1 Increased levels of YKL-40 in patients with chronic pancreatitis and secondary diabetes

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Background and aims: Circulating levels of the inflammatory glycoprotein YKL-40 and interleukin-6 (IL-6) are elevated in patients with type 2 diabetes. We aimed to evaluate YKL-40 levels in patients with chronic pancreatitis (CP) with and without secondary diabetes mellitus (DM) to investigate whether elevated plasma YKL-40 could play a primary role in the pathogenesis of type 2 diabetes or rather represent a consequence of the diabetic state.

Methods: Plasma levels of YKL-40 and IL-6 were measured during a 4h 50 g-oral glucose tolerance test (OGTT) in 8 patients with CP and non-insulin requiring secondary DM, 8 patients with CP and normal glucose tolerance (NGT), and 8 healthy control subjects (CTRLs).

Results: OGTT did not alter the levels of YKL-40 or IL-6 in any of the groups. Levels of YKL-40 and IL-6 were significantly ($P < 0.05$) higher in patients with CP and secondary DM (YKL-40: 113 [60-215] ng/ml (mean [95% confidence interval]); IL-6: 4.6 [2.3-9.1] pg/ml) compared to patients with CP and NGT (YKL-40: 42 [28-63] ng/ml; IL-6: 1.4 [0.8-2.4] pg/ml) and CTRLs (YKL-40: 46 [31-69] ng/ml; IL-6: 1.4 [0.8-2.4] pg/ml). Plasma YKL-40 showed a positive correlation with plasma IL-6.

Conclusions: Patients with CP and secondary non-insulin requiring DM are characterised by elevated levels of YKL-40 and IL-6 compared to CP patients with NGT and healthy subjects, suggesting that YKL-40 is not a primary mediator in the pathogenesis of DM, but rather a consequence of the diabetic state.
Interaction of lipids with the low grade inflammatory state: the association between variations of CHI3L1, YKL-40 levels and the lipid profile in a Danish population

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**Objective:** To describe the association between polymorphisms of CHI3L1, serum YKL-40 and levels of the differentiated lipid profile in a representative group of the Danish population.

**Material and methods:** 12 SNPs of CHI3L1 were genotyped and serum YKL-40 and parameters of the lipid profile were measured in 2656 healthy Danes.

**Results:** The differentiated lipid profile and obesity-associated parameters were analyzed according to YKL-40 quartiles. Cholesterol (p<0.0001) as well as triglyceride (p<0.0001) levels increased with each YKL-40 quartile, whereas BMI (p<0.0001) and waist-hip-ratio (WHR) (p<0.0001) were higher in the 3rd and 4th quartile. LDL levels increased slightly from the 1st through the 3rd quartile (p=0.006), whereas HDL did not change significantly (p=0.630). The highest YKL-40 quartile was associated with a 36% greater risk of hypercholesterolemia (OR 1.36 (95% CI 1.08; 1.72), p=0.009). YKL-40 correlated strongly with triglyceride (β=0.25, p<0.0001), but only weakly with cholesterol (β=0.09, p=0.011) and HDL (β=0.04, p=0.001). Higher total cholesterol levels were seen in individuals with minor homozygosity of rs872129 (p=0.047) and higher triglyceride levels were seen in individuals with minor homozygosity of rs12123883 (p=0.008). Minor homozygosity of rs12123883 was associated with a higher prevalence of low HDL (p=0.012).

**Conclusion:** Serum YKL-40 correlates with triglyceride levels in a representative group of healthy Danish citizens. This is partly explained by minor homozygosity of the polymorphism rs12123883, which is also associated with the prevalence of low HDL.
3 Glukosestofskiftet er påvirket efter fjernelse af L- og α-celler, men upåvirket efter fjernelse af K-celler

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\textbf{Hypotese og formål:} De enteroendokrine K- og L-celler secernerer glucose-dependent insulinotrop polypeptide (GIP) og glucagon like-peptide 1 (GLP-1) og α-cellerne i de langerhanske øer secernerer glukagon; derfor anses K-, L- og α-celler for at være essentielle for normal regulering af glukosestofskiftet. Formål med dette studie var at undersøge hvordan en akut fjernelse af Gip eller Gcg udtrykkende celler påvirker glukose stofskiftet.

\textbf{Metoder:} Udvikling af de to difteritoksin medieret cellulære knock-out mus (TgN(GIP.DTR) og TgN(GCG.DTR)). Undersøgelse af sukkerstofskiftet med oral- og intraperitoneal-glukosetolerancetest efter akut fjernelse af K-, L- og α-celler.

\textbf{Resultater:} Administration af difteritoksin til TgN(GIP.DTR) reducerede ekspressionen af Gip i proksimale jejunum, mens administration til TgN(GCG.DTR) reducerede ekspressionen af Gcg i både proximal jejunum, distal ileum samt indholdet af glukagon i pankreas.

Fjernelse af K-celler medførte reduceret GIP sekretion efter oral glukose stimulation, medens den orale og intraperitoneal-glukosetolerance var upåvirket. Hvor den intraperitoneal glukose tolerance var forringet efter kombineret L- og α-celle fjernelse og upåvirket efter isoleret α-celle fjernelse, var den orale glukose tolerance let forbedret efter kombineret L- og α-celle fjernelse, og markant forbedret efter isoleret α-celle fjernelse.

\textbf{Konklusion:} Vi introducerer to nye transgene musemodellever, der kan bruges til at studere effekterne, af K- eller L- og α-celle fjernelse samt efter isoleret α-celle fjernelse. Vores fund viser at K-cellerne ikke er nødvendige for glukose stofskiftet i normale mus, desuden understreger de α-cellens rolle i reguleringen af sukkerstofskiftet.
4 Involvement of SGLTs and $K_{atp}$ channels in the glucose induced secretion of Glucagon-Like Peptide 1 (GLP-1) from rat small intestine

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**Background and aims:** The development of specific secretagogues for endogenous glucagon-like peptide 1 (GLP-1) requires solid knowledge on the regulatory mechanisms of intestinal L-cells. This study was performed to investigate the involvement of the apical sodium-glucose co-transporter SGLT, and $K_{atp}$ channel activation in glucose mediated GLP-1 release in isolated perfused rat intestine.

**Methods:** Isolated vascularly perfused segments of rat small intestine ($n = 6-8$) were luminally perfused by 0.250 mL/min 20 % glucose containing 0.9 % NaCl, with or without the addition of the SGLT blocker Phloridzin (PZ; 1 mM, 0.250 mL/min luminal infusion), Diazoxide (DZ; 300 µM intra arterial infusion) or Tolbutamid (TBM; 185 µM intra arterial infusion); a $K_{atp}$ channel opening and -closing agent, respectively.

**Results:** Glucose infusion elicited a total outcome of GLP-1 of 296.1±69.07 fmol (AUC) vs. basal secretion = 103.4±11.97 fmol (2.96 fold change, p=0.018, n=11). Addition of PZ obliterated the glucose induced GLP-1 response (GLU+PZ; 138.8±23.33 vs. basal secretion136.9±19.56 fmol, p=0.943, n=8). GLP-1 outcome was increased 5.17 fold by GLU+DZ (530.6±78.04 vs.102.5±19.38 fmol, p=0.002, n=7), and 2.70 fold by GLU+TBM (439.8±55.16 vs. 162.9±24.6 fmol, p=0.005, n=6).

**Conclusion:** Blocking the glucose uptake via SGLT in the luminal L cell membrane significantly decreases glucose induced GLP-1 secretion from L cells of rat small intestine. In contrast, DZ caused an augmented response, not entirely reversed by TBM. We conclude that SGLT mediated signaling is likely to be involved in L-cell secretion, whilst the role of $K_{atp}$ closing is less clear.
The PNPLA3 rs738409 G-allele associates with a reduction in fasting levels of serum triglyceride and total serum cholesterol in middle-aged people with impaired glucose regulation

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Objective: Non-alcoholic fatty liver disease (NAFLD) is a common condition, associated with hepatic insulin resistance and the metabolic syndrome. We aimed at studying the potential impact of the NAFLD-associated PNPLA3 rs738409 G-allele on NAFLD-related metabolic traits including insulin resistance in hyperglycaemic individuals.

Design and Methods: We genotyped rs738409 in the population-based Inter99 cohort (n=6,116) examined by an oral glucose-tolerance test and a combined study-sample consisting of 192 twins (96 twin pairs) and a subset of the Inter99 population (n=63), examined by the hyperinsulinemic euglycemic clamp method (ntotal=255). We applied an additive genetic model. In Inter99 we examined for associations of rs738409 with metabolic traits related to hepatic steatosis (n=5,663) and associations with components of the WHO-defined metabolic syndrome. A meta-analysis in the combined study-sample was conducted to elucidate whether the rs738409 G-allele altered hepatic or peripheral insulin sensitivity. Study populations were divided into individuals with either normal glucose-tolerance (NGT) or impaired glucose regulation (IGR).

Results: Among 1,357 middle-aged IGR individuals, the rs738409 G-allele associated with decreased fasting serum triglyceride levels (per allele effect(β)= -9.2 % [-14.4%; -4.0% (95% CI)], p=3.3×10-5) and fasting total-cholesterol (β=-0.2 mmol/l [-0.3;0.01 mmol/l(95% CI)], p=1.0×10-4). No associations were found in 4,306 NGT individuals. Studies of the combined study-sample showed no impact on hepatic or peripheral insulin resistance in carriers of the rs738409 G-allele, yet, NGT individuals had significantly increased peripheral insulin sensitivity (Combined β=9.7 %[0.05%;18.8%(95% CI)], p=0.04).

Conclusion: Our findings suggest that the G-allele of PNPLA3 rs738409 associates with reduced fasting levels of total-cholesterol and triglyceride in IGR individuals
6 Studies of AGPAT6 variation and the relation to type 2 diabetes and metabolic traits in 12,068 Danes

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Aim: Type 2 diabetes, obesity and insulin resistance are characterized by hypertriglyceridemia and ectopic accumulation of lipids in liver and skeletal muscle. The AGPAT6 gene encodes a novel glycerol-3 phosphate acyltransferase, GPAT4, which catalyzes the first step in de novo triglyceride synthesis. AGPAT6-deficient mice show lower weight and resistance to diet- and genetically induced obesity. Here, we examined whether common or low-frequency variants in AGPAT6 associate with type 2 diabetes or related metabolic traits in a Danish population.

Methods: Eleven variants capturing the common and low-frequency variation of AGPAT6 were genotyped in 12,068 Danes from four study populations of middle-aged individuals. The case-control study involved 4,638 type 2 diabetic and 5,934 glucose-tolerant individuals, while studies of quantitative metabolic traits were performed in 5,645 non-diabetic participants in the Inter99 Study.

Results: None of the eleven AGPAT6 variants were robustly associated with type 2 diabetes in the Danish case-control study. Moreover, none of the AGPAT6 variants showed association with measures of obesity (waist circumference and BMI), serum lipid concentrations, fasting or 2-h post-glucose load levels of plasma glucose and serum insulin, or estimated indices of insulin secretion or insulin sensitivity.

Conclusion: Common and low-frequency variants in the AGPAT6 gene do not significantly contribute to type 2 diabetes susceptibility, or influence related phenotypic traits such as obesity, dyslipidemia or indices of insulin sensitivity or insulin secretion.
**7 Protein Metabolism in Human Skeletal Muscle after 72 hours Fasting**

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**Background:** Intermittent fasting increase maximum lifespan in several species and this effect is associated with reduced protein synthesis signaling. During fasting, a progressive loss of protein in human skeletal muscle is evident. Furthermore, fasting is associated with increased lipid oxidation and insulin resistance.

**Methods:** To understand the mechanisms that regulate skeletal muscle protein turnover during fasting, we investigated the response to 72 hours of fasting in 8 healthy men. Skeletal muscle protein metabolism was assessed using labelled phenylalanine tracer combined with arteriovenous catheterization technique. Insulin sensitivity was assessed by hyperinsulinemic-euglycemic clamp. In addition, substrate oxidation and intramyocellular signaling to protein synthesis and breakdown was assessed.

**Results:** Peripheral insulin sensitivity was reduced and substrate oxidation shifted toward lipid oxidation during fasting. Net muscle protein breakdown was increased, mTOR signaling to protein synthesis was reduced, and FOXO3a signaling to local protein breakdown was unaltered. Furthermore, insulin signaling to protein synthesis was impaired downstream of Akt. However, fasting did not affect the upstream kinases Akt and AMPK or amino acid sensitive phosphorylation of eIF2a.

**Conclusion:** This work defines the physiological adaptations to fasting. The findings suggest that the increased net protein breakdown is due to reduced mTOR mediated protein synthesis. Furthermore, impaired insulin signaling to protein synthesis is not due to amino acid deprivation or AMPK activation. Our findings suggest that inhibition of mTOR signaling is a central mechanism triggering reduction of protein synthesis in muscle during fasting – and perhaps increasing longevity in humans and other species.
8 Increased non-stimulated and $T_3$-stimulated reactive oxygen species (ROS) in human lymphocytes in patients with Diabetes Mellitus type 2

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**Aim:** To determine non- and $T_3$-stimulated ROS production in human lymphocytes of patients with Diabetes Mellitus type 2 (T2D) and control persons.

**Methods:** Nine patients with T2D and fifteen control persons with no history of diseases were included in the study. All patients were hypertensive and had no other signs of complications. They were treated with insulin, and/or metformin, and an ACE inhibitor. Blood samples were drawn and peripheral blood mononuclear cells (PBMC’s) were isolated by Ficoll-Paque Plus. One million cells were stimulated with 50 nmol/L $T_3$ for 90 min. $T_3$-stimulated and non-stimulated cells were labeled with 5-6-carboxy-2’-7’-dichlorodihydrofluorescein diacetate (carboxy-H$_2$DCFDA) and the fluorescence emission was measured by flow cytometry as a measure of ROS.

**Results:** Non- and $T_3$-stimulated ROS production were determined in human lymphocytes from patients with T2D and control persons. The non-stimulated ROS production in patients with T2D was significantly increased: 18840 relative fluorescence (a.u.) (interquartile range 17162-24247 a.u.) compared to control persons: 3893 a.u. (interquartile range: 2656-5687 a.u.) (p=0.007) (Figure 1). In addition, the $T_3$-stimulated ROS production was significantly increased in patients with T2D: 20.0% (interquartile range 20.6-39%) compared to control persons: 8.5% (interquartile range: 3.5-11.8%) (p=0.025).

![Figure 1: Non-stimulated reactive oxygen species in human lymphocytes from control persons (n=15) and patients with Diabetes Mellitus type 2 (n=9) in relative fluorescence (a.u.).](image)

**Conclusion:** The non- and $T_3$-stimulated ROS production in human lymphocytes were significantly increased in patients with T2D indicating that the patients with T2D are more sensitive to stimuli of ROS production.
9 Huntingtin-interacting protein 14 is a type 1 diabetes candidate protein regulating insulin secretion and beta-cell apoptosis

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Type 1 diabetes (T1D) is a complex disease characterized by the loss of insulin-secreting beta-cells. The disease has a strong genetic component and several loci are known to increase T1D susceptibility risk. However, only few causal genes have currently been identified. To identify novel T1D candidate genes, we performed an *in silico* “phenome-interactome analysis” on a genome-wide linkage scan dataset. This method prioritizes candidates based on their interactions to other proteins involved in diabetes. By this method, eleven genes were predicted to be likely disease genes in T1D, including the *INS* gene. A top-scoring candidate gene was huntingtin-interacting protein (HIP)-14/ZDHHC17. Immunohistochemical analysis of pancreatic sections demonstrated that HIP14 is almost exclusively expressed in insulin-positive cells in islets of Langerhans. RNAi knockdown experiments established that HIP14 is an anti-apoptotic protein required for beta-cell survival and glucose-stimulated insulin secretion. Hence, the current network biology approach is a valid method to identify genes of importance for T1D and may therefore represent the basis for developing new and targeted therapeutic approaches.
10 Clinical reliability of Continuous Glucose Monitoring System (CGMS) in detecting nocturnal hypoglycaemia in patients with type 1 diabetes and recurrent severe hypoglycaemia

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Background: A reliable method to detect biochemical nocturnal hypoglycaemia is needed. Continuous Glucose Monitoring (CGM) may reveal these episodes.
Aims: To evaluate reliability of nocturnal CGM in patients with type 1 diabetes at high risk of severe hypoglycaemia (SH).
Methods: 72 patients with type 1 diabetes (46 males; age 54±12 years, HbA1c 8.1±1.1%, duration of diabetes 30±14 years, 2 (2-20) episodes of SH last year) participated in a 2-year randomised crossover study of the ability of insulin analogues to reduce the incidence of SH in high-risk patients, i.e. ≥ 2 episodes of SH in the past year. Blinded CGMS was made 2 x 2 nights, totally 217 nights. Blood was drawn hourly from 23:00 – 7:00 for plasma glucose (PG) measurements (gold standard). Nocturnal hypoglycaemia was defined by three thresholds: <4, <3, and <2.2 mM. A valid episode of hypoglycaemia measured by CGMS lasted at least 20 min.
Results: 53% of the patients experienced at least one night with hypoglycaemia. The prevalences of nocturnal hypoglycaemia according to the three thresholds were 28%, 16%, 3% for PG and 33%, 12%, 3% for CGMS. The sensitivity of CGMS was 65% (95% CI: 53-77), 40% (24-56) and 17% (0-46), respectively. If only hypoglycaemic nights were taken into account, CGMS missed detection of 35% of hypoglycaemia <4, 60% <3 and 83% <2.2 mM (Figure). Among 1786 simultaneous pairs of measurements, 67% of the CGMS recordings were lower than PG and were on average 1.1 mM lower than PG (r=0.82; p<0.0001).

Conclusions: Reliability of CGM is inadequate in type 1 diabetic patients at high risk of severe hypoglycaemia. However, since nocturnal hypoglycaemia is usually unrecognized, CGM may benefit some high-risk patients.
11 Use of flexible intensive insulin therapy and an automated bolus calculator in type 1 diabetes

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**Aim:** To investigate the effects of flexible intensive insulin therapy (FIIT) and an automated bolus calculator (ABC) (Accu-Chek Aviva Expert) in a Danish type 1 diabetes population treated with multiple daily injections.

**Research design and methods:** The BolusCal Study was a 16-week randomized, controlled, three-arm parallel, clinical study. Patients aged 18-65 years in poor metabolic control (HbA1c 8.0-10.5%) were randomly assigned to the Control (n=8), CarbCount (n=21) or CarbCountABC arm (n=22). During a three-hour group teaching, the Control arm received general diabetes training not including carbohydrate counting. CarbCount patients were taught FIIT including carbohydrate counting. CarbCountABC received FIIT and carbohydrate counting training and patients were provided with an ABC.

