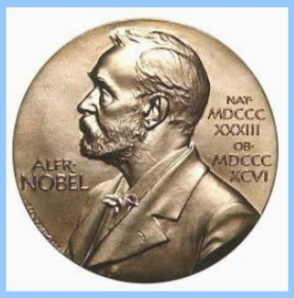
2012

Book of Abstracts
2012

Nobel Day Festivities
10th of December 2012



Traditionally, on 10th of December, the anniversary of Alfred Nobel's death, is awarded the Nobel Prize in Physiology or Medicine. School of Health and Medical Sciences shows attention to this day by organizing own research activities and festivities.

School of Health and Medical Sciences
Örebro University
10th of December 2012

Program Committee:
Nikolaos Venizelos, Professor
Allan Sirsjö, Professor
Olle Ljungqvist, Professor
Ulrica Nilsson, Professor

Book of abstracts, Nobel Day's Festivities 10th of December 2012

Preface

The"**Nobel Day Festivities"** were established 2009 by Biomedicine, Department of Clinical Medicine, School of Health and Medical Sciences at Örebro University, and is organized traditionally every year in order to notice the anniversary of Alfred Nobel's death (10th of December) with scientific activities including poster presentations and selected oral presentations by doctoral students, which are documented in this *"Book of abstracts".* Nobel day's activities are open and scheduled so that all students and personnel can attend the scientific activities. We warmly welcome you to enjoy all the good science that will be presented at Nobel Day.

The Organizers

Nikolaos Venizelos, Professor
Allan Sirsjö, Professor
Olle Ljungqvist, Professor
Ulrica Nilsson, Professor

Effect of persistent organic pollutants on tyrosine and tryptophan uptake in human fibroblast cells

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Objective: Bioaccumulation and biomagnification of persistent organic pollutants (POPs) like polychlorinated biphenyls (PCBs) and brominated flame retardants (BFRs) have drawn attention in the field of neuropsychiatry over the recent years [1]. Many neuropsychiatric disorders involve disturbances in the dopaminergic and serotonergic neurotransmitter systems. Both PCBs and BFRs have shown to inhibit the uptake of dopamine and serotonin into brain synaptic vesicles. Dopamine and serotonin are synthesized from the amino acids, tyrosine and tryptophan respectively, and the synthesis is partly dependent on the brain's availability of these amino acids. Altered transport of these amino acids has been observed in schizophrenia, bipolar disorder, autism and ADHD [2], which could lead to altered dopaminergic and serotonergic transmission. However, the reason for this disturbed amino acid transport is not known. The aim of this study was thus, to investigate the effect of PCBs on tyrosine and tryptophan uptake, along with the effect of BFRs on tyrosine uptake.

Material and Methods: The amino acid uptake was studied in human fibroblast cells after incubation with PCBs and BFR in different concentration for different timings and was carried out using the cluster tray method.

Results: Hexabromocyclododecane (HBCD), a BFR, significantly reduced the tyrosine uptake by approximately 20%, but the PCBs did not have any significant effect on either tyrosine or tryptophan uptake.

Conclusions: BFRs seem to affect the tyrosine transporter (s), further studies are required to reveal how this effect is exerted. While PCBs, do not prominently affect the amino acid transporters.

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All-cause mortality in 272 186 patients hospitalized with incident atrial fibrillation 1995-2008 – A Swedish, nationwide, long-term case-control study

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Aims To evaluate long-term all-cause risk of mortality in women and men hospitalized for the first time with atrial fibrillation (AF) compared to matched controls.

Methods and Results 272 186 patients (44% women) ≤85 years at the time of hospitalization with incidental AF 1995-2008 and 544 344 matched controls free of in-hospital diagnosis of AF were identified. Patients were followed via record linkage of the Swedish National Patient Registry and the Cause of Death Registry. Using Cox regression models, the long-term relative all-cause mortality risk, adjusted for concomitant diseases, in women versus controls was 2.15, 1.72 and 1.44 ($p<0.001$) in the age categories ≤65, 65 to 74 and 75 to 85 years, respectively. The corresponding figures for men were 1.76, 1.36 and 1.24 ($p<0.001$). Among concomitant diseases, neoplasm, chronic renal failure and chronic obstructive pulmonary disease contributed most to the increased all-cause mortality versus controls. In patients with AF as the primary diagnosis, the relative risk of mortality was 1.63, 1.46 and 1.28 ($p<0.001$) in women and 1.45, 1.17 and 1.10 ($p<0.001$) in men.

Conclusions AF was an independent risk factor of all-cause mortality in patients with incident AF. The concomitant diseases that contributed most were found outside the thromboembolic risk scores. The highest relative risk of mortality was seen in women and in the youngest patients compared to controls, and the differences between genders in each age category were statistically significant.

Keywords: Atrial fibrillation, mortality, gender, age, long-term.

Downregulation of platelet activation markers during long-term immobilization

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Introduction. Immobilization and sedentary lifestyle are risk factors for venous thromboembolism and cardiovascular disease, yet little is known about platelet function during long-term physical inactivity. Our aim was to investigate platelet activation markers and their coupling to standardized immobilization: platelet derived growth factor (PDGF-BB) and P-selectin.

Methods. We studied fifteen healthy females participating in the Women International Space simulation for Exploration study (WISE). Following a 20-day ambulatory control period the subjects underwent 60 days of bed rest in head-down tilt position (-6°) 24 h a day, finalized by 20 days of recovery. The subjects were randomized into two groups during bed rest: a control group (n=8) that remained physically inactive and an exercise group (n=7) that participated in both supine resistance and aerobic exercise training. Blood samples for analysis of platelet activation markers were collected at baseline (five days before bed rest), after 44 days of bed rest and eight days into the recovery period.

Results. Compared to baseline, the levels of P-selectin and PDGF-BB decreased after bed rest (by 55%, $p=0.01$ and 73%, $p<0.03$, respectively) and remained decreased in the recovery period (by 76%, $p<0.001$ and 78%, $p<0.02$, respectively, compared to baseline). Platelet count (baseline value for the exercise group 260 000/μL ± 34 000 and baseline value for the control group 210 000/μL ± 30 000) did not change during the bed rest study (two way repeated measurements anova, p=ns). There were no statistical differences between the physically inactive and the exercise group.

Conclusions. During long-term immobilization, a known risk factor for thrombosis, the levels of P-selectin and PDGF-BB decreased. Our findings indicate downregulation of platelet activation during immobilization.

Determination of Insulin Resistance in Surgery

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Objective: Insulin resistance has implications on surgical outcome. With increasing insulin resistance, complication rates rise. Golden standard method for its determination is the hyperinsulinemic normoglycemic clamp. The cheaper, easier HOMA method, that uses basal plasma levels of insulin and glucose, is often used instead. The argument made that the two methods correlate significantly. However, several publications using HOMA have challenged previous reports using the clamp, so we compared the methods to study if they are interchangeable or not.

Methods:113 surgical patients previously studied using the clamp and where data for basal insulin and glucose levels were available. Pre- and postoperative clamp and HOMA values were compared using regression- and correlation-analysis. Degree of agreement and interchangeability was studied both using kappa and the Bland-Altman test.

Results: All patients developed insulin resistance after surgery; span of change from hardly any insulin resistance to almost a 90% loss of preoperative insulin sensitivity. Both pre- and postoperatively HOMA and clamp were significantly correlated ($p<0.01$) but with r2 values 0.04 and 0.06 respectively. Regarding relative change, again the correlation was significant between the two methods, $p=0.011$, r2 value of 0.06.Bland-Altman test gave a large range for “limits of agreement” (±2SD). This poor intermethod agreement was further consolidated by a kappa value of 0.07.

Conclusion: The HOMA method does not determine the same measure as the clamp, probably due to that the clamp studies insulin when it is active, while HOMA does not. Data using HOMA method should not be mixed with data using the clamp.

Infant Dental Enucleation in a multi-ethnic population in Sweden: a retrospective study

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Objective: to examine the prevalence of Infant Dental Enucleation of the deciduous canine tooth (IDE), an East African traditional remedial procedure, in a multi-ethnic population of children residing in Sweden.

Methods: A retrospective cross-sectional study was conducted of the dental records of 1133 patients (582 boys, 551 girls, mean age in years 4.6, SD±1.4) regularly attending one Public Dental Health Clinic located in a multi-ethnic community in the County of Örebro. All patients were born within the years 2002-2006 and they had received a dental check-up in either of the years 2007 to 2009.

A registry was made of the sites of missing deciduous canines where no explaining history or registered reason could be found. In cases of documented national origin of the patient, the information was extracted.

Results: A variety of at least 34 countries of origin was recorded. Twenty-four (2%) of all the patients were registered to be missing one or more canines according to the criteria, thus being suggestive of a history of IDE. Significant difference was seen when comparison was made between patients of known East African origin, of whom 21% (21/101) manifested findings according to the criteria, and the rest of the population ($p<0.001$). No significant difference could be determined between the genders.

Conclusion: The prevalence of cases suggestive of IDE amongst the East African children points to a need for risen awareness and specific guidelines within the dental and health care communities in Sweden.

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Chronic cigarette smoke exposure impairs skeletal muscle regenerative capacity in murine COPD/emphysema model

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Objective: Cigarette smoke (CS) is a well established risk factor in the development of irreversible airflow limitation in COPD. In contrast, the extent to which CS exposure contributes to the development of the systemic manifestations of COPD, such as skeletal muscle dysfunction and wasting remains unknown. Decline in skeletal muscle regenerative capacity has been previously reported in COPD patients and might play an important role in the development of COPD-associated skeletal muscle abnormalities. To investigate the effects of chronic CS exposure on skeletal muscle regenerative capacity a mouse model of COPD/emphysema was used.

Methods: The129/SvJ mice were exposed to CS for 6 months, and the expression levels of important developmental regulators such as *Jarid2, Znf496* and *Notch1* as well as pivotal regulators of skeletal muscle myogenic program were studied. Additionally, number of fibers with centralized nuclei, accretion of myonuclei, animal body weight, and mean fiber cross-sectional area were assessed.

Results: Compared to controls, skeletal muscles from CS-exposed mice exhibited significantly decreased expression of *Jarid2*, coupled with enhanced expression of *Znf496, Notch1, Pax7, Fgf1* and *Myh3*. In contrast, expression levels of myogenin, marker of terminally differentiated muscle cells were reduced. Reduction in muscle fiber cross-sectional area and body weight were also observed in CS-exposed animals.

