

Fertility Clinic
Department of Obstetrics/Gynaecology
Holbæk Sygehus and University of Copenhagen

Clinical/laboratory skills

1. Fertility treatment
2. Polycystic ovary syndrome
3. Preconception care
4. IVF laboratory
5. Time lapse microscopy
6. Gamete/embryo freezing
7. WHO semen analyses
8. Fertility assessment and counseling

Research areas

1. Micro RNA as a predictor of metabolic syndrome in women with PCOS
2. Dynamic changes in gene expression during oocyte maturation
3. Weight loss prior to fertility treatment

Principal Investigator:

Anne Lis Mikkelsen, Chief Consultant / aleg@regionsjaelland.dk

**Department of Occupational and Environmental Medicine, Bispebjerg-
Frederiksberg University Hospital Copenhagen, Denmark**

We carry out research on consequences for health related to occupational and environmental exposure. In ReproUnion our focus is on reproductive health.

Our research addresses maternal exposures as well as exposures in early in life. In addition we are interested in environmental and occupational exposures and effects on reproductive outcomes.

We are an epidemiological research unit and major methods include:

1. Advanced biostatistics and epidemiological research
2. Registry linkages
3. Statistics Denmark
4. Proper conduct in epidemiological research
5. Recruitment of persons for population studies
6. Correct ethical conduct in human studies
7. Development of a national job exposure matrix

Specific research areas related to reproduction and fertility include:

Epidemiological Population Research

1. Fetal programming of semen quality within the Danish National Birth Cohort
 - a. Fetal exposure to environmental toxicants including over the counter analgesics
 - b. Maternal obesity diet and smoking
 - c. Maternal life events and stress
2. Fetal programming of obesity within the Danish National Birth Cohort
 - a. Maternal obesity
 - b. Maternal paracetamol
3. Indoor environment and reproduction (Maternal exposure to indoor semi-volatile PCBs and semen quality)

Epidemiological Register based Research

4. Infertility as a precursor for morbidity/ mortality

Occupational Epidemiology

5. Occupational exposure to toxicants and pregnancy outcomes
6. Stress and fertility
7. Shift work and reproduction

Principal Investigator:

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**The Fertility Clinic
Rigshospitalet
Copenhagen University Hospital, Denmark**

Clinical activity

- Conduct a total of 2.600 treatment cycles per year
- Do ART, IUI, OI, PGD, treatment of HIV or hepatitis infected patients
- Recurrent miscarriage clinic
- Fertility Assessment and Counselling function

Clinical/Laboratory skills

- ART laboratory
- Embryo selection
- PGD – but not PGS

Research areas

Optimizing ovarian stimulation, safety and quality aspects of ART, recurrent miscarriage, reproductive immunology, Fertility Assessment and Counselling

Type of conducted studies

Clinical randomized controlled trials, national registry-based cohort studies, observational studies, case-control studies

Clinical research areas

- Optimizing patient treatment protocols, AMH bases dosing algorithms
- Nurse conducted studies on vulnerable patients and single women undergoing donor sperm IUI
- Follicular activation studies
- Ovarian reserve assessment in patients and normal women
- Prediction of poor responders by AMH
- Fertility counselling
- Fertilization failures – laboratory aspects
- Luteal phase in ART and natural cycles
- Reproductive immunology
- Recurrent miscarriage

Principal investigators:

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Anders Nyboe Andersen, Professor / Anders.Nyboe.Andersen@regionh.dk

Department of Growth and Reproduction Rigshospitalet, University of Copenhagen

Appointed Global Excellence Centre in 2010, re-appointed in 2015. Tertiary referral centre in paediatric endocrinology, EAA certified Andrology Training centre. The department (www.reproduction.dk) hosts the international research centre EDMaRC (www.edmarc.net) and the secretariat of the National Center of Endocrine Disruptors (www.cehos.dk). Ongoing collaborative studies with Pharma; Novo Nordisk (GH in short SGA children), Ferring (free DNA in infertile men), Diurnal (Chronocort in CAH)

- 1 coordinating clinical professor, head of department (Juul)
- 1 clinical professor (Main)
- 2 adjunct professors (Toppari, Skakkebaek)
- 3 research team leaders (Jørgensen, Andersson, Rajpert-DeMeyts)
- 1 part-time professor (Kold Jensen)
- 4 senior researchers (Almstrup, Jørgensen, Frederiksen, Blomberg Jensen (currently Harvard))
- 18 junior researchers/PhD students

Alltogether the group is based on a multidisciplinary team including a total of 100 employees (doctors, nurses, molecular biologists, chemists, public health scientists, secretaries, technicians epidemiologists).

