LIETUVOS SVEIKATOS MOKSLŲ UNIVERSITETO LIGONINĖ
KAUNO KLINIKOS

Rare Diseases

Center of Rare and Undiagnosed Diseases
Kauno klinikos

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Contents

The Coordinating Center for Rare and Undiagnosed Diseases at Kauno klinikos

Head of the Center
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The Hospital of Lithuanian University of Health Sciences Kauno klinikos (Kauno klinikos) is the largest healthcare institution in Lithuania; it provides multidisciplinary healthcare services for both children and adults, including conservative and surgical treatments. The specialists of Kauno klinikos have participated in the development of the Lithuanian National Plan on the Activities Related to Rare Diseases and are actively involved in its implementation.

The Coordinating Center for Rare and Undiagnosed Diseases (CCRUD) at Kauno klinikos was established in 2012 (https://www.kaunoklinikos.lt/contacts/coordinating-center-for-rare-and-undiagnosed-diseases-/). CCRUD takes part in organization and coordination of all activities in the field of rare diseases at the hospital level in order to ensure qualified multidisciplinary healthcare services for patients with suspected or diagnosed rare disorders. The specialists of the CCRUD also provide consultations for medical professionals and patients on the logistic issues of healthcare for rare disease patients. Also CCRUD represents Kauno klinikos at national and international level in close collaboration with the Lithuanian University of Health Sciences.

All clinical departments at Kauno klinikos are providing services both for children and adults with rare disorders. This is a tertiary center where most of complicated or undiagnosed cases are being concentrated. In many cases, rare diseases affect multiple organs and are long-lasting; therefore, patients need careful diagnostic work-up, modern treatments and long-term follow-up by competent interdisciplinary teams which are available at Kauno klinikos. For this purpose, 25 functional competence centers for groups of specific rare diseases have been established in accordance with special professional interests and experiences of the dedicated staff. This allows a more structured approach to certain groups of rare diseases in providing multidisciplinary services of comprehensive tertiary level for patients from all around Lithuania and abroad as well as scientific research, education of professionals, patients and community, collaboration at national and international level, etc.

These competence centers are functioning according to the requirements set by European Commission (COUNCIL RECOMMENDATION of 8 June 2009 on an action in the field of rare diseases) and the Lithuanian National Plan on the Activities Related to Rare Diseases. Close collaboration with patient representatives ensures efficient feedback and progress in implementing patient-oriented care. Also, smooth transition of children with rare disorders from childhood to adult healthcare is available due to close collaboration between childhood and adulthood specialists at Kauno klinikos.

Since 2017, Kauno klinikos has received the full membership in the following European Reference Networks (ERNs): EURACAN (European Network for Rare Adult Solid Cancer), Endo-ERN (Rare Endocrine Conditions), ERN-EYE (Rare Eye Diseases), ERN-SKIN (Rare Skin Diseases).

In 2019, affiliated ERN partnerships have been received in additional 9 ERNs: ERN RARE LIVER (Rare Liver Diseases), ERN RITA (Primary Immunodeficiency, Autoinflammatory and Autoimmune Diseases), ERN LUNG (Rare Respiratory Diseases), ERN BOND (Bone Rare Diseases), ERN GUARD HEART (Rare and Low Prevalence Complex Diseases of the Heart), ERN ERNICA (Rare Inherited and Congenital (digestive and gastrointestinal) Anomalies), ERN EpiCARE (Rare and Complex Epilepsies), ERN EURO-NMD (Rare neuromuscular diseases), ERN ReCONNET (Rare and Complex Connective Tissue and Musculoskeletal Diseases). ERN memberships have opened new opportunities for progress in the field of rare diseases.

Kauno klinikos has been registered as a partner of ORPHANET. It also takes part in the EU collaborative project "Towards access to at least 1 million sequenced genomes in the EU by 2022". International Rare Disease Day is being celebrated annually by organizing a conference for medical professionals and patients, supported by broad campaign on rare diseases via different media sources, including the EURORDIS website.

Diagnostic and treatment possibilities of rare genetic, metabolic and autoimmune disorders are expanding within the recent years at Kauno klinikos. The international collaboration predisposes further development of healthcare provision for patients with rare diseases and of the scientific research. The staff of Kauno klinikos is open to any professional cooperation in this field of priority.

The Rare Eye Diseases Center of Kauno klinikos was established in 2015.

The aim of the Center is to coordinate and integrate activities of the departments involved in the Center to develop and implement high quality, timely diagnosis and treatment of rare eye diseases (RED).

The tasks of The Rare Eye Diseases Center (REDC) are:

- to provide qualified and specialized medical care to patients suffering from RED;
- to prepare methodological recommendations and teaching materials for the diagnosis and treatment of RED;
- to consult physicians on prevention, diagnosis, treatment and rehabilitation of RED;
- to analyze and evaluate the quality and results of diagnosis and treatment of RED;
- to introduce new methods of treatment of RED;
- to cooperate with patient organizations;
- to participate in European reference network dedicated to RED (ERN-EYE) network activities.

REDC is a member of ERN-EYE network since 2017. ERN-EYE consists of 29 health care providers in 13 full member countries and 15 HCPs in 7 affiliated partner countries across the European Union. ERN-EYE goals are to improve patient trajectory in the EU through the virtual clinic, reduce inequalities of patient care and the time of diagnosis, ensure molecular diagnosis, bring the diagnosis to the undiagnosed patients, facilitate involvement of patients in clinical trials, give access to innovations and provide tools for education.

The functional organization of REDC is related to ERN-EYE work groups; REDC provides clinical expertise in management of the most difficult diseases in four main fields of ophthalmology: Pediatric Ophthalmology, Retinal RED, Neuroophthalmology RED and Anterior eye segment RED. Analysis of the entire range of genes associated with hereditary ophthalmic disorders is carried out in Kauno klinikos because of the cooperation with geneticists and the next-generation gene sequencing.

Diagnostics and treatment is provided for children suffering from congenital cataract, lens position anomalies, congenital glaucoma, Coats disease, retinal dystrophies, aniridia, congenital ptosis and oculomotor disorders. The surgical treatment of congenital conditions is delivered by the most experienced surgeons of the Department of Ophthalmology. Retina experts diagnose retinal dystrophies and degenerations, retinal vasculopathies, provide laser treatment, vitreoretinal surgery and intravitreal injections. Inflammatory and hereditary optic neuropathies, optic atrophies, pupil and oculomotor disorders are diagnosed by neuroophthalmologists. Specialists diagnose and treat corneal dystrophies, lens position anomalies, iridogoniodysgenesis, glaucoma related RED, provide congenital cataract surgery, congenital glaucoma surgery, corneal transplantations (including DSEAK) and phototherapeutic keratectomy in Anterior eye segment RED.

The Department of Ophthalmology at Kauno klinikos is the largest center for diagnosis and treatment of eye diseases in Lithuania, providing about 88,000 consultations of adult patients and about 10,000 of children, proceeding more than 18,000 surgical procedures per year, covering the whole range of ophthalmic diseases. The staff of the Department of Ophthalmology consists of 267 people, of whom 68 are ophthalmologists.

