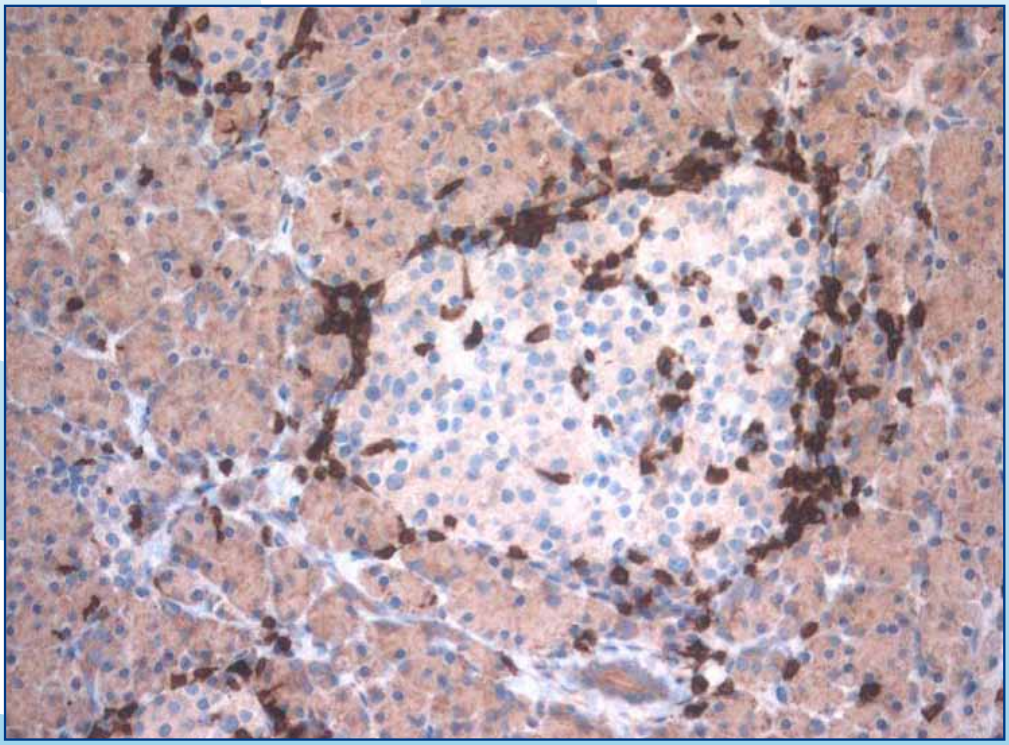
Oslo Diabetes Research Centre



ANNUAL REPORT 2011

CONTENT

Picture front page: The picture shows CD3 + T-cells surrounding and infiltrating a Langerhans islet with beta cells. This inflammation, named insulitis, is seen in recent onset T1D, as in this patient included in the DiViD-study (se page 7) The biopsy was collected approximately 4 weeks after T1D was verified.

Steering Committee for Oslo Diabetes Research Centre

- Kåre I. Birkeland, Professor dr.med.
- Knut Dahl-Jørgensen, Professor dr.med.
- Kristian F. Hanssen, Professor dr.med.
- Geir Joner, Professor dr.med.
- Benedicte Lie, Professor dr.philos.
- Dag Undlien, Professor dr.med.
- Trond G. Jenssen, Professor dr.med.
- Tore Henriksen, Professor dr.med.
- Jens Bollerslev, Professor dr.med.
- Jens Petter Berg, Professor dr.med.
- Beth Tyrdal, Research secretary

Board for Aker and Ullevål Diabetes Research Fund

- Knut Dahl-Jørgensen, Professor dr.med.
- Kristian F. Hanssen, Professor dr.med.
- Erik Schultz, MBA
- Per M. Thorsby, Consultant

Collaborating partners

Oslo University Hospital

- Harald Arnesen, Professor dr.med., Cardiology Dep
- Ragnheidur Bragadottir, Consultant dr.med., Ophthalmological Dep
- Magne Brekke, Consultant, Dep of Interventional Radiology
- Cathrine Brunborg, Statisticiane for Clinical Research
- Helene Holm, Midwife/Diabetes nurse, Dep of Obstetrics and Gynecology
- Peter Kierulf, Professor dr.med. (Em), Dep of Clinical Biochemistry
- Morten Fagerland, Ph.D., Centre for Clinical Research
- Leiv Sandvik, Ph.D., Centre for Clinical Research
- Ingard Holme, Professor, Centre for Clinical Research

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- Anders Hartmann, Professor, Dep of Nephrology
- Ludvig Sollid, M.D. Professor, Institute of Immunology
- Siri Vangen, Consultant dr.med., Centre for Women's health
- Haakon Stensæth, M.D., Dep Radiology
- Frode Lars Jahnsen, M.D. Ph.D., Dep of Pathology
- Bjørn Edwin, M.D. Ph.D., Dep of Surgery,
- Arne Rosseland, M.D. Ph.D., Dept of Surgery
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Department of Nutrition University of Oslo
- Lene Frost Andersen, Professor dr.philos.
- Christian A. Drevon, Professor dr.med.
- Per Ole Iversen, Professor dr.med.
- Svein Olav Kolset, Professor dr.philos.
- Hilde Nebb, Professor
- Margareta Wandel, Professor
- Line Grønning-Wang, Ph.D.

Norwegian Institute of public health
- Sidsel Graff-Iversen, Researcher Ph.D.
- Wenche Nystad, Ph.D.

Institute for general practice and public health, University of Oslo
- Gerd Holmboe-Ottesen, Professor dr.philos.
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- Finn Skårderud, Professor Ph.D.

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- Kristian Midthjell, Professor dr.med.

