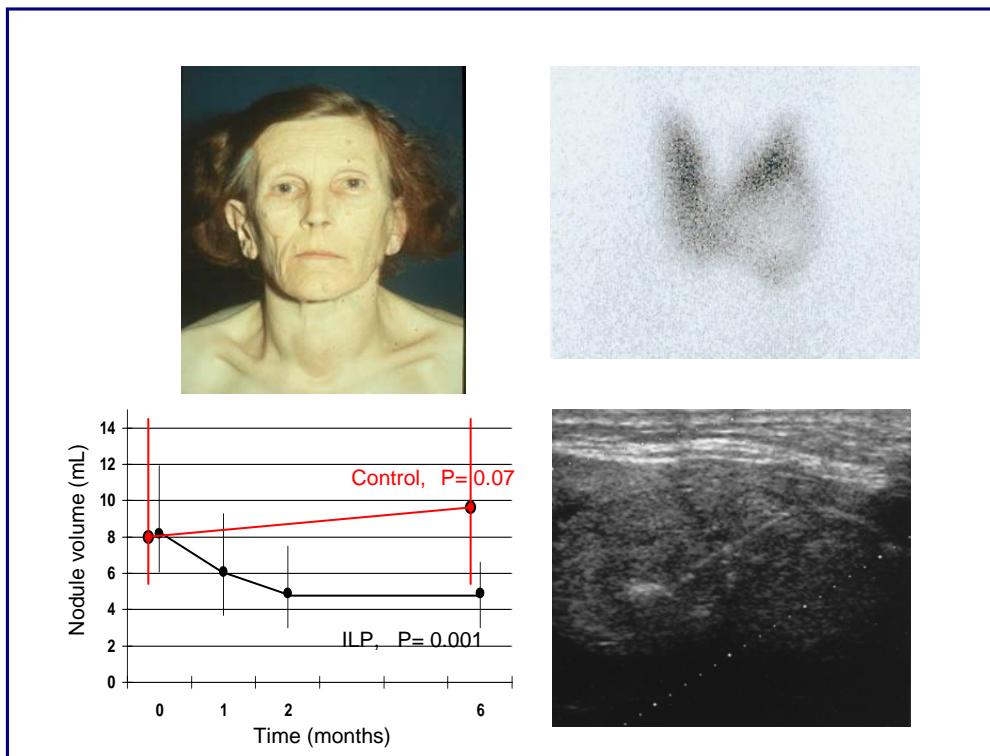


Annual Report 2004

EFE

**Endocrine Research Unit
Department of Endocrinology**

**Odense University Hospital
and
University of Southern Denmark**



Laser treatment of cold nodule in the thyroid gland

Legend to the front page figure (to be seen from top left clockwise)

Picture 1: Patient with solitary nodule in the thyroid gland.

Picture 2: Scintigraphic cold thyroid nodule. Lacking uptake corresponding to the nodule.

Picture 3: Ultrasonographic illustration of the laser fibre situated in the solid nodule.

Picture 4: Thyroid nodule volume before and 1, 2 and 6 months after laser treatment compared with the spontaneous course after 6 months' observation.

Table of Contents

Preface	4
EFE’s Research Committee	6
Six selected research stories from 2004	7
1. Odense Androgen Study in the Elderly (OASE)	7
2. Stem cell based transplantation as a future treatment of diabetes.....	9
3. We got eyes for you	12
4. Effect of ultrasound guided interstitial laser photocoagulation on benign solitary solid cold thyroid nodules – 1 versus 3 treatments.....	14
5. Relocation of lab – The Molecular Endocrinology Unit (KMEB)	16
6. Osteoporosis in men.....	167
Examples of current research projects in EFE	19
The Diabetes Research Group.....	19
The Pituitary Gland Research Group	21
The Molecular Endocrinology Unit (KMEB).....	22
The Bone and Calcium Research Group.....	23
The Thyroid Research Group.....	25
Researchers and technical/administrative staff in EFE – as per 31 December 2004	27
The Diabetes Research Group.....	27
The Pituitary Gland Research Group	29
The Molecular Endocrinology Unit (KMEB).....	30
Clinical Nursing Research Group	31
The Bone and Calcium Research Group.....	32
The Thyroid Research Group.....	33
Publications	35
Internal meetings and lectures 2004	44
Selected, invited lectures held by EFE members at international congresses and meetings ..	46
The Diabetes Research Group.....	46
The Molecular Endocrinology Unit (KMEB).....	46
Clinical Nursing Research Group	47
The Bone and Calcium Research Group.....	47
The Thyroid Research Group.....	48
Courses 2004 organised by the PhD Graduate School of Metabolism	49
Completed scientific theses 2004	52
Scientific awards	52
Financial support to EFE from institutions and foundations	53
Institutions and foundations	53
Commissioned research and support from pharmaceutical companies	57

Preface



In the field of endocrinology, much emphasis is put on evidence based practice, thus meaning that our diagnostics and treatment need to be based on research. I am therefore happy to see that, again in 2004, our activities have increased in all of the research groups of the Endocrine Research Unit (EFE). Our goal is, however, not to produce as many articles as possible, but to produce as good articles as possible. Therefore, I am happy to see that not only the number of articles increases – in 2004 we published more than 70 articles in peer reviewed journals – but also the quality improves. During the past years, the research unit has published articles in the Lancet, New England Journal of Medicine and Science. The last-mentioned article from Moustapha Kassem's research group has recently been published and will be included in next year's report, but it must be mentioned this year as it is the first time that the Department of Endocrinology publishes in this journal – probably the most prestigious journal in the world!

These days, problems of research recruiting are often mentioned, but I believe that the limit for genuinely interested candidates has probably been reached. In health sciences, the general annoying opinion is that PhD degrees serve only one purpose – achieving an end position. If this is the motivation for researching, you better not do it! As senior doctors/researchers, we need to put much emphasis on getting the new generation to understand the importance of research and its natural position – also in a clinical department. Researching is a lifestyle promoting good clinical practice and thereby excellent patient care. We must never forget that this is our goal. Researching for the sake of research may be justifiable in many basal research institutions, but not in hospital clinics. Therefore, I encourage new doctors (but also medical students) to try it! If you are turned on by research, you will have an exciting career – and become a good doctor.

In order to strengthen research training and attract talents, we have have established a research school within the framework of the Danish Research Agency, i.e. the PhD Graduate School of Metabolism or The PhD Graduate School of Functional Genomics and Proteomics as Applied to Metabolic Diseases (diabetes, obesity and osteoporosis). This year's courses and the programme for the PhD Summer Schhol have therefore been included in this annual report.

As earlier mentioned, there is a lot to be pleased with in EFE in 2004. Among others, the many prizes awarded to several persons at the department. Congratulations to Ole Hother-Nielsen, Kurt Højlund, Moustapha Kassem, Dorthe Nielsen, Lone Hammelsvang, Grete Kirketerp, Anne Holm Nyland, Lillian Petersen and Mette Rothmann.

We also need to congratulate The Molecular Endocrinology Unit (KMEB), which became a part of the Department of Endocrinology in 2004, for their new spectacular labs in Winsløwparken 25, now employing more than 20 researchers and technical/administrative staff working with especially stem cell and metabolic research. I hereby express our great thanks to the management of Odense University Hospital for making this possible.

This year's front page picture shows aspects of laser treatment of thyroid nodules. A new treatment developed by Laszlo Hegedüs' research group. This treatment is not offered by any other groups in the world. This is one example of how new research is of benefit to the patients.

As usual, I need to thank many persons on behalf of EFE. First, I would like to thank all patients and voluntary control persons, who have made themselves available for research. Second, our very steady and hard-working staff at the Department of Endocrinology and KMEB as well as our cooperating departments at Odense University Hospital, nationally and internationally. Especially, the cooperation with the Faculty of Science and Engineering at the University of Southern Denmark has been fruitful – and exciting.

As it appears from the report, we have received large amounts from private foundations (a special thanks to the VELUX FOUNDATION), but also from public and not least from Funen County. We are therefore indebted to politicians and administrators in Funen County. It is great to work in a county giving priority to innovation. We will make sure to pay back in the form of creating research results improving patient treatment and putting Funen on the map – also endocrinologically.

Henning Beck-Nielsen
Head of research, EFE
Department of Endocrinology

EFE's Research Committee



Marianne Andersen
Consultant, PhD
The Pituitary Gland
Research Group



Henning Beck-Nielsen
Professor, consultant, DMSc
Chairman
The Diabetes Research Group



Kim Brixen
Consultant, DMSc
The Bone and Calcium
Research Group



Tine Christensen
Research Secretary



Laszlo Hegedüs
Consultant, DMSc
The Thyroid
Research Group



Moustapha Kassem
Professor, consultant, DMSc
The Molecular
Endocrinology Unit (KMEB)



Anne Holm Nyland
Development nurse, MSc (nursing)
Clinical Nursing Research Unit

Six selected research storys from 2004

Examples of EFE's research areas.

1. Odense Androgen Study in the Elderly (OASE)

Kristian Wraae, MD, PhD student

Introduction

Male ageing is associated with sarcopenia, frailty, osteopenia, obesity, the metabolic syndrome and cardiovascular disease. To what extent the androgens affect these signs of ageing is still largely undetermined. A few studies have shown divergent results concerning the relation between ageing and serum levels of testosterone. It still remains to be shown whether there is a pure age-related decline in serum testosterone or whether other factors such as obesity, chronic illness or medication are responsible for the lower serum testosterone found in elderly men when compared with young men. To investigate these issues a cohort of 600 men aged 60 to 75 years is examined.

Objective

The aim of the study is to investigate the relation of testosterone (T) to body composition (BC) and physical performance (PP). Measures for BC are muscle mass (MM), bone mineral density (BMD) and fat mass (FM). Parameters for PP are maximum voluntary force (MVF), maximum oxygen uptake (VO₂max) and muscle power (P). We hypothesize that T is positively associated with MM, BMD and all PP parameters, but negatively associated with FM. We will furthermore examine whether life style, medication, chronic disease, hormones and binding proteins exert their actions on BC and PP solely through or independently of T. The levels of s-total and free T in this cohort will be compared with the s-total and free T levels from a cohort of young men aged 20 to 30 years. Furthermore the associations found between T and BC and PP in the two cohorts will be compared to investigate whether T plays the same role in the two groups.

Methods

All blood analyses are determined in fasting condition from venous samples drawn between 8 and 9 a.m. The influence of life style, medication, chronic disease, hormones and binding proteins on T, BC and PP are assessed by four questionnaires, a physical examination and blood tests. MM is

determined regionally (truncal, lower and upper extremities) and as total by Dual Energy X-ray Absorptiometry (DEXA), and specifically by MRI with cross sectional area of femoral and axial muscles. MVF of *m. biceps brachii* and *m. triceps surae* is measured isometrically. P is measured with the Nottingham Powerrig. VO₂max is determined on a Monark ergometer bike using a Jaeger Oxycon Pro. BMD is determined specifically (femoral and lumbar) as well as total bone mass is estimated by DEXA. The ratio of intraperitoneal area/volume of fat to total abdominal area/volume is determined by MRI, and likewise is also abdominal subcutaneous FM. Finally BMI and waist-to-hip ratio are measured.