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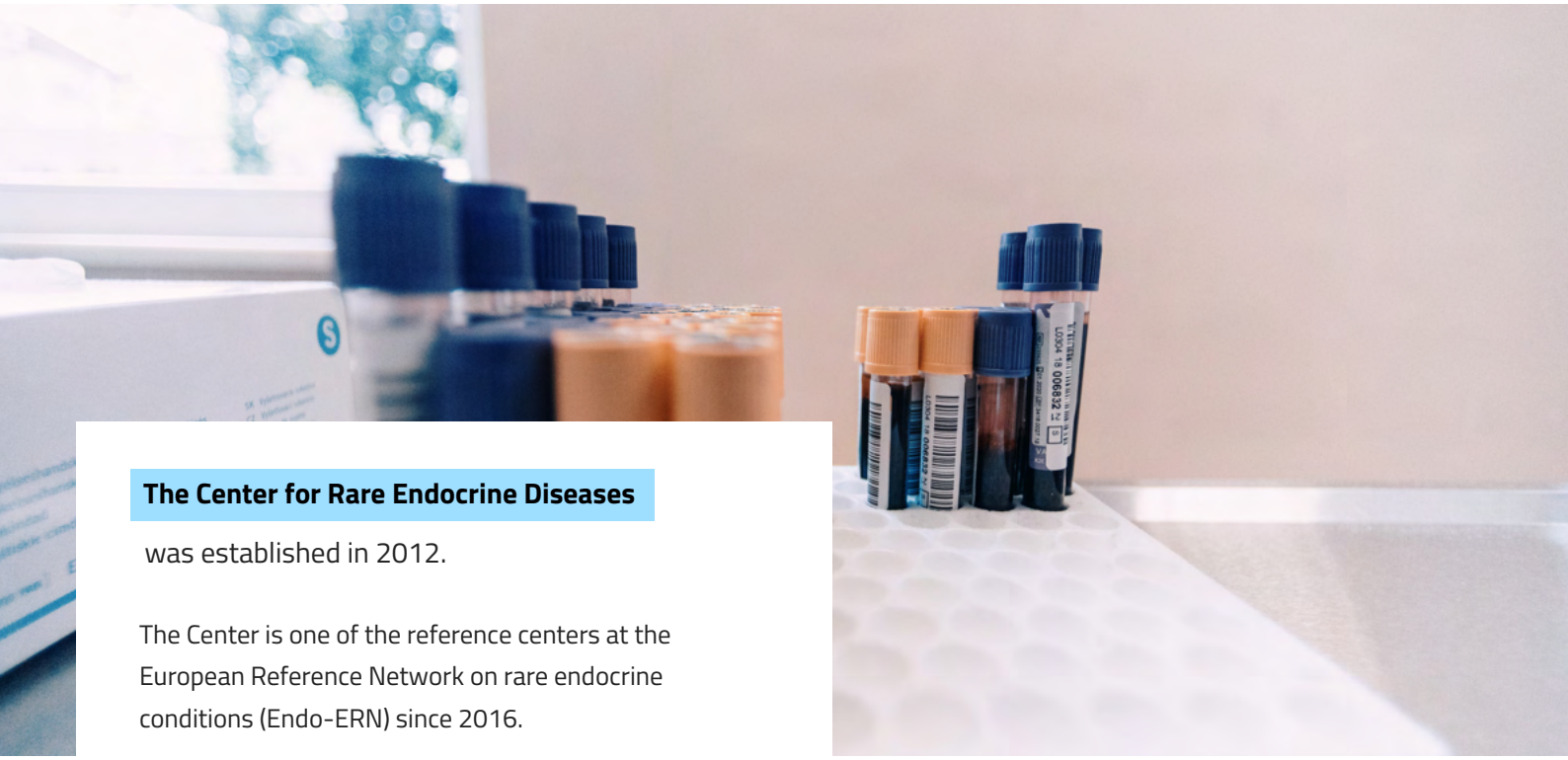

The Center for Rare Endocrine Diseases

was established in 2012.

The Center is one of the reference centers at the European Reference Network on rare endocrine conditions (Endo-ERN) since 2016.

The main clinical work, diagnostics and treatment, is conducted at the Department of Endocrinology of Kauno klinikos and covers over 30,000 outpatient appointments with more than 2,000 hospitalizations per year.

The Center closely collaborates with the Institute of Endocrinology of the Lithuanian University of Health Sciences, the Department of Genetics and Molecular Medicine, the Department of Radiology, General Surgery (Endocrine sector), the Department of Neurosurgery and many others. Since 2016, the next-generation sequencing analysis in genes, associated with monogenic diabetes (*GCK*, *HNF1A*, *HNF4A*) is available. After genetic assessment, specialists can customize the treatment method; in some cases, the insulin therapy can be discontinued.

The Center provides clinical expertise in the management of rare adrenal and pituitary gland diseases. The patient is fully examined using basic hormonal axis tests, dynamic-diagnostic tests (synthetic adrenocorticotropic hormone test, "salt" infusion test, cortisol suppression tests, etc.). Moreover, in collaboration with interventional radiologists, adrenal vein sampling or inferior petrosal sinus sampling can be performed. The multidisciplinary team of professionals provides access to a specialized medical or surgical treatment of these disorders seeking after a multifactor evaluation for a full recovery. Transsphenoidal pituitary surgery has been performed at Kauno klinikos since 1996. Stereotactic radiotherapy for pituitary adenomas treatment is available since 2019. Furthermore, the Department of Endocrinology proceeds in biomedical research with the latest drugs: growth hormone receptor antisense inhibitors for the treatment of acromegaly, another rare pituitary gland disease.

Experts in endocrinology, radiology, pathology, surgery and oncology take part in the multidisciplinary team for management of patients with thyroid tumors. The Multidisciplinary team meetings (MTM) are organized on a regular basis at least once a month to discuss treatment possibilities of thyroid cancer. The research is carried on to identify the significance of epigenetic markers for early diagnosis and long-term prognosis of papillary thyroid carcinoma in elderly patients at the Center.

The Center also provides a full range of assessments and access to specialized medical or surgical treatment of growth, gender developmental disorders, multiple endocrine neoplasia, genetic obesity, disorders of calcium and phosphorus metabolism. Strategy for the diagnosis and treatment of rare endocrine diseases is usually decided by a multidisciplinary team including specialists in various fields. If needed, consultations with international experts are organized through the Virtual Clinical Patient Management System (CPMS), available via Endo-ERN. In very rare cases, when there is an absence of the necessary diagnostic and treatment methods in Lithuania, patients are referred to specialized centers in other European countries.

The Center for Rare Endocrine Diseases at Kauno klinikos is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of rare endocrine diseases.

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The Center for Hemophilia and Coagulopathies was established in 2014.

Patients with hemophilia and other coagulopathies are diagnosed and treated in the Unit of Hematology in the Department of Oncology and Hematology and in the Unit of Hematology in the Department of Pediatrics.

The Center closely collaborates with other departments of Kauno klinikos: Department of Laboratory Medicine, Orthopedic Surgery, Genetics and Molecular Medicine, Rehabilitation and many others. Center performs all screening laboratory tests for suspected inherited and acquired disorders related to hemostasis defects, coagulation factors antigen and activity levels with standard and chromogenic laboratory assays, measure natural anticoagulants antigen and activity levels, determine acquired anticoagulants against clotting factors titer, evaluate global coagulation activity with tromboelastography. Abnormalities of congenital and acquired primary hemostasis are investigated with platelet function analyzer PFA and platelet aggregometry test. Genetic counseling is provided for patients with congenital bleeding disorders and their family members.

The center ensures a comprehensive multifactor evaluation and treatment of rare and complex inherited and acquired bleeding or thrombotic disorders for patients of all ages.

The Center offers clinical expertise in the diagnosis and management of inherited and acquired Hemophilia A and B, Willebrand disease, factor VII deficiency, other rarer clotting factors deficiencies. The multidisciplinary team of professionals provides access to specialized diagnostic, medical, surgical and rehabilitation assessment and treatment of these disorders. There is a possibility for an individualized treatment with plasma clotting factors, recombinant standard half-life and extended half-life factor VIII or IX in the Center. These drugs are administered according to individualized pharmacokinetic parameters. Since 2020, a non-factor replacement therapy with monoclonal antibody for patients with severe form of hemophilia A became available. Immune tolerance regiments are used for inhibitory neutralization in patients with congenital hemophilia A with inhibitors. For patients with acquired hemophilia A, measurement of inhibitors titers with modified Bethesda assay is performed, and treatment with bypassing and immunosuppressive agents is administered. Consultations regarding problematic hemostatic management before surgery or other interventional procedures are provided by specialists of the Center in timely manner.

In cooperation with the Department of Orthopedic Surgery, complex hip or knee joint replacement procedures for patients with hemophilia A and B are performed followed by extended rehabilitation and physiotherapy. Home treatment plans are also prepared.

The Center for Hemophilia and Coagulopathies is also a teaching center that actively participates in national and international projects, registries and implements scientific and research programs in the field of rare bleeding diseases. Since 2016, the Center has been recognized as the European Hemophilia Treatment Center.