University of Bergen, Haukeland University Hospital
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- Pål Rasmus Njølstad, Professor dr.med., Dep of Pediatrics
- Oddmund Søvik, Professor dr.med. (Em), Dep of Pediatrics
- Trond Markestad, Professor dr.med., Dep of Pediatrics

Bergen University College
- Marit Graue, Ph.D., Assoc. Professor

University of Northern Norway
- Svein Ivar Mellgren, Professor dr.med., Dep of Neurology

Sunnås sykehus
- Nils Hjeltnes, Consultant dr.med.

Others
- Jacob R. Larsen, M.D. Ph.D., Medical Director

International Collaborators
- Prof Vincent Monnier, CWRU, Cleveland, Ohio, USA
- Prof Timothy Lyons, Oklahoma University, Oklahoma, USA
- Prof Alicia Jenkins, University of Melbourne, Australia
- Prof Johnny Ludvigsson, Linköping University, Sweden
- Prof Mikael Knip, Helsinki University, Finland
- Prof Heikki Hyöty, University of Tampere, Finland
- Prof John Todd, University of Cambridge, UK
- Flemming Poicot, Jim McGuire and Jørn Nerup, Steno Diabetes Centre, Copenhagen, Denmark
- Prof John Gerich, Rochester NY, USA
- Prof Michael Stumvoll, Tübingen, Germany
- Prof Ashimina Mitrakou, Athens, Greece
- Prof Timon van Haeften, Holland
- Prof Allan Flyvbjerg, Aarhus, Denmark
- Prof Steve Chadban, Sydney, Australia
- Prof Olle Korsgren, Uppsala, Sweden
- Prof Gun Frisk, University of Uppsala, Sweden
- Prof Bart Roep, Leiden University, Holland
- Prof Chittaranjan Yajnik, KEM Hospital, Pune, India
- Prof Johan Wens,University of Antwerp, Belgium

Kristian F. Hanssen
Another satisfactory year!

We are here focusing on some few areas in our research. For a more comprehensive survey, see the individual reports from the research groups.

The groups in pregnancy and diabetes (Anne Karen Jenum/Kåre Birkeland and Tore Henriksen/ Jens Bollerslev) are very active. New results show that gestational diabetes is much more common than thought, at least in Oslo. By the traditional WHO criteria 13 % had gestational diabetes, even more striking is that in pregnant women of Western European origin 11 % had gestational diabetes. This reflects profound changes in life style behavior among young women in Oslo at least. They have changed diet, exercise and are more overweight than before. In ethnic minorities, 15 % had gestational diabetes by the WHO criteria.

By the newly proposed IADPSG criteria based on the HAPO study, the numbers are staggering: gestational diabetes 24 % in Western European origin and 37 % in ethnic minorities! We are on the road to classify gestational diabetes as the new normality in pregnancy! This has profound influence on society. The Directorate on Public Health have realized this point and appointed a group to council on this matter. We see here the close cooperation between research and practical management of diabetes as both Jenum, Henriksen and myself are part of this group.

Vitamin D is popping up everywhere and new and unfounded hypotheses are abundant. To try to sort out some of the hypotheses, the type 2 diabetes research group has performed a randomized controlled study on high dose vitamin D in subjects with type 2 diabetes and low serum vitamin D: DIVINE study. The results of the study are eagerly awaited.

We still do not know what initiates the autoimmune process in type 1 diabetes, but our research centre has several new and important projects in this field (see individual research groups).

Regarding late diabetic complications, the nephrology group (Trond Jenssen) together with Svein Kolset at the Institute of Nutrition and my group are studying the long term consequences of kidney transplantation versus combined kidney and pancreas transplantation on the development of new diabetic nephropathy.

We are also pursuing the putative mechanisms of late complications, mostly oxidative stress and advanced glycation (AGE). We have developed collaboration with professor Monnier's group in Cleveland, USA. He is one of the foremost researchers in the field worldwide and he has analyzed skin biopsies in the Oslo study by LC MS/MS. We have new and exciting results coming up at the EASD meeting in Berlin this autumn. Furthermore, in close cooperation with the Department of Neurophysiology at Oslo University Hospital and Neurological Department of University of Northern Norway in Tromsø we have analyzed thin fiber neuropathy in long standing diabetes, a new field.

The collaboration with Institute of Nutrition is evolving. Christian Drevon has developed the isolated myocyte model together with co-workers. Muscle is a fascinating organ much more than thought. The evolving role of muscle as an endocrine organ is exciting. Many peptides are secreted from muscle, especially during exercise and influence metabolic processes in other organs.

The annual seminar (Solstua seminar) had a main focus on lipidomics. People doing research on diabetes may be too focused on glucose metabolism. There are exciting developments in the understanding of lipid metabolism. There is so much more to lipids than cholesterol and triglycerides!

We had excellent contributors: Matej Oresic, Christian Drevon and Tore Henriksen. Oresic from the technical university in Helsinki covered new methods in lipidomics (LC MS/MS). He also presented new data showing that lipids in blood may predict the development of type 1 diabetes. Furthermore, one of the Ph.D. students funded by Norwegian Research Council will stay in Oresic's lab to develop the methods in Oslo.

The venue was fantastic too: Early sunny spring weather at the new hotel at the seaside in Son!

Organizational development:
We have regular meetings for the steering group and have developed by-laws for the research centre. Furthermore, we are developing strategic plan for the future research.

We have funded three researchers to form two independent investigators group: Sedegheh Gharagzlia / Anne-Marie Aas and Torild Skrivarhaug. The idea is to develop mentors for future Ph.D. students.

