



**EAA training Centre of Tartu University Hospital,
Estonia**

Andrology Center

Tartu University Hospital

L. Puusepa 1a

50406 Tartu

Estonia

Tel.: +37 2 7319323

Fax.: +37 2 7319401

Web: <http://www.kliinikum.ee/meestekliinik/>

Email: meestekliinik@kliinikum.ee

margus.punab@kliinikum.ee

Facebook: <https://www.facebook.com/meestekliinik>

Formation of the Andrology Centre in Estonia: chronological footsteps.

1993 – Initiation of andrological service at the Tartu University Hospital (TUH) by dr. Margus Punab (specialization in gynecology 1993; residential training in andrology/urology 1993-1996): first outpatient clinic for infertile men at the Women's Clinic.

1995 – First specialized semen laboratory established by the United Laboratories of TUH.

1996 – Andrological outpatient clinic joined the central outpatient clinic (policlinic) of the TUH in the vicinity of the semen laboratory.

1997 – The Centre was involved in first international collaboration projects with Nordic colleagues

March 2005 – establishment of an independent Andrology Centre at the TUH.

Andrological activities, previously scattered between different clinics (private and state owned) is now centralized into one center. The Andrology Center consists of the main unit in Tartu and the branch offices in Tallinn and Pärnu

Our unit works as a referral Centre for whole Estonia.

Present staff.

- Margus Punab, MD, PhD – director of the Center, andrologist-urologist, certified clinical andrologist by the EAA in 2004
- Olev Poolamets, MD – andrologist, head of the Tallinn branch office, affiliated member of the EAA, past president of the Nordic Association for Clinical Sexology
- Vladimir Vihljajev, MD – andrologist-sexologist
- Ruth Ladvá, MD – andrologist-GP
- Kristjan Pomm, MD - andrologist-GP
- Paul Korrovits, MD, PhD – andrology resident, research assistant
- Kristel Ehala-Aleksejev, MD – PhD student, specialist of internal medicine, nutritionist
- Ülo Sõmer, MD – GP (part time in Pärnu center)

The center has five laboratory technicians, six nurses and seven secretaries.

Scientific council.

Prof. Maris Laan – Institute of Molecular and Cell Biology, University of Tartu

Prof. Vallo Tillmann - Tartu University Children's Hospital

Prof. Reet Mändar - Institute of Microbiology, University of Tartu

Docent Margus Punab – Andrology Center

The aim of council is to generate and coordinate scientific activities of the Andrology Center.

Management of patients with andrological diseases.

Table 1 summarizes the statistics about clinical activity of the unit during the years 2009-2013. The unit provides diagnosis and treatment for a full range of andrological diseases. There are three main groups of patients (Table 2): male infertility, male sexual dysfunctions and prostate diseases. The specialists of the Andrology Center have also reception hours at the Youth Counselling Centres, Haapsalu Neurological Rehabilitation Center, and Estonian Multiple Sclerosis Centre (numbers not included in the statistics of Table 1).

Andrology center has access to a full range of modern diagnostic facilities (Table 3) either in our own center or in collaboration with partners' clinics and laboratories.

Table 1. Number of visits and lab examinations per year

	Tallinn					Tartu					Pärnu
	2009	2010	2011	2012	2013	2009	2010	2011	2012	2013	2013
Doctors visits	13933	13229	11451	12387	13168	8739	6886	6565	6619	6798	1213
Nurses visits	9248	9866	11439	10759	11540	2546	5255	5767	6701	6052	872
In total - visits	23181	23095	22890	23146	24708	11285	12141	12332	13320	12850	2085
Semen analysis	2237	2347	2530	2306	2606	2024	1883	1985	2350	2427	
Prostate secretion	2459	2718	2863	2512	3390	1572	2093	1994	2293	2395	289
In total lab tests	4696	5065	5393	4818	5996	3596	3976	3979	4643	4822	289

Table 2. Primary causes of consultation (approximate figures)

Male infertility	20 %
Sexual dysfunction	20 %
Genitourinary tract infections and prostatitis	25 %
Prostate diseases	15 %
Male hypogonadism	10 %
Other genital diseases	5 %
Male health	5 %

Table 3 Diagnostic facilities for clinical work-up of patients with andrological diseases.