Conclusion: Taken together, the current results provide evidence linking chronic CS exposure and ongoing damage/regeneration process as well as impaired regenerative capacity in skeletal muscles of CS-exposed mice.

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Low frequency of new or aggravated heart failure during long-term right ventricular pacing after radiofrequency ablation of the atrioventricular junction.

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Objective: Atrioventricular junction ablation (AVJA) is a highly effective palliative treatment in patients with pharmacological resistant atrial fibrillation (AF). However, after AVJA the patient becomes pacemaker dependent. Long-term right ventricular pacing has been reported to lead to worsening of heart failure (HF). We analyzed the incidence of new or aggravated HF in patients who had undergone AVJA.

Methods: 67 patients (36F: 31M) underwent AVJA because of AF between 2001 and 2011 in Örebro University Hospital. The mean age was 72 ± 8 years at the time of AVJA. The patients were followed for a period of 45 ± 27 months after AVJA. 22 patients were known to have paroxysmal AF, 4 patients persistent AF and 41 permanent AF. A second ablation procedure was needed to achieve complete junctional ablation in two patients. 33 patients (49%) had known clinical HF before AVJA.

Results: During the follow-up 15 % of patients (5/33) showed an aggravation of HF and 6 % (2/34 patients) developed new symptoms of HF. 18 of those with known HF (55 %) showed an improvement of HF. The remaining 10 patients had unchanged HF (30%). The all-cause mortality was 19,4 % and 3% died of HF. Death occurred at a mean time of 51 ± 33months after AVJA.

Conclusions: Long-term right ventricular pacing was not harmful in the majority of AF patients after AVJA. Aggravated or new HF was observed in only 10%, while 55% of those with known HF improved their symptoms during long-term follow up.

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Incidence of Hyperthyroidism in Sweden, in the years 2003 – 2005

Byström, Kristina[2], Abraham-Nordling, Mirna[1], Lantz, Mikael[3], Berg, Gertrud[4], Calissendorff, Jan[5], Filipsson, Helena[4], Jansson, Svante[4], Jörneskog, Gun[6], Karlsson, Anders[7], Lundell, Göran[8], Nyström, Ernst[4], Ohrling, Hans[9], Sjölin, Gabriel[11]Örn, Thomas[10], Törring, Ove[9], Hallengren, Bengt[3], Wallin, Göran[11]

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Introduction

The incidence of hyperthyroidism has been reported 23-93/ 100000 inhabitants / year in the world. Hyperthyroidism in Sweden is locally registered 26 - 43/100000. This study has evaluated the incidence for approximately 40% of the Swedish population. Sweden is considered iodine sufficient since long time iodine supplementation.

Methods

Patients with overt hyperthyroidism, were 2003 - 2005 prospectively registered in a multicenter study (Malmö, Karlskrona, Göteborg, Örebro, Eskilstuna / Katrineholm, Stockholm and Uppsala) organized by the "Swedish Thyroid Study Group" (Vetenskapsrådets Planeringsgrupp för Tyreoideasjukdomar). Patients were included if TSH was below <0.2 mIE/l, combined with increased freeT3 and/or free T4 levels. Hyperthyroidism due to thyroiditis, relapse of hyperthyroidism and exogenous thyrotoxicosis were excluded. The diagnosis (Graves' disease (GD), toxic multinodular goiter (TMG) and solitary toxic adenoma (STA)), smoking, initial treatment, occurrence of Thyroid Associated Ophthalmopathy (TAO) and demographic data were registered.

Results

2866 patients were diagnosed with *de novo* hyperthyroidism, incidence 27.1/ 100000 inhabitants (children included) / year. Subtypes were: GD 20.3/100000 (75%), TMG 3,9/100000 and STA 2.9 /100000 inhabitants/year. The incidence women / men, 4.3:1. TAO occurred at diagnosis in every fifth GD patient. Geographical differences were observed.

Conclusion

The incidence of hyperthyroidism is in the lower range compared to earlier reports in the literature. The incidence of TMG and STA hyperthyroidism is lower and GD increases in iodine sufficient areas compared to iodine insufficient countries, which is in accordance with these results, where 75% of the patients had GD.

FOXP3^{+} Regulatory T Cells and Risk of Lethal Prostate Cancer

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Objective: A challenge in prostate cancer (PCa) management is identifying potentially lethal disease at diagnosis. Disease outcomes are highly variable and no curative treatment exists for metastatic disease. Alternative immunotherapeutic approaches have recently emerged, but with low clinical response rates. FOXP3^{+} regulatory T cells (T_{regs}) may explain the poor efficacy due to their suppressive function on CD4^{+} helper T cells and CD8^{+} cytotoxic T cells.

Methods: To evaluate T_{regs} as a predictor of lethal PCa, we conducted a case-control study including 784 men diagnosed with PCa through transurethral resection of the prostate in Sweden. A triple IHC staining was performed to identify CD4^{+}, CD8^{+}, and FOXP3^{+} cells.

Results: In unadjusted analysis, we found no association between mean CD4^{+} T cells, mean CD8^{+} T cell or mean T_{regs} and odds of death from PCa. However, T_{regs} cells were associated with a nearly 2-fold increase in the odds of lethal PCa when comparing the highest to the lowest quartile. This association was independent of tumor stage, tumor percent and Gleason score.

Conclusions: Our data provides evidence that men with greater number of T_{regs} in their prostate tumor environment have an increased risk of dying of their disease.

Nitric oxide activates IL-6 production and expression in human renal epithelial cells

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Background/Aim: Nitric oxide (NO) and IL-6 are produced as part of the host response during urinary tract infection (UTI). IL-6 is believed to promote the inflammatory response but the precise function of NO in UTI is not known. We investigated whether NO can affect the host response in human renal epithelial cells by modulating IL-6 production and mRNA expression.

Methods: The human renal epithelial cell line A498 was infected with an uropathogenic *E. coli* (UPEC) strain and/or the NO-donor DETA/NO. The IL-6 production and mRNA expression were evaluated by ELISA and real time RT-PCR. IL-6 mRNA stability was evaluated by analyzing mRNA degradation by real time RT-PCR.

Results: Stimulation of cells with DETA/NO (1mM) caused a significant ($p<0.05$) increase in IL-6 production. The inhibition of p38 MAPK and ERK1/2 signaling significantly suppressed DETA/NO-induced IL-6 production. UPEC-stimulated IL-6 production was further increased (by 73□23%,$p<0.05$) in the presence of DETA/NO. The IL-6 mRNA expression increased 2.1±0.17 fold in the presence of DETA/NO while the UPEC-induced increase was pronounced (20±4.5 fold). A synergistic effect of DETA/NO on UPEC-induced IL-6 mRNA expression was found (33±7.2 fold increase). The IL-6 mRNA stability studies showed that DETA/NO partially attenuated UPEC-induced degradation of IL-6 mRNA.

Conclusions: NO was found to stimulate IL-6 in renal epithelial cells through p38 MAPK and ERK1/2 signaling pathways and also to increase IL-6 mRNA stability in UPEC-infected cells. This study proposes a new role for NO in the host response during UTI by modulating the transcription and production of the cytokine IL-6.

Reproducibility of the Nordic Orofacial Test – Screening in children and youth with cerebral palsy

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Objective: To evaluate interrater and intrarater agreement on the Nordic Orofacial Test–Screening (NOT-S) examination in children and youth with cerebral palsy (CP).

Methods: Two speech-language pathologists independently rated the NOT-S examination[1,2] from video-recordings of 48 subjects with CP (5-22 y) representing all CP-subdiagnoses and levels of gross motor function and manual ability. Thirty-one subjects were re-rated. Fifteen items in the domains 1-Face at rest, 2-Nose breathing, 3-Facial expression, 4-Masticatory muscle and jaw function, 5-Oral motor function, and 6-Speech, were rated in a 'Yes' (dysfunction observed)/'No' format, generating a score of 0-6.

Results. *Interrater agreement*. Twelve out of 15 items and five out of six domains showed acceptable unweighted kappa values (κ 0.46–1.00). The lowest kappa value was found for domain 4 (κ -0.04), though it had high interrater agreement (92%). The linear weighted kappa value for the NOT-S examination score was 0.65 (95% CI = 0.49–0.82). *Intrarater agreement.* All items and domains showed acceptable unweighted kappa values (items 0.53–1.00 and 0.43–1.00, domains 0.81–1.00 and 0.43–0.89) for both raters. The linear weighted kappa value for the NOT-S examination score was 0.81 (95% CI = 0.63–0.99) for rater A and 0.53 (95% CI = 0.31–0.76) for rater B.

Conclusions. Applied on children and youth with CP, the NOT-S examination has acceptable interrater and intrarater agreement. Health professionals with limited training in the NOT-S examination can use it. Together with the NOT-S interview, the full NOT-S constitutes a comprehensive screening of orofacial dysfunction.

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Bacterial recolonisation of the skin and wound contamination during cardiac surgery; a randomized controlled trial of the use of plastic adhesive drape compared with bare skin

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Background: Sternal wound infection after cardiac surgery is a serious complication.

Various peri-operative strategies, including plastic adhesive drapes, are used to reduce bacterial contamination of surgical wounds.

Aim: To compare plastic adhesive drape to bare skin regarding bacterial growth in cardiovascular surgery patients, and to measure the time to recolonisation.

Methods: This single-blinded randomized controlled trial (May 2010–May 2011) included 140 patients scheduled for cardiac surgery via median sternotomy. The patients were randomly allocated to the adhesive drape (chest covered with plastic adhesive drape) or bare skin group. Bacterial samples were taken pre-operatively and intra-operatively every hour during surgery until skin closure, in the wound and on the adjacent skin.

Results: Bacterial recolonisation on the skin showed progressive increases of *Propionibacterium acnes* and coagulase-negative staphylococci (CoNS) after 120 minutes, with significantly more growth in the adhesive drape group: respectively, 63% vs. 44% ($P = 0.034$) and 45% vs. 24% ($P = 0.013$). The only statistically significant difference in bacteria growth in the surgical wound was greater CoNS at the end of surgery in the adhesive drape group (14.7% versus 4.4%, $P = 0.044$). Disinfection with 0.5% chlorhexidine solution in 70% alcohol decreased CoNS but not *P. acnes*, and men had significantly more *P. acnes* than women.

Conclusion: Plastic adhesive drape does not reduce bacterial recolonisation, and actually seems to hasten it. *P. acnes* colonized men more frequently, and was not decreased by disinfection with chlorhexidine solution in alcohol.