Results

Initially a questionnaire providing us with basic demographic, social, occupational and other information about men from Funen aged 60 to 75 was randomly mailed to 4,964 men. Of these questionnaires, 89% were returned and 85.2% of the returned questionnaires had been completed. Afterwards 1,650 people received an invitation by mail to get an introduction to the project via telephone. Of these 1,650 people 50.8% accepted to be contacted. So far 762 people have been contacted in a randomly manner and of these people, 74% have agreed to participate in the project. In the beginning of April 2005, 550 people have been included in Odense Androgen Study in the Elderly.

2. Stem cell based transplantation as a future treatment of diabetes

Ulrik Frandsen, PhD, Assistant research professor

The Molecular Endocrinology Unit (KMEB)



Introduction

Conventional therapy of type 1 diabetes has failed to prevent the development of long-term complications, which are devastating to the patient and extremely costly to treat. The reason is that insulin administration by the patient will never be able to fully mimic the performance of the normal glucose-sensing beta-cell. Even slight fluctuations of blood sugar through many years are enough to cause accumulating events of irreversible chemical reactions eventually causing diseases such as heart and kidney failure and blindness. Ideally, a restoration of a functional beta-cell mass would be a preferred alternative treatment of diabetes as the beta-cell itself has the unique ability to sense blood glucose and to produce and secrete insulin just according to the needs. Today this can only be accomplished by transplantation of pancreas or islet cells to a diabetic recipient. James Shapiro and coworkers from University of Alberta, Canada, have recently shown that islet transplantation can restore normoglycaemia in diabetic patients for several years. It takes, however, 2–4 pancreases to yield sufficient islets to treat one person. Consequently, there will be a need for alternative beta-cell sources before islet transplantation can be considered as a treatment possibility for a large number of diabetes patients. Recent breakthroughs in embryonic stem cell technology together with increased understanding of the developmental biology of islet specification and maturation *in vivo* have, however, raised the hope that embryonic stem cells can be directed to differentiate *in vitro* into large quantities of insulin-producing cells to provide sufficient material for transplantations.

Derivation of human embryonic stem cells

Stem cell research is among the more recent areas of scientific discovery. Researchers only isolated stem cells from mouse embryos some 20 years ago; but it wasn't until 1998 that scientists successfully isolated human embryonic stem cells, when research teams at the University of Wisconsin and Johns Hopkins University independently derived human pluripotent cells. Embryonic stem cells are cells possessing two capacities believed to be unique: they are capable of seemingly limitless reproduction, and they can develop into any type of cell, tissue, or organ as they mature – and as such they are characterised as being pluripotent. Their ability to replicate

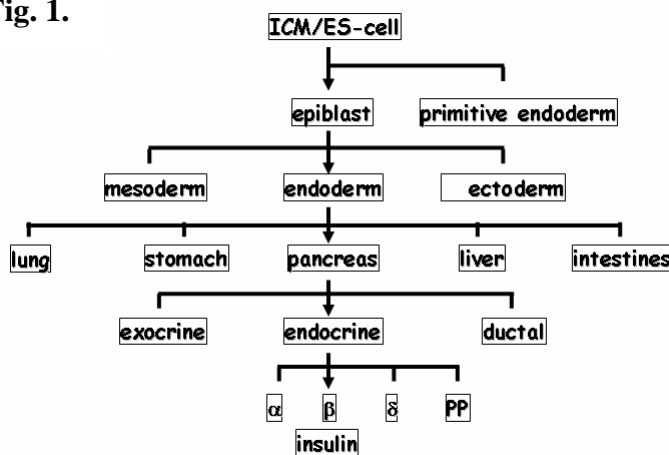
themselves indefinitely while remaining in an “undifferentiated” state means that embryonic stem cells offer a potentially unlimited source of cells for organ transplantation. Human embryonic stem cells are derived from surplus eggs that have been fertilized *in vitro* – in an *in vitro* fertilization clinic – and have afterwards been specifically donated for research purposes with the informed consent of the donors. These “blastocysts” are typically four or five days old and form a hollow, microscopic ball of about 150 cells. To derive stem cells, the inner cell mass of a blastocyst is isolated from the surrounding trophectoderm by immunosurgery and is subsequently transferred into a laboratory culture dish containing feeder cells. Over the course of several days and sometimes weeks, the cells of the inner cell mass proliferate and begin to crowd the culture dish. The cells are removed and put into several fresh culture dishes, and eventually an embryonic stem cell line becomes reality. Within the Department of Endocrinology and the Molecular Endocrinology Unit (KMEB) the technique to isolate and transplant islet cell has recently been established. KMEB has, furthermore, obtained the first permission given in Denmark to derive human embryonic stem cells from surplus embryos and two lines have until now been established and further five reference human embryonic stem cell lines have been imported from collaborators in Sweden and USA. In order to meet the future demand for transplantation material, much effort within KMEB is now being directed towards the establishment of protocols for the subsequent differentiation to functional insulin producing cells. In order to do so, a great challenge in stem cell biology will be to uncover the extra-cellular and intra-cellular mechanisms determining whether a progeny of a stem cell division self-renews or commits to a particular pathway of differentiation - the development of the earliest of the three germ layers – endoderm, mesoderm and ectoderm - from which all other tissue and organs develop.

Commitment of human embryonic stem cells to Endoderm-Derived Lineages (liver/pancreas)

Understanding the mechanisms regulating endoderm induction and tissue specific differentiation has become an area of intense investigation in our laboratory as the development of definitive endoderm and its subsequent patterning and differentiation lead to the formation of pancreas and liver (Fig.1). We have recently established an human embryonic stem cell differentiation protocol in our laboratory supporting the development of hepatocyte-like cells expressing genes and proteins indicative of hepatocyte development and maturation including hepatocyte nuclear factors (HNFs), alfa-fetoprotein (AFP), albumin (ALB), Tryptophan oxygenase (TO) and alpha1-antitrypsin (AAT) and we use this model system to investigate the signalling pathways committing an undifferentiated

embryonic stem cell to an endodermal cell type fate. We find our current results very promising due to the fact that pancreas and liver development are controlled by common signalling pathways *in vivo* but differ in their dependence on hedgehog signalling. Hedgehog signalling regulates various aspects of morphogenesis, including cell proliferation and differentiation in embryonic tissue. The mammalian hedgehog (Hh) genes, sonic (Shh), Indian (Ihh) and desert hedgehog (Dhh), encode secreted proteins that elicit concentration-dependent responses from target cells. In contrast to its inductive activities during the development of the liver, Shh inhibits pancreas morphogenesis and cell differentiation. Shh is excluded from developing pancreatic tissue and ectopic expression of Shh in embryonic pancreatic epithelium disrupts expression of pancreatic marker genes and pancreas morphogenesis. Inhibition of Hh signalling with cyclopamine, a plant-derived steroidal alkaloid specifically blocking smoothened (Shh receptor function), leads to ectopic budding of pancreatic structures and expression of pancreatic markers in stomach and duodenum. Thus, Shh functions to inhibit ectopic pancreas formation in the foremidgut area including the liver, thereby negatively regulating the growth and size of the developing pancreas. Consequently, inhibition of hedgehog signalling in human embryonic stem cell derived endodermal cells may be required for successful development along the pancreatic lineage. We are currently testing this hypothesis in our newly established hepatocyte cell culture model using small interfering RNAs (siRNAs) and other modulators of Shh signalling to silence Shh gene expression. Apart from the above-mentioned research, the KMEB stem cell research programme also includes the following research areas: 1) Derivation of new human embryonic stem cell lines without the use of xeno-proteins; 2) characterisation of conditions for the efficient growth and maintenance of human embryonic stem cells in culture; and 3) differentiation of human embryonic stem cells to mesoderm and derivative tissues.

Fig. 1.



The lineage tree illustrates the idea that at each step of development, from stem cell to a functional pancreas, decisions are made that affect the fate of cells. For example, an embryonic stem cell can be directed to one of the three germ layers, ectoderm, mesoderm or endoderm, which gives rise to the pancreas. The endoderm is, subsequently, divided into different organ regions such as lung, liver, stomach and pancreas. During pancreas formation, additional decisions are made to form the ductal, exocrine or endocrine lineages.

3. We got eyes for you

Mette Rothmann, Lone Hammelsvang, Lillian Petersen, diabetes nurses, Anne Holm Nyland, development nurse, MSc (nursing), RN, and Grete Kirketerp, head nurse, MPM, master student (nursing)



”We got eyes for you” is a development project focusing on nursing intervention in relation to the prevention of retina changes in diabetic patients.

The aim of the project is

- To investigate whether early nursing intervention by structured and differentiated instruction, guidance and dialogue for a general prevention of retina changes increases motivation and the ability to master blood glucose levels, hypertension, weight, exercise and social arrangements.
- To carry out a pilot project with a view to carrying out a follow-up study aiming at showing whether intervention through an eye school may prevent retina complications.

The following two research questions need to be answered

1. Will a participation in an eye school stay optimize the diabetic patients’ knowledge of retina and life style changes and self care ability?
2. Will new knowledge and new skills learned thourgh an eye school stay prevent further retina changes and thereby save sight?

Design and method

The target group of the study includes type 2 diabetic patients diagnosed with retina changes, phase 1-2. The study will be carried out as a pilot project. The design includes randomization to either control group or study group with 25 participants in each group. The control group will receive relevant care and treatment when arriving in the eye screening clinic. The study group will be

offered participation in an eye school giving relevant, preventive instruction – in total four lessons of 1½ hour during three months. The instruction may include: the anatomy and physiology of the eye, retina changes, prevention and treatment of retina changes, problems related to refraction, cataract, glaucoma and AMD (age-related macular degeneration), which may influence sight and life with retina changes.

The instruction is based on the concept behind the evidence based practice equally taking into consideration the diabetic patient's circumstances and values, the scientific evidence and the clinical expertise. Furthermore, Aron Antonowsky's concept of Sense of Coherence is considered to be an important educational pivotal point.

The data collection is carried out based on questionnaires and focus group interviews in both the control group and the study group. All participants are followed for a period of two years. The project respects the ethical guidelines for nursing research in the North. The project will be notified to the local ethics committee and the internal research committee of the department.

4. Effect of ultrasound guided interstitial laser photocoagulation on benign solitary solid cold thyroid nodules – 1 versus 3 treatments

Helle Døssing, MD, PhD student, consultant



Background

Nodular goitre is common in the adult population and the prevalence increases with age. Most benign, solitary, cold thyroid nodules are stationary or increase slightly in size over time. The vast majority of these nodules are benign. Thorough clinical and biochemical evaluation and the use of US-guided FNAB allow reduction of the number of diagnostic thyroidectomies and a non-surgical approach in patients with compressive symptoms. Interstitial laser photocoagulation (ILP) is a minimally invasive interventional procedure and the necrosis induced by the thermic energy can be delivered in a controlled fashion with no or only minimal damage to the surrounding tissue. The fact that we have recently demonstrated ILP to be feasible and well-tolerated has lead us to evaluate the efficacy and dose-response relationship, as well as the safety of US-guided ILP, on the volume of benign, solitary, solid, cold thyroid nodules. Additionally, we evaluated nodule related symptoms in this prospective randomized study comparing one ILP treatment with three treatment sessions.