The department includes a large outpatient clinic (11000 annual visits), hormone lab, LC-MS/MS lab, semen lab, histology lab, molecular biology lab (including cell lab).

Clinical/Laboratory skills (patient management)

- Male infertility work up
- Paediatric endocrinology expertise; growth and pubertal (ovarian/testicular) disorders
- Assessment of body composition (2 DXA scanners Lunar Prodigy)
- Automated boneage readings (BoneXpert); OPI project with Visiana and PC-PAL
- Gynecological endocrinology; reproductive hormone assessment (ultrasensitive FSH/LH, estradiol, testosterone, IGF-I, IGFBP-3, SHBG, AMH, inhibin B) and androgen metabolites by LC-MS/MS (Adion, DHEAS, Testo, 17OHP, corticosterone metabolites) in DANAK accredited lab)
- Andrological examination (incl. scrotal ultrasound) and management (incl infertility and hypogonadism).
- Histological expertise in testicular histology, infertility and DSD gonads (DANAK accredited)
- Semen cryopreservation, authorized semen bank
- WHO semen analysis (5-6000 analyses per year), automated assays including acrosome reaction
- Y chromosome microdeletions

Clinical Research

- Genetic polymorphisms, puberty timing and testicular function
- Stress, other lifestyle factors and testicular function
- Surveillance of semen quality in Denmark (1996-present)
- Activation of hypothalamo-pituitary.-gonadal axis in minipuberty
- Ano-Genital Distance as a postnatal readout of fetal androgen action (formation of the new international AGD consortium under EDMaRC)
- Endocrine disrupting chemicals (phthalates, phenols, parabens, UV filters) by LC-MS/MS, puberty timing and testicular function
- Male subfertility, testosterone deficiency and long term morbidity
- Disorders of Sex Development; diagnostic and management and therapeutic aspects (incl RCTs)
- Treatment of transgender adolescents.

- Sex chromosome disorders; Klinefelter and Turner syndrome, clinical aspects
- Testicular cancer, Leydig cell function and longterm follow up
- Hypogonadotropic hypogonadism (incl Kallman syndrome); genetic and therapeutic aspects

Basic research methodologies and projects

- Regulation of meiotic entry in fetal gonads
- Ex-vivo hanging drop model of fetal gonadal tissues, and adult testicular biopsies
- Standard molecular biology techniques, qPCR, Western blotting, etc.
- DNA sequencing (Illumina MiSeq machine), RNA seq,
- Fetal gonads from controls and patients with sex chromosome disorders (45X, 47,XXY, 45X/46XY)
- Isolation of testicular cells by laser capture microdissection,
- Microscopy including slide scanner, immunohistochemistry, in situ hybridization
- Epigenetic modifications, puberty timing and testicular function (DNA methylation, microRNA)

Principal investigators:

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Niels Jørgensen, Consultant / Niels.Joergensen@regionh.dk

Laboratory of Reproductive Biology
Rigshospitalet University Hospital of Copenhagen, Denmark

Clinical/Laboratory skills (patient management)

- Cryopreservation and transplantation of ovarian tissue
- Cryopreservation of testicular tissue

Research

Ovarian endocrinology; Cryobiology; Sex Differentiation and human foetal gonads; Foetal exposure to environmental toxicants, Human embryonic Stem cells; Molecular Genetic Reproductive Research; Molecular Reproductive Research.

