus nerve with MRI-guided HIFU. Neurophysiological investigations showed a significant reduction in nerve conductivity in the heat-treated vagus nerve in comparison to the non-sonicated side.

Conclusion: This study demonstrated that we were capable of delivering enough energy using MRI-guided HIFU to reduce function significantly in nerves (vagus) adjacent to the major vessels with large flow, which are suspected to reduce the effect of sonication due to the thermodynamic cooling of flowing blood. These encouraging results motivate our next step:

renal denervation.

- P22.03 Rasmus Hansen BLOOD BRAIN GLUCOSE TRANSPORT IN RELATION TO INCREASING BMI
Olesen EXPRESSION OF GLUT1 AND GLUT3 IN THE PREFRONTAL CORTEX

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Background and aims: Excess body weight is a major health problem, leading to increased mortality and morbidity. There seems to be a relationship between elevated BMI and reduced cognitive performance. Recent research links obesity to increased risk of Alzheimer's Disease (AD). Glucose enters the brain by facilitated diffusion across the Blood Brain Barrier (BBB). Under normal conditions, glucose transport across the BBB does not affect the cerebral glucose metabolism but under pathophysiological conditions, the transport of glucose can be rate limiting. In AD, the cerebral metabolic rate of glucose is decreased in the most affected regions. We hypothesize that chronic metabolic changes induce alterations in the glucose transport over the BBB and that this will be reflected when comparing obese and normal weight individuals.

Materials and methods: The BrainCloud contains gene expression data on 272 individuals. We examined GLUT 1 and 3 expressions in the human pre-frontal cortex. Analysis was done using ANCOVA.

Results: GLUT1 and 3 expressions in individuals with a BMI ranging 25-50 were statistically unaltered compared to normal BMI, whereas a BMI >50 had a significantly lower expression of GLUT1 ($p < 0.01$). The analysis found GLUT1 expression unaffected by sex, race and age. GLUT3 expression declined with age ($p < 0.01$), but was unaffected by sex and BMI. Comparing races, the expressions of GLUT3 were significantly lower in the non-white population ($p < 0.01$).

Conclusion: The results suggest that BBB glucose transport is stable at most metabolic conditions but may be affected in the morbidly obese. The effect is unrelated to age although an age effect occurring in old age cannot be excluded.

- P22.04 Kathrine OBESITY AND RISK OF INFECTION
Agergård
Kaspersen

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Background: Obesity is associated with increased risk of developing a range of diseases. However, the effect of obesity on the risk of infection among otherwise healthy individuals has not been established.

Methods: The project included 17,246 participants in The Danish Blood

Donor Study, which was initiated on 1 March 2010. All participants completed a standard questionnaire on e.g. smoking status, physical activity, diet, and various body measurements. Body mass index (BMI) was categorized as BMI<20, 20<=BMI. =BMI=BMI=30 (defined here as obesity). Infections among participants were identified as relevant ICD-10 codes in the National Patient Register. Cox proportional hazards analysis with BMI, age, current smoking status and sex as predictors was performed with risk time defined as time since inclusion.

Preliminary results: A total of 501 participants had one or more infectious disease diagnoses during 40,070,5 risk years. BMI>=30 were associated with an increased risk of infection (hazard ratio (HR)=1.37, p=0.029, 95% confidence interval (CI): 1.03-1.80). For current smoking, a similar increase in risk was found (HR=1.41, p=0.001, CI: 1.14-1.75) whereas age was found to be protective (HR=0.91, p=0.019, CI: 0.85-0.98).

Perspectives: Among healthy individuals, obesity was associated with an increased risk of all-course infection similar to the risk associated with smoking. Forthcoming analyses will include approximately 40,000 participants. Knowledge of an association between obesity and risk of infection would further support an early intervention against obesity and facilitate research in the interplay between metabolism and immune response.

P22.05 Julie Vendelbo
Nielsen NEUROINFLAMMATION IN DIABETES - A POSSIBLE LINK TO ALZHEIMER'S DISEASE? A MICROPET STUDY IN THE GK-RAT, AN ANIMAL MODEL OF TYPE 2 DIABETES

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Background: Alzheimer's disease (AD) affects an ever increasing numbers of patients as the population ages. It is estimated to affect 4 to 8% of the population aged above 65 years and up to 30% of those aged above 80 years. AD is a chronic disorder in which patients progressively develop dementia with loss of cognitive abilities and independence. This reduces their quality of life dramatically. Type 2 diabetes mellitus (DM2) is a major risk factor for AD. DM2 is characterised by hyperglycaemia and insulin resistance and causes a state of chronic inflammation in the body. We hypothesise that insulin resistance also leads to brain inflammation in the form of glial activation and contributes to the development of AD pathology (beta amyloid plaques and tau neurofibrillary tangles).

The aims of the project are to 1. Develop an in vivo rodent model to study inflammation in the brain, 2. Identify the localisation and the level of brain inflammation in a rodent model of DM2, and 3. Investigate the efficacy of an anti-diabetic GLP-1 analogue in reducing neuroinflammation.

Methods: The project is an ¹¹C-PK11195 microPET study in the GK rat. ¹¹C-PK11195 binds to the translocator protein expressed by activated microglia in the brain and so provides an in vivo inflammation marker. We plan to compare brain ¹¹C-PK11195 uptake in GK rats to that in the brain of

healthy Wistar rats, the background rats of the strain. Rats will be studied before and after GLP-1 treatment and PET findings compared with spinal fluid levels of cytokines and eventual brain histology.

- P22.06 Rasha
Abdelkadhem
Al-Saaidi
- THE MISSENSE MUTATION P.ARG471HIS CAUSES DILATED
CARDIOMYOPATHY THROUGH A DOMINANT NEGATIVE EFFECT

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Lamins (A- and B-type) are the main structural components of the nuclear lamina, an elastic network located on the inside of the inner nuclear membrane. Mutations in the LMNA gene encoding the A-type lamins, lamin A and lamin C are linked to different human genetic diseases affecting different tissues called laminopathies collectively. The most prevalent laminopathy is dilated cardiomyopathy (DCM). DCM is a hereditary cardiac disease characterized by cardiac ventricular chamber enlargement and reduced systolic function. It is unclear and debated whether DCM is caused by haploinsufficiency or dominant negative effects. In this present study, we investigated a heterozygous LMNA missense mutation, Arg471His to get a better understanding of the molecular disease mechanisms. Quantitative reverse transcriptase polymerase chain reaction (qRT-PCR), Western blotting (WB) and nano-liquid chromatography coupled with tandem mass spectrometry (nLC-MS) demonstrated that the transcript and the protein expression levels of lamin A and lamin C were not reduced in patients bearing the missense mutation p.Arg471His. Furthermore, immunofluorescence microscopy analysis showed normal levels of lamin A and lamin C proteins in patient fibroblast cells. nLC-MS analysis showed that the mutant protein is present in the cytoskeletal fraction of all patient fibroblasts with the missense mutation. These findings indicate that the p.Arg471His mutant protein is expressed and incorporated in the lamin filament and may cause DCM through a dominant negative effect.

- P22.07 Mikkel Svankjær
Thagaard
- DOES METFORMIN TREATMENT CAUSE VITAMIN B12 DEFICIENCY?

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Introduction: Metformin is a cornerstone in treatment of type 2 diabetes. A side effect of treatment is a decrease in plasma B12 (B12). This has led to the concern that individuals treated with metformin are in danger of developing B12 deficiency. Preliminary data from our laboratory derived from studies in a rat model indicate that, despite a metformin-induced decrease in plasma B12, a supernormal level of B12 is seen in the liver. The aim of the present study is to further elucidate trafficking of B12 in rats

treated with metformin.

Methods: Two groups of male rats (n=10 in each group) were given subcutaneous injections daily with metformin (250mg/kg/day) or saline for six weeks. After treatment the rats will be given a dose (0,5pmol) of ⁵⁷Co-B12 by gastric gavage and the next 24 hours housed in metabolic cages. The rats will then be sacrificed. Blood, faeces and organs collected for measurements of ⁵⁷Co-B12, endogenous B12 and markers B12 deficiency. We will also perform RT-PCR on selected genes related to the metabolism of B12.

Results: We expect to see a decrease in plasma B12 despite an accumulation of B12 in the liver. Measurements of labeled and endogenous B12 in the liver and in other organs will help us understand alterations in the distribution of B12 caused by treatment with metformin. The results of our RT-PCR assays will indicate if metformin causes changes in B12 metabolism at gene level, and may help in understanding the pathophysiological causes for changes in B12 metabolism.

Perspectives: This experiment may help us understand whether B12 deficiency should be a concern in patients treated with metformin.

P22.08 Vincent
Kalumire
Cubaka

HEALTH EFFECTS OF CONTEXT-SENSITIVE, PHYSICIAN-ASSISTED,
TRAINING-CENTERED SUPERVISION OF HEALTH CENTER PERSONNEL IN
RWANDA

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Background: Evidence shows that primary health care is a crucial component in building a cost-effective health system offering equal access to appropriate health services. Rwanda has an extensive primary health care system with health centers nationwide. A national monitoring system requires district hospitals to supervise health centers' performance. At the heart of supervision is a relationship between a supervisor and a supervisee. There are indications that this relationship is characterized by inspection and performance-scoring rather than support and problem-solving. Studies are needed from low-resource-settings to describe this and the type of supervision taking place, from the view of both supervisors and supervisees. Also, the role of primary care physicians in supervision is unclear.

Objectives and methods: To understand the characteristics of hospital supervision of health centers, and the relationship between supervisors and supervisees, through a qualitative study primarily using focus group discussions. This study will guide an intervention to measure the effects of introducing physician-assisted, training-centered supervision at selected health centers. Changes in indicators over time will be compared to control sites to evaluate the impact of the intervention.

Perspectives: Many low-income countries spend resources on supervision without clear policies to define the objectives, methods and expectations. Our study will explore methods for training-centered supervision that may be adapted in low-resource settings such as in Rwanda, including what

role a primary care physician may play in the supervision team.

- P23.01 Aisha Rafique TARGETING BIOACTIVE NANOPARTICLE-ENCAPSULATED 1,25 VITAMIN D TO MACROPHAGES IN VITRO AND IN VIVO FOR ANTI-INFLAMMATORY THERAPY

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Background: Vitamin D₃ is known for its physiological function in calcium and phosphate metabolism. Studies have shown that vitamin D₃ also plays important immunological roles and possesses anti-inflammatory and anti-fibrotic properties. Through tight regulation, Vitamin D is synthesized into its bioactive form in the kidneys and in macrophages. Macrophages are essential cells in initiating and sustaining inflammation by the production of inflammatory cytokines and blocking of macrophage cytokines by biological drugs have shown pronounced effects in inflammatory diseases.

Aim: The aim of this study, which was initiated in August 2013, is to examine the anti-inflammatory effects of the bioactive form of vitamin D₃ (1,25 D₃) encapsulated in nanoparticles targeted to macrophages in chronic inflammatory diseases.

Materials and methods: We have successfully prepared lipid nanoparticles (LNP) consisting of POPC and triolein containing 1,25 D₃ using millisecond microfluidic mixing. 1,25 D₃ Triolein-LNPs were quality tested by Dynamic Light Scattering and by HPLC and modified with macrophage-specific CD163 antibody. The anti-inflammatory effects of 1,25 D₃-LNPs are investigated in vitro in mouse monocyte macrophage cell line RAW 264.7 and in human monocyte derived macrophages by RT-qPCR, western blot analysis, flow cytometry, confocal microscopy and immunohistochemistry. We will subsequently select the most suitable nanoparticles and test them in a relevant animal model of inflammation.

Perspectives: This translational project holds promise for the utilization of the strong anti-inflammatory effects of the bioactive vitamin D in the systemic treatment of patients with inflammatory disorders.

- P23.02 Anne Winther Larsen EGFR POLYMORPHISMS AS PREDICTORS OF CLINICAL OUTCOME IN ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH EGFR-TKI

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Background: Mutations in the epidermal growth factor receptor (EGFR) have been confirmed as a predictor of efficacy for tyrosine kinase inhibitors (TKI) in non-small cell lung cancer (NSCLC). However, the EGFR mutated patients only represent approximately 15%, and not all clinical outcomes can be explained by the mutation. Therefore, there is a lack of novel biomarkers. Previous studies have demonstrated germline polymorphisms in

EGFR affecting the protein expression, and some of them have been correlated to a better clinical outcome on TKI treatment. A CA repeat polymorphism in intron 1 containing 14-21 repeats have showed higher EGFR expression with decreasing number of repeats. Two polymorphisms – 216G/T and -191C/A – located in the promoter region have shown to influence the expression level of EGFR. This study is designed to evaluate the role of these three polymorphisms in a cohort of NSCLC patients treated with a TKI.

Material and methods: Number of CA repeats in -216G/T and -191C/A will be evaluated in blood samples from 498 consecutive NSCLC patients treated with erlotinib. EGFR somatic mutation status is known in all patients. DNA has been extracted from blood using the QIAamp DNA mini kit. Regions containing the polymorphisms have been amplified by PCR and number of CA repeats will be evaluated by capillary electrophoresis and -216G/T and -191C/A polymorphisms by restriction enzymes and gel electrophoresis. The results will afterwards be correlated to PFS, OS, histology and EGFR somatic mutations.

Conclusion: The study will determine if the polymorphisms are potential predictors for clinical outcome under TKI treatment in advanced NSCLC patients.

P23.03 Konstantin Kazankov

SOLUBLE CD163, A MACROPHAGE ACTIVATION MARKER, IS INDEPENDENTLY ASSOCIATED WITH FIBROSIS IN PATIENTS WITH CHRONIC VIRAL HEPATITIS B AND C

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Macrophages are involved in liver inflammation and fibrosis. Soluble (s)CD163 is a specific marker of activated macrophages, and we investigated associations between sCD163 and biochemical and histological parameters of inflammation and fibrosis in 556 patients with chronic hepatitis C virus (HCV) and 208 patients with chronic hepatitis B virus (HBV) before anti-viral treatment. Scheuer histological scores of activity and fibrosis were obtained. Clinical, biochemical, and metabolic parameters were recorded. We measured sCD163 by ELISA. Soluble CD163 was higher in patients with HCV compared to HBV (3.7(interquartile range (IQR) 2.5-5.5) vs. 2.4(IQR 1.8-3.6) mg/L, p<0.001). sCD163 was associated with fibrosis stages, with highest levels in patients with advanced fibrosis (F≥3) (5.7(IQR 3.9-6.9) mg/L) and cirrhosis (F=4) (6.2(IQR 5.0-6.9) mg/L). sCD163 was a marker of fibrosis independent of other biochemical parameters and known risk factors. A sCD163-based Fibrosis Score, CD163-FS, had an area under the Receiver Operating Characteristics curve (AUROC) of 0.87 (95% CI: 0.82-0.92) for cirrhosis, 0.84 (95% CI: 0.80-0.88) for advanced fibrosis, and 0.78 (95% CI: 0.74-0.81) for

significant fibrosis. Compared to existing fibrosis scores, CD613-FS was superior to the AST to platelet ratio index (APRI) for all fibrosis stages and to FIB-4 for significant fibrosis. Conclusion: sCD163 levels are increased in patients with chronic viral hepatitis, reflecting macrophage activation. Increased sCD163 is associated with the severity of disease and predicts fibrosis. A sCD163-based fibrosis score, CD163-FS, is superior to APRI and FIB-4 for the diagnosis of significant fibrosis.

P23.04 Christina Demuth

IDENTIFICATION OF NOVEL ERLOTINIB RESISTANCE MUTATIONS BY EXOME SEQUENCING OF PLASMA DNA

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In 2004, a novel mutation in the epidermal growth factor receptor (EGFR) gene was found in non-small cell lung cancer (NSCLC). Today, we know that about 15% of the NSCLC patients harbour EGFR mutations. Different tyrosine kinase inhibitors (TKIs) that directly target the mutated EGFR protein have been developed and at the Dept. of Oncology, AUH, the TKI erlotinib is now a part of the routine treatment of EGFR mutation positive patients. Unfortunately, the response is temporary, and most patients develop resistance at some point. A new mutation in the EGFR gene, T790M, has been found to hinder binding of erlotinib to the EGFR protein, thereby causing resistance to the treatment.

Today, it is commonly known that DNA from cancer cells can be found in the blood plasma of a patient. We have a cohort of 23 patients harbouring EGFR mutations and who have been treated with erlotinib. From this cohort of patients, we have collected blood samples when the treatment was initiated (pre-treatment) and at the point where resistance developed (post-treatment). The post-treatment samples have been investigated to identify the T790M mutation. Of 23 patients, only 9 gained the T790M mutation, and the mechanism of development of resistance in the remaining 14 patients is therefore still unknown.

The aim of this project is to use exome sequencing to identify the mechanisms causing the erlotinib resistance in the remaining 14 patients. We want to sequence the exome of DNA isolated from the pre- and post-treatment blood samples. By doing this, we can exclude the patient-specific variations found in the pre-treatment samples and thereby identify mutations developed after treatment has started.

P23.05 Johan Frederik Berg Arendt

CANCER PROGNOSIS IN PATIENTS WITH ELEVATED PLASMA VITAMIN B12

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Background: We recently demonstrated that high plasma vitamin B12 levels were associated with increased cancer risk among patients referred

for plasma vitamin B12 measurement. Other studies have shown an increased mortality risk among cancer patients with high vitamin B12 levels. This population-based study aims to examine the survival among cancer patients with a plasma Cbl measurement prior to cancer diagnosis.

Methods: We will include all patients with a cancer diagnosis and vitamin B12 levels of 200-600 (reference range), 601-800 and >800 pmol/L prior to diagnosis during 1998-2010 from the Danish Cancer Registry and Laboratory Information Systems Database in Northern Denmark. Data on the use of B12 supplements and co-morbidity will be obtained through the Aarhus University Prescription Database and the Danish National Registry of Patients. B12 supplemented patients will be excluded and co-morbidity will be scored according to the Charlson Co-morbidity Index. Cox proportional hazard regression model will be used to assess mortality risk and Kaplan-Meier curves will be computed.

Results: Preliminary results will be reported.

Conclusion: We hypothesize that elevated vitamin B12 levels are associated with an increased cancer mortality.

P23.06 Peter Rubak

ASSESSING PLATELET FUNCTION: A NEW FLOW CYTOMETRY BASED ASSAY

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Background: Assessment of platelet function in whole blood by impedance aggregometry is increasingly used. However, it has recently been shown that this method is highly dependent on platelet count making it less suitable for examination of patients with thrombocytopenia.

Aim: To develop and validate a new flow cytometry assay for assessment of platelet function by determination of the glycoproteins CD62p, CD63 and bound fibrinogen expressed on the platelet surface.

Methods: Background noise and spectral overlap were minimised by titration of the following antibodies with specific fluorochromes: CD42b-PE, CD63-PCy7, CD62p-APC, anti-fibrinogen-FITC, isotype-PE and isotype-APC. The compensation matrix was validated with fluorescence minus one (FMO) controls. The agonists ADP, collagen, TRAP-6, ristocetin and arachidonic acid were titrated to an optimal concentration with maximum platelet response for CD62p, CD63 and bound fibrinogen.

Platelet function was measured before and after stimulation with agonists on 20 healthy volunteers and presented as percentage of platelets positive for CD62p, CD63 and bound fibrinogen.

Results: The isotype controls showed minimal non-specific antibody binding, and the FMO controls showed no spillover-induced staining. All agonists were titrated from maximum platelet response to no platelet response to find the optimal concentration. Reference intervals of the percentage of platelets positive for CD62p, CD63 and bound fibrinogen will

be presented for 20 healthy volunteers.

Conclusion: We have developed and validated a new flow cytometry assay for determination of platelet function. This assay will in future studies be validated in thrombocytopenia.

P23.07 Sidsel
Rødgaard-
Hansen

A SOLUBLE FORM OF THE MACROPHAGE-RELATED MANNOSE RECEPTOR (MR/CD206) IS PRESENT IN HUMAN SERUM AND ELEVATED IN CRITICAL ILLNESS

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Background: This study tests the hypothesis that the mannose receptor (MR/CD206), which is expressed primarily by macrophages and dendritic cells, can be found in a soluble form (sMR, sMR) in human serum. Furthermore, we wished to establish and validate an enzymelinked immunosorbent assay (ELISA) for sMR and to perform initial studies exploring the potential of sMR as a biomarker.

Methods: Western blotting identified a single band of approximately 170 kDa in human serum, and MALDI MS/MS of the purified protein confirmed it to be sMR. An ELISA was established and validated with a measurement range of 1 - 256 µg/L.

Results: The 95% reference interval was 0.10 - 0.43 mg/L based on measurements of serum samples from healthy individuals (n=217). Samples from hospitalised patients (n=219) revealed that more than 50% of patients had concentrations above 0.43 mg/L. Very high concentrations (up to 6.2 mg/L) were observed in critically ill patients with sepsis and/or severe liver disease.

Conclusions: This study documents, for the first time, the presence of sMR in human serum and describes an optimised ELISA suitable for quantitative measurements. Levels of sMR are strongly elevated in several disease states, including sepsis and liver disease, and the protein therefore shows promise as a new biomarker.

P23.08 Omar Majed
Abuyaman

THE SOLUBLE RECEPTOR FOR VITAMIN B₁₂ UPTAKE (SCD320) IS PRESENT IN EIGHT OUT OF TWELVE EXAMINED TYPES OF HUMAN BODY FLUIDS

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Background: Cellular uptake of vitamin B₁₂ (B₁₂) demands binding of the vitamin to transcobalamin (TC) and recognition of TC-B₁₂ by the receptor CD320. Recently, we have identified a soluble form of CD320 (sCD320) in human serum and shown it to be present in high concentrations in urine

(Abuyaman, et al. PLOS One 2013). Here we present data on the occurrence of this soluble receptor in an additional 10 different human body fluids.

Methods: We examined the sCD320 level in the following set of samples: 40 urine, 67 serum, 5 seminal plasma, 5 amniotic fluid, 5 breast milk, 6 synovial fluid, 110 cerebrospinal fluid (CSF), 6 cervical mucus, 6 saliva, 4 gastric juice, 3 nasal drainage, and 6 bronchial fluid samples. sCD320 concentration was measured by in-house ELISA. Gel filtration was performed on a Superdex 200 column.

Results: The median (range) of sCD320 expressed as pmol/L are 230 (60-550) in urine, 120 (73-840) in serum, 75 (65-153) in seminal plasma, 64 (55-67) in amniotic fluid, 37 (34-81) in breast milk, 36 (29-67) in synovial fluid, 18 (6-45) in cerebrospinal fluid, and 13 (0-61) in cervical mucus. sCD320 is not detected in saliva, gastric juice, nasal drainage, and in bronchial fluid samples. The molecular characteristics of cerebrospinal fluid and urine sCD320 as judged by gel filtration is identical to that observed for sCD320 in serum. Conclusions: We report, for the first time, the occurrence of sCD320 in other body fluids than serum and urine. The concentration is relatively low as compared to serum, and no sCD320 is detected in most of the exocrine secretions examined. The biological significance of the reported findings remains to be clarified.

P24.01 Mads Engel
Hauberg

MICRO-RNAS IN THE AETIOLOGY OF SCHIZOPHRENIA

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Several miRNAs have recently been implicated in schizophrenia, and it could be hypothesised that the disease in part could be explained by dysregulation of miRNA regulated gene networks. The goal of this research project is to further elucidate this using data from genetic studies and bioinformatics. As a preliminary step, publicly available miRNA databases will be searched and targets for newly identified miRNAs will be predicted. In a next step, genome-wide association data will be used to see if gene sets comprised of miRNAs and their respective targets or the miRNAs themselves are associated with schizophrenia. The miRNA gene sets found to be associated with schizophrenia will then subsequently be validated using bioinformatics evaluating among others eQTL and mQTL data as well as epistasis information. Finally, gene-set enrichment and pathway-based association analyses will be used to possibly infer the biological processes malfunctioning in schizophrenia patients.

P24.02 Michael
Aagaard
Andersen

PATHOPHYSIOLOGICAL INTERPLAY BETWEEN LRRK2 AND ALPHA-SYNUCLEIN IN THE MECHANISMS LEADING TO NEURONAL DYSFUNCTION AND NEURODEGENERATION IN PARKINSON'S DISEASE

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Parkinson's disease (PD) is a progressive neurodegenerative disorder that affects 1% of the population over 55 years of age. Lewy bodies and neurites are hallmarks of PD. PD is mostly a sporadic disease; however,

inherited forms of PD exist and are associated with mutations in genes encoding alpha-synuclein (SNCA) and Leucine-rich repeat kinase 2 (LRRK2). LRRK2 has been shown to be co-localized with α -synuclein in Lewy bodies in the brain of PD patients, and a potential pathophysiological interplay between LRRK2, α -synuclein and dysfunctions of the basal ganglia circuitry in PD is increasingly investigated.

While it has been hypothesized that inhibition of LRRK2 may be an attractive treatment option for familial forms of PD, it remains to be investigated whether this principle will also be efficient for treating sporadic PD. Accordingly, our project will focus on determining the pathophysiological interplay in vivo between two key proteins in PD, α -synuclein and LRRK2, in basal ganglia circuitry. Virally-mediated overexpression of α -synuclein in the substantia nigra will be performed in a LRRK2 knock out transgenic rat model. The viral-mediated overexpression of alpha-synuclein has been previously evaluated in wt rats, which shows a progressive pathology. The evaluation of the α -synuclein and LRRK2 interplay will be done by different behavioural, electrophysiological and biochemical readouts e.g. cylinder test, in vivo single unit recording in subthalamic nucleus, in vivo investigation of the corticostriatal plasticity (LTD and LTP), and in situ hybridisation in striatum with co staining of D1, D2-receptors, LRRK2 and pLRRK2, α -synuclein and pS129- α -synuclein.

P24.03 Trine Gjerløff

[¹¹C]DONEPEZIL PET: A METHOD FOR ASSESSING AUTONOMOUS DYSFUNCTION IN PARKINSON'S DISEASE?

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Background: Non-motor symptoms in Parkinson's disease (PD), such as dryness of mouth, nausea and constipation, often occur several years before motor symptoms and diagnosis. Impairment of the autonomous nervous system (ANS) is responsible for a large part of non-motor symptoms. Finding a method to assess dysfunction in ANS would be a valuable tool in early diagnosing of PD.

[¹¹C]donepezil is a PET ligand that binds to the enzyme acetylcholinesterase (AChE). AChE breaks down acetylcholine, which is the neurotransmitter of the parasympathetic nervous system (PNS), the part of ANS related to "rest-and-digest" functions.

Methods and materials: In our study, we plan to scan 20 PD patients with moderate PD symptoms and 20 healthy controls, using [¹¹C]donepezil PET. Each subject will undergo two scans, one of the abdomen and one of the brain and salivary glands.

We will estimate the function of the parasympathetic nervous system by comparing the PET signals of the two groups. In addition, the PET data will be analyzed for correlations with other autonomic measures - such as heart rate variability, gastric emptying time and salivary flow.

The study is conducted as a clinical trial in accordance with the guidelines

of Good Clinical Practice.

Results: Preliminary [¹¹C]donepezil PET scans on 7 healthy subjects have demonstrated a whole-body biodistribution largely in accordance with the known density of parasympathetic innervation.

Discussion: Preliminary findings indicate that [¹¹C]donepezil PET can be used to visualize PNS. We believe this tracer can be useful in future research and diagnostics in PD, but also in diabetes and other illnesses with PNS involvement.

- P24.04 Kristian Gaarn A SINGLE DOSE OF VORTIOXETINE OR KETAMINE, BUT NOT FLUOXETINE, INCREASES TRANSCRIPT LEVELS OF GENES INVOLVED IN NEUROPLASTICITY IN THE RAT PREFRONTAL CORTEX
Du Jardin
Nielsen

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Vortioxetine (Brintellix) and ketamine have antidepressant and pharmacological characteristics that may differentiate them from current antidepressants. The multimodal antidepressant, vortioxetine, has been shown to improve depression symptoms and may have a greater therapeutic effect on cognitive symptoms related to major depressive disorder than current standard SSRI treatment. Ketamine is a non-competitive NMDA receptor antagonist that has been shown to induce a rapid antidepressant effect in treatment-resistant patients. Major depressive disorder is associated with a loss of neurons, dendrites, and dendritic spines in the prefrontal cortex and hippocampus. The clinical efficacy of antidepressants may involve reversal of these processes. Moreover, glutamatergic signaling has a central role in the regulation of neuroplasticity. Here we investigate the effect of ketamine and vortioxetine on neuroplasticity at the gene transcript level. Male Sprague-Dawley rats received one dose (IP) of fluoxetine, ketamine, or vortioxetine 2, 8, 12, or 27 hours prior to harvesting of the prefrontal cortex and hippocampus. The mRNA levels of genes involved in neuroplasticity and glutamatergic signaling were measured by real-time qPCR. We found increased transcript levels of genes involved in dendritic spine density and metabotropic glutamatergic signaling in the prefrontal cortex 8 hours after treatment with vortioxetine or ketamine but not fluoxetine. These data indicate modulation of dendritic spine density and metabotropic glutamatergic signaling in the prefrontal cortex after acute vortioxetine and ketamine treatment. This may play a role in the therapeutic effects of these compounds.

- P24.05 Noemie Regine ANTI-INFLAMMATORY THERAPY VIA CD163-MACROPHAGES IN THE 6-
Virginie Tentillier OHDA PARKINSON'S DISEASE MODEL

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Parkinson's disease (PD) is characterized by the progressive degeneration of dopaminergic neurons in the substantia nigra (SN) and the presence in

cells of aggregated alpha-synuclein (α -syn) in Lewy bodies. Among other factors, inflammation seems to play a role in PD neurodegeneration. We have data suggesting infiltration of peripheral immune cells, specifically CD163+ macrophages, into the area of neurodegeneration in the 6-hydroxydopamine (6-OHDA) PD model. We hypothesized that the migration of CD163+ macrophages into the brain-injured area in PD may influence local microglia.

By enhancing the M2 profile of peripheral macrophages, these could in turn release anti-inflammatory molecules into the neurodegenerative area modifying local microglia response and resulting in neuroprotection. In a 6-OHDA rat model of PD, designed liposomes targeted for the scavenger receptor CD163 were used to deliver dexamethasone (Dexa) into peripheral macrophages. The liposomes were injected intravenously (i.v.) for 3 weeks in a treatment approach, with in parallel 3 control groups. Our data show that liposomes Dexa loaded CD163+ macrophages were able to reach the brain. The treatment improved motor functions. This paralleled a partial rescue of dopaminergic neurons in the nigro-striatal system. Injection of free Dexa resulted in significant weight loss that was not observed in animals treated with Dexa-loaded liposomes. Our data support the modulation of inflammation by targeting macrophages as a putative novel therapy in PD and the use of CD163 targeting a valid and non-invasive approach to modulate neuroinflammation in neurodegenerative diseases.

P24.06 Arnela
Mehmedbasic

SORLA IN THE RETINA

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SorLA is a mosaic 250 kDa type I membrane protein belonging to the Vacuolar protein sorting 10 protein (Vps10p) receptor family, which also includes Sortilin and SorCS1-3. It is expressed abundantly in the brain, but also in other tissues such as spinal cord, liver, adrenal glands and testis. Its expression levels in the eye and the retina are yet unknown.

We have sorLA $-/-$ mice which are viable and do not exhibit any visible abnormalities. However, our unpublished data have shown that these mice have a significant decrease in the total cell number of the inner nuclear layer (INL) of the retina when compared to wild type mice, indicating that sorLA may play a role in development or degeneration of the retina.

In order to investigate the significance and function of sorLA in the retina and the phenotype of the retina in sorLA $-/-$ mice, we will investigate the temporal and spatial expression patterns of sorLA in the retina. Protein and mRNA isolations from murine retinas will be performed at different time points, and mRNA and protein levels will be assessed by qPCR and western blotting, respectively. The spatial expression of sorLA in the retina will be investigated by immunohistochemical analysis of the murine retina using antibodies against sorLA and retinal cell specific markers. Hopefully, in the future, we will be able to determine the function of sorLA in the retina and

the molecular mechanisms leading to the decreased cell number.

P24.07 Maryam Ardalan

STEREOLOGICAL STUDY OF NEURONAL AND SYNAPTIC PLASTICITY OF HIPPOCAMPUS

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Background and aim: Depressive disorders are common, serious and associated with enormous morbidity. In this study, design-unbiased stereological methods are used to test the "neuronal plasticity hypothesis" in rat brain hippocampus as one of the main underlying mechanisms for anti-depressive effects of the drug Ketamine. The "neuronal plasticity hypothesis" describes structural and functional plasticity and cellular resilience. This includes the promotion of dendritic growth, axonal sprouting, increased neurogenesis, synaptic remodeling, and new synaptic connections within specific brain regions.

Material and method: After ketamine injection and perfusion fixation of the rat brains, hippocampus is isolated, straightened out and embedded in 5% agar. The straightened hippocampus is sectioned perpendicular to its longest axis at 65- μ m thickness on a vibratome. Two sets of sections are chosen based on a systematic sampling principle and a section sampling fraction of 1/12. There are 8-9 sections in each of the two sets. For examining synaptogenesis in stratum radiatum of CA1 - subregion of hippocampus, the length of CA1 stratum pyramidale is measured along the CA2-subicular (CA2-SUB) axis at light microscopy and used as a 1D sampling guide. By use of the physical disector and electron microscopy, the numerical density of synapses is estimated. The optical fractionator is used to estimate the total number of neurons and glial cells in selected hippocampal subfields and microvessel length is evaluated with global spatial sampling. The volume of different subfields of hippocampus is estimated by point counting using the Cavalieri estimator at light microscopy.

P24.08 Ali H. Rafati

SPATIAL DISTRIBUTION OF NEURONS IN LAYER-III OF MEDIAL PREFRONTAL CORTEX OF FLINDERS RATS WITH MATERNAL SEPARATION

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Background: The Flinders Sensitive Line (FSL) rat is a genetic animal model of depression and maternal separation (MS) of rats is an example of early-life adversity. The rat prefrontal cortex is a brain region in which maturation

occurs mainly during postnatal period. It has been shown that neurons in different layers of cortex are developed and organized vertically, in columnar-like structures. Early life stress can change structure and function of interneurons in medial prefrontal cortex (mPFC) of rats; it is expected that the columnar distribution of neurons from layer-II/III in mPFC might be affected. To test this hypothesis, we aimed to find differential degree of columnarity in layer-III of mPFC from the Flinders rat (FSL/FRL) and its environmental interaction, superimposed stress of maternal separation.

Material and method: We used coronally-sliced thick plastic sections (Nissl-stained) to record the spatial coordinates of neurons contained in two systematically-chosen samples per hemisphere of brain from layer-III of mPFC (bregma: 1.2-3.7) in three groups; FSL-control, FSL-MS and FRL-control. Each sample is a well-defined 3-dimensional region (x, y, z: 450, 150, 140 μm) containing up to two thousands neurons. Data acquisition was performed on a stereological microscopy system equipped with the NewCast software (100x oil objective). The volume of mPFC and layer-III were obtained by the Cavalieri estimator. The degree of columnarity of spatial arrays of neurons perpendicular to the mPFC surface will be analyzed by statisticians at CSGB by applying a new mathematical tool; the Cylinder K-function, recently developed by statistical collaborators in CSGB.

P25.01 Anne Kristine Amstrup

TREATMENT OF OSTEOPENIA WITH MELATONIN: EFFECT ON BONE MINERAL DENSITY, MUSCLE STRENGTH AND QUALITY OF LIFE

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Background: Melatonin is known for its regulation of circadian rhythm. The production falls with age, which explains why elderly may have disturbed sleep patterns. In vitro and vivo studies suggests that melatonin also may protect against bone loss through increased osteoblast- and inhibited osteoclast activity. However, so far human studies have not been performed.

Design and patients: Double-blinded randomised controlled study. Eighty post-menopausal women (aged 55-75) with osteopenia are randomized to receive 1mg, 3mg or placebo (daily - at night time) for 12 months.

Methods and results: Effects of melatonin on BMD, bone- structure and mass will be assessed through DXA-scans, pQCT, and QCT. Quality of life, sleep, and activity level will be assessed though questionnaires. Calcium-homeostasis will be analyzed through blood and urines samples. As safety parameters, balance and muscle function will also be performed.

Conclusion: Expected improvements in BMD, quality of life and sleep.

P25.02 Nikolaj Rittig

METABOLIC CHANGES DURING ACUTE INFLAMMATION WITH AND WITHOUT AMINO ACID SUPPLEMENT

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Background: Acute inflammation affects our metabolism and causes a catabolic state with loss of muscle tissue. The loss of muscle tissue is associated with worse outcome and higher socioeconomic costs. The optimal nutritional supplement during inflammation is not known.

Aim: To investigate metabolic effects of an amino acid supplement during acute inflammation using the homogeneous "human endotoxin model".

Design: A randomised crossover trial with 3 separate days of investigation: 1. Placebo day, 2. Endotoxin (1 ng/kg LPS from E. Coli) and 3. Endotoxin (1 ng/kg LPS from E. Coli) and amino acid supplement.

Material and methods: Eight young, healthy and lean males randomly received all 3 interventions. During each intervention, metabolic parameters were measured in a basal state and during a hyperinsulinemic euglycemic clamp. Glucose, fat and protein metabolism were quantified by tracer method calculations on arterial and venous differences. Signalling pathways were investigated in muscle and fat biopsies. An Oxycon calorimeter was used to quantify energy expenditure and the respiratory exchange ratio.

Status and results: Twenty-two of 24 trials are completed. Endotoxin caused discomfort, chills and a mild headache. No severe side effects occurred. The average increase in heart rate was 7.1 (± 2.8) during intervention 1 compared with 35.8 (± 6.0) during 2 and 38.1 (± 7.4) during 3. The maximal mean temperature increase was 0.6°C (± 0.4) during day 1 compared with 2.7°C (± 0.8) during day 2 and 2.4°C (± 0.7) during day 3.

Conclusion: We conclude that the human endotoxin model caused clinical signs of inflammation and are now awaiting metabolic analysis.

P25.03 Joan Bach
Nielsen

ETIOLOGY, ASSESSMENT AND TREATMENT OF POST-GASTRIC BYPASS SEVERE HYPOGLYCAEMIA

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Background: Roux-en-Y gastric bypass (RYGB) causes sustained weight loss and improves glucose metabolism; despite these favourable effects, there has been mounting concerns about severe post-RYGB hypoglycemia.

Aim: We aimed to examine 1. if glucagon-like peptide-1 (GLP-1) or other hormones are involved in the pathogenesis and 2. if continuous glucose monitoring can be used to diagnose post-RYGB hypoglycemia. In addition, we intended to investigate the available nutritional and pharmacological treatment options for managing post-RYGB hypoglycemia.

Methods and materials: Four groups (12-14 subjects) will be examined in a case-control study; 1. RYGB and hypoglycemia according to Whipple's

triad, 2. RYGB without hypoglycemia and/or dumping, 3. Sleeve gastrectomy, 4. Non-operated controls. In each of the 4 groups, 3 tests will be performed; 1. Oral glucose-tolerance test; 2. Isoglycaemic intravenous glucose infusion; 3. Mixed meal test (MMT). The subjects with post-RYGB hypoglycemia will be examined in a case-crossover study. They will be evaluated during a MMT under three different circumstances; 1. Control; 2. Iv. GLP-1 rec. antagonist (Exendin 9-39); 3. Sc. Somatostatin analogue. Pre- and post-prandial hormone levels will be evaluated for five hours. Acetaminophen absorption test to evaluate the gastric emptying rate.

Results: Student's unpaired t-test and two-way repeated measurements ANOVA will be used to evaluate the results from the case-control study and case-crossover study, respectively.

Conclusion: Ex 9-39 will be used to evaluate the hypothesis that post-RYGB hypoglycaemia is mediated by increased GLP-1 actions. A somatostatin analogue will be used to test whether an inhibition of gastro-pancreatic hormones will change the glucose metabolism.