**Results:** At 16 weeks, the within-group change in HbA1c was -0.1% (P=0.730) in the Control arm, -0.8% (P=0.002) in CarbCount, and -0.7% in CarbCountABC (P<0.0001) (Table 1). The between-group difference was insignificant. Adjusting for baseline HbA1c values in a regression model, the relative changes in HbA1c in CarbCount and CarbCountABC were -0.6% (P=0.082) and -0.8% (P=0.017), respectively, with a borderline significant between-group difference (P=0.056).

**Conclusions:** FIIT resulted in significantly improved metabolic control. The study suggests that the benefit of FIIT could be further improved with concurrent ABC usage.

**TABLE 1.**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CarbCount</th>
<th>CarbCountABC</th>
<th>Between-group difference (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>9.1 ± 0.7%</td>
<td>9.2 ± 0.6%</td>
<td>8.8 ± 0.7%</td>
<td>0.088</td>
</tr>
<tr>
<td>16 weeks</td>
<td>8.9 ± 1.1%</td>
<td>8.4 ± 0.9%</td>
<td>8.1 ± 0.4%</td>
<td>0.029</td>
</tr>
<tr>
<td>Within-group diff. (95%CI)</td>
<td>-0.1% (-1.0 – 0.7%)</td>
<td>-0.8% (-1.3 – -0.3%)</td>
<td>-0.7% (-1.0 – -0.4%)</td>
<td>0.175</td>
</tr>
<tr>
<td>Within-group diff. adjusted for baseline HbA1c (95%CI)</td>
<td>0.0% [reference]</td>
<td>-0.6% (-1.2 – 0.1%)</td>
<td>-0.8% (-1.4 – -0.1%)</td>
<td>0.056</td>
</tr>
</tbody>
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12 Cannabinoid Receptor Agonist Treatment In Severe Chronic Anorexia Nervosa

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Aim: The endocannabinoid system (EC) plays a constitutive role in feeding-related neuronal circuits. Associated with a deranged leptin signalling it may be involved in the pathophysiology of eating disorders (ED) and clinical data emphasise it as a potential therapeutic target. The aim of the present study is to reveal if treatment of severe chronic AN patients with cannabinoid receptor agonist (dronabinol) has significant effect on body weight, endocrine parameters, Eating Disorder Inventory profile, and motor restlessness assessed by accelerometry.

Method: The study is add-on, randomized, double blinded, placebo-controlled with a cross over design, including 24 patients with chronic AN. The 4 weeks of active treatment are separated by a wash-out period of four weeks. The recruitment phase is now closed.

Results: The median age at inclusion was 33 (range 19 - 62), with a median BMI of 15.84 (range 11.66 - 18.13). In an interim analysis performed on 19 participants we found a significant increase in weight during active treatment versus placebo, while no significant changes were observed in the secondary effect parameters. No significant adverse effects or dropouts have been registered.

Conclusion: Based on our preliminary results, dronabinol seems to be safe in women with chronic AN and may prove to be an important supplement in a multidisciplinary treatment strategy in the severest cases. Moreover, elucidating the effect on pharmacologic CB1 agonist stimulation on motor restlessness, leptin levels and other hormones may generate crucial progress in understanding the pathogenesis of AN.
13 Kvaliteten af glykæmisk kontrol samt patienttilfredshed hos patienter i behandling med insulinpumpe

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Formål: At etablere en database til overvågning af behandlingskvalitet og patienttilfredshed hos patienter med Type 1 diabetes i behandling med insulinpumpe.

Materiale og metoder: Behandling med insulinpumpe til patienter med Type 1 diabetes er påbegyndt ved diabetesambulatoriet i Fredericia i 2005. I 2009-2010 er der oprettet en database over disse patienter. Databasen indeholder både retrospektive og prospektive årlige data fra før pumpestart. Fra 2009-2010 er patienttilfredsheden vurderet ved udfyldelse af patienttilfredshedsskemaerne Diabetes Treatment Satisfaction Questionaire Status (DTSQs) and Change (DTSQc) Versions.

Resultater: Opgives som median med spændvidde. Per 31.12.2010 indeholder databasen 68 aktive patienter, heraf 33 mænd og 35 kvinder. Alderen er 41 (22-66) år, diabetesvarighed 21 (1-52) år, vægt 78 (53-124) kg og diabetesvarighed 2,2 (0-25) år. Glykeret hæmoglobin (HbA1c) er reduceret fra 8,0 (5,8-13,7) % ved baseline til 7,6 (6,1-9,5) % (p<0,01) det seneste år under pumpebehandling. Den forbedrede glykæmiske kontrol har kunnet fastholdes hvert år til og med >=4 år efter pumpestart (p<0,01). Ved baseline versus seneste år under pumpebehandling har hhv. 13 % og 24 % HbA1c <7 % samt 18 % og 3 % HbA1c>9 %. Antallet af tilfælde med alvorlig hypoglykæmi er reduceret under pumpebehandling (p<0,05). Tre tilfælde med ketoacidose er rapporteret. Vægt er uændret efter behandlingsskift. Der er betydelig tilfredshed med pumpebehandling med en DTSQs-score på 34,5 (27-36) i forhold til en score på 19 (12-33) (p<0,01) og en DTSQc-score på 16 (9-18) (p<0,01) på pumpebehandling i forhold til pennebehandling. For hvert af de enkelte aspekter af patienttilfredsheden er der større patienttilfredshed med insulinpumpebehandlingen (p<0,01).

Konklusion: Insulinpumpebehandling er ledsget af en forbedret glykæmisk kontrol, reduceret antal hypoglykæmiske tilfælde samt betydelig tilfredshed med diabetesbehandlingen.
14 Exercise Dependence: Validation of a screening tool, psychological characteristics and leptin levels

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Aims and hypothesis: Exercise dependence is characterised by excessive and obsessive exercise behaviour with potential negative physical, psychological and social consequences. The aim was to validate the screening tool Exercise Addiction Inventory (EAI) and we expected good psychometric properties. In the next part of the study psychological and hormonal profiles of the exercisers will be performed.

Methods: A total of 590 normal weight exercisers was tested with the EAI, which has a cut off score = 24. In the next part of the study 30 dependent versus 30 non-dependent exercisers are tested with NEO Personality Inventory to test personality profiles, with blood samples to measure leptin concentrations and DXA scans to determine body composition.

Results: Preliminary data demonstrate a prevalence of exercise dependence of 5.8\% (Figure 1). Males and individuals below 35 years have an increased risk of exercise dependence. There is no difference in Body Mass Index. The EAI has good psychometric properties with a Cronbach’s Alpha of 0.66.

![Figure 1](image_url)

Conclusion: Exercise dependence seems to exist in Danish sport cultures and the EAI may be a useful screening instrument. The next part of the study provides psychologic, endocrinologic and antropometric information about exercising individuals which can be useful in future prevention and treatment of exercise dependence.
15 Neurocognitive phenotype and personality profile in men with Klinefelter syndrome and their genetic vulnerability to psychiatric symptoms

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Background: Klinefelter syndrome (KS) is associated with increased risk of psychiatric disease and behavioral problems, as well as social problems. The background for these risks is not known.

Aim: The aim was to describe the cognitive function, personality traits and the vulnerability to psychiatric symptoms in patients with KS.

Methods: 41 KS patients and 41 age- and educational-matched control subjects participated. All participants were tested with standardized neuropsychological tests and 4 questionnaires investigating psychological problems.

Result: KS patients scored significantly lower in processing speed, working memory, verbal abilities and showed a selective deficit in executive function compared to control subjects, whereas visual cognitive abilities and cognitive response inhibition was preserved. The KS patients displayed significantly higher levels of cognitive failures, emotional distress and autism traits as reported in questionnaires. Furthermore symptoms of anxiety were also significantly higher among KS patients, whereas there were no difference in depressive symptoms between KS patients and control subjects. On the personality test KS patients scored high on the neuroticism scale, low on the extraversion scale and low on the conscientiousness scale. We could not discriminate between those KS receiving testosterone supplementation or those who did not, which is likely due to a small sample size.

Conclusion: Men with KS have deficits in several cognitive domains and have an altered personality phenotype. Furthermore our results suggest that KS patient may be associated with an increased genetic vulnerability to psychiatric symptoms. In future analyses, we are going to assess the neuroanatomical, neurofunctional, endocrine and genetic basis for the cognitive deficits, altered personality phenotype and increased psychiatric symptoms seen in KS patients. Whether testosterone therapy or other interventions can alleviate these deficits remain to be proven.
16 Long QT interval in Turner syndrome, relation to cardiovascular malformations, and presence of polymorphisms in genes related to long QT syndrome and hypertension

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Purpose: Prolonged QT interval has been described in both children and adult women with Turner syndrome (TS), which suggests presence of long QT syndrome (LQTS). However, the genetic background has never been examined. Therefore the aim of the present study was to assess the QT interval in a large cohort of adult TS and to explore the presence of mutations in the LQTS genes.

Methods: One-hundred-and-two adult TS patients were examined thrice with a mean follow-up of 4.7 ± 0.5 years (mean ± SD), and 67 healthy controls were examined once. QTc (Bazett’s formula) was measured by one blinded examiner (intra-observer variability 0.7 %). Echocardiography, 24-hour blood pressure and blood samples were performed. Thereafter, we determined the presence of polymorphisms in known genes related to LQTS (KCNQ1, KCNE1, KCNE2, KCNJ2, SCN5A) in the TS women with a QTc in the upper quartile.

Results: The mean QTc in TS (427.9 ms) compared to controls (389.1 ms) was prolonged (p < 0.001) and did not change over time (431.9 vs. 426.6 ms; p = 0.058). 45,X karyotype was associated with increased QTc prolongation when compared to other TS karyotypes (433.8 vs. 419.0 ms; p = 0.005). The presence of bicuspid aortic valve and elongated transverse aorta was significantly related to QTc (p = 0.026 and p = 0.022). Of the 23 TS with the longest QTc, 6 had missense mutations in major LQTS-genes (SCN5A and KCNH2), with one individual having 2 mutations (KCNE2 and KCNH2).

Conclusion: Preliminary data supports a significant prolongation of the QTc interval in TS. We found a high prevalence of mutations in the major LQTS genes, indicating a new probable cause of sudden death in TS.
17 Substrate oxidation in type 2 diabetes during acute exercise

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Background and aims: Exercise is recommended for the treatment of type 2 diabetes (T2D). However, few studies have examined the metabolic adaptations to acute exercise in T2D. The aim of the present study was to investigate the effect of acute exercise on whole-body glucose and lipid metabolism and signaling to glucose transport and storage in muscle of patients with T2D.

Methods: Insulin-stimulated glucose infusion rates (GIR) were studied in 12 patients with T2D and 11 glucose-tolerant controls by euglycemic-hyperinsulinemic clamps at rest and seven hours after 60 min of stationary bicycling at 60% of VO2max. Indirect calorimetry was performed during exercise (20 and 50 min) to calculate whole-body rates of glucose and lipid oxidation. Muscle biopsies were taken before and after each intervention.

Results: GIR were lower in diabetic individuals compared with controls in the rested (223 vs. 342 mg·min⁻¹·m⁻², P=0.03) and the post-exercise state (211 vs. 329 mg·min⁻¹·m⁻², P=0.02). Exercise had no effect on GIR in the diabetic (P=0.82) or the control (P=0.80) group. Glucose and lipid oxidation did not differ between groups during exercise. Lipid oxidation increased from 20 to 50 min of exercise in the diabetic group (98 vs. 172 mg·min⁻¹·m⁻², P=0.02) and tended to increase in controls (147 vs 223 mg·min⁻¹·m⁻², P=0.06). Lactate levels were significantly higher in the diabetic group throughout exercise.

Conclusion: During acute exercise, patients with T2D and controls show similar fuel utilization patterns. GIR was not improved by exercise in either group, and remained lower in patients with T2D. Determination of endogenous glucose production and signaling events in muscle are ongoing.
18 GLP-1 is also secreted from proximal rat intestine

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**Aim:** This study aimed to compare secretion of the incretin hormone glucagon-like peptide-1 (GLP-1) from the proximal and the distal small intestine using the in situ perfused rat intestine. GLP-1 is secreted from intestinal L-cells after intake of nutrients. Classically, L-cells are believed to be located primarily in the distal part of the small intestine and the colon.

**Methods:** Experiments were performed by in situ perfusing either the proximal or distal half of the small intestine in male Wistar rats. Intestinal secretion was stimulated by infusion with the phosphodiesterase inhibitor IBMX (1 mmol/L). Effluent concentrations of GLP-1 and PYY were subsequently measured. Furthermore, expression levels of *Glucagon* and *Pyy* in proximal small intestine were compared to expression levels in distal small intestine.

**Results:** Infusion of IBMX significantly increased GLP-1 secretion in the proximal small intestine from a basal level of 52.9±7.7 to peak level 277.5±54.2 µmol/min (n=7; p=0.0032). Comparable GLP-1 levels were observed from the distal intestine (345.0±18.2; n=7). In contrast, stimulation with IBMX resulted in a significant increase in PYY secretion in distal intestine from 37.2±3.9 to 175.7±29.0 µmol/min (p=0.0021), but had no effect on PYY secretion from the proximal intestine.

**Conclusion:** These results show that infusion of IBMX stimulates secretion of GLP-1 from both proximal and distal small intestine, whereas PYY secretion is only stimulated from the distal small intestine. Consequently, GLP-1 secretion is not limited to the distal part of the gastrointestinal tract and the early GLP-1 response could arise from direct stimulation of L-cells in the proximal small intestine.
19 Characterization of postprandial blood glucose regulation in GIP receptor knock-out mice

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Aim: Being an incretin hormone, Glucose-dependent Insulinotropic Polypeptide (GIP) augments glucose stimulated insulin secretion from the β-cells, and also glucagon secretion from the α-cells. However, the effect of GIP on glucose metabolism after fat and protein ingestion is not well characterized. Our aim was to characterize the impact of specific nutrients on blood glucose regulation in GIP receptor knock-out mice (GIPr KO). Our hypothesis is that GIP is necessary to stabilize blood glucose after a low/non-carbohydrate meal, by inducing hepatic glucose release via glucagon. Furthermore, we looked at the influence of anaesthesia on oral glucose tolerance test (OGTT).

Methods: Oral glucose/protein/fat/protein+fat/mixed-meal tolerance tests were performed in unanaesthetized GIPr KO and WT mice following an overnight fast. Blood glucose were repeatedly measured in the interval 0-150 min. Insulin were measure at 0 and 20 min. Nutrition was dissolved in water, with the addition of bile salts for fat mixtures. Specific nutrition doses were 8 calories/g of body weight.

Results: We found a profound impact on glucose metabolism following use of two forms of anaesthetics (isoflurane and hypnorm/midazolam). We were unable to detect any impact of the GIPr on blood glucose and insulin secretion following oral delivery of any of the used nutrients.

Conclusion: Use of anaesthesia has a profound impact on glucose metabolism and OGTT should only be performed in unanaesthetized mice. GIP is not important for the acute regulation of blood glucose or insulin secretion, following a carbohydrate deficient meal.
20 Transgenic rescue of adipocyte Glucose-dependent Insulinotropic Polypeptide (GIP) receptor expression restores high fat diet induced body weight gain

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Aim: The Glucose-dependent Insulinotropic Polypeptide receptor (GIPr) has been implicated in high fat diet (HFD) induced obesity and proposed as an anti-obesity target despite an uncertainty regarding the mechanism of action. The aim of this study is to distinguish between direct effects of GIP in adipose tissue and effects from an impaired entero-insular axis.

Method: To independently investigate the contribution of insulinotropic effects and direct effects on adipose tissue, we generated transgenic mice with targeted expression of the human GIPr to white adipose tissue or beta-cells, respectively. These mice were then cross-bred with the GIPr knockout strain.

Results: The central findings of the study are that mice with GIPr expression targeted to adipose tissue have a similar HFD induced body weight gain as control mice, significantly greater than weight gain in mice with a general ablation of the receptor. Surprisingly, this was due to an increase in total lean body mass rather than a gain in total fat mass. In contrast, GIP mediated insulin secretion does not seem to be important for regulation of body weight after high fat feeding.

Conclusion: The study supports a role of the adipocyte GIPr in nutrient dependent regulation of body weight and lean mass, but does not support a direct and independent role for the adipocyte or beta-cell GIPr in promoting adipogenesis.
21 Glucagon and the gut hormones GLP-1 and oxyntomodulin increase resting energy expenditure in man

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Background and aim: The satiety hormone oxyntomodulin (OXM) is a proglucagon product with body weight lowering effect. It binds to the glucagon-like peptide-1 (GLP-1) receptor and the glucagon receptor, but the mechanisms behind the body weight reducing effect of OXM remain elusive. We aimed to evaluate resting energy expenditure (REE) during infusions of: 1) saline, 2) GLP-1, 3) glucagon, 4) OXM, and 5) GLP-1+glucagon in healthy subjects.

Methods: Indirect calorimetry was used to measure oxygen consumption ($VO_2$), carbon dioxide production ($VCO_2$), respiratory quotient (RQ) and REE after a 3h-continuous infusion of either saline, GLP-1 (1 pmol/kg/min), glucagon (0.86 pmol/kg/min), OXM (3 pmol/kg/min) or glucagon+GLP-1 (same doses) in 15 healthy male volunteers (age: 22±2 years (mean±SEM); BMI: 23±0.5 kg/m²; HbA1c: 5.8±0.1%).

Results: Plasma glucose (5.1±0.1 mM) and triglyceride (1.0±0.1 mM) concentrations were similar during the calorimetric measurements. REE was significantly elevated in response to all peptide infusions compared to saline, with OXM eliciting the most pronounced increase in REE (Fig. A). GLP-1 alone and in combination with glucagon elevated RQ compared to saline whereas OXM decreased RQ (Fig. B).

Conclusion: These data suggest that GLP-1, glucagon and OXM increase REE. Also, our RQ results indicate that oxyntomodulin increases REE by other mechanisms than glucagon and GLP-1 - perhaps involving a shift of the metabolic substrate utilization towards lipid metabolism.

Figure 1. Resting energy expenditure (A) and respiratory quotient (B) during the five different infusions. Asterisks indicate significant differences from the saline infusion (Bonferroni-adjusted post hoc analysis: *$p<0.05$ and **$p<0.001$).
22 Impaired gastrointestinal-mediated glucose disposal in vagotomised subjects indicates an essential role of the vagus nerve for endogenous GLP-1 effects

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Background: GLP-1 is degraded by DPP-4, suggesting it may act locally before being degraded. Gastrointestinal-mediated glucose disposal (GIGD) describes the impact of all factors, including the incretin effect, on plasma glucose (PG) concentrations after oral glucose ingestion. We aimed to clarify the role of vagal innervation on the incretin effect and GIGD.

Methods: Ten truncally vagotomised subjects (due to duodenal ulcer) with pyloroplasty (68±2 years; fasting PG (FPG): 6.0±0.2mM), 10 subjects treated for oesophageal cancer with cardia resection including truncal vagotomy/pyloroplasty (65±2 years; FPG: 5.8±0.3mM) and 10 control subjects (67±1 years; FPG: 5.3±0.1mM) underwent 4h 50g-OGTT±concomitant DPP-4 inhibition (DPP-4i) and isoglycaemic glucose infusion (IIGI).