Material and Methods

Thirty euthyroid outpatients with a cytologically benign, solitary, solid and scintigraphically cold thyroid nodule causing local discomfort were randomised to one session of ILP (ILP-1) (n=15) or three monthly ILP sessions (ILP-3) (n=15) and followed for 6 months. At enrolment and at the 6 month evaluation, the patients were asked to rate pressure symptoms and cosmetic complaints on a visual 10 cm analogue scale. Immediately after termination of the ILP-procedure the patients were asked to rate the degree of pain/discomfort on a visual analogue scale and whether they would undergo the treatment again, as a surrogate marker of tolerability.

Under sterile conditions and preceded by local anaesthesia, the laser fibre-guided by ultrasound (US) was positioned in the thyroid nodule. The output power was dependent on the pre-treatment nodule volume and nodule position. The patients were investigated 1, 2 and 6 months after the treatment. Initially, and during follow-up, nodule volume, total thyroid volume, as well as thyroid function were investigated.

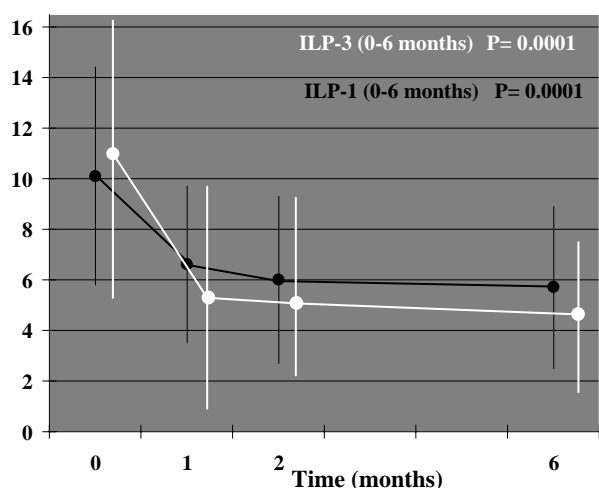
Results

In the ILP-1 group, mean thyroid nodule volume decreased from 10.1 ± 4.3 mL (SD) to 5.7 ± 3.2 mL ($P= 0.0001$) at 6 months' follow-up, corresponding to a mean decrease of $45\% \pm 13\%$. In the ILP-3 group, mean thyroid nodule volume decreased from 10.8 ± 5.5 mL to 4.6 ± 3.0 mL ($P=0.001$) during follow-up, corresponding to a mean reduction of $58\% \pm 17\%$. The overall mean difference between the two groups was 13% ($P=0.03$). In both groups pressure symptoms and cosmetic complaints were significantly reduced. The only side effect recorded was mild to moderate transient pain. No correlation between thermal energy deposition and nodule volume reduction could be demonstrated ($r= 0,08$; $p=0,67$). Thyroid function was unaltered throughout.

Conclusion

Ultrasound-guided ILP is a safe procedure. The additive effect of two supplemental treatment sessions results in a significant further mean decrease of 13%. In both groups ILP results in a satisfactory clinical response in the majority of the patients. ILP could become a non-surgical therapeutic option in selected patients with a benign, solitary, cold thyroid nodule.

Nodule volume (mL)



Thyroid nodule volume before and 1, 2 and 6 months after interstitial laser photocoagulation (ILP) treatment (mean± SD).

5. Relocation of lab – The Molecular Endocrinology Unit (KMEB)

Moustapha Kassem, professor, consultant, DMSc, Head of KMEB



The Molecular Endocrinology Unit of the Department of Endocrinology (also known as KMEB) has moved to a new building: Medical Biotechnology Center (MBC), Winsløwsparken 25 [please see www.mbc.sdu.dk]. MBC is a newly established center at the Faculty of Health Sciences, University of Southern Denmark. MBC is composed of seven research groups. Each is led by a professor and is composed of around 15-20 researchers. The strength of this center is that the research groups possess all state-of-the-art technologies within cell biology, molecular biology and immunology. This creates a strong and inspiring research environment. Each group has its own research projects and the interests of the groups cover areas like cancer biology, neurobiology and studies of neuro-inflammatory diseases, studies of cardiovascular diseases as well as stem cell biology, which is the area of research interest of KMEB. It is envisaged that the presence of KMEB in this new center should help establishing a strong connection between the basic research activities at the MBC and the clinical departments at Odense University Hospital.

The new premises



6. Osteoporosis in men

Morten Frost Nielsen, MD, House Officer

For the past 15 years, the prevalence of osteoporosis in women has been thoroughly analysed. Meanwhile, a long range of effective medical treatments has been developed. A new large project will now analyse the prevalence of and the risk factors (genetic, lifestyle factors, endocrine and other factors) for osteoporotic fractures in elderly Danish men. The Study of Osteoporosis and Male Ageing (SOMA) is a prospective study running for the next ten years. So far, 10,000 men from Funen aged 64-70 years have received a questionnaire and an invitation to participate in the study. However, by next year, the study will be extended to include in total 30,000 men from Funen.

Morten Frost Nielsen, who is at present House Officer at Sønderborg Hospital, is in charge of the study together with Bo Abrahamsen, consultant, PhD, Roskilde County Hospital Køge, and Kim Brixen, consultant, PhD, Department of Endocrinology, Odense University Hospital. Morten Frost Nielsen started his career in the field as medical substitute during his medical studies, and he was immediately swirled into the research work. “In order to develop evidence based programmes and treatment offers, we need to know the prevalence of the disease in the population and the mechanisms underlying the development of bone loss”, says Bo Abrahamsen and he continues: “In women, a long range of naturally appearing variations in the genes (genetic polymorphisms) has been shown to be of importance for the construction of peak bone mass and the later bone loss, whereas the importance of hereditary factors for bone mass and osteoporotic fractures in men has been poorly analysed”. Bone mineral density is known to be reduced in first degree relatives (i.e. parents and siblings) to men with bone fracture due to osteoporosis, but a large number of the hereditary factors important in women seem to be of minor importance in men. This also applies for e.g. polymorphisms in the genes for the vitamin D receptor and alpha-helix of type I collagen.

“We are pleased that the population supports our study”, says Morten Frost Nielsen, “70% of the respondents have chosen to respond to our questionnaire and have been included in our study”. All participants sustaining a future bone fracture will be called in for bone scanning and further investigations. Moreover, persons sustaining no fractures will be called in to represent the control group. “Thereby, it is possible to establish the factors underlying the development of osteoporosis

in men”. Morten Frost Nielsen hopes to begin a PhD study in 2006 on the basis of the data collected from the study.

Facts

Osteoporosis is a considerably individual and social health problem. The disease is related to reduced life quality and working capacity, and in elderly people it often leads to disablement further leading to placement in a residential home. The expenses for treatment of osteoporosis in 1999 in Funen County alone were estimated to be 120 million Danish kroner. Unfortunately, the problem is increasing. During the next 50 years, a doubling from 414,000 to 972,000 of the European prevalence of bone fractures is expected. The treatment of hip or back fractures in the European Union is thereby expected to occupy 30,000 hospital beds in 2010 and 56,000 more beds in 2050. The prevalence of osteoporotic bone fractures in men is especially increasing. From 1981 to 1993, the age-adjusted prevalence of hip fractures in men was increased by 30%, while the increase in women was only 5% during the same period.

Examples of current research projects in EFE

The Diabetes Research Group

Søren Feddersen, MSc, PhD student

Application of lipid mass spectrometry in the study of intracellular lipids and the Acyl-CoA binding protein function in yeast and skeletal muscle from type 2 diabetic subjects.

The aim of the project is to use and further develop HPLC and mass spectrometric based methods to map the cellular lipid profile in control and non-insulin dependent diabetic subjects by measuring important metabolites like long-chain acyl-CoAs, ceramides, triglycerides and phospholipids. In addition, a part of the project focuses on the role of the acyl-CoA binding protein in the regulation of gene expression and synthesis of complex lipids like ceramides and sphingolipids using the eukaryote *Saccharomyces cerevisiae* as a model system. Since most of the proteins we focus on have a mammalian counterpart our work may be directly relevant for mammalian systems. By combining genomic and proteomic technologies with lipid mass spectrometry, our understanding of the role of lipids in cell signalling and in the development of lipid-related disorders like non-insulin dependent diabetes mellitus will be greatly enhanced.

Kurt Højlund, senior house officer, PhD

Molecular mechanisms of mitochondrial dysfunction in skeletal muscle of patients with type 2 diabetes.

Most previous studies of skeletal muscle insulin resistance in type 2 diabetes (T2DM) have focused on the mechanisms underlying impaired glucose transport and glycogen synthesis. However, recent reports of perturbations in glucose and lipid oxidation and down-regulation of proteins involved in oxidative phosphorylation in muscle of patients with T2DM suggest a role for mitochondrial dysfunction. Oxidation of lipids and glucose takes place in the mitochondria leading to generation of ATP (coupled respiration), heat (uncoupled respiration) and free radicals. An intact mitochondrial function is necessary to obtain a normal insulin activation of glucose transport and glycogen synthesis. Therefore, abnormalities in the molecular mechanisms co-ordinating cytosolic storage and mitochondrial oxidation of lipids and glucose could play a pivotal role in the pathogenesis of skeletal muscle insulin resistance and T2DM. To elucidate the molecular

mechanisms of mitochondrial dysfunction in skeletal muscle of patients with T2DM, mitochondria isolated from skeletal muscle biopsies obtained from patients with T2DM and control subjects will be used for studies of coupled and uncoupled respiration, generation of free radicals and for proteome analysis of mitochondrial proteins. Insights into these mechanisms will improve our understanding of the underlying pathophysiology in T2DM and provide novel targets in the development of pharmaceuticals for the treatment of this disease.

Iben Brock Jacobsen, MD, PhD student

New aspects of insulin treatment.

The PhD thesis includes a descriptive and a clinical part involving two clinical studies of dysregulated type 1 diabetic patients. The review “Evidence based insulin treatment” describes and validates all randomized, clinically controlled studies published during the past 20 years and concerning the various insulin preparations and treatment regimens forming the scientific evidence for the treatment of adult type 1 diabetic patients. The clinical part of the thesis includes an intervention study concerning the combined effect of Metformin and insulin on HbA1c, lipids and blood pressure in obese, dysregulated type 1 diabetic patients. The second clinical study concerns the insulin analogue NovoRapid and its effect on nocturnal hypoglycaemia illustrated by measurements of diurnal profiles of blood glucose, plasma insulin, lipids, growth hormone, cortisol, glucagon, ghrelin and IGF-1.

Jørgen Jensen, MD, PhD student

Effect of growth and differentiation factors on the regeneration of beta-cells from stem cells isolated from porcine (pig) and human pancreas: Characterisation of morphology and gene expression in vitro and function in vivo by transplantation in diabetic mice.