P25.04 Sofie Hertz Rønn INVESTIGATIONS OF THE EFFECT OF MK-7 ON BONE AND GLUCOSE METABOLISM AND ARTERIAL CALCIFICATION

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Background: Osteoporosis, diabetes, metabolic syndrome and cardiovascular disease are common diseases in the Western world. Several evidence-based treatments are available for the treatment of osteoporosis, but since the condition is common, prevention of osteoporosis is important.

Osteocalcin (OC) is the major noncollagenous protein produced by the osteoblast. The exact role of OC is not clear; it most likely functions as a regulator of bone mineral maturation. OC undergoes post-translational γ -carboxylation of three glutamate residues. Vitamin K is a co-factor in this process converting undercarboxylated osteocalcin (ucOC) to carboxylated osteocalcin (cOC).

Research hypotheses: Vitamin K2 (MK-7) reduces undercarboxylated osteocalcin in postmenopausal women and reduces bone turnover and increases bone mineral density; increases insulin sensitivity and decreases indices of arterial calcification.

Methods: The trial is a randomized double blinded controlled clinical trial. 150 postmenopausal women with osteopenia are randomized to MK-7 375 μ g per os per day or placebo for 12 months.

Bone turnover is assessed by biochemical markers, bone mineral density, assessed by DXA- and HRpQCT-scans, insulin sensitivity, assessed by HOMA test, and indices of arterial calcification, assessed by pulse wave velocity.

Perspective: The study will provide new knowledge about the possible effects of MK-7 on bone and glucose metabolism as well as on arterial

calcification. Positive effects of MK-7 on one or more of the investigated endpoints would provide significant impact on the possibilities for preventing osteoporosis, diabetes, metabolic syndrome and heart diseases at the population level.

P25.05 Mette Bohl
Larsen

WHEY, CASEIN, AND POST-PRANDIAL LIPAEMIA; A 12-WEEK, RANDOMIZED, PARALLEL-CONTROLLED, HUMAN INTERVENTION STUDY

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Background: Obesity is becoming a world-wide epidemic, and food quality is important in changing this development. Milk protein, particular whey, has shown beneficial effects on several metabolic features. However, long-term human intervention studies are lacking. Post-prandial lipaemia (PPL) is an independent risk factor for cardiovascular disease. We measured PPL as triglyceride and apolipoprotein B-48 (ApoB-48) (chylomicron) responses.

Hypothesis: Whey protein improves postprandial lipid metabolism in humans with abdominal obesity.

Methods: A 12-week, randomized, double-blinded, human intervention study was performed. The daily intake of milk protein (whey or casein) was 60 g and the milk fat (different fatty acid composition) was 63 g. In total, 63 subjects were randomized into one of four diets. A high fat meal was consumed and changes from intervention baseline in post-prandial triglyceride, ApoB-48, free fatty acids, insulin, and glucose were measured. Two-way ANOVA was used as statistical model.

Results: 51 subjects completed the study. Baseline characteristics did not differ significantly between groups. Mean change in post-prandial triglyceride from baseline did not change significantly between groups consuming whey or casein. However, mean incremental area under the curve for ApoB-48 decreased significantly to whey compared to casein (by 431 mg/L, $p=0.025$). We observed no significant change in post-prandial TG, free fatty acids, glucose, or insulin.

Conclusion: 12-week whey consumption resulted in a decreased post-prandial chylomicron response to the high fat meal, while no change in TG was detected. This indicates a beneficial effect on PPL of whey compared to casein.

P25.06 Anke Elisabeth
de Beijer

CLINICAL PATHWAY FOR DIAGNOSIS AND TREATMENT OF TRIGGER FINGER AND CARPAL TUNNEL SYNDROME IN PATIENTS AT HOLSTEBRO REGIONAL HOSPITAL

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This study compares one-stop day-care surgery versus day-care surgery

with preoperative outpatient clinic assessment, in terms of waiting times, patient-related outcomes and process outcomes of a clinical pathway for patients with trigger finger and carpal tunnel syndrome.

Methods: The clinical pathway was developed by a multidisciplinary team. Patients were asked to present in the day care surgery unit to be diagnosed and if indicated and accepted by the patient operated the same day. Changes from standard to enhanced care included e.g. diagnostics and, if accepted by the patient, operation on the same day instead of after two visits. All patients were operated in local anesthesia instead of regional intravenous block. Standardized diagnostics, communication to patients and between healthcare staff and standardized post operative protocol

Patients were primarily selected based on their referral letter. In both groups, we measured patient-related outcomes (DASH, EQ5D) before surgery and after three and six months. Furthermore, waiting time before surgery and resource consumptions were measured.

Results: Preliminary data from the first 100 patients: Average throughput time with new clinical pathway is 117 minutes as opposed to 189 minutes for the standard care. Two patients (2%) did not qualify for surgery. The new pathway allows an average of 11 patients per sitting to be operated instead of six in the usual care group.

Conclusions: The preliminary analysis shows a reduction in in-hospital waiting-times of 42% and almost a doubling of patients diagnosed/treated in one sitting. From 6 patients to 11 patients in a 7-hour work day.

P25.07 Andreas Buch MOLECULAR MECHANISMS OF EXERCISE-INDUCED AUTOPHAGY IN
 Møller HUMAN SKELETAL MUSCLE: EFFECT OF SUBSTRATE AVAILABILITY

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The mechanism by which autophagy is induced by exercise remains largely unknown. Studies conducted in cultured cells suggest an important role of ULK1 in autophagy. ULK1 is negatively regulated by mTORC1 by phosphorylation at Ser757, and positively regulated by AMPK by phosphorylation at Ser555. As exercise strongly activates AMPK, signaling through AMPK/ ULK1 represents a potential mechanism of exercise-induced autophagy.

The purpose of the present study is to examine potential mechanisms of exercise-induced autophagy in human skeletal muscle, and to examine the effect of substrate availability on activation of these mechanisms.

Eight healthy subjects were investigated twice in a crossover study. Subjects completed a one-hour cycling exercise at 50% VO₂-max either with continuous glucose infusion, or following a prior 36 hour fasting period. Skeletal muscle biopsies were sampled before, immediately after and 30 minutes after exercise. Blood samples were collected continuously

throughout the protocol.

Glucose infusion increased plasma glucose levels during exercise, while fasting increased plasma FFA levels. Exercise increased ULK1 phosphorylation at Ser555 independently of glucose and FFA levels, while no differences were observed at Ser757. Exercise increased AMPK Thr172 and ACC Ser79 phosphorylation in both conditions, while mTOR Ser2448 phosphorylation increased at the glucose infusion day only.

In conclusion, exercise induces ULK1 Ser555 phosphorylation in human skeletal muscle independently of glucose and FFA levels in a pattern that mirrors AMPK activation. These results suggest signaling through AMPK/ULK1 as a potential mechanism of exercise-induced autophagy.

P26.01 Krystian Figlewski

TRANSCRANIAL DIRECT CURRENT STIMULATION AIDED REHABILITATION OF GAIT IN SUBACUTE STROKE. PILOT STUDY

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Background: Stroke is a common cause of gait impairment, which inhibits independent life. Consequently, regaining a normal gait is a major target in stroke rehabilitation. To facilitate motor recovery after stroke, a variety of experimental rehabilitation approaches have been tested. Recent developments include non-invasive brain stimulation techniques such as transcranial Direct Current Stimulation (tDCS). In neurophysiologic studies, an imbalance of interhemispheric interactions has been demonstrated which is believed to interfere with the recovery process. This imbalance can be ameliorated by upregulation of the excitability in the lesioned hemisphere with anodal tDCS.

Aim: (1) To evaluate the effect of a single session of anodal tDCS on corticomotor excitability and muscle force of knee extensors and (2) to assess whether these changes are correlated with change in gait speed following 4 weeks of gait training.

Study design and methods: Exploratory case study including 20 subjects with subacute stroke and gait impairment admitted to Hammel Neurocenter within 14 days from stroke onset. At baseline, corticomotor excitability is assessed by measuring motor evoked potentials (MEPs) evoked by transcranial magnetic stimulation (TMS) before and immediately after a single session of anodal tDCS. Afterwards, subjects receive 4 weeks of daily gait training combined with anodal tDCS. Effects of training are monitored by a 10-meter walking test and isokinetic strength performance of knee extensors. Also, data from MRI of the brain are obtained and related to the other findings (location of lesions, integrity of fiber connections).

P26.02 Henrique Fernandes

SIGNIFICANT CHANGES IN LOCAL CONNECTIVITY IN EARLY-ONSET BIPOLAR DISORDER WITH PSYCHOSIS

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Pediatric bipolar disorder (PBD) with psychosis (delusions and/or hallucinations) is currently not well understood in terms of its underlying neurobiology. The diagnosis of PBD is based primarily on taking clinical history, which is considerably more difficult to obtain from children and adolescents than from adults. The clinical diagnosis could potentially benefit from a better understanding of the underlying neurobiology of PBD, and in particular of the early structural changes in connectivity.

In the current study, we examined the changes in cognitive and structural connectivity in a group of 15 adolescents with PBD and psychosis compared to a 25 euthymic matched healthy controls, having constructed the connectomes using probabilistic tractography and diffusion tensor imaging.

We found significant differences in the structural connectivity of anterior regions within the so-called 'default mode' network including regions of the medial orbitofrontal cortices and precuneus. These results show that PBD is associated with changes in structural connectivity in regions involved in brain networks associated with emotional processing and regulation.

P26.03 Lene Duez

DETECTION OF INTERICTAL EPILEPTIC DISCHARGES BY MAGNETO-ENCEPHALOGRAPHY IN THE DANISH PRESURGICAL EPILEPSY EVALUATION

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Background: Magnetoencephalography (MEG) is increasingly used in the non-invasive evaluation of patients with refractory focal epilepsy. MEG records the changes in magnetic fields generated by the activity of the neural networks in the brain¹. EEG and MEG supplement each other in localizing the epileptic focus because MEG detects epileptic sources tangential to the skull and EEG detects both tangential and radial sources. The magnetic field recorded by MEG is not distorted by the brain, tissue, skull or scalp².

Method: MEG (Elekta Neuromag® TRIUX™) 306 channels and simultaneous EEG (60-70 channels) were recorded in 26 consecutive patients with focal epilepsy, referred for epilepsy surgery. Recording duration was one hour in resting conditions, with closed eyes. MEG and simultaneous EEG were manually viewed by skilled personal using CURRY Scan 7 Neuroimaging

Suite.

Results: MEG has revealed epileptiform discharges in 57% of the patients. 15 % had focal discharges seen only in MEG. In 75% of these patients, earlier conventional EEG had not been able to localize a focus. Focal discharges were seen in both MEG and in the simultaneous EEG in 42%.

Conclusion: MEG detects interictal focal epileptic discharges not captured by conventional EEG. This can lead to a better hypothesis on where to operate. Although the number of patients is low, since this is an ongoing project, we argue that MEG should be considered for epilepsy surgery candidates.

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P26.04 Lars Høj
Markvardsen

LONG-TERM TREATMENT WITH SUBCUTANEOUS IMMUNOGLOBULIN IN HIGH DOSES IS EFFECTIVE IN PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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Background: Subcutaneous immunoglobulin (SCIG) is superior to placebo treatment when administered for a 12-week period to maintain muscle strength in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). The present study evaluated whether SCIG is able to maintain muscle strength for one year in an open-label follow-up study.

Methods: Seventeen responders to intravenous immunoglobulin (IVIG) who had participated in a previous study of SCIG versus placebo in CIDP were included. After one IVIG infusion at baseline, all continued on SCIG treatment and were evaluated after 3, 6 and 12 months of SCIG therapy. The primary endpoint was changes in muscle strength evaluated by isokinetic dynamometry (IKS) in four affected muscle groups. The secondary endpoint was a composite score of muscle performance and function tests, including MRC-score, grip strength, 40-meter-walking test (40-MWT) and 9-hole-peg test (9-HPT).

Results: In three patients, the dose was increased due to clinical deterioration. The IKS value increased overall by 7.3% (P=0.03) and by 5.7%, 8.2%, and 6.8% after 3, 6, and 12 months; only the value after 6 months being significant (P=0.04). The overall composite score remained significantly unchanged after 3, 6, and 12 months. The MRC score increased significantly by 2.1% and 2.8% after 6 and 12 months. Grip strength 40-MWT and 9-HPT remained unchanged. No side effects were reported.

Conclusion: SCIG maintains muscle strength in patients with CIDP who respond to IVIG. SCIG is an alternative to IVIG in long-term treatment of

CIDP patients with complications to IVIG or in those who need a more flexible administration schedule.

P26.05 Kristian
Lundsgaard
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CITALOPRAM IN ACUTE STROKE

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Clinical background: Stroke is a widespread disease with approx. 12,000 new cases annually in Denmark. In total, 40-50,000 people currently live with the effects of the disease in Denmark.

Theoretical background: The cerebral serotonergic neurotransmission is widespread and may affect the cerebral regeneration after stroke. Neurons and platelets re-uptake serotonin via the serotonin transporter (SERT). SSRIs inhibit the SERT, hereby increasing the concentration of serotonin in the neuronal synapse and decreasing the concentration in the thrombocyte.

Hypothesis: SSRI treatment initiated during the acute phase after stroke prevents new ischemic events and facilitates rehabilitation.

Trial design: A randomized, double-blinded, placebo-controlled multicenter trial.

Inclusion criteria: Patients over 18 years admitted with clinically verified first-time ischemic stroke.

Study participants: Patients admitted with first-time ischemic stroke in the inclusion period 01.08.13 - 31.07.15 in the Departments of Neurology at Aarhus University Hospital, Aalborg University Hospital and Glostrup Hospital. A total of 600 patients will be included.

Intervention and randomization: Citalopram starting dose will be 10-20 mg per day. Maximal dosage is 20 to 40 mg. Treatment is discontinued after 6 months at the last clinical evaluation.

Primary outcome: Combined vascular death, myocardial infarction and re-stroke.

Secondary outcome: Death from any cause, vascular death, acute myocardial infarction, re-stroke, physical and intellectual disabilities, depression/tearfulness and fatigue.

P26.06 Gro Helen Dale

CAN EARLY TREATMENT WITH SOLU-MEDROL PREVENT VISUAL LOSS AFTER OPTIC NEURITIS?

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Background: Optic neuritis (ON) is an inflammatory disease that results in acute visual loss. ON may occur as an isolated episode, but is also known to

be associated with multiple sclerosis (MS) and neuromyelitis optica (NMO). The prognosis of ON is generally good, but significant visual impairment remains in 10% of the patients, and is typically more severe in patients with NMO than in patients with MS. Treatment with intravenous (iv) Solu-medrol speeds up recovery, but does not seem to affect the prognosis. However, there is a lack of studies investigating the effect of initiating treatment early in the acute phase.

Aim: The aim of this study is to investigate if early Solu-medrol treatment can prevent permanent visual loss, and whether this treatment is more efficient in patients with NMO than in patients with MS.

Material and methods: In this open, non-randomized follow-up study, we plan to include 100 patients with acute ON. The patients are evaluated with several tests, including visual acuity, optical coherence tomography, neurological examination and magnetic resonance imaging of the brain and spinal cord. In addition, bloodsamples are analyzed for important parameters such as NMO-Immunoglobulin G. Depending on the patients' visual acuity and co-morbidities, they are offered treatment with iv Solu-medrol for 3-5 days. Follow-ups are performed after 6 and 12 months.

Results: Preliminary results are expected in 2014.

Perspectives: Prevention of permanent visual impairment is of great importance to both the individual and society. If early treatment with Solu-medrol proves effective, this may result in a revised guideline for evaluation and treatment of ON.

P26.07 Erhard Næss-Schmidt

PATHOLOGY IN THE BRAIN AFTER MTBI? A MULTIMODAL MAGNETIC RESONANCE IMAGING STUDY

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Each year, more than 25,000 people in Denmark get the diagnosis of concussion or mild traumatic brain injury (mTBI) as a result of head trauma. Previous studies report 5 to 15% of a population with mTBI having persisting symptoms beyond 3 months.

Pathological findings after severe trauma can be detected by conventional clinical scan methods such as Computer Tomography (CT) and Magnetic Resonance Imaging (MRI), but it is often difficult to detect tissue pathology after mTBI with conventional MRI methods. Especially beyond the acute period, conventional scan methods lack the ability to detect pathology, although patients continue having physical, cognitive and emotional symptoms.

Several MRI techniques, which are not routinely used in the clinic, have suggested pathological changes in grey matter (GM), white matter (WM) and cortical connectivity after mTBI. Two of such methods are Diffusional Kurtosis Imaging and Diffusional Tensor Imaging which have shown a significant difference in MR-markers between individuals with mTBI and healthy controls in GM and several WM areas. In addition, more studies

have shown a correlation between DKI and DTI markers with post concussion symptoms (PCS) in multiple domains.

In the clinic, it is crucial to have imaging techniques that are not time-consuming, but sensitive enough to detect micro structural changes that can serve as biomarkers. Using a new optimized and short scan sequence with DKI and DTI, it is the purpose of this study to detect structural changes in the brains of people who have had a concussion, both acute and 3 months after the accident. Moreover, it is the purpose to compare the results of the MR-scans with the reported PCS.

P26.08 Johanne Liv
 Agger

PHARMACOLOGICAL TREATMENT OF MULTI-ORGAN BODILY DISTRESS SYNDROME. A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF THE EFFECTS OF IMIPRAMINE (STRESS-3) CLINICALTRIALS.GOV, NCT01518634

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Background: Bodily Distress Syndrome (BDS) is characterized by multiple persistent bodily symptoms not attributable to well-defined disease. BDS is related to centrally mediated pain conditions and has been shown to encompass functional somatic syndromes such as fibromyalgia, irritable bowel syndrome and chronic fatigue syndrome. The most severe form of BDS, multi-organ BDS, is characterized by symptoms from several organ systems.

While psychological interventions are effective in the management of multi-organ BDS, pharmacological treatment is sparsely investigated, with most trials focusing on single functional somatic syndromes. TCA treatment represents an easily available and affordable treatment option for patients with multiple somatic symptoms. It may have the potential of reducing both pain and other symptoms of bodily distress.

Objective: To examine the effects and safety of the TCA imipramine in patients with multi-organ BDS in a double-blind, placebo-controlled trial.

Methods: 140 consecutively referred patients with multi-organ BDS are randomized to either low-dosage imipramine or pill placebo. Primary outcome is patient-rated improvement measured by Clinical Global Improvement Scale after 12 weeks of treatment. Secondary outcomes are symptom level measured by Visual Analogue Scale and Symptom Checklist, and functional level (physical, mental and social) measured by the SF-36.

Results: Recruitment started early 2012. Flow chart will be presented.

Perspective: This study will evaluate the effects and safety of imipramine in patients with multi-organ BDS and elicit whether low dose TCA may play a role in the routine management of these severely affected patients.

P27.01 Chris Amdisen COMPARISON OF AN IMPLANTABLE ULTRASOUND PROBE AND MICRODIALYSIS FOR DETECTION OF GRADUAL RENAL VEIN OCCLUSION

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Introduction: One of the most feared complications to kidney transplantation is vascular occlusion, which often results in graft loss. We developed a model for stepwise reduction of renal venous blood flow. An implantable ultrasound probe and microdialysis were evaluated for detection of vascular occlusion.

Methods: In 20 pigs, implantable ultrasound probes were placed on the renal artery and vein. A microdialysis catheter was placed in the renal cortex. As gold standard a flowprobe was also placed on the renal artery. Following, two-hour baseline measurements, the pigs were randomised to gradual venous occlusion, complete venous occlusion, complete arterial occlusion or control.

Results: All parameters were stable through baseline. Glutamate and lactate increased significantly 45 minutes after a reduction of 2/3 in renal blood flow. The implantable ultrasound probe was not able to detect flow changes until renal blood flow had stopped. Microdialysis detected both arterial and venous occlusion, whereas the implantable ultrasound probe, could only detect vascular occlusions, on the side it were placed.

Conclusions: A new model for stepwise reduction of venous renal bloodflow was developed. Furthermore, the first comparison of the implantable ultrasound probe and microdialysis for detection of renal vascular occlusions, were made.

The implantable ultrasound probe, could only detect flow changes after a complete occlusion, whereas microdialysis was able to detect flow changes earlier, and changes after both arterial and venous occlusion. This study shows, that microdialysis is a better tool for detection of gradual vascular occlusions than the implantable ultrasound probe.

P27.02 Mette Tiedemann Skipper OPTIMIZING WHOLE BLOOD IMPEDANCE AGGREGOMETRY IN SEVERE THROMBOCYTOPENIA

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Evaluation of platelet function by impedance aggregometry is currently not possible in patients with thrombocytopenia.

This study aimed to investigate platelet aggregation (PA) in severe thrombocytopenia, using whole blood impedance aggregometry adjusted for

the platelet count (PC).

Citrated whole blood was obtained from 12 healthy volunteers, 7 cancer patient and 12 patients with primary immune thrombocytopenia (ITP). Thrombocytopenia was induced in the healthy whole blood. PA was evaluated by whole blood impedance aggregometry (Multiplate®) and expressed as area under the curve (AUC).

PC in the range of 10 to $39 \times 10^9/L$ was obtained in whole blood from healthy volunteers. In this group, linear regression analysis displayed a strong positive correlation between PC and PA (R-squared=0.84). The prediction equation of normal PA in thrombocytopenia was: $y = 19.9x - 145$ ($y = PA$, $x = \text{platelet count}$). The PA response was then indexed relatively to the prediction estimate of normal PA. The obtained PA index was 106% (64-130) [median (interquartile range)] in thrombocytopenia modelled from healthy whole blood, 10% (7-13) in cancer patients and 109% (65-147) in ITP patients. The difference in aggregation index observed between ITP and cancer patients was highly significant ($p=0.002$; Mann-Whitney U test). Aggregation in ITP patients was not significantly different ($p=0.73$) whereas aggregation in cancer patients was significantly reduced ($p<0.001$) when compared to the platelets from healthy volunteers.

The findings suggest that whole blood impedance aggregometry can be optimized to detect differences in platelet function even at very low platelet counts.

P27.03 Rikke
Hjortebjerg

METABOLIC FUNCTIONS OF THE IGF SYSTEM IN HUMAN ADIPOSE TISSUE

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Insulin-like growth factor I (IGF-I) and IGF-II mimic the metabolic effects of insulin and are considered to increase whole body insulin sensitivity. However, experimental studies indicate that in adipose tissue, IGF counteracts the effects of insulin and induces insulin resistance.

Metabolically unfavorable obesity associates with an excess accumulation of visceral adipose tissue (VAT) which is less insulin sensitive than subcutaneous adipose tissue (SAT). We recently demonstrated that cultures of VAT from obese subjects produced more IGF-I and -II than SAT. VAT also produced more IGFBP-4 and PAPP-A, two important regulators of IGF-action.

On this basis, it is hypothesized that locally produced IGF reduces the insulin sensitivity in VAT and in this way partake in the development of type 2 diabetes. To test the hypothesis and its clinical implications, this study aims to clarify the impact of IGFs and their regulatory proteins on glucose uptake in cultures of human VAT and SAT. Furthermore, the study aims to identify the factors and specific cell types that are responsible for the increased IGF-secretion, and investigate whether the large secretion of IGF-I, -II, IGFBP-4 and PAPP-A by VAT translate into circulating levels.

Finally, a potential effect of gastric inhibitory polypeptide (GIP), glucagon-like peptide 1 (GLP-1) and the GLP-1 analogue Victoza® on the IGF-system in adipose tissue will be examined. If we can substantiate that the IGF-system is involved in processes that lead to insulin resistance in adipose tissue, it may contribute to the development of potential new treatment strategies.

- P27.04 Julie Brogaard Larsen COULD VON WILLEBRAND'S DISEASE BE OVERLOOKED IN WOMEN USING COMBINED ORAL CONTRACEPTIVES?

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Introduction: Women of fertile age referred for diagnosis of von Willebrand's disease (vWD) are often treated with combined oral contraceptives (COCs) because of menorrhagia. Only a few previous studies have investigated the effect of COCs on von Willebrand factor (vWF), and the results of these are conflicting, but COCs could possibly cause an increase in vWF levels and thereby mask the disease in women taking COCs.

Aim: To investigate the influence of COCs on vWF in healthy women.

Methods and materials: We included two groups of healthy participants; 1) a group of women starting COC treatment and 2) a control group who did not receive COC treatment during the study. Blood samples were obtained at the time of inclusion (baseline) and after 3 months in both groups. The COC group began treatment after the baseline sampling. Analysis of vWF antigen (vWF:Ag), ristocetin cofactor (vWF:RCo) and collagen binding (vWF:CB), factor VIII clot (FVIII:C) and C-reactive protein (CRP) were performed in both groups, and ABO blood group was determined.

Results: We observed significant increases in median levels of vWF:RCo, vWF:CB, FVIII:C and CRP in the COC group. The increase was also significantly higher than the increase found in the control, except for vWF:CB. Median vWF:Ag levels did not change from baseline to 3 months in either group.

Conclusion: The present study indicates that COCs do have an influence on vWF in healthy women, possibly through an acute phase response. This may impair the diagnosis of vWD in women taking COCs.

- P27.05 Andreas Engel Krag ISCHEMIA-REPERFUSION INJURY IN EXPERIMENTAL MUSCLE FLAPS FOLLOWING HYPOTHERMIC OR NORMOTHERMIC ISCHEMIA

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Background: Reconstructive microsurgery involves a block of tissue to be replanted if amputated, or transferred as a free flap in order to reconstruct defects from e.g. tumor ablation or trauma. Free tissue transfer always

involves flap ischemia until blood supply is restored by microvascular anastomosis at the recipient site. The normal range of ischemia is 30-90 minutes for free flap revascularization. The tolerated time of ischemia varies according to the composition of the tissue to be transferred. Prolonged ischemia for various reasons causes aggravated ischemia-reperfusion injury resulting in flap tissue inflammation and microcirculatory thromboses. If severe, this leads to the no-reflow phenomenon and flap failure potentially catastrophic for the patient.

Aim: The aim of the study is to outline the cytokine and coagulation profile in experimental muscle flaps undergoing normothermic or hypothermic ischemia prior to reperfusion. We want to investigate the potential protecting effects of hypothermic ischemia against ischemia-reperfusion injury.

Methods and materials: The design is an experimental study in a porcine model. In each animal, a latissimus dorsi flap will be elevated and subject to four hours of ischemia by clamping of the vascular pedicle. In the experimental group, the flaps will be cooled to four degrees during ischemia (n = 8). In the control group, the flaps will be ischemic at body temperature (n = 8). Samples of flap venous blood and systemic venous blood will be collected during reperfusion. The concentration of pro-inflammatory cytokines and coagulation factors will be analyzed, and tissue samples will be harvested for immunohistochemistry.

P27.06

Abstract moved to session poster session 3

P27.07

Heidi Kristine Støve Nielsen

EXTRAMEDULLARY LEUKAEMIA IN CHILDREN WITH ACUTE MYELOID LEUKAEMIA

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Background: Extramedullary leukaemia (EML) is a relatively common finding in paediatric acute myeloid leukaemia (AML) and can present as leukaemic blast cells in the cerebrospinal fluid (CSF) (CNS disease) or as a solid tumour (myeloid sarcoma, MS). The prognostic significance of EML is

not clarified, and, consequently, the optimal treatment of the children presenting with EML at diagnosis of AML is unknown.

Hypothesis and aim: We hypothesized that the presence of EML has a significant impact on the prognosis in children diagnosed with AML. The aim of this study was to characterize the clinical and prognostic aspects of EML in children with AML.

Methods: Children diagnosed with AML and treated according to the NOPHO-AML 2004 protocol in the period of January 2004 to January 2013 in the Nordic countries and Hong Kong were eligible for inclusion in this study. The patients were classified by means of the presence of EML (CNS disease, MS or non-EML). CNS disease was defined as ≥ 5 leukocytes per μL of CSF and the presence of leukaemic blast cells on CSF cytopsin, and MS was defined as a tumour mass of myeloblasts or immature myeloid cells occurring in an extramedullary site. Data on characteristics, treatment and outcomes of the children will be collected from the NOPHO-AML database and compared. The Kaplan-Meier method will be used to calculate estimates of survival, and the prognostic factors will be examined in a multivariate analysis with the Cox proportional hazards regression model.

Results: From January 2004 to January 2013, 315 children were registered in the NOPHO-AML database. 33 (10%) of these children had CNS disease at diagnosis of AML and 49 (16%) children had MS.

P27.08 Anders
Gyldenkerne

GENERATION OF A MODEL DESCRIBING THE OPTICAL PROPERTIES OF THE CORNEA

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Background: The optical properties of the cornea after a surgical procedure are not yet fully understood. Corneal surgery treating nearsightedness or astigmatism has become very popular in recent years and many of the patients who have had these treatments are expected to be operated for cataract in the near future. In order for cataract surgery to yield the best optical result, it is crucial to know the effective refractive power of the cornea. Corneal refractive power cannot be directly measured by standard methods following corneal refractive surgery. However, a device from Oculus, the Pentacam HR, uses an advanced Scheimpflug camera for measuring numerous parameters concerning the cornea and provides highly detailed images. Recent studies suggest this device could be used for assessing refractive power following corneal refractive surgery.

Aim: To examine the effective optical properties of the normal and laser treated cornea using the Pentacam HR.

Methods: The optical properties will be examined by comparing changes in the front and back refractive curvatures of the cornea with changes in subjective refraction among patients who have undergone corneal surgery. The Pentacam measurements and clinical measurements of manifest refraction are readily available for more than 1000 eyes. The statistical analysis is expected to be carried out in a multivariate manner.

Perspectives: An effective model describing the corneal refractive powers would be of great benefit to the many patients who have undergone corneal refractive surgery, many of whom are expected to be operated for cataract in the near future.

P28.01 Signe Væth

DIAGNOSTIC TIME TREND AND AGE AND SEX DISTRIBUTION OF CHARCOT-MARIE-TOOTH DISEASE

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Background: Charcot-Marie-Tooth Disease (CMT) is the most common inherited neurological disease. More than 70 genes can cause CMT, today only 4 are analyzed. This diagnostic strategy is based on mutation prevalence outside Denmark. Little is known about the epidemiology of the disease in Denmark. The present investigation is part of a larger genetic study to establish a diagnostic platform for CMT.

Aim: A classification of Danish patients diagnosed with CMT in the period 1977- 2012, according to sex, age and date at diagnosis, and reliability of the diagnosis based on genetic analysis.

Material and methods: Records with diagnostic codes ICD8 33009 (atrophia mm. neuropathica, Charcot-Marie-Tooth) and ICD10 G60.0 (hereditary motor sensory neuropathy) from the period 1977- 2012 were retrieved from The Danish National Patient Register (DNPR). These data were linked with data on CMT patients who had a genetic analysis for CMT between 1990 and 2012 at the Department of Clinical Genetics in Aarhus or at Rigshospitalet.

Results: A total of 2002 patients (809 women) with CMT diagnosis were identified in DNPR. The number of new CMT diagnoses per year was fairly constant from 1977 to 1990, but increased by almost a factor 4 from 1990 to 2012. The increase was largest in the 0-9 year age group. The proportion of women was 40%, and the average age at first diagnosis was 45 years; both were fairly constant. A total of 684 patients (34%) have had a genetic analysis for CMT. Of the 1586 patients who were diagnosed after 1990, 631 patients (40%) have had a genetic analysis.

Conclusion: The frequency of CMT diagnosis has increased since 1990, where genetic testing was introduced.

P28.02 Luise Borch

THE EFFECT OF COMBINING TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) AND ANTICHOLINERGICS WHEN TREATING CHILDREN SUFFERING FROM URINARY INCONTINENCE AND AN OVERACTIVE BLADDER (OAB).

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Aim: To investigate a possible synergistic effect of combining sacral transcutaneous electrical nerve stimulation (TENS) and anticholinergics when treating children suffering from urinary incontinence and an overactive bladder (OAB).

Background: Daytime urinary incontinence in children is pathological from the child is 5 years old. It is a common disorder with a prevalence of 2-9% for 6-year-old children. Besides the physical consequences, the disorder is also psychologically malignant, and causes a low self-esteem. The disorder is heterogeneous and the symptoms are caused by different mechanisms, which are far from completely understood. The treatment of these children is far from effective in all cases. The primary treatment is urotherapy (bladder training) followed by anticholinergics (relaxes the bladder muscle). In recent years, studies have also shown an effect of TENS when used as mono therapy. Therefore in children where urotherapy has had no effect, it seems reasonable to combine treatment with anticholinergics and TENS, so that the treatment is aimed both at the detrusor muscle and the central nervous system at the same time.

Method: The study is double blinded, placebo controlled, prospective, and randomized. The study population includes 90 children from 5-14 years diagnosed with daytime urinary incontinence and OAB. The children are randomized into 3 groups of 30 children. Each group will receive 10 weeks of treatment with one of the following: 1) Active TENS + placebo Ditropan 2) Active TENS + active Ditropan 3) placebo TENS + active Ditropan.

Expected results: In the future, this study will result in a more effective treatment of this group of patients.

P28.03 Steven Brantlov BIOIMPEDANCE SPECTROSCOPY (BIS) PARAMETERS IN HEALTHY CHILDREN: RELATION TO AGE, WEIGHT, LENGTH AND BODY MASS INDEX (BMI)

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Background: There is a need for a quick and reliable method to determine fluid status in critically ill children. Current reference methods make use of dilution techniques. However, these are invasive, expensive, and require highly trained personnel. Bioimpedance spectroscopy (BIS) is non-invasive, quick, and inexpensive, and is therefore a viable alternative to such techniques. One BIS approach is to use total body fluid (TBF), and extra- and intracellular fluid (ECF, ICF), which are based on predictive equations and only proven in adults. Another approach is to use raw data values of the extracellular resistance (R_E) and intracellular resistance (R_I). These values are advantageous, since predictive equations are not required. The aim was to answer the following questions: is BIS a reliable method to determine fluid status? Does a relation exist between R_E and R_I and age, weight, length or body mass index (BMI)?

Methods: BIS measurements (whole body) were performed on 119 healthy children (M=69, F=50, ages=2-14 yr). The statistical analysis was based on evaluation of correlation coefficients (r).

Results: Data for boys and girls (combined) showed significant negative correlations between R_E and R_I and the following variables: age, weight, length and BMI (see Table).

Conclusions: A moderate to strong correlation does exist between the impedance values and BMI, and BIS appears to be a reliable method to determine fluid status in children.

Table:

R_E vs Age: $r=-.4$ $p=.0001$	R_I vs Age: $r=-.5$ $p<.0001$
R_E vs Weight: $r=-.5$ $p<.0001$	R_I vs Weight: $r=-.5$ $p<.0001$
R_E vs Length: $r=-.4$ $p<.0001$	R_I vs Length: $r=-.4$ $p<.0001$
R_E vs BMI: $r=-.6$ $P<.0001$	R_I vs BMI: $r=-.6$ $p<.0001$.

P28.04 Navid Sahebekhtiari

MITOCHONDRIAL PROTEOME CHANGES IN ETHE1- DEFICIENT MICE: INDICATION OF METABOLIC IMBALANCE

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Ethylmalonic encephalopathy (EE) is an autosomal recessive fatal disorder caused by homozygous gene variation in the ethylmalonic encephalopathy gene (ETHE1) which is characterized by early-onset of encephalopathy, microangiopathy, chronic diarrhea, and defective cytochrome C oxidase (COX) in muscle and brain. Biochemical hallmarks are high concentrations of C4 acylcarnithine in blood which also is characteristic of the fatty acid beta-oxidation defect short chain acyl CoA dehydrogenase deficiency (SCADD). Furthermore, ETHE1 is a mitochondrial sulfur dioxygenase involved in sulfide detoxification. Although the severe systemic consequences of dysfunction in sulfide detoxification become clear, further elucidation of molecular etiology of EE is essential both for treatment and also understanding other aspects of disease. Blocking in sulfide oxidation at the level of sulfur dioxygenase leads to severe dysfunctions in multiple pathways including cellular energy metabolism. This calls for large scale techniques to grasp the multiple pathways affected. The present studies apply large scale proteomics to get insight into the molecular effects behind this rare neurometabolic disorder. ETHE1-deficient and wild type mice are studied and preliminary results yielded more than thousand identified and quantified proteins. Furthermore, using DSP cross-linker, protein network of ETHE1 can be investigated. By using mass spectrometry based proteomics, we will map mitochondrial proteins and in addition probe for acetylation sites as an important regulatory post translational modification.

P28.05 Lilja Kristin

CHRONIC OROFACIAL PAIN PATIENTS EXPERIENCE PERCEPTUAL

Dagsdóttir

DISTORTIONS OF THE FACE

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Orofacial pain patients sometimes report that the painful area feels "swollen" or "differently", although there are no clinical signs of swelling i.e. perceptual distortion (PD).

The aim of the study was to determine the prevalence and magnitude of PD in chronic orofacial pain (OFP) patients.

Sixty OFP patients (mean age 50) were recruited and divided into 1) Traumatic Trigeminal Neuropathic Pain (TTNP), 2) Painful Temporomandibular Disorders (TMD) and 3) Atypical Facial Pain (AFP). Questionnaires for experience of PD, location and grading of the magnitude were developed and used in addition to sets of questionnaires to measure the contribution of psychological factors.

Mean pain intensity on a 0-10 Visual Analogue Scale was 5.5 ± 1.8 . A total of 73.3% of OFP patients reported PD. The highest prevalence was encountered for TTNP (90.5%). When asked about PD as perceived changes in size, 33 of the 44 patients (75%) expressed the PD as enlargements. Mean changes in perceived size was highest for TTNP patients ($52.9 \pm 6.4\%$), and somewhat lower for TMD ($27.9 \pm 5.7\%$) and AFP ($26.7 \pm 12.0\%$). 36 out of 44 (80.8%) linked the experience of PD directly to their pain.

Present pain intensity significantly predicted the degree of PD in TTNP patients ($R^2=0.35$, $p<0.05$). Correlation analysis revealed that PD ($n=60$) was positively correlated with dissociation scores ($R^2=0.25$, $p<0.05$).

This study has identified prevalence of PD in chronic OFP patients. PD appears to be highest in TTNP, perhaps because of the direct involvement of the somatosensory system. Further studies are needed in order to understand the underlying neurobiological mechanisms.

P28.06 Tanni Kjær
Borgbo

GENETIC VARIATIONS OF THE FOLLICLE STIMULATING HORMONE RECEPTOR AND THEIR IMPACTS ON FEMALE FERTILITY

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Background: The gonadotrophic hormone "Follicle stimulating hormone"

(FSH) are one of the main regulators of ovarian activity, with a massive impact on female fertility. An intricate interplay between the gonadotropins regulates the ovarian steroidogenesis, as well as follicle growth and oocyte development. Recently, a number of studies have shown that genetic variations of the gonadotropins and their receptors may affect the outcome of controlled ovarian stimulation (COS) during in vitro fertilization. However, it is still unknown how the genetic variations affect the downstream signaling pathways. To elucidate how polymorphisms of the gonadotropins and their receptors affect ovarian function, this study correlate the common genetic variations of the FSH receptor (FSHR) to ovarian gene-expression and steroid production in small human antral follicles.

Methods: Hormone levels of 252 small antral follicles from 82 women were analyzed by ELISA and correlated to the FSHR genotypes. Gene-expression analysis was performed by reverse transcriptase qPCR on RNA isolated from granulosa cells, and genotyping of the FSHR polymorphisms Ala307-Thr and Asn680Ser was performed by High Resolution Melt analysis.

Results: Significant differences in follicular hormone levels were observed between the FSHR receptor haplotypes in the small antral follicles. The haplotype AG³⁰⁷/AG⁶⁸⁰ had a significantly higher steroid production (estradiol levels, P = 0.03) compared to homozygote haplotypes.