The diabetes research in Oslo University Hospital is organized through Oslo Diabetes Research Centre which is a flexible and robust organization. However, the clinical work in adult diabetes in Oslo University Hospital is going through a difficult transitional phase as the practical organization for patients has still not been determined. To put it bluntly: There is no place for us anywhere!

I am reminded of the old game we used to play as children at Christmas time: The chair game (stol-leken).The music was playing, suddenly it stopped and there was one chair too few for the children playing. This child had to leave the game. We are in a similar situation for clinical diabetes: There is no room left for us! We trust that our administrators and the Hospital and University will extend their nice words in celebration talks into positive action to gather a strong environment for diabetes research in Oslo!

Political initiative:
On the political level, the ongoing obesity epidemic is really a challenge as it leads to a staggering rise in type 2 diabetes, also in Norway. However, very little has been achieved on the political level.

I have a dream: Jens Stoltenberg (the Premier Minister) is saying: Friends - we have a problem and we are going to face it in the following ways: By community actions - by legislation - by economic incentives and by health care actions. We are overruling Orkla, Rema, Meny, Kiwi, Rimi, McDonalds, Coca Cola, Statoil and Shell and will impose taxes on unhealthy food and reduce tax on healthy foods like vegetables, some fruits and fish. Advertisement for unhealthy food is curtailed. HURRAH!

Major Funding:
Regional Health Authority (Helse Sør-Øst), Oslo University Hospital, Medical Faculty, University of Oslo, Aker and Ullevål Diabetes Research Fund, Norwegian Research Council, Health and Rehabilitation, Norwegian Diabetes Association, EU grants.

Kristian F. Hanssen
Chairman Professor dr.med.

Leader	Work place	Research Area	Email
Kristian F. Hanssen (Chairman)	Department of Endocrinology, Oslo University Hospital	Diabetic late complications	k.f.hanssen@medisin.uio.no
Knut Dahl-Jørgensen (vice-chairman)	Pediatric Department, Oslo University Hospital	Diabetes in children and adolescents Etiology of type 1 diabetes, complications	knut.dahl-jorgensen @medisin.uio.no
Geir Joner	Pediatric Department, Oslo University Hospital	Epidemiology and etiology of type 1 diabetes, complications, mortality	geir.joner@medisin.uio.no
Benedicte Lie/ Dag Undlien	Department of Medical Genetics, Oslo University Hospital	Genetics and epigenetics of type 1 diabetes	b.a.lie@medisin.uio.no d.e.undlien@medisin.uio.no
Kåre I. Birkeland	Department of Endocrinology, Oslo University Hospital	Prevention and treatment of type 2 diabetes	k.i.birkeland@medisin.uio.no
Tore Henriksen/ Jens Bollerslev	Department of Endocrinology and Obstetrics, Oslo University Hospital	Diabetes and pregnancy	tore.henriksen@rikshospitalet.no jens.bollerslev@rikshospitalet.no
Trond Jenssen	Department of Nephrology, Oslo University Hospital	Diabetic nephropathy	trond.jenssen@rikshospitalet.no
Jens Petter Berg	Department of Biochemistry, Oslo University Hospital	Metabolomics of hyperglycemia	j.p.berg@medisin.uio.no

Group leader: Kristian F. Hanssen

Research Group: Diabetic late complications

Research focus:
Epidemiology and mechanisms of late complications.
The mechanism by which hyperglycaemia is so deleterious to large and small blood vessels is basically unknown. A leading hypothesis is that glycation (the chemical reaction between glucose or intracellular metabolites of glucose and proteins) and subsequent rearrangements (Advanced Glycation Endproducts AGE's) is a main culprit. We have developed unique assays for different AGE's (CML, hydroimidazolone and Glucosepane) in blood.
We have previously shown that serum AGE is associated with and predicts coronary heart disease in type 2 diabetes. Furthermore, that serum AGE is associated with micro-vascular complications.

Projects:

1. **30 years prospective study of late complications in type 1 diabetes (The Oslo Study).**

A. Prospective study: We have studied the progression of vascular changes, especially coronary vascular changes as measured by intravascular ultrasound (IVUS) and coronary angiography in the prospective Oslo Study and identified predictive parameters for this progression, especially AGE parameters.

B. Cross-sectional study: Assess both macro and microvascular status of the patients and associate with skin (measured in Dr. Monnier's lab, Cleveland, USA) and serum AGE. A number of parameters have been followed prospectively over 25 years, and have given valuable data for our cross-sectional study (together with many groups within OUS, especially dr. Brekke, Department of cardio-vascular radiology and dr. Fosmark, Department of Ophthalmology).

Specific aims:

- To study cardiac events; sub endpoints will be the vessel area stenosis, significant plaque (>0.5 mm) progression both on IVUS and coronary artery stenosis on coronary angiography.
- Serum and skin AGE, oxidative and inflammatory markers in relationship to complication status.

There are few studies that have examined long term complications and intensive diabetes treatment with such a long duration of the disease and it is a unique opportunity to study the relationship between complications and biochemical markers of complications.

2. **Glycation in the arterial wall.**
We are studying glycation modification in the arterial wall in atherosclerosis with and without diabetes by western analysis, immunohistochemistry and LC MS/MS (mass spectrometry). We have already discovered some modifications in the wall that might be involved in the increased propensity to atherosclerosis in diabetes.

3. **Advanced glycation of proteins and vascular complications in childhood diabetes** (together with Dahl-Jørgensens group).
Prospective study of early markers of atherosclerosis in a large group of adolescents with type 1 diabetes and controls - its relationship to glycation.