- Characterization of human small antral follicles and granulosa cells obtained from human small antral follicles
- Culture of human immature granulosa cells
- Isolation and culture of human preantral follicles
- IVM of human oocytes
- Isolation and culture of human spermatogonial stem cells
- Human foetal tissues and gonads; exposure to environmental pollutants
- Genetic polymorphisms of FSHR, LHR and PAPP-A
- Human embryonic stem cells: culture and differentiation protocols
- *In vitro* studies of sex steroid and gonadotropin receptors
- New concepts for ovarian stimulation, ovulation induction and individualized luteal phase support
- Immunohistochemistry of ovarian and testicular tissue
- Q-RT-PCR
- Confocal microscopy
- Measurement of ovarian hormones

Principal Investigator:

Claus Yding Andersen, Professor / claus.yding.andersen@regionh.dk

Fertility Clinic
Department of Obstetrics/Gynaecology
Hvidovre Hospital University Hospital of Copenhagen, Denmark

Clinical

- Fertility clinic (ART, IUI, TESA, donor semen)
- Gynecological surgery (hysteroscopy, laparoscopy, etc.)
- Obstetrics and antenatal care (more than 7000 deliveries per year)
- Special function in antenatal care of vulnerable patients

Clinical/Laboratory skills

- IVF laboratory
- Time lapse microscopy
- Gamete/embryo freezing

Research areas

Reproductive epidemiology, optimizing ovarian stimulation, safety and quality aspects of ART, preconceptional care, reproductive epigenetics, fertility assessment and counseling

Type of conducted studies

Meta-analyses and systematic reviews, national registry-based cohort studies, clinical randomized controlled trials, observational studies, case-control studies

Specific areas

- Nordic collaboration on short and long term outcomes of ART children (Committee of Nordic ART and Safety (CoNARTaS))
- Epidemiological studies based on the Danish ART registry and national health registries
- Optimizing “Freeze-all” strategies
- Optimizing patient treatment protocols (short GnRH-antagonist vs. long GnRH agonist protocol)
- Endometrial scratching and endometrial biopsy
- Prediction of poor responders by AMH
- Weight loss prior to fertility treatment
- Epigenetics in cord blood cells and embryos comparing different conception methods
- Fertility counseling clinic
- Qualitative studies on patient aspects
- Sex hormone manipulation and brain response

Principal Investigator:

Anja Pindborg, Professor / anja.bisgaard.pinborg@regionh.dk

**Urology Research Unit
Herlev Hospital
University Hospital of Copenhagen, Denmark**

Clinical skills

- Microsurgical vaso-vasostomy
- Microsurgical vaso-epididymostomy
- Microsurgical Testicular Sperm Retrieval (Micro-TESE)
- Microsurgical varicocelectomy
- Transurethral Resection of the Ejaculatory Ducts (TUR-ED)
- Assisted ejaculation (Penile vibratory ejaculation (PVS) & Electroejaculation (EEJ))
- Penile Implants
- Surgical treatment of Peyronie's Disease

Research

- Surgical sperm retrieval techniques
- Biology of non-obstructive azoospermia
- The effect of male infertility on sexual performance and sexuality
- Pregnancy outcomes in relation to location of retrieved spermatozoa
- Optimizing human semen cryopreservation
- Semen quality and reference values for "normal" semen parameters
- Factors influencing assessment of semen quality
- Male infertility problems (varicocele, hypogonadism, obstructive azoospermia etc.)

Principal Investigator: Jens Sønksen, Professor / jens.sonksen@regionh.dk

Reproductive Medicine Centre
Skane University Hospital – Malmö and Lund University, Sweden

Clinical/Laboratory skills (patient management)

- ART (IVF; ICSI; Intratuterie insemination)
- Male/female infertility work up
- Gynecological endocrinology
- Andrological examination (incl. scrotal ultrasound) and management (incl infertility and hypogonadism)
- Recruitment and investigation of gamete donors
- Gamete/embryo freezing
- Standard IVF/ICSI procedures
- Time lapse microscopy
- WHO semen analysis
- Sperm Chromatin Structure Assay

Research (Molecular Genetic Reproductive Research; Molecular Reproductive Research)