Conclusion: The genetic composition of the FSH receptor affects the downstream signaling of FSH in small human antral follicles, reflected in genotype specific differences in ovarian steroid production.

P28.07 Zahra Nochi

APPROACHES TO DECIPHERING THE BALANCE BETWEEN SURVIVAL AND DEATH MECHANISMS IN CELLS WITH MITOCHONDRIAL DYSFUNCTION

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Short-chain acyl-CoA dehydrogenase deficiency (SCADD) is an autosomal recessive fatty acid oxidation disorder which affects enzymes required to break down a certain group of fats called short chain fatty acids.

Indeed, SCAD deficiency in children with mitochondria dysfunction is indicated by elevated ethylmalonic acid in urine and/or butyrylcarnitine in blood. However, since these clinical symptoms are very unspecific and because many individuals with SCAD gene variations do not show significant clinical symptoms, as indicated from neonatal screening programs, it is discussed internationally whether SCAD gene variations are disease associated at all. Many biochemical geneticists consider this to be a biochemical phenotype with a very mild or no clinical phenotype. Therefore, many patients with SCAD gene variations do not get a diagnosis and proper treatment, and it is important to delineate whether children with such variations are at risk of developing disease during acute stress, such as fever and starvation.

The aim of the study is to explore whether acute stress exerted by glucose starvation and temperature elevation in chronic stressed cell shift the

balance to a more rapid death, and the treatment of the cells by agents, such as N-acetyl-L-cystein (NAC) and Resveratrol, which induce the survival mechanisms, can prevent cells death.

SCADD and control fibroblasts will be cultured in low and high glucose medium at 37C and 40C. After treatment the cells with NAC and Resveratrol at optimum time, cells will be harvested. Selected markers for oxidative stress, autophagy, and apoptosis will be determined by western blotting, or mass spectrometric techniques.

P28.08 Lu Xing

RENAL AQP1-3 EXPRESSION PATTERNS IN RESPONSE TO 1 WEEK CONGENITAL PARTIAL UNILATERAL URETERAL OBSTRUCTION IN RATS

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Background: Congenital hydronephrosis owing to partial unilateral ureteral obstruction (PUUO) is one of the most common urinary abnormalities in infancy and childhood. Renal aquaporins (AQP1-3) may be involved in the pathophysiologic changes in the obstructed kidney. This study investigated the renal expression of AQP1-3 in newborn rats with PUUO for 1 week.

Methods: Forty-nine newborn rats were allocated into 2 groups randomly: PUUO (n = 26) and SHAM (n = 23). The left PUUO was induced within 2 days of birth, and the kidney was harvested 1 week after surgery.

Results: Obvious renal pelvis dilatation was observed in all PUUO kidneys by HE staining. AQP1-2 mRNA was reduced in the PUUO group compared to the SHAM group, whereas AQP3 mRNA level was unchanged. AQP2-3 protein level was reduced in the PUUO group compared to the SHAM group. Immunohistochemistry staining of renal AQP2-3 showed weaker labeling in collecting duct principal cells in the obstructed kidney compared to sham kidneys, which was consistent with the results of western blot. However, AQP1 protein level was unchanged and showed no change in staining intensity in the proximal tubules and descending thin limbs.

Conclusion: These data demonstrate the expression of AQP1-3 in the PUUO rat kidney in the early stage of life. One week congenital PUUO in rats results in significant down regulation of renal AQP2-3 protein level, which may play a role in neonatal kidney impairment.

Key words: AQP1-3, newborn rats, PUUO, kidney

P29.01 Karen Toftdahl
Bjørnholdt DEXAMETHASONE FOR THE REDUCTION OF POSTOPERATIVE PAIN AFTER OUTPATIENT SHOULDER SURGERY: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Background: Dexamethasone has analgesic properties when given i.v. perioperatively; however, the optimal dose has not been determined. We tested the hypothesis that a dose of 40 mg improved analgesia after outpatient shoulder surgery compared to 8 mg.

Methods: This was a randomized, double-blind, placebo-controlled clinical trial conducted at Horsens Regional Hospital, Denmark. Patients scheduled for arthroscopic subacromial decompression and/or acromioclavicular joint resection as an outpatient procedure (n=101) were randomized to receive i.v. dexamethasone 40 mg (D40), dexamethasone 8 mg (D8) or placebo (D0) before surgery. The primary outcome was pain intensity rated on a numeric rating scale (NRS, 0-10) 8 h after surgery. Secondary outcomes were pain intensity, analgesic consumption, and side-effects during three days following surgery.

Results: Data from 73 patients were available for analysis (D40: n=25, D8: n=26, D0: n=22). Eight h after surgery pain intensity was [median (IQR)]: the D40 group: 2 (1-4), the D8 group: 2.5 (1-5), the D0 group: 4 (2-7). For the D40 and D8 groups, pain intensity was similar 8 h after surgery (P=0.46) and all other recording times. When the two active treatment groups were combined and compared to the D0 group, pain intensity was significantly lower 8 h after surgery (P=0.03), also regarding most pain recordings up to and including the next morning. No differences were found in analgesic consumption. No serious side-effects were observed.

Conclusions: Increasing the dexamethasone dose from 8 mg to 40 mg does not improve analgesia significantly after outpatient shoulder surgery.

P29.02 Kristian Andersen

EFFECT OF MANDIBULAR DISTRACTION OSTEOGENESIS ON THE TEMPOROMANDIBULAR JOINT: A SYSTEMATIC REVIEW OF ANIMAL EXPERIMENTAL STUDIES

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Distraction osteogenesis is frequently used to correct mandibular retrognathism and mandibular asymmetry of either congenital or acquired etiology. The aim of the present systematic review of animal studies was to test the hypothesis of no effect of mandibular distraction osteogenesis (DO) on the temporomandibular joint (TMJ). Inclusion and exclusion criteria were applied to all experimental studies found in a PubMed, Embase, Scopus and Cochrane Library search.

Results: A total of 289 articles were identified of which 17 met our inclusion

criteria.

Conclusion: All articles were evaluated to be at a high risk of bias. The direction of the vector applied may influence the effect of DO on the TMJ, and physiological rates may be well-tolerable to the constituents of the TMJ. The hypothesis of no effect of MDO on the TMJ could neither be confirmed nor rejected.

P29.03 Jens Bay
Vegger

ADDITIVE EFFECT OF PTH(1-34) AND ZOLEDRONATE IN THE PREVENTION OF DISUSE OSTEOPENIA IN RATS

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Introduction: Immobilisation is known to cause rapid bone loss. Can this be prevented by treatment with zoledronate (ZIn) and hPTH 1-34 (PTH) alone or in combination?

Materials and methods: Immobilisation was achieved by injecting 4 IU Botox (BTX) into the right hindlimb musculature. Seventy-two 16-weeks old female Wistar rats were randomized into 6 groups; baseline, control (Ctrl), BTX, BTX+PTH, BTX+ZIn, and BTX+PTH+ZIn. PTH dosage was 80 µg/kg given 5 days/week sc and ZIn dosage was 100 µg/kg given sc once at study start. The animals were killed after 4 weeks of treatment. The bone properties were evaluated using µCT, mechanical testing, and dynamic histomorphometry.

Results: BTX resulted in lower trabecular bone volume fraction (BV/TV) (-25%, $p < 0.05$), lower bone strength at the distal femur (F_{max}) (-19%, $p < 0.001$), and lower trabecular bone formation rate (BFR/BS) (-29%, $p < 0.01$) compared with Ctrl. PTH-treatment resulted in higher BV/TV (+31%, $p < 0.05$), higher F_{max} (+11%, $p < 0.05$), and higher BFR/BS (+297%, $p < 0.05$) compared with BTX. ZIn-treatment resulted in higher BV/TV (+36%, $p < 0.05$), higher F_{max} (+10%, $p < 0.05$), and lower BFR/BS (-93%, $p < 0.05$) compared with BTX. PTH+ZIn-treatment resulted in higher BV/TV (+70%, $p < 0.001$), higher F_{max} (+32%, $p < 0.001$), and higher BFR/BS (+59.0%, $p < 0.05$) compared with BTX.

Conclusion: BTX-induced immobilisation resulted in lower BV/TV, F_{max} , and BFR/BS. In general, PTH or ZIn alone prevented the BTX-induced osteopenia, whereas PTH and ZIn given in combination did not only prevent, but increased BV/TV and maintained F_{max} and BFR/BS compared with Ctrl.

P29.04 Mikkel Tøttrup

THE CONCENTRATION OF CEFUROXIME IN CORTICAL AND CANCELLOUS BONE CAN BE DETERMINED BY USE OF MICRODIALYSIS - A METHODOLOGICAL STUDY

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Background: Determining penetration of antimicrobials into bone tissue remains a difficult task. The most commonly used method is bone biopsy. Different approaches have been used. However, most seem to share methodological and practical limitations.

Aim: The aim of this study was to apply and validate microdialysis for measuring cefuroxime concentrations in bone tissue.

Methods: In vitro studies were conducted in order to determine in vitro recovery by gain and by loss, appropriate flow rate and the effect of temperature. The prerequisite that recovery remains constant over a relevant period of time was tested in vivo in pigs. In order to assess whether microdialysis in drill holes in cortical bone solely reflects bone concentrations, an experimental study in pigs was conducted where one of two symmetric drill holes in the tibia was sealed with bone wax. In all experiments, CMA 63 catheters were used. Flow rate was 2 µl/min and was produced by a CMA 107 precision pump. All samples were analyzed with an UHPLC-method. Intra-cortical placement of drill holes was verified by post mortem CT scan.

Results: Two µl/min was found to be an appropriate flow rate, producing acceptable recoveries. Recovery by gain was comparable to recovery by loss. Temperature had little effect on recovery. In vivo, recovery was found to be constant over time. No significant difference in key pharmacokinetic parameters could be detected between sealed and unsealed drill holes in cortical bone.

Conclusions: Microdialysis seems to be a reliable method for determination of the concentration of cefuroxime in bone tissue. Sealing of drill-holes does not significantly affect key pharmacokinetic parameters.

P29.05 Bahram
Ranjesh

APATITE FORMATION ON FAST-SETTING NOVEL MINERAL TRIOXIDE AGGREGATE AND DIAMETRICAL STRENGTH DEVELOPMENT IN VITRO

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Introduction: Calcium-silicate-based cements are widely used for sealing of root canals in dental treatments. Poor strength and long setting time prevent usages in the crown.

Novel calcium hydroxide releasing dental cement called iMTA, for prevention of dental diseases, has been developed at AU. iMTA releases hydroxyl and fluoride ions. Fast-setting and optional consistency support new possible dental applications.

Objectives: We evaluated 1) mineral precipitation on iMTAs in physiological solution (PBS), and 2) iMTAs diametral tensile strength (DTS)

development in humid condition.

Methods and materials: iMTAs powder varying in soluble fluoride and radiocontrast were mixed with hydration liquid containing 2% poly-carboxylic acid in specific powder-liquid ratios for practical consistencies. We measured DTS after 1, 28, and 180 days (n=12). Material behavior in PBS was assayed by SEM/EDX and Raman Spectroscopy on 1, 7, 28 and 56 days.

Results: Typical "cauliflower" hydroxyapatite morphology composing calcium and phosphate were observed on iMTAs. Raman shifts supported apatite nucleation since day1. By time, thickened β -type carbonated apatite formed on iMTAs surface. All iMTAs had higher DTS than Pro-root MTA on day1 ($p<0.05$) and day 28. After 180 days, DTS values increased however without statistical significance. Addition of 20% radiocontrast reduced the DTS significantly ($p<0.05$).

Conclusion: This study confirmed formation of carbonated apatite on iMTA surface that thickened by time. iMTAs gained DTS strength in humidity during 180 days. Investigations on iMTA-dentin interaction regarding gap repair, ion distribution from iMTA to dentin and dentin remineralization are in progress.

P29.06 Polina
Martinkevich

PRECISE AND FEASIBLE MEASUREMENTS OF LATERAL CALCANEAL LENGTHENING OSTEOTOMIES BY RADIOSTEREOMETRIC ANALYSIS (RSA)

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Background: Lengthening osteotomies of the calcaneus in children's orthopaedics are in general grafted with iliac crest bone. Artificial structural bone grafts have been introduced. The durability has not been documented by RSA. RSA has not previously been used in clinical studies of calcaneal osteotomies. Prior to a clinical study we did an RSA study on lateral calcaneal lengthening osteotomy (LCLO) in cadaver feet. The aim was to determine the feasibility and precision of marker-based RSA on LCLO with focus on the osteotomy and the calcaneal-cuboid (CC) joint.

Methods: The LCLO was performed in 3 fixed adult cadavers (6 feet). Tantalum markers were inserted in the anterior and posterior fragment of calcaneus and the cuboid. Lengthening was done with a plexiglas wedge. 24 double radiographic examinations were obtained with the osteotomy in zero distraction and approximately 1 cm, 1.25 cm and 1.5 cm distraction to mimic selected clinical situations. One foot was excluded from the study due to loose markers/osteotomy fracture. Another foot was excluded from the precision analysis of the CC joint due to unacceptable high condition number (CN) (>300). Precision was assessed as systematic bias and 95% repeatability limits (LOA).

Results: Systematic bias was in general below 0.1 mm for translations and 0.33° for rotations. LOA was in general below 0.46mm for translations and below 1.8° for rotations (x,y,z). Mean CN for the anterior and posterior

calcaneus, and the cuboid bone was 153, 53 and 120.

Conclusions: Marker-based RSA is feasible and precise method to assess migration in LCLO and in the CC joint, though less precise for rotation.

P29.07 Rubens Spin-Neto VARIATION IN VOXEL VALUE DISTRIBUTION AND EFFECT OF TIME BETWEEN EXPOSURES IN SIX CBCT UNITS

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Objective: To assess the variation in voxel value distribution in volumetric datasets obtained by six CBCT units, and the effect of time between exposures.

Methods: Six CBCT units were tested (Cranex 3D/CRAN; Scanora 3D/SCAN; NewTom 5G/NEWT; Promax Dimax 3/PROM; i-CAT/ICAT; 3D Accuitomo FPD80/ACCU). Two volumetric datasets of a dry human skull imbedded in acrylic were acquired by each CBCT unit at two sessions in separate days. Each session consisted of 20 exposures: 10 acquired with 30 minutes between exposures, and 10 acquired immediately after one-another. CBCT data were exported as DICOM files and converted to text files. The text files were re-organized to contain x-, y-, and z-position and grey shade for each voxel. The files were merged to contain one record per voxel for each exposure / session. For each voxel subtractions were performed between dataset 1 and the remaining 19 datasets (1 minus 2, 1 minus 3, etc...) in a session. Means, medians, ranges, and standard deviations for grey shade variation in the subtraction datasets were calculated for each unit and session.

Results: For all CBCT units, variation in voxel values was observed throughout the 20 exposures. A "fingerprint" for the grey shade variation was observed for CRAN, SCAN, and NEWT. For the other units the variation was (apparently) randomly distributed.

Conclusion: Large discrepancies in voxel value distribution (noise) are seen in CBCT images. This variation should be taken into account in studies that assess minute changes in CBCT images.

P29.08 Abhishek Kumar EFFECTS OF EXPERIMENTAL PAIN ON FINE JAW MOTOR CONTROL - A PLACEBO-CONTROLLED DOUBLE-BLINDED STUDY

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Background: The jaw motor system is structurally and functionally complex. Jaw motor system achieves fine motor control with the precise positioning of the mandibular teeth against the maxillary teeth. Craniofacial pain is a potential modifier of natural mastication and jaw motor control. Pain causes significant changes in maximum occlusal force and EMG activity as

compared to healthy individuals. Animal studies have indicated that noxious stimulation of TMJ might have a different motor effect compared to noxious stimulation of jaw muscles. However, other lines of research have indicated that adaptation of jaw motor function may be more complex and involve individual traits.

Objective: To investigate the influence of experimental pain on the neural control of jaw muscles during fine motor tasks such as splitting food in healthy participants with natural dentitions.

Methods: 20 healthy volunteers participate in four experimental sessions. In each session, participants receive injection with either 0.2 ml of monosodium glutamate (MSG)/0.2 ml of normal saline (NS) in either the masseter muscle/TMJ. The participants perform the 'Hold and split' task with food morsel at baseline, during intervention (MSG/NS) and post intervention. The force applied by the teeth to 'hold' and 'split' the food morsel and the corresponding EMG activity of jaw muscles will be recorded. In addition, participants will be asked how they perceive the interference of pain on their biting performance.

Results: Pending.

Conclusion: It is suggested that because pain is multidimensional in nature, motor control during pain cannot always be stereotypical and predictable, but shaped by individual traits.

P30.01 Malene Beck

QUIET PLEASE! BETTER MEALTIMES AT THE NEUROLOGY WARD:
A PH.D. STUDY (IN PROGRESS)

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Aim: This study aims to improve mealtimes for patients hospitalised following a stroke or other neurological diseases.

Background: A determined effort has been made to optimise the nutrition of hospitalised patients, however the organisation of the meal situation and its relational and aesthetic aspects have not received similar attention. This means that all other tasks continue with undiminished intensity when patient meals are served and eaten.

Method: 20 patients are included in the study. Based on 10 interviews and field observations, the study first describes how patients experience traditional hospital mealtimes. These findings combined with the principles of the British concept of 'protected mealtimes' form the basis of an intervention designed to create a sense of calmness and awareness towards the mealtimes. During the intervention 10 new patients are interviewed, now in a changed environment. Field notes and answers from all interviews are analyzed, compared and interpreted using the phenomenological- hermeneutic approach by Paul Ricoeur.

Findings: The preliminary impressions from the field observations performed in June 2013 suggest that meals in the traditional mealtime environment are being interrupted or skipped, and are associated with waiting times for

patients.

Conclusion: The patient's perspective combined with recommendations from the concept of protected mealtimes should ensure that patients experience mealtimes positively and that meals are an integrated part of their care and treatment. This new knowledge gained could form the basis of a modified food culture in hospitals and is expected to be generalisable to other danish hospitals departments.

P30.02 Jette Pedersen IS TRANSFER OF NUTRITIONAL RECOMMENDATIONS FROM SECONDARY SECTOR TO PRIMARY SECTOR AFFECTED BY THE PRESENCE OF A CLINICAL DIETICIAN IN HOSPITAL?

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Introduction: Undernutrition is common in old people admitted to hospital. Length of stay in hospital is short, and at discharge many patients are still undernourished. Transfer of information concerning nutrition from hospital to primary health care is essential to optimize nutritional care after discharge.

Aim: To investigate if the presence of a clinical dietician during hospitalization ensures transfer of information concerning nutritional recommendations from secondary to primary sector.

Material and method: A clinical dietician was available for the health professionals at the geriatric ward to support, ensure and control that patients at nutritional risk were offered a nutrition plan, including recommendations after discharge. Discharge information in the study period (1 May to 15 July 2011) was compared with two periods without dietician intervention, a before-intervention period (1 January to 30 April) and an after-intervention period (15 July to 30 September). Statistical analyses were performed by chi-squared test.

Results: A total of 318 patients at nutritional risk were included: 129 in the before-intervention period, 87 in the intervention period, and 102 in the after-intervention period. In the before-intervention period, a nutrition plan at discharge was transferred to the primary health care in 63% of discharges, versus 76% during intervention, and 89% in the after-intervention period ($p < 0.001$).

Conclusion: The intervention with a clinical dietician seems to enhance the health professionals' attention on nutritional issues and thereby improve the transfer of information concerning nutrition at discharge to the primary health care to optimize nutritional care.

P30.03 Anna Sundby WHOLE GENOME SEQUENCING - NEW POSSIBILITIES, NEW DILEMMAS

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Background: The development of whole genome sequencing (WGS) has made it possible to identify genetic variations associated with increased risk for many disorders. The use of WGS in genetic research raises new ethical and legal questions. This study explores ethical implications of WGS and focuses on potential research participants' attitudes towards findings and consenting procedures.

Methods: We have made a pilot study which includes 12 interviews: Six interviews with genetic researchers, three interviews with patients with schizophrenia and three focus group interviews with clinical counsellors, relatives of psychiatric patients and Danish blood donors. Currently, we are working on developing a web-based questionnaire to examine the attitudes to WGS research.

Preliminary results: The majority of the participants in the pilot study would participate in genomic research. Most of the genetic researchers supported a broad consent. Clinical counsellors and patients were concerned whether a broad consent would be an informed consent. Nearly all participants believed that pre- and post-test counselling is necessary. All participants expressed strong preferences regarding how and if findings should be returned. Relatives supported that children should be enrolled in genomic research and they believed that parents should have the right to know about research results pertaining to their children.

Conclusion: Attitudes toward feedback of findings vary across different groups of participants. There are both arguments for and against the broad consent. Researchers need to address how to handle consent and findings in WGS-research and do so in a way that respects the group's different attitudes.

P30.04 Nanna Rolving Rasmussen DOES A PREOPERATIVE COGNITIVE INTERVENTION AFFECT POSTSURGICAL PAIN, MOBILISATION AND LENGTH OF HOSPITALISATION IN LUMBAR SPINAL FUSION PATIENTS?

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Background: Postoperative outcome following spine surgery appears to be highly influenced by psychosocial factors like fear-avoidance belief and coping strategies. Cognitive behavioural therapy (CBT) seems to be a possible way of modifying these traits. In addition, it may be beneficial to initiate rehabilitation already prior to surgery. The effect of preoperative cognitive rehabilitation has not been investigated for lumbar spinal fusion (LSF) patients, although the surgical procedure is still related to prolonged

hospitalisation, postoperative pain and disability.

Aim: To examine if preoperative CBT can reduce postoperative pain and facilitate early mobilisation and thereby decrease length of hospitalisation.

Materials and methods: A total of 96 patients undergoing LSF were randomly allocated to either standard treatment or, in addition, preoperative CBT. The CBT intervention consisted of a short patient education focused on pain coping. Effects were measured on back and leg pain one month postoperatively, mobility on the first 3 postoperative days, and length of hospitalisation.

Results: There was no difference between groups concerning back pain ($p=0.33$) or leg pain ($p=0.14$), overall mobility ($p=0.35$) or length of hospitalisation ($p=0.1$). A total of 73% versus 50% (intervention vs control) had independent walking ability at postoperative day three ($p=0.085$).

Conclusion: Postoperative pain does not seem to be influenced by preoperative CBT. The intervention group tended to achieve independent mobility faster than the control group, but this did not affect length of hospitalisation.

P30.05 Rikke Aarhus

FAST-TRACK DIAGNOSTICS: EXPLORING HOW CANCER PATHWAYS FRAME CLINICAL ENCOUNTERS AND THE CONFIGURATION OF PATIENT AND HEALTH PROFESSIONAL IDENTITIES

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Background: Early and fast-track diagnostics are central to cancer treatment. Medical and technological enhancements continuously improve diagnostic processes. This implies implementing standardized pathways to ensure timely and evidence-based action to increase prognosis. While the importance of time and timeliness is well-established within diagnostics, we only have little knowledge of how increased focus on time affects organizations and people involved in them.

Aim: The aim of the project is to explore how fast-track diagnostics, with an inherent focus on time, tend to frame clinical encounters, experiences and the configuring of patient and health professional identities in cancer pathways.

Method: The project is based on a multi-sited, one-year ethnographic fieldwork in three different cancer pathways. The main methods applied are participant observation, unstructured interviews and semi-structured in-depth interviews. Data are coded throughout the fieldwork, re-read and analyzed with selected theoretical framework after completion of

fieldwork.

Perspectives: The project will improve the understanding of how medical and technological changes in diagnostic processes influence clinical encounters and individuals. In particular, it will add to our knowledge of how the focus on time in cancer pathways frames 1) experiences, 2) the conceptualization of cancer, 3) clinical encounters and 4) what it means to be a patient and a health professional.

P30.06 Louise Møldrup
Nielsen THE EFFECT OF SYSTEMATIC ASSESSMENT OF FUNCTIONAL ABILITY,
DEVELOPMENT OF REHABILITATION PLAN AND FOLLOW-UP AT HOME FOR
ELDERLY MEDICAL PATIENTS

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Background: Studies indicate that limitations in functional ability increase the risk of readmissions and mortality for elderly patients.

Aim: The aim of this study is to examine the effect of systematic assessment of functional ability, development of rehabilitation plan and follow-up at home. Furthermore, to examine the importance of intervention for the elderly patient's experience of consistency across sectors.

Methods: This study uses a comprehensive Mixed Method design and consists of two sub-studies:

1. The effect of systematic assessment of functional ability, development of rehabilitation plan, and follow-up at home is examined in a controlled randomized study. A risk of 16% is expected between the groups as regards readmission. With a two-sided significance level of 5%, a power of 80% and expected loss to follow-up at 10%, a total of 304 patients will be included 1:1 ratio. Patients in the intervention group receive an assessment of functional ability and a rehabilitation plan. The therapist from MVA, visits the patient the day after discharge and ensure the first training at home. Patients in the control group are referred to rehabilitation as usual. Primary endpoint is readmission. Secondary endpoints are: mortality, self-reported disability and quality of life measured with the Barthel-20, WHODAS 2.0 and EQ-5D. Readmission is estimated with relative risk.

2. The patient's perception and experience of is examined with a qualitative interview, with 10 selected individuals from the intervention group. A phenomenological approach is chosen, using a semi-structured interview guide. The analysis is performed by meaning condensation and analysis based on selected theory.

P30.07 Janni Lisander
Larsen WOMEN'S EXPERIENCE OF LIVING WITH SYSTEMIC LUPUS
ERYTHEMATOSUS: A QUALITATIVE STUDY

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Background: Systemic lupus erythematosus (SLE) is a rare chronic autoimmune disease, with a prevalence in Denmark of 22/100,000, most frequently affecting women. SLE may affect kidneys, lungs, heart and blood vessels. The course of disease is potentially lethal and unpredictable; fluctuating between active and stable phases thereby making profound impact on the life. Thus, SLE patients deal with existential uncertainty; they might experience restricted lifestyle and disrupted identity. The literature points out that it is important for patients to feel supported, but existential experiences are scarcely researched in chronic disease. Further, the literature does not clearly emphasize, which existential themes that are relevant for patients. This leaves a gap of knowledge which could prevent initiations of nursing support into important areas of life management.

Purpose: The purpose of this PhD project is to investigate such existential experiences as they unfold over the years in female patients with SLE. The study will shed light on the living experience of SLE, pointing out the meaning of existential experiences.

Method: Qualitative in-depth interviews, guided by Van Manen's Lifeworld Existentials (time, space, body, relationship) are presently performed with 15 women with SLE; they are followed over 1½ year with three interviews. Interviews are analyzed phenomenologic- hermeneutically by considering essential themes, reflecting and synthesizing on the text. Phenomenologic Existential theory will be used to interpret the experience of living with SLE.

P30.08 Jette Lauritzen THE MEANINGFULNESS OF PARTICIPATING IN SUPPORT GROUPS FOR INFORMAL CAREGIVERS OF OLDER ADULTS WITH DEMENTIA.

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Background: While the positive aspects of care such as fulfilment and companionship should not be overlooked, informal caregivers, often family members, experience multiple negative consequences when performing care-related tasks around-the-clock for older adults with dementia at home. The consequences, such as the perception of taking on a stressful responsibility that eventually will lead to a meaningless existence, depression, stress, anxiety and fatigue, are all identified risk factors for premature death among informal caregivers. These multiple challenges are often referred to as "the caregiver's burden". The Public Health Care Systems in western counties consider support groups for informal caregivers to be an effective and economical way to relieve the caregivers' stress and burden. It is, however, unclear if or how participating in support groups produces a meaningful outcome for the caregivers.

Aim: To explore how informal caregivers in urban and rural settings respectively, perceive the meaningfulness of participating in support

groups as a means to release stress and to ease the transition of the afflicted partner to respite care.

Method: The aim will be explored in three studies; I. A meta-synthesis is produced based on a peer-reviewed protocol. II. Ethnographic participant observation studies of support group meetings in rural and urban settings. III. Semi-structured individual interviews of informal caregivers in rural and urban settings. Content analyses based on the ICF model are performed on the qualitative data in both study II and study III.

P31.01 Sara Marie Hebsgaard

FROM BODILY SIGNS TO SYMPTOMS OF ILLNESS. AN ANTHROPOLOGICAL STUDY OF THE 'PATIENT INTERVAL'

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Background: One in five people diagnosed with cancer in Denmark experience symptoms for three months or more before seeking medical care (the patient interval). Existing studies of healthcare-seeking have primarily been conducted retrospectively and with a focus on already diagnosed patients. We do not know much about how or when everyday bodily changes, signs and sensations are experienced as symptoms of illness. Hence, there is a need to explore the social and interpretive processes that occur before people contact their doctor. This longitudinal study provides in-depth knowledge on how everyday life influences bodily experiences and symptom interpretation and vice versa.

Methods: The project is based on 12 months of ethnographic fieldwork in a Danish middle-class, suburban neighbourhood of single-family houses. Fifteen key informant households are followed through regular participant observation and 3 interviews. They will register symptom experiences for six months. Field notes, interview transcripts and symptom registrations will systematically be coded and analysed.

Perspectives: A longitudinal research design will generate new perspectives on the scientific knowledge about the time from symptom experience to healthcare-seeking. Following participants in their everyday life as it unfolds and exploring bodily experiences as they happen will broaden our understanding of symptom interpretation and healthcare-seeking practices among Danish middle-class households and will also provide us with an understanding of bodily changes and sensations as culturally embedded experiences. This can be used to explore reasons why some cancer patients report such a long patient interval.

P31.02 Linda Christie Andrea

SUSPECTED IMPINGEMENT SYNDROME - PREDICTORS OF EARLY CLOSURE OF TREATMENT

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Background: A large number of patients suspected of impingement syndrome are referred to an orthopaedic department for evaluation.

Purpose: We hypothesised that predictors of early closure of an episode of care (EOC) after first consultation are: Oxford Shoulder Score (OSS), diagnosis made by the orthopaedic surgeon, younger age, female sex, comorbidity, self-reported depression, language difficulties, unemployment, and ongoing (workers') insurance claim.

Materials and methods: All patients aged 18-63 suspected of impingement syndrome (based on referral letter) who provided questionnaire information and were seen at one of six orthopaedic departments in the Central Denmark Region during a 17-month period. Departments registered diagnosis, language difficulties, co-morbidity, and closure of the EOC. Remaining risk factors and Oxford Shoulder Score (OSS) were obtained from the questionnaire. Poisson regression was used for analysis.

Results: 1750 persons were included, 66.2% completed the questionnaire. 30% (14-38%) of the EOC were closed at first consultation. Patients with 'good' shoulder function (OSS>32) without impingement syndrome diagnosed had OR 2.6 (95% CI 1.85-3.54) for early closure of the EOC - compared to patients who had both impingement syndrome and 'poor' shoulder function (OSS≤32). None of the other risk factors considered were significant predictors.

Conclusion: 30% of the patients referred with suspected impingement syndrome had their EOC closed after the first consultation. Early closure depended on diagnosis and shoulder status. All other tested predictors showed no evidence. The perspective of GPs determining OSS when referring patients could be considered.

P31.03 Charlotte
Simonÿ

ISCHAEMIC HEARTPATIENTS ARE ENCOURAGED TO ENJOY PHYSICAL EXERCISES IN THEIR REHABILITATION

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Background: About 6,000 Danes are annually diagnosed with Unstable Angina Pectoris (UAP) or Non-STEMI (NSTEMI). Cardiac rehabilitation has been established to improve prognosis, and support the patients in moving forward towards a satisfying life. Evidence shows that the patients' perspective must be firmly addressed. Hence, further illumination of the individual's experiences of recovering is needed.

Aim: To present obtained knowledge about patients' experiences associated with physical exercises in the rehabilitation.

Method: A qualitative ethnographic study including field observations, focus group- and individual - interviews was conducted. 11 men and women

with UAP/NSTEMI were followed during rehabilitation. Fieldnotes and transcribed interviews were analyzed by a three-phased interpretation, inspired by Paul Ricoeur's phenomenological- hermeneutic approach.

Findings: Before training, the patients are afraid to exercise as they fear to overload the body and provoke a new heart attack. In a safe and encouraging environment with specialized physiotherapists and other heart patients, the participants grow confident and learn to enjoy training. They find that exercising is meaningful as it brings them well-being and a good quality of life. Furthermore, they discover that exercise is essential to prevent new heart attacks. They want to continue their training in order to improve health.

Perspectives: Through cardiac rehabilitation patients overcome anxiety and learn to appreciate physical activity. It is essential for both professional rehabilitation planners as well as future patients that physical exercise becomes enjoyable and meaningful when training.

P31.04 Bettina Kjær
Kristiansen

FOLLOW-UP OF ABNORMAL OR INADEQUATE TEST RESULTS IN THE DANISH CERVICAL CANCER SCREENING PROGRAMME: EFFECTS OF TWO INTERVENTIONS

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Denmark has a higher incidence of cervical cancer than other Nordic countries, although all Danish women (aged 23-65) are screened regularly to identify possible cervical dysplasia or asymptomatic invasive cancer.

Annually 40,000 women receive an abnormal or inadequate test result and a follow-up recommendation.

However, problems with delayed follow-up may threaten the effectiveness of the Danish Cervical Cancer Screening Programme as 20% of women are delayed and dysplasia potentially can progress into cancer.

Delayed follow-up occurs when women either consciously or unconsciously postpone follow-up, but the organization of the screening program may also play a role as communication of test results can fail in content or be delayed. This study evaluates two interventions designed to increase follow-up:

1) An RCT of the effect of a letter - with the test result and a recommendation for potential follow-up - sent to the women. The intention is to ensure that all women are notified about the test result and offered the opportunity to contact or be contacted by the GP in case of special needs. Furthermore, it is assessed whether the number of GP consultations regarding delivery of normal test results will decrease.

2) A retrospective cohort study of the effect of electronic reminders sent to the GP if the women have not had the recommended follow-up, thereby

providing the GP with an opportunity to remind the women.

The results will be of great importance to the future organisation of cervical cancer screening programmes in Denmark, and findings will also be applicable in countries with similar programmes.

- P31.05 Vita Ligaya CHANGES IN SELF-REPORTED SLEEP AND COGNITIVE FAILURES:
Ponce Dalgaard A RANDOMIZED CONTROLLED TRIAL OF A STRESS MANAGEMENT INTERVENTION

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Background: Danish clinics of occupational medicine have seen a rise in patients with work-related stress during several years. Systematic reviews indicate that cognitive behavioural interventions are more effective than other treatments in reducing stress symptoms. Only few studies have been done in patients with clinical levels of work-related stress.

Aim: To evaluate the efficacy of a cognitive behavioral intervention on self-reported sleep quality and cognition among patients with work-related stress.

Methods: Patients were included if fulfilling the following criteria: 1) sick leave due to work-related stress reactions, 2) a diagnosis of adjustment disorder or reactions to stress (ICD 10-diagnose codes: F43.2 - F 43.9 not PTSD) or mild depression. Participants (n=137) were randomized to either a treatment group (n=57) or a control group (n=80). The intervention comprised 6 sessions with a psychologist and the offer of a small work place intervention. Questionnaires were answered at baseline, after 4, and 10 months.

Results: Symptoms were reduced over time in both groups, showing significant within-group changes, but no significant between-groups treatment effect was observed at any time point. From baseline to 4 months there was a tendency for larger improvements in the intervention group. Although neither was significant, the results came close to significance on sleep complaints (p = 0.076) and distractions (p = 0.070) but not memory (p = 0.252).

Conclusions: The treatment was not superior to the control condition in reducing self-reported problems in sleep and cognition at any time point. Substantial improvements in symptoms over time were seen in both groups.

- P31.06 Christina Friis DISCONTINUATION OF NASAL CPAP IN PRETERM INFANTS - A
Jensen RANDOMIZED CONTROLLED MULTICENTER TRIAL

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Background: Nasal continuous positive airway pressure (nCPAP) is used as treatment of respiratory distress syndrome in preterm infants. The best way to discontinue the treatment is unknown and the treatment may be unnecessary prolonged. This increase risk of mechanical complications, increased length of stay in the Neonatal Intensive Care Unit (NICU) and potential increased risk of chronic lung disease. The aim of this study is to determine whether sudden discontinuation of nCPAP or gradual reduction in CPAP pressure prior to discontinuation is more efficacious measured primarily as the infant's weight at the date of the expected delivery.

Materials and methods: This is a randomized, open-label, controlled trial. Preterm infants born before 32 weeks of gestation and admitted to the NICU's at Aalborg University Hospital, and the Regional Hospitals of Randers, Viborg and Herning will be enrolled in this study, if some prespecified inclusion criteria are met. The study is performed between 1st September 2012 and 31th August 2014. Neonates are randomized to: 1) Gradual wean where the CPAP pressure is gradually reduced by 1 cmH₂O per day 2) Sudden discontinuation where the CPAP treatment are terminated. The discontinuation of the nCPAP is considered successful if the infants stay off nCPAP for three days. The primary endpoint is body weight at a gestational age of 40 completed weeks. Secondary endpoints are duration of CPAP therapy, oxygen therapy and length of hospital stay.

Results: Currently 58 patients have been enrolled in the study. We aim to include 300 patients at the end of December 2014.

P31.07 Mette Trads

QUALITY OF LIFE AMONG PATIENTS WITH CONSTIPATION

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Introduction: Constipation is often an overlooked problem in both hospital and home settings. 4-28% of the general population is estimated to be constipated. In patients with complex disorders, up to 70% suffer from constipation. Constipation increases the risk of postoperative complications, can prolong hospital stay and increase financial cost and staff nursing care time. Furthermore, constipation is suggested to have an impact on the patients' general health perception, emotional health, social functioning and mental health. A comprehensive systematic review is needed in order to assess and understand the impact of constipation on patients' quality of life. In addition, this knowledge will contribute to a better foundation for prioritizing and decision making in clinical practice.

Aim: To complete a systematic review in order to improve quality of care for patients with constipation.

Key words: constipation, defecation, obstipation, gastrointestinal disorders, quality of life, wellbeing social, physical, psychological, Bristol Stool Scale

- P31.08 Berit Skjødeberg THE EFFECT OF CONTINUING MEDICAL EDUCATION (CME) ON GP
Toftegaard CANCER RISK ASSESSMENT - PRELIMINARY RESULTS

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Background: Danish cancer patients have a lower survival and cancer at more advanced stages at treatment initiation compared to other Nordic countries. This has called for a focus on earlier diagnosis, i.e. earlier referral. However, cancer is a low prevalence condition with only 8-10 new cancer patients per general practitioners (GP) per year. Alarm symptoms of cancer have low positive predictive values of 3-8% in general practice. Nevertheless, cancer patients have increased GP visits 3-6 months before diagnosis. Therefore, the GP's ability to rationally assess the risk of cancer to facilitate early referral is critical. We need to know whether CME can alter GP cancer risk assessment.

Aim: To analyse changes in GP cancer risk assessment before and after CME in early cancer diagnosis.

Methods: We invited all 859 GPs in the Central Denmark Region. Within eight months, 689 GPs (80.2%) completed forms on patients they referred to cancer fast-track diagnosis, including a GP-assessed specific risk of cancer (0-100%). During the same period, the GPs were invited to a CME; a multifaceted three-hour course in early cancer diagnosis.

Results: 184 GPs (27%) received CME. 505 GPs (73%) did not receive CME. The CME group completed 622 forms before CME (mean risk of cancer: 38.7%) and 819 forms after (mean risk of cancer: 28.0%) ($p < 0.001$). The reference group completed 1653 forms before CME (mean risk of cancer: 39.8%) and 1208 forms after (mean risk of cancer: 38.8%) ($p = 0.525$).

Conclusion: A before-after analysis found that CME in early cancer diagnosis could lower the GP-assessed cancer risk on referred patients. Future analyses will clarify whether the GPs referred patients earlier.