4. **Coronary and glomerular morphology in kidney transplants - Long term study in two contrasting groups. PI: Trond G. Jenssen** (together with Svein Kolset, Institute of Nutrition).
Study the effect of long-term normoglycaemia vs hyperglycaemia on changes in the coronary arteries and the renal function and structure in type 1 diabetes patients. Two groups of patients with type 1 diabetes are studied, one group transplanted with a single kidney (HbA1c 8-8.5%), the other who received combined kidney-pancreas grafts and has obtained perfect normoglycaemia over the same period of time (HbA1c 4.5-5.5%).

- To investigate proteoglycans and glycosaminoglycans which are important components of the filter network of the basement membrane.
- To explore proteoglycans (syndecan-1) and macrophage transcription factors (Id-1) in blood samples as markers of early kidney changes.
- Advanced Glycation Endproducts (AGE, CML, hydroimidazolone) by immunohistochemistry

in the glomerulus and in serum samples to test the hypothesis that glycation markers can predict the development and progression of late complication (specifically early diabetic nephropathy and coronary heart disease).

A two year study with neurography as the primary end point.

5. **Prospective study of pre-eclampsia in pregnant type 1 diabetes** (in collaboration with research groups in Australia and US).

Group members:

- Kari Anne Sveen, Ph.D. student
- Terje Lund, Ph.D.
- Bente K.Kilhovd, Consultant dr.med.
- Tore J. Berg, Consultant dr.med.
- Dag Fosmark, Consultant Ph.D. (Department of Ophthalmology)
- Peter Torjesen, Ph.D.
- Martin Heier, Ph.D. student (together with Dahl-Jørgensens group)
- Lars Krogvold, Ph.D. student (together with Dahl-Jørgensens group)
- Milaim Pepaj, Ph.D.

Group Leader: Knut Dahl-Jørgensen

Group name: Childhood Diabetes

Research focus:

The group has four main research areas.
The first is the ethiology and prevention of type 1 diabetes and autoimmune diseases, especially focusing the role of viruses and the interaction with the immune system in pancreatic and thyroid tissue samples.
The second area is diabetes late complications. We have long term clinical studies on microvascular complications and the influence of glycemic control and advanced glycation. Recently the risk of early atherosclerosis in type 1 diabetes has been the focus in several of our studies, with measurement of vessel wall thickness (IVUS, IMT, MRI) and vessel elasticity, and biochemical markers, as well as clinical data and risk factors. In our large, nationwide clinical studies, now as part of the Childhood Diabetes Registry, we focus important issues as intensified insulin treatment and pumps, diabetic nephropathy, diet, physical activity, quality of life and psychosocial problems.

Projects:

Aethiology and prevention of type 1 diabetes and autoimmune diseases:

1. Diabetes Virus Detection Project
2. Nordic Diabetes Prevention Trial
3. Disease eliciting T cell epitopes in type 1 diabetes
4. Genetic studies of the importance of copy-number polymorphism in the development of type 1 diabetes
5. Viruses, genetics and autoimmunity in thyroiditis. A biopsy study

Diabetes late complications:

6. Atherosclerosis in Childhood Diabetes
7. Long term vascular changes in type 1 diabetes – Clinical aspects and biological markers – 27 years follow-up of the Oslo Study
8. Advanced glycation of proteins and vascular complications in childhood diabetes
9. Diabetic nephropathy: Hypertension and microalbuminuria in Norwegian children with type 1 diabetes

Clinical diabetes:

10. Norwegian Childhood Diabetes and Quality project (NCDQ) - a nationwide prospective population-based study for research and quality improvement by means of benchmarking
11. Dietary intake, meal pattern and physical activity in children and adolescents with type 1 diabetes
12. Diabetes in body and mind. The theory of the specific psychological processes in type 1 diabetes
13. Children and adolescents with diabetes - present state and future possibilities - A population-based study of factors affecting competences and treatment results in children and adolescents with type 1 diabetes
14. Childhood diabetes and celiac disease – a population based study
15. Serotonin receptor mutations, psychological state and metabolic control in childhood diabetes
16. A systematic, nationwide study of diabetes team resources in paediatric departments

Obesity and type 2 diabetes:

17. Pathways to social inequalities in childhood weight development and overweight in Norway. Sub-study of the Mother and Child National Cohort.

Group members:

Ph.D. students:

- Hanna Dis Margeirsdottir, MD, Pediatrician. Projects: 6, 8, 9, 10, 13
- Lars Krogvold, MD, Pediatrician. Project 1, 2, 3
- Kari Anne Sveen, MD, Physician. Project 7
- Dag Helge Frøisland, MD, Pediatrician. Project 12,14
- Martin Heier, MD, Pediatrician. Project 8
- Sara Hammerstad, MD, Endocrinologist. Project 5
- Unni Mette Køpp, MD, Pediatrician. Project 16

Master students:

- Siv Janne Kummernes, R.N. Diabetes specialist nurse. Project 15
- Ingvild Ellingsrud, Medical student. Project 13
- Marie D. Tonga, Medical student. Project 13

Postdoc:

- Stig Tollefsen, Ph.D. Project 1, 3
- Nina Øverby, Dietician. Project 10

Senior Independent Investigators:

- Hans Jacob Bangstad, MD, Ph.D., Professor. Project 9
- Jon Haug, Dr. Philos, Clinical psychologist. Project 11

Group leader: Geir Joner

Group name: Childhood diabetes and epidemiology group

Research focus:

Epidemiology of diabetes, type 1 diabetes aetiology and prevention nutritional factors and viral infections as risk factor for childhood onset type 1 diabetes.
Diabetes complications, epidemiology of complications, adverse pregnancy outcome, mortality.
Obesity, intervention programs, risk of type 1 diabetes.
Health care research (quality measurements, quality indicators, inequalities in therapy and access to specialized health services).