Keywords: Plastic adhesive drape, Recolonisation, Contamination, CoNS, *P. acnes*, Gende

Bone marrow stromal cells in primary and secondary myelofibrosis: Analysis of fibrosis-related gene expression in cultured cells.

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Objective: Primary myelofibrosis is a disease with genetic and environmental causes with severe impacts on the afflicted individual. Fibrosis is probably well imprinted in the stromal fibroblasts in which the phenotype is characterized by increased proliferation and overproduction of ECM components. Knowledge on the fibroblast gene expressions may enable us to understand the mechanisms underlying the disease. In this study we investigated 84 genes previously connected to fibrosis developments.

Methods: RNA isolated from explant cultures of bone marrow fibroblast from three myelofibrosis patient and three healthy subjects at passage 5-8 were subjected to microarray analysis using the agilent two-colour 4X44 K HD 60-mer oligo slide containing about 35000 probes. Only known human fibrosis genes with uncorrected p-value < 0.1 were considered.

Results: Fibrosis-regulated genes that are candidates for disease development included TGFβ signal transduction pathway genes TGFβ2, TGFβR2 and TGIF1, the proteinase inhibitors TIMP1, SERPINE1, the anti-apoptotic protein BCL2 and integrin-linked kinase.

Conclusion: This pilot study suggests that TGFβ pathways, proteinase inhibitors and anti-apoptotic proteins may contribute to myelofibrosis development by bone marrow fibroblasts. We are currently collecting more samples to verify these data.

Patients' experience of MRI-examination

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Objective: The aim of this study was to describe patient's experiences of an MRI- examination as a part of a larger study where patient's experiences of two different breath hold techniques were explored.

Method. After completed MR-examination patients (*n*= 28, 7 men and 21 women) were interviewed with semi-structured interviews. The interviews were transcribed and analyzed with qualitative content analysis.

Result: The patients experienced that they during the MRI-examination were trapped in a situation they could not control. They had to lie still in the tunnel surrounded by an annoying and ever ongoing sound. The patients described experiences of being lost in time during the examination, which was exemplified by experiences that the examination took very long, or surprisingly short, time. The patients were worried about doing wrong when holding their breath and when not being able to stay still. They held many questions and wonderings; for example they wondered about witch part of their body that were imaged or what would happen if they got at heart attack in the tunnel, would anyone notice? They also wished they had got information about different topics before the examination.

Conclusion: The patients experienced anxiety and claustrophobic feelings, as described in earlier studies (1, 2). They could not control the situation and feel trapped and lost in time. They described worries, wonderings and a wish for information. The findings are of importance for radiographers in their daily meetings with patients and when dealing with patient information.

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Mature miRNAs (miR-146a, miR-155 and miR-21) and IL-37 are differentially expressed in lymphocytic colitis and collagenous colitis patients compared to controls in mucosal colon biopsies.

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Objective: Microscopic colitis (MC) comprising collagenous colitis (CC) and lymphocytic colitis (LC) is a common cause of chronic diarrhea, whose histopathological features are observed on microscopic examination. In this study, we compared mature microRNA (miR-146a, -155 and -21) profiles, and gene expressions of IL-37, IL-10, IRAK-2 and IRAK-M, important regulators of Toll-like receptor (TLR) signaling pathway to regulate innate immune system from colon biopsies of CC and LC patients with non-inflamed controls.

Methods: Total RNA and microRNA were isolated from the fresh frozen mucosal colon biopsies of MC patients and non-inflamed controls. Reverse transcribed RNA and microRNA were analyzed using quantitative RT-PCR.

Results: A significant decrease of IL-37 gene expression, not previously observed in any chronic inflammatory disease, was found in CC patients (p=0.02). In contrast, there were significant increases in the levels of mature miR-146a (p=0.03), miR-155 (p=0.02) and miR-21 (p=0.01) in LC patients compared to controls. In CC patients, there was a tendency towards increased miR-155 expression (p=0.09) and a significant increase in miR-21 expression (p=0.01). Per contra, no significant differences were detected in IL-10, IRAK-2 and IRAK-M gene expressions between MC patients and controls.

Conclusion: The identification of differentially expressed miRNAs and IL-37 in colonic tissues further indicates the differences in immunopathogenesis between LC and CC. This study might form the basis of future diagnostic tests for MC and differentiation of the two subtypes of the disease, CC and LC.

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Abnormalities in CF airway epithelial cells: are these all related to the mutation in CFTR?

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Background/Aims: In cystic fibrosis (CF) the chloride (Cl^-) conductance by the cystic fibrosis transmembrane conductance regulator (CFTR) is defective. The question is, whether the defect in CFTR can explain all other abnormalities in CF airway epithelia. We aimed to investigate if the differences between CF and non-CF cells can be explained exclusively by the mutation in CFTR, and if pharmacological inhibition and activation of CFTR can induce changes in the mRNA expression of ENaC, iNOS, mucin and in wound healing.

Methods: We used CF and non-CF bronchial and submucosal gland cells. We performed qRT-PCR, and Western blot for the expression study of ENaC, iNOS, MUC (2, 5AC, and 5B). Wound healing, cell migration and proliferation studies were carried out by wound healing scratch, migration, and proliferation assays respectively. Cell cytotoxicity was assessed by the Neutral Red uptake assay.

Results: A link between mRNA expression of ENaC, iNOS, mucin, and wound healing time with mutated/activated CFTR proved to be complicated. CFTR inhibitor-172 showed unspecific and cytotoxic effect on the cells. Inhibition of ENaC with amiloride did not affect wound healing significantly.

Conclusion: It appears unlikely that the observed differences between CF-cells and non-CF cells (high ENaC, low iNOS, high MUC (2, 5B) expression and a delay in wound healing) could all be related to the mutated CFTR.

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Flagellin affects the expression of NOD1, NOD2 and NLRP3 in Cystic fibrosis bronchial epithelial cells

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Objective: Cystic fibrosis (CF) is associated with chronic airway infections caused by a number of bacteria, notably *Staphylococcus aureus, Psudomonas aeruginosa, Burkholderia cepacia* and *Haemophilus influenzae*. The innate immune system has evolved as a system for identifying and controlling microbial infections and is important in the pathophysiology of CF. The aim of the current study was to investigate the mRNA expression of NOD-like receptor (NLR) in cystic fibrosis bronchial epithelial cells.

Methods: This was done by detecting NOD1, NOD2, NLRP3 and NLRC4 using reverse transcription polymerase chain reaction in cystic fibrosis (CFBE), normal (16HBE), and corrected-CF (overexpressing the chloride channel CFTR) bronchial epithelial cells under unstimulated conditions and as well as after flagellin treatment.

Results: Unstimulated CFBE and corrected CF cells displayed lower mRNA expression of NOD2 and NLRP3 but no difference in the expression of NOD1 in CFBE cells while slight increase in corrected-CF cells was detected, compared to the wild-type 16HBE cells. Flagellin, which is a known dual ligand for NLRC4 and TLR5, caused a time-dependent decrease in the expression of NOD1, NOD2, and NLRP3 in CFBE cells, whereas a slight increase of mRNA expression of these receptors was detected in 16HBE as well as in corrected CF-cells. TLR5 but not NLRC4 mRNA was detected in the CFBE cells, which indicate that flagellin most probably signals through TLR5 to stimulate the innate immune system in the airway epithelium.

Conclusions: Apparently, flagellin promotes the immune response in normal cells, but weakens this response in CF cells, thereby allowing for other bacteria to colonize.

C10X Polymorphism in the *CARD8* Gene is Associated with Bacteremia

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Objective: The NALP3 inflammasome is a multiprotein complex in the cytosol that senses pathogen and danger-associated signals. Activation of the NALP3 inflammasome complex triggers the cleavage of caspase-1, which results in the maturation of pro-inflammatory cytokines IL-1β and IL-18. These cytokines are implicated in a variety of inflammatory processes, including severe infection like sepsis. Polymorphism C10X in *CARD8* gene *per se* or in combination with *NLRP3* (Q705K) has been associated with constitutive activation of NALP3 inflammasome and unregulated caspase-1 mediated maturation of IL-1β. These genetic variations lead to increased susceptibility and severity of auto-immune diseases, and are characterized by excessive IL-1β production. CARD8 has been implied to regulate the synthesis of IL-1β via interaction with caspase-1 and inhibition of NF-κB. The aim of the study was to investigate whether these polymorphisms influence susceptibility to blood stream infection (bacteremia).

Methods: The study included 70 bacteremia patients and 76 blood culture negative patients. A method was developed to extract human DNA from blood culture bottles. It was successfully applied to isolate human DNA from the study groups. Polymorphisms of Q705K and C10X were genotyped using Taqman assay. The results were compared to blood culture negative patients and 1003 healthy controls.

Results: The polymorphism C10X was significantly over-represented among patients with bacteremia compared to patients with negative blood culture and healthy controls (p=0.0002). There was no association with polymorphism Q705K, or combined polymorphisms.

Conclusion: Our findings show that patients carrying polymorphism C10X in the *CARD8* gene are at increased risk of developing bacteremia.

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TNF-α induced decrease in USP19 expression may disrupt hypoxia-inducible angiogenic pathway in COPD

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Objective: Decreased capillarization and impaired angiogenesis have been implicated in the development of skeletal muscle dysfunction in COPD. Whether systemic inflammation and increased circulatory levels of TNF-α might play a role in the capillary bed deterioration in skeletal muscles of COPD patients remains uninvestigated. Decreased capillarization in skeletal muscles of COPD has been associated with excessive ubiquitination and proteasomal degradation of HIF-1α, major molecular regulator of tissue angiogenesis. Besides VHL, which is well-documented controller of HIF-1α expression, ubiquitin specific protease 19 (USP19) has recently been identified as a novel regulator of HIF-1α protein stability. In this study, we have examined the effects of TNF-α on the expression of factors associated with the control of HIF-1α protein stability using murine C2C12 skeletal muscle cells as a model.

Methods: C2C12 cells were treated with TNF-α and expression levels of VHL, USP19, HIF-1α and VEGFA, were determined using qPCR and western blot.

Results: We found expression levels of VHL and USP19 to be down-regulated in cells treated with TNF-α when compared to controls. VEGFA levels were also decreased on both protein and mRNA level. Although TNF-α did not have a large effect on protein levels of HIF-1α, a slight decrease in protein levels was observed.

Conclusions: Our results suggest co-regulation of VHL and USP19 in murine skeletal muscle cells, supported by relative stability of HIF-1α protein levels. In addition, as it has been demonstrated that USP19 deficient cells have impaired response to hypoxia, this may have implications in understanding disruption of hypoxia-induced angiogenic pathways in COPD.