- P32.01 Maria Staub ANDROGEN DEPRIVATION THERAPY IMPROVES BIOCHEMICAL OUTCOMES
Ervandian IN PATIENTS TREATED WITH SALVAGE RADIOTHERAPY - A NATIONAL DANISH STUDY

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Background and objectives

Salvage radiotherapy (SRT) is considered standard of care in patients with biochemical failure after radical prostatectomy (RP). The benefit of

androgen deprivation therapy (ADT) in combination with SRT is unclear.

The purpose of this study was to compare biochemical outcomes in patients who received SRT with or without concurrent ADT.

Materials and methods

This study comprises the total cohort of patients receiving SRT in Denmark in the period 2006 to 2010. A total of 272 patients treated were included and analyzed retrospectively. The primary endpoint was biochemical failure after SRT defined as a PSA ≥ 0.2 ng/mL.

Results

One hundred fifty-two patients (52 %) received SRT alone and 120 (44%) received ADT in combination with SRT. The median follow-up from SRT was 3.4 (range, 0.7 – 6.7) years. The use of ADT decreased over time, resulting in a longer median follow-up (4.17 years) for patients receiving SRT and ADT compared to patients receiving SRT alone (2.81 years).

Patients who received ADT had higher pre-RP PSA levels ($p=0.039$), lower Gleason scores ($p=0.028$) and higher pre-SRT PSA levels ($p=0.001$) compared to patients who did not receive ADT.

Biochemical progression free survival was significantly longer in the patients receiving ADT compared to patients who did not receive ADT ($p=0.000$).

At the end of follow-up 51 % of the patients were without biochemical failure.

Conclusions

Patients who received combined therapy with ADT and SRT had a highly significant improved biochemical progression-free survival compared with patients who received SRT alone.

- P32.02 Mai Lykkegaard DOSIMETRIC IMPACT OF INTRA- AND INTER-FRACTION TUMOR MOTION
Schmidt AND ANATOMICAL CHANGES IN RADIOTHERAPY OF NSCLC

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The dosimetric impact of tumor motion and anatomical changes during radiotherapy (RT) of 16 patients with non small-cell lung cancer was investigated. The tumor was delineated in the mid-ventilation phase of a planning 4DCT scan (CT1), forming the clinical target volume (CTV). Typically, 66Gy was delivered in 33 fractions using daily conebeam CT (CBCT) with bony anatomy match for patient setup. The daily tumor shift relative to the spine was extracted from the CBCT scans as a measure of interfraction tumor motion. A second 4DCT scan (CT2) was acquired halfway through the treatment, and the tumor motion was extracted as a measure of intrafraction motion. Rigid bone registration was used to transfer the original plan from CT1 to CT2 thus mimicking the patient setup

procedure. The plan was recalculated on CT2 with and without inclusion of inter- and intrafraction tumor motion and the resulting CTV doses were compared with the planned CTV dose to investigate the dosimetric impact of both tumor motion and anatomical changes. Tumor intrafraction motion was largest in the CC direction [1-11 mm]. Tumor interfraction motion spanned 2.5 cm. The average absolute difference in mean CTV dose between CT1 and CT2 was 1.23 percentage point (pp) [0.1-3.9]. The average change in mean CTV dose when adding intra- and interfraction motion was 0.41 pp [0-1.9] and 1.08 pp [0.1-6.9], respectively. For most patients, the changes in the CTV dose were caused by anatomical changes rather than target motion. The anatomical changes had larger impact on the target dose distribution than internal target motion. Adaptive radiotherapy could be used to achieve better target coverage throughout the treatment course.

P32.03 Nina Munk Lyhne

DHANCA 27; TRANSORAL LASER ASSISTED MICROSURGERY FOR T1A GLOTTIC CANCER

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Background: Glottic cancer is, in Denmark, currently treated with accelerated radiotherapy (RT). The treatment is efficient, and the 5-year primary control rate is 95% for patients with T1aN0M0 glottic cancer, while control with salvage is 98%. Modern technology has made it possible to surgically remove the tumour by transoral laser assisted microsurgery (TLM). This treatment is faster, of less strain to the patient and probably cheaper. Unfortunately, it is unknown if cancer control is comparable in TLM and RT.

Aim: The aim is to investigate whether TLM is non-inferior compared to accelerated RT in treating patients with T1aN0M0 glottic cancer.

Materials and methodology: Patients operated radically with TLM will be included in this national study. Patients will be followed at least five years after the last cancer presentation. Voice quality will be evaluated at 6 months and after 3 years of follow up. The primary end-point is laryngectomy-free survival. Secondary end-points include primary control, control with salvage, survival, voice outcome, and costs. Data on TLM treated patients will be compared to a national historic cohort of 350 RT treated patients prospectively recorded in the DAHANCA database. 80 patients treated with TLM will be included.

Perspective: By comparing national cohorts of consecutive patients treated with TLM and RT respectively we will avoid selection bias. This study will provide better evidence of the value of TLM vs. RT compared to existing data. Outcome of this study will underlie the decision on whether to

implement TLM as a standard treatment for T1a glottis cancer in Denmark.

P32.04 Sara Correia Marques

MICRORNAS AS BIOMARKERS FOR DOXORUBICIN RESISTANCE IN POST-GERMINAL B-CELL MALIGNANCIES

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Doxorubicin (Dox) is a cornerstone of the first line therapy in Multiple Myeloma (MM) and Diffuse Large B-cell Lymphoma (DLBCL). Unfortunately, the overall survival rate of individuals diagnosed with these malignancies remains dismal, mainly due to tumor resistance, including resistance to Dox. We are interested in generating drug-specific gene signatures involved in prediction of treatment outcome and in the study of microRNAs (miR) involved in B-cell malignancies. Our hypothesis is that deregulated miRs are implicated in resistance to Dox. The project aims are 1) to generate a miR-based response signature to Dox, 2) to validate the clinical impact of selected miRs on chemosensitivity, and 3) to perform lentiviral transduction of B cells and study its impact on resistance in vitro. A systematic drug screen was performed on 15 DLBCL and 12 MM cell lines, which were then divided into sensitive and resistant groups based on GI₅₀ estimates. Using class comparison analysis on results of miR arrays, 3 miRs were identified with potential influence on resistance mechanisms. Their expression levels were validated by RT-qPCR in DLBCL cell lines and subsequently measured in 89 DLBCL primary clinical samples with a minimum of 3 years of follow-up. They will be analyzed in additional clinical samples for studies of prognostic impact. Functional studies of miRs specific for Dox sensitivity will be performed following manipulation of their expression in B cell lines with an optimized lentiviral vector system. Our expectations are to establish causal relationships between miR expression and chemotherapy response that support the development of individualized treatment strategies.

P32.05 Marianne Hjorth Skorstengaard

ADVANCE CARE PLANNING: A WAY TO IMPROVE END-OF-LIFE CARE

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Background: Communication about end-of-life issues is often suboptimal. A way to improve the quality of end-of-life care is Advance Care Planning (ACP). ACP is a discussion between an incurably ill patient, a health care professional and, if possible, a relative about preferences for end-of-life care.

Aim: The aim is to investigate if ACP is effective in relation to improving incurably ill patients' quality of life, satisfaction with health care services and psychological distress among both patients and bereaved relatives.

Research plan: The study is designed as a prospective randomised controlled trial. Eligible patients from the departments of oncology,

cardiology and respiratory medicine at Aarhus University Hospital will be included and randomised in two groups: one receiving usual care and one receiving usual care and ACP. ACP discussions will be documented in the hospital's Electronic Patient Files and send to general practitioners and community nurses with the patient's acceptance. Patients and relatives will be followed with questionnaires to monitor quality of life, satisfaction with provided care, anxiety and psychological distress. Patients' preferences of place of care and place of death will be registered. After death of the patient, depression, anxiety and degree of complicated grief among bereaved relatives will be measured. The randomisation of patients are planned to begin 1st November 2013.

Perspective: If ACP is found effective, it may have the potential to improve quality of end-of-life care for patients and their families and reduce the uncertainty that many patients and their relatives experience, with substantial psychological distress as a consequence.

P32.06 Anna Kirstine Winthereik IMPROVING END-OF-LIFE CARE BY CONTINUING MEDICAL EDUCATION AND ELECTRONIC DECISION MAKING SUPPORT FOR GENERAL PRACTITIONERS IN DENMARK – A RANDOMIZED CONTROLLED TRIAL

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Background: It has been shown beneficial to patients in end-of-life care to optimize the basic palliative care, in which the general practitioner (GP) has a pivotal role in the health care system, providing comprehensive and continued medical care.

The aim of the study is to investigate the effect of a complex intervention in general practice on GPs' awareness of and confidence in providing end-of-life care.

Method: A cluster-randomized controlled trial among 410 general practices in the Central Denmark Region. The participating general practices will be randomized into (a) receiving education in palliative care and electronic palliative support, (b) having access to electronic palliative support and (c) performing standard care as a control group. The end-of-life care delivered by the GPs to their deceased patients will be analysed based on register data related to the deceased patients and questionnaires to GPs.

Primary outcomes: Place of death of deceased patients, time spent at home and number of hospital admissions in the last three months of the patients' life.

Secondary outcomes: Number and kinds of contacts between GPs and patients, use of relevant medicine and of the 'Safety Box'. Finally GPs' confidence concerning palliative care will be assessed in questionnaires. The work is in progress and the intervention is planned to start February 2014.

Perspective: If this intervention improves the palliative awareness among GPs, it can improve the quality of the basic end-of-life care beneficial both to terminally ill patients and especially to patients suffering from non-malignant diseases, who are often overlooked when it comes to palliative care.

P32.07 Jakob Kristian Jakobsen PRE-TREATMENT DIAGNOSTIC CHARACTERISTICS OF 321 PENILE CANCER PATIENTS - A NATIONAL RETROSPECTIVE STUDY FROM DENMARK

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Introduction: In Denmark, squamous cell carcinoma of the penis (pSCC) is rare. A number of registry-based studies have characterized pSCC patients. We present the first national study based on detailed data from medical records.

Methods: Patients with pSCC seen at 3 university hospitals from 1 January 2000 to 31 December 2010 were identified and data retrieved from records.

Results: A total of 321 patients (mean age 65 (33-102) years) were referred from 50 clinics. 29 patients (9%) were acute referrals. 179 (56%) had phimosis at diagnosis. In 240 (75%) patients diagnosis was based on biopsy prior to referral. Further 34 patients were biopsied after referral. 24 of 61 (39%) punch biopsies did not sufficiently represent the tissue of deeper structures necessitating a re-biopsy before treatment strategy could be chosen compared to 4 of 210 (2%) knife-biopsies necessitating re-biopsy (χ^2 ; $p < 0.001$). In 35 patients (11%) the penile tumor was revealed unexpectedly during phimosis-surgery. In 176 of 296 (59%) patients with invasive tumor, either previous or simultaneous precancerous pathology was associated; in 99 patients (56%) carcinoma in situ, in 24 (14%) dysplasia, in 22 (12%) condyloma acuminata(CA), in 17 (10%) chronic balanitis and in 14 (8%) lichen sclerosus et atrophicus(LSA).

Discussion: Penile cancer is primarily handled in an elective setting, it is a clinical diagnosis most often confirmed by biopsy. In this retrospective study knife-biopsy necessitated significantly fewer re-biopsies than punch biopsies. Selection bias may exaggerate the figures but the tendency is very strong. As seen in other studies, phimosis, CA, balanitis and LSA are associated lesions.

P33.01 Maja Ølholm Vase EBV AND HLA-TYPE IN POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)

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PTLD following solid organ transplantation is a rare complication. It is a heterogeneous condition encompassing benign hyperplasia and genuine lymphomas. Epstein-Barr virus (EBV) plays a crucial role in lymphomagenesis.

Methods: We identified 102 PTLDs in 4308 transplants. All were evaluated by a hematopathologist and prepared for tissue micro array. Frequencies between groups were compared with Pearson's χ^2 , and survival analyses were performed using Kaplan-Meier.

Results: Of 102 PTLDs, 13 (13%) were early lesions, 7 (7%) were polymorph PTLDs and the remaining 82 (78%) monomorphic, frank lymphomas of which the majority consisted of Diffuse large B-cell lymphoma (61%). In the cohort, 48 (49%) patients had an EBV-positive tumor, 21 (21%) no evidence of EBV and the remaining no information with regard to EBV-status.

EBV-status was associated with time-to-PTLD ($p=0.002$), performance status ($p=0.009$) and B-symptoms ($p=0.047$). The 5-year overall survival was 59.23% (43.58-71.88) and 61.90% (38.08-78.80) in the EBV positive and negative groups, respectively (non-significant). The degree of HLA-A and -B mismatch did not influence the risk of developing PTLD (HLA-A mismatch $p=0.678$; HLA-B mismatch $p=0.220$) and EBV-status was also unaffected (HLA-A mismatch $p=0.138$; HLA-B mismatch $p=0.743$). HLA-A*02 and HLA-DR*04 were significantly underrepresented in patients with PTLD ($p=0.001$ and 0.036), but no association with EBV-status. Our results confirm the association with EBV and indicate that individuals carrying HLA-A*02 and -DR4 have reduced risk of developing PTLD. This may be useful in risk-stratification and monitoring. HLA-A*02 presents EBV-antigens, and may be protective against EBV-driven tumors.

P33.02 Anne Vestergaard

CLINICAL EXPERIENCE WITH ADAPTIVE RADIOTHERAPY FOR MUSCLE INVASIVE BLADDER CANCER

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Purpose: Large changes in bladder shape and size during a course of radiotherapy (RT) make adaptive RT (ART) appealing in treatment of muscle invasive bladder cancer. We are running a two-center clinical trial of ART for bladder cancer where the primary aim of the trial is to reduce gastro-intestinal morbidity.

Materials/methods: The present study reports preliminary results on the first nine bladder cancer patients included in the ART trial. All patients received 60 Gy in 30 fractions to the bladder; in four patients the pelvic lymph nodes

received 48 Gy simultaneously. Patients were set-up by use of cone-beam CT (CBCT) guidance. In our ART strategy, the first five fractions were delivered using large margins - the bladder contours from the CBCTs acquired prior to the first four fractions were used to create a library of three plans corresponding to a small, medium and large size bladder. Dose was calculated by summation of the selected plans calculated on the planning CT and compared to standard RT plans involving population-based margins.

Results: The median rectal volume receiving 50 Gy or more was 5% [0-41%], compared to 17% [0-62%] if the patients had been treated with standard, non-adaptive RT. For the bowel cavity, the median volume receiving more than 45 Gy was 269 cm³ [83-486 cm³], compared to 337 cm³ [126-553 cm³] if not treated with adaptation. No grade 3-4 gastro-intestinal morbidity was observed and three out of nine patients had grade 2 (33%) compared to 44% for standard RT.

Conclusion: Daily adaptive plan selection in RT of bladder cancer results in a considerable normal tissue sparing, and is expected to reduce the risk of gastro-intestinal morbidity.

P33.03 Mette Marie
Fode

TOWARDS BIOLOGY ADAPTED STEREOTACTIC BODY RADIATION THERAPY (SBRT) OF LIVER METASTASES

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Background: SBRT is a non-invasive method for ablation for lung and liver tumors. By SBRT, a large radiation dose is delivered with high precision to the tumor with limited exposure to the normal tissue. The evidence of SBRT is primarily based on small retrospective studies.

Materials and methods: Project 1: A retrospective study including 400 patients will identify potential prognostic factors for improved stratification of patients considered for SBRT for metastases. The primary endpoints are local control, progression-free survival and treatment related morbidity. Project 2: This pilot study will focus on tumor hypoxia as a possible cause of resistance in SBRT. Information from this study may allow for hypoxic manipulation. 15 patients referred for surgical resection of colorectal cancer liver metastases will undergo FAZA PET/CT prior to surgery for evaluation of the degree of tumor hypoxia. FAZA PET/CT will post-surgery be validated by pimonidazole staining and histological examination. Project 3: A phase II trial will evaluate functional treatment planning of SBRT in liver metastases. In 28 patients galactose PET/CT will be used for treatment planning with the purpose to spare the best functioning parts of the liver.

Results: The study is ongoing.

Conclusion: The project focuses on biological aspects, which could have significant influence on the outcome of SBRT of liver metastases, which so

far have not been studied.

- P33.04 Alexander Juhl
Andersen MID-TERM EVALUATION OF DELAYED UNILATERAL BREAST
RECONSTRUCTION AFTER MASTECTOMY

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Objective: The number of breast reconstructive procedures is increasing, and according to Danish guidelines, all women having undergone mastectomy are offered a breast reconstruction. The aim of the current study was to assess the mid-term subjective and objective outcome of different reconstructive methods.

Patients and methods: A total of 135 women who underwent a delayed unilateral breast reconstruction after mastectomy in the Central Denmark Region between January 2005 and July 2011 were included in the study. Data were collected from the patient charts, a study specific questionnaire evaluating the satisfaction with the breast reconstructive procedure, and a clinical follow-up visit.

Results: 117 (87%) women answered the questionnaire and 64 (47%) participated in the follow-up visit. The median follow-up time was 3.8 years. Women reconstructed with abdominal based flaps were more pleased with their aesthetic outcome, compared to women who received reconstructions based on implants, latissimus dorsi or thoracodorsal flaps. The objective evaluation did not reveal any significant difference between the reconstructive methods. There were no significant differences in major complications between the groups. Complications did not have an impact on the subjective or objective aesthetic outcome.

Conclusion: Women reconstructed with an abdominal flap were significantly more pleased with the aesthetic result of their breast reconstruction. This was not supported by the clinical evaluation. No difference in the overall satisfaction with having received a breast reconstruction or the perceived gain in quality of life was found between the different reconstructive procedures.

- P33.05 Mette Eline
Brunbjerg IMMEDIATE BREAST RECONSTRUCTION WITH ACELLULAR DERMAL MATRIX

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Introduction: Every year, 4500 Danish women suffer from breast cancer. For many patients, the cancer diagnosis and the possible removal of one or both breasts results in major psychological stress. These side-effects to treatment are sought reduced with the use of external breast prosthesis or reconstruction of the breast. Breast reconstruction should be seen as part of the psychosocial as well as the functional rehabilitation process that

patients undergo during and after the final treatment of their breast cancer.

The aim of the study is to contribute to fast and complete rehabilitation of women undergoing breast reconstruction after surgical removal of the breast tissue. This is done by identifying the most optimal method for breast reconstruction comparing two methods for implant-based breast reconstruction. A one-stage method where the breast is reconstructed using a fixed size silicone gel implant and porcine acellular dermal matrix (ADM), and a two-stage procedure where an expander is later replaced with a fixed size silicone gel implant. Porcine acellular dermal matrix undergoes a process that eliminates all cellular elements from the tissue leaving only the intact extracellular matrix. The matrix provides a scaffold, promoting integration of the connective tissue thus being revascularized and repopulated by the patient's own cells.

Hypothesis: Immediate one-stage implant-based breast reconstruction using ADM is superior to immediate two-stage implant-based breast reconstruction regarding frequency of postoperative complications, aesthetic appearance and costs.

Method: 40 patients divided in two groups consecutively undergo surgery. Follow-up period is two years.

P33.06 Søren Haack

DIFFUSION WEIGHTED MRI ACQUISITION WITH HIGH ACCELERATION FACTOR FOR IMPROVING ACCURACY FOR USE IN RADIOTHERAPY PLANNING

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Introduction: Diffusion Weighted MRI (DW-MRI) has potential for monitoring treatment response during radiotherapy (RT). A major obstacle is the sensitivity of EPI based DW-MRI to B0 inhomogeneity leading to geometrical distortions. New coil technology allows the use of higher acceleration factors (AF). This study examines if DW-MRI with right-left (RL) phase-encoding (PE) and higher AF factors can reduce distortions compared to the standard anterior-posterior (AP) PE direction AF = 2.

Materials and methods: A geometrical phantom and 4 volunteers underwent MRI including DW-MRI ($b=0, 150$ and 600 s/mm²) using different AF and different PE. Distortions were evaluated by comparing the DW-MRI with T2 weighted images. Rod points in the phantom were identified in both image sets and difference in position was calculated. For volunteers the prostate was contoured and the Jaccard Similarity index (JI) used for comparison.

Results: Mean rod displacement was reduced from 3.99 ± 0.58 mm (AP, AF =2) to 2.21 ± 0.36 mm (RL, AF =4).

Volunteers: Mean JI was increased ($p=0.015$) from 0.58 ± 0.08 (AP, AF =2) to

0.74±0.06 (RL, AF=4). There was no significant difference (p=0.27) for the ADC for AP, AF =2 (ADC=1.41±0.02 10⁻³ mm²/s) and RL, AF =4 (ADC=1.38±0.06 10⁻³ mm²/s).

Conclusions: For phantom and in-vivo data, the RL DWI acquisition resulted in the smallest distortion at same AF. When RL acquisition is used, it is possible to increase the AF to 4. The study demonstrated that the ADC value is not significantly different for the two acquisition methods. It is demonstrated that geometrical distortion of pelvis DW-MRI can be reduced when optimizing the image acquisition relative to the coil design.

P33.07 Kennet Sønderstgaard Thorup IMPROVING DIFFUSION WEIGHTED MRI FOR QUANTITATIVE BODY TUMOUR CHARACTERIZATION. PARTIAL VOLUME CORRECTION AND ISOTROPIC IMAGING STRATEGIES

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In this PhD study, the first step will focus on understanding the basic limitations for quantitating diffusion and perfusion parameters based on body DWI. Particular focus will be placed on limitations related to motion and the most optimal way of minimizing these effects by using different scan parameters.

Materials and methods: To evaluate the impact of motion, an MRI diffusion model is being developed. The model is based on the 4d extended cardiac torso phantom, and can simulate motion due to both breathing and heartbeat. The model makes it possible to scale multiple values like: breathing frequency, signal to noise ratio (SNR), tumor size, uniformity, and placement. It is also possible to test the effect of different scan parameters, such as navigated, cardiac trigger, resolution, TE and TR.

Results: Initial results show that the model is delivering a good approximation to real life scan results in healthy volunteers. Decreasing the SNR gradually and looking at the root mean square error of the intravoxel incoherent motion (IVIM) parameters showed that the pseudodiffusion (D*) is the most sensitive parameter and requires a SNR over 20 to be reliable. The most stable was the diffusion coefficient (D), which had small variation even down to 10 SNR. The perfusion fraction (f) was very stable until 20 SNR, but was still acceptable with a SNR of 10.

Perspectives: Quantitative knowledge of motion influence on accuracy of quantitative DWI parameters will be the basis for further improvement of quantitative tumor characterization. The model will be used to optimize scan parameters for the remaining parts of this PhD study.

P33.08 Susanne Rylander THE POSSIBILITY TO REDUCE RECTAL DOSE BY REMOVING THE ULTRASOUND PROBE PRIOR TO DELIVERY OF HIGH-DOSE-RATE BRACHYTHERAPY IN PROSTATE CANCER

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Purpose: Transrectal ultrasound (US) is the standard imaging modality for High-Dose-Rate (HDR) brachytherapy (BT) in prostate cancer patients. In order to preserve the same patient set-up as during the US planning, the treatment is typically delivered with the probe positioned in the rectum. However, it is an open question whether the removal of the probe before delivery may reduce rectum dose. The purpose of this study was to compare the rectum dose for when the probe is present and not present in the rectum during delivery.

Material and methods: T2-weighted (T2W)-MRI based BT treatment planning was performed after US guided needle implantation for 18 fractions of BT in 9 prostate cancer patients. BT was delivered in 2 fractions of each 8.5 Gy preceded by 46 Gy given in 23 fractions of external beam radiotherapy. T2W-MR- and US images were co-registered based on the BT needle implant. The same optimized treatment plan, based on MRI contouring, was applied on both MR- and US images. Rectal doses were estimated for the two rectum scenarios, as well as the rectum-prostate separation evaluated at base plane, reference plane and apex plane.

Results: The median rectum-prostate separation increased by removing the probe by 7 mm (2-14) at the base plane and 2 mm (0-8) at the apex plane. At the reference plane, no difference was observed. In the scenario where the probe was removed, the mean rectum doses D_{5cc} , D_{2cc} and $D_{0.1cc}$ were lower during BT delivery (decrease of 0.7 Gy (max 1.6 Gy), 0.7 Gy (max 1.5 Gy) and 1.1 Gy (max 4.6 Gy)), respectively).

Conclusions: The results implied that the dose to rectum can be reduced by removing the probe prior to the delivery of BT.

P34.01 Morten
Nørgaard
Andersen

MACROPHAGES AND THERAPY RESISTANCE IN MULTIPLE MYELOMA - NOVEL TARGETS FOR TAILORED THERAPY

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Background: Macrophage infiltration is associated to poor prognosis in most human cancers, and "tumor-associated macrophages" (TAMs) can promote tumor growth by performing several pro-tumor functions, e.g. suppression of adaptive immunity and promotion of chemotherapy resistance. TAMs are phenotypically anti-inflammatory, but they are also highly plastic cells, and can be switched to a pro-inflammatory phenotype by appropriate stimuli. Importantly, TAMs express high amounts of the scavenger receptor CD163, which is solely expressed on cells of the monocyte/macrophage-lineage. CD163 can be shed from the cell surface and become a soluble protein (sCD163), which can be measured in serum.

Preliminary results: We examined serum values of sCD163 in 104 multiple

myeloma (MM) patients. Serum sCD163 was associated to established prognostic factors, and was itself an independent prognostic marker of overall survival (HR=1.82, p=0.01). Moreover, in a co-culture model with human MM cells, TAMs were able to protect MM cells from apoptosis induced by melphalan.

Objectives and experiment plan: We will characterize the interplay between cancer cells and TAMs in MM, in vitro and in vivo, especially concerning mechanisms responsible for the chemo-protective effect of TAMs. Material from patients and cell cultures will be analysed to identify favourable targets within TAMs. The aim is to abolish the chemo-protective effect of TAMs, by delivering an inhibitor of potential targets, e.g. STAT3, specifically to the TAMs, using CD163 as a gateway in a liposome-based delivery system. The advantage from targeting TAMs with tailored therapy will be evaluated in vitro, as well as in a mouse model.

- P34.02 Maria Cathrine
Corneliussen
Vest Schmidt HYPODONTIA AND OVARIAN CANCER - THE CONNECTION BETWEEN DENTAL AGENESIA AND EPITHELIAL CANCERS, ESPECIALLY OVARIAN CANCER

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Aim: To examine possible genetic factors causing a predisposition to the development of epithelial cancers. This could aid us in the identification of high-risk families and thereby to offer them diagnostic examinations as a means of screening and thus diminish their risk of developing cancer.

Introduction: Ovarian cancer is known as the 'silent killer'. A tumor can reach a substantial size before causing any symptoms, which is one of the reasons why ovarian cancer is often diagnosed too late with considerably negative effect on the prognosis. A small American study showed a surprising connection between hypodontia and ovarian cancer. A similar connection has been shown to colon cancer. Our hypothesis is that this is caused by genetic mutations.

Materials and methods: To confirm the connection between hypodontia and ovarian cancer, all women referred to the Departments of Obstetrics and Gynecology in Aarhus and Copenhagen, who are given the diagnosis ovarian cancer, will be asked to fill in a validated questionnaire regarding their dental status, as will a matched control group. We will distribute the same questionnaire to already known families with genetic predisposition to cancer (HBOC and HNPCC) to see if this confirms a connection.

A sample of blood from high-risk families (suffering from ovarian cancer and hypodontia) will be reserved for later genetic analysis. This will be screened for relevant target genes based on the current literature.

- P34.03 Jill Rachel Mains DIFFUSION-WEIGHTED MRI (MR-DWI) AND DYNAMIC CONTRAST-ENHANCED CT (DCE-CT): A COMPARATIVE PILOT STUDY

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Objectives: A pilot study to elucidate correlations between MR-DWI and DCE-CT using renal cell tumors and metastases.

Methods: 8 patients in a phase II trial with immunotherapy and bevacizumab and with technically sufficient scans in both modalities were included. DCE-CT and MR- DWI scans were performed at baseline, 5 and 10 weeks using Philips iCT or Brilliance 64 CT-scanners and a Philips Achieva 3T MR-scanner. Analysis was performed blinded to treatment group. Perfusion (P, ml/min/100 ml) and blood volume (BV, ml/100 g) were calculated using a Philips Extended Brilliance workstation v. 4.5.2 (max slope method). MR-DWI was obtained using a standard single-shot EPI sequence during free breathing. B-values of 0, 10, 30, 50, 100 and 1000 were obtained. Monoexponential fitting was used to calculate ADC_{low} (b-values 0, 10, 30 and 50) and ADC_{high} (b-values 100 and 1000). Perfusion fraction (Fp) was calculated as $(SI_{ADC_{low}} - SI_{ADC_{high}}) / SI_{ADC_{low}}$ where SI denotes signal intensity at B=0. Osirix v. 5.6 and Microsoft Excel software were used.

Results: Our analysis using mixed-models linear regression and log-transformed data showed a significant correlation between ADC_{low} and BV ($p=0.040$) as well as between Fp and BV ($p=0.018$).

Conclusion: In this preliminary study, a significant correlation was found between DCE-CT and low b-value MR-DWI. Larger studies are needed to verify these findings.

P34.04 Ninna
Aggerholm-
Pedersen

THE INFLUENCE OF HYPOXIA ON SARCOMA PATIENTS' RESISTANCE TO CHEMOTHERAPY AND IRRADIATION THERAPY

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Background: The incidence of sarcoma is about 300 in Denmark each year, and the prognosis for these patients is poor. One reason is that these tumours have a poor response to chemotherapy and radiotherapy. Our Department has shown that hypoxia inside the tumors is a poor prognostic factor in sarcoma, and a hypoxia induced gene profile (HIGP) has been identified in head and neck cancer. The aim of this study is to identify hypoxia in human sarcoma by identifying a HIGP and to investigate the impact of this profile on OS and response to treatment.

Material and methods:

Study I: An already validated tumor HIGP of head and neck cancer will be explored in diagnostic biopsies from STS patients (cohort 1; 30 patients) by using qPCR and microarrays. The HIGP obtained from these result will be correlated to oxygen tension measurement (from the tumor) performed on

each patients.

Study II: cohort 2: A cohort of 60 STS patients selected from the sarcoma database are matched to cohort 1 according to patient characteristic and tumor histology. The presence of the HIGP will be correlated to the OS of these patients.

Study III: Validation of the HIGP is done in an independent data set. Cohort 3: A cohort of 600 patients selected from the sarcoma database according to tumor histology and treatment modality. Cohort 3 are tested for HIGP (by qPCR) and correlated to response to chemotherapy and OS.

Conclusion/perspectives: The HIGP found in head and neck cancer may be a universal classifier, which can be transferred to other cancer types. If a HIGP correlates with overall survival or is predictive in regard to response to treatment in STS, it could be the target for development of new treatment modalities.

P34.05 Mary Nguyen
Nielsen

PROSTATE CANCER, COMORBIDITIES AND RISK OF VENOUS
THROMBOEMBOLISM

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Background: We examined the overall risk of VTE among prostate cancer (PC) patients and the impact of comorbidities and biologic (causal) interaction on risk of VTE.

Methods: This was a nationwide registry-based matched cohort study. PC patients diagnosed in the period 1995-2010 were identified from the Danish Cancer Registry and the Danish National Registry of Patients. Each PC patient was matched to 5 cancer-free men, by age and comorbidity level (Charlson Comorbidity Index). Follow-up was from PC diagnosis until first-time VTE, death, emigration, or end-of-follow up (31-Dec-2011). We used a competing risk model to estimate the 5-year cumulative incidence of VTE in the PC and matched cohorts. Cox proportional-hazards regression was used to estimate adjusted Incidence Rate Ratios (IRR). Finally, we computed the Interaction Contrast (IC) and the proportion of the 5-year cumulative incidence of VTE that could be attributed to biologic interaction. The IC is the "departure from the risk difference, contrasting from what would be expected if no interaction were present" (Rothman, Modern Epidemiology).

Results: We included 43,084 PC patients and 208,555 cancer-free men. The 5-year cumulative incidence of VTE was 3.0% for PC patients and 1.5% for the matched cohort. The VTE rate per 1000 person-years was 6.0 (95% CI 5.6, 6.4) for PC patients and 3.1 (95% CI 2.9, 3.2) for the matched cohort. The interaction between PC and comorbidity levels accounted for 5% of the 5-year cumulative incidence of VTE.

Conclusion: PC patients have an increased risk of VTE compared with cancer-free men. However, biologic interaction between PC and comorbidities is minimal.

P34.06 Anne Wandler THE BIOLOGICAL AND PROGNOSTIC SIGNIFICANCE OF MICRORNAS IN MELANOMA

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Background: Melanoma is a potentially aggressive cancer with an aggressive increase in incidence in Denmark as well as many other countries. The diagnosis and prognosis of melanoma are based on histopathology and immunohistochemistry. MicroRNAs (miRNAs) are short molecules known to regulate many biologically important pathways primarily by limiting the translation of mRNAs. MiRNAs are involved in the development and progression in a variety of cancers, including melanoma. By in situ hybridisation (ISH) the origin of miRNAs in tissue can be visualised. We aim to investigate the biology of miRNAs in melanoma formalin-fixed paraffin embedded (FFPE) tissue and to explore the potential use of miRNAs as prognostic and diagnostic biomarkers by ISH.

Hypothesis: 1. Melanoma and benign nevi differ in miRNA expression in routine FFPE tissue, 2. MiRNA ISH can distinguish nevi from melanoma, 3. ISH and immunohistochemistry can visualise deregulated miRNAs and their cellular targets and 4. Deregulated miRNAs in melanoma correlate to prognosis.

Materials and methods: 1. RNA from FFPE tissue will be submitted to a miRNA array profiling to detect miRNAs that are deregulated in melanoma, 2. Array data will be validated by PCR and ISH on a new tissue cohort, 3. A large cohort of melanoma tissue has been established as tissue microarrays and upon these the expression of the deregulated miRNAs will be examined by ISH. An association of miRNAs to potential molecular targets will be evaluated through co-localisation with immunohistochemistry on the same cohort and 4. The association between deregulated miRNAs and clinical outcome will be investigated in the tissue microarray cohort.

P34.07 Kristine Raaby INVESTIGATING THE ROLE OF LUNG FIBROBLASTS IN NON-SMALL CELL LUNG CARCINOMAS
Jakobsen

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Background: Cancer-associated fibroblasts (CAFs) have been shown to be a predominant component of the tumor-stroma in different types of cancer including Non-small Cell Lung Carcinomas (NSCLC). It has been proposed that CAFs can influence cancer cells by upregulating mesenchymal markers through TGF- β 1 and by activating the EGFR system. The exact role

of CAFs in NSCLC is still unclear, as is the mechanism by which CAFs are generated.

Aim: To investigate communication between NSCLC cells and CAFs in different experimental settings, with focus on exosomes in inter-cell signaling. As a model system we have chosen to work with the lung adenocarcinoma cell line H1568 and the lung fibroblast cell line Wi-38.

Methods: In-direct co-culture: Cancer cells are grown at the bottom of a 6-well plate and fibroblasts grown on a 1 mm pore insert placed in the well, but without direct contact with the cancer cells. Cancer cells are harvested and analyzed for gene expression profiles.

Addition of fibroblast-derived exosomes: Wi-38 cells are grown for 2 days in medium with exosome-depleted serum. From the medium, we isolate exosomes using ExoQuick TC (Systems Bio). The exosome pellet is added to the medium of H1568 cells grown in a 6-well plate, and after a time course incubation cancer cells are harvested and analyzed for gene expression profiles.

Perspectives: We envisage that the used methodology will generate novel basic knowledge concerning the interplay between cancer and fibroblast cells in the tumor environment with consequences for tumor cell proliferation and metastasis.

P35.01 Ditte Louise
Egeskov
Munkedal

AN AUDIT ON THE SURGICAL QUALITY ON COLON CANCER SPECIMENS

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Background: Laparoscopic colon cancer surgery (LAP-CCS) was implemented at Aarhus University Hospital in 2008 for right and left side tumors only. Same year the technique of complete mesocolic excision was introduced.

Aim: To evaluate whether LAP-CCS was associated with any changes in the distance between the tumor and the closest arterial tie and the distance between the nearest bowel wall and the same tie compared to open surgery.

Method: The study contains a consecutive series of 162 patients, who had undergone curative surgery (83 laparoscopic and 79 open) at Aarhus University Hospital in the period of 2008-2011. The measurements were done by using tissue morphometry on specimen pictures.

Results: With LAP-CCS, the distance between the tumor and the tie was significantly increased with 26.8 mm (15.1mm; 38.4mm) (p-value<0.001) and the distance between the nearest bowel wall and the tie with 26.9 mm (16.7mm; 37.2mm) (p-value<0.001) in multivariate analysis including age, gender, BMI, right or left tumor location, tumor stage, and year of surgery.

Conclusion: With LAP-CCS, it is possible to obtain at least as long a distance to the arterial tie as with open surgery at Aarhus University Hospital. This

study supports that LAP-CCS can be beneficial in the effort to reach a high tie.

P35.02 Susanne Hass CORTICAL EVOKED POTENTIALS IN RESPONSE TO RAPID BALLOON DISTENSION OF THE RECTUM AND ANAL CANAL

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Background: Ano-rectal sensory function is crucial to the continence mechanism. However, neurophysiological studies of the ano-cerebral-axis are hampered by a paucity of methods. Rapid balloon distension (RBD) has been introduced to describe the cerebral response to rectal distension. We aimed at recording cortical evoked potentials in response to RBD of both the rectum and the anal canal and tested within-day reproducibility of the latter.

Methods: 19 healthy women underwent standard clinical ano-physiological evaluation. Afterwards, they received 30 RBDs in the rectum and the anal canal at intensities corresponding to sensory and unpleasantness thresholds. In the anal canal, stimulation at unpleasantness level was repeated after 4 min. Evoked potentials were recorded on an electroencephalographic cap.

Results: Repeated stimulation of the anal canal generated evoked potentials with similar latencies but smaller amplitudes compared to those of the rectum. Reproducibility was lower than what has been reported from the rectum and alignment to the N2 component revealed latency jitter. Consequently, the best feature was N2P2 peak-to-peak amplitude with an intra-class correlation coefficient (ICC) of 0.7 and a coefficient of variation (CV) of 18 %. However, the spectral content of the single sweeps was reproducible with ICCs for all bands > 0.8 and corresponding CVs < 7%.

Conclusions: Cortical potentials evoked from the rectum can be reliably evaluated by visual inspection and averaging, but electrophysiological evaluation of the tonic anal sphincters is challenged by latency jitter. CEPs proved reproducible, when analyzing them through single sweep spectral band analysis.

P35.03 Lise Hald
Nielsen HYPERTENSION AND URINE PROTEASE ACTIVITY IN PRE-ECLAMPSIA

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Pre-eclampsia (PE) is a common disorder of pregnancy that complicates 4-7% of all pregnancies. It is a serious condition with acute proteinuria and hypertension. PE involves a substantial risk of low birth weight and is a frequent cause of iatrogenic delivery of the preterm infant.

Pathogenesis of pre-eclampsia is unknown but is believed to be initiated by the placenta. The primary placental disorder results in renal glomerular injury with endothelioses and subendothelial fibrin deposits and a defective barrier for protein. Established PE is associated with paradoxical suppression of the renin-angiotensin-aldosterone system (RAAS). Suppression of the RAAS begins at the same time with the occurrence of PE and correlates with severity.

We believe that a sodium channel (ENaC) in the kidneys is activated by plasmin found in the urine of patients with preeclampsia. Activation of ENaC causes increased influx of sodium and is responsible for the state of salt retention seen in preeclampsia. This will increase blood pressure and secondarily suppress RAAS by a negative feedback mechanism. We will test this hypothesis through an intervention study with a low-sodium vs. a high-sodium diet. The study may offer an explanatory model for a number of key pathophysiological observations in established preeclampsia.

Since microalbuminuria in pregnant pregestational diabetes patients predicts the development of preeclampsia, we believe that this is also due to plasmin loss from plasma to urine. Thus we want to test the relationship between measurable plasmin / plasminogen in the urine early in pregnancy and the development of preeclampsia in patients with type 1 diabetes.