Projects:

1. **Prospective study of diabetes in children and adolescents in Norway.** Study ongoing since 1989 collecting data on all newly-diagnosed cases of diabetes 0-17 years in Norway and biobanking. Personal, clinical data and biological samples for studies on the epidemiology and etiology of diabetes.PI: Prof. Geir Joner Co-PI: Prof. Pål R. Njølstad (Bergen) and Prof. Dag E. Undlien (Oslo). Collaborators: Lars Chr. Stene and Torild Skrivarhaug (Oslo).

2. **Epidemiology of complications, mortality and causes of death in Norway 1973-2010.** Clinical follow-up of different national cohorts of diabetes patients diagnosed 1973-1982, 1989-1998 and 1999-2010. Studies trends in mortality, temporal changes in causes of death and risk factors for premature death. PI: Torild Skrivarhaug. Co-PI: Prof. Geir Joner. Collaborators in clinical endocrinology, pathology and forensic medicine.

3. **Pregnancy outcome in families with type 1 diabetes.** Ph.D.-project. A study on pregnancy complications, malformations, prematurity and perinatal mortality in families where the mother or father has t1d. Record-linking between the Norwegian Childhood Diabetes Registry and the Medical Birth Registry of Norway. Ph-student Ingvild Eidem (MD). PI: Lars Chr. Stene. Collaborators: Prof. Tore Henriksen, Prof. Kristian F. Hanssen and Siri Vangen (MD, Ph.D.).

4. **Clinical characteristics/detailed description of phenotype of newly diagnosed children with diabetes;** 1000 newly diagnoses cases from the Norwegian Childhood Diabetes Registry with HLA, autoantibodies, family history and clinical data. PI: Prof. Geir Joner, Collaborators: Torild Skrivarhaug, Prof. Dag Undlien, Lars Chr. Stene, Prof. Pål R. Njølstad.

5. **Maternal virus infections and nutrition in pregnancy as risk factor for type 1 diabetes in children.** Ph.D.-project. Linking the Norwegian Childhood Diabetes Registry with serum samples from a cohort of 30 000 pregnant women. Studies on the role of vit. D, fatty and viral infections in the etiology of t1d. Ph student Ingvild Menes Sørensen. PI: Geir Joner, Co-PI: Lars Chr. Stene. Collaborators: Prof. Anne Eskild and Prof. Pål Jenum.

6. **The MIDIA-study.** The MIDIA-study, a prospective cohort study initiated at the NIPH in 2001. Newborns have been screened for HLA genes conferring risk for type 1 diabetes and enrolled for follow-up if carrying the high-risk genotype. These are followed with serial blood samples for islet autoantibody testing

and identification of biomarkers, as well as with very frequent stool samples for molecular identification of infections. The aim is to identify enteral viral infections as risk factors for t1d in children. PI: Per Magnus, NIPH. Collaborators: Kjersti Skjold Rønningen and Lars Chr. Stene.

7. **The MOBADIA study:** The Norwegian Mother and Child Cohort is established with data and biological samples from mother and child in pregnancy and by time of delivery. The cohort is set up to study causes of disease in mother and their offspring. This unique database will be linked to the Norwegian Childhood Diabetes Registry to study environmental risk factors and gene-environment interactions related to t1d. PI: Lars Chr. Stene. Co-PI: Prof. Geir Joner. Several national and international collaborators.

8. **Health consequences of obesity in children and adolescents.** Ph.D.-project. Follow up of a cohort of children and adolescents who was enrolled in an interventions project at Oslo University Hospital. Focus on cardiovascular risk factors and the effect of intervention. Ph.D. student Magnhild Pollestad Kolsgaard. PI: Prof. Geir Joner.

Group members:

- Group leader: Geir Joner, MD, Ph.D. Senior consultant at Dept. of Pediatrics, Oslo University Hospital Ullevål. Professor, Institute of Health and Society, Faculty of Medicine. University of Oslo. Project Manager. Supervisor for Ingvild Menes Sørensen and Magnhild P. Kolsgaard.
- Lars Chr. Stene, MSc, Ph.D., Researcher, Norwegian Institute of Public Health, Division of Epidemiology. Supervisor for Ingvild Eidem and Ingvild Menes Sørensen. Research area is etiology of type 1 diabetes and gene-environment interaction.
- Torild Skrivarhaug, MD, Ph.D., Director, The Norwegian Childhood Diabetes Registry. Research on diabetes complications and mortality. Supervisor for Vibeke Gagnum.
- Ingvild Menes Sørensen, MD, Ph.D. student. Research project: “Maternal virus infections and nutritional status during pregnancy and risk of type 1 diabetes in children.”
- Ingvild Eidem, MD, Ph.D. student. Research project: Pregnancy outcome in families with type 1 diabetes.
- Magnhild P. Kolsgaard, MSc (clinical nutritionist), Ph.D. student. Research project: Health consequences of obesity in children and adolescents (Subproject in “The Oslo Adiposity Intervention Study”).
- Kjersti S. Rønningen, MD, Ph.D., Senior researcher. Research area is etiology of type 1 diabetes with focus on environmental factors. The MIDIA-project.
- Vibeke Gagnum, MD. Planning to apply for Ph.D.-studies on a mortality project within our group.

Group leaders: Benedicte Lie/ Dag E. Undlien

Group name: Immunogenetics and epigenetics of autoimmune diseases

Research focus:

Our main research focus is to identify and characterize genetic factors which predispose to type 1 diabetes and other autoimmune diseases. We also explore epigenetic mechanisms and the functional relevance of risk variants regarding their influence of gene expression, as well as their clinical relevance on disease progression.