Results: Isoglycaemia was obtained. Peak PG during OGTT and IIGI were similar in vagotomised subjects (13.8±0.8 vs. 13.2±0.6mM; 13.9±0.8 vs. 13.9±0.8mM, p=NS), and higher than in controls (9.3±0.5 and 8.8±0.4mM, p<0.0009). GLP-1 secretion was 5-fold higher and gastric emptying faster (time to peak paracetamol 38±7 and 33±7 vs. 77±8 min, p<0.002) in vagotomised subjects after OGTT compared to controls. The incretin effect was similar in all groups (48±6% (duodenal ulcer), 50±5% (cardia resection) and 53±4% (controls), p=NS). In vagotomised patients, isoglycaemia during IIGIs was obtained using 26±2g (duodenal ulcer) and 26±3g (cardia resection) glucose (p=NS) compared to 18±2g in controls (p<0.02 and p<0.05 vs. the two vagotomised groups), resulting in GIGD of 49±4 and 48±6% in the vagotomy groups (NS) and 63±4% in control subjects (p<0.02 and P<0.05).

Conclusions: Vagotomized subjects have impaired glucose homeostasis. Despite higher OGTT-induced GLP-1 levels (likely due to pyloroplasty-associated accelerated gastric emptying), the incretin effect was not elevated in vagotomised subjects. This, together with reduced GIGD, suggests that vagal innervation is important for the effect of GLP-1 and thereby maintenance of normal glucose homeostasis.
The impact of dipeptidyl peptidase 4 inhibition on glucose tolerance and gastrointestinally-mediated glucose disposal in healthy subjects

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Background and aim: Inhibitors of the enzyme dipeptidyl peptidase 4 (DPP-4), which under normal circumstances degrades and thereby inactivates the incretin hormones glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1), are thought to exert their antidiabetic effect by increasing the incretin effect. We aimed to describe the impact of DPP-4 inhibition on glucose tolerance and gastrointestinally-mediated glucose disposal (GIGD) in healthy subjects in order to elucidate 1) the mode of action of DPP-4 inhibition and 2) the physiological mechanisms underlying the incretin effect.

Methods: Ten healthy subjects (age: 40±16 years; body mass index: 24±3 kg/m², fasting plasma glucose: 5.1±0.2 mM; HbA1c: 5.3±0.1%) were subjected to 50 g-oral glucose tolerance test (OGTT) and isoglycaemic iv glucose infusion on separate days with and without (randomised) preceding administration of the DPP-4 inhibitor sitagliptin (100 mg). GIGD was calculated using the formula: GIGD (%) = 100% × (glucose_{OGTT} - glucose_{IIGI} / glucose_{OGTT}).

Results: Isoglycaemia was obtained during both conditions (with and without DPP-4 inhibition) in all subjects. No significant impact of DPP-4 inhibition on fasting plasma glucose (5.1±0.1 vs. 4.9±0.1 mM, p=0.3), glucose tolerance (evaluated as area under curve: 1,351±20 vs. 1,339±35 mM×240 min, p=0.7) or peak plasma glucose (8.5±0.4 vs. 8.1±0.3 mM, p=0.3) during OGTT was observed. Similar amounts of glucose during the iv infusions were needed to obtain isoglycaemia (24.2±2.0 vs. 22.1±2.3 g, p=0.4) resulting in similar GIGD values with and without DPP-4 inhibition (51.6±3.9 vs. 55.7±4.5%, p=0.4).

Conclusions: Our data suggest that acute inhibition of DPP-4 (and elevation of active incretin hormone levels) does not increase GIGD significantly and has limited effects on fasting plasma glucose, glucose tolerance and peak plasma glucose concentrations after OGTT in healthy subjects.
24 Incretin-induced amplification of insulin secretion is impaired following glucose homeostatic dysregulation in healthy subjects

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Background and aims: Type 2 diabetes is characterised by impaired insulinotropic effect of the incretin hormones glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). It remains unclear whether this impairment is a primary pathophysiological defect or a consequence of glucose intolerance. Therefore, we aimed to investigate the insulinotropic effect of GIP and GLP-1 compared to placebo before and after 12 days of glucose homeostatic dysregulation in healthy subjects.

Materials and methods: The insulinotropic effect was measured using hyperglycaemic clamps and infusion of physiological doses of GIP, GLP-1 or saline in 10 healthy Caucasian males before and after intervention using high calorie diet, sedentary lifestyle and administration of prednisolone (37.5 mg/day) for 12 days.

Results: The intervention resulted in insulin resistance according to the homeostatic model assessment (1.2±0.2 vs 2.6±0.5, p=0.01) and glucose tolerance deteriorated as assessed by the area under curve (AUC) for plasma glucose during OGTT (730±30 vs 846±57 mM×2h, p=0.021). The subjects compensated for the induced insulin resistance by significantly increasing their post intervention insulin responses during saline infusion by 2.9±0.5 fold; thus, disposition index was unchanged. In contrast, the insulin responses to GIP or GLP-1 were only weakly up-regulated (1.78±0.3 and 1.38±0.3 fold, p=0.001 vs saline).

Conclusions: These data show that impairment of the insulinotropic effect of both GIP and GLP-1 can be induced in healthy male subjects without risk factors for type 2 diabetes indicating that the reduced insulinotropic effect of the incretin hormones observed in type 2 diabetes most likely is a consequence of insulin resistance and glucose intolerance rather than a primary event causing type 2 diabetes.
Preserved postprandial GLP-1 responses in cholecystectomized subjects: no evidence of a physiological role of gallbladder emptying in postprandial GLP-1 release

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Aim: Preclinical studies suggest that gallbladder emptying - via bile acid-induced activation of the G protein-coupled receptor TGR5 in intestinal L cells - plays a significant role in the secretion of the incretin hormone glucagon-like peptide-1 (GLP-1) and postprandial glucose homeostasis. We hypothesized that human gallbladder emptying potentiates postprandial release of GLP-1 and aimed to evaluate whether cholecystectomized patients exhibit impaired postprandial GLP-1 secretion.

Methods: Ten cholecystectomized subjects (age: 49±4 years (mean±SEM); BMI: 25±0.4 kg/m²; HbA1c: 5.9±0.1%) and 10 healthy age-, gender- and BMI-matched control subjects (age: 48±4 years; BMI: 24±0.5 kg/m²; HbA1c: 5.7±0.1%) were studied. None had any family history of diabetes and all had normal oral glucose tolerance according to 75 g-oral glucose tolerance test (OGTT). Subjects received a 2,200 kJ-standardized fat-rich liquid meal during which blood samples were drawn and duodenal aspirate (for evaluation of intraduodenal bile acid concentrations) was collected through a duodenal tube placed fluoroscopically.

Results: Similar fasting plasma glucose levels were observed in the two groups (5.4±0.1 (mean±SEM) vs. 5.2±0.1 mM, P=0.2) whereas postprandial plasma glucose (PPG) excursions were exaggerated in the cholecystectomized group compared to control subjects (1,431±31 vs. 1,313±36 mM×240 min, P=0.023). Similar fasting plasma GLP-1 concentrations were observed in the two groups, and subjects without a gallbladder exhibited preserved postprandial responses of GLP-1 compared to the carefully matched healthy control subjects (3,707±400 vs. 3,165±287 pM×240 min, P=0.29).

Conclusions: Cholecystectomized subjects exhibit preserved postprandial GLP-1 responses suggesting that the physiologically important role of gallbladder emptying for postprandial GLP-1 release indicated by preclinical studies is of less importance in humans. Thus, the physiological relevance of potentiation of GLP-1 release via bile acid-induced activation of TGR5 in small intestinal L cells is questionable in humans.
Improvement in psoriasis after treatment with the glucagon-like peptide-1 receptor agonist liraglutide - a case report

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Background and aim: Glucagon-like peptide-1 (GLP-1) is an incretin hormone that is essential for glucose homeostasis. During the last years, various GLP-1 receptor (GLP-1R) agonists have been marketed and are increasingly used for the treatment of patients with type 2 diabetes. Moreover, studies have demonstrated clinical relevant and sustained effects of GLP-1R agonists on weight loss in obese patients.

Methods: This case includes a 59-year old man suffering from type 2 diabetes for five years with inadequate glycaemic control (HbA1c 8.9%, body mass index 29.3 kg/m², body weight 91.8 kg). His diabetes had been controlled previously with diet restrictions, metformin therapy 500 mg twice daily and premixed insulin 20 IE twice daily. His medical history included a 15-year long history of plaque psoriasis. Treatment with the GLP-1R agonist liraglutide was initiated at 0.6 mg once daily, and titrated to 1.8 mg once daily after five weeks of treatment.

Results: The patient experienced marked improvement in his psoriasis immediately after start of liraglutide treatment. Itching stopped within days, scaling was reduced and spots of normal skin emerged. After 3 months, psoriasis was still improving. Excellent glycaemic control (HbA1c 5.9%) as well as a weight loss of approximately 8 kg during 3 months was moreover obtained. The effect of liraglutide on psoriasis set in before weight loss occurred.

Conclusion: The GLP-1R agonist liraglutide markedly improved psoriasis in a patient treated for type 2 diabetes. Randomized clinical trials are needed to reveal whether this effect is reproducible in other patients with psoriasis.
27 GLP-1 receptors in psoriatic skin - a target for new treatment?

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Background and aim: Psoriasis vulgaris is a chronic inflammatory skin disease affecting 2-3% of the Western population. Recent case reports suggest that treatment with glucagon-like peptide-1 (GLP-1) receptor agonists may result in clinical improvement of the disease. The aim of the present study was to investigate if GLP-1 receptors are present in healthy and psoriatic skin, respectively.

Methods: We included 6 patients with psoriasis and 6 healthy subjects in the study. Punch biopsies were taken from lesional and non-lesional skin and preserved for histological and immunohistochemical staining and gene expression analysis. In addition, a blood sample was drawn from all patients.

Results: RNA was isolated from the skin biopsies (submerged into RNAlater) and validated by expression of house keeping genes. Further analyses are on-going. The first preliminary staining of the formaldehyde-fixed biopsies indicates the presence of GLP-1 receptors in human skin biopsies.

Conclusions: These preliminary results suggest that there might be GLP-1 receptors in the human skin, thus providing a possible explanation for the positive effect of treatment with GLP-1 receptor agonists seen in psoriasis.
28 Subclinical Thyroid Disease and Risk of New-onset Atrial Fibrillation

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Background: It is still uncertain if subclinical thyroid disease or “high-normal” thyroid function are risk-factors for atrial fibrillation (AF).

Objectives: To examine the risk of AF in relation to thyroid function.

Methods: Patients consulting their general practitioner from 2000–2009 in Copenhagen, Denmark, who underwent thyroid blood tests, were identified by individual-level linkage of nationwide registries. Patients with a history of thyroid disease, AF or related medication were excluded. Risk of AF was analyzed using cumulative incidence plots and Poisson regression models to gain Incidence Rate Ratios (IRR).

Results: Of 525,100 individuals in the study population (mean age 51.7 years [SD ±18.0]; 39.5% males) 504,113 (96.0%) were euthyroid, 1,474 (0.3%) had clinical hypothyroidism, 10,679 (2.0%) subclinical hypothyroidism, 3,421 (0.7%) clinical hyperthyroidism and 5,414 (1.0%) subclinical hyperthyroidism. A ”dose-dependent” increased risk of AF was found in two levels of subclinical hyperthyroidism (TSH <0.1, 0.1–0.2 mU/L): IRR 1.8 [95% CI: 1.5–2.2], IRR 1.5 [1.2–2.0] and in “high-normal” levels of euthyroidism (TSH 0.2–0.4 mU/L): IRR 1.3 [1.2–1.5]. Both clinical and subclinical hypothyroidism was associated with a lower risk of AF.

Conclusions: Subclinical hyperthyroidism and “high-normal” thyroid function is a significant risk-factor for AF, whereas hypothyroidism is associated with decreased risk of AF.

Cumulative incidence of atrial fibrillation in relation to thyroid function (age > 65 years)
29 Individual changes in thyroid function after iodine fortification: 11-year follow-up of the DANTHYR C1 cohort

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Objective: To evaluate individual changes in thyroid function after iodine fortification in a population.

Methods: The DANTHYR C1 cohort examined in 1997 and re-examined 11 years after. 2,036 individuals with no prior thyroid disease and with a baseline serum level within the normal reference range for TSH (0.4-3.6 mU/L) were included in the analysis. The nationwide mandatory program for iodization of salt was initiated in 2000.

Results: During the 11 years of follow-up, a significant increase in mean TSH was measured; 1.30 mU/L (CI 1.27-1.32) to 1.40 mU/L (CI 1.32-1.45), P<0.0001. Subjects living in the area of Copenhagen (with mild iodine deficiency at baseline and sufficient iodine intake at 11 years follow-up) had the most pronounced increase (1.32 mU/L (CI 1.28-1.36) to 1.50 mU/L (CI 1.44-1.56), p<0.0001), whereas in subjects living in Aalborg (with moderate iodine deficiency at baseline and mild iodine deficiency at 11 years follow-up) the increase was not significant (1.27 (CI 1.24-1.31) to 1.31 (CI 1.26-1.37), p=0.0589). The baseline lower TSH quartile was positively associated with low TSH at follow-up (< 0.4 mU/L), and the frequency decreased with increasing TSH baseline value (Fig. 1). The frequency of high TSH (> 3.6 mU/L) at follow-up also associated with baseline TSH quartile.

Conclusion: Iodine fortification leads to an increase in TSH level, signalling a general shift in the thyroid disease pattern. The more pronounced increase in Copenhagen might be explained by iodine induced hypothyroidism and/or less thyroid autonomy. TSH in the upper and lower quartile of the normal reference range is a risk factor for development thyroid dysfunction.
30 Incidence of painless thyroiditis in Denmark as evaluated by consecutive 99m-Tc pertechnetate thyroid scintigraphics

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Introduction: The incidence of painless thyroiditis (PT) varies hugely in the literature which might in part be due to different reporting and perhaps different iodine intake. PT is characterized by lack of uptake on a thyroid scintigraphy in a non-tender thyroid gland, elevated anti-TPO antibodies, no fever, no history of increased iodine intake, and a normal sedimentation rate.

Objective: to establish the incidence of PT in Denmark, which is an iodine replete area.

Methods: Scintigraphies were performed over a period of close to 10 years on 6001 consecutive patients, of which 2349 had a hyperthyroid episode. Two-hundred and four had lack of uptake on a Tc-99m pertechnetate scintigraphy, of which 13 were lost to follow up, leaving 191 for analysis. As a control measure, 215 consecutive patients referred during one year with hyperthyroidism were also analysed from patient records.

Results: Ten patients were categorized as PT, corresponding to an incidence of approximately 0.41/100,000 person years. Approximately 0.43% of all hyperthyroid patients had PT based on evaluation by scintigraphy. Based on the scintigraphy analysis only one out of 230 consecutive biochemically established hyperthyroid patients should have PT. Reassuringly, this patient was identified and no further patients with PT were found in this cohort.

Conclusion: Painless thyroiditis is an extremely rare disease in Denmark as compared to reported incidence rates in the literature.
31 Hospitalsbehandlede thyroideapatienters arbejdsliv – resultater fra en kvalitativ undersøgelse

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Formål: At belyse faktorer af betydning for hospitalsbehandlede thyroideapatienters arbejdsliv.
Resultater: Tre overordnede temaer havde betydning for interviewpersonernes arbejdsliv:
2. Sygdommens diffuse karakter medførte tvivl om gyldigheden af de oplevede begrænsninger. Diskrepans mellem de oplevede mentale begrænsninger og resultater fra biomedicinske prøver medførte negativ selvevaluering
3. Begrænsningerne oplevedes som svære at tackle og italesætte over for omgivelserne. På arbejdspladsen oplevedes begrænsningerne som individets eget ansvar og blev ikke tacklet sygdomsspecifikt (f.eks. valgtes afspadsering frem for sygefravær), ligesom arbejdspladsen ikke involveredes i sygdommen.
Konklusion: Kvalitative interviews viste, at problemer med at skelne sygdomsbetingede begrænsninger fra normal funktion kan gøre det vanskeligt for thyroideapatienter at håndtere deres -sygdom i arbejdslivet. Denne hypotese vil blive testet i fremtidige kvantitative undersøgelser og kan forhåbentlig lede til bedre identifikation af rehabiliteringsbehov blandt thyroideapatienter.
32 Hyperthyroidism, rather than autoimmunity, seems to determine quality of life in patients with Graves' disease

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Purpose
To evaluate relationships between clinical variables and thyroid-specific quality of life (QoL) in Graves' hyperthyroidism.

Methods
The ThyPRO-questionnaire was completed by 168 cross-sectional, clinically well-described outpatients with Graves' hyperthyroidism. ThyPRO measures thyroid-related QoL in 13 scales: Goitre-, Hyperthyroid-, Hypothyroid-, and Eye symptoms, Depressivity, Anxiety, Tiredness, Cognitive problems, Emotional susceptibility, Impaired Social life, Daily life, Sex life and Cosmetic concern. Data were analyzed within a QoL framework, both univariately and multivariately. The clinical variables entered were thyroid volume, low TSH, high fT4, high fT3, high TSH, low fT4, low fT3, CAS, NOSPECS, TPO-Ab and TSHR-Ab.

Results
In initial pairwise analyses, all clinical variables were related to one or more QoL scales. However, in the path analysis multivariate model only hyperthyroid function, i.e. lower TSH and higher fT3 was related to QoL scales. Low TSH and high fT3 both affected Hyperthyroid Symptoms (standardized partial regression coefficient r=-0.28 and 0.28 respectively, p<0.01 for both), which in turn was related to all three well-being scales (Tiredness r=0.45, p<0.0001, Cognition r=0.32, p=0.003, Susceptibility r=0.26, p<0.0001) as well as Impaired Daily life (r=0.41, p<0.0001). fT3 also had a direct relationship with Tiredness (r=0.16, p=0.029), Impaired Daily life (r=0.16, p=0.026) and Impaired Sex life (r=0.38, p<0.0001).

Conclusion
When analyzed univariately, many clinical measures were related to thyroid-related QoL. However, when analyzed multivariately, QoL was related solely to thyroid hyperfunction through hyperthyroid symptoms. QoL was not associated to TSHR-Ab or TPO-Ab levels indicating only minor influence of autoimmunity per se on QoL in patients with Graves’ disease.
Is the association between overt hyperthyroidism and mortality explained by confounding? A nation-wide register-based study of Danish twins

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**Background:** Overt hyperthyroidism (OH) has repeatedly been associated with a number of potential lethal conditions such as pulmonary embolism, stroke and coagulopathy. In addition, OH has also been connected with an increased mortality. However, the link between OH and mortality could be the result of common genetic and environmental factors affecting both OH and mortality. Investigating twin pairs discordant for OH can minimize this potential confounding.