P35.04 Marie Krarup
Schrøder

THE EFFECT OF GENDER ON ANTIDIURESIS

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The discovery of gender and age differences in the occurrence of various illnesses has sparked an interest in gender differences in other physiological systems. To date a gender difference in the V2 receptor (V2R) mediated antidiuretic function has been reported inconsistently. The sparse evidence suggests a greater renal sensitivity to the antidiuretic hormone Arginine Vasopressin (AVP) in women due to a greater response at the V2R level. The difference may develop or increase with age and cause elderly women to be more prone to side effects to treatment with the synthetic AVP analog dDAVP. The aim of our studies is to investigate the occurrence and cause of a gender difference in V2R function.

Three studies have been designed to elucidate the various aspects of a gender difference. In study 1, four age groups are subjected to low dose graded infusion of dDAVP. Antidiuretic response is evaluated by correlating Urine Osmolality and Volume to Plasma levels of dDAVP. In study 2, V2R are quantified using a PET-CT scanner. A tracer specific to the V2R in the kidneys will be developed in collaboration with the department of nuclear

medicin, Aarhus University hospital. In study 3, the genetic expression of V2R mRNA is analyzed. V2R mRNA will be quantified in renal cells exfoliated into the urine and compared to the expression of household genes known to display little or no gender difference.

Our hypothesis is that women are more sensitive to the actions of AVP and dDAVP. The increased sensitivity is mediated by a greater expression of the V2R gene. The greater V2 receptor gene expression causes women to have a greater renal density of V2R.

P35.05 Jacob Gamst ATRIAL FIBRILLATION AND RISK OF ARTERIAL THROMBOEMBOLISM FOLLOWING HOSPITALIZED PNEUMONIA: A POPULATION-BASED COHORT STUDY

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Background: The risk of arterial thromboembolic events (ATE) is up to 3-fold increased in the weeks following pneumonia. It is unknown if the risk is higher in patients with atrial fibrillation (AF).

Objectives: To examine the impact of AF and related treatment with vitamin K antagonists (VKA) on the risk of ATE following pneumonia.

Methods: We included all adults with first-time pneumonia hospitalization in northern Denmark from 1997 through 2012. Patients with a diagnosis of AF within 5 years preceding pneumonia admission were identified. In patients with and without AF, we computed the cumulative incidence of ATE within 30 days of admission with death as a competing risk. By Cox regression we compared the risk of ATE in AF patients to that in non-AF patients, adjusting for age, heart failure, hypertension, diabetes, prior stroke, vascular disease, and sex. Among patients with AF, we further compared users to non-users of VKA by Cox regression.

Results: Of the 88,315 included patients, 10.1% had a prior diagnosis of AF. The cumulative incidence of ATE within 30 days after pneumonia was 5.2% in AF patients and 3.6% in patients without AF. The corresponding adjusted hazard ratio (aHR) associated with AF was 1.06 (95% confidence interval (CI): 0.96 - 1.18). Among pneumonia patients with AF, an aHR for ATE of 0.74 (95%CI: 0.61 - 0.91) was observed when comparing users to non-users of VKA.

Conclusion: After confounder adjustment, AF was not associated with increased risk of ATE following hospitalized pneumonia. Preadmission use of VKA reduced the risk of ATE substantially in AF patients.

P35.06 Baris Isak LASER-EVOKED CUTANEOUS SILENT PERIODS IN PATIENTS WITH CHEMOTHERAPY-INDUCED POLYNEUROPATHY

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Background: Laser evoked potentials (LEPs) are one of the most reliable tools that assess of peripheral and central nociceptive pathways following the stimulation of A-delta (A δ) and C fibres. Whereas, cutaneous silent period (CSP) is a brief pause in voluntary contraction following the stimulation of peripheral A δ and slow A-beta afferents. CSPs can be evoked with laser (Ls-CSPs) or electrical stimulation (EI-CSP).

Objective: In this study, we wanted to see if Ls-CSPs could identify the patients with distal polyneuropathy.

Methods: Twelve women with distal polyneuropathy due to chemotherapy were compared with 12 age- and sex-matched healthy subjects. Nd:YAP laser was used to evoke Ls-CSPs, and LEPs. EI-CSPs, Ls-CSPs, and LEPs were obtained after palmar stimulation of the right median sensory nerve. We recorded CSPs from the right APB muscle and LEPs from the left temporo-parietal cortex. The CSPs were evaluated based on latencies and durations. LEPs were evaluated with N1, N2, P2 latencies, N1 amplitudes (baseline to peak), and N2P2 amplitudes (peak to peak).

Results: The N2P2 amplitudes were lower ($36.69 \pm 12.71 \mu\text{V}$ vs. $47.34 \pm 14.45 \mu\text{V}$, $P = 0.0488$), EI-CSP durations were longer ($29.83 \pm 16.04 \text{ ms}$ vs. $27.9 \pm 9.79 \text{ ms}$, $P = 0.002$), and Ls-CSP durations were shorter ($9.66 \pm 10.83 \text{ ms}$ vs. $20.5 \pm 8.01 \text{ ms}$, $P = 0.004$) in the patient group. The Ls-CSP durations were more sensitive (50%) than LEP-N2P2 amplitudes (25%) and EI-CSP durations (8.3%).

Conclusions: The Ls-CSPs were the better than the other tests to identify the patients with distal polyneuropathy since they evaluate mainly the peripheral A δ -fibres starting from the free nerve endings.

P35.07 Line Pedersen NO AND COX PRODUCTS ARE INVOLVED IN HYPOXIA-INDUCED DILATATION OF RETINAL VESSELS

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Background: Retinal hypoxia with consequent changes in the blood perfusion is a central feature in the most common vision threatening diseases. The aim of the study was to examine the effects of inhibiting cyclo-oxygenase (COX) and NO-synthesis on hypoxia-induced relaxation of retinal vessels in humans.

Methods: In twenty healthy persons aged 20-55 years, the resting diameter and the diameter response secondary to isometric exercise and flicker stimulation of retinal vessels were studied using the Dynamic Vessel Analyzer (DVA) before and during breathing of a hypoxic gas mixture. The

examinations were performed before and during intravenous infusion with the NOS inhibitor L-NMMA and were repeated on a second day after administration of the COX-inhibitor diclofenac eye drops.

Results: Hypoxia induced a significant increase in the resting diameter of arterioles and venules ($p < 0.0001$) which was reversed by the infusion of L-NMMA. Diclofenac significantly reduced arteriolar contraction induced by isometric exercise ($p = 0.04$), whereas hypoxia significantly reduced L-NMMA induced contraction of retinal venules ($p = 0.0005$). Flicker-induced dilatation of retinal arterioles was increased by L-NMMA ($p < 0.0001$) whereas dilatation of retinal venules was significantly reduced during hypoxia and was reversed by L-NMMA ($p < 0.0001$).

Conclusion: Diameter changes of retinal vessels during hypoxia are influenced by inhibiting the synthesis of NO and COX products. This may point to new treatment strategies to diseases characterised by retinal hypoxia and disturbances in retinal perfusion.

P35.08 Sanne Shiroma Harsløf PAIN, QUALITY OF LIFE, ADHESIONS AND RECURRENCE AFTER LAPAROSCOPIC VENTRAL HERNIA REPAIR: A CLINICAL, RANDOMIZED, PROSPECTIVE, DOUBLE-BLINDED STUDY OF THREE TYPES OF MESH FIXATION

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Objectives: The aim of this study is to test three types of mesh fixation in laparoscopic ventral hernia repair regarding immediate and long-term effects on pain, quality of life, adhesion formation and recurrence.

Hypothesis: Non-traumatic fixation of mesh will cause less pain than any other type of fixation.

Design: A clinical randomized, prospective, double-blinded study

Participants: 75 patients with ventral hernias between 2 cm -7 cm. Patients will only be enrolled if otherwise suitable for surgery.

Interventions: Laparoscopic ventral hernia repair with implantation and fixation of mesh.

Randomization between three types of mesh fixation will be performed:
Tissue glue (Glubran IITM) - 25 patients
Non-absorbable traumatic fixation (ProTackTM) - 25 patients
Absorbable traumatic fixation (SecurestrapTM) - 25 patients

After surgery, patients will participate in the following at different time points:

Fill out questionnaires (Dolo TestTM, Pain Diary, SF-36TM, Carolinas Comfort ScaleTM)

Clinical examination

MR scan (once at 24 months)

Follow-up visits at: 1 month, 6 months, 12 months and 24 months.

Measures:

Primary endpoint: Pain on the 2nd postoperative day.

Secondary endpoint: Pain (at other time points than above), quality of life and recurrences.

Perspectives: This study will be the first to compare the effects of three types of mesh fixation on the central endpoints pain and recurrence, in a randomized, prospective design. The results may provide an evidence base for selection of method of mesh fixation.

P36.01 Christina
Kjærgaard
Rasmussen

INTER-OBSERVER VARIATION IN DIAGNOSING ADENOMYOSIS USING TWO- AND THREE-DIMENSIONAL TRANSVAGINAL ULTRASOUND

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Objectives: To investigate inter-observer variation (IOV) in identification of adenomyosis by two- and three-dimensional (2D and 3D) transvaginal ultrasonography (TVS). To evaluate improvement in agreement between experienced and inexperienced sonographers during the time of learning.

Methods: 103 premenopausal women scheduled for hysterectomy or transcervical resection of the endometrium (TCRE) were enrolled and divided into three groups: A (first 34), B (next 34) and C (last 35). An experienced and an inexperienced sonographer independently performed 2D and 3DTVUS examinations. Pattern criteria for adenomyosis were systematically evaluated during 2DTVUS. Six months after examination, adenomyosis was again evaluated using stored 3DTVUS including junctional zone thickness (JZt: $\geq 12\text{mm}$) and irregularity (JZdif: maximum-minimum thickness $>5\text{mm}$) in the first 70 patients.

Results: 2DTVUS diagnosis of adenomyosis showed substantial agreement (κ (CI): 65(50-79)) in 103 patients. Presence of anechoic lacunae (AL) and/or myometrial cysts (MC) had substantial agreement, while criteria of heterogeneity (HG), asymmetric corpus myometrium (ACM) and linear striations (LS) had fair agreement. There was a steady increase in agreement for the diagnosis of adenomyosis in group A, B and C (κ (CI): 47 (18-76), 63 (37-89) and 82 (62-100)). 3DTVUS reached moderate agreement (κ (CI): 46(23-68)) in the first 70 patients. Presence of AL and/or MC had moderate agreement, while HG, ACM and LS had slight-fair agreement. There was fair agreement in evaluation of JZt and JZdif.

Conclusions: In a standardized diagnostic set-up, IOV was improved to substantial levels after 68 examinations. 3DTVUS did not improve IOV.

P36.02 Ditte Lou
Langhoff
Gantriis

A CASE-CONTROL STUDY OF THE HOME ENVIRONMENT AMONG 7-YEAR OLD OFFSPRING OF PARENTS WITH SCHIZOPHRENIA OR BIPOLAR DISORDER

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Background: Several high-risk studies and meta-analyses indicate that an inadequate home environment may pose an increased risk for later development of psychopathology in children of parents with schizophrenia (sz) and bipolar disorder (bd). However, there are only few studies of the home environment among children at high risk and these studies often lack methodologically strong designs.

Design: This is a case-control study comprising a cohort of 500 children at age 7 with one, two or none of the parents registered with sz or bd. The cohort is established using Danish National Registers. Parents with sz or bd are matched with controls on gender and geography. Researchers are blind to the diagnosis of the parents.

Objective: To characterize the home environment among children at familial high risk for developing psychopathology with the hypothesis: Increasing levels of psychopathology in parents with sz or bd is associated with increasing levels of inadequate home environment.

Measurements: Level of support and stimulation in the home are assessed with a semi-structured interview with the child and the parent (MC-HOME). The parent's relation to the child is explored through the description of emotions concerning the child (R-FMSS). Level of daily life stress for the child is measured by a questionnaire (modified version of DLSS). The child's exposure to parental mental illness is assessed as the number of months the child has lived with the ill parent and visualized on a time line that is filled out with all parents.

Current status: Data collection was commenced in December 2012 and is ongoing. 138 families are included and 77 have completed assessment.

P36.03 Jennie Maria
Christin Strid

ULTRASOUND/MAGNETIC RESONANCE IMAGE FUSION GUIDED
LUMBOSACRAL PLEXUS BLOCK

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Introduction: Ultrasound (US) guided lumbosacral plexus block (Supra Sacral Parallel Shift, SSPS) offers an alternative to general and spinal hip surgery anaesthesia and perioperative analgesia including opioids in elderly patients with severe comorbidity.¹ The complex anatomy of the lumbosacral region decreases the accuracy of the block, but it may be improved with guidance by image fusion of magnetic resonance (MR) and US.²

Aim: We aim to estimate the effect and the distribution of lidocaine after SSPS guided by US compared to SSPS guided by US/MR image fusion with neurological mapping, pharmacokinetic assays, and MR visualization. We

hypothesize the success rate to be highest for US/MR image fusion guidance.

Methods: We will include 24 healthy volunteers in a double-blinded random controlled trial with crossover design. Supine MR datasets will be acquired and uploaded in an advanced US system. All volunteers will receive SSPS blocks with lidocaine guided by US and by US/MR image fusion one week apart. Bedside US/MR image fusion will allow real-time 3D guidance of the needle. Block of the L2-S1 nerves, plasma lidocaine, and MR visualization of lidocaine will be estimated.

Perspectives: US/MR image fusion guided SSPS may provide a safe and effective alternative to traditional anaesthesia and minimize the need for opioids in fragile hip surgery patients.

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P36.04 Rune Wilkens INTESTINAL PERFUSION IMAGING IN CROHN'S DISEASE (CD)

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CD is a chronic inflammatory bowel disease that often evolves in puberty or adolescence. Symptoms of CD depend on gastrointestinal disease location, severity and extra intestinal involvement. The diagnosis is based on clinical symptoms, endoscopy, medical imaging and histology. European guidelines suggests that magnetic resonance imaging enterography (MRE) together with ultrasound (US) are the most suitable cross sectional imaging modalities for assessing disease extent, severity and activity due to specificity, sensitivity and non radiation technique. Ultrasound is furthermore widely assessable, non-expensive, patient friendly and thus easily repeatable. Increased perfusion and neovascularization is known to be a crucial component of inflammation and thus active disease.

The aim is to investigate the perspectives of ultrasound in CD and compare US with MRE for measuring intestinal perfusion in the diseased bowel segment. We do so in 3 sub studies; 1) Direct comparison of time intensity curve parameters obtained in Contrast Enhanced US (CEUS) and dynamic MRE for quantification measurements. 2) The same procedures will be investigated preoperatively in patients with CD referred for elective surgery with histology analyses of the surgical specimens serving as gold standard. 3) Comparing ultrasound Elastography prior to surgery and compare the findings with biomechanical testing (impedance planimetri) and results will also be correlated to degree of collagen in the intestinal wall.

Bowel wall perfusion can hopefully add further details on disease activity and is easily repeatable for evaluation over time for assessing a flare or follow the success of medical treatment.

P36.05 Mads Skipper THE LINKS BETWEEN ORGANIZATIONAL, GROUP, AND INDIVIDUAL MEDICAL POSTGRADUATE WORKPLACE LEARNING IN PEDIATRIC DEPARTMENTS

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Introduction: Studies have shown how doctors learn in the workplace. However research is needed to answer, how organizational structures such as training programs and work organization influences actual clinical workplace learning.

Aim of study: To elucidate the significance of work organization, to adapt and develop training to the reality of the clinical departments.

Research question: What is the explanatory link between:

- a) Learning culture and the organization of work
- b) Group of junior learners and senior doctors
- c) Individual learners?

How do senior doctors' espoused theories of learning influence their way to organize and plan the medical training of junior doctors (theories in use)?

Studies:

- 1) Thematic literature review regarding workplace learning and organization in postgraduate medical education with a focus on multi-level research that links individual, group, and organizational learning.
- 2) Thematic analysis of qualitative data from "3-hour meetings" regarding the educational environment in the departments at Aalborg University Hospital from 2006 to 2012.
- 3) Ethnographic field study, to study the underlying norms, policies, and objectives of consultants responsible for postgraduate medical education and junior doctors.
- 4) Exploratory focus group study with consultants responsible for medical education and junior doctors.

Perspective: The study will contribute to the budding literature on linking individual learning with group, community of practice, organization and political systems, by focusing on the perceived and observed reality in relation to learning opportunities in daily clinical practice and on barriers in the organization.

P36.06 Katrine Fuglsang HIGHLIGHTS ON RECURRENCE AFTER SURGERY DUE TO CERVICAL CANCER

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Objective: After surgery due to cervical cancer, women are offered to attend a follow-up program 10 times during five years with the purpose for early diagnosis of recurrence. The aim of this study is to evaluate the follow-

up program, which has remained unchanged for 20 years even though reminding and concerning women, who we consider healthy after surgery.

Methods: A retrospective longitudinal study of women attending follow-up program after surgery due to cervical cancer at the Department of Gynecology and Obstetrics, Aarhus University Hospital.

524 patients were identified from 1996 to 2011 with the diagnosis of cervical cancer combined with a surgical procedure. From the national pathological database and patient files information was extracted. Information was stored in Epidata. Associations were calculated using stratified analysis and logistic regression.

Results: 133 (25%) women of 524 needed further treatment. 45 (12%) women of 391 treated by surgery had recurrence. Symptoms of recurrence and non-regional recurrence were negatively associated with survival. Diagnosis of recurrence at a scheduled control was positively associated with survival. Only 4 (9.5%) cases of recurrence were diagnosed by PAP-smear.

Conclusions: Evaluation on the follow-up program is valuable and might inspire to adjustments. By tradition a gynecological examination is processed along with a cytological test from the top of the vagina and a vaginal exploration. The results imply failing success in diagnosing recurrence by cytological test and a tendency for poorer outcome for patients debuting with symptoms in between scheduled follow-up visits.

P36.07 Zhanyuan Kang TNF-ALPHA AND IL-17A-INDUCED S100A7 EXPRESSION IS REGULATED BY A P38 MAPK AND ERK1/2 DEPENDENT MECHANISM IN CULTURED HUMAN KERATINOCYTES

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The antimicrobial peptide S100A7 is known to be overexpressed in lesional psoriatic skin and is believed to play a role in the pathogenesis of psoriasis. However, little is known about the signalling pathways involved in the regulation of S100A7 expression. Using quantitative PCR analysis we demonstrated that stimulation with TNF α and IL-17A in combination resulted in a significant and synergistic induction of S100A7 mRNA and protein. The TNF α and IL-17A mediated induction of S100A7 mRNA and protein was mediated by a p38 MAPK and ERK1/2 dependent mechanism, as demonstrated by the use of p38 MAPK and ERK1/2 inhibitors. Furthermore, we found that TNF α and IL-17A enhanced p38 MAPK but not ERK1/2 phosphorylation. Taken together, our results demonstrated that the TNF α /IL-17A-induced S100A7 mRNA and protein expression were mediated by a p38 MAPK and ERK1/2 dependent mechanism in cultured human keratinocytes.

P36.08 Anders Grejs THE CARDIAC EFFECT IN PROLONGED HYPOTHERMIA AFTER CARDIAC ARREST

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Background: In Denmark, we have 3500 out of hospital cardiac arrests every year. The chance of surviving at least 30 days has increased over the last 10 years from 5 to 10%. This improvement is believed to be primarily due to better pre-hospital treatment.

There is evidence that post cardiac arrest therapeutic hypothermia improves the neurological outcome and survival after 6 months.

The duration, exact temperature and effect on the heart and circulation have, however, still not been fully investigated.

Methods: The PhD is a sub-study in a multicentre study, where resuscitated pre-hospital cardiac arrest patients, who are still comatose, are randomised to 24 versus 48 hours therapeutic hypothermia ($\pm 33^{\circ}\text{C}$).

During the PhD programme, the cardio protective effect of the hypothermia will be studied through bloodsamples (Troponin T, CK-MB, CoPeptin, NT-proBNP, proANP and Adrenomedullin), echocardiography, use of inotropics and frequency of arrhythmias.

Results: The multicenter study uses the Cerebral Performance Categories Scale as the primary outcome. My PhD study will have several outcomes/ hypotheses:

- Bloodsamples: reduced release of Troponin T in the 48 hrs group
- Echocardiography: increased contractility during hypothermia; S₁Max
- Inotropics: Increased use of inotropics in the 48 hrs group
- Arrhythmia: More arrhythmias in the 48 hrs group

Perspective: To our knowledge, about 65% of the mortality is due to neurological damage after hypoxia. It is very important to look into what should be focused upon during the post-resuscitation hypothermia period to investigate the factors contributing to survival and improving the condition for the heart and circulation.

P37.01 Esben Nielsen FUCHS' ENDOTHELIAL DYSTROPHY: CLINICAL CHARACTERISTICS, TREATMENT OUTCOME, AND PATHOLOGY

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Background: Fuchs' endothelial dystrophy is an eye disease characterized by changes on the inner side of the cornea, which causes poor vision. The only effective treatment option is corneal transplantation. However, there are several unresolved matters regarding both the disease as well as the treatment that warrant further studies:

1. For reasons unknown, visual acuity is often subnormal after DSAEK, despite clear corneas.
2. The functional state of transplanted endothelial cells after DSAEK is unknown.
3. The cause of the disease is unknown, but CollagenVIII may play a

crucial role.

Materials and methods: 1. A controlled prospective trial of DSAEK patients is being undertaken. The aim is identify the cause for subnormal visual performance with to level II evidence. 2. We will monitor the ability of the endothelial cells to dehydrate the cornea after corneal oedema has been induced by applying custom-made contact lenses. 3. In an immunofluorescence study of Fuchs' ED tissue the amount of CollagenVIII will be determined.

Results: Data are still too preliminary to warrant analysis.

Perspectives: Better understanding of the effects and outcomes after DSAEK surgery will help surgeons to further optimize the procedure for patients and further knowledge of the pathology in Fuchs' ED is necessary before working towards a non-surgical treatment approach.

P37.02 Sidsel Hastrup EFFECT OF CENTRALIZATION OF ACUTE STROKE; AND OPTIMIZATION OF THE PRE-HOSPITAL PHASE

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Introduction: Stroke is frequent with approx. 12,000 annual incidents in Denmark (DK). Acute treatment is crucial for the patient's quality of life and daily function. Modern treatments reduce the extent of brain damage; and in case of TIA effectively prevent the development of stroke. Thrombolysis (iv rt-PA) is a well-documented treatment for acute ischemic stroke. The sooner iv rt-PA is started, the more effective it is. Trombectomy and intra-arterial thrombolysis (EVT) are other acute treatments for ischemic stroke. Although iv rt-PA has been used since 2004 in DK, only around 15% receives the treatment and the proportion of major strokes treated with EVT is only a few percentages. To increase the number and rate of success of acute stroke treatment, an optimization of both the pre- and intrahospital organization is required.

In 2012, a comprehensive centralization of suspected acute stroke/TIA was implemented in the Central Denmark Region (RM), DK to improve the quality of assessment and treatment.

Study 1: Objective: To develop of a rapid ambulance protocol to identify patients with stroke and distinguish between major and minor stroke to improve referral of patients with acute stroke to the relevant vascular unit offering iv rt-PA only/or EVT.

Study 2a: Objective: To examine the effects of centralization of acute stroke treatment exclusively to highly specialized stroke centers with thrombolysis in RM.

Study 2b: Objective: To examine the impact, quality and economy of the neurovascular outpatient clinics in RM - and to investigate whether it is

possible to identify patients who can safely be handled in an outpatient clinic by using a risk assessment system developed for this purpose.

P37.03 Anne-Mette Haase

GASTROINTESTINAL MOTILITY AND SLEEP PATTERNS ASSESSED BY AMBULATORY TRACKING OF TELEMETRIC CAPSULES COMBINED WITH POLYSOMNOGRAPHY

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Introduction: We introduce a novel ambulatory telemetric capsule system (3D-Transit) which in conjunction with polysomnography shows the associations between depth of sleep and gastrointestinal motility.

Material and methods: 3D-Transit (Motilis Medica SA) consists of ingestible electronic capsules, an extracorporeal portable detector, and visualization software. Changes in capsule position and orientation reflect gastrointestinal contractile activity and progression. Sixteen healthy subjects (9 females, median age 34 years) ingested two capsules. One- in the morning, and another in the evening. Polysomnography was carried out as an unattended portable sleep study.

Results: Median total sleep-time was 6.6 h (range 5.1-7.5) with a median arousal index of 7.6 per hour sleep (range 4.9-16.9), and a median Wake time after sleep onset (WASO) of 26 minute (range 7-84). Gastric contraction frequency did not exceed 2 to 4 contractions per minute and there were no changes in frequency comparing each sleep stage with nocturnal wake periods. The amplitude of the contractions however, decreased significantly during sleep. The speed of progression through the small intestine did not change with depth of sleep compared with wake periods. There was no association between the sleep stages and the occurrence of colonic propagating movements whereas basic colonic activity was significantly lower during deep sleep compared with wake periods.

Conclusion: This novel ambulatory capsule technique (3D-Transit) in combination with polysomnography allows minor invasive and completely ambulatory investigation of associations between sleep patterns and gastrointestinal motility.

P37.04 Morten Thingemann Bøtker

PREHOSPITAL TRIAGE OF PATIENTS WITH SEVERE DYSPNEA USING POINT-OF-CARE N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE. THE PREBNP STUDY

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Background: Dyspnea is a dangerous symptom. Prehospital telemedicine data from patients with suspected acute myocardial infarction show a very high long-term mortality close to 40% in patients with unresolved dyspnea. A cardiac cause is found in half of these patients and this subgroup with dyspnea of cardiac origin display a particularly high hazard rate of 60%. Measurement of cardiac biomarkers in the prehospital setting may aid in identification of patients with dyspnea of cardiac origin thereby improving triage, early treatment, and ultimately outcome.

Aim: To evaluate if addition of cardiac biomarker measurement to the routine physical examination in patients with severe dyspnea in the prehospital setting leads to an improvement in triage and early treatment.

Study design: Randomized controlled study

Study population: Patients over the age of 18 years with severe dyspnea according to predefined criteria that require dispatch of an emergency physician in the prehospital setting are included (n = 700).

Study period: January 15, 2014 to February 1, 2015

Randomization: Patients will be randomized to one of two strategies:
1) triage according to routine clinical assessment by emergency physician
2) triage with supplementary measurement of the biomarker N-terminal pro-Brain Natriuretic Peptide

End-points: The primary end point is the proportion of patients with dyspnea of cardiac origin triaged to department of cardiology. Secondary end points are time to correct treatment (loop-diuretics, nitroglycerin, β -agonists, ACE-inhibitors and cortisone) and length of hospital stay.

P37.05 Anders
Rosendal
Korshøj

INDIVIDUALIZED DEEP BRAIN STIMULATION TREATMENT OF CHONIC NEUROPATHIC PAIN

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Objectives: We aim to provide efficient treatment for chronic pain patients beyond reach of conventional therapy. We will test the hypotheses, that

1) deep brain stimulation (DBS) treatment of the cingulate cortex (dACC) effectively alleviates refractory pain,

2) ^{11}C -Carfentanil and H_2^{15}O PET and new noninvasive brain stimulation (focused TMS) can be used to optimize patient selection for surgery and individualize DBS treatment,

3) neuromodulation reduces blood flow and increases opioid binding in pain centres.

Background: Chronic pain affects 7-8% of the western population and is very difficult to treat. Neuromodulating treatments are used when pharmacotherapy has failed. The effect is often unsatisfactory, due to ineffective methods of patient selection and treatment planning. We will

overcome these challenges by implementing a new and rational brain target for stimulation and noninvasive techniques to predict the individual outcome and optimal electrode target.

Methods: We will include ten patients with refractory chronic pain and ten healthy subjects. Participants will undergo clinical examination, quantitative sensory testing and pain mapping. We will conduct ^{11}C -Carfentanil and H_2^{15}O PET brain imaging to evaluate pain center blood flow and opioid binding and subsequently test for clinical pain relief by focused TMS of the dACC followed by repeated PET imaging. We will then implant DBS electrodes into the bilateral dACC brain areas. Patients will be followed for 5 years postsurgery and control PET imaging will be performed.

Perspectives: The project is initiated in the beginning of 2014 and will potentially provide new standards for treatment of severe pain and DBS in general.

P37.06 Tommy
Kjærgaard
Nielsen

CONTRAST ENHANCEMENT ON CT FOLLOWING RENAL CRYOABLATION - WHEN SHOULD TREATMENT FAILURE BE CONSIDERED?

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Introduction: Renal cryoablation is a valid treatment option for localized pT1a renal cancer. Treatment success is typically defined as absence of contrast enhancement (CE) on follow-up imaging. We investigate the development of cryolesions that demonstrate CE on follow-up CT after renal cryoablation.

Materials and methods: A retrospective review of cryoablation procedures from 2005 to 2012. A total of 113 patients with a localized pT1a biopsy verified malignant renal lesion was identified. 34 patients experienced postoperative CE. Mean age was 43 (59-66) yr. Mean tumor size was 25 (22-28) mm. RCC-subtypes: Clear cell (79%), Papillary (12%), Chromophobe (6%), Collecting duct carcinoma (3%).

Results: A total of 31 patients (29%) were found to have CE on the initial follow-up CT and additional 3 patients had delayed CE (defined as no CE on prior CT). Spontaneous resolution was observed in 15 patients (44%) with a median time to resolution of 12 (3-45) months. A total of 10 patients (29%) underwent re-ablation, with a median time to re-ablation of 12 months (1-27). Only 13% experienced spontaneous resolution if attenuation levels exceeded 39 HU compared to 39% with lower attenuation levels ($p=0.004$).

Conclusion: Contrast enhancement is a frequent finding and is evident in 29% of patients on the initial follow-up CT after 6 months. Early re-treatment before 12 months follow-up should be carefully evaluated as spontaneous resolution is a common observation. Residual unablated tumor should be considered if attenuation levels exceed 39 HU on contrast

enhancement CT.

- P37.07 Aja Neergaard Greve A CASE-CONTROL STUDY OF ASSOCIATIONS BETWEEN SOCIAL COGNITION IN PARENTS WITH SCHIZOPHRENIA OR BIPOLAR DISORDER AND THEIR 7-YEAR OLD OFFSPRING

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Background: There is growing evidence that social cognitive deficits are state independent and can be detected both in patients and their unaffected relatives. Social cognitive deficits may reflect increased genetic risk of developing schizophrenia (SZ). Research has been much less extensive regarding social cognitive deficits in bipolar disorder (BD).

Objectives: Characterize the possible associations between social cognitive deficits in parents with SZ or BD and in their offspring.

Design: A case-control study. We aim to establish a cohort of 500 children, age 7, with one, two, or no parents with SZ or BD (200 pair of parents where at least one of them is diagnosed with SZ, 100 pair of parents where at least one of them have been diagnosed with BD and 200 pair of control parents without SZ and BD). The cohort is identified from the Danish Civil Registration System and the Danish Psychiatric Central Research Register. The parents are matched on gender and geography. Researchers are blind to the diagnoses of the parents. Measurements: Social cognitive domains (Theory of Mind (ToM) and Emotion Recognition (ER)) are assessed in one of the biological parents and their offspring using Animated Triangles task and Emotion Recognition task. Neurocognition, IQ and psychiatric symptoms are also measured.

Perspectives: This study investigates whether ToM and ER are potential endophenotypes for SZ and BD. A later follow-up of these children will add important clues to a better understanding of the causal role of genetic and environmental factors.

Current status: Data collection started December 2012, 122 families are included and 70 families have completed the assessment.

- P37.08 Mikkel Petersen EVALUATION OF MR BASED FIBER TRACKING AS A TOOL IN DEEP BRAIN STIMULATION FOR MOVEMENT DISORDERS

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Deep brain stimulation (DBS) is an efficient treatment for advanced stages of Parkinson's disease and other movement disorders such as dystonia and

essential tremor. In DBS surgery, an electrode is implanted with high precision into a neuro-anatomical target where it through electrical impulses modulates nearby neurons. Planning of the procedure is carried out using a combination of conventional CT and MR imaging together with a stereotactic frame attached to the patient's skull. The choice of implant target is based on the visual interpretation of the MR images combined with landmark anatomy and surgical experience. Though an efficient treatment, the mechanism-of-action of DBS is currently poorly understood.

In this project, we are working to implement diffusion tensor imaging (DTI) as a part of the pre-surgical planning. DTI is an advanced MRI technique that allows us to non-invasively identify dominant fiber tracts within the brain through the use of probabilistic fiber tracking. Our aim is to combine DTI and fiber tracking with knowledge of the specific area in the brain that is being stimulated and utilize this to learn more about which fiber tracts are being modulated and where they project to in the brain. Correlation between clinical outcomes and electrode placement will allow us to evaluate the best areas to stimulate and potentially in the future use this to assist in targeting when planning DBS surgery.

At the current stage, we have finalized a new MRI protocol including DTI sequences and have begun enrolling future DBS candidates into the project.

P38.01 Pernille Libach
Hansen

USE OF GENERAL PRACTICE, DIAGNOSTIC INVESTIGATIONS AND PRESCRIPTIONS IN THE YEAR PRECEDING COLORECTAL CANCER DIAGNOSIS

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Background: Colorectal cancer (CRC) is one of the most common cancers in Denmark with a low 5-year survival compared to e.g. other Nordic countries. It is estimated that 90% of patients diagnosed with CRC present symptomatically to primary care. However, less than half of these present with alarm symptoms, which makes it a challenge for the general practitioner to discriminate malign from benign disease. Further, cancer patients are seen more often in general practice in the months prior to diagnosis.

Aim: To describe the amount of daytime consultations, haemoglobin measurements and medicine prescriptions for haemorrhoids and obstipation in general practice in the year preceding incident colorectal cancer diagnosis. Furthermore, to analyse whether patients with distant disease at the time of diagnosis have different activity patterns than patients with local disease.

Methods: A population-based case-control-like cohort study will be conducted using registry data. Cases are all patients aged 40-80 years diagnosed with a primary colorectal cancer (C18-20) in 2004-2010. Using incidence density sampling, ten gender- and age-matched controls from the same general practice as the case will be randomly selected.

Analysis: Cases and controls will be compared according to consultation

rate, haemoglobin measurements and medicine prescriptions. Similar comparisons will be made between CRC patients with different tumour stages.

Perspectives: This study will provide knowledge that can optimize diagnostic investigations for CRC in general practice. It will give new information about when to suspect CRC as a possible diagnosis, which can have an effect on earlier diagnosis of CRC.

P38.02 Wajd Abbas
Hassan

IGFBP-2 AUTOANTIBODIES AS A SEROLOGICAL BIOMARKER IN THE DIAGNOSIS AND PROGNOSIS OF CANCER

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Introduction: Insulin-like growth factor binding protein (IGFBP)-2 is over-expressed in malignancies and is associated with tumor growth, metastasis and relapse. Hence, IGFBP-2 is considered to be a human tumor antigen (TAA) and a possible progression-dependent biomarker in cancer diagnosis. In addition, specific immunity against IGFBP-2 has been reported in several cancer types with increased IGFBP-2 expression. IGFBP-2 antibodies (Abs) can magnify the signal when IGFBP-2 expression is low or even undetectable in early stages of cancer.

Aim: The current study aims to investigate whether circulating IGFBP-2 Abs in combination with IGFBP-2 can be used as a diagnostic biomarker to improve early cancer detection and as a prognostic biomarker in cancer treatment.

Methods and end-points: An in-house assay will be established for the measurement of serum concentration of IGFBP-2 Abs. This method will be applied to serum samples from patients with lung and breast cancer (grade and stage divided) and healthy control subjects. Cancer patients will be statistically compared to healthy controls and relationships between cancer stage and IGFBP-2 Ab level will be investigated. In addition, IGFBP-2 immunohistochemistry will be performed on 75 lung cancer tissue samples to compare the cellular IGFBP-2 expression in tissues with serum levels of IGFBP-2 and IGFBP-2 Abs. The value of IGFBP-2 Abs as a serological biomarker may reveal novel strategies in early cancer diagnosis as well as follow-up of progression and relapse.

P38.03 Kristoffer
Backman Nøhr

QUANTITATIVE EEG REACTIVITY IN COMATOSE NEUROSURGICAL PATIENTS

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Quantification of EEG reactivity may improve reliability and sensitivity of the usual qualitative assessment of EEG reactivity in comatose neurosurgical patients.

In this study, we investigate quantitative measurements of EEG reactivity

including which frequency bands are most affected and how they correlate with outcome.

Seven comatose neurosurgical patients undergoing 24 hour EEG recording were subjected to four noxious stimulations of 30 seconds duration separated by at least 2 minutes. Average power at F3 and F4 in the alpha, delta, and theta bands during stimulation was divided by average power of the 30 seconds period prior to stimulation yielding reactivity ratios (RR) of the three frequency bands. Quantitative reactivity in a frequency band was defined as a RR different from 1. A preliminary 3-8 weeks evaluation of outcome was done by the Cerebral Performance Category (CPC) Scale.

Mean RR of the alpha, theta, and delta band varied between 0,865-1,494, 0,824-2,357, and 0,831-1,437, respectively. Four patients had quantitative reactivity in one or more bands. RR in the alpha band was increased in one patient (CPC 2-3), in the theta band in two patients (CPC 1-2 and 2-3), and in the delta band in one patient (CPC 3-4). One patient had a decrease in RR in the delta band and had a CPC of 5. Of the three patients who showed no reactivity one had a CPC of 3 and two had a CPC of 5. Five patients were partly sedated, one of which had a CPC of 5.

It seems possible to achieve a quantitative measure of reactivity. In this study, we found no obvious systematic correlation with outcome, but larger studies are required.

P38.04 Anne Bank
Boisen

LOW-GRADE SYSTEMIC INFLAMMATION IN ADOLESCENT OFFSPRING OF MOTHERS WITH TYPE 1 DIABETES

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Background: Offspring born to mothers with type 1 diabetes (T1DM) are more susceptible to develop obesity, prediabetes, type 2 diabetes (T2DM) and cardiovascular disease in adulthood. Evidence from both human and animal studies strongly supports an etiology of adverse fetal programming as a consequence of a hyperglycemic environment. Though it is now widely accepted that chronic low-grade inflammation in adipose tissue is directly involved in the development of T2DM little is known about inflammatory changes in offspring of T1DM mothers.

Objective: To investigate the association between fetal exposure to in-utero hyperglycemia and the level of low-grade systemic inflammation in adolescent offspring of women with T1DM.

Methods: A national follow-up study including 275 adolescent offspring of women with T1DM born during the period 1993-1999 and 304 controls matched for age, sex and postal code as a marker of socioeconomic status. At follow-up subjects aged 13-20 years are characterized by plasma levels

of high-sensitivity C-reactive protein (hs-CRP), macrophage specific marker sCD163, mannose receptor, mannose binding lectin (MBL) and soluble membrane attack complex (sMAC). Participants are further characterized by an oral glucose tolerance test and anthropometric measurements.

P38.05 Khoa Manh Dinh THE DANISH BLOOD DONOR STUDY: NASAL COLONISATION WITH AMONG HEALTHY DANES AND THE ASSOCIATION TO C-C CHEMOKINE RECEPTOR TYPE 5 DELTA 32 DELETION

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Background: Staphylococcus aureus (SA) is a commensal but it is also a potent pathogen that can cause a wide variety of infections. Approximately 25-30% of the healthy adult population are carriers of SA in their vestibulum nasi. Colonisation is a complex interaction between the bacteria and its host. The recent report of a toxin, Leukotoxin ED, from SA that attacks cells by binding to the C-C chemokine receptor type 5 (CCR5) adds another factor that may affect the interplay between host and bacteria.