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Risk factors for development of postoperative sore throat and hoarseness after endotracheal intubation in women

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Objective: Postoperative sore throat (POST) and postoperative hoarseness (PH) are common but disturbing complications following endotracheal intubation (1, 2). Therefore, identification of risk factors associated with POST and PH would add to our knowledge of predictors of poor outcome in our patients.

Methods: This was a secondary analysis of prospective, cross-sectional data (n=100 women). Eight different variables were analyzed in order to detect possible association between endotracheal intubation and the development of POST or PH. At the Post-Anaesthesia Care Unit, the patients rated their POST and PH. Bivariate analyses with Chi-Square test was used and the odds ratio (OR) and confidence interval (CI) were calculated for each significant variable.

Results: A total of 97 women completed the study. Three variables were found to be significant risk factors for the development of POST: age >60 yrs, endotracheal tube size 7.0 and the use of throat pack. The only risk factor found to be significantly associated with developing PH was a cuff pressure ≤ 20 cm H2O.

Conclusion: Patient-reported outcome measures research is based on the knowledge that anesthetists get insight into how the patient perceives different situations. Therefore, it is important to increase our knowledge of the patients at risk and the conditions under which this risk increases.

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Test-retest reliability of the Orthotics and prosthetics users´ survey

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Objective: The Orthotics and prosthetics users' survey (OPUS) consists of five independent modules for self-report: Lower extremity functional status (LEFS), Upper extremity functional status (UEFS), Client satisfaction with device (CSD), Client satisfaction with services (CSS), and Health-related quality of life (HRQoL). Each module consists of 10-28 items rated on 4- or 5-point Likert scales giving a Rasch derived measure on a 0–100 unit scale. The aim was to investigate the test-retest reliability and calculate the smallest detectable difference (SDD) with users of different prosthetic and orthotic devices.

Methods: Sixty-nine outpatients at the Department of prosthetics and orthotics, Örebro, Sweden, completed OPUS on two occasions separated by a two-week interval. This resulted in 18–67 valid responses per module. Intraclass correlation coefficient (ICC; version 1,1), Bland-Altman plots and paired t-tests were used to investigate the reliability. The SDD, the smallest change in a person's test scores that can be interpreted as a real difference, was calculated for a 95% confidence level. An ICC>0.75 and a SDD<10.0 were considered acceptable.

Results: The ICC ranged from 0.77 to 0.96 for the modules. The t-tests and Bland-Altman plots did not reveal any systematic differences between the response occasions. The SDD was acceptable for HRQoL (7.4 units) but was larger than acceptable for the other modules (12.1-16.6 units).

Conclusions: The test-retest reliability was satisfactory for all five OPUS modules. On all modules but HRQoL, relatively large changes are needed to achieve statistical significance when assessing individuals.

Monocyte interaction with *Porphyromonas gingivalis* ATCC33277

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Objective: Monocytes have long known to be the sentinel cells of innate immunity. *Porphyromonas gingivalis* DNA, cell wall lipopolysaccharide, fimbriae, outer membrane proteins and gingipains (trypsin like cysteine proteases) are all recognized by the monocytes. Also, the bacterial DNA has been traced in sites of atherosclerotic lesions, leading to speculate if monocytes are the carriers of the periopathogen to a distant site of inflammation. Here we have analyzed the monocyte like THP-1 cell interaction with periopathogen *Porphyromonas gingivalis* ATCC 33277.

Methods: Pro-inflammatory cytokine, interleukin-8 production has been quantified by Enyme linked immunosorbent assay. The effect of gingipains in cleaving interleukin-8 has been clearly elucidated by use of selective gingipain inhibitors. Cell invasion of the bacteria has been demonstrated by antibiotic protection assay and scanning confocal microscopy. Using FITC labeled bacteria.

Results: The results show an increase in interleukin-8 levels 24 hours post-infection and the levels were still higher when arginine gingipains were inhibited. Viable bacteria have been retrieved from the cells 1.5hours, post-infection demonstrating cell invasion. However, 24 hours post-infection, viable bacteria could not be retrieved. Confocal images show the bacteria in the cytoplasm following infection.

Conclusions: The findings suggest that gingipains tend to cleave inflammatory mediators in order to evade the immune surveillance which helps the bacteria to be transported to distant sites where they persist to trigger the exisiting inflammation further.

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No touch vein graft harvesting technique results in more normal vein grafts and less development of atherosclerosis in coronary by-pass sugery. Short-term angiographic and IVUS data from a longitudinal randomized trial

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Objective: A new "no touch" (NT) vein graft preparation technique where the entire vein wall is preserved had a low occlusion rate at 17 months angiographic follow-up compared to routine (C) vein graft preparation. This study evaluated possible mechanisms by means of angiographic and intravascular ultrasound (IVUS) findings in patent vein grafts.

Methods: In a prospective randomised by-pass study 124 grafts in group NT and 127 grafts in group C were patent at 17 months follow-up and were evaluated angiographically in a scale from 0 (normal) to 2 (significant stenosis). Fifteen grafts in group NT and 14 grafts in group C were evaluated by IVUS according to intimal hyperplasia, plaque burden and graft lumen volume.

Results: The cineangiogram showed more normal vein grafts (77,4% v 66,1%; $p < 0,05$) and less grafts with significant stenosis (3,3% v 7,1 %; $p < 0,05$) in group NT compared to the C-group. IVUS revealed larger lumen volume (124,1 + 45,8 v 92,4 + 25,5; $p < 0,05$), more normal vein grafts (33,3% v 7,2%; $p < 0,05$) and less vein grafts with multiple hyperplasia lesions (0% v 42,8%; $p < 0,05$) in the NT-group compared to the C-group

Conclusions:
The preserved vein wall using the no-touch vein graft harvesting technique improves the short-term coronary by-pass results.

References

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Porphyromonas gingivalis and bacterial complex-like nanoparticles induce platelet activation and immune responses via TLR2.

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Platelets are considered to have important functions in inflammatory processes as key players in innate immunity. Platelets are rapidly activated by different stimuli e.g subendothelial collagen, but also by PAMPs in the circulation that are recognized by TLRs expressed on platelets surfaces, with subsequent release of inflammatory and immune modulating factors. The periodontal pathogen *Porphyromonas gingivalis* has been found in atherosclerotic plaques, indicating that it may spread via the circulation. *P. gingivalis* can interact with, and activate platelets via TLR2-receptors, in a similar manner as the synthetic lipopeptide Pam_3CSK_4.
We aimed to investigate the effects of *P. gingivalis* and how Pam_3CSK_4 immobilized onto nanoparticles, resembling bacterial complexes, affects platelet derived immune responses.

Pam_3CSK_4 was immobilized onto silica particles by means of ECD/NHS-chemistry. *P. gingivalis* was cultured and used as viable bacteria as well as heat killed. To investigate how the different stimuli affected platelet aggregation, platelets were stimulated with Pam_3CSK_4, Pam_3CSK_4-coated particles, viable or heat killed *P. gingivalis*. ELISA was conducted to examine the release of RANTES/ CCL5 after *P. gingivalis* stimulation.

Treatment with Pam_3CSK_4-coated particles resulted in platelet activation and aggregation. Confocal-microscopy revealed that platelets bound to the particle surface and formed aggregates with nearby platelet-particle complexes. *P. gingivalis* stimulation led to a dose-dependent aggregation, comparable to Pam_3CSK_4-stimulation. Heat killed bacteria did not stimulate the platelets.

Platelets are activated by nanoparticles, resembling bacterial complexes, and by viable *P. gingivalis* whereas heat-killed *P. gingivalis* does not activate platelets. These results further clarify platelets as active players in sensing bacterial infections.

Microscopic colitis patients demonstrate a Th1/Th17 and CTL-associated gene expression profile

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Objective: Data on the local cytokine profile in microscopic colitis (MC) is limited. This study investigates the expression of different gens encoding proteins involved in T helper (Th) cell and cytotoxic T lymphocytes (CTL) differentiation in mucosa of MC patients.

Methods: Mucosal biopsies from CC, LC patients, as well as LC or CC patients in histological remission (LC-HR) and CC-HR, UC, non-inflammed diarrhoea patients and non-inflamed controls were analysed by real time qRT-PCR.

Results: No genes were upregulated in non-inflamed diarrhoea patients compared to controls. IFN-_, mainly from CD4+ Th1 and CD8+ CTL, were markedly upregulated in CC (22-fold) and LC (19-fold), more than in UC (12-fold) and LC-HR (9-fold) but not in CC-HR. IL-12p35, was also significantly upregulated in CC (3-fold), and LC (2-fold) but not in LCHR, CC-HR and UC. In addition transcription factor for Th1/CTL; T-bet was slightly upregulated in CC (2-fold; $p < 0.01$) and in UC (3-fold), but no change in LC, LC-HR and CCHR. Genes involved in Th17 differentiation; IL-6, IL-21, IL-17 and IL-23 were significantly induced in CC and LC compared to controls, albeit less than in UC patients. Th17 cell chemokine; CCL20 was markedly induced in UC but not in CC and LC group. In addition, Th17/Th22/CTL related cytokine IL-22 was significantly induced in CC, LC and UC patients. LC-HR and especially CC-HR patients had normalized mRNA levels of the above cytokines compared to LC and CC patients.

Conclusion: MC patients demonstrate a mixed Th1/Th17 and CTL mucosal cytokine profile.