Location	Tartu	Tallinn	Pärnu
History and physical examination	Andrology Unit (AU)	AU	AU
Semen and prostate secretion analysis	AU	AU	AU
Ultrasound examination	AU	AU	AU
Uroflow test	AU	AU	AU
Vibrostimulation	AU	AU*	AU
Endocrine testing	TUH Central lab	TUH Central lab	TUH Central lab
Pathology	TUH Pathology department	TUH Pathology department	TUH Pathology department
Microbiology and STD testing	TUH Central lab	TUH Central lab	TUH Central lab
Genetic analyses	TUH Central lab	TUH Central lab	TUH Central lab
Flow cytometry	TUH Central lab	TUH Central lab	TUH Central lab
Andrological operations	TUH Clinics of	TUH Clinics of	TUH Clinics of Surgery

	Surgery	Surgery	
Urological operation	TUH Clinics of Surgery	North Estonian Regional Hospital	Pärnu Hospital, TUH Clinics of Surgery
IVF, ICSI, TESA	TUH Women`s Clinic	IVF clinics in Tallinn	TUH Women`s Clinic
Sperm cryopreservation	TUH Women`s Clinic	TUH Women`s Clinic West-Tallinn central Hospital	TUH Women`s Clinic, West-Tallinn central Hospital
Bone density	AU / TUH Dept. of Internal Medicine	East-Tallinn Central Hospital	AU / TUH Dept. of Internal Medicine
Electron microscopy, FISH, molecular biology	Research facilities of collaborators		

Infertility work-up.

In Tartu and Tallinn offices specialized semen analysis laboratory has been established.

Semen analysis is performed according to WHO (2010).

Care for infertile patients has been organized stepwise: diagnostic, conservative treatment together with lifestyle modification, assisted reproductive techniques (ART) or/and operative treatment. Decisions for ART procedures are based on collaboration with partner gynecologist. In certain indication varicocele operations were performed. Microsurgical operations in male seminal ducts were started in 1994, but with introduction of TESA, lost their actuality during some recent years.

Genetics.

Y chromosome microdeletion screening deletions are performed according to EAA recommendations. Laboratory has participated in the external EAA/EMQN quality control program.

For CF mutation screening we use extended APEX (arrayed primer extension), test which allows us to analyze 246 most common CFTR gene mutations detected in Caucasians.

Cytogenetic analysis are performed in TUH Central laboratory. Chromosomes are analyzed by Trypsin –Giemsa banding technique. Other methods, such as R-, Q-, AgNOR and fluorescence in situ hybridization (FISH) methods, were used for the identification of chromosome abnormalities.

- Pathology tests are performed in collaboration with TUH Pathology department which has a wide experience in standard histological techniques, histomorphometry and immunohistochemistry.

- Hormonal analysis is performed in collaboration with the TUH Central laboratory under appropriate internal and external quality control.
- Microbiological tests are performed in collaboration with TUH Central laboratory

Male sexual dysfunction

Basic diagnostic work-up includes clinical examination, hormonal tests and test treatment course. In non-responders to pharmacological treatment Doppler ultrasound examination of penis blood vessels are performed. In selected cases also neurological test will be applied. Treatment contains elements of sexual therapy and lifestyle modification. Majority of patients get pharmacological treatment. In rare cases patients will be referred to penis prosthesis operations.

Prostate diseases

Diagnostic work-up starts with standard questionnaires (IPSS, NIH-CPSI). According to clinical indications blood tests for cancer markers, uroflowmetry and ultrasound examinations were used.

Diagnosis of prostatitis is always based on test of prostate specific material (prostate secretion, semen). Cytological and biochemical tests have been introduced to detect inflammatory process in these secretions. Conservative treatment of prostatitis and LUTS patients is performed in our unit but patients with diagnosed prostate cancer are referred to the Department of Urology.

Surgical activity

Two staff doctors have skills to perform andrological operations. The range of operations is limited to (noncancerous) diseases of penis, scrotum and includes also TESA procedures in partner IVF clinics. Patients who need for more advanced operations are referred to consultant urologists.

The Andrology Unit is involved in the following clinical training and educational programmes.

1. Andrology Residency: Our Hospital teaches a five-year residential programme in Andrology (as a subspecialist of urology) based on EAA recommendations for andrology training.
2. Current program of training consist of the following parts:

Urology	10 months
Paediatric urology	1 month
Oncology	1 month
Gynaecology	5 months
Laboratory medicine	2 months
Endocrinology	1 month
Radiology	1 month
Genetics	1 month
Andrology	33 months

2. The unit serves as training base for residents in Andrology, urology, dermatovenereology and gynaecology.
3. The unit is responsible for a two yearly 20-hour (elective) course in andrology and urological andrology included in teaching program of medical students.
4. Our clinicians give lectures on Andrology, reproductive biology, sexology at postgraduate courses organized by other departments (urology, gynaecology, internal medicine).
5. Biannually the unit organizes workshops in actual topics of andrology and sexology, open for all clinicians.

Research activities.