A possible treatment of diabetes is transplantation of insulin-producing islet cells. As the effect depends on the number of islet cells, it is often necessary to use islet cells from several donors. There is, however, a lack of donor organs, wherefore methods to increase the number of islet cells either from existing islet cells or from stem cells need to be developed. Pancreas from both animals and humans contain stem cells with potential for developing into insulin-producing islet cells by influencing several known factors. The aim is therefore to characterise the effect of these factors on stem cells from new-born pigs. The results will be used as model for experiments with pancreas tissue from humans.

Vibe Skov, Master of agronomy, PhD student

Gene expression profiling by DNA chips and subsequent bioinformatic analysis for identification of genes and biochemical pathways associated with type 2 diabetes.

Biopsies from skeletal muscle and adipose tissue from 50 diabetic patients and 50 control persons will be provided for investigation. Bioinformatics and gene expression microarrays (GEM) will be applied to gain insight into the molecular pathophysiology of type 2 diabetes. The simultaneous monitoring of thousands of genes in parallel can identify genes and entire biochemical pathways dysregulated at the transcriptional level. Bioinformatic software programmes and databases will be used as data mining tools. Three investigations are planned. First, genes and biochemical pathways altered between diabetic subjects and controls will be examined. Second, it will be investigated if any functional relationships exist between biochemical pathways in adipose tissue and skeletal muscle. Third, diabetic patients will be grouped into subtypes according to their expression profile and phenotype and a classification system will be constructed.

The Pituitary Gland Research Group

Dorte Glintborg, MD, PhD student

Aspects of endocrinology and metabolism in hirsute patients - The effects of insulin sensitizing in polycystic ovary syndrome.

Hirsutism is defined as an increased growth of terminal hair in a male pattern and is observed in 10-20% of reproductive aged women. In two studies, some of the endocrine and metabolic disturbances in hirsute patients are characterised. Part study 1 is a population based study in 340 patients referred with hirsutism. The results of the study showed a low prevalence of endocrine diseases in the hirsute population (3.4%), whereas insulin resistance and type 2 diabetes were prevalent. In part study 2, 30 patients with PCOS were randomized to PPARgamma agonist treatment or placebo. Fourteen healthy females were studied as controls. The results from the study showed severe insulin resistance including both oxidative and non-oxidative glucose metabolism in PCOS patients compared with controls. PPARgamma agonist treatment was followed by significantly increased insulin sensitivity and increased growth hormone secretion, whereas testosterone levels and levels of luteinising hormone did not change significantly.

Thue Kvorning, MSc, PhD student

Effects of testosterone on the adaptation to strength training.

Introduction: The specific mechanisms and the interaction between resistance training, levels of circulating hormones, cellular effects, muscle hypertrophy and increased strength still need to be examined. We suggest that testosterone plays a major role in stimulating these local changes. Therefore, the aim of this study is to investigate the importance of testosterone for increase in muscle hypertrophy and muscle strength gain during a controlled training study.

Hypothesis: Strength training with suppression of testosterone inhibits the local adaptation to this training stimulus, wherefore a less pronounced increase in muscle hypertrophy and a smaller increase in muscle strength are seen after the training period compared with the placebo group.

Methods: The participants are divided into two groups practising the exact same strength training programme by which we expect testosterone to increase acutely. By treatment with Zoladex, we exclude the effects of testosterone on the muscles during and after strength training. When comparing the treatment group with the placebo group it is possible to investigate the importance of testosterone in the adaptation to strength training.

Torben Leo Nielsen, MD, PhD student

Odense Androgen Study in young men (OAS).

The first part of this project is a cohort study of 800 young men aged 20-29 years. Relations between androgens, oestrogens, growth factors, lipids, lipid hormones, body composition, muscle strength, oxygen uptake, life quality and sexual function are studied. In addition to anthropometric measurements, DEXA and MR scanning are also used to decide body composition (muscle, fat, bone mineral content). Finally, the importance of birth weight, gene polymorphisms (e.g. androgen receptor, MTHFR, LRP5) and life style factors are also studied for the correlation between sex hormones, body composition and muscle function.

The Molecular Endocrinology Unit (KMEB)

Studies of the human mesenchymal stem cells.

The aim of this project is to develop a new isolation procedure for human mesenchymal stem cells from the bone marrow as well as studies of the mechanisms of differentiation of these stem cells into osteoblasts, chondrocytes and adipocytes.

Establishing human embryonic stem cell lines and developing methods as well as studies of the mechanisms of differentiation of these stem cells into endoderm (and insulin-producing cells) and mesoderm (osteoblast and chondrocytes).

Studies on the isolation of endothelial stem cells from the bone marrow and their characterisation in vitro and in vivo.

In addition, we will develop clinical protocols for using these cells in the treatment of various ischaemic conditions (e.g. ischaemia after myocardial infarction and lower extremities ischaemia)

Malthe Kristiansen, MD, PhD student

Isolation and characterisation of human mesenchymal stem cells from bone marrow and their potential use in therapy.

The discovery of stem cells, which have clonogenic and self-renewing capabilities and are able to differentiate into multiple cell lineages both *in vivo* and *in vitro*, have shown great promise in tissue regeneration therapy. This has led to clinical investigations attempting to use implantation of bone marrow derived from stem cells to repair damaged tissues. The results have been encouraging with improvement in both subjective and objective measures of tissue function.

The PhD project involves two parts:

- 1) Isolation and characterisation of stem cells from bone marrow in an attempt to identify subpopulations of stem cells with the greatest therapeutic abilities.
- 2) Clinical application of bone marrow derived stem cells in two clinical settings:
 - a. Myocardial infarction.
 - b. Severe limb ischaemia due to atherosclerosis.

The Bone and Calcium Research Group

Comparison of MXA, MRX and clinical evaluation of X-rays of column.

The project is carried out in collaboration with Trine Torfing and Dana Jensen, Department of Radiology, Odense University Hospital, and will explain whether a new method for measurement of the height of the *vertebrae* (can be carried out by bone scanning) can replace conventional X-ray examinations. If so, this will result in a faster examination of the patients and they will be exposed to a smaller radiation dose than before.

Polymorphisms in the MTHFR gene in relation to "peak bone mass" in men.

The project is carried out in collaboration with the Pituitary Gland Research Group, Department of Endocrinology, Odense University Hospital, and it will explain whether a large number of frequently appearing genetic variations in the MTHFR gene is of importance to the maximum peak bone mass in men. The study includes 800 randomly selected men from Funen aged 20-30 years.

Cost effectiveness analysis of a programme for systematic tertiary prophylaxis of osteoporotic fractures in patients with recent hip fracture - preliminary results of a Markov analysis.

Using a newly developed model for the measurement of cost effectiveness of osteoporotic medical treatment (Danish Osteoporosis Outcome Model), we have analysed the effect of carrying out a systematic detection among patients treated for hip fractures in collaboration with the Centre for Applied Health Services Research and Technology Assessment and the department of Orthopaedic Surgery, Odense University Hospital. The results of the study will be presented at the European Calcified Tissues Society's Congress in June 2005 and Dr. Jesper Ryg, PhD student, has been awarded the "Young Investigators' Award" for this work.

Nis Nissen, MD, PhD student

Bone structure and hip geometry in relation to strength in the proximal femur.

Hip fracture is one of the most serious consequences of osteoporosis. The incidence of hip fractures increases exponentially with age in both women and men. Bone Mineral Density (BMD) is a strong predictor of the risk of hip fracture. It is shown that the geometry of the hip is a predictor of hip fractures independent of BMD. The purpose of the PhD study is to improve the estimate of the risk of hip fracture. The geometry of the proximal hip is measured on the screen of DXA scans of the hip. The theory is tested on cadaver bones as a case-control-study. Also a cross-sectional study to describe the natural variation of the geometry of the hip is included. Data from the Danish Osteoporosis Prevention Study is used in the study to investigate the structural parameters of the proximal femur from the menopause and 10 years ahead.

The Thyroid Research Group

Daniel El Fassi, MD, clinical assistant

B-lymphocyte depletion in the treatment of Graves' disease.

Graves' disease is a prevalent autoantibody mediated autoimmune disease affecting approximately 2% of the adult population. B-lymphocytes are implicated in autoimmune diseases as (auto)antigen presenting cells, and as precursor cells for the (auto)antibody producing plasma cells. Employing a controlled clinical trial, we investigate the efficacy of therapeutic B-lymphocyte depletion by the monoclonal antibody Rituximab in patients with Graves' disease. It is our hope that this novel treatment may become an option in the treatment of particularly Graves' eye disease. An extensive national and international network has been established in order to gain insight into the immunological changes occurring during B-lymphocyte depletion. The scope is to broaden our understanding and treatment of Graves' disease, in particular, and autoimmunity in general.

Pia Skov Hansen, MD, PhD student

The relative importance of genetic and environmental effects in the regulation of thyroid function and size. A study of healthy Danish twins.

Overt thyroid diseases such as autoimmune thyroid disease and goitre are common. These complex diseases develop on the basis of genetic susceptibility interacting with environmental triggers. The diagnosis is based on measurements such as thyroid function (i.e. thyrotropin (TSH), triiodothyronine (T3) and thyroxine (T4)) and thyroid size. Health and disease are defined by a continuum of biological traits. The study of thyroid homeostasis in healthy individuals is crucial in trying to understand the pathways eventually leading to thyroid disease. A total of 1,380 individuals (690 twin pairs) were included in the study. A sub-sample including 520 individuals was investigated using ultrasound. Intraclass correlations for serum TSH, free T4 and T3 concentrations as well as for thyroid volume were consistently higher for monozygote than for dizygote twin pairs. 64% (95% CI 57-70%) of the variation in serum TSH concentration were due to additive genetic effects, while unique environmental effects explained the remaining part of the variation. Genetic effects explained 65% (95% CI 58-71%) and 64% (95% CI 57-70%) of the variance for serum free T4 and free T3 concentrations, respectively. For thyroid volume 71% (95% CI 61-78%) of the total variance was explained by genetic factors. The measured covariates were only responsible for a minor part of the variation.

Viveque Egsgaard Nielsen, MD, PhD student

Prospective randomized double blind study of the effect of recombinant human TSH for the effect of radio-iodine in benign nodular goitre.

The PhD thesis deals with the effect of pretreatment with 0.3 mg recombinant human TSH (rhTSH) on the effect of radioiodine treatment and on thyroid size and function in patients with non-toxic nodular goiter. A novel principle is introduced based on prospective, randomized double-blind investigations. In connection with this, we investigate the acute effects of rhTSH on thyroid size (measured by ultrasonography) both in healthy individuals and in patients with non-toxic nodular goiter. These investigations are designed as double-blinded cross-over studies. Thus, overall, the investigations are divided into four categories listed below:

1. Prospective randomized double-blind study of pretreatment with 0.3 mg recombinant human TSH for the effect of radioiodine in non-toxic multinodular goiter.
2. Prospective randomized double-blind study of the pretreatment with 0.3 mg recombinant human TSH for the effect of radioiodine on thyroid size and function in patients with a very large (>100 ml) goiter.
3. Does administration of 0.9 mg recombinant human TSH affect thyroid function and volume in healthy individuals? A randomized double-blind cross-over trial.
4. Does administration of 0.3 mg recombinant human TSH affect thyroid function and volume in healthy individuals and in patients with multinodular non-toxic goiter? A randomized double-blind cross-over trial.