Doubtful association between diverticulitis and colorectal cancer: A systematic review of the literature

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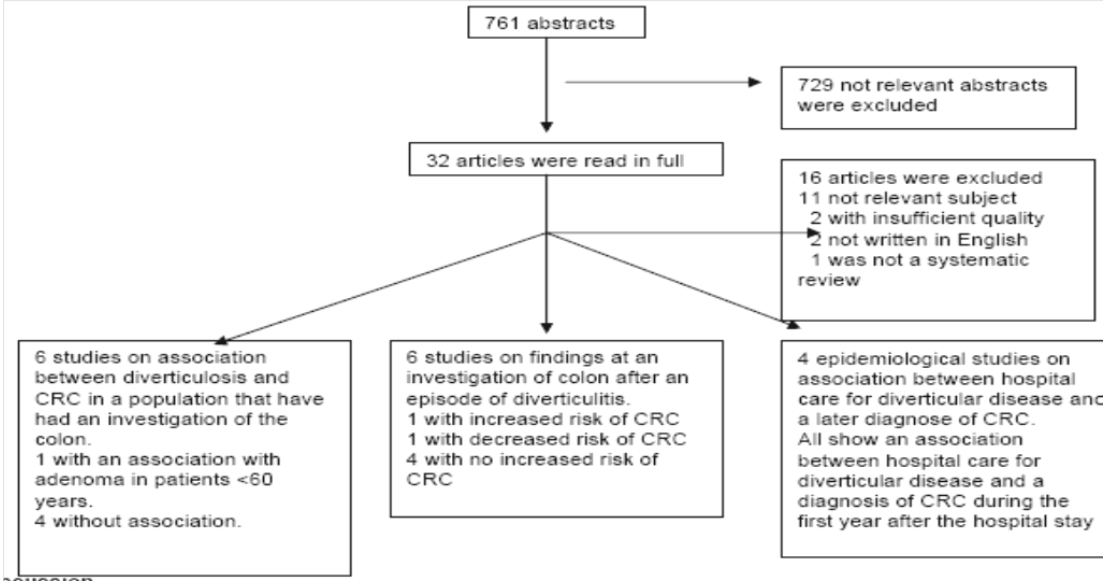
Bakground: Diverticulosis in colon is common with an incidence of 65% at age 85 years. Colo-rektal cancer (CRC) is the third most common type of cancer on the global level. Between 10-25% of people with diverticulosis will be affected with diverticulitis. After an episode of diverticulitis an examination of colon to exclude CRC is made. The objective with this review of the literature is to evaluate if an examination of colon is always necessary.

Method: A systematic search of the literature in PubMed, Cochrane and the TripDatabase from 1990-01-01 to 2012-01-31 of articles published concerning the association between CRC and diverticulosis or diverticulitis was performed. Two independent reviewers examined the literature according to a prespecified protocol.

Results:



Discussion: The number of studies examining the association between CRC and diverticular disease of the colon are few and of varying quality. The epidemiological support for an association between hospital stay for diverticular disease of the colon and CRC is based data from Swedish registers and is relatively strong. There are difficulties to generalise these data to patients med mild symptoms treated in open care.

Summary

- Findings of colo-rectal neoplasia is not more common in patients with diverticular disease than without it. (Limited evidence, ++oo)
- Examination of the colon after an episode of diverticulitis is not clearly necessary. (Limited evidence, ++oo)
- Patients that has been hospitalised for diverticular disease have an increased risk of beeing diagnosed with an CRC 1-2 years after the admission (Fairly strong evidence, +++o)

A comparative genomic study in schizophrenic as well as in bipolar disorder patients based on microarray expression profiling meta-analysis.

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Background: Schizophrenia, affecting almost 1% and bipolar disorder affecting almost 3-5% of the global population constitute two severe mental disorders.

The aim of this study was to perform and interpret results of a comparative genomic profiling study in schizophrenic and in patients with bipolar disorder as well as in healthy controls, and try to relate and integrate the results with an aberrant amino acid transport through cell membranes. Especially we focused in genes and mechanisms involved in amino acid transport through cell membranes at genome-wide gene expression level. We performed microarray analysis on raw data derived from four different studies.

Methods: The microarray data were downloaded from NCBI´s GEO datasets. Microarray expression profiling analysis was performed, using the GENE ARMADA software, followed by a computational analysis. GCRMA background adjustment, quantile normalization and median polish summarization were used for pre-processing the raw data.

Results: Our microarray analysis and meta analysis of the downloaded datasets demonstrate genes and GO terms associated with ion transport dysregulation (potassium ion transport, sodium ion transport, calcium ion transport and binding probably resulting in a disturbed primary active transport and difficulty in maintaining transmembrane Na+ and K+ gradients. Characteristic dowregulation of ATP1A3 (ATPase, Na+/K+ transporting, alpha 3 polypeptide), the enzyme which is responsible for establishing and maintaining the **electrochemical gradients** of **Na** and **K** ions across the **plasma membrane** is indicated in the differentially expressed gene lists of two of our datasets (schizophrenic and bipolar patients). Also downregulation of P-type ATPases is reported in the datasets. In one dataset the gene SLC7A8 which encodes the L-type amino acid transport protein, the most responsible transport protein system for the transport of tyrosine and tryptophan across the cell membranes was downregulated.

Conclusion: The disturbed primary active transport occurring from our study indicates difficulty in maintaining transmembrane Na+ and K+ gradients. This fact should result in disrupted secondary active amino acid transporters Systems A, X−AG, N and y+, as they couple amino acid transport to the electrical and chemical gradients initiated by primary active transport. Amino acid exchangers, Systems ASC, y+L and L, that transport amino acids by antiport mechanisms may have a reduced availability of secondary active transported amino acids that they need for the exchange, resulting in a disrupted transport of amino acids mainly transported through this third mechanism (such as tyrosine).

Effects of ΔNp73ß on Cisplatin Treatment in Colon Cancer Cells

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Background: p73 can activate transcription of p53-responsive genes, thereby inhibiting cell growth. An alternative promoter in the TP73 gene gives rise to an N-terminally truncated isoform of p73, ΔNp73, which lacks the transactivation domain of the full length TAp73 protein. TAp73 is considered pro-apoptotic, and ΔNp73 anti-apoptotic.

Methods: We overexpressed ΔNp73ß in p53 wild type and p53 mutant colon cancer cell lines and further exposed the cells to cancer therapeutic drug cisplatin.

Results: Cisplatin decreased the protein expression levels of ΔNp73ß in a dose-dependent manner, and both TAp73 and p53 were upregulated after cisplatin treatment. Further, clonogenic potential and cell viability were decreased, and apoptotic cells increased, in p53 mutant and in p53 wild type cells. Cellular viability was significantly higher in ΔNp73ß -cells than mock-transfected cells. However, ΔNp73ß overexpression did not affect the cellular susceptibility to cisplatin.

Conclusion: The overexpression of ΔNp73ß increases viability in p53 wild type and p53 mutant colon cancer cells, and cisplatin induces the degradation of ΔNp73ß in a dose-dependent manner.

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Impact of PINCH expression on survival in colorectal cancer patients with or without adjuvant chemotherapy

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Background: The adaptor protein PINCH is overexpressed in the stroma of several types of cancer, and is an independent prognostic marker in colorectal cancer. In this study we further investigate the relationship of PINCH and survival regarding the response to chemotherapy in colorectal cancer.

Results: Paraffin-embedded tissue sections from 251 primary adenocarcinomas, 149 samples of adjacent normal mucosa, 57 samples of distant normal mucosa and 75 lymph node metastases were used for immunohistochemical staining. Stromal staining for PINCH increased from normal mucosa to primary tumour to metastasis. Strong staining in adjacent normal mucosa was related to worse survival independently of sex, age, tumour location, differentiation and stage (p=0.044, HR, 1.60, 95% CI, 1.01-2.52). PINCH staining at the invasive margin tended to be related to survival (p=0.051). In poorly differentiated tumours PINCH staining at the invasive margin was related to survival independently of sex, age and stage (p=0.013, HR, 1.90, 95% CI, 1.14-3.16), while in better differentiated tumours it was not. In patients with weak staining, adjuvant chemotherapy was related to survival (p=0.010, 0.013 and 0.013 in entire tumour area, invasive margin and inner tumour area, respectively), but not in patients with strong staining. However, in the multivariate analysis no such relationship was seen.

Conclusions: PINCH staining in normal adjacent mucosa was related to survival. Further, PINCH staining at the tumour invasive margin was related to survival in poorly differentiated tumours but not in better differentiated tumours, indicating that the impact of PINCH on prognosis was dependent on differentiation status.

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Reoperation for chronic pain after groin hernia surgery. A population-based study

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Objective: To describe the measures at reoperations for chronic postoperative inguinal pain in a population based sample, and to evaluate the results in terms of remaining pain and quality-of-life.

Methods: All patients who had undergone surgery for chronic pain after previous groin hernia surgery 1999-2006 were identified in the Swedish Hernia Register (n=237).
Data on the surgical technique used were abstracted from the medical records. The patients were asked to answer a set of questions including SF-36, the Inguinal Pain Questionnaire (IPQ) and other questions in order to evaluate the prevalence of pain after reoperation.

Results: The study group consisted of 95 males and 16 females, mean age 53 years. Continued pain after reoperation was present in 19 %. In 27 % of cases an intervention aimed at suspected ilioinguinal neuralgia was performed. The mesh was removed completely in 28 % and partially in 13 %. A suture at the pubic tubercle was removed in 13 % of cases.
A decrease in pain was reported by 69 patients (62%), no change in pain by 21 patients (19%) and increase in pain in 21 patients (19%). There was no significant difference in outcome between the techniques applied. Quality-of-life was reduced compared to the general population.

Conclusions: Patients reoperated for chronic pain after hernia surgery often report a reduction in pain, but impairment was also seen. The natural course of chronic pain and selection of patients makes it difficult to draw firm conclusions regarding measures at reoperation.

Lithium-induced hyperparathyroidism, LHPT

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Objective: Lithium is used primarily in the treatment of bipolar disorder. Garfinkel (1973) presented the first case of lithium-induced hyperparathyroidism (LHPT). Since then c. 200 cases of surgically treated LHPT have been described in English literature. In the general population the prevalence of hyperparathyroidism (HPT) is approximately 1%. Hitherto, no studies have shown conclusively the prevalence of LHPT, which is the aim of this study.

Method: Two study populations have been identified, namely Örebro County (population c.300,000) and the catchment area for Ryhov County Hospital, Jönköping (c.130,000). The health records of all patients treated with lithium are reviewed for biochemical values including calcium, parathyroid hormone, vitamin D, creatinine and phosphate, and even if they have been operated on earlier because of HPT.

Result: This study is still in progress; so far 260 health records have been reviewed. Preliminary results show that in the first 100 patients studied there are 10 indisputable cases of HPT and a further 21 suspected cases, where complementary blood tests are required in order to differentiate diagnosis and aetiology. Secondary hyperparathyroidism due to hypovitaminosis D occurred clearly in 5 cases. Only one patient had been operated for HPT.

Conclusion: Preliminary results suggest a markedly higher prevalence of LHPT in comparison to the general population, possibly as high as 10%. An expansion of the current blood test controls is required in order to properly distinguish and diagnose deviating biochemical values. The study illustrates an associative role of lithium in the development of HPT.