- Genetic polymorphisms and individualized ovarian hyperstimulation
- Genetic polymorphisms in androgen receptor gene
- *In vitro* studies of sex steroid and gonadotropin receptors
- Prostate cancer and male subfertility
- Sperm DNA damage and male fertility
- Cancer and male reproductive function
- Male subfertility, testosterone deficiency and long term morbidity
- Male cancer and health of the offspring (epidemiological and molecular studies)

Principal Investigator:

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**Department of Translational Medicine
Clinical Medicine, Lund University Hospital, Sweden**

Research:

- Proteomics

Principal Investigator: Johan Malm, Professor / johan.malm@med.lu.se

Department of Occupational & Environmental Medicine

Lund University, Sweden

Research:

- Reproductive Epidemiology
- Register studies

Principal Investigator:

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**Fertility Clinic, Department of Obstetrics/Gynecology
Herlev/Gentofte Hospital, University of Copenhagen, Denmark**

Synopsis:

We are a university hospital based infertility center offering a comprehensive range of investigations and treatments in gynecological endocrinology and reproductive medicine. Our program provides high quality academic led clinical care in a multi-disciplinary environment including a team of doctors, embryologist, nurses, bioanalysts and administrative staff delivering consistently high success rates. We aim to provide a high quality service that places our patients and couples at the center of their management. The clinic is involved in a large portfolio of studies promoting a culture of evidence-based practice and we support and encourage research and education involving all team members. We seek to translate our clinical findings into top-quality, state-of-the-art care for patients with reproductive disorders and incorporate this into the ReproUnion collaboration.

Clinical management

- Reproductive medicine and gynecological endocrinology including exogenous hormonal treatment.
- Fertility clinic (IUI, IVF, ICSI, TESA, semen and oocyte donation, gamete and embryo cryopreservation, fertility awareness)
- Reproductive surgical procedures: hysteroscopic and laparoscopic treatment of fibroids and endometriosis
- PCOS clinic. Metabolic and thrombogenic effects of endogenous and exogenous sex steroids. Intervention trials according to PCOS phenotypes
- Obstetrics and antenatal care (more than 7000 deliveries per year)
- Gynecology. All kind of benign gynecology and selected gynecological oncology (cervical and endometrial cancer)

Laboratory skills

- IVF laboratory
- Time lapse microscopy
- Gamete/embryo freezing

Staff:

- Clinical professor, head of reproductive medical unit (Skousby)
- Clinical professor , epidemiology and infertility (Kesmodel)
- Part time professor (Macklon)
- Head of laboratory unit (Grøndahl)
- Associate professor, infertility (Bungum)
- Associate professor, infertility and reproductive surgery (Nøhr)
- Expert trainee and consultant (Sopa)
- 4 ph d students
- The majority of the nurses and bioanalyst staff is ESHRE certified

Main Research areas

- “Mapping”the follicular and endocrinological environment to explore the determinants for the “gate-keeping” in natural and stimulated cycles of the number and development of follicles as well as the inter-cyclic variation and endometrial receptivity
- Impact of aromatase inhibitor on supraphysiological estrogen and progesterone levels in stimulated cycles
- Reproductive epidemiology
- PGS
- Oocyte and Embryo morphokinetic, time lapse
- Folliculogenesis (expression array and next generation sequencing of oocytes and follicle cells)
- Female Meiosis (chromosome stability)
- Gene expression profiling of follicle cells (biomarker)
- MicroRNA in spent culture medium (biomarker)
- DNA methylation profiling in follicle cells
- GL-P1 intervention in women with PCOS. Impact on clinical expression and long term co-morbidity

Other specific areas

- Endometrial scratching and endometrial biopsy
- Weight loss prior to fertility treatment
- Multi center studies on embryo morpho kinetics in relation to female age and outcome (Fertility database)
- Age and ovarian reserve: DNA methylation age profile and telomere length
- Ovarian response and OHSS risk: Expression and DNA methylation profiling of follicle cells
- Chromosome stability and age
- HPV as risk factor for infertility and pregnancies

Type of conducted studies

Meta-analyses and systematic reviews, national registry-based cohort studies, clinical randomized controlled trials, observational studies, case-control studies

Principal Investigator:

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