Researchers and technical/administrative staff in EFE – as per 31 December 2004

The Diabetes Research Group

Researchers

Henning Beck-Nielsen, professor, DMSc, head of research (consultant, Department of Endocrinology, Odense University Hospital)

Michael Gaster, MD, PhD (Department of Endocrinology, Odense University Hospital)

Jan Erik Henriksen, MD, PhD (consultant, Department of Endocrinology, Odense University Hospital)

Ole Hother-Nielsen, MD (consultant, Department of Endocrinology, Odense University Hospital)

Kurt Højlund, MD, PhD (Senior House Officer, Department of Endocrinology, Odense University Hospital)

Dorte Møller Jensen, PhD (Senior Registrar, Department of Endocrinology, Odense University Hospital)

Claus Bogh Juhl, PhD (Senior Registrar, Department of Endocrinology, Odense University Hospital)

Peter Stæhr, MD, PhD (Department of Cardiology, Odense University Hospital)

Birgitte Vind, MD (clinical assistant, Department of Endocrinology, Odense University Hospital)

Knud Yderstræde, PhD (consultant, Department of Endocrinology, Odense University Hospital)

PhD students

Søren Feddersen, MSc (Institute of Biochemistry and Molecular Biology, University of Southern Denmark)

Iben Brock Jacobsen, MD (Department of Endocrinology, Odense University Hospital)

Jørgen Erik Jensen, MD (Department of Endocrinology, Odense University Hospital)

Vibe Skov, Master of agronomy (Human MicroArray Center, Odense University Hospital)

Other students

Malene Just Pedersen, medical student (pre-graduate research student, the Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

External researchers

Klaus Brusgaard, MSc, PhD (molecular biologist, Department of Clinical Biochemistry, Genetics and Pharmacology, Odense University Hospital)

Aase Handberg, DMSc, PhD (Senior House Officer, Clinical Biochemistry, Randers Central Hospital)

Klaus Levin, PhD (staff specialist, Clinic I, Bispebjerg Hospital)

Pernille Poulsen, PhD (post.doc., Steno Diabetes Center, Gentofte)

Allan Vaag, DMSc, PhD (consultant, Steno Diabetes Center, Gentofte)

Jørgen Vinten, professor (The Faculty of Health Sciences, University of Southern Denmark)

Henrik Støvring, MSc (researcher, Institute of Public Health, General Practice Research Unit, University of Southern Denmark)

Technical/administrative staff

Tine Christensen, research secretary

Lone Hansen, technician

Vibe Jensen, research nurse

Helle Krüger, technician

Charlotte Olsen, technician

The Pituitary Gland Research Group

Researchers

Marianne Andersen, PhD (consultant, Department of Endocrinology, Odense University Hospital)

Magdalena Andries, MD (House Officer, Medical Department, Odense University Hospital)

Claus Hagen, DMSc (consultant, Department of Endocrinology, Odense University Hospital)

Anne Pernille Hermann, PhD (consultant, Medicinsk Afdeling, Kolding Sygehus)

Rene Støvning, PhD (staff specialist, Department of Endocrinology, Odense University Hospital)

PhD students

Dorte Glintborg, MD (Department of Endocrinology, Odense University Hospital)

Torben Leo Nielsen, MD (Department of Endocrinology, Odense University Hospital)

Thue Kvorning, MSc (Institute of Sport Sciences and Biomechanics, University of Southern Denmark)

Kristian Wraae, MD (Department of Endocrinology, Odense University Hospital)

External researchers

Anette Fløgstad, DMSc (staff specialist, Medical Department, Aabenraa Hospital)

Joanna Ganc-Petersen (Senior House Officer, Department of Orthopaedic Surgery, Fredericia Hospital)

Technical/administrative staff

Ellen Andersen, technician

Henny Hansen, technician

Annagrethe Jeppesen, technician

Jane Nielsen, technician

The Molecular Endocrinology Unit (KMEB)

Researchers

Bassem Abdallah, MSc, PhD (assistant research professor, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Jorge Burns, MSc, PhD (assistant research professor, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Helle Christiansen, MSc (research assistant, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Ming Ding (associate research professor, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Ulrik Frandsen, MSc, PhD (assistant research professor, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Chen Li, MSc (assistant research professor, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Moustapha Kassem, professor, DMSc (consultant, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Steen Broch Laursen, PhD ((to 1 November) associate research professor, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Amer Mahmood, MSc (research assistant, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Ann Dorte Pørneki, MSc (research assistant, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Yu Zhentao, post.doc. (The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

PhD students

Malthe Kristiansen, MD (The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Other students

Mandana Azaldi (master student, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Nicholas Ditzel (master student, The Molecular Endocrinology Unit, Department of Endocrinology, Odense University Hospital)

Technical/administrative staff

Lone Christiansen, technician

Karin Dyrgaard, technician

Tina Hansen Barbisan, research secretary

Irene Lynfort, technician

Tina K.L. Nielsen, technician

Hanne Thayssen, technician

Clinical Nursing Research Group

Lone Hammelsvang (nurse, Department of Endocrinology, Odense University Hospital)

Grete Kirketerp, MPM, MSc student (head nurse, Department of Endocrinology, Odense University Hospital)

Dorthe Nielsen, MSc student (nurse, Department of Endocrinology, Odense University Hospital)

Anne Holm Nyland, MSc (nursing), RN (development nurse, Department of Endocrinology, Odense University Hospital)

Lillian Petersen (nurse, Department of Endocrinology, Odense University Hospital)

Mette Rothmann (nurse, Department of Endocrinology, Odense University Hospital)

The Bone and Calcium Research Group

Researchers

Bo Abrahamsen, PhD (consultant, Medical Department, Roskilde County Hospital Køge)

Kim Torsten Brixen, associate professor, PhD (consultant, Department of Endocrinology, Odense University Hospital)

Charlotte Ejersted, PhD (Senior House Officer, Department of Endocrinology, Odense University Hospital)

Lis Stilgren, PhD (Senior House Officer, Department of Endocrinology, Odense University Hospital)

PhD students

Palle Mark Christensen, MD

Anne-Christine Bay Jensen, MSc (Clinical Research Unit, Vejle Hospital)

Kent Kramme, MD (Department of Endocrinology, Odense University Hospital)

Nis Nissen, MD (Department of Endocrinology, Odense University Hospital)

Jesper Ryg, MD (Department of Endocrinology, Odense University Hospital)

Other students

Kariatta Koroma (medical student)

External researchers

Mikkel Højbjerg (House Officer, Hjørring Hospital)

Morten Frost Nielsen (House Officer, Sønderborg Hospital)

Rasmus Wulff (House Officer, Kolding Hospital)

Technical/administrative staff

Donna Arbuckle-Lund, technician

Elsebeth Byrge, secretary

Alice Christensen, secretary

Jeanett D. Jacobsen, secretary

Anette R. Madsen, technician

Bente Tøt, technician

Kirsten Westermann, technician

The Thyroid Research Group

Researchers

Steen Joop Bonnema, PhD (consultant, Department of Endocrinology, Odense University Hospital)

Thomas Heiberg Brix, MD, PhD (Senior House Officer, Department of Endocrinology, Odense University Hospital)

Daniel El-Fassi, MD (clinical assistant, Department of Endocrinology, Odense University Hospital)

Laszlo Hegediüs, DMSc (consultant, Department of Endocrinology, Odense University Hospital, ½ Novo Nordisk scholar)

PhD students

Helle Døssing, MD (consultant, Department of Otorhinolaryngology, Odense University Hospital)

Pia Skov Hansen, MD (Department of Endocrinology, Odense University Hospital)

Viveque Egsgaard Nielsen, MD (Department of Endocrinology, Odense University Hospital)

External researchers

Finn Noe Bennedbæk, PhD (staff specialist, Department of Endocrinology, Herlev County Hospital)

Malene Boas, MD (clinical assistant, House Officer, Department of Growth and Reproduction, Rigshospitalet)

Dorte Hansen, PhD (House Officer, Paediatric Department, Odense University Hospital)

Esther Jensen, MD (staff specialist, Department of Clinical Biochemistry, Genetics and Pharmacology, Odense University Hospital)

Kirsten Ohm Kyvik, PhD (associate professor, Institute of Public Health, Epidemiology, University of Southern Denmark)

Claus H. Nielsen, MD, PhD (Senior House Officer, Institute of inflammation research and Tissue Type Lab, Rigshospitalet)

Torquil Watt, MD (clinical assistant, Endocrine Clinic, Abdominal Center, Rigshospitalet)

Publications

1. *Abdallah BM, Jensen CH, Gutierrez G, Leslie RG, Jensen TG, Kassem M.* Regulation of human skeletal stem cells differentiation by Dlk1/Pref-1. *J Bone Miner Res* 2004; 19: 841-52.
2. *Abdallah BM, Stilgren LS, Nissen N, Kassem M, Jorgensen HR, Abrahamsen B.* Increased RANKL/OPG mRNA Ratio in Iliac Bone Biopsies From Women with Hip Fractures. *Calcif Tissue Int* 2004; Nov 18 [e-pub].
3. *Abildgaard N, Brixen K, Eriksen EF, Kristensen JE, Nielsen JL, Heickendorff L.* Sequential analysis of biochemical markers of bone resorption and bone densitometry in multiple myeloma. *Haematologica* 2004; 89: 567-77.
4. *Abrahamsen B og Brixen K.* Osteodensitometri. *Ugeskr Læg* 2004; 166: 578-82.
5. *Abrahamsen B, Nielsen TL, Hangaard J, Gregersen G, Vahl N, Korsholm L, Hansen TB, Andersen M, Hagen C.* Dose-, IGF-I- and sex-dependent changes in lipid profile and body composition during GH replacement therapy in adult onset GH deficiency. *Eur J Endocrinol* 2004; 150: 671-9.
6. *Andersen-Ranberg K, Wiik A, Høier-Madsen M, Jeune B, Hegedüs L.* High prevalence of autoantibodies among Danish centenarians. *Clin Exp Immunol* 2004; 138: 158-63.
7. *Bayer Y, Neumann S, Meyer B, Rüschenhoff F, Reske A, Brix TH, Hegedüs L, et al.* Genome-wide linkage analysis reveals evidence for four new susceptibility loci for familial euthyroid goiter. *J Clin Endocrinol Metab* 2004; 89: 4044-52.
8. *Beck-Nielsen H.* The combined effect of triple therapy with rosiglitazone, metformin and insulin aspart in type 2 diabetic patients: response to Davidson and Mikhail. *Diabetes Care* 2004; 27: 1847-48.