Head of the Center:
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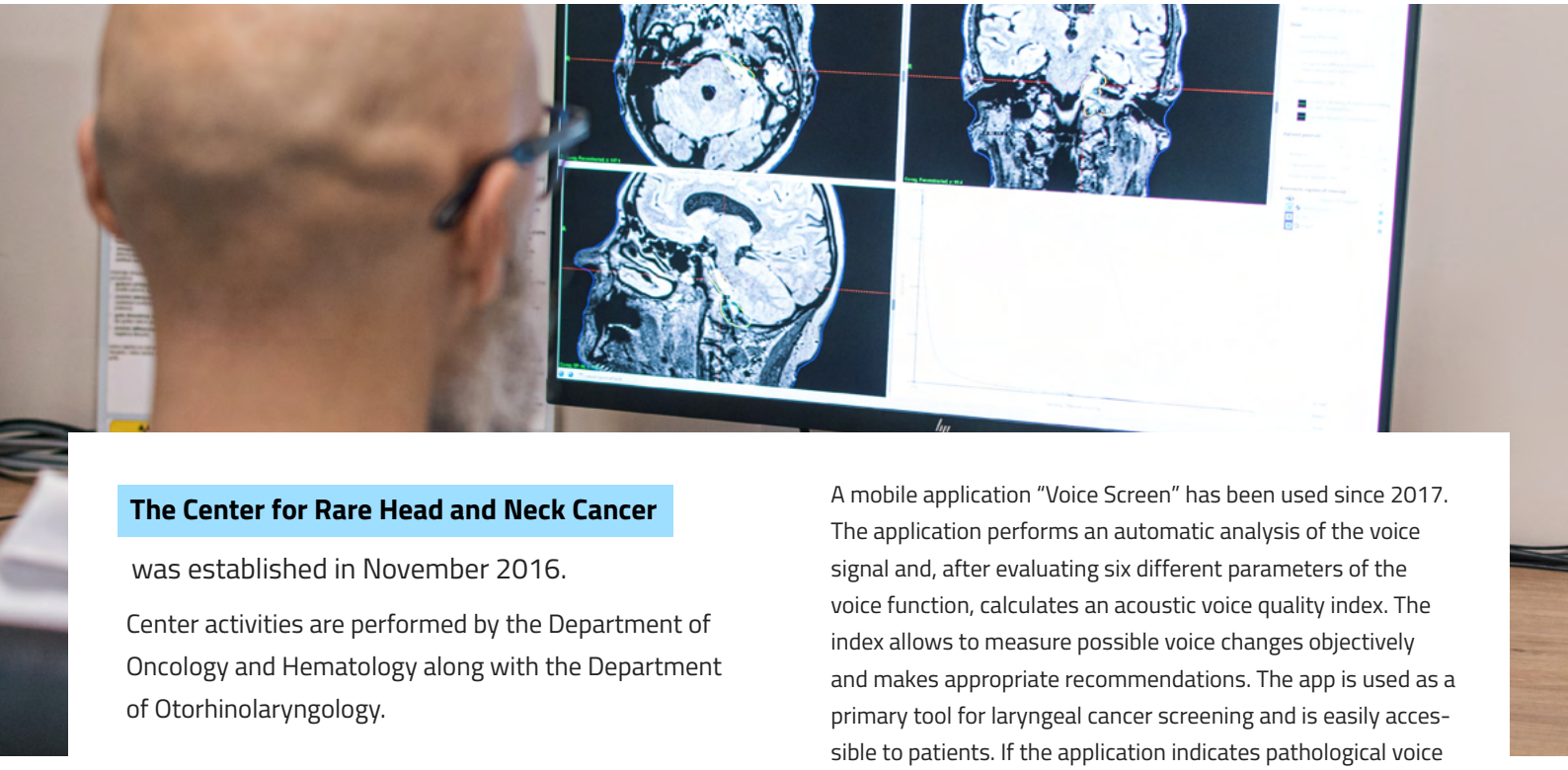

The Center for Rare Head and Neck Cancer

was established in November 2016.

Center activities are performed by the Department of Oncology and Hematology along with the Department of Otorhinolaryngology.

Several factors make this Center a unique one in Lithuania: its structure, coordination of multidisciplinary activities, specialist competence, as well as many years of experience in the field of rare head and neck cancer. Due to the mentioned qualities, the Center ensures the highest level of services for patients with rare head and neck tumors.

The Center is the only treatment center in Lithuania, which is qualified to perform sentinel lymph node biopsy, high dose brachytherapy and re-irradiation (using conformal radiotherapy, stereotactic body radiotherapy or brachytherapy) for head and neck cancer patients. Radiation therapy is planned by using new and advanced diagnostic methods, such as positron emission tomography/computed tomography (PET/CT). Merging of different radiological examinations ensures extra accuracy of the treatment. All patients are treated with intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT).

Additionally, the Gamma Knife unit in Kauno klinikos is currently used to treat tumors of the nasopharynx, paranasal sinuses and skull base.

Since June 2016, Department of Otorhinolaryngology has been equipped with Karl Storz OR1TM integrated operating theatre. It is the first operating theatre of this kind in the Baltic region, characterized by cutting-edge technological advances. It ensures high safety standards, hygiene, ergonomics and work efficiency. The operating room is equipped with the necessary endoscopic and navigational instruments. There is a possibility to store medical images in the hospital information system and broadcast the surgical procedures directly to the training rooms to ensure specialized education.

A mobile application "Voice Screen" has been used since 2017. The application performs an automatic analysis of the voice signal and, after evaluating six different parameters of the voice function, calculates an acoustic voice quality index. The index allows to measure possible voice changes objectively and makes appropriate recommendations. The app is used as a primary tool for laryngeal cancer screening and is easily accessible to patients. If the application indicates pathological voice changes, the patient is referred for further examinations to otorhinolaryngology specialist. The gadget is currently available in seven different languages.

The range of laboratory and genetic testing is constantly expanding: new effective immunogenic marker tests were implemented for use in cases of squamous cell carcinoma of the larynx and mouth floor. Scientific research project of correlations between telomere length and the phenotype of laryngeal squamous cell carcinoma is being performed. Furthermore, a number of single nucleotide polymorphism and miRNA studies in the field of head and neck cancer are currently ongoing.

Since 2020, the Center for Rare Head and Neck Cancer has been participating in a project organized by the European Cooperation in Science and Technology (e-COST) on the topic "Interception of Oral Cancer Development (INTERCEPT)". The Center cooperates in fields of Biobank and Biomarkers, as well as Health Economics and Ethics.

In 2017, the Baltic States Head and Neck Oncology Association was established. The aim of the Association is to promote the development of head and neck oncology in the Baltic States through medical science and practice, to coordinate the activities of the Association members, to represent the interests of Association members and meet other public interests. In April 2018, during the European Congress of Head and Neck Oncology (ECHNO) in Rome, the Baltic Head and Neck Association became a member of the European Head and Neck Society (EHNS).