**Method:** We first conducted a classical case-control study in the background population with (n=4895) and without (n=19580) OH, and then a case-control study of twin pairs discordant for OH (n=1264). Risk estimates were calculated by COX regression analysis.

**Results:** In the Danish background population, mortality was increased by 23% in subjects with OH (Hazard ratio, HR = 1.23, 95% CI 1.17-1.30). The impact of OH on mortality remained significant after adjusting for the degree of comorbidity (HR = 1.14, 95% CI 1.08-1.20). Irrespective of zygosity, OH was also associated with an increased mortality (HR = 1.43, 95% CI 1.09-1.88) in twins discordant for exposure. However the effect of OH on mortality attenuated and was non-significant within monozygotic pairs (HR = 0.95, 95% CI 0.60-1.50) whereas it was significant within dizygotic pairs (HR = 1.80, 95% CI 1.27-2.55).

**Conclusion:** This is the first study, which on a nation wide level, investigated whether OH is linked to increased mortality. Our finding supports the notion that the link between OH and mortality could be causal although it is to some degree influenced by shared genetic determinants.
34 Serum selenium is low in newly diagnosed Graves`disease and autoimmune hypothyroidism. A population based study

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Aim: To compare s-Se values in patients with newly diagnosed autoimmune thyroid disease and controls from the Danish population.

Methods: s-Se was measured (in triplicate by a fluorimetric method) in patients with newly diagnosed Graves` disease (GD) (n = 97) and autoimmune overt hypothyroidism (AIH) (n = 96), and for comparison, in euthyroid subjects with high serum levels of TPO-Ab (TPO-Ab > 1500 U/ml, n = 92) and in random controls (n = 830). Patients and controls were consecutively included from two population based surveys. Data were analysed in univariate and multiple linear regression models to adjust for possible confounders.

Results: S-Se was lower in patients with GD than in controls (mean (SD), GD: 89.9 µg/l (18.4); controls: 98.8 µg/l (19.7), p < 0.01). This was confirmed in a multivariate linear regression model adjusting for age, sex, mineral supplements, smoking, geographical region and time of sampling (p < 0.01). In a univariate model, s-Se was similar in patients with AIH (mean (SD): 98.4 µg/l (24.9)) and in controls (p = 0.86). In the multivariate model however, s-Se was lower in patients with AIH compared to controls (p = 0.04). There was no significant difference in s-Se between euthyroid participants with high TPO-Ab and controls (univariate: p = 0.97; multivariate: p = 0.27).

Conclusion: In a carefully controlled, population based study, patients with newly diagnosed GD and AIH had significantly lower s-Se compared with random controls. This observation supports the postulated link between inadequate Se supply and overt autoimmune thyroid disease.
**35 “GravThyr” - Subclinical hypothyroidism and miscarriage**

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**Aim of the Study:** To estimate the prevalence of subclinical hypothyroidism (SH) and thyroperoxidase antibody (TPOab) positivity and miscarriages among women of reproductive age.  
**Methods:** Data from the General Suburban Population Study (GESUS) in Naestved were evaluated to estimate the prevalence of subclinical hypothyroidism and TPOab in women. SH was defined as raised serum concentrations of thyroid stimulating hormone (TSH) > 3.4 mU/l and normal levels of free thyroxine (10-26 pmol/l) and triiodothyronine (1.2-1.8 nmol/l). A cut-off of 60 mU/l was used for TPOab.  
GESUS is an ongoing population study initiated in 2010. In June 2011 more than 10.000 participants had attended this large health study, which includes a comprehensive questionnaire, collection and analysis of blood samples, ECG, blood pressure and bioimpedance measurements.  
**Results:** The prevalence of subclinical hypothyroidism was 10% (180/1716). In total, 25% of women with SH reported at least one miscarriage compared to 22% in the control group (fig. 1). The prevalence of elevated TPOab was 13% (229/1755). Of these, 26% of the women reported at least one miscarriage compared to 22% in the control group. None of the differences were statistically significant. The prevalence of miscarriage was 20% (986/4969) in all women independent of age, other diseases, medication etc.  
**Conclusion:** There was no significant difference in the prevalence of miscarriage in the population. The cut-off of TSH was lower compared to other studies. Further analysis of this study will estimate the cut-off of TSH (subclinical hypothyroidism), which causes a significant increased frequency of miscarriage.

**Fig. 1:** Subclinical hypothyroidism and miscarriage.
36 Urinary sulphate excretion is a predictor for progression of diabetic nephropathy

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Aim: Hydrogen sulphide has widespread physiological effects, including vasoregulation. Hydrogen sulphide levels are reduced in many pathophysiological states, including diabetes and end stage kidney disease. We aimed to determine if urinary sulphate excretion, as a proxy for hydrogen sulphide, could predict progression of diabetic nephropathy.

Method: We conducted a post-hoc study of a prospective, randomized, unmasked, controlled trial, studying the effects of low/normal protein diet, following 82 type 1 diabetic patients with progressive nephropathy for 4 years. Sulphate excretion was measured by ion exchange chromatography in 24h urine at baseline and used to predict the combined endpoint of End Stage Renal Disease or death for all patients and the rate of decline in GFR, for 72 patients with minimum one year follow-up and 3 measurements of ⁵¹Cr-EDTA plasma-clearance. The cohort was divided at the median sulphate excretion (11mmol/day).

Results: Events occurred in 26.8% of the patients with sulphate excretion below the median compared to 9.8% above (p=0.059). Cox regression revealed a relative risk of kidney failure or death of 3.0(0.9-9.3) for the group with lower sulphate excretion (p=0.064). Sulphate excretion was significantly associated with the rate of decline in GFR (p=0.016,r=-0.28). In linear regression models including age, gender, blood pressure, Hba1c, smoking, albuminuria and diet group, sulphate excretion was highly significant (p=0.0002), furthermore adjusted r² increased from 6% to 23% when sulphate was included.

Conclusion: High urinary sulphate excretion was significantly associated with slower rate of decline in GFR in diabetic nephropathy, during four years of follow-up, independent of known progression promoters.
Effect of aliskiren, irbesartan and the combination on urinary levels of angiotensinogen and renin in patients with type 2 diabetes, hypertension and albuminuria

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Introduction and aim: Urinary levels of RAAS components are considered to reflect the intrarenal renin-angiotensin-aldosterone system (RAAS). We measured urinary levels of angiotensinogen and renin to gain information on treatment response to aliskiren and irbesartan treatment.

Material and methods: We measured urinary levels of angiotensinogen and renin in 19 patients with type 2 diabetes, hypertension and albuminuria, during 2 month treatment periods with placebo, aliskiren 300 mg once daily, irbesartan 300 mg once daily and the combination. Levels were correlated with levels of albuminuria and changes in urinary markers were correlated with change in albuminuria. Urine/plasma (U/P) concentration ratios of markers were also compared.

Results: We found a significant reduction in urinary renin compared to placebo during aliskiren treatment (-3.3 [5.0] pg/ml, p=0.006), and during combination treatment (-3.2 [4.8] pg/ml, p=0.005). The reduction with irbesartan was not significant (-0.7 [2.7], p=0.25). Irbesartan treatment led to a significant reduction in urinary angiotensinogen (0.05 [0.09] pmol/ml, p=0.021) and so did combination therapy (0.09 [0.09] pmol/ml, p<0.001), but not aliskiren treatment. Urinary angiotensinogen was associated with albuminuria during all treatment periods. A significant association between change in urinary renin and albuminuria was found during aliskiren treatment, r²=0.273, p=0.013, but not in the other treatment periods. Angiotensinogen U/P correlated strongly to albuminuria, suggesting it as a marker of glomerular damage.

Conclusion: Aliskiren monotherapy led to a reduction in urinary renin, and the change was correlated to change in albuminuria. This could point to a specific renal effect of renin inhibition.
38 Én ud af tre patienter henvist til Type 2 diabetes klinikken, Steno Diabetes Center (SDC) har obstruktiv søvnapnø

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Formål: Obstruktiv søvnapnø (OSA) er associeret med høj kardiovaskulær morbiditet og mortalitet. Vi ønskede derfor, at undersøge prævalensen af OSA blandt type 2 diabetes (T2DM) patienter henvist til SDC.


Resultater: I alt deltog 180 patienter (Mænd; 61 %, Alder; 59.7±10.5 år, BMI; 31.8±6.7 kg/m², Diabetesvarighed 8.2±6.3 år, HbA1C; 7.3±1.2 %). Heraf scorede 104 (61%) højt for OSA på spørgeskemaet, og i alt 77 patienter (43 %) blev efter ApneaLink undersøgelse henvist til søvnklinik. Foreløbig er 49 patienter udredt med PG, heraf er 44 fundet at have OSA. Dette svarer til en estimeret prævalens af OSA blandt de 180 patienter på i alt 34 %. ApneaLink positive (n=77) patienter havde sammenholdt med dem, der var uden symptomer (n = 77) eller tegn på OSA på ApneaLink (n=26) højere BMI (34.3±7.4 versus 30.3±5.7 kg/m², p<0.001), højere HbA1C (7.6±1.3 versus 7.2±1.1 %, p=0.008) og lavere Hdl-cholesterol (1.1±0.3 versus 1.3±0.4 mmol/l, p=0.003). Grupperne var sammenlignelige med hensyn til: blodtryk, albuminuri, p-creatinin, retinopati, LDL-kolesterol, behandling med antidiabetika, RAS-blokade samt statiner.

39 Does intensive multifactorial treatment of screen detected diabetes affect aortic stiffness? ADDITION Denmark

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Aim: Aortic stiffness is an independent risk factor for cardiovascular disease (CVD). In microalbuminuric type 2 diabetes patients, intensive multifactorial treatment of type 2 diabetes reduces the risk of CVD by more than 50%. The aim of this study was to examine the effect of intensive multifactorial treatment on aortic stiffness in a population with screen-detected diabetes.

Methods: As part of a population based screening and intervention study in general practice, 1533 Danes aged 40-69 years were diagnosed with screen-detected diabetes. The general practitioners were randomised to provide either intensive multifactorial treatment or routine care. At 6-year follow-up, a random subsample of 427 patients had measurements of aortic stiffness by carotid-femoral pulse wave velocity (PWV). The effect of the intervention on PWV was analysed by mixed effect models adjusted for clustering (all patients within a practice were randomised to either intensive treatment or routine care), mean blood pressure and heart rate at follow-up to account for its direct functional effects on PWV. We additionally adjusted for age and sex.

Results: From the study sample at follow-up, mean age was 65.7 years (SD: 9.8), 260 patients (61%) were men, mean PWV was 9.54 m/s (SD: 2.12), and 270 patients (63%) were in the intensive treatment group. Patients receiving intensive treatment had a 0.43 m/s lower PWV than patients receiving routine care (Table 1).

Conclusion: Intensive multifactorial treatment of screen-detected diabetes in general practice has a beneficial effect on aortic stiffness. Extrapolating our results based on estimates from cohorts with baseline PWV, the effect observed in our study would correspond to a 2% lower risk of CVD and a 3% lower risk of all cause mortality over a period of 10 years.

Table 1: Intensive treatment versus routine care

<table>
<thead>
<tr>
<th>Pulse wave velocity [m/s] (95% CI)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Model 1  -0.44 (-0.86 ;-0.01)</td>
<td>0.048</td>
</tr>
<tr>
<td>Model 2  -0.43 (-0.79 ;-0.06)</td>
<td>0.024</td>
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Model 1: adjusted for clustering (general practice), mean blood pressure and heart rate at time of measurement
Model 2: model 1 + adjustment for age and sex
40 Discrepancy between tonometric ambulatory and cuff-based office blood pressure measurements in patients with type 1 diabetes

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Objective: Hypertension (HTN) is often diagnosed by office blood pressure (OBP) despite ambulatory blood pressure (AMBP) being superior in predicting adverse outcome. Tonometric brachial blood pressure (BP) can be calculated from radial pulse waves, allowing for frequent and undisturbed measurements. We investigated the agreement between AMBP and OBP in HTN diagnostics in patients with type 1 diabetes (T1DM).

Methods: Cross sectional study including 676 Caucasian T1DM patients, 373(55%) men, age (mean±SD) 55±13 years. AMBP was measured with a tonometric watch-like device (BPro), while OBP was measured with a cuff-based oscillometric or auscultatoric device and obtained from medical records. Valid AMBP and OBP measurements were available on 569 patients. AMBP or OBP values ≥130/80mmHg defined HTN. Elevated AMBP with normal OBP defined masked HTN and normal AMBP with elevated OBP defined isolated clinic HTN.

Results: Mean±SD 24-hour AMBP was lower than mean OBP, 128±15/75±10 vs. 136±14/76±8mmHg; (p<0.001). HTN with both AMBP and OBP was present in 256(45%), normal BP in 103(18%), isolated clinic HTN in 153(27%) and masked HTN in 57(10%). In 37%, AMBP and OBP disagreed in diagnosing HTN, while 313(55%) patients did not reach the target of BP <130/80mmHg.

AMBP measurements with the BPro device were well-tolerated and successful in 98%, 92% would volunteer for a repeat measurement and 83% preferred the BPro to a conventional cuff-based device.

Conclusion: In T1DM, tonometric AMBP measurements are feasible. In 37% of patients AMBP and OBP disagree in HTN diagnosis. The majority of patients did not reach target BP despite regular follow-up.
Increased arterial stiffness is independently associated with cerebral infarctions and white matter lesions in patients with type 2 diabetes despite good blood pressure and lipid control

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**Aim:** Patients with type 2 diabetes (T2DM) have increased risk of cardiovascular disease (CVD) including stroke. The risk of CVD is traditionally assessed using office blood pressure (BP) and lipid profile. Increased arterial stiffness predicts cardiovascular events in the general population. We investigated if arterial stiffness was associated with cerebrovascular disease in patients with T2DM and sex- and age-matched controls.

**Methods:** 90 patients with newly diagnosed T2DM and 90 sex- and age- matched controls were examined. Arterial stiffness was assessed by aortic pulse wave velocity (PWV), and cerebrovascular disease by cerebral infarctions and severity of white matter lesions (WMLs) on MRI scans of cerebrum. A blinded reviewer rated WMLs a.m. Breteler (no/slight changes=0, moderate=1, severe=2).

**Results:** Antihypertensive treatment and lipid lowering treatment was more frequent in diabetic patients, who consequently had lower office BP (126+/- 12 vs 131+/-14 mmHg systolic, p=0.01) and lower lipid levels. Despite this, diabetic patients had significantly higher PWV compared to controls, (9.2+/-2.0 vs 8.0+/-1.6 m/s, p<0.0001). PWV was higher in patients with cerebral infarctions (9.9 vs 8.5 m/s, p=0.002) and PWV increased across Breteler categories (8.2+/- 1.7 vs 9.3+/-2.0 vs 9.4+/-2.1 m/s, p<0.001 for trend).

PWV remained independently associated with severity of WMLs (p<0.01) and cerebral infarctions, (p<0.02) after adjustment for the following covariates: age, sex, diabetes, mean arterial pressure, smoking, statins and BMI in multivariate regression.

**Conclusion:** Despite good BP and lipid control, PWV was substantially higher in T2DM patients. PWV is independently associated with WMLs and cerebral infarctions. PWV may represent a clinically relevant parameter in the evaluation of CVD risk in T2DM.
42 Gustatory sweating – a common late diabetic complication?

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Hypothesis and aims: Gustatory sweating is a manifestation of autonomic neuropathy and is characterised by profuse sweating after ingestion of food. It has been reported to occur more often in patients with long-standing diabetes with severe peripheral and autonomic neuropathy. Most reports on gustatory sweating have been case reports suggesting it to be a rare late diabetic complication. The aim of this study was to determine the prevalence of gustatory sweating in an unselected cohort of patients with type 1 diabetes.

Methods: A questionnaire with 8 questions concerning gustatory sweating was designed and mailed to 745 patients with Type 1 diabetes (49% male, age: 51.5±14.7 years, duration of diabetes: 26.7±14.5 years, HbA1c: 8.1±1.1%) attending Steno Diabetes Center. The response rate was 89.3%. Patients were classified as having gustatory sweating if they reported to suffer from sweating on the face, scalp or upper body during or immediately after ingestion of food. Patients with gustatory sweating indicated to have increased sweating as compared with others. Clinical data were extracted from patient records.

Results: A total of 43 (6.5%) patients were classified as having gustatory sweating. Gustatory sweating was not associated with peripheral neuropathy, retinopathy or elevated albumin excretion rate. Patients with and without gustatory sweating were similar concerning sex, age, duration of diabetes, blood pressure and HbA1c. A trend towards a higher BMI in patients with diabetic gustatory sweating was seen (26.6 kg/m² vs. 25.4 kg/m², p=0.06). Patients with gustatory sweating more often also had gastroparesis: 18.6% vs. 5.2%, p<0.001.

Conclusion: Symptoms of diabetic gustatory sweating was seen in 6.5% of patients with longstanding Type 1 diabetes. Gustatory sweating was associated with symptoms of diabetic gastroparesis but not with other micro vascular complications.
43 Improvement in symptoms of diabetic gastroparesis in both Type 1 and Type 2 diabetes by treatment with a ghrelin receptor agonist

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**Hypothesis:** Administration of a ghrelin receptor agonist diminishes symptoms of diabetic gastroparesis in Type 1 and Type 2 diabetes.

**Objectives:** To characterize the effects of a ghrelin receptor agonist on symptoms of gastroparesis and to determine whether type 1 and type 2 diabetic patients responses are different.

**Methodology:** Patients with diabetes, delayed gastric emptying and upper gastrointestinal symptoms were randomized to 10, 20 or 40 mg ghrelin receptor agonist or placebo. Symptoms were evaluated by patient-reported symptom severity scales (0-5) on days 8, 15, 28 (treatment) and 42, 58 (follow up). Effects were assessed by changes in symptom scores from baseline compared to end of treatment.

**Results:** Findings: 92 patients \{females 65%; age 49.9 ± 11.9 years; 91% Caucasian; BMI 28.8 ± 5.1; 60% type 1; ~70% on insulin; HbA1c 8.3 ± 1.5%; PAGI-SYM 3.0 ± 0.8; breath test t1/2 GE 193 ± 51 min\} received treatment (22, 21, 23 and 26 patients received 10, 20, 40 mg ghrelin receptor agonist and placebo, respectively). Significant improvements versus placebo were observed in individual symptoms across all ghrelin receptor agonist dose groups with a maximum improvement at the 20mg dose. Importantly, significant improvement vs. placebo was observed with 20mg ghrelin receptor agonist for each of prevalent symptoms for this patient population; magnitude of the effects was similar in type 1 and type 2 diabetic patients.