9. *Beck-Nielsen H, Alford F, Hother-Nielsen O.* Insulin Resistance in Glucose Disposal and Production in Man with specific reference to Metabolic Syndrome and Type 2 Diabetes. In: Kumar S, O'Rahilly S, eds. Insulin resistance – insulin action and its disturbances in disease. London: Wiley, 2004: chapter 6.
10. *Bonnema SJ, Bennedbaek FN, Veje A, Marving J, Hegedüs L.* Propylthiouracil before 131I therapy of hyperthyroid diseases: effect on cure rate evaluated by a randomized clinical trial. *J Clin Endocrinol Metab* 2004; 89: 4439-44.
11. *Bonnema SJ, Nielsen VE, Hegedüs L.* Long-term effects of radioiodine on thyroid function, size and patient satisfaction in non-toxic diffuse goitre. *Eur J Endocrinol* 2004; 150: 439-45.
12. *Brix TH, Hansen PS, Kyvik KO, Hegedüs L.* Aggregation of thyroid autoantibodies in first-degree relatives of patients with autoimmune thyroid disease is mainly due to genes. A twin study. *Clin Endocrinol* 2004; 60: 329-34.
13. *Brixen K, Christensen PM, Ejersted C, Langdahl BL.* Teriparatide (biosynthetic human PTH(1-34)) – A new paradigm in the treatment of osteoporosis. *Basic Clin Pharmacol Toxicol* 2004; 94: 260-70.
14. *Brixen K, Kassem M, Abrahamsen B.* Drugs used in osteoporosis. In: du Souich P, Erill S, Orme M, eds. *The IUPHAR Compendium of Basic Guidelines for Pharmacological Research in Humans.* Irvine: IUPHAR, 2004: 366-77.
15. *Brixen KT, Christensen PM, Ejersted C, Langdahl BL.* Gennembrud i behandlingen af osteoporose. *Leder i Ugeskr Læg* 2004; 166: 2649.
16. *Brusgaard K, Kjeldsen A D, Poulsen L, Moss H, Vase P, Rasmussen K, Kruse TA, Hørder M.* Mutations in endoglin (ENG) and in Activin Receptor-Like Kinase 1 (Alk1) among Danish patients with Hereditary Hemorrhagic Telangiectasia. *Clin Gen* 2004; 66: 556-61.

17. *Christiansen JJ, Gravholt CH, Fisker S, Svenstrup B, Bennett P, Veldhuis J, Andersen M, et al.* Dehydroepiandrosterone supplementation in women with adrenal failure: impact on twenty-four hour GH secretion and IGF-related parameters. *Clin Endocrinol* 2004; 60: 461-69.
18. *Damm P, Jensen DM, Ovesen P.* Hvornår har man gestationel diabetes? *Ugeskr Læg* 2004; 166: 3518-19.
19. *De Vroede M, Bax NMA, Brusgaard K, Dunne M, Groenendaal F.* Laparoscopic diagnosis and cure in 2 cases of neonatal focal hyperinsulinism. *Pediatrics* 2004; 114: 520-22.
20. *Fink T, Abildtrup L, Fogd K, Abdallah BM, Kassem M, Ebbesen P, et al.* Induction of adipocyte-like phenotype in human mesenchymal stem cells by hypoxia. *Stem Cells* 2004; 22: 1346-55.
21. *Gaster M, Beck-Nielsen H.* The Reduced Insulin Mediated Glucose Oxidation in Skeletal Muscle from Type 2 Diabetic Subjects may be of Genetic Origin – Evidence from Cultured Myotubes. *Biochem Biophys Acta* 2004; 1690: 85-91.
22. *Gaster M, Brusgaard K, Handberg A, Højlund K, Wojtaszewski JFP, Beck-Nielsen H.* The primary defect in glycogen synthase activity is not based on glycogen synthase kinase-3 activity in diabetic myotubes. *Biochem Biophys Res Comm* 2004; 319: 1235-40.
23. *Gaster M, Handberg A, Schurmann A, Joost HG, Beck-Nielsen H, Schroder HD.* GLUT11, but not GLUT8 or GLUT12, is expressed in human skeletal muscle in a fibre type-specific pattern. *Pflugers Arch* 2004; 448: 105-13.
24. *Gaster M, Rustan AC, Aas V, Beck-Nielsen H.* Reduced lipid oxidation in skeletal muscle from type 2 diabetic subjects may be of genetic origin: evidence from cultured myotubes. *Diabetes* 2004; 53: 542-48.

25. *Glintborg D, Henriksen JE, Andersen M, Hagen C, Hangaard J, Rasmussen PE, Schousboe K, Hermann AP.* The prevalence of endocrine diseases and abnormal glucose tolerance tests in 340 Caucasian, premenopausal women with hirsutism as primary diagnosis. *Fertil Steril* 2004; 82: 1570–79.
26. *Hagen ML, Hellmers M, Abrahamsen B, Hagen C.* Østrogeneres molekylære virkemekanismer – Basale aspekter. *Ugeskr Læg* 2004; 166: 1216.
27. *Hagen ML, Hellmers M, Abrahamsen B, Hagen C.* Østrogeneres molekylære virkemekanismer – Kliniske aspekter, herunder industrielle østrogener og fytoøstrogener. *Ugeskr Læg* 2004; 166: 1220.
28. *Hansen L, Gaster M, Oakeley EJ, Brusgaard K, Damsgaard Nielsen EM, Beck-Nielsen H, et al.* Expression profiling of insulin action in human myotubes: induction of inflammatory and pro-angiogenic pathways in relationship with glycogen synthesis and type 2 diabetes. *Biochem Biophys Res Commun* 2004; 323: 685-95.
29. *Hansen PS, Brix TH, Bennedbæk FN, Bonnema SJ, Kyvik KO, Hegedüs L.* Genetic and environmental causes of individual differences in thyroid size: a study of healthy Danish twins. *J Clin Endocrinol Metab* 2004; 89: 2071-77.
30. *Hansen PS, Brix TH, Sørensen TIA, Kyvik KO, Hegedüs L.* Major genetic influence on the regulation of the pituitary-thyroid axis. A study of healthy Danish twins. *J Clin Endocrinol Metab* 2004; 89: 1181-87.
31. *Hansson M, Tonning A, Frandsen U, Petri A, Rajagopal J, Englund MC, et al.* Artifactual insulin release from differentiated embryonic stem cells. *Diabetes* 2004; 53: 2603-9.
32. *Hegedüs L.* Thyroid nodule. In: Martini L, ed. *The Encyclopedia of Endocrinology and Endocrine Diseases*. San Diego: Academic Press, 2004; 4: 521-29.

33. *Hegedüs L*. The thyroid nodule. *N Engl J Med* 2004; 351: 1064-71.
34. *Hegedüs L*. Thyroid ultrasonography as a screening tool for thyroid disease. *Thyroid* 2004; 11: 879-80.
35. *Hegedüs L, Brix TH, Vestergaard P*. Relation between cigarette smoking and Graves' ophthalmopathy. *J Endocrinol Invest* 2004; 27: 265-71.
36. *Heldgaard PE, Olivarius NF, Hindsberger C, Henriksen JE*. Impaired fasting glycaemia resembles impaired glucose tolerance with regard to cardiovascular risk factors. *Diabetic Medicine* 2004; 21: 363-70
37. *Holten MK, Zacho M, Gaster M, Juel C, Wojtaszewski JF, Dela F*. Strength Training Increases Insulin-Mediated Glucose Uptake, GLUT4 Content, and Insulin Signaling in Skeletal Muscle in Patients With Type 2 Diabetes. *Diabetes* 2004; 53: 294-305.
38. *Hyltoft Petersen P, Blaabjerg O, Andersen M, Jorgensen LG, Schousboe K, Jensen E*. Graphical interpretation of confidence curves in rankit plots. *Clin Chem Lab Med* 2004; 42: 715-24.
39. *Højlund K, Hansen T, Lajer M, Henriksen JE, Levin K, Lindholm J, Pedersen O, Beck-Nielsen H*. A novel syndrome of autosomal-dominant hyperinsulinemic hypoglycemia linked to mutation in the human insulin receptor gene. *Diabetes* 2004; 53: 1592-98.
40. *Højlund K, Mustard KJ, Staehr P, Hardie DG, Beck-Nielsen H, Richter EA, et al*. AMPK activity and isoform protein expression are similar in muscle of obese subjects with and without type 2 diabetes. *Am J Physiol Endocrinol Metab* 2004; 286: E239-44.
41. *Jensen E, Petersen PH, Blaabjerg O, Hansen PS, Brix TH, Kyvik KO, Hegedüs L*. Establishment of a serum thyroid stimulating hormone (TSH) reference interval in healthy adults. The importance of environmental factors, including thyroid antibodies. *Clin Chem Lab Med* 2004; 42: 824-32.

42. *Jensen DM, Damm P, Moelsted-Pedersen P, Ovesen P, Westergaard JG, Moeller M, Beck-Nielsen H.* Outcomes in Type 1 diabetic pregnancies: A nation-wide population based study. *Diabetes Care* 2004; 27: 2819-23.
43. *Justesen J, Mosekilde L, Holmes M, Stenderup K, Gasser J, Mullins JJ, Seckl JR, Kassem M.* Mice deficient in 11beta-hydroxysteroid dehydrogenase type 1 lack bone marrow adipocytes, but maintain normal bone formation. *Endocrinology* 2004; 145: 1916-25.
44. *Justesen J, Pedersen SB, Stenderup K, Kassem M.* Subcutaneous adipocytes can differentiate into bone-forming cells in vitro and in vivo. *Tissue Eng* 2004; 10: 381-91.
45. *Kassem M.* Mesenchymal stem cells: biological characteristics and potential clinical applications. *Cloning Stem Cells* 2004; 6: 369-74.
46. *Kassem M, Kristiansen M, Abdallah BM.* Mesenchymal stem cells: cell biology and potential use in therapy. *Basic Clin Pharmacol Toxicol* 2004; 95: 209-14.
47. *Lauenborg J, Hansen T, Jensen DM, Vestergaard H, Mølsted-Pedersen L, Hornnes P, et al.* Increasing incidence of diabetes after gestational diabetes mellitus – A long-term follow-up in a Danish population. *Diabetes Care* 2004; 27: 1194-99.
48. *Lauenborg J, Hansen T, Jensen DM, Vestergaard H, Mølsted-Pedersen L, Hornnes P, et al.* Increasing Incidence of Diabetes After Gestational Diabetes. *Obstet Gynecol Surv* 2004; 59: 696-97.
49. *Levin K, Hother-Nielsen O, Henriksen JE, Beck-Nielsen H.* Effect of troglitazone in young first-degree relatives of patients with type 2 diabetes. *Diabetes Care* 2004; 27: 148-54.
50. *Lindholm J, Hagen C, Kosteljanetz M, Kristensen LØ, Laurberg P, Weeke J.* Relation between Pre- and Post-Dexamethasone Test Cortisol Values in Cushing's Disease. In *J Endocrinol Metab* 2004; 2: 74-77.