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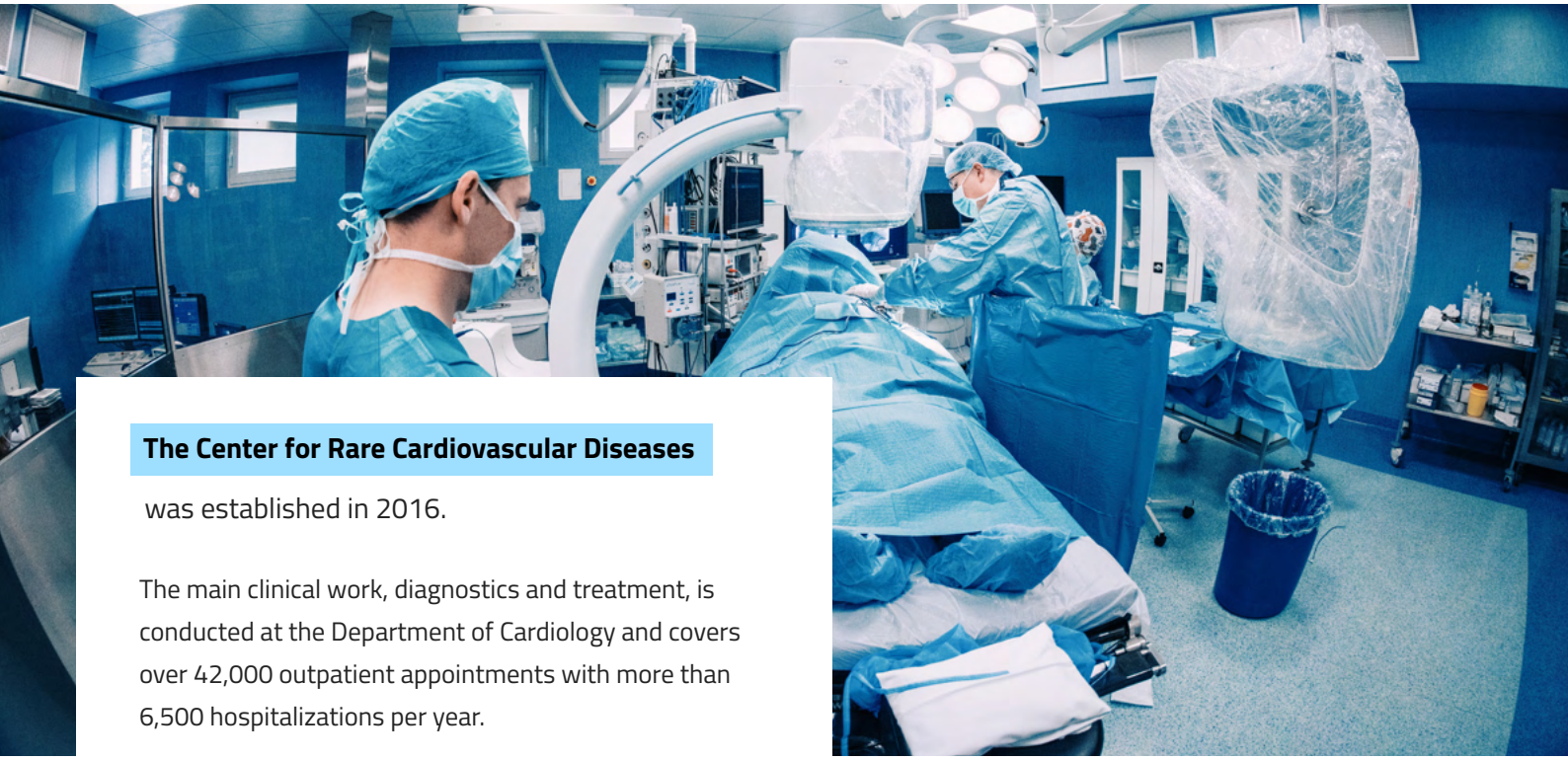

The Center for Rare Cardiovascular Diseases

was established in 2016.

The main clinical work, diagnostics and treatment, is conducted at the Department of Cardiology and covers over 42,000 outpatient appointments with more than 6,500 hospitalizations per year.

The Center closely collaborates with the Institute of Cardiology of the Lithuanian University of Health Sciences, the Department of Cardiac, Thoracic and Vascular Surgery, the Department of Genetics and Molecular Medicine and many others. Since 2019, cardiogenetics program is available both at diagnostic and research level. The next-generation sequencing enables analysis of up to 238 genes associated with familial cardiopathies (channelopathies, rare arrhythmias, cardiomyopathies, aortic diseases and sudden cardiac death).

The experienced team of the Unit of Cardiac Arrhythmias operates within modern electrophysiology laboratories. The University hospital was the first institution in Lithuania where treatment of complex cardiac arrhythmias and implantation of pacemakers became available in 1963. Nowadays, the Center provides a comprehensive multifactorial evaluation and interventional treatment of rare and complex arrhythmic disorders for patients of all ages.

The Center provides clinical expertise in management of inherited heart muscle disorders, metabolic and neurological disorders with cardiovascular manifestations, complex and rare congenital heart disease, heart tumors, and end-stage heart failure. The multidisciplinary team of professionals provides access to specialized medical, surgical and electrophysiological assessment and treatment of these disorders. A wide spectrum of catheter interventions, such as valve replacements, vascular procedures, closure of septal defects and left atrial appendage are available.

The Center also provides a full range of open-heart cardiac surgery for congenital and acquired heart diseases including those with the most complex anatomy, surgery for hypertrophic obstructive cardiomyopathy, benign and malignant heart tumors. Experts in cardiology, pathology, oncology and radiology take part in the multidisciplinary team for management of patients with heart tumors. The implantation of ventricular assist devices, heart and heart-lung transplantations are performed for the end-stage heart failure patients.

The Center for Rare Cardiovascular Diseases at the Hospital of Lithuanian University of Health Sciences Kauno klinikos is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of rare cardiovascular diseases.

Since 2019, the Center is an Associated National Center in ERN GUARD-Heart – European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart.

Head of the Center:
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The Center for Rare Neurosurgical Diseases

was established in 2016

In the same year, it became the full member of EURACAN (European Network for Rare Adult Solid Cancer) network (domain 10 – Rare cancer of the brain and spinal cord).

The Center for Rare Neurosurgical Diseases provides comprehensive and multidisciplinary world-class care for patients suffering from neurosurgical disorders. The Center is coordinated by the Department of Neurosurgery at the Kauno klinikos, which provides world-class medical care services for adults and children. Here the neurosurgeons routinely use cutting-edge technological advances (intraoperative MRI, intraoperative CT, intraoperative ultrasound, etc.) to treat complex cerebrovascular diseases, brain and spinal tumors, skull base pathologies at the Department of Neurosurgery. Patients from all around the country are referred to the Department to get treatment for arteriovenous malformations, cavernous angiomas, carotid-cavernous fistulas, ischemic and hemorrhagic strokes, complex brain aneurysms. Patients suffering from epilepsy, Parkinson's disease, tremor of various etiology, torsion dystonia, choreoathetosis, hemiballismus and other forms of extrapyramidal hyperkinesias are also evaluated and treated at the Center for Rare Neurosurgical Diseases. The surgical operations for congenital and acquired cerebrospinal fluid circulation disorders (various types of hydrocephalus, cerebral cysts, etc.) and congenital deformations of skull, spine, brain and spinal cord (craniosynostosis, Chiari malformation, myelomeningocele, etc.) are also performed.

At the Center for Rare Neurosurgical Diseases, the most advanced radio surgery instrument, Gamma Knife (Leksell Gamma Knife Icon), is used for treatment of various brain tumors, cerebrovascular malformations and functional disorders.

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The Center for Rare Gastrointestinal and Liver Diseases is a medical center, which is a functional unit at the Department of Gastroenterology of Kauno klinikos.

The Center was established in 2012 and is the leading, highly specialized center providing clinical care for multiple patients with a variety of rare gastrointestinal and liver pathologies.

Since 2019, the Center has been an affiliated partner in the RARE-LIVER network of European Reference Networks.

Gastroenterology is the largest clinic of digestive diseases in the Baltic States: 60 inpatient beds, an outpatient unit and Endoscopy unit with modern diagnostics.

The team of the Center employs new clinical research and treatment techniques according to the EU university clinic standards (interventional endoscopic and ultrasound procedures, contrast ultrasound procedures, transjugular intrahepatic portosystemic shunt formation (TIPS), transarterial chemoembolization (TACE), transjugular liver biopsy), manometry/pH-metry, capsular endoscopy, fecal microbiota transplantation, etc.), in order to improve health and quality of life of people with rare gastrointestinal and liver diseases.

More than 2,800 patients each year are treated in wards. Furthermore, more than 14,000 endoscopy procedures: ERCP, EUS, enteroscopy, capsule endoscopy, and other endoscopic procedures are performed each year in Endoscopy unit.

In carrying out scientific activities, the Center closely cooperates with Digestive System Research Institute. Collaboration takes place with specialists from various Departments: pathologists, pediatric and adult surgeons, radiologists, geneticists, immunologists, pediatric and adult anesthesiologists, intensive care specialists, obstetricians-gynecologists.

The Center closely works with patient organizations. Locally, the Center works with the Crohn's and Colitis Association of Lithuania in the development of high quality service for patients with PSC/UC, AIH/UC, PSC/UC/CCC. We closely work with PSC Patients Europe (PSCPE), and together we have developed adn published the PSC Brochure for GP. Taken into account our expertise in RLD, we believe that the Center will bring additional clinical, research and educational value for rare liver diseases and serve as a valuable partner for all associated stakeholders across Lithuania and Europe. The team based at the Kauno klinikos works towards the development and application of new clinical approaches in order to improve health outcomes of people living with rare liver diseases.

The Center for Rare Gastrointestinal and Liver Diseases is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of rare gastrointestinal and liver diseases.