Projects:

1. Correlation between genetic risk variants for type 1 diabetes and other autoimmune diseases and their gene expression in the immunologically important thymus
2. Influence of genetic risk variants for type 1 diabetes on gene expression in the immunologically important thymus
3. Study epigenetic variation and their relevance to type 1 diabetes and other autoimmune diseases
4. Differences and similarities between genetic predisposition to type 1 diabetes and celiac diseases addressed in individuals with both diagnosis
5. Copy number variations and predisposition to autoimmune diseases
6. Influence of genetic risk variants on disease progression assessed in rheumatoid arthritis, a disease sharing many risk factors with type 1 diabetes

Group member:

- Marte K. Viken, post doc
- Gry BN Nordang, Ph.D. student
- Marthe Mæhlen, Ph.D. student
- Nimo Hatinoor, masterstudent
- Siri Flåm, technician
- Teresia Wangensteen, MD, Ph.D.
- Beate Skinningsrud, MSc, Ph.D.
- Magnus Dehli Vigeland, Ph.D., postdoc
- Kristina Gervin, MSc, Ph.D. student
- Morten C. Eike, Ph.D., post doc
- Hanne Hjorthaug, MSc, research assistant
- Alice Stormyhr, MSc, research assistant

Group leader: Kåre I. Birkeland

Group name: Research group for type 2 diabetes

Research focus:

Our group aims to increase knowledge about the factors that lead to type 2 diabetes and its complications so as to be able to prevent the development of the disease and its complications. Our research includes basic and clinical studies in diabetes pathophysiology, single- and multi-center randomized controlled trials (RCTs) and observational, epidemiological studies with emphasis on ethnic minority groups.

Research facilities:

We work in close collaboration with the Hormone Laboratory, a core facility for endocrine research in Oslo University Hospital with a broad repertoire of analytical methods including immunoassays, GC/MS, LC/MS, molecular biology etc. Together we run the Diabetes Research Laboratory situated within the outpatient diabetes clinic, with facilities for oral and intravenous glucose tolerance tests, meal tests, hyper- and euglycaemic clamp studies with tracer methodology, muscle and fat biopsies, indirect calorimetry and measurements of VO2max. Furthermore, we collaborate closely with basic medical research groups at Dept. of Nutrition, Institute of Basic Medical Sciences, University of Oslo; Research Institute for Internal Medicine, Oslo University Hospital; and the Norwegian School of Sport Sciences.

Our most important studies in 2011 were:

1. The STORK-Groruddalen Research program: a population-based, prospective cohort study of pregnant women living in three districts of Oslo, a large proportion being ethnic minorities. The cohort comprises 823 women and their offspring, and constitutes a large database for present and future research into the biochemical, clinical and psychosocial factors that determine gestational diabetes, offspring birth weight/ body composition and future health for mother and child.
2. The DIVINE study; a single center, researcher-initiated RCT of high dose vitamin D (cholecalciferol) to subjects with type 2 diabetes and hypovitaminosis D, with main study endpoints being the effects on insulin sensitivity and insulin secretion.
3. The ABCD (Asker and Bærum Cardiovascular Diabetes Study) was a RCT of intensive vs. conventional multifactorial intervention to reduce complications in patients with type 2 diabetes. We are currently collecting long term follow-up data.
4. Life-style intervention in subjects after bariatric surgery – effects on BMI, nutritional factors and markers of cardiovascular risk.
5. MyoGlu – the effect of exercise training on myokin expression and secretion.
6. Several multicenter pharmacological studies in diabetes, the most important being ORIGIN, PROactive follow-up, LEADER, TECOS.

Group members:

- Kåre I. Birkeland, MD, Ph.D., professor II, group leader
- Anne Karen Jenum, MD, Ph.D., senior researcher at Institute for Health and Society, Department of General Practice, UiO and professor II at University College of Oslo
- Anne-Marie Aas, Ph.D., Assistant professor II, Department of Nutrition,
- Hanne Løvdal Gulseth, MD, Ph.D., post doc
- Erlend T. Aasheim, MD, Ph.D.
- John Willy Haukeland, MD, Ph.D., consultant gastroenterologist
- Ingrid M Fange Gjelstad, Ph.D., post doc
- Per Medbøe Thorsby, MD, Ph.D. student
- Cecilie Wium, MD, Ph.D. student
- Kirsti Bjerkan, Ph.D. student
- Line Sletner, MD, Ph.D. student
- Kjersti Mørkrid, M.Phil, Ph.D. student
- Anne Pernille Ofstad, MD, Ph.D. student
- Anh Trahn, MD, Ph.D. student
- Torgrim Langleite, MSc, Ph.D. student
- Susanna Hanvold, MSc, Ph.D. student

Research nurses:
- Åse Halsne and Gøril Vinje
- Bioengineer Lise Marit Amlie

Medical students:
Tuva Wyller, Sara K. Fidjeland, Hildegunn Grødal, Thea Drivnes, Nina Marie Aamodt, Hanna Jervell Heyerdahl

Group leaders: Tore Henriksen/ Jens Bollerslev

Group name:
Diabetes and Pregnancy

Research focus:
STORK Rikshospitalet is a part of the Thematic group ”Perinatal nutrition” at Faculty of Medicine, University of Oslo. Its main research focus is metabolic, nutritional, neuroendocrine and vascular aspects of maternal-fetal interactions, especially in terms of fetal growth and development. The role of maternal metabolic status (adipose adiposity, plasma glucose, lipids and endocrine and inflammatory parameters) has been studied. More recently the role of placenta has gained increasing interest based on the previous findings in the STORK-project. Placenta is a metabolically highly active organ that governs the maternal organism during pregnancy, but which may also be modified by maternal factors in terms of functional capacity. For this reason has currently developed a method for study of human placental function in vivo.