51. *Ling C, Poulsen P, Carlsson E, Ridderstrale M, Almgren P, Wojtaszewski J, Beck-Nielsen H, et al.* Multiple environmental and genetic factors influence skeletal muscle PGC-1alpha and PGC-1beta gene expression in twins. *J Clin Invest* 2004; 114: 1518-26.
52. *Malmström J, Lindberg H, Lindberg C, Bratt C, Wieslander E, Delander E-L, Särnstrand B, Burns JS, et al.* Transforming growth factor-beta specifically induces proteins involved in the myofibroblast contractile apparatus. *Mol Cell Proteomics* 2004; 3: 466-77.
53. *Meunier PJ, Roux C, Seeman E, Ortolani S, Badurski JE, Spector TD, Beck-Nielsen H, et al.* The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis. *N Engl J Med* 2004; 350: 459-68.
54. *Nielsen CH, Hegedüs L, Leslie RGQ.* Autoantibodies in autoimmune thyroid disease promote immune complex formation with self antigens and increase B cell and CD4⁺ T cell proliferation in response to self antigens. *Eur J Immunol* 2004; 34: 263-72.
55. *Nielsen LR, Ekbom P, Damm P, Glümer C, Frandsen MM, Jensen DM, et al.* Hemoglobin A1c levels are significantly lower in early and late pregnancy. *Diabetes Care* 2004; 27: 1200-01.
56. *Nielsen TL, Wraae K, Brixen KT, Andersen M, Hagen C.* Odense Androgen Study. *Ugeskr Læg* 2004; 166: 1449-51.
57. *Nielsen VE, Bonnema SJ, Hegedüs L.* Effects of 0.9 mg recombinant human thyrotropin on thyroid size and function in normal subjects: a randomized, double-blind, cross-over trial. *J Clin Endocrinol Metab* 2004; 89: 2242-47.
58. *Nielsen VE, Bonnema SJ, Hegedüs L.* The effects of recombinant human thyrotropin, in normal subjects and patients with goitre. *Clin Endocrinol* 2004; 61: 655-663.
59. *Nyland AH, Kirketerp G, Kragh-Sørensen A, Møller K, Hagen B.* På Bølgelængde – et serviceskolekoncept. *Klin Sygepl* 2004; 18: 67-71.

60. Rejnmark L, Vestergaard P, Jensen LB, Bärenholdt O, Nielsen SP, Abrahamsen B, Brixen K, et al. Response rates to oestrogen treatment in perimenopausal women: Five-years data from The Danish Osteoporosis Prevention Study (DOPS). *Maturitas* 2004; 15: 307-20.
61. Rejnmark L, Vestergaard P, Kassem M, Christoffersen BR, Kolthoff N, Brixen K, et al. Increased fracture risk in women treated with beta blockers. *Calcif Tissues Int* 2004; 75: 365-72.
62. Rix M, Hertel NT, Nielsen FC, Jacobsen BB, Hojberg AS, Brixen K, et al. Cushing's disease in childhood as the first manifestation of multiple endocrine neoplasia syndrome type 1 (MEN1). *Eur J Endocrinol* 2004; 151: 709-15.
63. Schousboe K, Visscher PM, Erbas B, Kyvik KO, Hopper JL, Henriksen JE, Heitmann BL, Sørensen TIA. Twin Study of Genetic and Environmental Influences on Adult Body Size, Shape, and Composition. *Int J Obes Relat Metab Disord* 2004; 28: 39-48.
64. Schwarz P, Brixen K, Laursen LC, Nielsen LP. Inhalationssteroider og risiko for osteoporose – update. Review. *Rationel Farmakoterapi* 2004; 8: 1-3.
65. Serakinci N, Guldberg P, Burns JS, Abdallah B, Schrodder H, Jensen T, Kassem M. Adult human mesenchymal stem cell as a target for neoplastic transformation. *Oncogene* 2004; 23: 5095-8.
66. Stenderup K, Rosada C, Justesen J, Al-Soubky T, Dagnaes-Hansen F, Kassem M. Aged human bone marrow stromal cells maintaining bone forming capacity in vivo evaluated using an improved method of visualization. *Biogerontology* 2004; 5: 107-18.
67. Stilgren LS, Rettmer E, Eriksen EF, Hegedüs L, Beck-Nielsen H, Abrahamsen B. Skeletal changes in osteoprotegerin and receptor activator of nuclear factor – KB ligand mRNA levels in primary hyperparathyroidism: effect of parathyroidectomy and association with bone metabolism. *Bone* 2004; 35: 256-65.

68. *Stæhr P, Hother-Nielsen O, Beck-Nielsen H.* The role of the liver in Type 2 diabetes. *Rev Endocrin Metab Dis* 2004; 5: 105-10.
69. *Støvring H, Andersen M, Beck-Nielsen H, Green A, Vach W.* Stigende diabetesprævalens og faldende mortalitet på Fyn. *Ugeskr Læg* 2004; 166: 1905-07.
70. *Tan Q, Brusgaard K, Kruse TA, Oakley E, Hemmings B, Beck-Nielsen H, Hansen L, Gaster M.* Correspondance analysis of microarray time-course data in case control design. *Biomed Inf* 2004; 37: 358-65.
71. *Westergaard LG, Yding Andersen C, Erb K, Laursen SB, Rasmussen PE, Rex S, Teisner B.* Serum concentrations of PP14 (Glycodelin) in relation to hormonal parameters and outcome of ART in women undergoing ovarian stimulation with GnRh agonist and gonadotropins. *RBM Online* 2004; 8: 91-98.
72. *Wulff R, Abrahamsen B, Ejerdsted C, Christensen PM, Brixen K.* Komplians ved behandling af osteoporose med bisphosphonater. *Ugeskr Læg* 2004; 166: 49-53.
73. *Wulff R, Koch Holst A, Nielsen TL, Andersen M, Hagen C, Brixen K.* Morphometric X-ray absorptiometry (MXA): Reference data for vertebral dimensions in a population based sample of young Danish men. *Acta Radiol* 2004; 45: 859-65.

Internal meetings and lectures 2004

3 February: Christian Mogensen: Hypokalaemia.

10 February: Lectures by the Diabetes Research Group.

17 February: Tue Hassenkam, Nano-Science Center, University of Copenhagen: Bone strength estimated nano-technically.

24 February: Claus Juhl: Insulin pulsation.

2 March: Søren Sindrup, Department of Neurology, OUH: Diabetic neuropathy and Ulrik Hintze: Autonome neuropathy and heart function.

9 March: Lectures by the Thyroid Research Group: 1) Esther Jensen, staff specialist, Department of Clinical Biochemistry, Genetics and Pharmacology, OUH: Definition of serum calcitonine (on Immulite) as routine method at the department and 2) Ole Blaabjerg, MSc, Department of Clinical Biochemistry, Genetics and Pharmacology, OUH: Establishment of serum calcitonine (on Immulite) as routine method at the department.

16 March: KMEB lecture by Professor, PhD, Jørgen Kjems, Institute of Molecular Biology, Aarhus University: Control of Gene Expression by siRNA and miRNA expression.

23 March: Christian Mogensen: Malaria in Africa – PhD project.

30 March: Bone radiology - hands-on. Joint meeting with the Department of Radiology, OUH.

13 April: Viveque Egsgaard Nielsen: Recombined TSH and radio-iodine treatment of non-toxic goitre.

20 April: Troels Andreassen, Institute of Anatomy, Aarhus University: Anabolic effects of PTH on bone tissue and healing of fractures.

27 April: Niels Elkjær, Department of Ophthalmology, OUH: Octopus perimetry.

11 May: Kim Brixen: Patient safety – new law and new possibilities.

18 May: Lectures by KMEB.

25 May: Steen Bonnema: The good medical department (DGMA) - cross section study 2003/2004.

8 June: Svend Stenvang: Meningitis and pneumonia.

15 June: Consultant, DMSc Jesper Hallas, Medical Department, OUH: Practical AK treatment.

7 September: Lectures by the Bone and Calcium Research Group: Diseases in the calcium receptor: 1) Morten Frost Nielsen: A family of autosome dominant hypoparathyroidism; 2) Kim Brixen: Polymorphies in the calcium receptor; and 3) Moustapha Kassem: Auto-antibodies against the calcium receptor.

5 October: Lectures by the Pituitary Gland Research Group: Claus Hagen: Prolactin – new aspects.

19 October: Claus Lykkelund Petersen: Plasma glucagon response to insulin-induced hypoglycaemia and arginine in normal subjects and alloxan diabetic rats.

9 November: Aase Handberg, Randers Central Hospital: CD36 and diabetes.

16 November: Niels Elkjær, Department of Ophthalmology, OUH: Octopus perimetry.

23 November: Lectures by the Diabetes Research Group: Henning Beck-Nielsen: Hypoglycaemia.

30 November: Torben Bjerregaard Larsen, Department of Clinical Biochemistry, Genetics and Pharmacology, OUH: AK treatment and self-monitored AK treatment and Kirsten Bahrt, Roche a/s: Presentation of apparatus CoaguChekS to be employed in connection with self-monitored AK treatment on Skejby, Brødstrup and Gentofte Hospitals.

7 December: Course in treatment of cardiac arrest.

14 December: Christoffer Hedelund: Amputation frequency by diabetic ulcers – an estimation from the center in Køge.

18 December: EFE Christmas seminar. Invited speaker: Head of clinic, professor, DMSc Liselotte Højgaard, Department of Clinical Physiology and Nuclear Medicine, Rigshospitalet: PET-scanning.

Selected, invited lectures held by EFE members at international congresses and meetings

The Diabetes Research Group

Henning Beck-Nielsen, professor, consultant, DMSc

- Twin studies of beta-cell function, Baltic Summer School, Lund, Sweden (25-27 August).
- The combined effect of Triple Therapy with Rosiglitazone, Metformin and Insulin Aspart in Type 2 Diabetic patients – a new treatment based on self-monitored blood glucose values and timely adjusted treatment schemes, Taiwan, Hong Kong (12-22 September).
- The Dysmetabolic Syndrome. Danish Society for Internal Medicine, symposium on The Metabolic Syndrome, Herlev, Denmark (11 November).

Kurt Højlund, Senior House Officer, PhD

- Increased intramyocellular lipid content in type 2 diabetes may involve dysregulation of the liver X receptor. Galileo – Innovators in Diabetes and Metabolic Syndrome, Venice, Italy (21-23 October).

The Molecular Endocrinology Unit (KMEB)

Moustapha Kassem, professor, consultant, DMSc

- European Calcified Tissue Society Annual meeting, Nice, France (5-9 June).

- European Calcified Tissue Society Training Course on Mesenchymal Stem Cell, Wuerzburg, Germany (14-16 June).
- American Society of Bone and Mineral Research Annual Meeting, Seattle, USA (1-5 October).
- Stem cells and telomerase, British Society for Cancer Research, Cyprus (12-16 October).

Clinical Nursing Research Group

Grete Kirketerp, head nurse, MPM, and *Anne Holm Nyland*, development nurse, MSc (nursing), RN.

- Implementing evidence based practice. The 3rd Conference of Clinical Practice – Research and Development in Nursing (August).