**End of Treatment Change from Baseline over Placebo* in Prevalent (>90% of Patients) Symptoms of Gastroparesis – 20mg Dose**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>All patients (n=21)</th>
<th>p-value</th>
<th>Type1 (n=10)</th>
<th>Type2 (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>-1.0</td>
<td>0.029</td>
<td>-1.0</td>
<td>-0.9</td>
</tr>
<tr>
<td>Early satiety</td>
<td>-0.9</td>
<td>0.022</td>
<td>-0.9</td>
<td>-1.2</td>
</tr>
<tr>
<td>Postprandial fullness</td>
<td>-1.0</td>
<td>0.019</td>
<td>-1.4</td>
<td>-0.4</td>
</tr>
<tr>
<td>Bloating-stomach large</td>
<td>-0.9</td>
<td>0.018</td>
<td>-0.9</td>
<td>-0.8</td>
</tr>
<tr>
<td>Upper abdominal pain</td>
<td>-0.7</td>
<td>0.042</td>
<td>-0.7</td>
<td>-0.7*Placebo:</td>
</tr>
<tr>
<td>type 1 =15; type 2=11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Ghrelin receptor agonist treatment represents a possible novel treatment of severe symptomatic gastroparesis in both type 1 and type 2 diabetic patients.
44 Cardiovascular Autonomic Neuropathy in Type 1 and Type 2 Diabetes and associations with Albuminuria, Retinopathy, Peripheral Neuropathy, Pulse Pressure and Obesity (The DAN-study)

Jesper Fleischer; Knud Yderstraede; Elisabeth Gulichsen; Poul Erik Jakobsen; Hans Henrik Lervang; Ebbe Eldrup; Hans Nygaard; Lise Tarnow; Niels Ejskjaer
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Objective: To identify the presence of subclinical cardiovascular autonomic neuropathy (CAN) in a cohort of individuals with diabetes in four outpatient clinics in Denmark and to evaluate the association between CAN and other risk factors.

Method: The DAN-Study is a Danish multi-center study focusing on diabetic autonomic neuropathy. Over a period of twelve months, 382 type 1 and 271 type 2 individuals with diabetes were tested for CAN. Patients were randomly recruited and tested during normal visits to outpatient clinics at four Danish hospitals. The presence of CAN was quantified by measuring cardiovascular reflex tests (valsalva, response to standing and deep breathing) and analysis of heart rate variability in time and frequency domain. In order to describe possible associations, multivariate analysis with CAN as the dependent variable was performed.

Results: Besides heart rate above 80 (p≤0.001) and age above 60 years (p<0.02) in both type 1 and type 2 patients multiple ordinal logistic regression analysis revealed that in Type 1 diabetes patients CAN was associated with microalbuminuria (p=0.015), macroalbuminuria (p=0.005), and proliferative retinopathy (p=0.021). Among Type 2 diabetes patients CAN was associated with high pulse pressure (p<0.001) and BMI above 35 kg/m² (p=0.025).

Conclusion: In this cross-sectional observational study CAN is associated with proliferative retinopathy, micro- and macroalbuminuria in type 1 diabetes patients, whereas in Type 2 diabetes patients CAN is associated with pulse pressure and obesity.
45 Opgørelse over adrenalektomier på Syddansk Binyrecenter, OUH 2006-2010 (2011)

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¹. Endokrinologisk afd. M, Odense Universitetshospital, 2. Urologisk afd. L, Odense Universitetshospital

Introduktion: Et adrenalt incidentalom defineres som en tilfældigt fundet tumor i binyren > 1cm. Ved fund af et adrenalt incidentalom må hormonoverproduktion og eventuel malignitet afklares.


Metode: Retrospektiv opgørelse over adrenalektomerede patienter ved urologisk afdeling L, Odense Universitetshospital. Indikationer for adrenalektomi var tumor > 4 cm, hormonoverproduktion, Hounsfield units (HU) over 10 eller tumortilvækst > 1cm.


Primær henvisningsårsag var adrenalt incidentalom (n=63, 74%) og symptomer på hormonoverproduktion (n=22, 26%). Ved præoperativ udredning havde 37/85 (44%) patienter hormonoverproduktion: katekolamin (n=19), kortisol (n=11), aldosteron (n=6) og chromogranin A (n=1).

17/63 (27%) patienter primært henvist med incidentalom havde hormonoverproduktion: katekolamin (n=12), kortisol (n=3), aldosteron (n=2).

Histologi viste følgende diagnoser (n=85): fæokromocytom (n=19), adrenokortikalt adenom (n=38), myolipom/lipom (n=6), hyperplasi (n=9), adrenalt karcinom (n=1), metastase (n=3), adrenalt karcinom/metastase (n=1), teratom/dermoid cyste (n=3), ganglioneurom (n=1), schwannom (n=1) og infarkt (n=1), ikke oplyst (n=2).

Konklusion: Antallet af adrenalektomier var stigende gennem perioden. 74% af opererede tumores var incidentalomer. 27% af patienter primært henvist med incidentalom havde hormonoverproduktion, hvilket bekræfter vigtigheden af endokrinologisk udredning.
46 Mutationer i KCNJ5 (K⁺ kanal) i aldosteronproducerende binyreadenomer

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Metoder: Tumorvæv blev udtaget fra paraffinfikserede operationspræparater fra patienter med histologisk verificeret Conn syndrom (n=10). Tumorvævet blev identificeret mikroskopisk af patolog. Fra tumorvævet blev kromosomalt DNA udvundet og et 261 basepar stort fragment af KCNJ5 genet blev herefter opformeret ved PCR og sekventeret med Sanger sekventering.


Konklusion: Mutationer i KCNJ5 kan forklare patogenesen ved aldosteronproducerende binyreadenomer. Germinalcellemutationer kan genfindes i blod og fund af somatiske cellemutationer bringer forhåbninger om at disse kan genfindes i frit DNA i plasma. Hermed er håbet at en sikker Conn syndrom diagnose i fremtiden kan stilles præoperativt uden brug af invasive procedurer.
47 Decreased osteoprotegerin levels during testosterone therapy in ageing men were associated with changes in regional fat distribution

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Objective: The cardiovascular effects of testosterone therapy are currently debated. Osteoprotegerin (OPG) is an independent marker of cardiovascular risk. We investigated the effect of testosterone therapy on OPG levels in ageing men with low normal bioavailable testosterone levels.

Design: A randomized, double-blinded, placebo-controlled study of six months testosterone treatment (gel) in 38 men, aged 60-78 years, with bioavailable testosterone < 7.3 nmol/l, and waist circumference > 94 cm.

Methods: Clinical evaluation, OPG, and C-reactive protein measurements. Fat mass was established by dual x-ray absorptiometry measuring lean body mass and total fat mass and magnetic resonance imaging measuring visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT). Responders were defined as testosterone treated patients with increased LBM ($\Delta$ LBM positive). Data were presented as median (interquartile range).

Results: Testosterone treatment was followed by decreased total fat mass, decreased SAT and unchanged VAT. OPG levels decreased during testosterone treatment (from 2.0 (1.9 – 2.5) to 1.9 (1.6 – 2.2) ng/ml, p<0.05 vs. placebo), whereas CRP levels were unchanged. In responders for testosterone treatment (n=14), $\Delta$OPG levels were inversely associated with $\Delta$SAT (r= -0.60, p=0.03) and positively associated with $\Delta$VAT (r= 0.56, p=0.04).

Conclusion: OPG levels decreased during testosterone treatment suggesting decreased cardiovascular risk. Decreased OPG levels were associated with changes in regional fat distribution and future studies are needed to determine the association between OPG and regional fat mass distribution.
48 Adipokines, and central fat mass have a higher impact on peak GH during the GHRH+arginin test than the insulin tolerance test

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Background & aim: The stimulated GH response, which is used for diagnostic purpose, has been shown to be significantly reduced in obesity. This confounding effect is of particular interest in patients with a low pretest probability a GH deficiency. We studied the association between adipokines and peak GH in response to two standard GH stimulation tests.

Subjects and Methods: Thirty healthy subjects with BMI 24 (19-30) kg/m² underwent a GHRH+arginin test and an ITT on two separate visits. Measurements included GH, adiponectin and leptin concentrations, BMI, waist circumference and total and abdominal fat mass assessed by DEXA.

Results: Peak GH in response to the GHRH+arg test was negatively correlated to BMI (r = -0.5; p = 0.005) and waist circumference (r = -0.7; p<0.001). Peak GH was furthermore positively correlated to adiponectin (r = 0.53; p=0.003), but not to leptin (r=0.03). Only waist remained independently related to peak GH after adjustment for adiponectin and gender.

Peak GH in response to the ITT was negatively correlated to total (r = -0.4; p=0.05) and abdominal (r = -0.4; p=0.07) fat mass, whereas not to BMI or waist circumference (p>0.4), nor to adiponectin (r = -0.11; p=0.6), or to leptin (r = -0.26; p=0.2).

Conclusion: Our data indicate that central fat accumulation has a more prominent inhibitory effect on the results of the GHRH+arg test as compared to the ITT. The mechanism behind these differences in response is not clarified. Adipokine concentrations were not superior to simple waist measurement for prediction of the peak GH response.
49 Relationship between growth hormone activity and markers of inflammation - a randomized cross-over study in healthy volunteers treated with growth hormone and a growth hormone receptor antagonist for three weeks

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¹Department of Internal Medicine O, Endocrine unit, Herlev Hospital, University of Copenhagen
²Department of Endocrinology and Internal Medicine, Aarhus University Hospital
³Medical Research Laboratories, Institute of Clinical Medicine, Health, Aarhus University
⁴Faculty of Health Science, Copenhagen University, Denmark

Introduction The growth hormone (GH)/insulin-like growth factor-I (IGF-I) axis may modulate inflammatory processes. However, the relationship seems complicated as both pro- and anti-inflammatory effects have been demonstrated.

Methods/design Twelve healthy volunteers (mean age 36, range 27-49 years) were treated in random order with increasing doses of GH for three weeks (1st week 0.01, 2nd week 0.02, 3rd 0.03 mg/day/kg) or a GH receptor antagonist (pegvisomant) (1st week 10, last two weeks 15 mg/day), separated by eight weeks of wash-out. Circulating levels of the pro-inflammatory cytokines tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), IL-1β and the acute phase proteins (APPs) CRP, haptoglobin, orosomucoid, YKL-40 and fibrinogen were measured.

Results During GH treatment IGF-I (median 131 IQR 112-166) vs. 390 (322-524) μg/L, p=0.002) increased together with TNF-α (0.87 (0.74-1.48) vs. 1.27 (0.80-1.69) ng/L, p=0.003), IL-6 (1.00 (0.83-1.55) vs. 1.35 (0.80-4.28) ng/L, p=0.045) and fibrinogen (9.2 (8.8-9.6) vs. 11.1 (9.4-12.4) μM, p=0.002). By contrast orosomucoid decreased (18.0 (16.3-23.8) vs. 22.0 (17.0-29.3) μM, p=0.036) and CRP increased (1.00 (0.62-1.77) vs. 1.43 (0.71-3.29) mg/L, p=0.074) without an increase in pro-inflammatory cytokines.

Conclusions GH/IGF-I action appears to modulate the initial stage of the inflammatory response as well as down stream processes elucidated by levels of APPs. The data suggest a complicated relationship not allowing any simple conclusions as to whether GH/IGF-I actions have mainly pro- or anti-inflammatory effects in vivo.
50 Acute presentation of craniopharyngioma in children and adults

Egil Husted Nielsen, Jens Otto Jørgensen, Per Bjerre, Marianne Andersen, Claus Andersen, Ulla Feldt-Rasmussen, Lars Poulsgaard, Lars Østergaard Kristensen, Jens Astrup, Jesper Jørgensen, Jörgen Lindholm and Peter Laurberg

Departments of Endocrinology and Neurosurgery, Aarhus University Hospital Aalborg and Aarhus, Copenhagen University Hospital Copenhagen, Herlev and Glostrup, Odense University Hospital Odense

Objective: To study the clinical phenotype of patients presenting with craniopharyngioma, including variations according to age, gender, calendar year period, and to estimate the frequency of acute symptoms.

Material and methods: In a retrospective cohort of all Danish craniopharyngioma patients (n = 189) diagnosed during the period 1985-2004, initial symptoms, clinical findings and neuroimaging results were systematically collected from medical records. Subgroups based on age, gender and calendar year period were compared using Pearson’s Chi-square test or Fisher’s exact test, as appropriate.

Results: Acute symptoms related to vision, cranial nerve function or intracranial pressure were reported in 24 patients (13%); most frequently among children, who also more often presented with hydrocephalus. Cold intolerance and depression were more frequent among adults. Frequencies of common endocrine and non-endocrine characteristics were similar among men and women. Hypopituitarism was observed in 26 to 56% of children and 26 to 82% of adults, respectively. The use of CT and MRI differed between the first and second half of the study period. Clinical symptoms and signs did not differ between the two half-periods.

Conclusions: Acute symptoms were seen in 13% of patients with newly diagnosed craniopharyngioma and, like hydrocephalus, more commonly among children than adults. Presenting symptoms and the extent of hypopituitarism were largely similar in men and women and across the study period.
51 ANTINOCICEPTIVE EFFECT OF PASIREOTIDE ON OCTREOTIDE-RESISTANT ACROMEGALY-RELATED HEADACHE

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Department of Medical Endocrinology PE 2132, Rigshospitalet, Copenhagen University, Denmark

Background: Headache often occurs as incapacitating symptom among the patients with acromegaly. Growth hormone (GH) involvement in the pathophysiologic mechanism and an analgesic effect of somatostatin analogues has been described, but the exact mechanism is not clear. Whether the pan somatostatine (sst)-receptor agonists are superior as concern the antinociceptive effect than the more selective ones is not evidenced.

Case report: A 21-year old woman, diagnosed with acromegaly, presented with visual disturbances, dizziness, and incapacitating headaches lasting for 8 months. She had several daily attacks of headache, resistant to high doses of regular pain-killers. MRI disclosed a pituitary macroadenoma (27x20mm) with suprasellar propagation. Preoperative neuroendocrine values on oral contraceptives: elevated mean spontaneously GH (>120miU/L); elevated IGF-1 (1249 ng/ml; +9 SD); low-normal free T4 (13.4 pmol/l (14-23 pmol/l)); low levels of FSH <0.2 iU/l and LH <0.1 iU/l; low-normal response to Synacthen® test (peak cortisol: 904 nmol/l). The patient underwent two transcranial operations with significant reduction in tumour size. Different combinations and multiple doses of Octreotide, Sandostatin LAR® and Somavert® were tried; nevertheless IGF-1 remained high and the headaches were getting worse. Pasireotide-Pegvisomant combination was introduced with prompt marked headache-relief, persisting until few days before next injection. IGF-I finally normalized (246 ng/ml; +0.45 SD, mean spontaneous GH 39.6 miU/L). Last MRI revealed no change of the remnant macroadenoma size.

Conclusion: This case illustrates that Pasireotide may have a superior antinociceptive effect, as compared to other somatostatin analogues. Very possibly pan-sst receptor antagonists may be superior to selective sst2 agonists regarding their antinociceptive effect, but further studies are needed to clarify this.
52 In vitro metabolic characterization and functional identification of myotubes established from in vivo insulin resistant patients with polycystic ovary syndrome (PCOS)

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1Department of Endocrinology, Odense University Hospital, Odense; 2Department of Clinical Research, University of Southern Denmark, Odense; 3Clinic for Molecular Endocrinology (KMEB), Department of Endocrinology, Odense University Hospital and Medical Biotechnology Centre, University of Southern Denmark; 4Department of Clinical Biochemistry and Pharmacology, Odense University Hospital; 5Department of Clinical Pathology, Odense University Hospital, Odense

Background: Polycystic ovary syndrome (PCOS) is characterised by insulin resistance.
Objective: To investigate if in vivo insulin resistance was conserved in myotubes from patients with PCOS and to identify a possible contribution of mitochondrial dysfunction to in vivo insulin resistance.
Methods: Myotubes were established from 28 insulin resistant PCOS patients and 14 healthy age and weight matched controls. A subgroup of patients were evaluated before and after pioglitazone treatment (n= 9). Glucose uptake and oxidation, glycogen synthesis, glycogen synthase activity and lipid uptake were measured by radiotracer techniques, RT-PCR and enzyme kinetic analysis and mRNA levels of the genes PLEK, SLC22A16 and TTBK were determined. Mitochondrial function was determined in 8 randomly selected patients by measuring ATP synthesis (with and without ATP use) and mitochondrial mass quantification.
Results: Glucose oxidation, glucose uptake, glycogen synthesis, glycogen synthase activity and lipid uptake did not differ significantly in myotubes established from patients compared to controls at baseline or during insulin stimulation. Pioglitazone treatment had no significant effect on metabolic pathways or in mRNA levels of PLEK, SLC22A16 and TTBK, as detected in vivo. Measures of mitochondrial function did not differ significantly in myotubes established from PCOS patients vs. controls.
Conclusion: We found no evidence that the in vivo insulin resistance in skeletal muscle of PCOS patients is of primary origin, but rather due to acquired defects. This is supported by the conserved primary mitochondrial function and comparable mitochondrial mass in myotubes established from PCOS patients.
Sammenhængen mellem fødselsvægt og polycystisk ovariesyndrom hos 523,757 danske kvinder

**Baggrund:** Polycystisk ovariesyndrom (PCOS) er karakteriseret ved insulinresistens og forøget risiko for type 2 diabetes mellitus (DM). Tidligere studier har demonstreret en sammenhæng mellem både lav og høj fødselsvægt og en forøget risiko for type 2 DM.

**Formål:** At afklare om der er en association mellem fødselsvægt og risiko for PCOS i voksenlivet.


**Resultater:** Risikoen for PCOS var signifikant forøget hos kvinder med fødselsvægt > 4.500 gram (IRR = 1,57 (95 % CI 1,21-2,03)) sammenlignet med kvinder med fødselsvægt 3.000-3.499 gram. Risikoen for PCOS var uafhængig af størrelse for gestationsalder. Kvinder født af mødre med en diabetes-diagnose havde forøget risiko for PCOS i forhold til kvinder født af mødre uden diabetes. Hos kvinder født af diabetiske mødre var sammenhængen mellem fødselsvægt og risiko for PCOS omvendt i forhold til den totale studiepopulation.

**Konklusion:** Vores data tyder på øget risiko for PCOS hos kvinder født med en fødselsvægt > 4,500 gram. Risikoen for PCOS er ligeledes forøget hos kvinder født af mødre med en diabetes-diagnose, men hos denne population er risikoen for PCOS højest hos kvinder født med lav fødselsvægt.
54 Hemoglobin A1c as a tool for the diagnosis of type 2 diabetes in 208 premenopausal women with polycystic ovary syndrome

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Objective: To study hemoglobin A1c (HbA1c) as a tool for diagnosing diabetes and to study HbA1c as a cardiovascular risk marker in patients with polycystic ovary syndrome (PCOS).

Methods: A retrospective observational study at an academic tertiary-care medical center. Two hundred eight premenopausal women with PCOS participated. Patients underwent clinical evaluation (Ferriman-Gallwey score, body mass index, waist, blood pressure), hormone analyses (T, sex hormone-binding globulin, fasting lipids, insulin, glucose, HbA1c), transvaginal ultrasound, and 2-hour oral glucose tolerance tests (OGTT) measuring capillary blood glucose (BG) at 0 (BG 0) and 120 (BG 120) minutes, insulin, and C-peptide.