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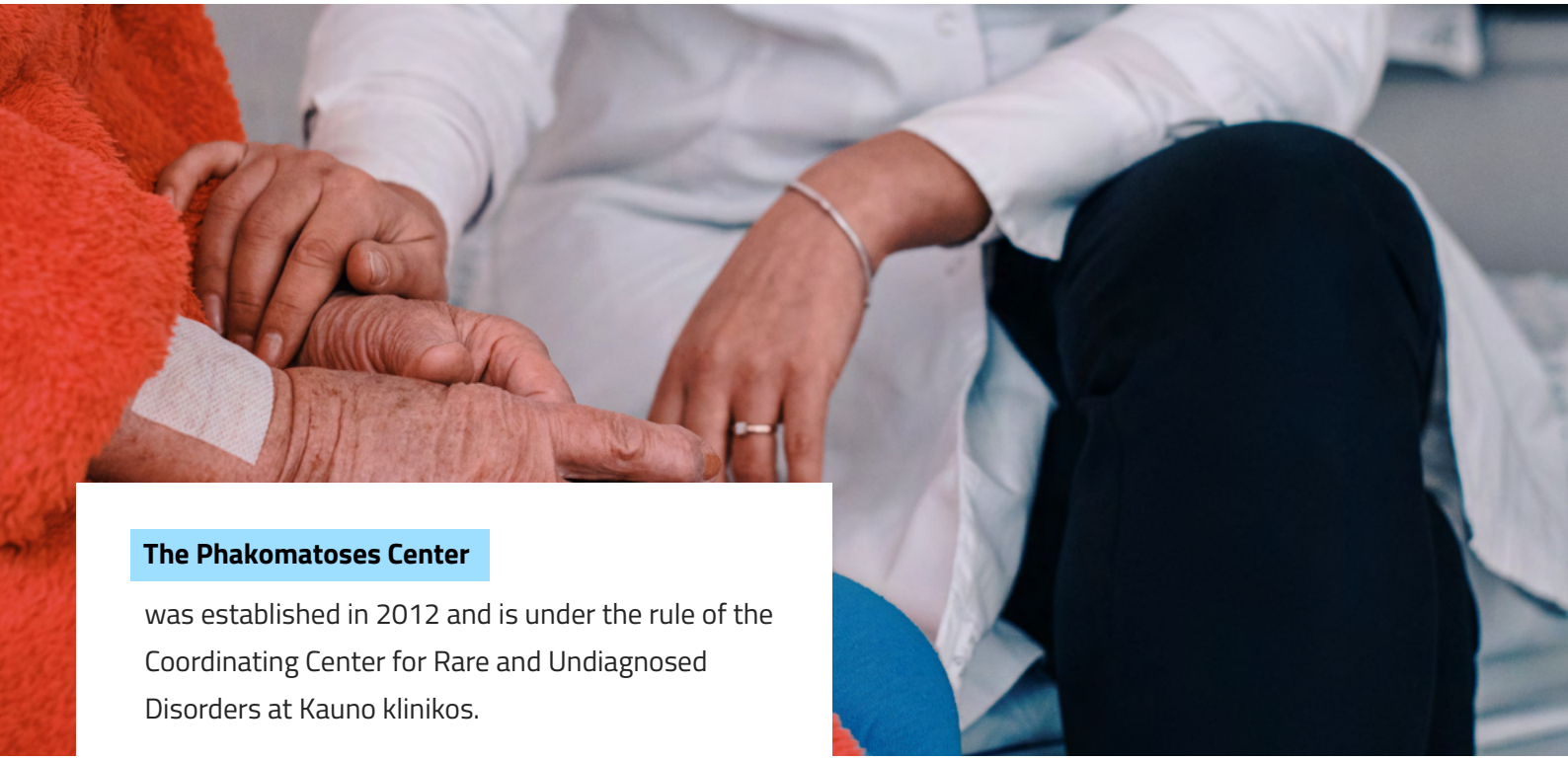

The Phakomatoses Center

was established in 2012 and is under the rule of the Coordinating Center for Rare and Undiagnosed Disorders at Kauno klinikos.

Each patient with a newly established diagnosis of a phakomatosis undergoes extensive investigations of all organs at risk, including radiology (CT, 1.5T and 3T MRI, SPECT, PET, with or without general anaesthesia), electrophysiology, laboratory, etc., with the plan for further treatment and multidisciplinary follow-up being developed and implemented by using the "green corridor" principle, according to the recognised international guidelines. Tuberous sclerosis is managed according to the official hospital-based protocol. Modern surgery and medical treatments for phakomatoses-related epilepsy and tumours (optic glioma in neurofibromatosis type I, and subependymal giant cell brain astrocytoma/renal angiomyolipoma in tuberous sclerosis) with plasma level monitoring are available and provided by experienced paediatric and adult specialist team: neurologists, neurosurgeons, nephrologists, dermatologists, radiologists, gastroenterologists, cardiologists, oncologists, haematologists, developmental specialists.

The Phakomatoses Center closely collaborates with the Department of Genetics and Molecular Medicine in making the genetic diagnosis and counselling of most phakomatoses; the Department of Neurosurgery which is experienced in peripheral nerve/brain tumor and epilepsy surgery (including gamma-knife, vagus nerve stimulation) and has wide international collaborations; the Institute of Neuroscience of the Lithuanian University of Health Sciences, and other relevant departments. Kauno klinikos holds full or affiliated membership of 13 different ERNs, so most of the Phakomatoses Center medical team members are involved in the rare disease activities of at least some of them (EpiCare, ERN Skin, ERN GUARD-Heart, EURACAN, ERN Eye, ERN RARE-LIVER).

The Phakomatoses Center has close collaboration with the Lithuanian University of Health Sciences and is involved in undergraduate and postgraduate education, also in research activities. The Center maintains the databases of patients with phakomatoses attending Kauno klinikos and has been involved in the international TOSCA (TuberOus SClerosis registry to increase disease Awareness) registry. As a part of the EU/Lithuania project "The Establishment of Rare Childhood Disease Competence Centre at the Hospital of the Lithuanian University of Health Sciences Kauno klinikos", the Phakomatoses Centre developed guidelines "Childhood Tuberous Sclerosis: Diagnostics, Treatment and Long-term Follow-up" (see Publications at www.kaunoklinikos.lt/contacts/coordinating-center-for-rare-and-undiagnosed-diseases-/ (Phakomatoses Centre).

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The Center of Primary Immunodeficiency

was established in 2012.

In Kauno klinikos, patients with primary immunodeficiency have been diagnosed and treated since 1999. The Center carries out testing and treatment of patients with Primary Immunodeficiency (PID) in accordance with current international standards. The Department of Immunology and Allergology carries out the activities of the Center and performs the functions assigned to it. The Department of Immunology and Allergology consists of the Outpatient clinic, Day care unit and the Laboratory of Immunology. Specialists consult patients of all age groups who are expected to have immune pathology related to allergy or other diseases. In Kauno klinikos, about 400 pediatric and adult patients are annually screened and treated for immunodeficiency conditions.

New diagnostic and treatment approaches of immune response in chronic or autoimmune diseases, transplantation, allergen challenge and immunotherapy are introduced every year.

The Center of Primary Immunodeficiency in Kauno klinikos has been a member of the *Jeffrey Modell Foundation* International Network since 2012 (www.info4pi.org/information-booth/find-an-expert). This facilitates the on-demand examination of patients and specialized treatment in primary immunodeficiency centers in other countries. The Center participates in J Project to increase the competence of medical professionals working in the field of PID and to improve patient examination and treatment. In 2015, the Center of Primary Immunodeficiency in Kauno klinikos was officially listed in Orphanet (www.orpha.net) as an expert center meeting the qualification requirements for such centers. Since 2019, the Center has been an associated national center in ERN RITA – European Reference Network on immunodeficiency, autoinflammatory and autoimmune diseases.

The Center closely collaborates with other departments of the Hospital in diagnosing and treating patients with immunodeficiency. Bone marrow transplantation is performed in the Department of Oncology and Hematology. Therefore, there is a possibility of bone marrow transplantation for patients with severe uncorrected primary immunodeficiency. Patients with end-stage organ damage may undergo transplantation other than bone marrow transplantation (including kidney, heart, lung, heart-lung complex, liver, etc.). In 2014, for the first time in Lithuania, a successful lung transplantation for a patient with primary immunodeficiency (common variable immunodeficiency) was performed. It was one of the 20 cases in the world at the time.

The Center of Primary Immunodeficiency is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of immunodeficiency disorders.

Head of the Center:
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The Center for Rare Cancer of the Neuroendocrine System was established in 2013.