Methods: The study will comprise 3,000 participants from the Danish Blood Donor Study. Nasal samples will be obtained with sterile swabs from the vestibulum nasi by trained personnel and subsequently cultured. Whole blood samples are collected in the main study and genotyping for the CCR5 Δ32 deletion is complete. All participants completed a standard questionnaire on smoking status, alcohol consumption, physical activity, diet and various body measurements etc.

Results: We hypothesize that the frequency of SA colonisation is different between carriers and non-carriers of the CCR5 Δ32 deletion. We expect the deletion in CCR5 affects the relationship between the host and SA colonisation.

Perspectives: The protective effect of a defective CCR5 against the SA Leukotoxin ED sheds new light on the interaction between the host and bacteria. CCR5 is today a target for a potent antiretroviral drug, maraviroc, used in the treatment of HIV. Our study may help to explain if CCR5 affects the relationship between the host and SA. In a subsequent study, we will follow the participants and compare the risk of invasive infection between carriers and non-carriers of the CCR5 32 deletion.

P38.06 Tobias Pilgaard LACK OF IMPROVEMENT IN INCIDENCE AND CASE-FATALITY OF FIRST
Ottosen TIME HOSPITAL ADMISSION WITH INTRACEREBRAL HEMORRHAGE IN DENMARK 2004-2012

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Background: The mortality from ischemic stroke has declined substantially in the last decades. Less is known about the epidemiology of intracerebral hemorrhage (ICH).

Objectives: To examine trends in incidence of first hospitalization due to ICH and subsequent 30-days case-fatality in Denmark 2004-2012.

Methods: We performed a nationwide population-based cohort study. Patients with first hospitalization due to ICH were identified in the Danish Stroke Registry and followed using the Danish Civil Registration System. We calculated the standardized incidence rates of hospitalization for ICH. Using 2004 as reference, we used multivariable logistic regression with 95% confidence interval to estimate the odds ratio (OR) of death according to year of admission adjusting for age, gender, atrial fibrillation, hypertension, previous myocardial infarction, diabetes, smoking, alcohol intake, and quality of in-hospital stroke care.

Results: We identified 7850 patients with incident ICH (51.7 % men, median age 74 years). The overall standardized incidence rate (SIR) was 20.9 per 100.000 person years (95% CI: 19.5-22.3) and slightly higher among men compared with women. The SIR remained stable throughout the study period (2004: 20.7 (95% CI: 19.3-22.1) vs. 2012: 18.2 (95% CI: 16.9-19.5)). The average 30-day case-fatality was 31.2%. The adjusted OR for 30-day case-fatality was 1.24 (95% CI: 0.94-1.64) when comparing 2012 with 2004.

Conclusions: The incidence rate of first hospitalization due to ICH and subsequent case-fatality have remained stable in Denmark in recent years despite increased focus on modifiable risk factors and improved early in-hospital stroke care.

P38.07 Pia Carstensen
Simonsen DEVELOPMENT OF A NEW CLASSIFICATION SYSTEM OF COMORBIDITY, TREATMENT COMPLEXITY, SEQUELAE AND COMPLICATIONS IN UROLOGICAL CANCER SURGERY

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Background: Cancer patients undergoing treatment can be classified according to dissemination and extend of the cancer but also by comorbidities which may affect the choice of treatment and influence the outcome of this. Current classification systems mainly focus on either comorbidity or complications after a given treatment modality without linking the two together. There is therefore a need for a uniform classification system that includes organ specific comorbidities, treatment complexity, complications and sequelae in order to make a systematic investigation of these relevant correlations.

Bladder cancer patients are often older people with multiple comorbidities as they are often heavy smokers. Radical cystectomy is a complex procedure with a 75% post-operative risk of complications, which makes

this patient group ideal for developing a new classification system.

Methods: Between 1992 and 2013, 1200 bladder cancer patients have undergone radical cystectomy at Aarhus University Hospital. They are registered in a database that includes vital and oncological parameters, comorbidity and complications. The classification system will be developed based on this database but aims to cover all types of treatment in urological malignancies.

With the different organ systems in the vertical direction and pre-, intra- and postoperative complications in the horizontal direction, a matrix is developed for all patients. In each field, a numeric code equals different comorbidities, complications and sequelae. Based on this matrix, it will be possible to identify links between organ specific comorbidities and complications dependent on treatment modality.

P38.08 Christophe
Henri Valdemar
Duez

QUANTIFIED EEG REACTIVITY PREDICTS BOTH GOOD AND POOR
OUTCOME. A PILOT STUDY ON CARDIAC ARREST PATIENTS

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Question: EEG reactivity (EEG-R) to noxious stimulation is an important prognostic parameter in comatose patients. Assessment of reactivity however, relies on a visual qualitative evaluation prone to subjective interpretations. The aim of this study was to test if QEEG analysis has a potential as an objective and sensitive method for the evaluation of EEG-R.

Methods: We conducted EEG in 14 lightly sedated out-of-hospital cardiac arrest (CA) patients during the first 12 to 24 hrs of therapeutic hypothermia. We marked three periods of 30 seconds both with and without noxious stimulation, and used the average to calculate a stimulation/rest ratio in the alpha, theta and delta bands. Then we compared the alpha/ theta-, alpha/delta-, and theta/delta ratios. Outcome was assessed by the Cerebral Performance Category Score (CPC) 28 days after CA.

Results: Alpha/delta reactivity ratio (ADRR), defined as the ratio of the alpha/delta ratio during noxious stimulation to the alpha/delta ratio without stimulation, was the best predicting parameter. All 9 patients with an ADRR below 1 (range 0.32 - 0.95) , i.e. a decrease in alpha-power and/or an increase in delta-power during stimulation, had a good outcome (CPC 1-2) and 4 of 5 patients with an ADRR of more than 1 (range 1.11- 1.43) had a poor outcome (CPC 4-5). One patient with an ADRR of 1.12 had a good outcome (CPC 2).

Conclusions: This pilot study suggests that quantification of EEG-R by ADRR may predict both good and poor outcome in sedated CA patients, even within the first 24-hours of therapeutic hypothermia.

Abstracts Student chairmen

CH.01 Jacob Johnsen IDENTIFICATION OF THE OPTIMUM REMOTE LIMB ISCHEMIC PRECONDITIONING PROTOCOL IN AN EXPERIMENTAL MOUSE MODEL OF CARDIOPROTECTION

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Background: Remote ischemic preconditioning (rIPC) by short periods of ischemia and reperfusion to a limb is known to evoke an innate response in organisms that protects against subsequent lethal cardiac ischemia and reperfusion injury. This finding has been widely confirmed in experimental and clinical trials.

In the original studies by Przyklenk et al. and Kharbanda et al., four cycles of 5 min. ischemia and reperfusion were used as preconditioning protocol, and this protocol has been adapted in the majority of subsequent studies within the field. However, the optimum remote limb preconditioning protocol has never been investigated.

Hypothesis: Intensifying the rIPC stimulus by two limb rIPC or by increasing the number of rIPC cycles might give rise to a more pronounced degree of cardioprotection. The protection by limb rIPC diminishes within a couple of hours after the rIPC stimulus.

Method: In total, 70 male C57BL/6 mice were subjected to single-limb rIPC (four or six cycles) or two-limb rIPC (two, four, six or eight cycles) or control according to group. Following the rIPC-stimulus, hearts are subjected to ex-vivo retrograde buffer perfusion a.m. Langendorff. An additional 30 mice were allocated to rest 1, 1½ or 2 hours after rIPC and prior to isolated perfusion. Cardioprotection was evaluated by measuring infarct size and post-ischemic hemodynamic performance.

Results: Preliminary results identify 6 cycles of limb-rIPC as the optimum preconditioning protocol with no additional effects in the two limb preconditioning groups. This preconditioned state lasts less than two hours.

CH.02 Søren Brandt SPECIFIC INACTIVATION OF THE EPITHELIAL SODIUM CHANNEL (ENAC) IN
Poulsen KIDNEY CONNECTING TUBULE: EFFECT ON SODIUM AND POTASSIUM
HOMEOSTASIS

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Introduction: In the kidney, ENaC is crucial for Na⁺ reabsorption, but it is also involved in the excretion of K⁺. ENaC is expressed in the late distal CNT and

CD of the kidney, where it is tightly regulated by the steroid hormone aldosterone. Inactivation of the α ENaC subunit of ENaC in the CD does not disturb Na^+/K^+ balance in mice. However, α ENaC deletion in both the CNT and CD causes disturbance in Na^+ and K^+ balance on standard and challenging diets. We investigated the importance of ENaC in the CNT by deleting α ENaC in a part of the CNT in mice.

Materials and methods: Mice with Cre-recombinase expressed under the control of the V-ATPase B1-subunit promoter (these mice express Cre in a portion of the CNT cells) were crossed with floxed Scnn1a mice.

Results: On standard diet KO, mice showed no phenotype. On low Na^+ diet (7 days), KO mice showed increased urinary Na^+ excretion (on day 3, 4 and 5) but the effect disappeared on day 7. Similarly, no difference was found in blood Na^+ or blood K^+ on day 7. On a 2% K^+ diet (4 days), mice showed no phenotype except from increased blood aldosterone. When challenged with a 5% K^+ diet (2 days), however, KO mice decreased their food intake, lost weight, and excreted less K^+ through the urine.

Conclusion: Data indicate that a partial inactivation of ENaC in the CNT is critical when ingesting high amounts of K^+ (5% diet). However, the kidney function is not affected during moderate K^+ intake (2% diet). On low sodium diet (0.01%), inactivation of ENaC initially decreased the Na^+ excretion, but the effect disappeared after seven days. Thus, the kidney may to a certain degree compensate for the inactivation of ENaC in the CNT.

CH.03 Jeppe Skov

EFFECT OF GLUCAGON-LIKE PEPTIDE-1 ON KIDNEY FUNCTION IN HEALTHY MALES

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Glucagon-like peptide-1 (GLP-1) is an incretine hormone with multiple actions in addition to control of glucose homeostasis. GLP-1 is known to cause natriuresis in humans but the effects on basic renal physiology are still partly unknown. GLP-1 has been linked to release of atrial natriuretic peptide (ANP) in mice and this GLP-1 - ANP axis is found to mediate all antihypertensive effects of GLP-1.

We examined twelve healthy young males in a randomized, controlled, double-blinded, single-day, cross-over trial to evaluate the effects of two hours GLP-1 infusion on kidney functions. Glomerular filtration rate (GFR) and renal plasma flow (RPF) were assessed with ⁵¹Cr-EDTA and ¹²³I-hippuran, respectively, using a constant infusion renal clearance technique based on timed urine sampling. Plasma was analysed for renin-angiotensin-aldosterone system components and proANP was measured as a marker of ANP secretion.

GLP-1 had no significant effect on either GFR or RPF but fractional urine

excretion of lithium increased 9% ($p=0.013$) and renal sodium clearance increased 40% ($p=0.007$). Angiotensin II decreased 19% ($p=0.003$) while proANP, renin, aldosterone, and the urinary excretion of angiotensinogen showed no significant changes. GLP-1 did not affect blood pressure but induced a small transient increase in heart rate.

Although GLP-1 markedly reduces proximal tubule sodium reabsorption, the acute effects on GFR and RPF are very limited in healthy humans. GLP-1's ability to reduce angiotensin II concentration is a novel finding and may be important in a possible prevention of diabetic nephropathy. Our data cannot confirm the existence of a GLP-1 - ANP axis in humans.

CH.04 Therese Koops ESTIMATING HERITABILITY FOR TIME-TO-EVENT DATA USING TWINS AND
 Grønberg PSEUDO-OBSERVATIONS

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Background: Twin studies are an important part of genetic epidemiology. The roles of genetic effect, shared environment, and unique environment can be explored by comparing traits in monozygotic and dizygotic twins. A popular measure of genetic effect is heritability; the proportion of phenotypic variance attributable to genetic variance. There are well-established methods to estimate heritability for continuous and binary traits, but there is a need for methods to estimate heritability for time-to-event data. The aim of this study is to establish such a method for twin data.

Methods: In time-to-event data, individuals are followed for different lengths of time and some individuals might be lost to follow-up (censored) for example because of emigration. This difference in length of follow-up needs to be adjusted for in the statistical analysis. If full follow-up time was available for every individual, standard regression models could be applied. A way of achieving this with censored data is to use a technique based on pseudo-observations. The pseudo-observation approach to heritability will be evaluated in a simulation study.

Perspectives: The pseudo-observation approach to heritability will make it possible to estimate heritability for time-to-event data such as time to diagnosis, and thus examine the relationship between genetics and environment in this setting.

CH.05 Anto Praveen THE IMPORTANCE OF BRD1 GENE IN AFFECTIVE BEHAVIOUR AND ITS
 Rajkumar RELATION TO DEPRESSION
 Rajamani

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Introduction: Schizophrenia and bipolar disorder associated Bromodomain containing 1 gene (BRD1) is involved in epigenetic regulations of brain through histone acetylation. We have recently developed a constitutive knock-out mouse heterozygous for Brd1 (Brd1^{+/-}) and aimed to investigate their affective behaviours and neurobiology.

Methods: We employed behavioural experiments to assess their locomotion, cognition, anxiety and depressive equivalent behaviours. Cortical serotonin and striatal dopamine levels were assessed by HPLC. Neuronal morphology of Anterior Cingulate Cortex (ACC) pyramidal neurons was studied by Golgi-cox staining and Imaris 3-D image analyses. Next Generation RNA sequencing by Illumina HiSeq™ 2000 evaluated differentially expressed genes (DEG) in their Amygdala and Hippocampus CA3.

Results: Female Brd1^{+/-} mice exhibited significantly more anhedonia ($p < 0.01$) and behavioural despair ($p < 0.01$). Their depressive phenotype could be reversed by both Imipramine and Fluoxetine. They had significantly less serotonin in their frontal cortex ($p = 0.03$) and less striatal dopamine ($p = 0.01$). Their ACC neurons had significantly shorter dendrites, less branches and less dendritic spine density ($p < 0.001$). Cell signalling, neuron development and transcription regulation associated genes were significantly enriched among the DEG in their amygdala and Hippocampus.

Conclusions: Depressive phenotype and its reversibility by antidepressants indicate the validity of female Brd1^{+/-} mice as a novel model for MDD. Female Brd1^{+/-} mouse model may help further studies evaluating the epigenetic changes and neurodevelopmental abnormalities, pertinent to MDD.

CH.06 Lise Tornvig
Erikstrup

A COMPARISON OF VANCOMYCIN, METRONIDAZOLE AND A COMBINATION OF VANCOMYCIN AND METRONIDAZOLE FOR THE TREATMENT OF INFECTION IN A MOUSE MODEL

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Objective: The aim of our study was to examine if *C. difficile* infected mice treated with a combination of vancomycin and metronidazole had a better outcome than mice treated with vancomycin or metronidazole alone.

Methods: C57BL/6 mice were divided into five groups: An uninfected and infected control group treated with placebo, and three infected groups treated with either vancomycin or metronidazole alone, or a combination of vancomycin and metronidazole. In order to establish infection, the normal enteric flora was disrupted by pre-treating the mice with an antimicrobial mixture. Mice were challenged with *C. difficile* or PBS by oral gavage. Post-infection mice were started treatment for ten days. Mice were monitored for 20 days with weight and a clinical score. Stool samples were

examined for bacterial load and the presence of *C. difficile* toxin.

Results: After challenge with *C. difficile* the infected mice developed signs of clinical illness with loose stools or diarrhoea and weight loss. Some mice developed severe illness and were euthanized. The uninfected control group did not show any signs of clinical illness. None of the mice in the vancomycin treated group died during the acute infection compared to a mortality of 17%, 33% and 67% in the combination, metronidazole and placebo group, respectively.

Conclusion: In the treatment of acute *C. difficile* infection in C57BL/6 mice vancomycin was superior compared to metronidazole. A combination of vancomycin and metronidazole did not improve the clinical or microbiological outcome. Hence, vancomycin seems to be the best choice for treating acute *C. difficile* infection in mice.

CH.07 Mohamed Ahmed Hassan COMPLIANCE AND TOXICITY OF THE HYPOXIC RADIOSENSITIZER NIMORAZOLE IN THE TREATMENT OF PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)

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Purpose: To evaluate the compliance and toxicity of the hypoxic radiosensitizer nimorazole (NIM) in patients with HNSCC.

Methods: A retrospective study of patients with HNSCC treated in Denmark. All patients treated with radical RT (\pm CT) [66-70 Gy; 33-35 fractions; 2 Gy/fraction; 5-6 fractions/week] concomitant with the hypoxic radiosensitizer NIM. NIM was administered as oral tablets in doses of 1.2 g/m² body surface area in connection with the first daily radiation fraction. A second daily dose of 1gm was given in connection with the second fraction in the accelerated fractionation regimen. The compliance was estimated as the percentage of the initially prescribed dose, which was received by each patient. The main side-effects were recorded.

Results: A total of 1049 patients were investigated. 58% of patients received the full prescribed total dose. Among the 260 patients with dose reductions due to known side effects, (87%) were due to nausea/vomiting. All side effects ceased when treatment was interrupted. Female patients were significantly more likely to have dose reduction (OR 2.02; 95% CI 1.50-2.70), and nausea/vomiting. Patients aged more than 70 years were significantly more likely to have dose reduction. Patients who received less than 1100mg/m² were significantly less likely to have dose reduction (OR 0.58; CI 0.44-0.78), and nausea/vomiting, compared to those who received 1100-1300mg/m². The compliance was also less in the group of patients received accelerated chemo-radiotherapy (OR 1.70; CI 1.20-2.50) with more association with nausea/vomiting (OR 2.09; CI 1.40-3.10).

Conclusion: The compliance to nimorazole is fair, with tolerable acute, non long-lasting, toxicity.

CH.08 Kristine Rømer Thomsen RECONCEPTUALISING ANHEDONIA: NOVEL PERSPECTIVES ON BALANCING THE PLEASURE NETWORKS IN THE HUMAN BRAIN

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Anhedonia, the lack of pleasure, has been shown to be a critical feature of a range of psychiatric disorders. Yet, it is currently measured primarily through subjective self-reports and as such has been difficult to submit to rigorous, objective scientific analysis. New insights from the emerging neuroscience of pleasure hold considerable promise in improving our understanding of anhedonia, and provide useful objective measures to aid subjective self-report. Here, we review the state-of-the-art of pleasure research and specifically the established principles of wanting, liking and learning. We propose that anhedonia can be viewed as unbalancing of these processes over time, thereby departing from the longstanding view of anhedonia as reduced hedonic impact (i.e. liking). Specifically, we review the evidence suggesting that patients suffering from anhedonia show impairments in wanting and learning processes, while liking processes are surprisingly intact. We show how anhedonia is heterogeneous across major psychiatric disorders and discuss implications for diagnosis and treatment of anhedonia.

CH.09 Lene Hee Christensen QUANTITATIVE SONOELASTOGRAPHY OF THE UTERINE CERVIX BY INTERPOSITION OF A SYNTHETIC REFERENCE MATERIAL

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Objective: To develop a reference material allowing for quantitative elastography of the uterine cervix with the calculation of the approximate tissue stiffness expressed as Young's modulus (N/mm^2) and to test the equipment on phantoms from a clinical perspective regarding the distance dependence and the influence of a heterogeneous material.

Design: Methodological study.

Setting: Aarhus University Hospital.

Population: Six mid- and five term-pregnant women.

Method: Elastography is based on tissue compression by the transducer during B-mode scanning followed by computerized analysis of changes in the speckle distance. Reference caps and phantoms with Young's moduli between $0.07 - 0.40 \text{ N}/\text{mm}^2$ were made of silicone and oil. By using reference caps, the approximate Young's moduli of the cervixes were calculated from strain ratios obtained by elastography.

Results: The recordings of the phantoms revealed that the calculation of the approximate Young's moduli became unreliable at distances above 10-15 mm from the transducer. This bias was increased at a phantom which

included a soft layer imitating the cervical canal. The approximate Young's modulus obtained from the anterior cervical lip was 0.08 N/mm² in mid- and 0.03 N/mm² in term-pregnant women, $p = 0.01$.

Conclusion: The reference cap constitutes a promising tool for quantitative elastography of the anterior cervical lip. Results from the posterior lip are less plausible due to the distance to the transducer and the heterogeneity introduced by the cervical canal. The method might be used as a supplement to cervical length assessment when evaluating women at risk of preterm delivery and when planning induction of labor.

CH.10 Maj Høygaard Nicolaisen ORAL HEALTH IMPACT AFTER REPLACEMENT OF A MISSING POSTERIOR TOOTH WITH A FIXED DENTAL PROSTHESIS

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Introduction and aim: Missing one or more teeth may be associated with compromised oral function and social stigmatization. The aim of this study was to examine if changes occur in oral health-related quality of life by replacing a missing posterior tooth with a fixed dental prosthesis (a dental bridge).

Methods: Thirty-four patients (13 men, 21 women) aged 32-66 years with one missing posterior tooth received a 3-unit fixed dental prosthesis. Control group: 20 healthy fully dentate individuals with normal occlusion and subjectively and objectively clinically sound teeth. The oral health-related quality of life was evaluated with the Oral Health Impact Profile (OHIP-14) form. This questionnaire consists of 14 questions and is designed to measure self-reported oral functional limitation, discomfort and disability. Low OHIP scores indicate better oral comfort. The patient group was assessed before treatment and 2 weeks, 3 months and 1 year after treatment. The control group completed the OHIP questionnaire once.

Results: Before treatment, the patients reported (median 9.5) a statistically significant higher ($p < 0.001$) OHIP score, i.e. lower self-reported oral health, compared to the control group (median 3.0). Three and 12 months after treatment, the patients' OHIP scores were reduced (median 3.0 and 3.5, respectively) to the level of the control group. This reduction in the OHIP scores, i.e. increase in self-reported oral health, was statistically significant ($P < 0.001$).

Conclusions: Missing a posterior tooth has an impact on physical, emotional and social functioning. Replacement of a missing posterior tooth improves the self-reported oral health significantly.

CH.11 Lene Rahr Wagner THE ASSOCIATION OF ORAL CONTRACEPTIVE (OC) USE ON THE RISK OF ANTERIOR CRUCIATE LIGAMENT (ACL) INJURY; A POPULATION-BASED CASE-CONTROL STUDY USING THE DANISH KNEE LIGAMENT RECONSTRUCTION REGISTRY

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Introduction: ACL injuries are reported to be higher in women than in men. A possible association between the use of OCs and a potential protective effect on the risk of ACL injuries are suggested, but this still remains unclear. Therefore, the aim of this study was to evaluate the association between use of OC and the risk of sustaining an ACL injury.

Methods: We conducted a population-based case-control study and identified 5,389 ACL operated women from the Danish ACL registry and 10,778 controls without ACL ruptures in a period from 2005-11. We used logistic regression to calculate the odds ratio (OR) of having ACL lesion according to OC use. Information on redeemed OC prescriptions (PS) as a proxy for OC use was extracted from the prescription database. OC use was divided into non-, ever-, new-, long-term-, and former user. A dose-response calculation of OC use was performed.

Results: Ever users of OC's compared with nonusers were associated with a decreased risk of sustaining ACL rupture of 14% (OR= 0.86; 95% CI: 0.80-0.93). Also, the risk of sustaining ACL injury among long-term- and former users was 10% and 22% lower than for non users. For new user, no association was found. When evaluating the duration of OC use on the risk of sustaining ACL rupture, we found a dose-response association, with 15%, 21%, and 26% reduction in risk using 1-10, 11-20, and 21-30 PS over a ten year period, respectively. No association was found using more than 31 PS.

Conclusion: The principal finding of this study is that OC use may have a protective effect on the risk of ACL injury, although the causal association is uncertain and does not justify using OC for prophylactic purpose.

CH.12 Lene Nyboe

DISTURBED BODILY EXPERIENCES IN PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA

L. Nyboe

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Introduction: Patients with schizophrenia often have disturbed bodily experiences that might hinder their engagement in physical activities. In the research project "Metabolic syndrome in patients with first-episode schizophrenia" the correlation between disturbed bodily experiences and physical activity is investigated.

Methods and material: The study is a clinical, prospective, observational study. For all participants, the disturbed bodily experiences, comprising morphological changes, bodily estrangement, cenesthetic disturbances, bodily disintegration, hypochondrias, motor disturbances, are assessed using items from "Examination of Anomalous Self Experience" and "The Body Awareness Scale". All patients consecutively assigned to the OPUS project and inpatients in the Central Denmark Region having an ICD-10 diagnosis of first-episode schizophrenia (18-45 years) is the population of interest (N=100). In comparison in-patients with ICD-10 diagnosed

depression and healthy controls matched on age, gender and level of education are also included.

Results: In all, 101 patients with first-episode schizophrenia have been included in the study. Disturbed bodily experiences are prevalent in 75% of the patients. There is a significant correlation between severity of disturbed bodily experiences and low levels of physical activity. Results from the specific analyses will be presented.

Conclusions: Disturbed bodily experiences are common in patients with first-episode schizophrenia and negatively correlated to physical activity-level.

CH.13 Bjørn Bay

FERTILITY TREATMENT AND THE RISK OF MENTAL DISORDERS IN CHILDHOOD AND ADOLESCENCE: A REGISTER-BASED COHORT STUDY

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Objective: To assess long-term mental health of children born after fertility treatment by comparing their risk of mental disorders with that of spontaneously conceived children.

Methods: In a cohort study, information from Danish national health registers was cross-linked by the personal identification number assigned to all citizens in Denmark. We included all children born in Denmark from 1995 to 2003 (33,139 children conceived after fertility treatment; 555,828 children after spontaneous conception) with follow-up in 2012 when the children were 8-17 years old. The absolute risk (AR) and hazard ratio (HR) of mental disorders were estimated while adjusting for potential confounding variables.

Results: The risk of mental disorders in children born after in vitro fertilization or intracytoplasmic sperm (IVF/ICSI) injection was low, and compared to spontaneously conceived children the risk was not increased, except for a borderline increased risk of tic disorders (HR 1.4 (1.0-1.9), AR 0.3%). In contrast, children born after ovulation induction with or without insemination (OI/IUI) had a low, but significantly increased risks of any mental disorder (HR 1.2 (1.1-1.3), AR 4.1%), autism spectrum disorders (HR 1.2 (1.1-1.4), 1.5%), hyperkinetic disorders (HR 1.2 (1.1-1.4), AR 1.7%), conduct, emotional, or social disorder (HR 1.2 (1.0-1.5), AR 0.8%), and tic disorders (HR 1.5 (1.2-2.0), AR 0.4%). There was no systematic risk related to any specific type of hormonal medication.

Conclusions: An increased risk of mental disorders was observed in children born after OI/IUI, while children born after IVF/ICSI were found to have overall comparable risk with children conceived spontaneously.

CH.14 Tue Kjølhedede LONG-TERM PROGRESSIVE RESISTANCE TRAINING IMPROVES FUNCTIONAL CAPACITY FOR PEOPLE WITH MULTIPLE SCLEROSIS

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Introduction: Exercise therapy has become an important part of rehabilitation for people with Multiple Sclerosis (PwMS), with progressive resistance training (PRT) proving to be a safe and effective way of improving maximal muscle strength (MMS). However, most conducted studies are of relatively short duration and conflicting results exist regarding the effects of PRT on functional capacity (FC). Thus, one purpose of this study was to elucidate the effects of long-term PRT on FC in PwMS.

Methods: 35 PwMS were randomized to perform either 24 weeks of supervised PRT (n=18) or constitute a non-training control group (n=17). Measures of FC included; timed 25ft walk test, 2min walk test, 5-time sit-stand and stair climb test. Additionally, the 12-item MS Walking Scale (MSWS12) was completed. MMS was measured as peak torque of the knee extensors and flexors. Baseline values, within and between groups changes (post-pre) was compared between groups using Student's t-test.

Results: 32 of 35 PwMS completed the study. For all patient characteristics, MMS and FC, training and control group were similar at baseline. After 24 weeks of supervised PRT, the improvements in MMS and all measures of FC were higher for training than for control group. Within the control group no changes were observed in any measures, while the training group improved in all measures of MMS and FC ($p < 0.05$). No difference in changes between groups was observed for MSWS12, however within training group a tendency to improvement was observed ($p = 0.06$).

Conclusions: This long-term study supports earlier short-term findings and further strengthens the contention that PRT is capable of improving MMS and FC for PwMS.

CH.15 Ioanna Milidou INFANTILE COLIC, HYPERKINETIC DISORDER, AND EMOTIONAL AND BEHAVIOURAL PROBLEMS IN CHILDHOOD - THE DANISH NATIONAL BIRTH COHORT

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Background: Infantile colic is considered a transient problem, but infants with colic may have persistent behavioural problems. We studied the association between history of infantile colic and attention deficit, hyperactivity, emotional and behavioural problems.

Materials and methods: Data on crying symptoms in infancy and Strengths and Difficulties Questionnaire (SDQ) scores at 7 years were available for 39,000 singletons from the Danish National Birth Cohort. SDQ scores in the upper 10% of community samples were characterized as abnormal. We compared infants with and without infantile colic by estimating odds ratios (OR) for abnormal SDQ scores using logistic regression and hazard ratios (HR) for diagnosis of hyperkinetic disorder (HKD, ICD10 F90.0-F90.9) using Cox regression.

Results: Infants with infantile colic had an increased risk of abnormal scores in all SDQ difficulties subscales (OR [95% confidence intervals]: emotional symptoms 1.6 [1.4-1.8], conduct problems 1.5 [1.3-1.7], attention deficit/hyperactivity 1.5 [1.3-1.8], relation with peers 1.4 [1.2-1.6], and total difficulties score 1.6 [1.4-1.9]), and an increased risk of HKD diagnosis (HR 1.4 [1.1-1.9]). Results were similar after adjustment for gestational age, birth weight, intrauterine exposures, and maternal SDQ symptoms.

Conclusion: Infants with infantile colic had higher risk of emotional, behavioural, attention deficit/hyperactivity problems, and for being diagnosed with HKD. This may indicate that infantile colic is an early symptom of these underlying conditions.

CH.16 Gitte Susanne Rasmussen EXPLORING THE NEEDS OF STRUCTURED PATIENT EDUCATION IN FAMILY MEMBERS TO YOUNG PERSONS WITH PSORIASIS

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Young people with the chronic autoimmune skin disease psoriasis struggle to make their disease fit into everyday life and minimise its influence on appearance and functioning. Parents' ability to seek and understand appropriate advice is decisive for the emotional impact of the disease on their children and young persons. Serious long-term impact of the disease on the life course has emphasized the importance of early preventive intervention like patient education, focusing on the factual needs and preferences of the participants, including their involvement in the designing process.

The aim of this paper was to assess the needs of patient education as a precondition for planning aims and objectives in a structured programme targeted at family members to young people and children with psoriasis. Interpretive description is used as a research strategy and provides a logical structure and philosophic rationale for the design decisions made in this project, aimed to generate credible and meaningful disciplinary knowledge. The preliminary framework is based on theories about self-management, health literacy as well as illness and body perception. The

sample was purposively and theoretically generated, and data were constructed through focus group discussions, individual interviews and questionnaires including 25 young people and 4 closely related family members. This poster presents some exploits of the dialectic between theory and the data in the analysis process. We argue that health literacy capacity facilitates parents understanding of what psoriasis can do to the young person, the stigmatizing process and the "inside and outside" of the illness.

CH.17 Charlotte Green CHALLENGES OF EDUCATIONAL RESEARCH
Carlsen

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Objectives: Societal changes demand efficient surgical training. Deliberate clinical operative training within a short time- frame may be this future model. This study set out to measure the effect of such a fast-track training module applied in laparoscopic cholecystectomy.

Design and participants: 35 Danish surgical specialty trainees (registrars) were randomized to either a fast-track module with performance of 20 procedures or standard clinical training. The performed laparoscopic cholecystectomies were blindly rated by three raters using GOALS. Due to heavy drop-outs only 10 completed the study.

Results: Data show significant effect of the fast-track program on the skills score compared to standard training at one year follow-up despite equal number of performed procedures in the two groups.

Conclusion: Fast-track show promising effect as an efficient, clinical skills training in surgical training of more advanced level. However, inter-rater reliability was low and only few trainees completed the study due to a number of reasons. Challenges in educational randomized studies will be discussed.

CH.18 Helene Kirkegaard MATERNAL PREPREGNANCY FAT DISTRIBUTION IN RELATION TO GESTATIONAL WEIGHT GAIN AND BREASTFEEDING DURATION: THE CORONARY ARTERY DEVELOPMENT IN YOUNG ADULTS (CARDIA) STUDY

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Background: Maternal obesity is more than body mass index (BMI). Fat may be stored in the abdomen and/or at the hips and thighs which affects the body and its metabolism differently. Fat distribution may also influence

maternal reproductive health, but very little is known about this aspect due to difficulties in recruiting women before conception.

Aim: We examined how prepregnancy waist circumference (WC) and BMI independently were associated with gestational weight gain and breastfeeding duration.

Methods: From the CARDIA study we included 807 women with 1,071 births between 1985 and 1996. At baseline, follow-up year 2, 5, 7, and 10, BMI and WC were measured and information on potential confounders was collected. Prepregnancy measures were obtained from the examination closest to the conception date. Recall information on gestational weight gain was collected at year 10 and on breastfeeding duration at year 7 and 10. We did complete case analyses using linear and logistic regression.

Results: Adjusted for BMI and other potential confounders, a 5 cm increase in WC was related to -1 kg (95% CI -1.54; -0.46) gestational weight gain and -8.7 days (-14.4; -3.1) in duration of breastfeeding. Also, the BMI-adjusted OR for 'ever' breastfeeding compared to 'never' was 0.92 (0.88; 0.96) per cm increase in WC. In contrast, the WC-adjusted OR was 1.13 (1.04; 1.22) for per BMI unit increase when 'ever' was compared to 'never'.

Conclusion: The findings suggests that measuring maternal WC in addition to BMI before pregnancy is more informative than just BMI, and abdominal and hip/thigh fat mass may contribute differently to gestational weight gain and breastfeeding duration.

CH.19 Ane Birgitte AUTISM SPECTRUM DISORDERS IN CHILDREN OF PARENTS WITH
Telén Andersen INFLAMMATORY BOWEL DISEASE - A NATIONWIDE COHORT STUDY IN
DENMARK

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Background and aim: Inflammatory bowel disease (IBD) and autism spectrum disorders (ASD) may share genetic and environmental risk factors. We examined whether parental IBD is associated with an increased risk of ASD in offspring.

Methods: We conducted a registry-based nationwide cohort study including children born alive in Denmark from 1 January 1994 to 31 December 2009, with follow-up throughout 2010. IBD in parents and ASD in offspring were identified using inpatient and outpatient hospital diagnoses. We computed risk of ASD and crude and adjusted incidence rate ratios (aIRR) with 95% confidence intervals (CI) using Cox proportional-hazards regression. We evaluated risk of ASD according to maternal and paternal IBD, and separately for maternal and paternal Crohn's disease (CD) and ulcerative colitis (UC). Children with parents free of IBD were the comparison cohort.

Results: We identified 1,005,330 children during the study period. Among them, 11,888 (1.2%) had a parent with IBD and 8087 (0.8%) had a diagnosis of ASD during up to 17 years of follow-up. The 10-year risks of ASD were

0.7% among children of parents with IBD and 0.9% among children of parents without IBD. The aIRR for ASD among children with parental IBD was 0.8 (95% CI: 0.6-1.0), and results were similar regardless of parent of IBD origin or whether a parent had CD or UC. The estimates were similar for different ASD subtypes.

Conclusion: We found no evidence of an increased risk of ASD among children born to parents with IBD.

CH.20 Malene Schou
Nielsson PREVALENCE OF BACTEREMIA IN THE INTENSIVE CARE UNIT: A DANISH CROSS-SECTIONAL STUDY

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Introduction: Bacteremia is associated with increased morbidity and mortality, and bacteremia prevalence has been estimated to be 15% during ICU admission. Limited data exist on how prevalence of bacteremia differs by age among ICU patients.

Objectives: To determine bacteremia prevalence among ICU patients in relation to age.

Methods: We used population-based medical and administrative registries to identify a cohort of 47,579 patients admitted to 1 of 12 ICUs in Northern Denmark during 2005-2011. We obtained information on bacteremia within 7 days of ICU admission; information on pre-existing morbidity according to Charlson's Comorbidity Index and surgery performed within 7 days of ICU admission. We estimated bacteremia prevalence at ICU admission (defined as bacteremia within 7 days of ICU admission), and compared prevalence between age groups (15-49, 50-64, 65-79, 80+ years of age) by prevalence odds ratios (PORs) computed by logistic regression, stratified by type of admission (medical, acute/elective surgical), adjusting for sex and pre-existing morbidity.

Results: Of the 47,579 patients, only 1,627 (3.4%) of the patients had bacteremia at ICU admission. In medical patients < 50 years prevalence of bacteremia at time of admission was 2.6% while prevalence in all age groups above 50 years were 6-7%. Prevalence was lower among acute/elective surgical patients and was below 1% for elective surgical patients regardless of age.

Conclusions: Bacteremia prevalence at ICU admission was increased in patients ≥ 50 years compared with patients aged 15-49 years. There was, however, no further increase in PORs with advancing age above 50 years.

CH.21 Charlotte K. FAMILIAL COLORECTAL CANCER RISK EXCLUDING FAMILIES WITH

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Background: Colorectal cancer (CRC) risk is reportedly increased 2-fold if at least one first degree relative (FDR) is affected with CRC, increasing to 3-4 fold if multiple FDRs are affected or if one FDR was diagnosed young. However, previous studies have not excluded high risk families with Lynch syndrome/Hereditary Non Polyposis Colorectal Cancer or Familial Adenomatous Polyposis. We investigated familial risk of CRC after excluding these high risk families.

Methods: We identified FDRs to CRC probands diagnosed 1995-1998 using Danish population registries. Family history of CRC was assessed at date of the proband's diagnosis using Danish medical registries. FDRs living without CRC at this date were included in the follow-up cohort. Each FDR was matched on age and gender with 10 individuals from background population. Cox proportional hazard modeling was used to estimate hazard ratios (HR) to compare the risk of CRC in the FDRs to the comparison cohort.

Results: 4182 FDRs from 1060 families were included. The risk estimates were: At least one FDR with CRC HR=1.78 (95% CI: 1.46, 2.17), 1 FDR diagnosed after age 50 HR=1.68 (95% CI: 1.32, 2.14), 1 FDR diagnosed before age 50 HR=1.86 (0.72, 4.82), and multiple affected FDRs HR=2.04 (95% CI: 1.39, 2.98).

Conclusion: Once excluding high risk syndromes, the overall risk in FDRs to CRC patient was comparable with results of previous studies. The risk of CRC in individuals with multiple FDRs with CRC or one FDR diagnosed young seem, however, lower than reported previously.

CH.22 Jesper Padkær Petersen THE UGT1A1*28 POLYMORPHISM AND ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN, A CASE-CONTROL STUDY

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Oxidative stress is a possible risk factor in the development of acute lymphoblastic leukemia (ALL) in children. Bilirubin is a potent endogenous antioxidant of possible clinical relevance, and the UGT1A1*28 polymorphism is the main known genetic cause of variation in plasma bilirubin

amongst whites in Western Europe.

In a case-control study of 665 incident cases of ALL in childhood (age at onset 1-14 years) in Denmark 1982-2011 and 1379 controls, we explored, whether the UGT1A1*28 allele was associated with a lower risk of ALL in childhood.

Secondary analysis was done on age at onset in three groups (1-4 years, 5-9 years and 10-14 years), and on the ALL subtypes precursor B cell, T cell and t(12;21) positive status.

Cases were identified in The Danish Registry of Childhood Cancer, and genotypes were estimated from dried blood spots stored in The Danish Newborn Screening Biobank.

We found no association between ALL in childhood and UGT1A1*28 genotypes. The sex and birth decade-adjusted odds ratio was 1.01 (0.88-1.17) for heterozygotes and 1.03 (0.78-1.36) for homozygotes. Also, no associations were found in the secondary analyses.