Results: Twenty patients were diagnosed with type 2 diabetes during OGTT. The sensitivity and specificity of HbA1c ≥6.5% for the diagnosis of diabetes were 35% and 99%, respectively, compared with the diagnosis established by OGTT. Hemoglobin A1c showed closer correlation with waist, body mass index, and lipid profile than BG 120, suggesting that HbA1c could be a cardiovascular risk marker.

Conclusion: The clinical utility of HbA1c for diagnosing impaired glucose tolerance and type 2 diabetes in PCOS in daily practice is low. Long-term prospective studies are needed to determine whether HbA1c is superior to glucose levels as a cardiovascular risk marker in patients with PCOS.
55 Metabolic Syndrome and Glutamic Acid Decarboxylase (GAD) Autoantibodies Post Partum in Women with Previous Gestational Diabetes Mellitus (GDM)

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Aim Women with previous GDM have increased risk of subsequent diabetes (primarily type 2) and metabolic syndrome. However, GDM is a heterogeneous condition and GAD-autoantibodies could be a predictor of later type 1 diabetes. Our hypothesis is that women with previous GDM and GAD-autoantibodies have clinical features that resemble type 1 diabetic patients. The aim of this study therefore is to describe the metabolic profiles 3 months post partum in GAD autoantibody(ab)-positive women versus GADab-negative women with previous GDM.

Methods During 1997-2010 407 women with previous GDM were tested post partum with fasting blood samples, oral glucose tolerance test (OGTT) and clinical examination. The median time for OGTT was 98 days post partum, the women had a median age of 32.5 years and 79% had Caucasian background.

Results

<table>
<thead>
<tr>
<th></th>
<th>GADabpos(n=22)</th>
<th>GADabneg(n=385)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SystolicBP(mmHg)</td>
<td>120(113-122)</td>
<td>120(112-130)</td>
<td>0.70</td>
</tr>
<tr>
<td>DiastolicBP(mmHg)</td>
<td>79(74-80)</td>
<td>80(70-85)</td>
<td>0.65</td>
</tr>
<tr>
<td>Cholesterol(mmol/l)</td>
<td>5.04(4.6-5.5)</td>
<td>5.1(4.4-5.8)</td>
<td>0.71</td>
</tr>
<tr>
<td>HDL(mmol/l)</td>
<td>1.3(1.1-1.5)</td>
<td>1.3(1.1-1.6)</td>
<td>0.52</td>
</tr>
<tr>
<td>LDL(mmol/l)</td>
<td>3.0(2.5-3.4)</td>
<td>3.0(2.5-3.6)</td>
<td>0.94</td>
</tr>
<tr>
<td>Triglycerides(mmol/l)</td>
<td>1.2(0.8-1.9)</td>
<td>1.3(0.9-1.9)</td>
<td>0.45</td>
</tr>
<tr>
<td>F-insulin(pmol/l)</td>
<td>33.0(28.0-56.0)</td>
<td>53.0(33.0-82.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>F-C-peptid(pmol/l)</td>
<td>520(374-715)</td>
<td>759(562-1035)</td>
<td>0.02</td>
</tr>
<tr>
<td>F-glucose(mmol/l)</td>
<td>5.2(5.1-5.8)</td>
<td>5.0(4.6-5.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>2-hours-glucose(mmol/l)</td>
<td>7.8(6.9-9.6)</td>
<td>7.1(6.1-8.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hba1c(%)</td>
<td>5.4(5.2-5.8)</td>
<td>5.4(5.2-5.7)</td>
<td>0.88</td>
</tr>
<tr>
<td>BMI pregestational</td>
<td>27.0(23.7-33.5)</td>
<td>28.7(24.3-33.5)</td>
<td>0.28</td>
</tr>
<tr>
<td>BMI postpartum</td>
<td>31.2(23.7-35.7)</td>
<td>29.0(25.4-33.1)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Table 1: Phenotype of GADab-pos versus GADab-neg women. Data given as median (IQ-range) or numbers (%). Total number is less than n for some variables due to missing values.

Conclusions: GADab-positive women had significantly lower fasting insulin, lower fasting c-peptide, higher fasting glucose and higher 2-h-glucose than GADab-negative women. These findings suggest that GADab-pos women with previous GDM have phenotypic characteristics similar to type 1 diabetes patients. And furthermore, GADab-neg women from this population resemble the clinical features of type 2 diabetes.
56 Differential effects of 36 hours of fasting on plasma triglyceride levels in LBW subjects compared with matched controls

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Context: Low birth weight (LBW) is a risk factor for insulin resistance, T2D and dyslipidaemia. The thrifty LBW phenotype may ensure survival during sparse nutritional conditions, but may be associated with adverse metabolic traits in an affluent society. We hypothesized that LBW subjects may benefit from short term fasting compared with normal birth weight (NBW) controls.

Study design: 18 NBW and 21 LBW young men were subjected to a 36hr fast. Six NBW and 7 LBW subjects participated in a control study. Plasma triglyceride (p-TG) levels were measured after 12, 24, 30 and 36 hours fasting, after an IVGTT and after a subsequent meal test.

Results: No differences in p-TG were found at baseline. The p-TG levels were significantly lower in the LBW subjects compared to NBW controls after 36hr fasting (0.77±0.16 vs. 0.93±0.26 mmol/L, P<0.02), the IVGTT (0.67±0.15 vs. 0.84±0.16, P=0.001), as well as after the meal test (0.92±0.24 vs. 1.11±0.32, P=0.038).

Whereas the NBW subjects studied in both settings displayed similar p-TG levels, the LBW subjects studied during both metabolic states showed significantly lower levels of p-TG’s after 36hr compared with 12hr (0.80±0.18 vs. 1.00±0.18, P<0.04) as well as after the meal test (0.86±0.20 vs. 1.36±0.43, P=0.009).

Conclusion: 36hr fasting is associated with a differential and beneficial change of p-TG levels among LBW subjects compared with NBW controls. The data support the idea of LBW subjects being less capable to cope with the current affluent Western lifestyle, and it may be speculated if a reduced meal frequency could be preferable among LBW subjects.
Impact of restricted maternal weight gain on fetal growth in obese women with type 2 diabetes

**Objective:** To explore the fetal growth in relation to gestational weight gain in obese women with type 2 diabetes mellitus (T2DM).

**Study design:** A retrospective cohort study of 58 singleton pregnancies in obese women (BMI ≥ 30 kg/m²) with T2DM who gave birth in January 1st 2008 to October 8th 2011. The women were recommended to gain ≤ 5 kg in total during pregnancy, which is less than generally recommended by the Institute of Medicine (IOM). Birth weight was evaluated by z-score to adjust for gestational age and gender. Large for gestational age (LGA) and small for gestational age (SGA) were defined as a birth weight > 90th or < 10th percentile, respectively.

**Results:** Seventeen women (28%) gained ≤ 5 kg, and were less obese before pregnancy and needed less insulin during pregnancy. Pregnancy outcomes are shown in table 1.

<table>
<thead>
<tr>
<th>n:</th>
<th>Weight gain ≤ 5 kg</th>
<th>Weight gain &gt; 5 kg</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prepregnancy BMI (kg/m²)</td>
<td>33.5 (30-52.7)</td>
<td>36.8 (30-48.2)</td>
<td>0.037</td>
</tr>
<tr>
<td>HbA1c at first visit (%)</td>
<td>6.7 (5.1-8.1)</td>
<td>6.7 (5.3-13.2)</td>
<td>0.365</td>
</tr>
<tr>
<td>HbA1c at last visit (%)</td>
<td>5.7 (5.4-6.6)</td>
<td>6.0 (4.8-8.2)</td>
<td>0.620</td>
</tr>
<tr>
<td>Weight gain in total (kg)</td>
<td>3.7 (-4.7-5.0)</td>
<td>12.1 (5.5-25.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Insulin treatment before first visit</td>
<td>5 (29%)</td>
<td>11 (27%)</td>
<td>0.843</td>
</tr>
<tr>
<td>Insulin treatment at last visit</td>
<td>17 (100%)</td>
<td>38 (93%)</td>
<td>0.256</td>
</tr>
<tr>
<td>Insulin doses at last visit (IU/kg)</td>
<td>0.72 (0.12-1.80)</td>
<td>1.29 (0.50-2.75)</td>
<td>0.003</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3134 (1278-3870)</td>
<td>3364 (1070-4432)</td>
<td>0.120</td>
</tr>
<tr>
<td>Gestational age at birth (days)</td>
<td>268 (221-284)</td>
<td>262 (206-280)</td>
<td>0.039</td>
</tr>
<tr>
<td>z-score</td>
<td>-0.53 (-3.41-1.96)</td>
<td>1.04 (-2.45-3.89)</td>
<td>0.007</td>
</tr>
<tr>
<td>LGA</td>
<td>2 (12%)</td>
<td>17 (41%)</td>
<td>0.051</td>
</tr>
<tr>
<td>SGA</td>
<td>3 (18%)</td>
<td>5 (12%)</td>
<td>0.864</td>
</tr>
<tr>
<td>Neonatal Hypoglycaemia</td>
<td>3 (19%)</td>
<td>20 (51%)</td>
<td>0.051</td>
</tr>
<tr>
<td>Jaundice, requiring phototherapy</td>
<td>0</td>
<td>8 (20%)</td>
<td>0.100</td>
</tr>
</tbody>
</table>

Conclusion: In obese women with T2DM, maternal gestational weight gain ≤ 5 kg was associated with a higher gestational age at delivery, a more proportionate birth weight and a trend towards lower rates of LGA infants and neonatal morbidity.
**58 Insulin requirements in type 1 diabetic pregnancy: Do twin pregnancies require twice as much insulin as singleton pregnancies?**

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**Objective:** To evaluate the pregnancy-induced changes in insulin requirements in women with type 1 diabetes during twin pregnancy compared with singleton pregnancies.

**Methods:** Through three databases; an ultrasonic, diabetic and obstetric, 15 women with type 1 diabetes expecting twins from 2000-2011 were identified. Insulin requirements at 8, 14, 21, 27 and 33 weeks and pregnancy outcome were compared with 108 singleton pregnancies from 2004-2006.

**Results:** The twin group was comparable with the singleton group apart from a shorter diabetes duration (median 11 (range 1-20) years vs. 16 (1-36), p=0.03) and a lower BMI (23.0 (18.8-27.3) kg/m² vs. 24.3 (17.3-43.8), p=0.01) in women expecting twins. Throughout pregnancy, HbA₁c was similar in twin and singleton pregnancies. The increment in total insulin requirement from before pregnancy until 33 weeks tended to be higher in twin pregnancies compared with singleton pregnancies (103% (36-257), from 45 IU/day (21-79) to 92 IU/day (60-157) vs. 71% (-20-276), from 50 IU/day (22-102) to 90 IU/day (43-198), p=0.07). In twin pregnancies, the total insulin requirement was 8% (-28-28 IU/day) lower at 14 weeks compared to pre-pregnancy values (p=0.50). The weekly increase in daily insulin dose between 14 and 27 weeks was higher than in singleton pregnancies (3.0 IU (0.9-4.9) vs. 1.5 IU (-1.5-5.9), p=0.008) and remained stable from 27 to 33 weeks.

**Conclusions:** In women with type 1 diabetes, total insulin requirements doubled throughout twin pregnancies and were 45% higher, with a steeper increase between 14 and 27 weeks, as compared with singleton pregnancies.
59 Comparison of treatment with insulin detemir or glargine in pregnant women with type 1 diabetes

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Objective: To compare glycemic control and pregnancy outcome in women with type 1 diabetes treated with either insulin detemir or glargine.

Methods: Review of all medical records of 113 singleton pregnancies in women with type 1 diabetes with a living fetus at 22 gestational weeks between January 2007 and August 2011 using either insulin detemir (n=67) or glargine (n=46) before and during pregnancy.

Results: Baseline characteristics were similar in the two groups except from parity (primipara, 67% in the detemir group vs. 46% in the glargine group, p=0.023). HbA1c was comparable throughout pregnancy (median 6.6% (range 5.6-9.8) vs. 6.8% (5.4-10.1) and 6.1% (5.1-7.6) vs. 6.2% (4.8-7.2) at 8 and 33 weeks, respectively). No differences regarding severe hypoglycemia (23% vs. 23%) or preeclampsia (14% vs. 18%) were seen. Total insulin dose was higher in the detemir group at 33 weeks (1.11 (0.47-2.22) IU/kg vs. 0.97 (0.37-2.60), p=0.044). No perinatal deaths were observed. One in each group was born with a major congenital malformation. The prevalence of preterm delivery was 31% vs. 35% (NS) and 46% vs. 26% infants were large for gestational age (p=0.030). The annual prevalence of patients using long-acting analogs increased from 12% in 2007 to 58% in 2011.

Conclusions: Glycemic control and pregnancy outcome were comparable in women using insulin detemir or glargine with a low rate of severe complications. However, a higher prevalence of large for gestational infants in women on detemir was seen. The use of long-acting insulin analogs during pregnancy is increasing.
60 Adrenaline response to hypoglycemia in early and late pregnancy is comparable despite increased incidence of severe hypoglycemia in early type 1 diabetic pregnancy

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Aim: To explore the adrenaline response to asymptomatic hypoglycemia during pregnancy in women with type 1 diabetes and its relation to severe hypoglycemia in early pregnancy.

Methods: Observational study of 107 consecutive pregnant women with type 1 diabetes (median duration 16 years (range 1-36) and HbA1c 6.6% (4.9-10.5) in early pregnancy) and 22 healthy pregnant women. At 8, 14, 21, 27 and 33 weeks (diabetic women) and at 15, 28 and 34 weeks (healthy women) blood was sampled for measurements of adrenaline and glucose. Each woman’s measurement of serum glucose was matched with her corresponding adrenaline concentration. Severe hypoglycemia was recorded prospectively.

Results: During normoglycemia (serum glucose >3.9 mmol/l), adrenaline concentrations were lower in late pregnancy compared with early pregnancy in both diabetic women (17 (2-131) pg/ml vs. 20.5 (7-111), p=0.02) and healthy women (13 (5-49) pg/ml vs. 21 (10-37), p=0.046). In diabetic women, asymptomatic hypoglycemia (serum glucose ≤3.9 mmol/l) occurred in 70 (65%) in at least one (1-4) blood sampling during pregnancy. Adrenaline concentrations at asymptomatic hypoglycemia were at comparable levels at 8 and 33 weeks (30 (5-164) pg/ml vs. 29 (9-152), p=0.79), lower in women with diabetes duration over 16 years (5 (-25-59) vs. 14 (-44-146) pg/ml, p=0.02), but comparable in women with or without severe hypoglycemia in first trimester (24 (14-164) pg/ml vs. 33 (5-86), p=0.35).

Conclusion: Adrenaline response to asymptomatic hypoglycemia was present at comparable levels in early and late pregnancy, declined with longer diabetes duration and was not associated with severe hypoglycemia in early pregnancy.
61 Recommended number of samples for monitoring of iodine nutrition after iodine supplementation

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**Background:** Iodine fortification of food has been applied in many iodine deficient regions. As both iodine deficiency and excess are unfavourable, it is recommended to monitor the iodine intake of the target population by measuring the median urinary iodine excretion (UIE) in groups of people. It remains to be elucidated if an iodization program affects the size of the subpopulation to study for estimating iodine intake of the population with a certain precision.

**Aim and Method:** We describe variations in UIE as measured in spot urine sampled in each participant once monthly for 13 months. Group 1 (G1, n=16) was studied before and G2 (n=21) after implementation of the Danish iodization program.

**Results:** G1 / G2 (207 / 265 samples) median (2.5 – 97.5 percentile) UIE were 50.0 / 98.0(15.2 – 155 / 32.0 - 295) µg/L. Median individual coefficients of variation (CV) were G1 / G2: 39 / 43% (Mann-Whitney p=0.92), and the group based CV 57% in both groups. No trend was seen between mean UIE during the year and individual variation (Spearmans Rho 0.01, p=0.54) or at a group level (Jonckheere-Terpstra p=0.37). The number of samples needed to reliably estimate the UIE level of a population was estimated to 122 in G1 and 126 in G2.

**Conclusion:** The iodization program led to a substantial increase in UIE, but variations in UIE were unchanged both at the individual and the group level. Consequently, the number of samples needed to reliably estimate the UIE level of a population did not differ between these populations with a two-fold difference in median UIE levels.
62 Metabolic function one month after hemithyroidectomy for benign euthyroid goiter – preliminary results after first postoperative visit

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Introduction: We present preliminary results of 7 patients (2 men, 5 women, mean age 54) from their first visit one month after hemithyroidectomy. In January 2012 we expect to present preliminary results of 15 patients. It is well known that TSH is increased after hemithyroidectomy. Thyroid hormones have major influence on mitochondrial function. The mitochondrial membrane potential (MMP) is believed to be a measure of stimulation by thyroid hormone. MMP can be determined by flow cytometry analysis of fluorescence of mononuclear blood cells.

Aim: To examine if increased serum TSH affects body weight and mitochondrial function 1, 3, 6 and 12 months after hemithyroidectomy for benign euthyroid goiter.

Method: Prospective, observational cohort study of 30 patients who undergo hemithyroidectomy for benign euthyroid goiter. Height, weight, waist circumference and body fat percentage is measured. A venous blood sample is analyzed for TSH, free T4 and total T3. The fluorescence of MitoTracker Green- and Tetramethylrhodamine methyl ester-stained MNBCs is measured by flow cytometry.

Results: One month after hemithyroidectomy for benign euthyroid goiter TSH is increased (p=0.017) and free T4 decreased (p=0.027). Total T3 shows a trend towards a lower value (P=0.128) and body weight is increased (p=0.017). Examination of MMP shows a trend towards decreased values although not statistically significant, see figure 1.

Conclusion: Postoperative alteration of mitochondrial function might be the link between decreased thyroid function and increased body weight after hemithyroidectomy. The study is ongoing and we await more results.

Figure 1: Percentage alteration of fluorescence of TMRM-stained MNBCs measured by flow cytometry before and one month after hemithyroidectomy.
Pre-stimulation with recombinant human thyrotropin (rhTSH) improves the long-term outcome of radioiodine therapy for multinodular nontoxic goiter

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Objective: To evaluate the long-term outcome of recombinant human TSH (rhTSH) augmented radioiodine (131I)-therapy for benign multinodular nontoxic goiter (MNG).

Patients and methods: Between 2002 and 2005, 86 patients with a MNG were treated with 131I in two randomized, double-blind, placebo-controlled trials. 131I-therapy, was preceded by 0.3 mg rhTSH (n=42) or placebo (n=44). In 2009, eighty patients completed a follow-up (FU) visit, including determination of thyroid volume (TV), thyroid function, and patient satisfaction by a visual analogue scale (VAS).