Projects:
1. Maternal and placental aspects of fetal growth (Ph.D. student: Marie Cecilie Paasche Roland).
2. Metabolic syndrome in pregnancy (Ph.D. student: Camilla Margrethe Friis).
3. The STORK-Placenta Study: Studies of Functional Properties Human Placenta In Vivo (Post doc. Trond M. Michelsen and Ph.D. student).
4. Fetal placental endocrine interaction (Kristin Godang, Jens Bollerslev).

Group members:
- Tore Henriksen, seksjonsoverlege/professor II, leder
- Jens Bollerslev seksjonsoverlege/professor II
- Guttorm Haugen, seksjonsoverlege/professor II
- Thomas Åbyholm, avd.overlege/professor II
- Svein Olav Kolset, professor I
- Marit Veierød, professor I
- Elisabeth Qvigstad, post doc., dr.med.
- Bjørg Lorentzen, overlege, dr.med.
- Nanna Voldner, undervisningsjordmor/Ph.D.
- Trond Michelsen, konst.overlege/post doc.
- Thor Ueland, Ph.D.
- Kathrine Frey Frøslie, Ph.D. student
- Marie Cecilie Paasche Roland, Ph.D. student
- Camilla Hoff, Ph.D. student
- Kristin Godang, BcS

Group leader: Trond Jenssen

Group name:
Diabetic Nephropathy

Research focus:
Cardiovascular risk factors and diabetes after organ transplantation. Pancreas and islet cell transplantation. Molecular and morphological changes in the diabetic kidney.

Projects:
1. New onset diabetes after transplantation (NODAT). Occurrence, Pathogenesis, Risk factors, Follow-up and Treatment.
2. Pancreas transplantation. Long-term development of diabetic and non-diabetic complications.
3. Islet cell transplantation.
4. Metabolic risk factors for graft and patient survival in renal transplant patients.
5. Molecular changes in transplanted kidneys, with emphasis on diabetes, the basement membrane and proteoglycans.

Group members:
- Professor Trond Jenssen OUS Rikshospitalet
- Ole Øyen, MD, Ph.D. OUS Rikshospitalet
- Jørn Petter Lindahl, MD OUS Rikshospitalet
- Rune Horneland, MD OUS Rikshospitalet
- Professor Anders Hartmann OUS Rikshospitalet
- Ingrid Moss Kolseth, MD OUS Rikshospitalet
- Karsten Midtvedt, MD, Ph.D. OUS Rikshospitalet

- Professor Svein O. Kolset — University of Oslo
- Ivar Eide, MD — OUS Rikshospitalet
- Trine Reine, Ph.D. — University of Oslo
- Professor Finn Reinholt — OUS Rikshospitalet
- Annicke Stranda, Ph.D. — University of Oslo

Group leader: Jens P Berg

Group name: Metabolomics of hyperglycemia

Research focus:

Diabetes is a group of metabolic disorders characterized by hyperglycemia. Our research aims to increase our understanding of the mechanisms leading to and the metabolic consequences of increased blood glucose by studies of small molecule metabolite profiles. We have established methods of metabolomics and multivariate data analysis, which allows the detection and quantitation of compounds in large mixtures, such as the products of metabolism in biological fluids and tissues.

In addition we focus on the use, quality control and interpretation of measures of glycemic control such as HbA1c and glycated albumin.

Projects:

1. Studies of metabolic profiles in gestational diabetes; in collaboration with dr. Anne Karen Jenum.
2. Head of working group for the evaluation of diagnostic use of HbA1c in Norway.

Groups members:

- Jens Petter Berg, MD, Ph.D., Professor
- Daniel Sachse, Ph.D. student

Chairperson of the Registry: Torild Skrivarhaug

Name: The Norwegian Childhood Diabetes Registry (NCDR)

Research focus:

The main research focus in this population-based, nation-wide childhood-onset diabetes registry:

- Epidemiology in childhood-onset diabetes, focusing on incidence, prevalence, classification of childhood-onset diabetes in Norway, ethnicity and long-term complications and mortality.
- Quality in childhood diabetes care – a nation wide prospective population-based study for research and quality improvement by means of benchmarking.
- Clinical childhood diabetes, especially focusing on quality of life, diabetes treatment, co-morbidity, eating disorders and the transition from paediatric to adult diabetes care.
- Diabetes in children, a global comparative study, with focus on the differences in I) epidemiology of type 1 and type 2 diabetes, II) in treatment, treatment guidelines and key clinical outcome data in different paediatric departments in different countries (Argentina, Canada, India, Norway, Rwanda, South Africa).

Projects:

Epidemiology

1. Incidence and prevalence of childhood-onset type 1 diabetes in Norway. This is the first time The Norwegian Prescription Database at the National Institute of Public Health and The Norwegian Childhood Diabetes Registry are linked with the purpose to give information about incidence of childhood onset type 1 diabetes and completeness of The Norwegian Childhood Diabetes Registry.
2. Classification of childhood-onset diabetes in Norway. The aim of this project is to study the epidemiology of different forms of diabetes and to classify incident cases on the basis of family history, clinical data, C-peptide, autoantibodies and HLA-genotypes.
3. Childhood diabetes and ethnicity in Norway. The aim of this project is to access the ethnic differences in T1DM in Norway and to compare the incidence of T1DM among child migrants in Norway with respect to their ethnic backgrounds or countries of origin in these regions.

4. The signification of analyzing Zn-antibodies at the diagnosis of T1D in children.
5. Time trends in mortality in childhood-onset type 1 diabetes: A nationwide population based cohort study. Aims: To evaluate absolute and relative mortality rates for childhood-onset T1D, the effects of sex and age at diagnosis, and the cause of death. To examine short and long time trends in mortality. To assess socioeconomic status as a risk factor for mortality in T1D.