The Bone and Calcium Research Group

Kim Brixen, consultant, PhD

- What is new in bisphosphonates. Davos, Switzerland (24-26 March)
- XXVth European Symposium on Calcified Tissues, Nice, France (5-9 June)
- 26th Annual Meeting of the American Bone and Mineral Research Society (ASBMR), Seattle, USA

The Thyroid Research Group

Laszlo Hegedüs, consultant, DMSc

- Treatment of multinodular non-toxic goiter. The New England Thyroid Club, Massachusetts Medical Society Conference Center at Waltham Woods, Boston, USA (2 April).
- Evaluation of rhTSH usage in the treatment of non-toxic multinodular goiter. Symposium on innovative approaches for the treatment of benign and malignant thyroid disease. The Endocrine Society Annual Meeting 2004, New Orleans, LA, USA (16-19 June).
- Advantages and disadvantages of radioiodine (131-I) therapy in benign multinodular non toxic goiter. Has the time come for rhTSH usage? Belgian Thyroid Club, Brussels, Belgium (4 December).
- Role of ultrasonography in benign and malignant thyroid neoplasias. 10th Annual Symposium of the Dutch Thyroid Club, Amsterdam, The Netherlands (15-16 December).

Steen Bonnema, consultant, DMSc

- Management of nodular goiter. A review. Annual Congress of the European Association of Nuclear Medicine. Helsinki, Finland (September).
- Management of goitre. A review. German Society for Nuclear Medicine. Würzburg, Germany (15 October).

Courses 2004 organised by the PhD Graduate School of Metabolism

- 7 – 18 June:** **Advanced applied fluorescence microscopy.**
Course directors: Associate professor Susanne Mandrup and associate professor Nils Færgeman, Institute of Biochemistry and Molecular Biology, University of Southern Denmark.
- 30 August –
2 September:** **DNA-MicroArray technology in clinical and basic research.**
Course director: Professor Torben Kruse, Human MicroArray Center, Odense University Hospital.
- 26 - 29 September:** **PhD Summer School in Functional Genomics and Proteomics as Applied to Metabolic Diseases.**
Course director: Professor Henning Beck-Nielsen, Department of Endocrinology, Odense University Hospital.
See programme on page 50.
- November:** **Advanced methods of protein chemistry: mass spectrometry/ proteomics.**
Laboratory course in advanced protein chemistry and mass spectrometry.
Course director: Associate professor Ole Nørregaard Jensen, Institute of Biochemistry and Molecular Biology, University of Southern Denmark.

Programme
PhD Summer School 2004
Functional Genomics and Proteomics as Applied to Metabolic Diseases
26 – 29 September 2004

Sessions:

- I Basic Technologies
- II Metabolic Regulation
- III Metabolic Regulation continued
- IV Type 2 Diabetes and Mitochondria
- V Genetics
- VI Workshops on Metabolic Regulation
- VII Bone Biology

Lecturers:

- Professor *Henning Beck-Nielsen*, Dept. of Endocrinology, OUH
- Dr. *Jean-Marie Delaissé*, Clinical Research Unit, Vejle Hospital
- *Jan Fleckner*, Novo Nordisk A/S
- Assistant research professor *Ulrik Frandsen*, KMEB, OUH
- Senior House Officer *Aase Handberg*, DMSc, Clinical Biochemistry, Randers Central Hospital
- Dr. *Torben Hansen*, Steno Diabetes Center, Gentofte
- Professor *Cecilia Holm*, University of Lund, Sweden
- Senior House Officer *Kurt Højlund*, PhD, Dept. of Endocrinology, OUH
- Professor *Jens Knudsen*, Institute of Biochemistry and Molecular Biology, SDU
- Professor *Karsten Kristiansen*, Institute of Biochemistry and Molecular Biology, SDU
- Professor *Torben Kruse*, Human MicroArray Center, OUH

- Associate professor *Kirsten Ohm Kyvik*, Institute of Public Health, SDU
- Professor *Larry Mandarino*, Arizona State University, USA
- Professor *Matthias Mann*, Institute of Biochemistry and Molecular Biology, SDU
- Professor *Jan Nedergaard*, The Wenner-Gren Institute, Stockholm University, Sweden
- Dr. *Claus Nerlov*, European Molecular Biology Laboratory, Monterotondo, Italy
- Assistant professor *Akhilesh Pandey*, McKusick-Nathans Institute of Genetic Medicine, Baltimore, USA
- Professor *Leena Peltonen-Palotie*, National Public Health Institute, Helsinki, Finland
- Professor *Stuart Ralston*, University of Aberdeen, United Kingdom
- Professor *Kent Sahlin*, Institute of Sports Science and Clinical Biomechanics, SDU
- Professor *Jonathan Seckl*, School of Molecular and Clinical Medicine, Edinburgh University, United Kingdom
- Dr. *Victor Zammit*, Hannah Research Institute, Ayr, United Kingdom
- Consultant Allan Vaag, DMSc, PhD, Steno Diabetes Center, Gentofte

Completed scientific theses 2004

Master theses

- **Patricia Anne-Marie Zeemann**. Proteome analysis of membrane proteins in human mesenchymal stem cells (24 June).

PhD theses

- **Lis Stilgren**. Molecular mechanisms of parathyroid hormone action on the skeleton in primary hyperparathyroidism (25 June).

Scientific awards

- **Ole Hother-Nielsen**, consultant, DMSc
The Bagger-Sørensen Foundation Honor Bursary (DKK 50,000)
- **Kurt Højlund**, Senior House Officer, PhD
Helmer Lausten's Memory Bursary (recommended by the Danish Diabetes Foundation) (DKK 50,000)
- **Moustapha Kassem**, professor, consultant, DMSc
The Danish Mason Research Award (DKK 100,000)
- **Dorthe Nielsen**, nurse
The Bone & Joint Decade 2000-2010 (DKK 10,000)
- **Mette Rothmann, Lone Hammelsvang, Lillian Petersen, diabetes nurses**
Anne Holm Nyland, development nurse, MSc (nursing), RN, and Grete Kirketerp, head nurse, MPM, MSc student (nursing)
The Bagger Sørensen Foundation, prize essay regarding the project We got eyes for you.

Financial support to EFE from institutions and foundations

EFE has been supported by the following contributors:

Institutions and foundations

	DKK
• The A. J. Andersen Foundation	
<i>H. Døssing</i>	24,000
• The Alfred Benzon Foundation	
<i>B. Abdallah</i>	25,000
..... and a 1 year research scholarship	
• The Johan Boserup and Lise Boserup Bursary	
<i>V.E. Nielsen</i>	30,000
• The M. Brogaard and Wife Memory Foundation	
<i>U. Frandsen</i>	25,000
• The Hertha Christensen Foundation	
<i>K. Brixen and R. Scheller</i>	5,000
• The Consultant Bursary Committee, Odense University Hospital	
<i>V.E. Nielsen</i>	15,000
<i>T.L. Nielsen</i>	25,000
• The Danish Bone Society	
<i>J. Ryg</i>	5,000
• The Danish Diabetes Foundation	
<i>H. Beck-Nielsen</i>	200,000

<i>U. Frandsen</i>	40,000
<i>M. Gaster</i>	40,000
<i>D. Glintborg</i>	70,000
<i>D.M. Jensen</i>	4,500
<i>T.B. Nielsen</i>	60,000
• The Danish Medical Association's Research Foundation	
<i>D. Glintborg</i>	50,000
<i>J.E. Jensen</i>	20,000
• The Danish Research Agency, The Danish Medical Research Council	
<i>H. Beck-Nielsen</i> (3 year framework grant of each)	500,000
<i>H. Beck-Nielsen</i> (scholarship for M.J. Pedersen)	139,175
<i>H. Beck-Nielsen</i> (3 year grant for co-financed PhD scholarships of each)	150,000
<i>M. Ding</i>	600,000
<i>U. Frandsen</i>	200,000
<i>A. Handberg</i>	300,000
<i>P.S. Hansen</i>	1,120,000
<i>O. Hother-Nielsen</i>	300,000
<i>M. Kassem</i>	400,000
<i>S.B. Laursen</i>	300,000
• The Danish Rheumatism Association Foundation	
<i>M. Ding</i>	120,000
• Danish Stem Cell Research Center (DASC)	
<i>M. Kassem</i>	300,000
• The Danish Thyroid Association	
<i>S. Bonnema</i>	12,500
<i>V.E. Nielsen</i>	50,000

• The Foundation of 17.12.1981	
<i>P.S. Hansen</i> (PhD scholarship).....	150,000
• Funen County Foundation of Medical Research	
<i>D. Glintborg</i>	20,000
<i>V.E. Nielsen</i>	32,000
• The Funen County and Province Funds	
<i>H. Beck-Nielsen</i>	400,000
• The Eva and Henry Fränkel Memory Foundation	
<i>M. Kristiansen</i>	55,000
• The Poul and Erna Sehested Hansen Foundation	
<i>J.E. Henriksen</i>	75,000
• The Health Foundation of the Sick-Benefit Association	
<i>K. Brixen</i>	100,000
• The Bernard and Marie Klein Bursary for Diabetes Research	
<i>U. Frandsen</i>	10,000
<i>K. Højlund</i>	10,000
• Manager Jacob Madsen's and Wife Olga Madsen's Foundation	
<i>D. Glintborg</i>	20,000
<i>M. Kassem</i>	15,000
• The Medical Promotion Foundation, The A.P. Møller and Wife Chastine Mc-Kinney Møller Foundation of General Purposes	
<i>B. Abrahamsen</i>	75,000
<i>P.S. Hansen</i>	35,000
<i>K. Højlund</i>	40,000

<i>J.E. Jensen</i>	20,000
• The Music Publishers Agnes and Knut Mørk's Foundation	
<i>D. El-Fassi</i>	50,000
• The Novo Nordisk Foundation	
<i>B. Abrahamsen</i> (clinical research scholarship)	220,000
<i>J. Burns</i>	125,000
<i>M. Gaster</i>	150,000
<i>A. Handberg</i>	162,383
<i>L. Hegedüs</i> (3 year research grant, per year).....	333,333
<i>O. Hother-Nielsen</i>	250,000
<i>K. Højlund</i>	250,000
• The Regional Development Plan, Funen County	
<i>H. Beck-Nielsen</i>	12,000,000
• University of Southern Denmark, Institute of Clinical Research	
<i>H. Beck-Nielsen</i>	96,000
<i>M. Kasseem</i>	200,000
<i>V.E. Nielsen</i>	37,952
<i>V.E. Nielsen</i>	22,000
<i>T.L. Nielsen</i>	80,000
• University of Southern Denmark, 7 PhD scholarships (approx.).....	2,450,000
• The VELUX FOUNDATION	
<i>H. Beck-Nielsen</i>	3,000,000

Commissioned research and support from pharmaceutical companies

Approx. DKK 2,5 million

- Aventis Pharma (DKK 25,000)
- AstraZeneca (DKK 710,500)
- DeveloGen (DKK 365,500)
- Eli Lilly (DKK 120,000)
- Genzyme (DKK 100,000)
- GlaxoSmithKline (DKK 54,400)
- Maxygen (DKK 150,000)
- Novartis (DKK 290,000)
- Roche (DKK 718,000)
- Servier (DKK 51,000)