Major areas of research:

1. Male fertility and its risk factors
2. Male infertility
3. Genetic aspects of male infertility
4. Male aging
5. Prostatitis, leukocytospermia, oxidative stress

Major international scientific grants

1. European Commission (EU 5. framework) – Envir.Reprod.Health (QLK4-CT-1999-01422) 2002-2004
2. European Commission (EU 5. framework) – European Male Aging Study (QLRT-2001-00258) 2001-2009

Major local scientific grants

1. Oxidative stress, prostatitis and male infertility - ETF8022 - 01.01.09 - 31.12.12
2. Determinants on men's health: psychosocial factors in men with prostate diseases – influence to the help-seeking behavior and to the utilization of screening methods – ETF7979 - 01.01.09 - 31.12.12
3. Development of novel non-invasive biomarkers for fertility and healthy pregnancy. European Regional Development Fund - 01.09.2012-31.08.2015

4. Competence Centre on Reproductive Medicine and Biology. European Regional Development Fund - 01.09.2009 to 31.08.2015
5. Causes of male factor infertility with special emphasis to the male accessory gland infection- PUT181 - Estonian Research Council – 1.01.2013-31.01.2016

Recent publications (2010-2014):

1. Alcohol and male reproductive health: a cross-sectional study of 8344 healthy men from Europe and the USA. Jensen TK, Swan S, Jørgensen N, Toppari J, Redmon B, Punab M, Drobnis EZ, Haugen TB, Zilaitiene B, Sparks AE, Irvine DS, Wang C, Jouannet P, Brazil C, Paasch U, Salzbrunn A, Skakkebaek NE, Andersson AM.
Hum Reprod. 2014 Jun 3.[Epub ahead of print]
2. Reproductive physiology in young men is cumulatively affected by FSH-action modulating genetic variants: FSHR -29G/A and c.2039 A/G, FSHB -211G/T.
Grigorova M, Punab M, Punab AM, Poolamets O, Vihlajev V, Zilaitienė B, Erenpreiss J, Matulevičius V, Laan M. PLoS One. 2014 Apr 9;9(4)
3. Semen quality in middle-aged males: associations with prostate-specific antigen and age-related prostate conditions. Ausmees K, Korrovits P, Timberg G, Erm T, Punab M, Mändar R. Hum Fertil (Camb). 2014 Mar;17(1):60-6.
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5. Male infertility: decreased levels of selenium, zinc and antioxidants.
Türk S, Mändar R, Mahlapuu R, Viitak A, Punab M, Kullisaar T. J Trace Elem Med Biol. 2014 Apr;28(2):179-85.
6. Late-onset hypogonadism and mortality in aging men. Pye SR, Huhtaniemi IT, Finn JD, Lee DM, O'Neill TW, Tajar A, Bartfai G, Boonen S, Casanueva FF, Forti G, Giwercman A, Han TS, Kula K, Lean ME, Pendleton N, Punab M, Rutter MK, Vanderschueren D, Wu FC; EMAS Study Group. J Clin Endocrinol Metab. 2014 Apr;99(4):1357-66.
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8. Male infertility workup needs additional testing of expressed prostatic secretion and/or post-massage urine. Punab M, Kullisaar T, Mändar R. PLoS One. 2013 Dec 9;8(12)
9. Low prolactin is associated with sexual dysfunction and psychological or metabolic disturbances in middle-aged and elderly men: the European Male Aging Study (EMAS). Corona G, Wu FC, Rastrelli G, Lee DM, Forti G, O'Connor DB, O'Neill TW, Pendleton N, Bartfai G, Boonen S, Casanueva FF, Finn JD, Huhtaniemi IT, Kula K, Punab M, Vanderschueren D, Rutter MK, Maggi M; EMAS Study Group. J Sex Med. 2014 Jan;11(1):240-53.
10. Decline of seminal parameters in middle-aged males is associated with lower urinary tract symptoms, prostate enlargement and bladder outlet obstruction.
Ausmees K, Korrovits P, Timberg G, Punab M, Mändar R.
Int Braz J Urol. 2013 Sep-Oct;39(5):727-40.
11. Increased levels of hydrogen peroxide and nitric oxide in male partners of infertile couples. Kullisaar T, Türk S, Kilk K, Ausmees K, Punab M, Mändar R.
Andrology. 2013 Nov;1(6):850-8.

12. The ability of three different models of frailty to predict all-cause mortality: results from the European Male Aging Study (EMAS). Ravindrarajah R, Lee DM, Pye SR, Gielen E, Boonen S, Vanderschueren D, Pendleton N, Finn JD, Tajar A, O'Connell MD, Rockwood K, Bartfai G, Casanueva FF, Forti G, Giwercman A, Han TS, Huhtaniemi IT, Kula K, Lean ME, Punab M, Wu FC, O'Neill TW; European Male Aging Study Group. *Arch Gerontol Geriatr*. 2013 Nov-Dec;57(3):360-8.
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20. The association of frailty with serum 25-hydroxyvitamin D and parathyroid hormone levels in older European men. Tajar A, Lee DM, Pye SR, O'Connell MD, Ravindrarajah R, Gielen E, Boonen S, Vanderschueren D, Pendleton N, Finn JD, Bartfai G, Casanueva FF, Forti G, Giwercman A, Han TS, Huhtaniemi IT, Kula K, Lean ME, Punab M, Wu FC, O'Neill TW. *Age Ageing*. 2013 May;42(3):352-9.
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