Results: In both groups, TV was further reduced from one-year to final FU (71 months). The mean goiter volume reductions (GVR) obtained at one-year and final FU (i.e. 59.2 ± 2.4% (SEM) and 69.7 ± 3.1%, respectively) in the rhTSH group were significantly greater than those obtained in the 131I alone group (i.e. 43.2 ± 3.7% and 56.2 ± 3.6%, respectively, p = 0.001 and 0.006), corresponding to a gain of 24% at final FU. At last FU the reduction in compression VAS scores was significantly greater in patients receiving rhTSH (p=0.05). Additional therapy (thyroid surgery or 131I) was required more often in the placebo group (9/44) compared to (2/42) the rhTSH group (p=0.05). The prevalence of hypothyroidism at one-year (9% and 43% in the placebo and rhTSH group, respectively (p < 0.0001) increased to 16% and 52%, respectively, at the last FU (p=0.001).

Conclusion: Enhanced GVR in rhTSH-augmented 131I therapy improves the long-term reduction in goiter-related symptoms and reduces the need for additional therapy compared with plain 131I therapy. Overall patient satisfaction is benefitted, despite a higher rate of permanent hypothyroidism.
64 Rygning induceret hæmning af NIS er ledsaget af tegn på jodmangel hos gravide og nyfødte, men synes ikke at hæmme jodid passage over placenta

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Baggrund: Det er påvist, at placenta indeholder NIS (natrium iodid symporter), som er jodid transporter i thyroidea og mamma, men det er uvist, i hvor høj grad NIS er involveret i aktiv transport af jodid fra mor til foster over placenta. Thiocyanat akkumuleres hos rygere, passerer placenta og er vist at hæmme NIS i thyroidea og mamma.

Hypotese: Såfremt NIS er af betydning for jodid transport over placenta, forventes forskel i biokemiske tegn på jodmangel hos rygende mødre og deres fostre.

Metode: 140 gravide kvinder klassificeret som rygere (n = 50) eller ikke-rygere (n = 90) baseret på måling af cotinin i serum og urin. Data indsamlet før jodberigelsen i Danmark, 1/3 af kvinderne (n= 46) tog regelmæssigt jodtilskud. Thyreoglobulin (Tg) er anvendt som markør for jodmangel.

Resultater: Ingen signifikant forskel i Tg (median) ryger vs. ikke-ryger blandt mødre og deres fostre; maternel Tg 14,5 vs. 13,8 μg/l, p = 0,34, navlesnors blod Tg 31,7 vs. 38,3 μg/l, p = 0,94. Signifikant forskel i Tg (median) ryger vs. ikke-ryger blandt mødre uden jodtilskud og deres fostre; maternel Tg 34,8 vs. 22,8 μg/l, p = 0,001, navlesnors blod Tg 74,2 vs. 53,0 μg/l, p = 0,017, men den relative medianstigning i Tg fandtes ikke signifikant forskellig mødre og fostre imellem; maternel 52,6% vs. navlesnors blod 40,0%, differens 12,6% (95% CI -12; 37%), p > 0,3.

Konklusion: Maternel rygning øger risikoen for jodmangel hos mor og foster. Vore biokemiske data giver ikke holdepunkter for, at NIS er af væsentlig betydning for jodid transport over placenta.
65 Risk of thyroid malignancy in thyroid incidentalomas detected by 18F-fluorodeoxyglucose positron emission tomography. A systematic review

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Background: The expanding use of 18F-fluoro-deoxy-glucose positron emission tomography (18F-FDG-PET) has led to the identification of increasing numbers of patients with an incidentaloma in the thyroid gland. The aim of this study was to review the risk of malignancy in thyroid incidentalomas found with 18F-FDG PET or PET/CT imaging.

Methods: Studies evaluating thyroid carcinomas discovered incidentally on 18F-FDG PET were systematically searched in the PubMed database from 2000 up to 2011. Studies were eligible for inclusion if they investigated thyroid incidentalomas found with 18F-FDG PET or PET/CT in patients or healthy volunteers. The main exclusion criteria were lack of confirmed diagnoses, investigation of diffuse uptake only, or investigation of patients with one predefined disease only.

Results: Twenty-two studies met our criteria comprising a total of 125754 subjects. 1994 (1.6%) had an unexpected focal hypermetabolic activity, while 1056 of 53370 individuals (2.0%) had a diffuse hypermetabolic activity in the thyroid gland. Diagnostic confirmation was obtained in 1051 of 1994 patients with a focal uptake (366 corresponding to 34.8% were malignant), and 168 of 1056 patients with diffuse uptake (7 corresponding to 4.4% were malignant). In the eight studies reporting individual maximum standard uptake values (SUV), the mean maximum SUV value was 4.8 (SD3.1) and 6.9 (SD 4.7) in benign and malignant lesions, respectively, (p< 0.001).

Conclusions: Incidentally found thyroid nodules, using 18F-FDG-PET, are at high risk of harbouring malignancy if uptake is focal. SUV-values are significantly higher in malignant than in benign nodules. The pronounced inhomogeneity and other shortcomings of the studies are discussed.
Is there evidence of increased mortality in hypothyroidism? A critical review

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Background: Overt hypothyroidism (OH) is common with a lifetime risk around 5%. OH is usually preceded by subclinical hypothyroidism (SCH), which is even more prevalent. Hypothyroidism has been linked with e.g. cardiac dysfunction, atherosclerosis, hypertension and coagulopathy. Intuitively the increased morbidity is expected to shorten lifespan.

Method: We have searched PubMed and reviewed the literature pertaining to whether SCH or OH is associated with an increased mortality. Study results were pooled by the method of DerSimonian and Laird.

Results: Study findings are inconsistent, and the pooled data neither demonstrate an increased mortality in SCH (HR: 1.17 95% CI: 1.00-1.37) nor in OH (HR: 1.24 95% CI: 0.94-1.62) individuals.

Conclusion: We found no increased mortality in hypothyroid individuals after pooling the data. The main concern is, however, that none of the eligible studies were adequately designed to answer whether SCH and/or OH cause an increased mortality. Due to major shortcomings in all studies we have discussed the potential influence of: study population dissimilarities; phenotype classification and misclassification; non-thyroidal illness; drug interference; major co-morbidities; differences in length of follow-up and number of Levothyroxine treated individuals. Having done so, we found no evidence of a systematic bias and thus maintain that there is no scientific proof of an increased mortality in either SCH or OH. Future studies should take the above shortcomings and potential genetic confounding into consideration. The latter can be achieved by studying twins discordant for the phenotype in question.
**67 Alcohol consumption is protective for development of autoimmune hypothyroidism – a population-based study**

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**Introduction + aim:** Alcohol consumption is an important (protective) risk factor for a number of autoimmune diseases, but virtually nothing is known on the possible association between alcohol consumption and overt autoimmune hypothyroidism.

**Design:** a case control study of patients with incident autoimmune overt hypothyroidism (n=140) prospectively identified in a Danish population-based study, and of age- and sex-matched controls with normal thyroid function and no history of thyroid disease (n=560) recruited simultaneously from the same population and undergoing the same investigational program.

**Methods:** participants gave information on alcohol intake, smoking habits, and family history of hypothyroidism. We analyzed the association between various alcohol intake patterns and development of hypothyroidism in univariate and multivariate models.

**Results:** hypothyroid cases had a lower reported alcohol consumption compared with the controls (median units of alcohol (12g) per week: 3 vs. 5 units, p < 0.013). Odds ratios (OR) (univariate model) for developing hypothyroidism were significantly lower among subjects who consumed alcohol compared to alcohol abstainers (abstainers: 0 units/week, reference, OR = 1.00): consumers of 1-10 units/week: OR (95% confidence interval): 0.58 (0.35-0.96); 11+ units/week: 0.40 (0.21-0.78)). Odds ratios were similar in multivariate models including smoking habits and family history of hypothyroidism: 1.00/0.59 (0.35-0.99)/0.41(0.21-0.79). No interaction was found with regards to sex or age, and neither did we find any interaction comparing type of alcohol (wine vs. beer).

**Conclusion:** alcohol consumption seems to confer considerable protection against development of overt autoimmune hypothyroidism - in women and men, at all ages, and regardless of type of alcohol consumed.
68 Association between real-time nodule elastography and “classical” malignancy risk markers by ultrasonography in a prospective patient study before thyroid surgery

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Purpose: To assess thyroid nodule elasticity score in relation to accepted ultrasonographic risk markers of malignancy (solid nodule, hypoechogenicity, microcalcifications, absent halo sign, irregular margins, oval shape, intranodular vascularisation).

Methods: We examined 324 thyroid nodules in 105 (F/M 86/19) patients (mean age±SD, 53±12y) assigned for thyroid surgery. Indications for surgery were: Solitary euthyroid thyroid nodule (n=26), Multinodular euthyroid goitre (n=50), Multinodular toxic goitre (n=11), Graves’ hyperthyroidism (n=3) and Thyroid cyst (n=15).

Elastography was performed by real-time, free-hand technique, using Hi Vision 900, Hitachi with a linear probe 10-5 MHz. Nodules with a diameter > 5mm were classified by risk markers and scored in 4 classes of hardness (ElasticityScore: A-D, ES A+B=soft and ES C+D=hard).

Histopathology was obtained in the 224 nodules removed.

Results: Elasticity scores were A/B/C/D: 25(7.7%)/188(58.0%)/89(27.5%)/15(4.6%), (not applicable, n=7). Soft=213(65.7%), hard=104(32.1%).

Numbers of ultrasonographic risk markers were 0/1/2/3/4/≥5: 1(12.7%)/122(37.7%)/95(29.3%)/39(12.0%)/17(5.2%)/10(3.1%).

Risk markers correlated: absent halo sign to microcalcifications/irregular margins/hypoechoic nodule (r=0.214,p<0.001)/(r=0.344,p<0.001)/(r=0.204,p<0.001). Microcalcifications to irregular margins/solid nodule/oval nodule shape (r=0.216,p<0.001)/(r=0.175,p=0.002)/(r=0.117,p=0.036).

Intranodular vascularisation to solid nodules/hypoechoic nodules (r=0.127,p=0.022)/(r=0.130, p=0.019).

Contrary to this, elasticity score did not correlate to any of these risk markers.

Histopathology (n=224) revealed 5 malignant (2 PTC and 3 FTC) and 219 benign nodules, and an extranodular microfocus of PTC. Malignant nodules had from 1 to 4 risk markers, 4 nodules had ES=B and 1 nodule had ES=D.

Conclusion: In an unsorted group of Danish patients assigned for thyroid surgery, thyroid nodules with malignancy risk markers by conventional ultrasonography were very common. Many of these risk markers correlated, but surprisingly this was not the case for elastography. The 5 histopathology verified malignant nodules were not statistically different from the 319 benign nodules when evaluated by conventional ultrasonography or elastography.
69 Varigheden af kontakten til diabetesambulatorium, risikostratificering og ressourceforbrug for type 2 diabetes patienter henvist fra almen praksis

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Formål: At undersøge varigheden af kontakten til diabetesambulatoriet for type 2 diabetes patienter henvist fra almen praksis, samt at foretage risikostratificering ved tilbagehenvisning. Desuden beregning af ressourceforbruget i ambulatoriet.


Resultater: Hovedparten af patienterne blev ved afslutningen stratificeret til højrisiko-niveau uden forskel i stratafordelingen mellem patienter fulgt i ≤12 mdr. eller >12 mdr. før afslutning. Efter gennemsnitligt 6 ambulatoriebesøg og en mediantid på 10 måneder (spændvidde 1-64) var 105 patienter returneret til diabeteskontrol i almen praksis, mens 20 % fortsat var tilknyttet ambulatoriet efter 6 år. Halvdelen var afsluttet efter 18 måneder. Ud fra DRG-ydelsestakst var godtgørelsen gennemsnitligt 1763 euro pr. afsluttet patient.

Konklusion: Risikostratificering er ikke et brugbart værktøj til at forudsige varigheden af kontakten til diabetesambulatoriet, muligvis fordi individuelle faktorer, der ikke indgår i stratificeringen har været afgørende for, hvornår patienten blev afsluttet. Der mangler strategier til at afkorte varigheden af kontakten til diabetesambulatoriet. De henviste patienter har høj grad af diabetiske komplikationer, også ved afslutning til videre kontrol i almen praksis, hvilket understreger vigtigheden af kvalificeret opfølgning, samt en effektiv kommunikation mellem sektorerne for at nedsætte behovet for genhenvisning til specialiseret behandlingsintensivering.
70 All-cause mortality rates in patients with type 1 diabetes mellitus compared with the non-diabetic population from Denmark 2001–2010

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Aims: We compiled up to date estimates of the absolute and relative risk of all-cause and specific cause mortality in patients with type 1 diabetes at the Steno Diabetes Center relative to the non-diabetic part of the population.

Materials and methods: We selected patients with type 1 diabetes (n=4,872) from the electronic patient record at Steno Diabetes Center. Baseline was 19 May 2001; patients were followed until 31 December 2009. Deaths occurring in the follow-up period were identified. Poisson regression was used to model cause-specific mortality rates by age, diabetes duration and calendar time for each specific cause of death, according to sex.

Results: The study comprised 31064 person-years of follow-up of type 1 diabetes. In 2004 the mortality rates among men and women were 8/6 per 1000 p.y. at age 40 years and 28/23 per 1000 p.y. at age 70 years. The mortality rate in the diabetic population decreased 4% per year, compared with 2% per year in the non-diabetic part of the population. The standardised mortality ratio decreased with age, from 4.0 at age 50 years to 2.5 at age 70 years, identically for men and women. The predominant cause of death in patients with type 1 diabetes was cardiovascular disease.

Conclusions/interpretation: Despite advances in care, mortality rates in the past decade continue to be greater in patients with type 1 diabetes than in those without diabetes; however the mortality rate in diabetes patients decreased faster than that of the non-diabetic population.
71 Gastrointestinally-mediated glucose disposal in patients with maturity onset diabetes of the young (MODY)

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Background & aim: Maturity onset diabetes of the young (MODY) is a clinically and genetically heterogeneous subgroup of non-autoimmune diabetes, which constitutes about 1-2% of all diabetes. In the current study we aimed to evaluate gastrointestinally-mediated glucose disposal (GIGD) in patients with MODY2 (mutations in the glucokinase gene) and MODY3 (hepatocyte nuclear factor 1α gene mutations) and in a group of matched healthy subjects.

Material & methods: Ten MODY3 patients (age: 31±3 years (mean±SEM); body mass index (BMI): 24±1 kg/m²; fasting plasma glucose (FPG): 8.4±0.8 mM; HbA1c: 7.0±0.3%), 9 MODY2 patients (age: 43±5 years; BMI: 24±2 kg/m²; FPG: 7.3±0.3 mM; HbA1c: 6.7±0.2 %) and 10 healthy subjects (age: 40±5 years; BMI: 24±1 kg/m²; FPG: 5.1±0.2 mM; HbA1c: 5.3±0.1%) were examined on two separate occasions: 4h 50 g-oral glucose tolerance test (OGTT) and isoglycaemic iv glucose infusion (IIGI).

Results: Patients with MODY3 and MODY2 were glucose intolerant evaluated from area under curve during OGTT (3,041 ±302 mM×4h vs. 2,139 ±59 mM×4h, \( p=0.0126 \)) when compared with healthy subjects (1,351 ±20 mM×4h; \( p<0.001 \) and \( p<0.001 \), respectively). Isoglycaemia during IIGIs was obtained using 37±4 g and 30±3 g of glucose in patients with MODY3 and MODY2, respectively \( (p=NS) \), and 24±2 g in healthy subjects \( (p=0.01 \) and \( p=0.11 \), respectively), resulting in GIGD \( [100\%\times(\text{glucoseOGTT} - \text{glucoseIIGI/}\text{glucoseOGTT})] \) of 26±8% and 41±5% in patients with MODY3 and MODY2, respectively \( (p=NS) \) and 52±4% in the healthy control subjects \( (p=0.01 \) and \( p=0.11 \), respectively).

Conclusion: As expected the MODY patients had reduced glucose tolerance during an OGTT. Interestingly only the MODY3 patients demonstrated an impaired GIGD when compared to healthy subjects. These differences in GIGD are most likely explained by differences in the aetiology and glucose tolerance between MODY3 and MODY2 patients.
Cystisk fibrose relateret diabetes. Et dansk retrospektivt fødselskohortestudie

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Formål: Formålet med dette studie er at undersøge, om der er sket en ændring i forekomsten af cystisk fibrose (CF)-relateret diabetes (CFRD), om det er muligt at identificere risikofaktorer for udviklingen af CFRD, samt om tilstedeværelsen af CFRD forværrer overlevelsen.


Resultater: I alt 50 (32%) patienter udvikler CFRD og prævalensen for CFRD er 29% ved kohortens afslutning. CFRD er sjælden før 10 års alderen, mens 40% af de 30-36 årige har CFRD. Prævalensen for CFRD blandt de 11-16 årige er i 1990: 13%, 1995: 10%, 2000: 14% og 2005: 13%. I samme periode er forekomsten af kroniske infektioner blandt 10 årige faldet fra 36% til 5% (p=0.001). Forekomst af CFRD er stærkt associeret til CF mutationer i klasse I og II (P=0.003). Forekomst af CFRD har ikke en signifikant påvirkning på BMI, lungefunktion eller overlevelsesraten i dette materiale.

Konklusion: Antallet af patienter, der udvikler CFRD, inden de bliver 17 år, har ikke ændret sig i studieperioden på trods af et signifikant fald i forekomsten af kroniske infektioner. Prævalensen for CFRD stiger med alderen. Patienter med CF mutationer i klasse I og II har en større risiko for at udvikle diabetes. CFRD påvirker ikke overlevelsesraten i dette materiale.
73 STATUS: THE DANISH CENTER FOR STRATEGIC RESEARCH IN TYPE 2 DIABETES - THE DD2 STUDY

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Aims: The main aim of the DD2 study is to use the present knowledge to improve quality of life for type 2 diabetes (T2D) patients in Denmark: 1) by implementing international guidelines and a new organization plan for all newly-diagnosed T2D patients, 2) by establishing a national register that enrolls 10,000 newly-diagnosed T2D patients a year, and 3) by following this T2D cohort through the unique Danish register. The main outcomes are expected to be improved individual care and an increased knowledge of the clinical course. This original main part of the DD2 study is conducted in collaboration with the Danish healthcare system, the national health authorities and the Danish Diabetes Association.

Status: Patient enrollment started in May 2011, and has since increased exponentially. This is due to a continuous increase in the number of participating diabetes outpatient clinics and general practitioners (GP’s).

In the Region of Southern Denmark 200 GP’s have signed to participate in patient enrolment. Additionally, we will invite 1000 GP’s from the Capital Region of Denmark to start in January 2012. During 2012, we aim to invite GP’s from the remaining regions. At present fifteen outpatient clinics, located nationwide, have started enrolment and another ten starts within six months.