CH.23 Anne Brosbøl-Ravnborg SYNERGY BETWEEN VITAMIN D₃ AND TOLL-LIKE RECEPTOR AGONISTS REGULATES HUMAN DENDRITIC CELL RESPONSE DURING MATURATION

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Background: Maturation of human dendritic cells (DC) can be inhibited by vitamin D₃ and vitamin D₃ deficiency has been associated with immune-mediated diseases, including multiple sclerosis. A recent study shows that the influence of vitamin D₃ on TLR4 ligand-induced activation of antigen presenting cells (APC) is dependent on the order of VDR and TLR4 engagement. To further study the interplay between TLR agonists and vitamin D₃, we examined the maturation and cytokine profile of DC differentiated in vitro.

Methods: Monocyte-derived DCs were treated with vitamin D₃ during differentiation, and maturation was induced with TLR2 and TLR4 agonists. DC surface expression of HLA-DR, CD14, CD40, CD80, CD83, and CD86 was analyzed by flow cytometry, cytokine secretion was quantified by ELISA, and expression of vitamin D₃ receptor (VDR) was detected by Western blotting.

Results: One of the earliest changes to LPS-induced maturation was an increase in CD83 expression, which was inhibited by vitamin D₃. In addition, vitamin D₃ inhibited other markers of DC differentiation and maturation. Vitamin D₃ acted in synergy with the TLR2 and TLR4 agonists in inducing IL-6, IL-8, and IL-10, whereas it completely blocked LPS-induced secretion of IL-12. The synergy occurred at concentrations where neither vitamin D₃ nor the TLR agonists alone induced measurable cytokine secretion. The TLR2 and TLR4 agonists enhanced the level of VDR.

Conclusions: Vitamin D₃ and TLR agonists acted in synergy to alter secretion of cytokines from human DC in a direction that may provide an anti-

inflammatory environment.

- CH.24 Thomas Nordstrøm Kjær RESVERATROL AMELIORATES PSORIASIS-LIKE SKIN INFLAMMATION: AN ANIMAL STUDY

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Background: Psoriasis is a disease of skin- and systemic low-grade inflammation. Pro-inflammatory cytokines (e.g. IL-6, IL-1 β , TNF- α) from both keratinocytes and T-lymphocytes produce the inflammation seen in psoriasis. The effects of some of these cytokines are mediated by NF κ B. Resveratrol (RV) is a naturally occurring compound found in grapes, nuts and berries, and possesses anti-inflammatory effects in macrophage/adipocyte cell lines, cultured adipocytes and in human tissue explants. RV is a known NF κ B inhibitor.

Aim: To evaluate effects of RV on psoriasis-like skin inflammation in mice.

Method: Imiquimod crème induces a psoriasis-like skin inflammation in BALBc/AnNTac mice. Thirty BALBc/AnNTac mice were distributed into 3 groups of 10; controls, Imiquimod (IMQ), Imiquimod-resveratrol (IMQ-RV). The groups IMQ and IMQ-RV received a daily dose of 62.5 mg of 5% Imiquimod cream on their back and right ear. The controls received 62,5 mg daily dose of vehicle cream on their back and right ear.

RV was added to the feed of the IMQ-RV group (400 mg/kg animal/day). The IMQ and control groups were given standard feed. The animals were weighed on day 0 and 7. Thickness of a skinfold on the back (day 7) and thickness of the right ear (day 0 and 7) was measured using a caliper. Skin erythema, scaling and thickness were evaluated day 0, 2, 4 and 7 using the Psoriasis Area Severity Index.

Results: We induced a psoriasis-like skin inflammation in mice treated with IMQ. The IMQ-RV group had significantly lower PASI score and thickening on both the ear and the skinfold on their back compared to the IMQ group. The ear fold thickness in the IMQ-RV group was reduced to the level the the control group.

- CH.25 Marie Juul Ørnstrup RESVERATROL INHIBITS PROLIFERATION, BUT PROMOTES DIFFERENTIATION OF HUMAN OSTEOBLASTS

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Background: Resveratrol (RSV) is a natural polyphenol which activates SIRT1, inhibits NF κ B, and has antiinflammatory properties. RSV stimulates both proliferation and differentiation of some osteoblastic cell lines. In rodent studies (ovarectomy- and immobilisation-studies) RSV treatment prevented the expected bone loss.

Aim: To investigate osteoblast proliferation and differentiation under normal conditions and inflamed conditions, with and without resveratrol stimulation.

Methods: Human bonemarrow-derived mesenchymal stem cells isolated from bone marrow aspirates of 13 healthy adult donors. Each donor provided cells to 4 different cultures (control, +RSV, +LPS, +LPS and RSV), and after 18 days of stimulation markers of proliferation and differentiation were measured.

Results: Lipopolysacharid (LPS) induced a significant increase in IL6 production in the osteoblastic cellcultures ($p < 0.05$). Co-stimulating with RSV tended to reduce the IL-6 production, but not significantly. The LPS-induced inflammatory state led to significant increase methyleneblue ($p = 0.001$), but did not affect alkaline phosphatase (AP) and P1NP. RSV alone caused a significant decrease in methyleneblue ($p = 0.02$) but also when added in addition to LPS ($p < 0.001$). AP were significantly increased in both RSV treated cultures ($p < 0.05$, $p < 0.05$, respectively)

Conclusion: LPS induces inflammation, which, in turn, stimulates proliferation, but has no effect on osteoblast differentiation. RSV did not counteract the LPS-induced inflammation, so its bone-protective effect is probably through other pathways. RSV alone, and when costimulating with LPS, inhibit proliferation of human osteoblasts, but increases differentiation.

CH.26 Ravikiran Mahadevappa EFFECT OF KIDNEY SPECIFIC INACTIVATION OF MEGALIN ON NEPHRON NUMBERS AND GLOMERULAR FILTRATION RATE IN MICE

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Megalin, a scavenger receptor expressed in kidney proximal tubular epithelial cells, plays a major role for the tubular reabsorption of filtered molecules. Megalin is expressed very early during nephrogenesis and may play a role for normal renal development. Observations in humans suggest that the absence of megalin may be associated with progressive, renal insufficiency. To examine the role of megalin expression for long term renal function we analyzed glomerular filtration rate (GFR), proteinuria, and morphology in conditional megalin-deficient mice produced using the cre-recombinase gene and wnt4 promoter, as previously described by our lab. Mice were analyzed at 6 months and at 12 months of age. Nephron number was calculated using the physical dissector method and GFR was measured as urinary FITC-inulin clearance. We did not observe a difference in GFR between megalin knockout mice and wild type mice at 6 months of age. However, the GFR was reduced at 12 months age, both in megalin knockout mice and wild type mice. Furthermore, these observations were supported by equal nephron number counts both at 6 months and at 12 months of age. These results indicates that absence of megalin do not influence nephron number and GFR thereby maintaining normal kidney physiology.

CH.27 Tine Kjærsgaard CD320 IS THE KEY ROLE PLAYER FOR PLACENTAL UPTAKE OF TC-B₁₂ - MEGALIN MAY NOT PLAY A SIGNIFICANT ROLE

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Receptor-mediated endocytosis is an important mechanism by which cells internalize biomolecules. One of these biomolecules is the complex of transcobalamin-vitamin-B₁₂ (TC-B₁₂), which is known to be endocytosed either by the multi-ligand receptor protein megalin or the somewhat smaller membrane receptor protein known as CD320. Whereas megalin expression is limited to a few tissues, including kidney and placenta, CD320 is almost ubiquitously expressed.

TC-B₁₂, and in particular B₁₂, plays a crucial role in any cell and is limiting for cell division and maturation. B₁₂ is naturally also important during fetal development however the mechanism for its maternal-fetal transport across the placenta is largely still unknown.

Both megalin and CD320 are expressed in human placenta, presumably within the syncytiotrophoblasts, but until now their exact role during endocytic placental uptake and transfer of TC-B₁₂ remain speculative.

The aim of this project was to characterize the localization and function of megalin in human placenta, by using syncytiotrophoblast-like cell models. During these studies, where the endocytic uptake of ¹²⁵I-TC-B₁₂ was studied in different syncytiotrophoblast-like cell models, e.g. JEG-3 and BeWo cells, we discovered that megalin may play only a minor role during this uptake. We have now investigated this further and have also included CD320 in our studies. Our recent results add significant knowledge to our understanding of TC-B₁₂ uptake in syncytiotrophoblasts of human placenta and to the function of CD320 in human placenta.

CH.28 Jean Farup WHEY PROTEIN AUGMENTS MYOGENIC STEM CELL POOL FOLLOWING MUSCLE DAMAGING EXERCISE

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Introduction: Turnover of skeletal myocellular components is partly dependent on muscle stem cells. Since the nuclei of myocytes are post mitotic, addition of new nuclei as well as repair of and formation of new myocytes rely on recruitment of a pool of myogenic stem cells, named satellite cells (SC). Therefore, the ability to activate the SCs in regeneration processes after muscle damage is critical.

Methods: Human subjects completed muscle damaging eccentrically

based exercise. In the immediate hours and in the two days following exercise, subjects received either whey protein (WHD) or iso-energetic carbohydrate placebo (PLA). Muscle biopsies, blood samples and functional muscle measures were collected before, 24, 48 and 168 hours following exercise and analyzed for markers of muscle damage and activation of SCs. Results: Increases in serum creatine kinase, muscle soreness and a decrease in muscle function were observed, with no major differences between groups. Analysis of SCs revealed an increase in the WHD group ($\approx 200\%$), which was not evident in the PLA group. The increase was primarily in SC associated with type II muscle fibers.

Discussion: Our results suggest that type II fibers are more sensitive to muscle damaging exercise or that type II fiber contain a higher intrinsic capacity for activating SCs. Furthermore, these findings suggest that SCs are sensitive to amino acid supplementation which may have clinical implications for muscle recovery.

CH.29 Christina Maar
Andersen PSYCHOMETRIC PROPERTIES OF THE DANISH VERSION OF THE
RELATIONSHIP SCALE QUESTIONNAIRE

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Background: There is a growing interest in how patients' attachment styles may affect their illness behaviour and how physicians' attachment styles may affect clinical outcomes. The Relationship Scale Questionnaire (RSQ) is a widely used measure of adult attachment, but the psychometric properties of the Danish translation of the scale have not been determined. The objective was to assess data quality and to validate the proposed factorial structure of the Danish RSQ.

Methods: All 835 GPs in the Central Denmark Region were invited to participate in the study and received the RSQ. A confirmatory factor analysis (CFA) was conducted to establish the four proposed prototypes of the RSQ (secure, fearful, dismissing and preoccupied). Data quality was assessed by mean, median and missing values, and for each prototype floor and ceiling effects, average inter-item correlations, and Cronbach's α was assessed.

Results: The response rate was 72%. The item response was high (98.8-97.5%). No floor or ceiling effect was found for any of the four prototypes. The internal consistency in the prototypes was low with inter-item correlations, ranging from 0.10 to 0.35 and Cronbach's α 0.34 to 0.70. The χ^2 test of model fit for the CFA indicated a poor comparative fit ($\chi^2 = 1159.007$, $df = 112$, $p < 0.001$), and all of the goodness-of-fit tests were violated (CFI = 0.621, TLI = 0.540, SRMR = 0.122, and RMSEA = 0.127).

Conclusion: The four proposed prototypes of the RSQ were not supported by the CFA. As the low internal consistencies of the RSQ subscales also pose some concerns about the factorial properties of the scale, it is recommended that an explorative analysis is conducted.

CH.30 Marie Beck Iversen IDENTIFICATION OF A NOVEL INNATE ANTIVIRAL MECHANISM WORKING PRIOR TO THE ACTION OF INTERFERONS

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Epithelial surfaces constitute a major portal of entry for infections. Herpes simplex virus 2 (HSV-2) is a leading cause of infections at genital mucosal surfaces. The innate immune system sense pathogens and induces antimicrobial effector molecules. Especially the type I interferons (IFN) are well established to have a crucial role in the innate antiviral response. The aim of this project is to describe and characterize an identified early immune response elicited by vaginal HSV-2 infection prior to the production and function of IFNs.

Results: After genital HSV-2 infection, type I IFN was detected in vaginal washes on day 2 post infection (p.i.), and IFNAR^{-/-} mice exhibited elevated viral titer on day 2 but not on day 1 p.i. By contrast, mice deficient in CXCR3, the receptor for CXCL9 and 10, displayed pronounced signs of disease compared to wild type (WT) mice and had elevated virus titer on day 1 p.i. Interestingly over a panel of cytokines, CXCL9 and 10 were selectively upregulated in vaginal washes on day 1 after HSV-2 infection. In the female genital tract, neutrophils but not NK cells were recruited on day 1 p.i. and this occurred through a CXCR3-dependent mechanism.

Conclusion: Our data indicate the existence of an antiviral pathway triggered by genital HSV-2 infection prior to the induction of IFNs. This innate immune reaction is dependent on CXCR3 likely through CXCL9/10 driven recruitment of neutrophils.

CH.31 Morten Leif Stilund BIOMARKERS FOR TREATMENT EFFICACY AND PROGNOSIS IN MULTIPLE SCLEROSIS

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Background: We have previously established the potential of soluble CD163 (sCD163), a macrophage/microglia specific protein, as a candidate biomarker in a panel of diagnostic biomarkers for multiple sclerosis (MS).

Hypothesis and aim: Soluble CD163 has potential, as a biomarker in serum and cerebrospinal fluid (CSF) samples, to optimize management of MS treatment and MS prognostics. We intend to investigate sCD163 together with other biomarkers, both novel and well-known, in a panel of MS biomarkers for treatment and prognostics.

Methods: Paired samples of serum and CSF were collected from patients (n=183) during MS diagnostic work-up. In a follow-up one year after

diagnosis, patients (n=98) with MS or clinically isolated syndrome (CIS) were re-examined with magnetic resonance imaging and asked to participate with re-sampling of CSF and serum. More than 25 patients agreed to have their CSF and blood re-examined. These samples are now analysed with enzyme-linked immunosorbent-assays, flow cytometry and time-resolved immunofluorimetric assays for a series of biomarkers.

Results: Assays are in progress and data are pending.

Perspectives: Among the challenges for optimal diagnostics and treatment of MS is the heterogeneity in both presentation and disease course of patients with MS. Additionally, new therapeutics for symptomatic treatment are continuously introduced. Thus, there is increasing international focus on the development of optimal biomarker panels for monitoring of treatment efficacy. As a specific marker for macrophage activation and inflammation, known to be significantly elevated in MS CSF, sCD163 has potential as a useful component in an optimised biomarker panel.

CH.32 Troels Rønn
Kjær

STRUCTURAL CHARACTERIZATION OF MANNAN-BINDING LECTIN AND ITS ASSOCIATED PROTEINS

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The ability of pattern-recognition molecules (PRMs) to bind foreign markers, so-called pathogen-associated molecular patterns (PAMPs), is central to the innate immune defence. The complement system is an important defence mechanism within the innate immune system, and consists of soluble and membrane bound proteins in extracellular fluids capable of reacting towards specific molecular patterns associated with, e.g., pathogens and necrotic cells.

The oligomeric mannan-binding lectin (MBL) is the most studied PRMs of the complement system. Upon recognition and binding to a suitable pattern of carbohydrates MBL ensures activation of associated serine proteases, such as MASP-2. Activated MASP-2 cleaves complement factors C2 and C4 and initiates the downstream activation of the complement cascade.

I am studying the interaction between MBL and its associated proteins. I have purified and separated MBL into distinct oligomers, and I am currently investigating the interaction between MBL and some of the associated proteins that we have produced recombinantly.

We have suggested a model of the activating complex of the lectin pathway, a complex of tetrameric MBL together with a dimer of MASP. Our recent small angle x-ray scattering data of the complex confirms our model.

We are currently trying to crystallize one of the MBL associated proteins and are pursuing electron microscopy imaging of the activating complex.

By describing the interaction of these complexes, we believe we can

provide a basis for understanding the molecular mechanisms leading to activation of the lectin pathway of complement activation. Such know-how may be of clinical relevance in inflammatory conditions.

CH.33 Per Qvist

THE SCHIZOPHRENIA ASSOCIATED GENE GOVERNS NORMAL BEHAVIOR, COGNITION AND NEUROTRANSMISSION IN MICE

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The bromodomain-containing 1 gene (BRD1) has repeatedly been found associated with schizophrenia with particularly SNPs in the putative promoter region of BRD1 being replicated across studies. BRD1 encodes a transcription factor which chromatin interactome is enriched with schizophrenia-associated genes. We hypothesize that disrupted BRD1 expression contributes to schizophrenia etiology through dys-regulated transcriptional control of genes acting at key schizophrenia pathways.

In the present study, we establish that BRD1 promoter risk variants correlates with reduced BRD1 expression as a result of decreased transcriptional drive. Accordingly, we have created a genetically modified strain of mice (Brd1^{+/-} mice) in which disruption of Brd1 expression results in a broad range of schizophrenia-associated behavioral and cognitive phenotypes combined with changes in neurochemistry, altered GABAergic signaling and seizure susceptibility. In line with a function in histone modification, we show that Brd1 regulates the expression of genes with suggested roles in neurotransmission.

Our study links the genetic association of BRD1 to schizophrenia pathogenically relevant endpoints and presents the first rodent model that, through transcriptional regulation, mimics the polygenic nature of schizophrenia.

CH.34 Simon Mølgaard SORTILIN AND SORCS2 IN THE GABAERGIC SYSTEM OF THE HIPPOCAMPUS
Jensen

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GABAergic interneurons in the hippocampus play a critical role in the central nervous system as proper GABAergic function is central for higher brain processes such as memory and cognition. A dysfunction of the GABAergic system has been implicated in several psychiatric illnesses, e.g. depression and schizophrenia. GABAergic interneurons constitute a diverse population, and are characterized by their anatomical, electrophysiological

and biochemical make-up such as the calcium-binding proteins parvalbumin, calretinin and calbindin. Sortilin and SorCS2 are members of the Vps10p-domain receptor family. They are highly expressed in the central nervous system, where they are important components in synaptic plasticity. Furthermore, SorCS2 has been identified as a risk-gene for schizophrenia and bipolar disorders. Studies have shown that mice lacking sortilin or SorCS2 show reduced cognitive skills. However, the role of sortilin and SorCS2 within the GABAergic system is far from characterized. In the Dentate Gyrus, almost all of the interneurons marked by parvalbumin or calretinin express high levels of both sortilin and SorCS2 in the ventral part, whereas this is not seen in the dorsal part. Deficiency of either sortilin or SorCS2 leads to non-responsiveness to Brain Derived Neurotrophic Factor (BDNF), a critical signaling molecule in the process of learning. Although no apparent developmental effect is observed in mice deficient of sortilin or SorCS2, the acute response seems affected upon stimulation with BDNF. This indicates that sortilin and SorCS2 are important for learning and lack of either receptor can lead to a dysfunctional GABAergic system in the hippocampus.

CH.35 Jonatan
Pallesen

A STUDY OF METHODS FOR AGGREGATING ASSOCIATION SIGNALS OVER REGIONS IN GWAS DATA

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GWAS association analysis is most commonly performed by SNP. However, it is often desirable to aggregate the analysis over genes or genomic regions. There is no consensus on which method to use for estimating the association of a gene or region. In this study we implemented and compared 18 readily available methods applicable for this purpose and evaluated them based on their power and ability to maintain the type 1 error rate.

The type 1 error rate was estimated by simulating 20,000 samples for each of 8 scenarios, with varying sizes and linkage disequilibrium compositions, for which the null hypothesis is true. For the methods that had an acceptable type 1 error rate, we evaluated the power in 144 different scenarios with different regions size, linkage disequilibrium structures, minimal allele frequencies and levels of association. For each scenario 1,000 samples were simulated and the significant findings recorded.

CH.36 Ming Sun

SUSTAINED DRUG DELIVERY DEVICE FOR TREATMENT OF BREAST CANCER BONE METASTASES

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Bone metastasis is one of the leading causes of death in breast cancer patients. The current treatment is performed as palliative therapy and the

adverse side effects can compromise the life quality of patients. To effectively treat bone metastasis and avoid the limitation of current strategy, a local sustained anticancer agent delivery device (DESCALYMR_DOX) is introduced in this study. The drug-release kinetics was investigated by loading two different concentrations of doxorubicin into the scaffold. It showed a dose-dependent manner of drug release. The Cell viability test, DNA quantification showed that the tumor inhibitory effect is sustained up to 4 weeks in vitro. Subcutaneous implantation of DESCLAYMR_DOX in athymic mice resulted in significant growth inhibition of human tumor xenografts of breast origin and decelerated multi-organ metastases. Fluorescence images visualizing doxorubicin showed a sustained release of drug from DESCLAYMR scaffold in vivo. Furthermore, locally use of DESCLAYMR_DOX implantation reduced the incidence of cardio-toxicity of doxorubicin. The results suggest that DESCLAYMR_DOX can be used in reconstructive surgery by supporting the structure after bone tumor resection as well as having a sustained release of anticancer drugs to prevent tumor recurrence.

CH.37 Xiao Ma

THE IMPACT OF MICROGRAVITY ON HUMAN FOLLICULAR THYROID CANCER CELLS

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The Random Positioning Machine (RPM) is a three-dimensional rotating device, widely used for ground-based simulated microgravity cell culturing. In this study, we used it for poorly differentiated thyroid cancer research. FTC-133 cells were cultured on a RPM for 10 days. Comparing the results from RPM with short-term (22 seconds, parabolic flight campaign (PFC)) and long-term (10 days, Shenzhou-8 Space mission) microgravity, we evaluated differences between real (Space) microgravity and ground-based simulated microgravity. 128 secreted cytokines and more than 2000 differentially expressed genes were revealed by multianalyte profiling technology and microarray analysis, respectively. In addition, 63 significantly regulated transcripts after 22s of microgravity during a PFC were detected by microarray as well. Genes in several biological processes including apoptosis (182), cytoskeleton (80), adhesion/extracellular matrix (98), proliferation (184), stress response (268), migration (63), angiogenesis (39), and signal transduction (429) were differentially expressed.

Genes and proteins involved in the regulation of cancer cell proliferation and metastasis such as IL6, IL8, IL15, OPN, VEGFA, VEGFD, FGF17, MMP2, MMP3, TIMP1, PRKAA, and PRKACA were similarly regulated on the RPM and spaceflight conditions. The resulting effect was mostly anti-proliferative. Gene expression during PFC was often regulated in the opposite direction.

In summary, microgravity is an invaluable tool to explore new targets in anti-cancer therapy and can be simulated in some aspects in ground-

based facilities.

CH.38 Yujia Cai

TARGETED GENOME EDITING BY LENTIVIRAL PROTEIN TRANSDUCTION OF ZINC-FINGER AND TAL-EFFECTOR NUCLEASES

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Engineered nucleases, like zinc-finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs), have emerged as versatile new tools for efficient and precise genomic editing. The relevance of these technologies for future clinical use and biological experimentation relies on safe and effective means of delivering nucleases to cells of interest. Here we adapt lentiviral vectors as carriers of designer nuclease proteins, providing efficient targeted gene disruption in lentivirally transduced cell lines and primary cells. By co-packaging pairs of ZFN proteins with donor RNA in 'all-in-one' lentiviral vectors, we establish lentiviral transduction of ZFN proteins for targeted correction, modification, and insertion of genes. In addition, evidence of targeted gene disruption and repair by lentivirus-delivered TALEN proteins demonstrates the possibility of expanding the repertoire of custom-designed nucleases delivered by this approach. Our findings generate a new platform for safe and efficient use of designer nucleases in genome engineering.

CH.39 Jonas Jensen

DENTAL PULP STEM CELLS SEEDED ON MODIFIED POLYCAPROLACTONE SCAFFOLDS PROMOTES OSTEOGENIC DIFFERENTIATION IN VITRO

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Introduction: Dental pulp cells (DPSCs) have been hypothesized as an alternative source of stem cells for bone tissue engineering. The aim was to determine their efficacy on three different polycaprolactone (PCL) scaffolds.

Methods: PCL was plotted into a three-dimensional grid structure (PCL scaffold). A modified scaffold was created by infusing the pure PCL scaffold with hyaluronic acid + TCP followed by lyophilization to create a micro-porous hydrophilic coating (HT-PCL scaffold). Another scaffold was developed by infusing a homogenous mixture of PCL, water and 1,4-dioxane and afterwards perform a thermal induced phase separation (TIPS) followed by lyophilization. This NSP-PCL scaffold was structurally graded with micro- and nanopores. A total of 132 scaffolds (Ø=10mm, h=5mm) were used. DPSCs were cultured using proliferation medium for 7 days and thereafter osteogenic medium. After day 1, 7, 14 and 21, 10 scaffolds were collected for further analysis. Following analyses were performed to validate cell viability: Scaffold cellularity by quantifying the amount of dsDNA, ALP activity, live/dead staining (confocal microscopy), histology, SEM, RNA extraction and RT-PCR (GAPDH, Ubiquitin, ALP,

Collagen type I, BMP-2, Runx2 and bone sialoprotein /osteocalcin).

Results: The HT-PCL and NSP-PCL scaffold promoted osteogenic differentiation compared with pure PCL scaffold. Cell proliferation and migration into the scaffold was best facilitated on the HT-PCL scaffold compared to both the pure PCL scaffold and the NSP-PCL scaffold, making this a promising scaffold for further in vivo studies.

CH.40 Halldór Bjarki Einarsson

FOREIGN BODY GIANT CELLS MEDIATE DEGRADATION OF POLYCAPROLACTONE IN VITRO AND IN VIVO

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Introduction: In tissue engineering polycaprolactone (PCL), has been suggested as a promising template of choice for cartilage and bone repairing. The aim of our study is to investigate the in vitro and in vivo effect of foreign body giant cells (FBGC) attached to PCL.

Materials and methods: We have developed an in vitro system of human monocyte-derived macrophage fusion and FBGC formation. PCL fibers with 1 µm fluorescent carboxylated microspheres at the ratio 1:5 were prepared by using electrospinning. Characterization of PCL fibers post 7 days of culturing was performed by using scanning electron microscopy and confocal imaging. Quantitative investigation for foreign material degradation in vitro and in vivo (porcine animal model) was performed by using newCast software. For protein and gene analysis we used time-resolved immunofluorimetric assay, flow cytometry and qPCR.

Results: Our non-normal distributed data and Wilcoxon-Mann-Whitney tested indicate cells of the monocyte-macrophage lineage to mediate degradation of PCL via engulfment of 1 µm microspheres within PCL foreign body constructs. The outcome is enhanced in the presence of T cells. In addition, we demonstrate for the first time, FBGC to shed sβ₂ integrins during the process. Furthermore, our experimental data show PCL to induce deposits of complement components, which has led us to a new hypothesis; that the observed phagocytosis of microspheres within our constructs is due to foreign body opsonization by complement components secreted by the FBGC pre-cursor cells.

Conclusions: Apparently, cells of the monocyte-macrophage lineage, including FBGC, are capable of degrading foreign bodies such as PCL.

CH.41 Paula Fernandez Guerra

PROTEOMICS AND CELLULAR OXIDATIVE STRESS STUDIES IN FIBROBLASTS FROM CLASSIC MAPLE SYRUP URINE DISEASE PATIENTS

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Mutations in any of the three different genes BCKDHA, BCKDHB, and DBT encoding for the E1 α , E1 β , and E2 components of the branched chain α -ketoacid dehydrogenase (BCKDH) complex can cause Maple Syrup Urine Disease (MSUD), a rare inherited metabolic disorder (1:185,000). To study the molecular effects of mutations in BCKDH, we performed targeted and discovery proteomics on cultured fibroblasts from classic MSUD patients with mutations in BCKDHA (p.R40fs) or BCKDHB (p.R285X). Targeted proteomics by SRM (selective reaction monitoring) confirmed these mutations as protein null mutations. In both cases, the other E1 subunit was not detected in a soluble protein fraction. Relative mRNA abundance showed normal levels for wild-type genes or 20% down-regulation for E1 α or E1 β mutant. All together indicates that monomers of E1 α and E1 β could be unstable. Discovery proteomics by iTRAQ relative quantification showed that the protein profile of classic MSUD was associated with different biological processes: intracellular signalling, oxidative stress, structural remodelling, and neuronal pathways. These biological processes have oxidative stress as a common feature. Cellular oxidative stress studies in fibroblasts from classic MSUD patients showed increased mitochondrial superoxide level together with increased protein oxidative damage. In response to oxidative stress, we found activation of the cellular antioxidant response by increased levels of Heme oxygenase 1, Ferritin heavy chain and ATP-dependent Lon protease. These results could contribute to understand aetiology and symptoms associated with classic MSUD patients, as well as highlight new possible therapeutic targets.

CH.42 Priscila Corraini IMPACT OF MEASUREMENT ERROR ON THE ABILITY TO ASSESS PERIODONTITIS PROGRESSION

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Aims: To compare the intra-examiner reliability of the direct and indirect methods of obtaining clinical attachment level (CAL) measurements, and to quantify the impact of less-than-perfect reliability of the two methods on our ability to assess periodontitis progression.

Material and methods: Of 192 subjects volunteering in a prospective study on non-surgical periodontal therapy, 151 were eligible and 148 were clinically examined at baseline and approximately one week later. At both time points, a single trained examiner performed measurements of probing depth (PD), direct CAL (CAL_{DIR}) and gingival recession (GR) in 6 sites per tooth in all teeth, excluding third molars. The indirect CAL (CAL_{IND}) was calculated on the basis of PD and GR measurements.

Results: Agreement was observed in 65%, 62%, 69% and 84% of the duplicate CAL_{DIR}, CAL_{IND}, PD and GR recordings, respectively. In over half of the patients, measurement error frequencies did not allow for detection of possible CAL changes ≥ 2 mm using a false-positive rate $\leq 5\%$. True observations of CAL change were clearly more evident in patients classified as "less extensive" rather than "extensive" periodontitis. If a maximum false-positive of 20% were allowed for, it would be possible to detect CAL_{DIR} changes ≥ 1 mm in around 3% of the subjects, whereas such changes could not be detected using CAL_{IND} recordings. Using higher thresholds to define progression or remission, detection of CAL changes with low false-positives was also more likely using direct method recordings.

Conclusions: To assess periodontitis progression or monitor periodontal patients, CAL_{DIR} recordings are preferable over CAL_{IND}.

CH.43 Janni Majgaard ABNORMAL URINARY EXCRETION OF ENAC&GAMMA; IN RESPONSE TO
Jensen HYPERTONIC SALINE IN CHRONIC KIDNEY DISEASE. A CASE CONTROL
STUDY

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Introduction and aims: Renal handling of sodium and water is abnormal in chronic kidney disease (CKD). We wanted to test the hypothesis that this phenomenon is caused by abnormal activity in the aquaporin2 water channels (AQP2) and/or the epithelial sodium channels (ENaC) in the distal nephron.

Methods: We compared 23 patients with CKD and 24 healthy controls at baseline conditions and after 3 % hypertonic saline infusion. The subjects consumed a standardized diet four days prior to the study day. We measured urinary concentrations of AQP2 (u-AQP2), gamma subunit of ENaC (u-ENaC γ), free water clearance (C_{H₂O}), urinary output (UO), fractional excretion of sodium (FE_{Na}), plasma concentrations of vasopressin (AVP), renin (PRC), Angiotensin II and Aldosterone (Aldo). GFR was measured by constant infusion clearance technique using ⁵¹Cr-EDTA as reference substance.

Results: At baseline, GFR was 34 ml/min in patients and 89 ml/ml in controls. There were no differences in u-AQP2 or u-ENaC γ , but p-Aldo, p-AVP and FE_{Na}, were significant higher in patients compared to controls. After hypertonic saline infusion, u-ENaC γ decreased in patients (-23 %), but increased in healthy controls (20 %). U-AQP2 increased to the same extent in both groups. Patients with CKD had a lower decrease in C_{H₂O} and UO, but the increase in FE_{Na} and p-AVP were similar. PRC, p-Ang II and p-Aldo decreased in both groups.

Conclusions: In response to hypertonic saline, patients with CKD exhibited a reduced concentrating capacity and a decrease in u-ENaC γ compared to healthy controls. The abnormal decrease in u-ENaC γ might be an

adjustment to compensate for an exaggerated reabsorption of sodium in proximal tubules.

CH.44 Nikolaj Grøndal PRIMARY VASCULAR INTERVENTIONS AMONG MORE THAN 50,000 PARTICIPANTS IN A RANDOMIZED SCREENING TRIAL FOR VASCULAR DISEASE (VIVA)

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Introduction: Population based screening for abdominal aortic aneurysms (AAA) has been proven to reduce the AAA-related mortality and to be cost-effective at the long-term. Whether additional screening for peripheral arterial disease (PAD) and hypertension (HT) influence the rate of vascular interventions is not known but holds the potential to influence cost effectiveness of such a combined screening offer.

We report the impact on primary vascular interventions after 2 years of follow-up.

Material/methods: More than 50,000 men aged 65-74 were randomized 1:1 to a vascular screening program where PAD, potential HT and AAA were diagnosed. Data was cross-linked to The Danish Vascular Registry (DVR) containing detailed information on the individuals and the performed vascular procedures. Survival and comparative statistical analysis by non-parametric methods was used to describe freedom from surgery and the hazard ratios (HR) in the two groups by each indication for vascular intervention.

CH.45 Karen Axelgaard Lorentzen HYALURONIC ACID INDUCE ATHEROSCLEROSIS DEVELOPMENT THROUGH INCREASED VESSEL STIFFNESS AND ENDOTHELIAL DYSFUNCTION

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Diabetic macroangiopathy is characterised by vessel wall thickening arising from extracellular matrix accumulation, in particular Hyaluronic Acid (HA). To explore the pathophysiological role of disseminated HA accumulation in the arterial wall in vivo; we created a transgenic mouse model with HA overexpression in the smooth muscle cells. The model showed increased vessel stiffness and strength. Additionally, we observed accelerated atherosclerosis development when crossed with atherogenesis prone mice. Together with results suggesting that vessel wall stiffening causes endothelial dysfunction and susceptibility to atheromatosis, we propose that the HA accumulation has a definitive influence on the development of diabetic macroangiopathy.

In this study, we examine whether HA itself attributes to the increase in mechanical stiffness and how crosslinking of HA, collagen and elastin is affected when HA is present in excessive amounts. Furthermore, we investigate how the endothelium is affected through vessel relaxation studies.

We show that increased vessel stiffness persists after HA is removed by hyaluronidase treatment ($p \leq 0.005$, $n=5$). Investigations into crosslinking of the ECM reveal that HA accumulation leads to a 229% ($p=0.001$, $n=8$) increase in HA linked to a HA stabilizer. Contractility measurements show an endothelial dysfunction in the male transgenic mice; thus, we are currently investigating several factors involved in the NO/O₂⁻ balance.

Based on these findings, we suggest that the alteration in HA crosslinking is crucial to the enhanced mechanical stiffness and thus to the increase in atherosclerotic susceptibility.

CH.46 Jannik Bertelsen SHARED CARE: A NEW APPROACH TO CARDIAC REHABILITATION, BUT DOES IT INCREASE REFERRAL AND PARTICIPATION?

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Background: Cardiac rehabilitation (CR) reduces mortality and morbidity, but CR is challenged by underutilization and lack of adherence. Attendance may potentially be improved by bringing CR closer to the patient in a model of shared care CR (SC-CR) involving Municipal Health Care Centers (MHCC) and the patient's general practitioner (GP) earlier and to a greater extent. We investigate if CR after a shared care model can increase referral, accept and adherence in a randomized controlled trial (RCT) against hospital-based CR.

Materials and methods: In 4 Danish hospitals, patients were screened after admission. If diagnose was acute coronary syndrome (ACS) and eligibility criteria were fulfilled, patients were invited to join the trial with phase II CR as either hospital-based (H-CR) or SC-CR. In SC-CR, the patient has one visit in the hospital and afterwards the GP is in charge of risk factor reduction supported by educational interventions at the MHCC regarding smoking cessation, nutrition, exercise and mental health.

Results: 1146 patients admitted with ACS were screened. 826 were excluded, 7 missed. Main causes for exclusion were age ≥ 80 (270 patients) and heart failure (104 patients). 313 (27.3%) met the inclusion criteria and 212 (68%) accepted participation in the trial. 53 (25%) women and median age was 60. Among rejecters, the median age was 64 and 29% were women. Main reason for rejecting the trial was lack of desire to participate or inability to commit. Among the patients included, 82 (39%) had hypercholesterolemia at admission and 79 (37%) hypertension.

Conclusion: Rejection was primarily based on lack of knowledge to SC-CR, but proximity is not the only thing to consider.

CH.47 Morten Christian Bay Grauballe BLOCKING OF KEY SIGNALING PATHWAYS IN TYPE 2 DIABETES AND PERIODONTITIS

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In diabetic patients, there is a correlation between elevated levels of Receptor for Advanced Glycation End-products (RAGE) and the development of systemic complications. The amount of RAGEs can be influenced by inflammation such as periodontitis, which is associated with elevated levels of the pro-inflammatory cytokine TNF- α . The level of TNF- α is also elevated when Advanced Glycation End-products (AGE) activate RAGE. Furthermore, glucose metabolism is influenced by TNF- α and elevated levels can lead to hyperglycemia.

The present study aims at elucidating the interplay between diabetes and periodontitis by blocking some of the key signalling pathways in both diseases.

Methods: Diabetic Zucker rats and their lean littermates are divided into 6 treatment groups with and without periodontitis. Anti-TNF- α treatment is provided with Etanercept®, and Anti-RAGE treatment with RAGE-antibody. Diabetic state is evaluated by OGTT, HOMA, and weight and blood glucose are measured continuously. Systemic markers of inflammation are evaluated in plasma. Periodontitis is evaluated by registration of alveolar bone loss, and oral microbiota is determined by microbe identification array.

Results: RAGE and TNF- α antibodies affect the metabolism in diabetic rats with a significantly faster clearance of sugar (OGTT) and a lower insulin resistance (HOMA); systemic of inflammation are being evaluated; there was no difference in bone loss between treatment groups. The microbiological profile appeared to be dependent on the diabetic state.

Conclusion: Antibody treatment with RAGE and TNF- α may change the diabetic state which again may change the oral microbiota in diabetic Zucker rats.

CH.48 Jay Rai MOLECULAR STUDIES OF PYRUVATE DEHYDROGENASE COMPLEX

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Pyruvate dehydrogenase (PDH) is a central multi-subunit enzyme, which links glycolysis to the citric acid cycle. Accordingly, mutations of PDH cause a deficiency syndrome with deleterious effects on brain development in human. Dependent on a cell's actual need, PDH is tightly regulated by phosphorylation/de-phosphorylation which implies the formation of

transiently stable macromolecular complexes that to date are structurally poorly characterized. By using the yeast *Saccharomyces cerevisiae* as a model, we established genetically modified strains characterized by the stable addition of purification tags facilitating biochemical purification of macromolecular assemblies formed around PDH-associated proteins, including the alpha subunit as well as four regulatory genes coding for kinases and phosphatases, respectively, known to interact with the enzyme's core. In addition to sequences for purification, the tags contain fluorescent protein labels suitable for locating the respective proteins in vivo. We also designed double tagged yeast strains in order to facilitate the purification of PDH by tandem affinity purification. Notably, gradient ultracentrifugation of PDH complexes containing genetic modifications in sucrose gradients indicates that only genetic tags of a certain size and/or placement allow a formation of macromolecular complexes. Moreover, we use the PDH system to investigate the advantages of chemical cross-linkers at different steps of the purification procedure in order to stabilize fragile macromolecular complexes, ultimately leading to a better characterization of such assemblies by structural biological methods.