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Short- and Long-Term Individual Variation in Cardiac Troponin in Patients with Stable Coronary Artery Disease

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Background: A rise and/or fall of cardiac troponin (cTn) is a prerequisite for the diagnosis of acute myocardial infarction. Defining significant changes requires knowledge of both biological and analytical variation. The short-term biological variation of high sensitivity cTn (hs-cTn) assays in healthy individuals is 3-48%. However, healthy individuals may not be representative for patients in whom cTn measurement is often of clinical importance. Therefore, we studied the individual variation of hs-cTn assays in patients with symptoms of stable coronary artery disease.

Methods: Twenty-four patients scheduled for elective coronary angiography were included. Blood samples were drawn once at enrolment and serially at six 4 hour intervals on the day prior to coronary angiography. cTn was determined by hs-cTn assays from Abbott Laboratories (premarket cTnI assay) and Roche Diagnostics (Elecsys®_cTnT assay with two different lots).

Results: The short-term individual variation in cTnI was 14%, the reference change value (RCV) 49%, and RCV-lognormal (rise/fall) 54/-35%. The corresponding values for cTnT were 7%, 23% and 26/-21%. The long-term variation for cTnI was 24%, the RCV 69%, and RCV-lognormal (rise/fall) 97/-49%. The corresponding values for cTnT were 11%, 32% and 37/-27%.

Conclusions: The short-term individual variation of cTn in patients with symptoms of stable coronary artery disease is similar to the biological variation previously demonstrated in healthy individuals. Our results suggest that a change in cTn concentrations of >50% can be used in attempting to diagnose acute myocardial injury. However, to detect significant long-term changes in cTn concentrations, larger changes will be required.

Improvement of food distribution to home living elderly people by using action research approach

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The study was performed in accordance with action research approach and included four phases: look, think, act and evaluate.

Look phase was performed in the three steps:

1. To gain insight into and describe the experiences of elderly home-living people who receive meals from municipality
2. To explore various professional's experiences of involvement in the food distribution process in order to get a comprehensive understanding of the organization and responsibilities and roles
3. To describe decision makers views on the food distribution service

Think phase was performed in the three steps:

1. To reflect on what was important for the elderly people relating to their receiving meals distributed by the municipality
2. To reflect on what the various involved professionals identify as most important to develop in the food distribution chain
3. To reflect over suggested developmental areas and choose one of them and reflect over how to perform action and evaluation

Act phase was performed in two steps:

1. The knowledge in nutrition as developmental area was chosen to focus action on
2. The way how to develop nutrition knowledge, the information letters, was chosen
3. The information letters were developed I collaboration with professionals and elderly people
4. The 1700 information letters were distributed

The evaluation phase was performed in three phases:

1. The preliminary outcomes were given as feedback to involved representatives from various professionals
2. The finally outcomes were given as feedback to decision makers
3. Final feedback resulted in three future actions

Outcomes from look and think phase are:

1. The food distribution receivers expressed feelings of: to not have influence over food products the meals were made from, to feel isolated and confined at home due to difficulties getting out of the house and expressed sincere gratitude for the meal service from the municipality.
2. The various professionals expressed that: food distribution is a fragmentary intervention where comprehensive perspective and roles of responsibility are lacking, the fragmented organization seemed strictly divided and limited by constrains regarding time and money, the necessary observations and structured following up of nutrition status for food distribution receivers is missing, and that knowledge in nutrition need to be continuously developed.
3. The decision makers found areas to require facilitation for change related to food distribution: the monitoring of the food distribution receiver's health and wellbeing, to focus on involved professional's competence in nutrition and to create a forum for inter-professional communication.

Porphyromonas gingivalis infection involves modulation of fibroblast-derived immunoregulatory mechanisms

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Objective: *Porphyromonas gingivalis* is a key pathogen in paradontitis, an inflammatory disease leading to destruction of bone and tooth-supporting tissue. *P. gingivalis* possess a number of patogenic properties to enhance growth and survival, including proteolytic gingipains. Accumulating data shows that gingipains are involved in the regulation of host inflammatory responses (1). By characterising the effects of *P. gingivalis* on fibroblast inflammatory responses, the aim was to determine if *P. gingivalis* infection modulates fibroblast immunoregulatory mechanisms.

Methods: Primary human fibroblasts were pre-stimulated with tumor-necrosis factor-α (TNF- α) and cocultured with *P. gingivalis*. Gingipain inhibitors were used to explore the effect of gingipains. CXCL8 were measured with ELISA and the relative levels of various inflammatory mediators were determined by a cytokine assay.

Results: TNF-α-triggered CXCL8 levels were completely abolished by viable *P. gingivalis*, whereas heat-killed *P. gingivalis* did not suppressed CXCL8. CXCL8 accumulation was partially restored by arginine-gingipain inhibitor. Fibroblasts produced several inflammatory mediators, notably chemokines, all of which were suppressed by viable *P. gingivalis*.

Conclusion: These findings provide evidence that fibroblast-derived inflammatory signals are modulated by heat-instable gingipains, whereby the bacteria can escape killing by the host immune system and promoting its own growth and establishment. In addition, we show that fibroblasts are important mediators of inflammation in response to infection and thereby play a crucial role in determining the nature and magnitude of the invasion of immune cells.

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The Q705K variant in the *NLRP3* gene confers protection against Myocardial Infarction in women of northern Swedish population.

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Objective: Inflammation is a multifaceted process underlying the pathophysiology of acute Myocardial Infarction (MI). Variations in the inflammasome-related NLRP3 gene have been associated with the risk for various inflammatory diseases. We hypothesize that Q705K polymorphism in *NLRP3* gene may therefore confer susceptibility to risk of MI.

Methods: FIA cohort comprising of 1016 controls and 555 MI patients was used to genotype rs35829419 in the NLRP3 gene using TaqMan SNP assays. C- reactive protein (CRP) was measured in the study participants by using ELISA assay.

Results: No significant association was found between the variant rs35829419 and MI. However, the minor allele A of the rs35829419 polymorphism conferred a protective effect against the risk of developing MI in women (*P*= 0.033). Moreover the minor allele A of rs35829419 polymorphism was also found to be associated with the increased CRP levels of men in the control subjects (*P*= 0.042).

Conclusions: The study suggests a gender specific association of the Q705K polymorphism to MI and CRP levels. The deregulation of *NLRP3* gene mediated by rs35829419 polymorphism confers protection against MI in women but has no effect on MI susceptibility in men. However, the rs35829419 polymorphism was found to increase the CRP level among men, thereby revealing the influence of Q705K polymorphism in elevating the basal active state of innate immune response.

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Postoperative pain following Abdominal Hysterectomy. A double-blind comparison between continuous infusion or patients controlled intra-peritoneal injection of localanesthetics

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Objective: Local anaesthetics injected intra-peritoneally (i.p.) have been found to decrease postoperative pain (1,2). This double-blind randomized study was performed to compare continuous infusion or patient controlled bolus injection of local anaesthetics i.p.

Methods: Two multi-hole catheters were placed intra-peritoneally at the end of the surgery in 40 patients undergoing elective abdominal hysterectomy were randomized into two groups:
Group P: Patients self-injected 10 ml of the study drug (levobupivacaine 1.25mg/ml) into the i.p. catheter as needed and had continuous saline infusion 10 ml/h into the second catheter.
Group C: Patients received a continuous infusion of 10 ml/h of the study drug i.p. through one catheter and 10 ml saline as bolus as needed. Morphine i.v. was administered as rescue medication. Pain, time to walk, drink, eat, return of gastrointestinal (GI) function, home readiness and home discharge were recorded.

Results: Morphine consumption during 0-24h was lower in Group P compared to Group C, mean difference -12.6 mg (95% CI -23.6 to -1.5, p = 0.027). No differences in median pain scores were found between the groups at any time point. Earlier return of GI function was found in Group P *vs*. Group C (1.5 vs. 2.2 days, p = 0.003), which also resulted in earlier home readiness
(1.9 vs. 2.7 days, p = 0.042).

Conclusion: A significant opioid-sparing effect was found when patient controlled levobupivacaine was administered i.p. as needed compared to those who received continuous infusion. This was associated with a faster return of gastro-intestinal function and home readiness.

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Cytokine Profile in a Cohort of Healthy Blood Donors Carrying Polymorphisms in Genes Encoding the NLRP3 Inflammasome

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Background: The NLRP3 inflammasome has been recognized as one of the key components of the innate immunity by sensing a diversity of insults. Inflammasome activation results in the maturation of the pro-inflammatory cytokines interleukin (IL)-1β and IL-18. Increased production of IL-1β is found in patients with gain-of-function polymorphisms in genes encoding the NLRP3 inflammasome. Since approximately 5% of the Swedish population are heterozygote carriers of these combined gene variants, their impact on inflammasome status and a relationship on disease development is therefore highly relevant to study. The present study investigates levels of inflammasome-produced cytokines as a measure of inflammasome activation in healthy individuals carrying Q705K polymorphism in the *NLRP3* gene combined with C10X in the *CARD8* gene.

Materials and Methods: Genotyping of 1006 healthy blood donors was performed for the polymorphisms Q705K in the *NLRP3* and C10X in the *CARD8* genes. IL-1β, IL-18, IL-33, as well as a number of other pro-inflammatory cytokines, were analyzed by Luminex or ELISA in plasma from individuals carrying the polymorphisms and in age and gender matched non-carrier controls.

Results & Discussion*:* The prevalence of the polymorphisms was in line with previous studies. Plasma levels of IL-1β and IL-33 were elevated among carriers of combined Q705K/C10X polymorphisms compared to controls, whereas no difference was found for IL-18 and the other cytokines measured. These data suggest that the combination of these two polymorphisms creates inflammasomes with increased basal activation state, which might provide a more favourable innate immune response. In spite of this, it could also represent the mechanisms by which the inflammatory loop is triggered into a long-term inflammatory phenotype.

Effect of cytokines, oxidative stress and nitrosative stress on tyrosine uptake in human fibroblasts: role of antioxidants

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Objective: Aberrant transport of tyrosine and tryptophan (precursors for dopamine, noradrenaline and serotonin) is one of the explanations for the disturbed dopaminergic, noradrenergic and serotonergic neurotransmission indicated in many neuropsychiatric disorders. A plausible explanation for the aberrant transport of tyrosine and tryptophan could be due to altered functionality of the amino acid transporters or general membrane dysfunction. These processes could arise through high levels of nitric oxide (NO) and reactive oxygen species (ROS), which could lead to nitrosative and oxidative stress (1). Cytokines can cause increased levels of NO and ROS, and altered levels of different cytokines are indicated in various neuropsychiatric disorders Moreover, antioxidants are proven to be effective in the management of certain psychiatric disorders as therapeutic adjutants.