Clinical diabetes

6. Co-morbidity in children and adolescents with type 1 diabetes. This is a sub study of The Norwegian Childhood Diabetes Registry assessing competencies and coping; factors affecting functional and dysfunctional behaviour in children and adolescents with diabetes.
7. A systematic nationwide study of diabetes team resources in paediatric departments. The aim of this project is to assess the multi disciplinary resources allocated to different paediatric departments treating diabetes in Norway and the relation to key clinical outcome data.
8. A national, population based study of the double diagnosis of celiac disease and type 1 diabetes. The aim is to investigate the relationship between type 1 diabetes and celiac disease and to explore the extent of symptoms, treatment and quality of life.
9. Ethnicity and diabetes in the Nordic countries. This project is collaboration between the Nordic Childhood Diabetes Registries (Sweden, Denmark, Iceland and Norway). The aim is to assess if ethnicity is an independent factor influencing metabolic control in children and adolescents with type 1 diabetes residing in Nordic countries.
10. Co-morbid diabetes and eating disorders – an exploration of prevalence, psychological correlates and diabetic control. This project is a collaboration between the Norwegian Childhood Diabetes Registry and the Regional Eating Disorder Service (RASP) at Oslo University Hospital, Ullevål. The aims of this study are to 1) explore the cognitive and behavioural correlates of comorbid type 1 diabetes and eating disorders, 2) assess the prevalence and co-morbid type 1 diabetes and eating disorders in Norway.
11. Diabetic nephropathy: Microalbuminuri and hypertension in Norwegian children with type 1 diabetes.
12. Treatment in childhood type 1 diabetes and the transition from paediatric to adult diabetes care – a prospective, populationbased, nationwide study. The aims are to 1) assess the extensiveness of treatment with insulin pump in children and adolescents in Norway and to find the predictors for successful insulin pump treatment, 2) to describe and evaluate the practices of transition from paediatric to adult diabetes care.
13. Diabetes in children, a global comparative study
    - The implementation of guidelines in clinical practice – Benefits and challenges exemplified by international guidelines in Diabetes Mellitus in children.
    - Diabetes: A neglected disease in sub-Saharan Africa.
    - The importance of a psychosocial focus in the treatment and management of type 1 diabetes in children. A comparison between Norway and Australia.
    - The choice of insulin regimen and target of glycemic control in children with type 1 diabetes mellitus – A comparative study of Canada and Norway.
    - Stigmatization of children with chronic diseases, exemplified by type 1 diabetes mellitus. Differences between India and Norway.

Group members:

- Torild Skrivarhaug, Consultant dr.med., Director of the Norwegian Childhood Diabetes Registry
- Geir Joner, Consultant dr.med., Professor
- Knut Dahl-Jørgensen, Consultant dr.med., Professor
- Siv Janne Kummernes, R.N., Diabetes nurse, Masterstudent
- Ann Kristin Drivvoll, MSC
- Lars Christian Stene, MSc, Ph.D., Researcher, Norwegian Institute of Public Health
- Hans Jacob Bangstad, MD, Ph.D., Professor
- Per Thorsby, MD, Ph.D. student
- Dag Helge Frøisland, MD, Ph.D. student
- Line Wisting, Master in psychology, Ph.D.
- Vibeke Gagnum, MD

International collaboration:
EURODIAB
The Nordic Childhood Diabetes Registry Study Group

Publications:

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Gjelstad IMF. Dietary fat and the metabolic syndrome – The LIPGENE dietary intervention study, Ph.D. University of Oslo.

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ISBN: 978-82-8264-309-2. Dissertation January 24th 2012.

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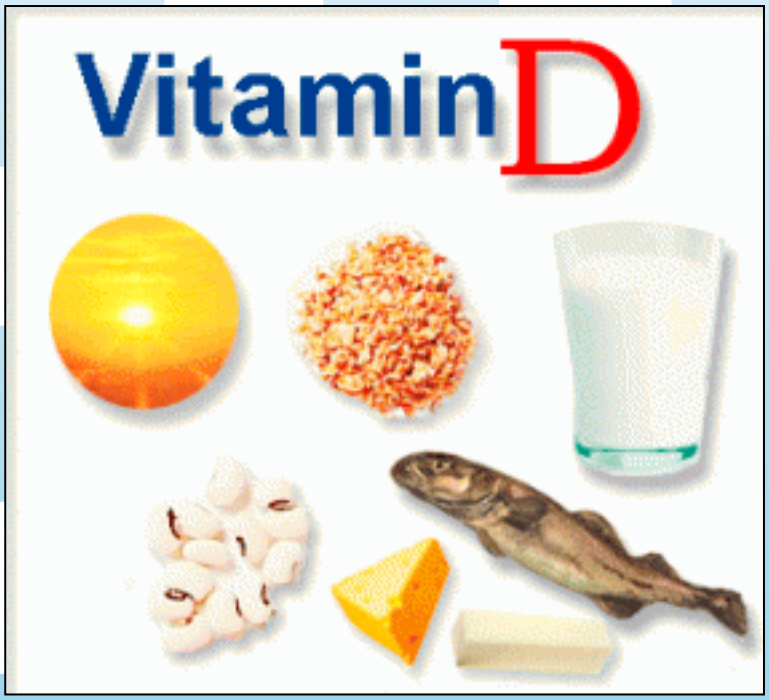

Vitamin D og diabetes er "hot".
Se undersøkelser om lavt vitamin D hos gravide og økt forekomst av type 1 diabetes hos barnet (se side 12). D vitamin og insulinresistens ved type 2 diabetes (se side 10).