CH.49 Marie Louise Schmitz

ACUTE ISCHEMIC STROKE AND LONG-TERM CLINICAL OUTCOME AFTER INTRAVENOUS THROMBOLYSIS: A NATIONWIDE PROPENSITY SCORE-MATCHED FOLLOW-UP STUDY

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Background: Acute thrombolytic therapy with intravenous tissue-type plasminogen activator (tPA) reduces the risk of disability at 3 months after ischemic stroke. Data on long-term clinical outcome in tPA treated patients are scarce. We examined the long-term risk of death, recurrent ischemic stroke and myocardial infarction (MI) in tPA treated patients as compared to non-tPA treated patients.

Methods: Based on linkage of population-based Danish medical registries, we conducted a nationwide follow-up study of acute ischemic stroke patients diagnosed between 2004 and 2011. We identified 3270 tPA treated patients and 2164 could be propensity score matched with a 1:1 ratio with tPA eligible ischemic stroke patients who were not treated with tPA. By using Cox regression analysis, we estimated hazard ratios (HR) while controlling for age, stroke severity, comorbidity, quality of early stroke care and use of stroke prevention drugs during follow-up.

Results: The median follow-up time was 3.1 years. In total, 26.3% died during follow-up whereas 9.0% had recurrent ischemic stroke and 2.7% had a myocardial infarction. The tPA treated patients had a lower risk of death (adjusted HR, 0.65; 95% confidence interval (CI), 0.51-0.82) and MI (adjusted HR, 0.18; CI 0.03-0.92) as compared to the untreated group. There was no significant difference in the occurrence of recurrent ischemic stroke (adjusted HR, 0.85; CI 0.60-1.19).

Conclusion: tPA treated patients had an improved long-term clinical

outcome when compared with propensity score-matched non-tPA treated ischemic stroke patients. Better insight about why the long-term clinical prognosis after tPA appears to be more favorable is needed.

CH.50 Ann Mosegaard THE INFLUENCE OF BODY COMPOSITION ON INSULIN SENSITIVITY,
Bak GROWTH HORMONE AND INSULIN SIGNALING AND SUBSTRATE
METABOLISM AFTER 72 HOURS OF FASTING

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We aim to study and compare metabolic flexibility in obese and lean individuals after 72 hours of fasting. Obese subjects have high levels of free fatty acids (FFAs) in their blood and FFAs are both protein sparing but also cause increased insulin resistance. Prolonged fasting is equally associated with reduced sensitivity to insulin. Obesity leads to low growth hormone (GH) levels, whereas fasting is accompanied by high GH and FFA levels. It is likely that obese individuals are more capable of fasting than lean individuals due to increased activation of GH signaling and subsequent protein sparing.

In lean and obese subjects, we want to study substrate metabolism and signaling pathways in fat and muscle tissue after stimulation with growth hormone and during fasting.

Material and methods: 8 lean (BMI 19-23) and 8 obese (BMI 32-40) healthy young men are examined on 4 occasions: (i) after an overnight fast of 12 h (ii) after 72 h of fasting (iii) after an overnight fast of 12 h with a bolus injection of GH (0,005 mg/kg) at the beginning of the study day (iv) after 72 h of fasting with inhibition of lipolysis (T. acipimox 250 mg) during the last 12 hours of the fasting period.

The test subjects will go through a 6 hour study period which includes a 2 hour hyperinsulinemic euglycemic clamp (30 mU/m²/min). Biopsies from muscle and adipose tissue will be obtained and analyzed with molecular biology methods. Substrate metabolism will be assessed with tracer techniques and relevant hormones and metabolites will be measured.

CH.51 Gitte Bloch EFFECTS OF VITAMIN D SUPPLEMENTATION BEFORE AND DURING
Rasmussen PREGNANCY: A RANDOMIZED CONTROLLED TRIAL

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Background: Vitamin D (25OHD) deficiency is common among women of childbearing age. The level of 25OHD is important for the pregnancy. Vitamin D deficiency in pregnant women is associated with low birth weight, neonatal hypocalcaemia and pre-eclampsia. Literature is

conflicting - and the effects of supplementation during pregnancy on maternal, perinatal and infant health are based on limited evidence.

Aim: To investigate effects of vitamin D supplementation in women with 25OHD < 50 nmol/L, before, during, and after pregnancy.

We hypothesized that maternal vitamin D status, before and during pregnancy, is correlated with birth weight, and maternal intake of vitamin D has a positive effect on birth weight and pregnancy outcome.

Methods: A controlled, double-blinded randomized trial. Women all with wish of pregnancy and 25OHD.

CH.52 Mikkel Mylius
Rasmussen

SACRAL ANTERIOR ROOT STIMULATION IMPROVES BOWEL FUNCTION IN PATIENTS WITH SPINAL CORD INJURY

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Background: Even though introduced in 1976, the clinical effect of the sacral anterior root stimulator (SARS) on neurogenic bowel dysfunction is sparsely investigated. Our objective is to evaluate the long-term effects of SARS on bowel symptoms in a large, well defined cohort of patients with spinal cord injury.

Material and methods: A cross-sectional study of patients undergone surgery at the Department of Neuro-Urologie, Werner-Wicker Clinic, Bad Wildungen, Germany between September 1986 and July 2011. N = 587. A total of 277 SARS was available for analysis.

Results: Satisfaction with SARS was 10 (range: 0-10) on a visual analog scale (VAS) score, and 242 (87 %) used SARS for their bowel emptying procedure. Median Neurogenic bowel dysfunction score was 17 (range: 11-21), declining to 11 (range: 9-15) at follow-up, p < 0.0001; median St. Marks score changed from median 4 (range: 0-7) to 4 (range: 0-5), p = 0.01; median Cleveland constipation score changed from 7 (range: 6-10) to 6 (range: 4-8), p < 0.0001. Median VAS score for bowel symptoms changed from 6 (range: 4-8) to 4 (range: 2-6), p < 0.0001. Finally use of suppositories, digital evacuation, mini enemas and patients totally dependent on assistance during defecation declined after SARS surgery.

Conclusions: SARS has the potential to be one of the few treatment methods targeting multiple organ dysfunctions following spinal cord injury.

CH.53 Jesper
Jeppesen

CAN CARDIAC SYMPATHETIC INDEX MEASURED WITH HEART RATE VARIABILITY ANALYSES BE USED TO DETECT EPILEPTIC SEIZURES?

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Tachycardia is often seen during epileptic seizures, but it is also a characteristic result of physical exercise. In order to assess whether focal epileptic seizures can be detected by short term moving window Heart Rate Variability (HRV) analysis, we modified the geometric HRV method, Lorenzplot, to consist of only 50 R-R intervals pr. analyzed window. From each window we calculated the Cardiac Sympathetic Index (CSI) and compared the maximum CSI of the patient's epileptic seizures with that of the patient's own exercise and non-seizure sessions as control. The 11 patients analyzed all had complex partial seizures (CPS) (30 temporal, 1 frontal) during their 1-5 days Video/EEG long term monitoring. All CPS with electroencephalographic correlation were selected for the HRV analysis. The CSI was correspondently calculated after each heart beat depicting the prior 50 R-R intervals at the time. CSI showed a higher maximum peak during seizures than exercise/non-seizure (103-256%) for 7 of 11 patients within 2 seconds before till 86 seconds after seizure onset time even though exercise maximum HR exceeded that of the seizures. The 7 patients with higher CSI maximum during seizures vs. exercise/non-seizure had a tendency of higher maximum HR during seizures than the remaining 4 patients. The results indicate a sudden and inordinate sympathetic shift in the sympathovagal balance of the autonomic nervous system just around seizure-onset for certain patients. This new modified moving window Lorenzplot-method seems promising as an easy and inexpensive way of constructing a portable ECG-based epilepsy alarm for certain patients with epilepsy who needs aid during seizure.

CH.54 Juan Manuel Shiquetomi Medina

THERMAL EPIPHYSIODESIS MADE WITH RADIO FREQUENCY ABLATION, RFA IN A PORCINE MODEL

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Introduction: Anisomelia is often treated with epiphysiodesis. Current used techniques may lead to complications. RFA may be a less risky method. It involves the application of energy resulting in local thermal coagulative necrosis.

Objective: Development of a new technique for epiphysiodesis using RFA in an experimental porcine model.

Methods: Six 35 kg pigs and two 25 kg non-mature pigs were used. A control leg was randomly selected and the contralateral physis was treated at two ablation sites (lateral and medial). Under general anesthesia, a

probe was inserted and the ablation performed. T₁, T₂ and water content MR images were obtained right after the procedure; 12 weeks later for 6 animals, and 6 months later for the last 2 ones. The length of both tibiae was measured immediately after the ablation and at the end of the study.

Results: Both legs were equal at the beginning of the study and, overall, there was a leg length difference (P=0.006) in average of 4.8mm (SD=2.25, Median=3.88) at the end. For the 12 week follow-up, we found an average leg length difference of 3.9mm (SD=1.286, Median=3.666, P=0.014), and for the 6 month one we found a difference of 8.11mm in average. No damage to the surrounding cartilage structures was found. The animals could walk normally after the anesthesia, and no signs of pain or discomfort were presented during the follow-up period.

Discussion and conclusion: Epiphysiodesis using RFA is an innovative technique that may represent an alternative way of treatment that potentially involves less scarring, less exposure to X-rays, and reduces the risk of injuring the surrounding structures compared to current methods.

CH.55 Lotte Vinge

DYNAMOMETRIC MEASUREMENT OF MUSCLE STRENGTH AND FATIGUE IN MYASTHENIA GRAVIS

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Background: Myasthenia gravis (MG) is characterized by alternating muscle weakness and fatigue as a result of impaired neuromuscular transmission. In patients with MG muscle strength is expected to gradually decrease combined with increased fatigability during the day.

Aim: The objective of this study was to determine diurnal and day-to-day variation in muscle strength and fatigability in patients with generalized MG using isometric dynamometry and validated clinical evaluation scales.

Methods: By dynamometry isometric muscle strength at the shoulder, knee and ankle was determined on 10 patients and 10 healthy control subjects using the Biodex System 3 PRO dynamometer. Change in isometric muscle strength was measured during the day to determine diurnal variation and day-to-day variation. Furthermore, muscle fatigue was assessed at the shoulder and knee during repetitive maximal voluntary isometric contractions. The findings were compared to the clinical evaluation scales MG Composite and QMG (Quantitative MG score).

Results: Pending.

CH.56 Miao Wang

SURVIVAL ANALYSIS OF THE BREAST CANCER SUBTYPES IN SPINAL METASTASES

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Introduction: Preoperative evaluation of prognosis among patients with spinal metastases is a challenge for the spine surgeon to choose optimal treatments. Breast cancer is one of the most common tumors that involve the spine. Estrogen receptor (ER), Progesterone receptor (PgR) and Human epidermal growth factor receptor 2 (HER-2) status are the key factors for determine subtypes and well-known factors predicting response to the adjuvant treatment.

Aim: The aim of this study was to investigate the influence of breast cancer subtypes on survival of breast cancer patients with spinal metastases.

Methods: We included 151 pt. from Aarhus and Copenhagen. The ER, PgR and Her-2 status data were retrieved from Danish Breast Cancer Group. We used survival analysis. We created Kaplan-Meier curves. P value less than 0.05 was consider significant.

Results: ER group, Median survival time of ER (+) and ER (-) were 23.1 and 10.6m. PgR group, The median survival time of the PgR(+) and PgR(-) were 40.8 and 14.7 m. HR group, The median survival time of the HR(+) and HR(-) were 23.1 and 10.6m. Her-2 group, The median survival period of the Her-2 (+) was 25.1m, Her-2(-) was 13.9m.

Conclusion: The mortality rates differ according to subtype. Receptor positive patients have better prognosis compared with the negative subtypes. Surgeries that are more aggressive could be considered in those patients with positive biomarkers based on the potential better prognosis.

CH.57 Lene Hjelle
Tauris

WEB-BASED ENURESIS (NE) BIOBANK

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To establish a web-based NE Biobank and elucidate possible genetic variants causing different NE phenotypes in children and explore international diversities in NE phenotypes and inheritance patterns.

We envision a triad; a website, a Biobank and a secure database. The website allows patients to upload their clinical data and flow-volume-charts from home. The data uploads to local servers. A central server in Aarhus will retrieve all data directly. All Centers get administrators, who create access for their patients to the website. DNA from patients and their biological parents (control groups) will be isolated from blood or saliva samples and then stored in the Biobank. Genetic data will be compiled with clinical data in a secure database. We will invite highly esteemed International Centers of Incontinence to contribute to this Biobank. What might be found in one center will be verified in correlation to a different international center. Data will be standardized and patients compared across borders. To organize the Biobank, there will be a board of directors, i.e. members from each incontinence center, one industrial representative

and one impartial member to scrutinize processes. By-laws will entail rules on publication rights as well as rules for the use of partitioned data. Patenting of possible new findings will also be addressed.

The website is established, the first patients have been included, and biological samples stored in the Biobank.

Establishment of a web-based biobank gather unique data from enuretic patients worldwide and make genetic analysis possible on large populations concurrently, and finally making a platform for future global research in the field.

CH.58 Kresten Rickers EXPERIMENTAL REPAIR OF THE ANNULUS FIBROSUS USING MESENCHYMAL STEM CELLS AND A POLYCAPROLACTONE SCAFFOLD IN A PORCINE MODEL

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Background: At an early age, the intervertebral disc (the cartilaginous disc between the vertebral bones) starts to degenerate. Water content diminishes, and the disc develops tears, herniations, and loses height. There is at present no effective treatment for these age-related changes. We are looking into new ways of treating the intervertebral disc using biochemical factors, stem cells, and biomaterials, to prevent back pain. The focus is on the annulus fibrosus (the outer ring of the intervertebral disc). Tears in the annulus fibrosus progress into disc herniations, and the inner substance, the nucleus pulposus, leaks out. Surgery removes the herniation and relieves the pain. But the defect in the disc is not repaired. This experimental study investigates annulus fibrosus healing.

Method: The approach to repair the defect was to plug the defect and suture the plug to the surrounding tissue. A polycaprolactone scaffold was used as a plug. Scaffolds were developed and produced in collaboration with iNANO, Aarhus University. Ex vivo tests to measure motion changes were done in collaboration with the VU Medical Centre, Amsterdam. The plugs were tested in a porcine herniation model. Eight Danish landrace pigs underwent surgery. A defect was made in the intervertebral disc and repaired with a scaffold. Three months later the pigs were killed. The ability of the scaffold to stay in the annulus fibrosus will be examined. MRI and histology will be used to describe tissue integration and degeneration. Degeneration will furthermore be scored by histology and MRI.

Perspective: Depending on results, this method could be applied in the clinical setting.

CH.59 Sepp de Raedt VALIDATION OF A COMPUTER NAVIGATION SYSTEM FOR PERIACETABULAR OSTEOTOMY: PRELIMINARY RESULTS

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Introduction: The development of a computer navigation system allows for real time feedback on the three-dimensional correction applied during periacetabular osteotomy (PAO) surgery in patients with hip dysplasia. The system reports standard radiological angle measurements to quantify the acetabular coverage.

Aim: To validate the angle measurements reported by the computer navigation system using manual measurements using pre- and post-operative CT images.

Methods and materials: Radiological angle measurements were performed manually on pre- and post-operative CT images and using the Biomechanical Guidance System (John Hopkins, Baltimore, USA). All measurements were performed in the Bergmann frame of reference defined by the centers of the femoral heads and the most anterior aspect of the L5-S1 joint. We compared measurements of the center-edge angle of Wiberg and the acetabular index of Tönnis. We calculated the concordance correlation coefficient (CCC), average difference and the 95% limits of agreement for the first five patients operated on.

Results: For the center-edge angle, we found a CCC: 0.92, Avg. Diff.: -0.17, 95% LOA [-5.1;4.7]. For the acetabular index we found a CCC: 0.95, Avg. Diff.: 0.228, 95% LOA [-3.7;4.2].

Discussion: We found a good correlation between manual and the BGS reported angle measurements with limits agreement within +/-5 degrees. This variation is within the range expected for inter- and intra-rater variability. These preliminary results suggest that surgical navigation may be a valuable asset in PAO surgery and in the future may be especially useful for less experienced surgeons while in training.

CH.60 Stina Lou

KNOWING THE FOETUS: ON THE INTERCONNECTEDNESS OF BIOMEDICAL TECHNOLOGY AND HUMAN EXPERTISE

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Ultrasound monitoring is a common prenatal practice in most western countries. However, images and knowledge produced by ultrasound are always incomplete, temporal and contested. Something may not show or may not be seen on the images, and interpretation may be ambiguous. In this uncertain field, sonographers aim to produce trustworthy images and accountable knowledge of the foetus. But how?

During 5 months of ethnographic fieldwork at an obstetric ultrasound clinic in Denmark, empirical data was generated, while participating in the daily

realities of sonographers and observing more than 400 ultrasound scans. Here, sonographers put the ultrasound probe on the pregnant belly to produce blurry black-and-white images on a computer screen. Seeing the foetus generated knowledge and simultaneously knowing was a prerequisite for seeing. Furthermore, this circular seeing and knowing the foetus depended on doing. The sonographers actively produced the images, as they found their way through layers of fat tissue, navigated through shadows cast by the ribs and sensed the place and position of the foetus. Their aim was to produce images that could be trusted to represent the 'real'.

However, fieldwork made apparent that doing and knowing 'real-ness' is a complex matter. In my presentation, I will discuss what goes on 'backstage' when knowledge on the fetus is produced and shared.

CH.61 Connie Timmermann A PALLIATIVE ENVIRONMENT: CARING FOR SERIOUSLY ILL HOSPITALIZED PATIENTS

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Background: The hospital environment is often dominated by clinical sensory impressions and less attention is given to aesthetics and homeliness. In light of this, the hospital environment in general has significant potential in relation to optimizing the hospital environment into a more supportive and palliative care setting.

Aim: The aim of this study was to explore how seriously ill patients experienced being in the hospital environment and the meaning they assigned to the environment.

Method: A qualitative study design was applied using Ricoeur's phenomenological-hermeneutic theory of interpretation. Twelve patients participated while hospitalized at a teaching hospital in Denmark. Broad and open-ended qualitative interviews were conducted and combined with observations in the hospital environment.

Findings: The findings showed that the patients experienced that aesthetic decorations created a sense of homeliness that reinforced their positive thoughts and feelings in a vulnerable situation. Furthermore, by bringing some of their personal items or undertaking familiar tasks, patients were able to maintain a sense of self and to some extent a familiar and known daily rhythm. This showed to be important for the patients' sense of well-being and positive emotions.

Conclusion and implications: The results stress the importance of an aesthetically pleasing and home-like hospital environment as part of palliative care as such setting supports the patients' experience of well-being, relief and positive emotions. Such knowledge could encourage the development of new policies regarding appropriate care settings, which in turn would result in an overall improved palliative care.

CH.62 Lotte Dahl LIFE AFTER CANCER - CHANGING THE PARADIGM OF FOLLOW-UP FOR

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Objective: Evidence now reveals that attending a follow-up program may not improve low-stage gynecological cancer patients' survival. The aim of this study was to explore quality of life after cancer for low-stage gynecological cancer patients attending the standardized follow-up program. Further aim was to explore health professionals' views of and experiences with the existing follow-up program. On the basis of the above, the overall aim was to develop a screening tool to identify the vulnerable patients with specific rehabilitations needs.

Materials and methods: By shifting between qualitative and quantitative methods, the topic under inquiry was investigated as profound as possible. We used observation and semi-structured individual interviews with seven patients attending a follow-up program. Furthermore, three focus group interviews were conducted with six doctors and six nurses specialized in onco-gynecology. The qualitative studies provided input for putting down a questionnaire. Low-stage gynecological cancer patients were included in the questionnaire study and asked at: time of diagnosis, 1 month, 6 months and 12 months after surgery.

Results: The majority of the patients seem to have the personal resources or coping mechanisms to rise again and have a good life after cancer. But a group of patients do not, and may have some special rehabilitation needs. From our preliminary data, it seems that our screeningtool will be able to identify this group of patients with special needs in regard to psycho-social rehabilitation.

Conclusion: It seems to be possible to identify low-stage cancer patients with psycho-social rehabilitation needs using our screening-tool.

CH.63 Louise Mahncke IMPLEMENTING DIRECT ACCESS TO CHEST CT SCANS IN GENERAL PRACTICE; METHOD, ADAPTION AND OUTCOME

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Background: Lung cancer is the leading cause of cancer death in Western Europe. Early detection is crucial as the prognosis strongly depends on the disease stage at diagnosis. Chest X-ray is the principal diagnostic tool for General Practitioners (GPs), but implies a potential risk of false negative results, while computed tomography (CT) scans have a high sensitivity. The aim of this study was to describe the usage and outcome of direct access to chest CT from general practice.

Methods: We conducted a cohort study nested in a randomised study. A total of 120 general practices with 276 GPs were randomised into two groups. Intervention GPs were offered a technological upgrade providing direct access to chest CT combined with a Continuing Medical Education (CME) meeting on lung cancer.

Outcomes: Referral rate, number of lung cancers diagnosed, required additional diagnostic work-up and GP variations in use.

Results: During a 19-month period, 648 patients were referred to CT (0.18/1000 adults on GP list/month). Half of the scanned patients needed further diagnostic work-up, and 15 (2.3%) of the scanned patients had lung cancer; 60% in a localized stage. In total, 2/3 of the GPs used the CT. The GP referral rate was 61% higher for CME participants compared to non-participants.

Conclusion: Of all patients referred to CT, 2.3% were diagnosed with lung cancer with a favourable stage distribution. Half of the referred patients needed additional diagnostic work-up. Whether open access to chest CT will provide earlier diagnosis of lung cancer is yet unknown. Results of the randomised trial are needed before any recommendations can be made.

Trial reg.: Clinicaltrials.gov: NCT01527214.

CH.64 Tinne Laurberg ASSOCIATION OF INTRINSIC SUBTYPES BASED ON PAM50 WITH RESPONSE TO POSTMASTECTOMY RADIATION THERAPY: RESULTS FROM TWO INDEPENDENT RANDOMIZED TRIALS OF HIGH-RISK BREAST CANCER PATIENTS

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Background: Today the majority of breast cancer patients receive radiation therapy (RT) regardless of tumor characteristics.

Aim: To assess if intrinsic subtypes (defined by research-based PAM50 classifier) have a predictive value associated to RT. The testing was done among pre-menopausal women from two independent postmastectomy randomized adjuvant radiation trials with more than 20 years follow-up.

Methods: Formalin fixed paraffin embedded (FFPE) tissues (n = 128) were collected from the British Columbia trial (BC) and fresh frozen samples (n = 83) were available from a similar study by the Danish Breast Cancer Cooperative Group (DBCG 82b). Gene expression profiles were done using Nanostring nCounter® for FFPE samples and Microarray for fresh frozen samples. Tumors were classified into intrinsic subtypes: Luminal A, Luminal B, Her2-enriched, Basal-like and Normal-like, based on the PAM50 classifier. Hazard ratios (HR) presented on Kaplan-Meier probability plots

were for local-regional relapse (LRR) after more than 20 years.

Results: In the BC study, patients treated with RT had a significant lower incidence of LRR. When the tumors were classified into intrinsic subtypes, the RT lowered the incidence of LRR significantly among Luminal A tumors. There was no significant effect of RT among the other subtypes. These findings were validated in the DBCG study. Data from the two studies were pooled, HR for LRR associated with RT in the cohort: 0.40 (0.23 to 0.69), P= 0.0006 and for luminal A tumors: HR=0.16 (0.04 to 0.58), P=0.0014.

Conclusion: RT significantly decreases LRR and especially Luminal A tumors seem to be sensitive for RT.

CH.65 Marie-Louise Feddern

CHRONIC PAIN AFTER RECTAL CANCER TREATMENT. A POPULATION BASED CROSS-SECTIONAL STUDY

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Introduction: The aim of the investigation was to examine the prevalence of and factors associated with chronic pain after rectal cancer treatment.

Methods: This is a population-based, cross-sectional, questionnaire study of chronic pain in Danish patients treated for rectal cancer from 2001 to 2007.

Results: Informative answers were obtained from 1369 patients (80%). Their mean age at surgery was 65 years [range 26- 90]. The median time since surgery was 6.7 years [range 4- 10]. A total of 427 patients (31%) reported having chronic pain in the pelvic area or lower extremities, and 173 (13%) had pain daily. Pain in other parts of the body was associated with the presence of pain in the pelvic region (OR: 4.8 [3.6; 6.3] p<0.000. 9% missing data). Regression analysis show association with chronic pain in the pelvic region or lower extremities for patients being of female gender (OR: 1.9 [1.5; 2.40] p<0.00), having undergone abdomino perineal excision (OR: 1.72 [1.21; 2.46] p=0.003), Hartmanns procedure (OR: 1.74 [1.05;2.86] p=0.31), and total mesorectal excision (OR: 1.38 [1.004; 1.88] p=0.047) compared to partial mesorectal excision. Chronic pain was associated with age at surgery younger than 55 years compared to older than 75 years (OR:1.69 [1.07; 2.66] p=0.025). Chronic pain was not associated with time since surgery (OR: 1.02 [0.95;1.09] p=0.6). To the question: "Is your pain a result of your rectal cancer treatment", the patients answered 'Yes' in 66%, 'no' in 7% and 'do not know' in 23%.

Conclusion: Chronic pain after rectal cancer treatment is a hidden, but common problem associated with female gender, type of surgery, and young age at surgery.

CH.66 Sandy Mohamed Ismail Mohamed

PARAMETRIAL BOOST BY MIDLINE BLOCKED EBRT FIELDS COMPARED WITH INTERSTITIAL BRACHYTHERAPY FOR LOCALLY ADVANCED CANCER CERVIX

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Purpose: Parametrial boost (PB) by external beam radiotherapy (EBRT) is used to increase the dose to the paracervical region. Midline block is used to protect organs at risk (OAR). Yet, the efficacy of EBRT PB has not been systematically evaluated. An alternative technique for boosting is combined intracavitary & interstitial brachytherapy (IC/IS) BT. In our study we compare both techniques.

Material and method: We evaluated 51 consecutive patients with parametrial involvement at diagnosis. At BT, 23 patients had persistent parametrial involvement necessitating IC/IS BT. For the 23 patients, we compared IC BT plus PB, to the delivered IC/IS BT. PB field was created as an external beam AP/PA field of 9 Gy/5fx, with midline block conformed to the isodose line 85Gy and of at least 4cm width. For the PB scenario, summation of doses from EBRT plus an optimised IC BT plan & PB fields were used. The physical 3D dose distribution was converted to the EQD2. DVH parameters obtained in total EQD2 for target & OAR D_{2cm^3} . Testing the impact of organ movement was done by shaking the EQD2 dose map 1cm bilaterally and reading out the DVH parameters. Volume irradiated to at least 60Gy was measured.

Results: Midline blocked fields significantly increases dose by 5-9 Gy to the D_{2cm^3} of the rectum, sigmoid, bladder and bowel as compared to IC/IS BT, but was robust in terms DVH parameters for the shaken dose map. Mean HR CTV D90 were comparable for both techniques. The PB resulted in a significantly higher V60 compared to the IC/IS ($p=0.004$), which may result in increased clinical morbidity.

Conclusion: IC/IS BT compared to IC BT plus PB by EBRT spares better the OAR and deliver a more conformed RT.

CH.67 Helene Myrtue
Nielsen HYPERMETHYLATION OF LEPTIN OBSERVED IN MYELOFIBROSIS PATIENTS:
COULD LEPTIN HAVE A TUMOR SUPPRESSOR FUNCTION?

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Constitutive activation of the JAK2/STAT pathway is associated with the hematopoietic stem cell malignancies essential thrombocytosis (ET), polycythemia vera (PV), and myelofibrosis (MF). They depict a biological continuum with MF being the most severe disease. MF patients have severe bone marrow fibrosis resulting in extramedullary hematopoiesis. The

myeloid cell lineage is characterized by abnormal proliferation and maturation. Leptin is an adipokine with pleiotropic functions initiating the JAK/STAT pathway. Using the 450K platform for genome-wide DNA methylation profiling, we identified differential methylation of the leptin promoter in sorted MF blood cells at the time of diagnosis. Pyrosequencing confirmed leptin hypermethylation in 13/16 granulocyte MF samples when compared to healthy controls (P=0.0274, Mann-Whitney test) whereas all analyzed MF CD34+ cell samples displayed leptin hypermethylation (P=0.0017, Mann-Whitney test). Allele-specific methylation analysis using the rs2167270 SNP revealed heterogeneous methylation of both alleles in 9/11 heterozygous MF samples. Leptin hypermethylation was furthermore observed in cell lines of both myeloid and lymphoid origin. Higher leptin expression levels were observed in UKE-1 and SET2 cell lines after decitabine treatment. To evaluate whether leptin hypermethylation is involved in other chronic myeloproliferative neoplasms, we analyzed 46 whole blood samples and found 5/17 ET, 4/19 PV, and 3/10 CMPN hypermethylated in the leptin promoter. Our results suggest the implication of leptin in a wide variety of hematological malignancies, however, its tumor suppressor function is still unknown and needs further investigation.

CH.68 Marie Louise Bønnelykke-Behrndtz INFILTRATION OF ELASTASE-ACTIVATED NEUTROPHILS (NE); SIGNIFICANT CORRELATION TO TUMOR CELL PROLIFERATION (KI67) IN ULCERATED MELANOMA

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Background: Neutrophils are one of the dominant inflammatory cell-type infiltrating an ulcerated melanoma. However, their role and activated status is largely unknown. In mice studies, neutrophil elastase, provided by neutrophils, is found to have a direct impact on tumor cell proliferation, with poorer prognosis to follow (Houghton, 2010).

Aim: Evaluate the heterogeneity of ulcerated melanoma and estimate the density of elastase-activated neutrophils correlated to tumor cell proliferation.

Material and methods: The status (presence vs. absence), extent (% of the total tumor length) and the type (infiltrative vs. attenuative) of ulceration were estimated from H&E sections in 385 melanomas. An objective estimate of the density of granulocytes (cd66b+), elastase-activated neutrophils (NE) and melanoma cell proliferation (Ki67/MelanA) were evaluated by immunohistochemistry and computer assisted image analysis.

Results: Multivariate analysis showed that ulceration is a heterogeneous phenomenon, where an attenuative type of ulceration (HR=2.14) and excessive ulceration (HR=2.50) were independent factors for melanoma-

specific survival. Categorizing patients into groups of no ulceration, minimal/infiltrative-, minimal/attenuative- and excessive/attenuative ulceration, a decreasing 10-years survival was found between the groups, respectively. The density of elastase-activated neutrophils and Ki67 positive tumor cells were significantly correlated (Spearman 0.28 ($p < 0.0001$)), and increased within the groups, inversely related to survival.

Conclusion: Infiltration of elastase-activated neutrophils is suggested to play an important role in inflammation induced tumor cell proliferation.

CH.69 David Christoffer Hansen COMPARING ION COMPUTED TOMOGRAPHY UNDER CLINICAL CONSTRAINTS

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Introduction: Ionizing radiation with MV x-rays is a common treatment for many types of cancers, but has a number of adverse side effects due to damage to healthy tissue. Radiation therapy using charged particles such as protons has the potential to provide significant healthy tissue sparing in comparison. This is however limited by our ability to accurately predict the range of the charged particles within the patient. A better prediction of the range can be obtained by replacing the conventional x-ray CT scan with an ion CT. In this work, we present a method for comparing resolution and accuracy of ion CT scans using different ions in an unbiased manner with respect to patient dose.

Methods: A digital phantom was created in the Monte Carlo code Geant4. Ion CT scans of the phantom were simulated in 4 different scenarios: protons at 230 MeV and 330 MeV, helium ions at 230 MeV/u and carbon ions at 430 MeV/u. Doses for each of the scans were evaluated by defining an ion CT dose index (ICTDI), and images reconstructed for a 10mSv dose. Range estimation accuracy and resolution was evaluated.

Results: 230 MeV protons demonstrated the lowest resolution of 5.15 linepairs/cm, with 230 MeV/u helium ions having the highest resolution of 6.95 linepairs/cm. Helium ions had the smallest maximal systematic error of 0.34% and carbon ions the highest of 4.47%.

Conclusion: We have presented a new method for comparing ion CT implementations and shown that helium ions yield the highest resolution and most accurate reconstruction at clinically acceptable dose levels. 330 MeV protons gave a better spatial resolution, but lower accuracy than 230 MeV protons.

CH.70 Cathrine Bach MEASUREMENT OF FETAL DNA IN PLASMA OF PREGNANT WOMEN

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Background: Pre-eclampsia affects 3-5% of pregnant women and is one of the leading causes of maternal, fetal and neonatal morbidity and mortality worldwide. Preeclampsia is one of the most common causes of pre-term birth and intra-uterine growth restriction.

Early detection is essential to keep the pregnancy ongoing and thereby prevent premature birth.

No effective test for prediction of preeclampsia exists, many biomarkers has been identified but most non-specific.

Cell-free fetal DNA (cffDNA) in maternal blood has opened a new perspective in this field. Several studies indicate a rise in level of cffDNA in maternal plasma in certain conditions associated with placental pathology e.g. preeclampsia and HELLP. Most existing research is based on Y-chromosome DNA in plasma of pregnant women carrying male fetuses. Thus, a gender-independent marker is necessary.

Aim: 1. To develop a method to measure fetal DNA in maternal blood independently of the gender of the fetus. 2. To investigate the association between the level of cffDNA in the maternal blood and the function of the placenta.

Method: Maternal and fetal DNA differs in methylation pattern. By using a methylation-sensitive restriction enzyme that digests hypomethylated (maternal) sequences and leaving hypermethylated (fetal) DNA intact, the fetal fraction can be quantified by PCR.

A retrospective study compares the levels of cffDNA from pregnant women who develop preeclampsia with uncomplicated pregnancies.

Results: Using a methylation array, we have identified regions at chromosome 1, 9 and 11 with different methylation between maternal blood and CVS. Suggesting these can be used as gender-independent measurement of cffDNA.

CH.71 Mette Julsgaard A POPULATION-BASED STUDY: DO WOMEN WITH CROHN'S DISEASE BREASTFEED?

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Aim: Medical treatment of Crohn's disease (CD) is important for induction and maintenance of remission. We aimed to assess how medical treatment of women with CD in the postpartum period was associated with breastfeeding behaviour. Furthermore an association between breastfeeding and risk of relapse was investigated.

Methods: Women with CD in North Western Denmark, who had given birth between 2000 and 2005 among a population of 1.6 million. Diagnoses and birth outcome were confirmed by population-based medical databases. Breastfeeding behaviour, relapse, medical treatment and counseling regarding medical treatment were investigated by questionnaires. Medical treatment was additionally confirmed through regional prescription databases.

Results: Of 132 women, 105 (80%) fulfilled the questionnaire. Overall 59 (56%) received medical treatment in the postpartum period, of whom 50 (85%) breastfed their infants on an average period of 5 months. In the 46 women (44%) who did not receive medical treatment 42 (91%) breastfed their infants on an average period of 7 months. More than 40% (95% CI 28.1-54.3) of the women had received counseling on medical treatment and breastfeeding, most often by a gastroenterologist. Among the women in medical treatment, 11 of the 50 women (22%) who breastfed their infants experienced a relapse compared with 4 of the 9 women (44%) who did not breastfeed their infants.

Conclusion: The majority of women with CD breastfed their infants and breastfeeding behaviour did not differ by medical treatment status. Breastfeeding showed a trend towards reduced risk of relapse among women in medical treatment.

CH.72 Eva Sædder

IDENTIFICATION OF HIGH RISK MEDICATION: A LITERATURE REVIEW

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Background: High-risk medication can be defined as "medications with an increased risk of causing significant patient harm when used in error".

Aim: To create a list of drugs that caused serious medication errors from a systematic literature review.

Methods: A literature search was performed in Embase, Psychinfo, Pubmed, Cinahl and the Cochrane Library. In addition, a search in the publicly available National Agency for Patients' Rights and Complaints database, the homepage of The Patient Insurance Association and the Danish Patient Safety Database. Search terms were: medication errors, adverse drug reactions, pharmaceutical preparations, drugs, drug toxicity, adverse effects, drug induced disease, drug interactions, iatrogenic disease, drug therapy, errors, side effects (drugs) and safety.

Result: 4352 references of which 135 met inclusion criteria. 621 medication errors were found in 507 patients. 142/621 were fatal. Lack of treatment: 75/621, lack of monitoring: 68/621, not considering a reduced renal function: 37/621. Top 10 of fatal drugs included 72% of all drugs causing fatal events. Top 20 of non-fatal drugs included 84% of all drugs. The 2 lists consisted of 23 different drugs/drug classes and represented 81% of all

serious medication errors. Methotrexate, warfarin, NSAIDs, digoxin, opioids, acetylic salicylic acid and betablockers were represented in the TOP 10 of both lists and comprised 47% of all serious medication errors.

Conclusion: Seven drugs were involved in 47% of serious medication errors. Keeping focus on 7 drugs can potentially reduce hospitalizations, prolonging of hospitalizations, disability, life-threatening conditions and death by almost 50%.

CH.73 Betina Hansen CHARLSON COMORBIDITY INDEX SCORE, AGE, AND GENDER IN ACUTE MEDICAL PATIENTS ACCORDING TO REASON FOR ADMISSION

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Background: There is a limited knowledge about the main reasons for admission of acute medical patients and such data are important for health care planning.

Objective: To examine the distribution of primary diagnoses assigned after an acute medical hospital admission, and the gender, age, and Charlson Comorbidity Index score (CCI score).

Methods: A study population of acute hospital admissions to the medical wards in Denmark during 2010 was identified through the Danish National Patient Registry (DNPR) covering all Danish hospitals. The first primary discharge diagnosis in the registry was included as the main reason for admission and classified according to the chapters in the International Classification of Diseases (ICD-10). Other variables included were gender, age, and CCI score.

Results: The study included 264,265 acute medical patients. Among the main reasons for admission, cardiovascular diseases were the most prevalent (19.3%) and the Z-diagnoses from ICD-10 (Factors influencing health status and contact with health services) were the second most prevalent (16.6%). The CCI score was comparable between these two groups, but the patients with cardiovascular diseases were older. The median age of the total population was 64 years (IQR 47-77 years) and approximately 60% had a low CCI score, but all variable differed widely between the diagnostic groups.

Conclusion: In conclusion, our study describes the main reasons for acute hospital admission to medical wards with cardiovascular diseases and Z-diagnoses being the most prevalent. This is important knowledge when planning the future organization of the healthcare system.

CH.74 Birgit Sørensen Skoffer ASSOCIATIONS BETWEEN MUSCLE STRENGTH AND FUNCTIONAL CAPACITY IN PATIENTS SCHEDULED FOR TOTAL KNEE ARTHROPLASTY

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Background: Impairment of the knee extensor muscle strength in patients with knee osteoarthritis is well documented. Furthermore, pain and reduced functional capacity in combination with severe radiographic osteoarthritis are the main findings resulting in total knee arthroplasty (TKA).

Purpose: 1) To compare knee extensor and flexor muscle strength in the leg awaiting TKA with the opposite leg in patients with end-stage osteoarthritis scheduled for TKA 2) to evaluate the association between muscle strength and functional capacity.

Methods: Fifty four patients, mean age 70.3 (SD 7.0) years, scheduled for TKA were included. Patients were tested six weeks before TKA with isometric, isokinetic muscle strength and functional capacity (sit-to-stand test and walking).

Results: Isometric knee extensor strength of the affected leg was weaker than the non-affected leg ($p=0.02$), while no difference was found for knee flexor strength ($p=0.93$). Both knee extensor and flexor strength were associated with functional capacity tests. Generally, isokinetic strength showed stronger associations to the functional tests than the isometric strength. The sit-to-stand test demonstrated the strongest association to muscle strength, both for knee extensor and flexor strength.

Discussion: The study indicates preoperative deficit in muscle strength of the affected leg. It also shows that activities such as sit-to-stand and walking are dependent on both knee extensor and knee flexor strength, which should be taken into account when planning rehabilitation programs before and or after TKA.

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