The main clinical work – diagnostics and treatment is conducted at the Department of Oncology and Haematology and covers over 20,000 outpatient appointments with more than 20,000 Chemotherapy Day Care Department visits and 6,500 hospitalizations per year.

Kauno klinikos has a full spectrum of specific diagnostic and treatment interventions for rare neuroendocrine cancer. Along with biochemical tests and all imaging possibilities (CT, MRI, PET-CT, SPECT-CT, tectrotide scintigraphy, J-123-MIBG scintigraphy), a full range of endoscopic diagnostic and treatment procedures are available (enteroscopy, capsule endoscopy, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography, mucosectomy, etc.). NET patients are consulted by experienced clinical geneticists regarding hereditary syndromes, including multiple neuroendocrine neoplasia type 1 and 2 in the Department of Genetics and Molecular Medicine of Kauno klinikos. A full spectrum of laboratory genetic evaluation including all exome sequencing is available, too.

An entire range of diagnostic and treatment minimally invasive procedures are performed (biopsies from all visceral organs including pancreas, liver, lung, also bone, thyroid, lymphnodes, soft tissue) under CT, US control at the Department of Radiology in the Hospital. The Center also provides a full range of surgery (minimally invasive, wide open surgery, including liver and lung transplantation) for different types of gastrointestinal, pulmonary neuroendocrine benign tumors and cancers, including pancreatic, thymic, lung, small intestine, colorectal, etc.

A wide spectrum of modern radiotherapy is available in the Center: stereotactic radiotherapy, brachytherapy, IMRT, IGRT and image control for planning of dosage are used. Also the Gamma knife for many kinds of local and metastatic cancer is used in the Center. The modern radiopeptide therapy is used for the treatment of advanced somatostatin receptor expressing neuroendocrine tumors in the Department of Nuclear Medicine. All kinds of systemic cancer treatment are available in the Center (somatostatin analogs, targeted agents, immunotherapy and chemotherapy).

The Center provides clinical expertise in the management of gastroenteropancreatic neuroendocrine tumors, bronchial neuroendocrine tumors, thymic neuroendocrine tumors, adrenal and paraganglial tumors, medullary thyroid carcinoma, lung carcinoids and neuroendocrine carcinomas. In the Center, diagnosis of neuroendocrine cancer is confirmed histologically for around 150–170 new patients every year. Experts in pathology, medical oncology, radiation oncology, gastroenterology, endocrinology and radiology take part in the multidisciplinary team for management of patients with neuroendocrine tumors.

The Center for Rare Cancer of the Neuroendocrine System at the Hospital is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of rare neuroendocrine cancers.

Kauno klinikos holds a full European Reference Network for Rare Adult Cancers (ERN EURACAN) membership in the domain of Rare cancer of the brain and spinal cord since 2017.

The Ministry of Health confirmed that the Hospital of Lithuanian University of Health Sciences Kauno klinikos has been endorsed by the Ministry of Health of the Republic of Lithuania as an approved health care provider and an expert in the field of Rare cancer of the neuroendocrine system of the European Reference Network for Rare Adult Cancers (ERN EURACAN) in accordance with legal and regulatory requirements of the Republic of Lithuania on the 20th of March 2021. Kauno klinikos is ready to expand its expertise in Rare cancer of the neuroendocrine system domain of the ERN EURACAN.

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The Pulmonary Hypertension Center

was established in 2012.

The center takes care of various forms of pulmonary hypertension. The diagnosis and treatment of pulmonary hypertension are conducted at the Departments of Pulmonology or Cardiology. All the patients are constantly discussed by a multidisciplinary team composed of pulmonologists, cardiologists, radiologists, rheumatologists. There are also dedicated cardiosurgeons, genetic specialists and gastroenterologists. The specialized nurse is the integral member of this health care team.

Currently, there are approximately 150 patients with pulmonary hypertension treated in the center. Most of the patients are from group one (idiopathic/hereditary, associated with connective tissue diseases) and four (chronic thromboembolic pulmonary hypertension), according to the World Health Organization (WHO). All routine investigations for this pathology, including right heart catheterization, heart magnetic resonance imaging, ventilation/perfusion scan, genetic counseling, are completely available at the site. Our center is one the two Lithuanian referral centers for this pathology.

Kauno klinikos is the only hospital in the Baltic States where the lung or heart/lung transplantation has been performed since 2007.

The modern medical treatment (endothelin receptor antagonists – bosentan, ambrisentan, macitentan), phosphodiesterase type 5 inhibitors – sildenafil, soluble guanylate cyclase stimulators – riociguat, prostacyclin receptor agonist-selexipag) including parenteral prostanoids (treprostinil) is available and fully reimbursed for patients. The Interventional Cardiology Unit is prepared for the baloon pulmonary angioplasty (BPA) program. Patients are sent for thrombintimendarterectomy to Amsterdam University Hospital, and all cases have been successful so far.

The Hospital of Lithuanian University of Health Sciences Kauno klinikos is the active associated member of ERN-LUNG in the area of pulmonary hypertension. The unclear or complicated cases are discussed in the Clinical Patent Management System (CPMS). There is an intense cooperation with Amsterdam University Hospital, Pulmonary Hypertension Centre of Hammersmith Hospital in London, Riga Stradins University Hospital, etc. There is also very good cooperation with patient organization (PHA Europe).

The Pulmonary hypertension center of Kauno klinikos participates in the international European COMPERA registry and clinical trials.

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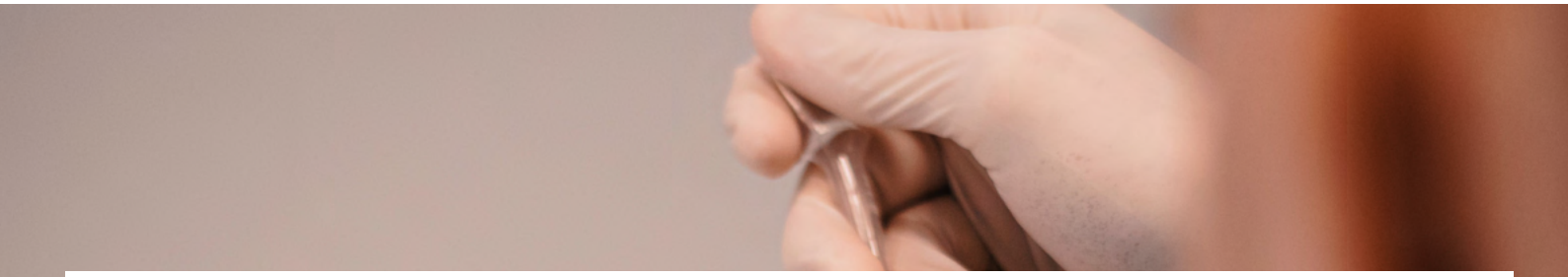

The Adult Cystic Fibrosis Center

was established in 2012 on the initiative of the Department of Pulmonology, taking into account the complexity of patients and the subtlety of diagnostic tests and treatment options.

The activities of the Center are carried out in one of the leading institutions in Lithuania, providing top-level (third-level) care of physicians of various specialties.

It is estimated that there are about 60 cystic fibrosis patients (including children and adults) in Lithuania. Two-thirds of them are supervised in Kauno klinikos; new ones are coming every year, and this number is growing.

The Center closely collaborates with the Department of Pediatrics. People with cystic fibrosis are usually cared for from childhood and referred to adult pulmonologists from the age of 18. Due to the peculiarities of the disease and possible damage to many organs, comprehensive care by professionals with experience in cystic fibrosis is required. Laboratory physicians, gastroenterologists, radiologists, dietitians, physical medicine doctors, and physiotherapists are actively involved in the activities of the Adult Cystic Fibrosis Center to achieve the best results.

The basic and innovative diagnostic tests are applied: a wide range of blood tests, lung function, radiological, sweat samples, genetic tests, including gene sequencing, are performed. The physicians adjust personalized treatment, which includes not only drugs that thin the bronchial secretions, antibiotics, digestive enzymes, but also an important part of the treatment is nutrition planning, specialized physiotherapy procedures. A cough assistant is used as needed to help remove the viscous secretion from the airways. The ports are implanted in all cases when long-term, frequent intravenous antibiotic treatment is required, or the patient has poor venous access.