Aims and Methods: The present study aimed to assess the effect of cytokines (TNFα, IFN-γ, and IL-1β), hydrogen peroxide (H_2O_2) and NO on tyrosine uptake and to further investigate the role of α-tocotrienol (an antioxidant) in counteracting the effect of H_2O_2 on L-[^{14} C] tyrosine uptake in cultured fibroblasts by using the cluster tray technique (2).

Results: Treating the fibroblasts with cytokine mixtures, H_2O_2 and NO resulted in tyrosine uptake inhibition. Treatment of fibroblasts with the antioxidant α-tocotrienol in combination with H_2O_2 reversed the inhibitory effect of H_2O_2 on tyrosine uptake.

Conclusions: Taken together the results of this study indicate that cytokines, NO and H_2O_2 can affect the functioning of tyrosine transporters of human fibroblasts and provides a probable mechanism of action for antioxidant α-tocotrienol that can be used as an adjuvant therapy for psychiatric disorders.

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Holding the patient's life in my hand: Swedish nurse anesthetists' perspective of advocacy

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Background: The concept advocacy is particularly appropriate in the perioperative nursing environment since anesthesia often puts the patient in an unconscious state. The patient has to rely on the nurse anesthetist to speak up for him/her, and for maintaining his/her dignity and safety.

Method: In order to describe the nurse anesthetists' perspective of advocacy in nurse anesthesia care data was collected through individual interviews with a purposive sample of 20 Swedish nurse anesthetists. The interviews were analysed by means of qualitative content analysis.

Findings: The main theme, "Holding the patient's life in my hand", was the Swedish nurse anesthetists' perception of advocacy. It embraced providing a dignified care, providing a safe care and a moral commitment. Moreover advocacy included an ethical, moral and medical responsibility in relation to the patient.

Conclusion: Advocacy has vast impact and influences the nurse anesthetist's professional role. The findings reveal that by practicing advocacy in their daily work e.g. when protecting patients from harm and treating them respectfully; the nurse anesthetists' contributes to the wellbeing and health of the individual. A humanistic work environment where the nurse anesthetists can make their voices heard and where their opinion regarding the patient's best is taken seriously is desirable since all health professionals have to have focused on the patient's best.

Calm or Not Calm: The Question of Anxiety in the Perianesthesia Patient

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Objective: Preoperative anxiety can be a major problem for the patient. Three distinct dimensions of preoperative anxiety are known: fear of the unknown, fear of feeling ill, and fear for life. The aim of this study was to investigate whether patients feel anxiety (calm or not calm) preoperatively before undergoing an elective day care surgery and also to elucidate the factors contributing to a patient's current state of mind.

Methods: A prospective study with 161 American Society of Anesthesiologists I–II outpatients scheduled for elective surgery was conducted. In a questionnaire the patients were asked to state if they were feeling calm or not and to describe factors contributing to their current mood. If responding that they did not feel calm, the participants were asked to rate the level of anxiety on a Numeric Rating Scale, 1–10.

Results: The results showed that 57% (n=91) of the participants stated that they did not feel calm. A significantly higher proportion of women did not feel calm (65%), P , .05. Significantly more participants with a previous experience of surgery felt calm (90%), P , .01. In all, 190 statements were submitted. The results show that nearly half of the participants felt calm before surgery. The reasons were earlier positive experiences, feeling of security and caring, being well-informed, and having positive expectations.

Conclusions: This indicates a need before surgery to routinely document and evaluate the individual patient's state of mind and reasons for the state of mind. This individual preoperative care can make it possible to provide emotional support, decrease anxiety, and give the patient a more positive surgical experience.

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ERG rearrangement status and castration resistant prostate cancer

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Objective: *ERG* rearrangement, most commonly leading *TMPRSS2-ERG* fusion, is suggested to be a sign of a more aggressive disease associated with prostate cancer specific death. Few studies have examined the association between ERG rearrangement and castration resistant disease, despite strong biologic rationale given that *TMPRSS2* is androgen regulated. We aimed to investigate if there is an association between *ERG* rearrangement status and time to castration resistant prostate cancer (CRPC).

Methods: We utilized 205 patients who were hormonally treated. CRPC was classified as two consecutive rises in PSA >3ng/ml after hormonal therapy. *ERG* rearrangement was assessed by fluorescence in situ hybridization.

Results: *ERG* rearrangement was more common among men who developed CRPC (36% vs. 27%). Having the rearrangement led to 84% increased risk of becoming castration resistant. After adjusting clinical variables, 54% increased risk of CRPC.

Conclusions: Our data suggest that patients with *ERG* rearrangement have an increased risk of CRPC and also were more likely to be hormonally treated earlier due to onset of symptoms or signs of disease progression. The results from our study indicate that the *ERG* rearrangement is a sign of a more aggressive disease and, if confirmed, could potentially be used to identify patients less likely to respond to hormone treatment.

Being born in Sweden increases the risk for type 1 diabetes - a study of migration of children to Sweden as a natural experiment.

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Background: The incidence of type1diabetes mellitus (T1DM) among children and adolescents in the world exhibit major differences with the highest rates in Scandinavia and Sardinia. This has been hypothesized to be an effect of an interaction of genetics and environmental factors. In this study we compared the risk of T1DM in three categories of residents with an origin in low incidence regions in the world; adoptees, immigrants and Swedish-born with foreign-born parents.

Methods: Register study in a study population in the age 6-25 years that consisted of 24,252 international adoptees, 47,986 immigrants and 40,971 residents with two foreign-born parents with an origin in Eastern Europe, East Asia, South Asia and Latin America and a comparison group of 1,770,092 Swedish-born residents with Swedish-born parents. Retrieval of a prescription of insulin during 2006 was used as an indicator of T1DM. Logistic regression analysis was used to test the hypothesis.

Main results: The odds ratios (OR) for T1DM were lower than the Swedish majority population for residents with an origin in the four low incidence regions with the lowest OR (0.10-0.14) for those with an origin in East Asia.
For Swedish-born the ORs for T1DM were highest in all four study groups. By a separate calculation excluding the indigenous Swedish children an OR of 1.68 (CI 1.03-2.73) was revealed for Swedish–born in the two other categories compared to international adoptees after adjustment for region of origin. The risk of T1DM did not vary by age at adoption in international adoptees or by age of immigration in immigrants.

Conclusions: Country of origin is an important determinant for T1DM in immigrant populations. The higher risk for T1DM in Swedish-born with an origin in low incidence regions in the world compared with adoptees from the same regions may imply that exposures in utero or very early infancy and/or early lifestyle changes may be important risk factors for T1DM.
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East Africans in Sweden have a high risk for diabetes type 1*.

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Short title: Childhood diabetes in East Africans

Objective: To investigate the prevalence of diabetes type 1 in children with an origin in Sub-Saharan Africa in Sweden.

Research design and Methods: Nationwide register study based on retrieved prescriptions of insulin during 2009 in children 0-18 years. The study population consisted of 35 756 children in families with an origin in Sub-Saharan Africa and 1 666 051 children with native Swedish parents.

Results: The odds ratio (OR) for insulin medication in Swedish-born children in families originating in East Africa was 1.29 (1.02-1.63) compared with offspring of native Swedish parents, after adjustment for age and sex, and less common in children who themselves were born in East Africa; OR 0.50 (0.34-0.73). Offspring of parents from other parts of Sub-Saharan African had a comparatively low risk for insulin medication.

Conclusions: This study indicates that Swedish-born children with an origin in East Africa have a high risk for diabetes type 1.

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Chronic cigarette smoke exposure disturbs hypoxia-induced angiogenesis signaling pathway in mouse skeletal muscle

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Objective: Smoking is a major risk factor for the development and progression of chronic obstructive pulmonary disease (COPD). Patients with COPD exhibit different systemic manifestations such as skeletal muscle dysfunction which directly correlates with high morbidity and poor quality of life. However, the impact of cigarette smoke exposure on skeletal muscles of COPD patients is unknown.
Methods: Here, we used 129/SvJ mice to investigate the effects of 6 months of cigarette smoke (CS) exposure and the effects of cigarette smoke extract (CSE) in C2C12 on expression of molecular elements of hypoxia-induced angiogenesis and muscle capillarization.

Results: Skeletal muscle of CS exposed mice showed increased expression of von Hippel-Lindau (VHL), Ubiquitin-conjugating enzyme E2 D1 (UBE2D1) and Prolyl hydroxylase domain 2 (PHD2). On the other hand expression of Hypoxia-inducible factor 1 (HIF-1α) and vascular endothelial growth factor (VEGF) was decreased. However, C2C12 cells treated with cigarette smoke extract (CSE) did not show any difference in the expression of *VHL*, *UBE2D1*, *PHD2*, *HIF-1α* and *VEGF*. Additionally, chronic CS exposed mice exhibited decreased skeletal muscle capillarization, decreased muscle fiber cross sectional area and decreased exercise endurance.

Conclusion: In summary, the findings show that mice skeletal muscles exposed to CS but not C2C12 exposed to CSE have disturbance in hypoxia-induced angiogenesis pathway which might contribute to deterioration of skeletal muscle structure and function.

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The development of a person transfer assessment tool for person transfers in dementia care settings

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Objective: Person transfer situations in dementia caregiving are complicated to be assessed. Limitations of existing assessment tools for transfer activities are that they do not take into account the complexity of cognitive decline, unpredictable motor behaviour or the social conditions of the context. There is a great need for new measures in this area. The ultimate purpose is to be able to identify problematic person- and environment-related bio-psychosocial factors, which could then be positively influenced by treatment strategies in these transfer situations.

Method: A conceptual framework for the person transfer assessment instrument was developed based on the literature, expert opinions, and video observations of person transfer situations in dementia context. The framework for behaviour assessment in person transfers is based on key domains from the bio-psychosocial model, both on the caregiver and the person with dementia. Items cover the whole range of domains that could be of importance in performing the person transfer situation. The measure needs also to be sensible for showing changes in the performance due to interventions.

Result: The initial list of 30 items was reduced to 17 in the first outline of the measure. Nine items are related to caregiver's behavioural actions and eight items to the behavior of the person with dementia. Contextual and background factors, e.g. medical diagnosis, prescribed medication, environmental factors and cues are also considered as important. The items are rated between 0 and 10. We are currently pilot-testing the measure, and finishing the development of the measure.

Low levels of stress resilience in adolescence and increased mortality risk: a national cohort study of Swedish men

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Objective: Previous studies suggest adverse affects of psychosocial stress on morbidity and mortality,[1,2] but it is unclear whether low levels of stress resilience in late adolescence influence all-cause and disease-specific mortality risk.