A total of 686 patients are enrolled in DD2 - increasing with 35 patients a week. We believe that this will increase to 75 patients a week in early 2012. The goal is to enroll 200 patients a week and we aim to reach this in early 2013. Scientific publication will be published from March 2012.
74 The burden of diabetes in Denmark: Using the National Diabetes Register to assess the individual and population components

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Aims: Describe the diabetes occurrence in Denmark in terms of incidence, prevalence and mortality, and in particular the time-trends. To describe the National Diabetes Register and the research potential in it.

Methods: The National Diabetes Register (NDR) was established in 2006, and covers the entire Danish population from 1995 to 2010. It is based on existing registers in Denmark, and was established to provide information of diabetes patients to the National Indicator Project (NIP).

Results: Incidence rates of diabetes have been increasing until about 2005, after this time the incidence rates have been largely constant. The number of diabetes patients will increase to about 300,000 in 2020. The prevalence of diabetes in 2009 was 19% for men aged 75 and 17% for women aged 85. The mortality ratio versus the non-diabetic population was about 3.5 at age 50, but only 1.5 in age 80. The years of life lost to diabetes was 7 years at age 50, 5 years at age 60 and 3 years at age 70.

Conclusion: The burden of diabetes in Denmark is large for the individual patient but decreasing, but increasing in terms of numbers. The number of diabetes patients is expected to increase in the coming years as a result of population structure not from increasing incidence. The National Diabetes Register provides an invaluable source of information for identification of the entire population of diabetes patients in Denmark, and provides the basis for a continuously updated overview of the population burden of diabetes.
75 Glycaemic control after total pancreatectomy

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**Aim:** To evaluate the glycaemic control after total pancreatectomy.

**Methods:** Records of all patients treated by total pancreatectomy since 2007 were investigated. The first 12 patients were mainly treated with supplementary doses of rapid insulin during the first postoperative period. They were compared to patients introduced to a new regimen with long-acting insulin analog detemir (0,3 IU/kg) and continuous intravenous infusion of glucose (3g/h) from the second day after operation.

**Results:** A total of 33 patients, median age 64 years, underwent pancreatectomy mainly for malign conditions. 61% got surgical complications during admission and one died. At last follow-up (median 15 months), 69% were still alive. The patients received intravenous isotonic glucose for a median of 8 (range 2-22) days and begun solid food after 10 (range 3-35) days. Total parenteral nutrition was given to 13 patients (39%) for a median of 7 (range 1-35) days. The first 14 postoperative days, the overall median p-glucose were 10,2 (range 3,6-19,7) and 11,9 (range 3,4-22,8) mmol/l in the new and old regimen, respectively. At least one p-glucose <2,2 mmol/l occurred in, 16% (n=3) vs 27% (n=3), respectively. All were asymptomatic. Later, two patients in the new group developed severe hypoglycaemia with seizures or coma, both shortly after interruption of intravenous glucose infusion. The median weight loss after one month was 5,5 kg (range -18,0-+7,5) and HbA1c after three months was 7,8% (range 6,7-8,7).

**Conclusion:** Early application of long-acting insulin seems beneficial after total pancreatectomy. However, there is still room for improvement and more focus on carbohydrate intake needed.
76 Weight loss for patients with type 2 diabetes after sustained low-intensity lifestyle intervention and intensified treatment

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**Background**: Patients with type 2 diabetes treated intensively tend to increase in weight, and the increased weight is associated in the deterioration of metabolic risk factors.

**Methods**: This was a 4 year follow-up of 186 patients (115 men and 71 women) treated at a Norwegian hospital. The study evaluated changes in general and abdominal obesity, metabolic risk factors, and the medical treatment.

**Results**: During follow-up for median 11.5 months, dose of statins, metformin, and insulin was increased significantly as was the number of antihypertensive drugs ($P < 0.001$). Patients underwent a sustained low-intensity lifestyle intervention and had a significant weight loss during the follow-up ($P = 0.030$). At the end of the study, 154 patients were abdominally obese patients and treated with a higher number of antihypertensive drugs ($P = 0.022$, $\chi^2$ test), and a higher dose of statins ($P = 0.0072$), and of insulin (IU/kg/d, $P = 0.0061$) than 32 abdominally lean patients, and they had also higher triglycerides ($P = 0.0074$), and lower HDL cholesterol ($P = 0.010$). In multiple linear regression analysis, BMI - but not waist circumference - was significantly associated with dose of insulin (IU/kg/d) and waist circumference – but not BMI - was significantly associated with number of antihypertensive drugs and dose of statins (mg/d), and the levels of triglyceride and HDL cholesterol.

**Conclusion**: Patients with type 2 diabetes may gain from a combination of lifestyle intervention and intensive medical treatment.

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Purpose: To evaluate the ability of a compact and portable scanner using radiographic absorptiometry (RA) to identify major osteoporotic fractures.

Methods: The study included a cohort of 15,542 men and women aged 18–95 years, who underwent a BMD scan in DANHES 2007–2008. BMD scans of the middle phalanges of the 2nd, 3rd and 4th digits of the non-dominant hand were performed with RA system (Alara MetriScan®). Data from DANHES were merged with information on fractures from the Danish National Patient Registry (NPR) comprising the International Classification of Diseases (ICD-10). New or Incident fractures were defined as having occurred between the date of DANHES and the end date of follow-up (27–40 months). Major osteoporotic fractures (vertebral fractures, humerus fractures, forearm fractures and hip fractures) were used in the analyses. Fracture events were calculated as “persons with fracture” and analyzed using logistic regression models.

Preliminary results: A total of 2.01% (n=312) of the participants had experienced a new fracture since participation in DANHES. T-score was significantly lower in subjects with fracture -0.89 vs. 0.49; p<0.01 (unadjusted) and -0.21 vs. 0.50; p<0.01 (adjusted for age, gender, previous fracture, height and weight and smoking). Odds ratios for fracture were 2.33 for T-score between -1 and -2.5 (95% CI: 1.69–3.21), and 2.99 for T-score≤-2.5 (95% CI: 1.95-4.60) compared with T-score>-1 when adjusted for potential confounders.

Conclusion: Phalangeal BMD measurement using RA is associated with prevalence of major osteoporotic fractures and may be used in fracture risk prediction.
78 Parathyroidectomy Improves Estimated Bone Strength in Female Patients with Primary Hyperparathyroidism. A 1-year Prospective Controlled Study using HR-pQCT based Finite Element Analysis

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OBJECTIVE: In this 1-year prospective controlled study, high resolution peripheral quantitative computed tomography (HR-pQCT) was used to evaluate changes in bone geometry, microarchitecture and estimated strength in female patients with primary hyperparathyroidism (PHPT) before and one year after parathyroidectomy (PTX), compared to healthy controls.

SUBJECTS AND METHODS: Twenty-seven women successfully treated with PTX (median age 62 years, range 44-75) and 31 controls (median age 63 years, range 40-76) recruited by random sampling from the general population were studied using HR-pQCT and finite element analysis of the distal radius and tibia.

RESULTS: In both radius and tibia, cortical (Ct.) volumetric bone mineral density (vBMD) and Ct. thickness increased or were maintained in patients and decreased in controls (p<0.01). Radius cancellous bone architecture was improved in patients through increased trabecular number and decreased trabecular spacing compared with changes in controls (p<0.05). No significant cancellous bone changes were observed in tibia. Estimated failure load by finite element modeling increased in patients in radius but declined in controls (p<0.001). Similar, albeit insignificant changes in failure load were found in tibia.

CONCLUSION: This study showed that females with PHPT had improvements in cortical bone geometry and increases in cortical and trabecular vBMD in both radius and tibia along with improvements in cancellous bone microarchitecture and estimated strength in radius one year after PTX, reversing or attenuating age-related changes observed in controls.
79 PTH(1-84) Replacement Therapy in Hypoparathyroidism (HypoPT): a Randomized Controlled Trial on Pharmacokinetics and Dynamic effects Following 24 Weeks of treatment

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In HypoPT, lack of PTH necessitates treatment with calcium and vitamin D analogues in order to avoid hypocalcemia. To study if replacement with the missing hormone possesses advantages, we randomized 62 patients with HypoPT to 24-wks with a daily SC injection in the thigh of PTH(1-84) 100 μg or similar placebo, as add-on to conventional therapy. After 24 weeks, we performed a 24h biochemical monitoring on 39 patients to assess effects on diurnal variations in calcium-phosphate homeostasis. Following injection, blood samples were obtained at 17 time points and urine in six time intervals.

During the 24-wks of therapy patients on PTH reduced daily dose of calcium and active vitaminD by 75% and 73%, respectively. P-PTH levels rose immediately, reaching a peak level of median 246 (IQR: 181–396) pg/ml at the first time point of measurement (15 min). Thereafter, PTH levels decreased gradually reaching pre-dosing levels after app. 16h, with a plasma t½ of 4.2 (IQR 4.0–5.8)hrs. PTH caused significant changes in the diurnal rhythms of p-Ca²⁺ and 1,25(OH)2D levels, with rising levels reaching a peak app. 8h following the injection. Asymptomatic hypercalcemia (>1.32 mmol/l) was present in 41% of PTH treated patients. Despite hypercalcemia, renal excretion of calcium was significantly lower 4-8h PTH- compared with the placebo-group, and 24h u-calcium did not differ between groups.

In conclusion, a fixed dose of 100 μg/d PTH(1-84) may be too high, as hypercalcemia developed in some patients. However, PTH decreased urinary calcium losses in the hour following injection. Accordingly, PTH may possess advantages compared with conventional treatment if administered in doses adapted to the patient’s needs.
80 Differential expression of vitamin-D-metabolizing cytochromes P450 in human adipose tissue depots

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Objective: The activation of vitamin D is catalyzed by the 25-hydroxylases (CYP2R1, CYP2J2, CYP3A4 and CYP27A1) and the 1α-hydroxylase (CYP27B1). Vitamin D is stored in adipose tissue (AT), and circulating levels of 25-vitamin D are low in obesity. We aimed to determine whether these CYPs are expressed in AT and whether their expression differ in lean and obese women.

Methods: Visceral (VAT) and subcutaneous (SAT) adipose tissue biopsies were obtained from 20 obese women and from 20 lean women during abdominal surgery. Relative gene expressions were measured using RT-PCR.

Results: CYP2R1, CYP2J2, CYP27A1, CYP27B1 and CYP24A1, but not CYP3A4, were all expressed in AT. Expression of CYP27A1 were 36 % lower in SAT than in VAT (P=0.007 and P=0.003, for lean and obese women, respectively). Interestingly, expression of CYP2J2 was 2.8 fold higher in SAT than in VAT of lean women (p <0.0001) and 3.6-fold higher than in SAT of obese women (P<0.00001). Expression of the 1α-hydroxylase, CYP27B1, was 2-fold higher in SAT than in VAT for lean women (P= 0.03), but in obese women the expression was 44% lower in SAT than in VAT (P=0.0496). In SAT, the expression of CYP27B1 was 2-fold higher in lean than in the obese (P<0.0001). There were no differences in the expression of CYP2R1 between AT depots.

Conclusion: Three 25-hydroxylases were expressed in AT along with the 1α-hydroxylase. Expression differed in SAT and VAT and in lean and obese women. This implies that local activation of vitamin D is possible within AT.
Evaluation of bone mineral density, kidney function and arterial stiffness in long-standing type 1 diabetic patients with or without diabetic nephropathy

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**Aim:** Estimate bone mineral density (BMD) and relation to kidney function and arterial stiffness among 371 long-standing, type 1 diabetic patients.

**Methods:** Cross sectional evaluation of a prospectively followed cohort 141 patients with diabetic nephropathy (DN) (55% men; age [mean±SD] 53±9 years, 42±8 years of diabetes, duration of DN 22±6 years) and 230 with persistent normoalbuminuria (50% men, 58±10 years, 40±10 years of diabetes). Femoral and lumbar spine BMD(g/cm²) was measured by dual energy x-ray absorptiometry (DXA). Osteopenia and osteoporosis were defined by any T-score from -2.5 to -1.0 and <-2.5, respectively. Glomerular filtration rate (GFR, ^51^Cr-EDTA) were determined in DN and estimated GFR (eGFR, MDRD formula) in normoalbuminuric patients. Pulse wave velocity(PWV) was measured by SphygmoCor and 24h pulse pressure(PP) by the BPro watch device.

**Results:** Among patients with DN, 73(52%) and 36(26%) had osteopenia or osteoporosis, respectively compared to 124(54%) and 32(14%) of normoalbuminuric patients(\(p=0.013\)). 34% of males with DN vs. 14% with normoalbuminuria had osteoporosis(\(p<0.001\)) and lower age-sex matched Z-scores(\(p<0.001\)). Among women, only femoral Z-scores were different. In addition, ambulatory 24hPP were elevated in osteoporosis patients compared to osteopenia and normal BMD(\(p=0.033\)). Among normoalbuminuric patients, both 24hPP and PWV were elevated in osteoporosis patients(\(p=0.023\) and 0.028, respectively). However, baseline eGFR levels did not change with declining BMD.

**Conclusion:** The risk of osteoporosis was highest among male type 1 diabetes patients and long-standing DN and femoral BMD correlated with renal function and arterial stiffness. Hence, screening and treatment of osteoporosis in patients with impaired renal function and arterial stiffness should be considered.
Bone mineral density is reduced in half of Danish insulin dependent type 2 diabetes patients

Trine Wellov Boesgaard on behalf of The CIMT Trial Group

Hypothesis and Aim: Prevalence and incidence of low bone mass in type 2 diabetes patients (T2DM) varies between populations and anatomical region. The prevalence of osteoporosis in Denmark is uncertain but estimated: around 20% in women and 10% in men age 55-59 years increased to 30% and 15% in 60-64 years old Danes. We want to evaluate the prevalence and risk factors for osteopenia and osteoporosis in Danish T2DM.

Method: Bone Mineral Density (BMD) was measured by Dual Energy X-ray Absorptiometry (DXA) in 424 of 435 T2DM recruited to the CIMT trial from 8 diabetics clinics in the greater Copenhagen area. Inclusion criteria were age>30 years, HBA1c>7.0% and eGFR>60 ml/min. Anthropometric measures, glycaemic status, plasma lipids and eGFR were determined. Osteopenia was defined by any T score -1 to -2.5 and osteoporosis as any T score<-2.5. BMD measured in (g/cm²).

Results: A total of 424 patients (65% men): age 61±9 years, HBA1c 8.5±1.0%, eGFR 144 ml/min (range 44-289 ml/min). The prevalence of osteopenia was 44% (men 46%, women 41%) whereas only 4% (men 3%, women 5%) had osteoporosis. Patients with osteopenia and osteoporosis had lower BMI, waist, hip, BP and eGFR than patients with normal BMD, p<0.03. Glycaemic-control did not differ between groups. Difference in age: 60±9 vs. 62±8 were seen when comparing non-osteoporosis vs. osteopenia/osteoporosis, p=0.05. Patients with reduced eGFR had lower femoral hip neck and total femoral BMD, p<0.001.

Conclusion and perspective: Almost half of T2DM patients had reduced BMD which is more frequent than expected in age matched non diabetic controls in the Danish population. This was most pronounced in patients with impaired renal function.
83 Treatment of vitamin D insufficiency with oral loading doses of cholecalciferol

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Aim: To minimize the duration of vitamin-D insufficiency, current treatment regimes are initiated with an oral bolus dose of cholecalciferol. We have previously developed an algorithm (# Dekristol caps/Vigantol mL = (80 nmol/L - initial [s-25-OH-d-vit]) / 7 nmol/L) for determining the dosage of this bolus, aimed at reaching a serum 25-OH vitamin-D of 80 nmol/L. Our main aim was to investigate the accuracy of this algorithm.

Materials: A retrospective study of 88 patients attending the out-patient clinic with low vitamin-D status. 60 patients had been treated with a bolus dose of cholecalciferol, estimated by the algorithm, as either capsules (Dekristol, 20.000 IU/capsule) or drops (Vigantol, 20.000 IU/mL), along with supplementation treatment consisting of Unikalk Forte 2 to 4 tbl./day (1520-3040 IU). 28 patients received supplementation treatment alone (no-bolus group).

Results: The average baselines were <25 nmol/L (below the assay's detectable range) in the bolus group and 32,0 nmol/L in the no-bolus group. Follow-up samples were taken after 116 (±70) days. Both groups had received daily supplementation of cholecalciferol, averaging at 1787 IU and 1924 IU respectively. At the follow-up, the bolus group had an increase in s-25-OH-vitamin-D of 34,9 nmol/L - significantly higher (P=0,005) than in the other group (19,0 nmol/L). The bolus treated patients had a s-25-OH-vitamin-D of 55,9 nmol/L, 95% CI 46,3-58,9 - significantly lower than the desired value of 80 nmol/L (P<0,001).

Conclusion: Our findings suggest that our treatment regime wasn't sufficient to increase the serum 25-OH vitamin-D to 80 nmol/L. Based on present data we have developed a new algorithm incorporating patient BMI, which we plan to validate in a prospective study.
84 Gamle henvist til DXA skanning i osteoporoseklinikken i Aalborg

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**Baggrund:** Der er ofte fokus på peri- & post-menopausale kvinder i evalueringen af osteoporose, men andre grupper af befolkningen undersøges også ved hjælp af DXA.

**Formål:** At karakterisere gruppen af 65+ årige kvinder sammenlignet med peri-post-menopausale kvinder henvist til DXA skanning.

**Metode:** Data analyseres på 1000 kvinder på 65 år eller derover, der har fået lavet DXA skanning i osteoporoseklinikken ved Aalborg Sygehus fra 1/1 2010, sammenlignet med kvinder på 50-64 år undersøgt i samme periode. Demografi og risikofaktorer blev bedømt ud fra spørgeskema, henvisning, og medicinlister. DXA skanning blev foretaget.

**Resultater:** Kvinder var gradvist lavere (p<0.001), mens BMI kun var lavere hos 90år+ (22.7 vs 24.1 kg/m², p<0.001). Antal risikofaktorer steg alene ved alder 80år+ (<80/ 80+år: kvinder; 1,57/2,48. p<0.001). Når alder blev ekskluderet havde kvinder på 65+/70+år henvist til DXA skanning flere risikofaktorer end yngre kvinder (p=0.05/0.03). Risikoprofil ændredes med alder. Familær disposition var den hyppigste risikofaktor i den yngre og aftog med alder (<65/ 65-80/ 80+år: 51/29/15%, p<0.001), mens fraktur tiltog som betydnende faktor og var hyppigste i den ældre gruppe (19/ 35/ 48%, p<0.001). T-score <-2,5 sås hos 32/ 43% af henviste med alderen <65/ 65år+, og betydnende herfor var alene BMI (OR, 95-CI: 4.8; 2.5-9.2), alder (1.7; 1.4-2.1) og rygning (1.3, 1.1-1.7) i multivariate logistisk regression.

**Konklusion:** Alder påvirker risikofaktorers antal og type hos gamle kvinder sammenlignet med peri-/ post-menopausale kvinder henvist til DXA skanning i Nordjylland.