The center operates in an organized manner and is patient centered. Contact visits take place according to the plan, but there is also an active telephone monitoring. In case of exacerbation with the need for hospital treatment, patients are usually hospitalized on the referral day. To optimize infection control, patients with cystic fibrosis are hospitalized in single wards. To facilitate the mobility of persons with cystic fibrosis, the physician caring for the patient contacts the cystic fibrosis specialist closest to the patient's location abroad, provides medical information on the health condition and simplifies access to a specialist in case of deterioration if the trip is short-term, or coordinates further monitoring and treatment in case of the long-term trip.

In 2013, the Adult Cystic Fibrosis Center was the first one from Lithuania involved in the activities of the European Cystic Fibrosis Society Patient Register. The generalized analysis of the data of the Register provides an opportunity for health care professionals and scientists to see and identify new trends in the development of the disease, identify the most effective treatments, create clinically-based new studies to introduce new, pathogenically active drugs into treatment practices. This would not be possible in separate specialized centers due to the small number of patients with cystic fibrosis. The unifying activities of the registry expand the possibilities of cooperation with other cystic fibrosis centers in Europe. The Adult Cystic Fibrosis Center actively participates in reviewing and editing the annual reports published by the European Cystic Fibrosis Society Patient Registry. In 2019, the Department of Pulmonology of Kauno klinikos, where the Adult Cystic Fibrosis Center is located, has become an affiliated Center for Rare Diseases of European Reference Targets. This further facilitates collaboration with foreign professionals in improving diagnostic fields, treatment, and care for cystic fibrosis.

The Center also carries out scientific activities. In 2013, a textbook was published for medical students, internists, resident doctors, and patients with cystic fibrosis, their relatives and anyone interested in cystic fibrosis. Periodically, peer-reviewed articles summarizing the Centre's performance are published. From 2020, Master's thesis in physiotherapy is underway "Change in quality of life, physical capacity and respiratory parameters by applying a long-term physiotherapy program to patients with cystic fibrosis" (Lithuanian University of Health Sciences Bioethics Edition No. BEC-SR (M)-28, received on 16 November 2020).

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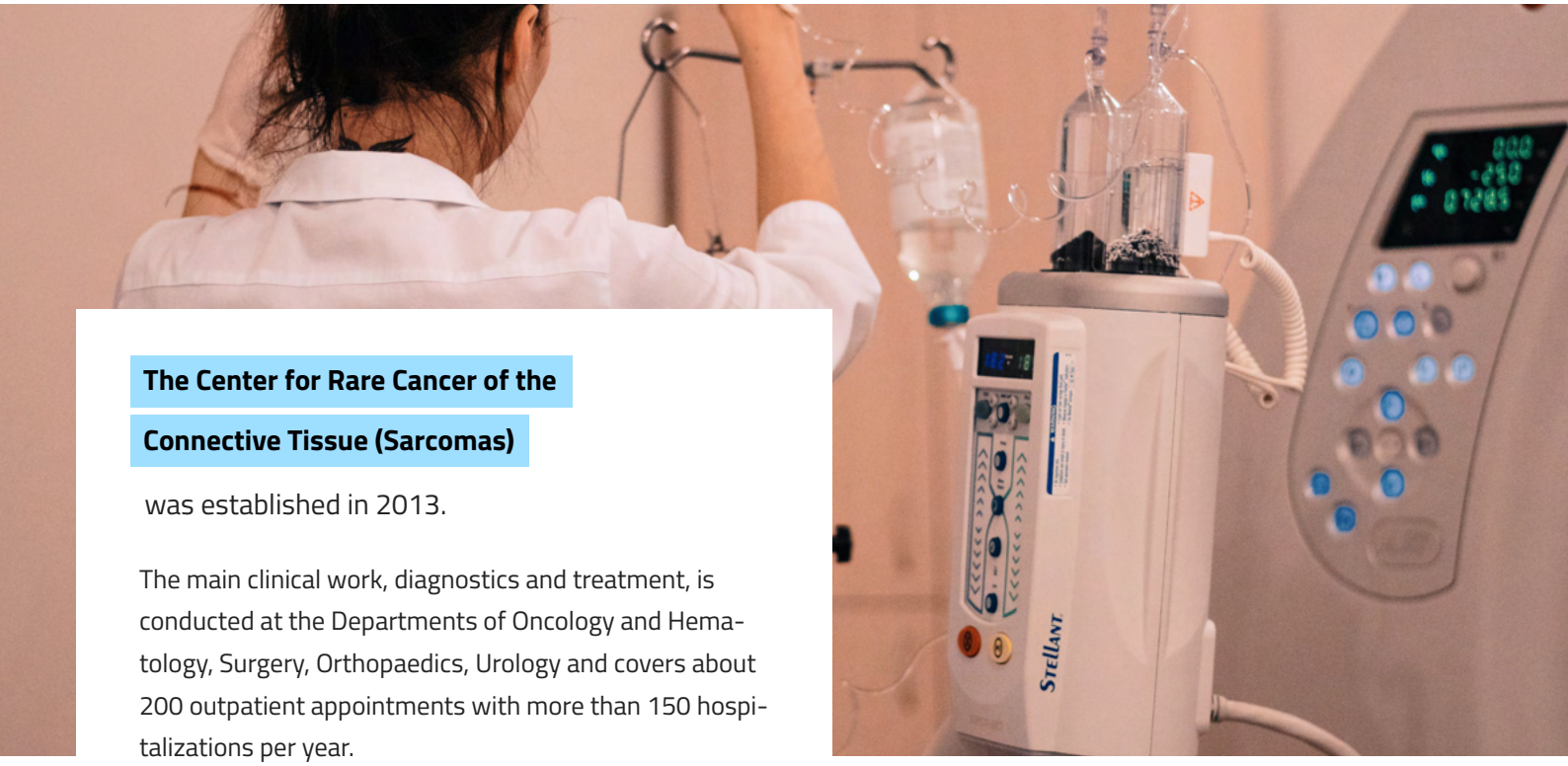

The Center for Rare Cancer of the Connective Tissue (Sarcomas)

was established in 2013.

The main clinical work, diagnostics and treatment, is conducted at the Departments of Oncology and Hematology, Surgery, Orthopaedics, Urology and covers about 200 outpatient appointments with more than 150 hospitalizations per year.

The Center closely collaborates with the Institute of Oncology of the Lithuanian University of Health Sciences, the Department of Cardiac, Thoracic and Vascular Surgery, Radiology, the Department of Genetics and Molecular Medicine and many others. Oncogenetic program both at diagnostic and research level has been available since 2013. The next-generation sequencing enables analysis of dozens of genes associated with sarcomas (translocations, fusion genes, point mutations, etc. for Ewing sarcomas, GIST, various syndromes and others).

The experienced team of the Sarcomas Center operates within modern surgery procedures for all sarcoma localizations: limbs, retroperitoneal, thoracic, the spinal and others. The Center also provides a full range of complex and expanded surgeries including limb sparing, various grafts and implants, also for those with the most complex anatomy (for example, retroperitoneal, axial sarcomas). Experts in surgery, pathology, oncology (both in medical oncology and radiotherapy) and radiology take a part in the multidisciplinary team for management of patients with sarcomas.

Kauno klinikos was the first institution in Lithuania where treatment of complex modalities such as radiotherapy, chemotherapy (later biological therapy) and surgery became available in 1980. Nowadays the Center provides a comprehensive multifactor evaluation and interventional treatment of all types of sarcomas (soft tissue, GIST, bone) for patients of all ages.

The Center provides clinical expertise in the field of radiotherapy in neoadjuvant and adjuvant setting, for both radical and palliative purposes, with various techniques such as intensity modulated radiotherapy (IMRT), stereotactic radiotherapy, the Gamma knife and others for management of all the types and localizations of sarcomas according to international guidelines. The multidisciplinary team of professionals provides access to specialized medical, surgical and laboratory assessment and treatment of these malignancies. High dose chemotherapy and Hematopoietic stem cell transplantation (for example, for Ewing sarcoma), chemotherapy for outpatients and inpatients for prolonged and bolus peripheral as well as central vein infusions, regional hyperthermia in addition to systemic chemotherapy are also available.

The Center for Rare Cancer of the Connective Tissue (Sarcomas) at Kauno klinikos is also a teaching center that actively participates in national projects, registries and implements scientific programs in the field of sarcomas.