Methods: A representative cohort of 244,907 male conscripts born between 1952 and 1956 was followed to an average age of 54 years using information from Swedish registers. Stress susceptibility relevant to military performance was measured at conscription using a semi-structured interview with a psychologist. Cox regression estimated the association of stress resilience with mortality, after adjustment for powerful predictors of socioeconomic conditions throughout life, health and mortality risk.

Results: Lowest stress resilience (21.9% with scores 1-3) compared with the highest (23.8% with score 7-9) are associated with increased mortality risk, producing adjusted hazard ratios (HR) with (95% confidence intervals) of 1.6 (1.5, 1.7) for all-cause, 1.3 (1.2, 1.6) for cardiovascular and 1.3 (1.1, 1.4) for cancer mortality. Associations of low stress resilience with suicide are higher in earlier adulthood (before age 35 years) than later life, with HR of 2.8 (2.3, 3.4) and 1.6 (1.4, 1.9), respectively.

Conclusions: Low stress resilience is associated with increased mortality, particularly from suicide in early adulthood, but also cardiovascular disease and cancer. This provides strong new evidence of the role of stress and stress resilience in determining disease and mortality risk. Disease prevention programmes concerned with psychosocial stress should take into account the roles of both stressful exposures and individual stress resilience that may be determined prior to adulthood.

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Diastolic function improves after resolution of Takotsubo cardiomyopathy

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Objective: Takotsubo cardiomyopathy (TSC) is a condition of reversible left ventricular (LV) systolic dysfunction. However, the impact on diastolic function (DF) manifestations of TSC has not been widely investigated (1). We performed a retrospective analysis of DF in patients (pts) with TSC during acute and recovery phase.

Methods: We studied 27 pts (64±11 yrs, F 24) diagnosed with TSC. All pts had echocardiogram acutely and about 3 months later at follow-up. LV systolic ejection fraction (EF) was assessed as well as standardized diastolic function variables, including E wave velocity and tissue doppler of mitral annuli (E'). LV diastolic dysfunction stages were recorded, according to guidelines (2), in 16 pts. Data was analyzed using paired t-test and chi-square test.

Results: Acutely DF was observed in 13 pts (81 %) compared to 6 pts (37 %) at recovery ($p<0.001$). Recovery was associated with significant improvement in systolic and diastolic parameters including E' and E/A ratio. Improvement in E' was linearly related to the improvement in EF ($p=0.02$).

Conclusions: TSC is associated with acute impairment of DF, which improves during recovery. Recovery parallels systolic recovery in TSC.

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20-Year Results after Sector Resection with or Without Postoperative Radiotherapy for Stage I Breast Cancer: A Randomized Trial

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Background: Postoperative radiotherapy after breast-conserving surgery (BCS) of early breast cancer significantly reduces the risk of local relapse. Our study was one of the first trials to confirm this. Between 1981-1988, 381 women diagnosed with breast cancer stage I was randomised to BCS with (XRT group) or without (non-XRT group) postoperative radiotherapy. The purpose of this updated analysis was to report the results with a minimum follow-up of 20 years.

Methods: Data for each woman on newly reported breast tumours and/or date and cause of death, was collected from the Patient Registers at Dpt. of Social Wellfare, Sweden. Life-table curves and cumulative-incidence estimates of the outcome were obtained.

Results: The cumulative incidence of local recurrence after 20 years in the XRT-group was 11,5% and 25.8% in the non-XRT group, RR 0.42 (95%CI 0.26-0.68). At the end of follow up 50.4% of the women in the XRT group had died as compared to 54.0% in the non-XRT group RR 0.91(95%CI 0.71-1.18). The cumulative incidence of local recurrence or a contralateral cancer was 22.4% in the XRT-group and 31.4% in the non-XRT-group, RR 0.74 (95%CI 0.51 – 1.08). In an anticipated low-risk group of women, the cumulative incidence of local recurrence was 5.1% in the XRT-group and 14.5% in the non-XRT-group, RR 0.39 (95% CI 0.15-1.00), p=0.051.

Conclusion: In our trial the addition of radiotherapy after BCS resulted in an absolute risk reduction of 14.3% concerning local recurrence. Postoperative radiotherapy did not affect overall mortality or breast cancer death. In a subgroup of women □55 years, without lobular or comedo cancer, the risk of local recurrence even without radiotherapy was approx. 10% lower than in all women. The risk of having a local recurrence was highest in the first 5 years after diagnosis. After 5 years no further difference in local recurrence between the groups was observed.

Global Protein Analysis in Fibroblasts from Oral Carcinoma

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Objective: Oral cancer still remains a drastic disease with an incidence that has increased over the last century. The 5-year survival rate is around 33%, evidence that additional therapies are required. Development of a solid tumor is dependent of a supporting tissue that surrounds the tumor cells. This tumor stroma consists of different non-transformed cells of which the fibroblasts are the most abundant. Targeting the tumor stroma together with the transformed carcinoma cells might provide therapeutic opportunities. Targeting tumor stroma is also attractive since cytotoxicity could be minimised. In this study, cancer-associated fibroblasts were subjected to proteomics analysis for the identification of proteins that could be implicated in oral cancer prognosis and treatment.

Methods: Cultures of cancer-associated fibroblasts were established from two pairs of oral normal mucosa and oral cancer tissues. Proteins were extracted from the cells and 2-dimensional electrophoresis and mass spectrometry were employed in order to identify any differentially expressed proteins between sample pairs.

Results: Peroxiredoxin-1 and Transgelin-2 were found to be highly expressed in the oral cancer fibroblasts cultures while absent in normal oral mucosa fibroblasts. Peroxiredoxin-1 is an anti-oxidant enzyme and one of the TLR4 ligands utilized by cancer cells for their progression. Transgelin is involved in actin cross-linking and thereby cytoskeletal remodelling presumably important for various cell movements and mechanical processes.

Conclusion: This pilot study of cancer-associated fibroblasts suggests that these cells produce TLR4 ligands that may be important for cancer progression. It also suggests that cancer-associated fibroblasts overexpress an actin-regulating protein that has implication for cellular mechanical property.

Can the pain be eliminated by physical training?

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Introduction
Musculoskeletal complaints from neck and shoulders are frequently described among employers working with near activities as ordinary office- or computer work. About thirty percent describe complaints as a sense of discomfort up to severe muscle pain in the neck and shoulder area[1,2]. These complaints could be due to visual ergonomics or other individual interactions with the environments in the office-landscape.

IEA definition of visual ergonomics
Visual ergonomics is the multidisciplinary science concerned with understanding human visual processes and the interactions between humans and other elements of a system. Visual ergonomics applies theories, knowledge and methods to the design and assessment of systems, optimizing human well-being and overall system performance. Relevant topics include, among others: the visual environment, such as lighting; visually demanding work and other tasks; visual function and performance; visual comfort and safety; optical corrections and other assistive tools.
A recent theory describes the hypothesis of that such visual demanding work (due to unfavorable lightning, not sufficient visual discrimination for the visual task) could impact on the muscles in the neck scapular area as they interact in many ways[4]. Neck complaints are more often described among those with a need of refractive visual correction a or spectacles[3]. Individuals with visual impairment or decreased visual performance, could therefore be presumed to have more complaints in neck and shoulders, which also was concluded in a county comprehensive survey. Physiotherapists are rare or seldom an ordinary profession in the treatment of Low vision patients in our Swedish Low vision clinics. This research concerns a special method "guided sensorimotor training", as a method to heal and strengthen the individuals in their own training in dealing with awareness of a better posture or motion in order to prevent musculoskeletal complaints. During 2009 the project received funds from the health insurance (Försäkringskassan och Vårdalstiftelsen) to perform the project in order to prevent sick leave due to neck and shoulder complaints.

Aim: Ergonomic advice as well as physiotherapy has been noticed to have high impact on treatments concerning chronic pain. This study was performed, to clarify if "guided sensorimotor training" could reduce chronic neck pain among visually impaired patients.

Method:A questionnaire was sent to all patients at the age of 16-67 years old, who had visited the Low vision clinic during the past decade. The questionnaire contained questions about neck and shoulder pain, visual performance and postural control . Those with the most pronounced complaints were offered to take part in the intervention. Randomised allocation, was used to split the group in two halves, where one half had the intervention at first and the other half was considered as referents (and offered the intervention later on).Data concerning Visual acuity, Visual Function and performance, Eye hand coordination, Musculoskeletal complaints, Postural sway and occurrence of muscular trigger points was collected before and after the intervention period, which concerned 12 sessions during 8-10 weeks.

Result: The intervention was very appreciated among all of the low vision clinics participants. The Musculoskeletal complaints were significantly reduced after the intervention. (mean diff -1.7w4 ; p<=.0001) as well as the results from the self administered questionnaire concerning balance and postural control (mean diff -1.11 p = 0.002), but the results were not stable over time.

Conclusion: Interdisciplinary treatments, concerning visual ergonomics from a wider perspective, can be very fruitful.

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The TGF-beta And Notch Signaling Pathway Are Activated By *Porphyromonas gingivalis* in Aortic Smooth Muscle Cells

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Background: *Porphyromonas gingivalis* is the main cause of periodontal disease. *P. gingivalis* has also been found being able to gain access into the bloodstream and attach to vascular wall[1]. A great number of epidemiological studies indicate that there is an association between *P. gingivalis* infection and cardiovascular disease[2-4]. The aim of this study is to investigate how *P. gingivalis* change the gene expression profiling of human aortic smooth muscle cells (AoSMCs).

Methods: In order to elucidate the association between P. gingivalis infection and AoSMCs, the AoSMCs were exposed to *P. gingivalis* for 24h. Fluorescence microscopy was used to find if P. gingivalis can invade the AoSMCs. Human genome microarray was used to show how *P. gingivalis* change the gene expression profiling of AoSMCs.

Results: Through fluorescence microscopy, we found *P. gingivalis* can invade the AoSMCs. A total of 982 genes were identified as differentially expressed genes with the threshold ($\log_2$ fold change >|1| with adjust p-value <0.05) from microarray results. Those genes were significantly related to rheumatoid arthritis and atherosclerosis in disease ontology analysis. Using pathway analysis, we found the up-regulated genes enriched in 14 pathways and down-regulated genes enriched in 7 pathways. NOTCH and TGF-beta are two of those pathways were being activated.

Conclusions: This study demonstrates the activation of TGF-beta and NOTCH signaling pathways in AoSMCs by live *P. gingivalis*. This further supports the association between periodontitis and cardiovascular diseases.

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