Head of the Center:
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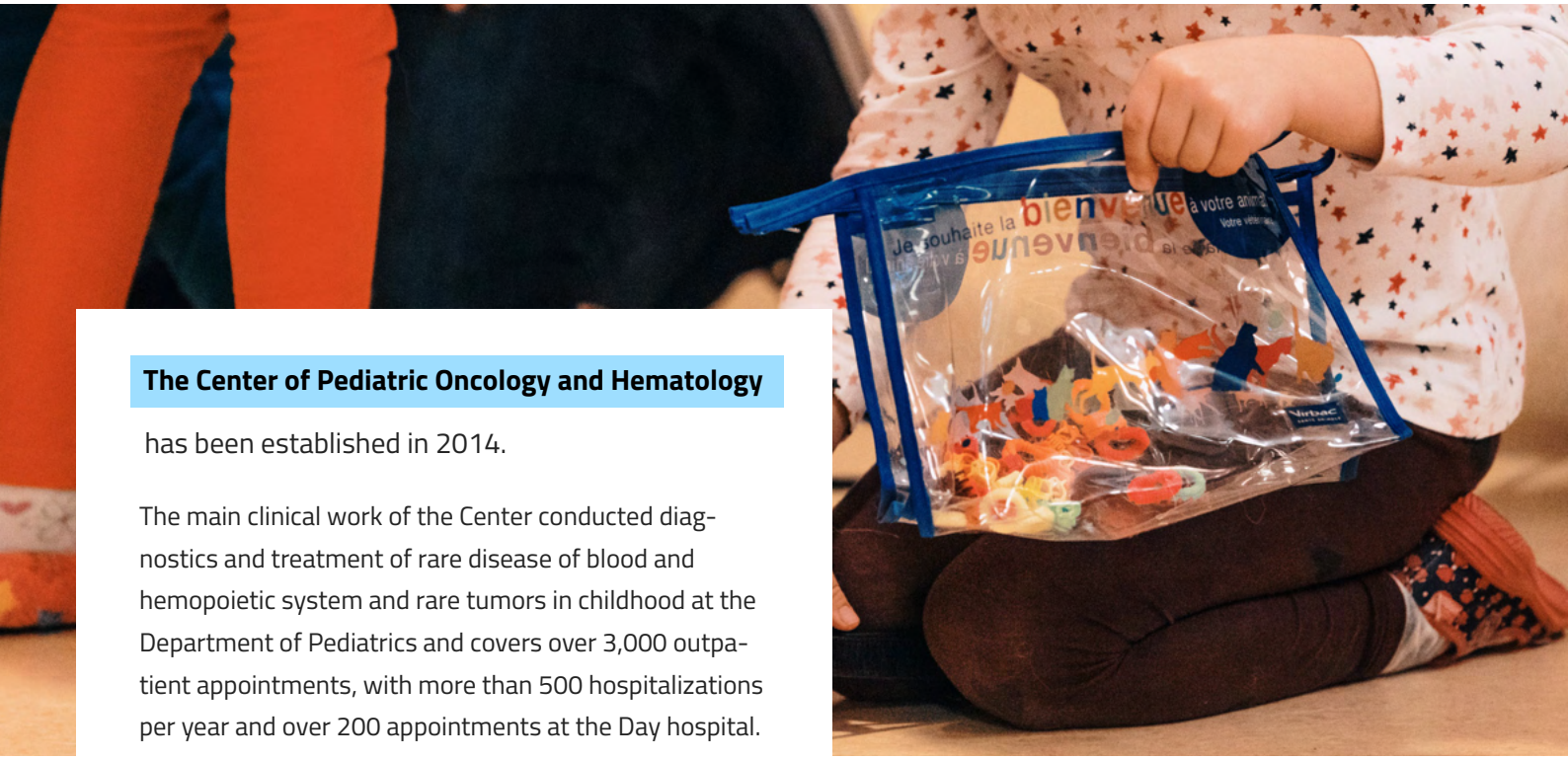

The Center of Pediatric Oncology and Hematology

has been established in 2014.

The main clinical work of the Center conducted diagnostics and treatment of rare disease of blood and hemopoietic system and rare tumors in childhood at the Department of Pediatrics and covers over 3,000 outpatient appointments, with more than 500 hospitalizations per year and over 200 appointments at the Day hospital.

The Center closely collaborates with the Departments of Neurosurgery, Pediatric Surgery, Orthopedics, the Department of Pathology, Radiology, the Department of Genetics and Molecular Medicine and many others. The Center has been working on oncogenetic research program since 2019. The analysis of both somatic mutations from the tumor tissue and germ-line mutations is available and widely applied in our clinical work. The next-generation sequencing enables syndromes, coagulopathies, pathology of the platelets).

The specialists of the Center of Pediatric Oncology and Hematology have over 20 years of experience in diagnostics and treatment of pediatric tumors of the central nervous system. There are more than 30 new cases of brain tumors are diagnosed and treated every year in the Center. The Center provides complex diagnostic and treatment of pediatric solid tumors (tumors of the bone, soft tissues, kidney and others), lymphomas. Since 2018, the follow-up after the cancer treatment became available in the Outpatient Department, where the experienced specialists (pediatric neurologists, endocrinologists, orthopedics, nephrologists and others) provide the consultation according with international follow-up protocols.

The Center collaborates with international partners (NOPHO – Nordic Society of Pediatric Hematology and Oncology; SIOP – International Society of Pediatric Oncology), participates in Pediatric Solid tumors and Brain tumors working groups. Our specialists provide clinical expertise in the management of rare tumors, bleeding disorders, anemias of childhood and neonatal hematologic pathology. The multidisciplinary team of professionals provides access to specialized medical, surgical and radiologic assessment and treatment of these rare disorders.

There are wide spectrum of interventions, such as biopsy, removal of the tumor, modern radiotherapy, radionuclide imaging, the implantation of the central catheters and special reservoirs, making the treatment of aggressive tumors easier available in the Center.

The Center of Pediatric Oncology and Hematology at the Hospital of Kauno klinikos is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of rare tumors and disease of the blood in children.

Head of the Center:
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The Center for Neuromuscular Diseases

has been established in 2012.

In 2018, the Center of Pediatric Neuromuscular Diseases was reorganized into the Center of Pediatric Neuromuscular Diseases, with the aim to provide and develop multidisciplinary care for both pediatric as well as adult patients with neuromuscular disorders. Based on the already developed care model for pediatric patients, the newly established Centre consists of two dedicated teams of pediatric and adult specialists with expertise in NMD area. The teams were formed according to the international criteria, and they work in close collaboration to ensure timely diagnosis and comprehensive care. The specialists of the Centre for Neuromuscular Diseases are involved in education of healthcare specialists and research activities as well. In 2019, Kauno klinikos was endorsed by the Ministry of Health of the Republic of Lithuania as the national reference center for participation in the activities of the European Reference Networks on Rare Neuromuscular Diseases (ERN EURO-NMD).

More than 1,200 patients with rare neuromuscular conditions (1,100 adults and 100 children) are consulted each year in the Outpatient Neurology Department. More than 330 adults requiring differential diagnosis or multidisciplinary evaluation are examined and treated in inpatient settings. About 40 children are hospitalized in the Pediatric Neurology Unit for clinical evaluation, laboratory tests, electroneuromyography, physical capacity and endurance testing, muscle biopsy and pathological evaluation, genetics counselling and genetic testing every year.

Regular comprehensive assessment of patients with neuromuscular conditions is carried out during short-term hospitalizations in the Neurology Department as well as the Pediatric Department, organized in advance in agreement with the patient, caregivers and specialists of the multidisciplinary team. Intensive treatment and monitoring of patients with advanced conditions are provided in intensive care units of the Hospital.

Depending on the diseases and complications, various treatments are applied. For example, treatment of spinal muscular atrophy with nusinersen or risdiplam, treatment of Duchenne muscular dystrophy with steroids and ataluren, management of myasthenia gravis with medications and plasmapheresis, treatment of cardiomyopathy and respiratory complications, adaptation and maintenance of non-invasive and invasive ventilation devices, treatment of endocrine disorders and osteoporosis, surgical correction of deformities, etc. Hospital of Lithuanian University of Health Sciences Kauno klinikos was the first hospital in Lithuania where the treatment with nusinersen intrathecal injections was initiated for children with spinal muscular atrophy. If necessary, cooperation is carried out with neuromuscular specialists from foreign centers.

Here patients and their families are provided with information about the disease, treatment, psychosocial problem solving options and patient organizations in the Center.

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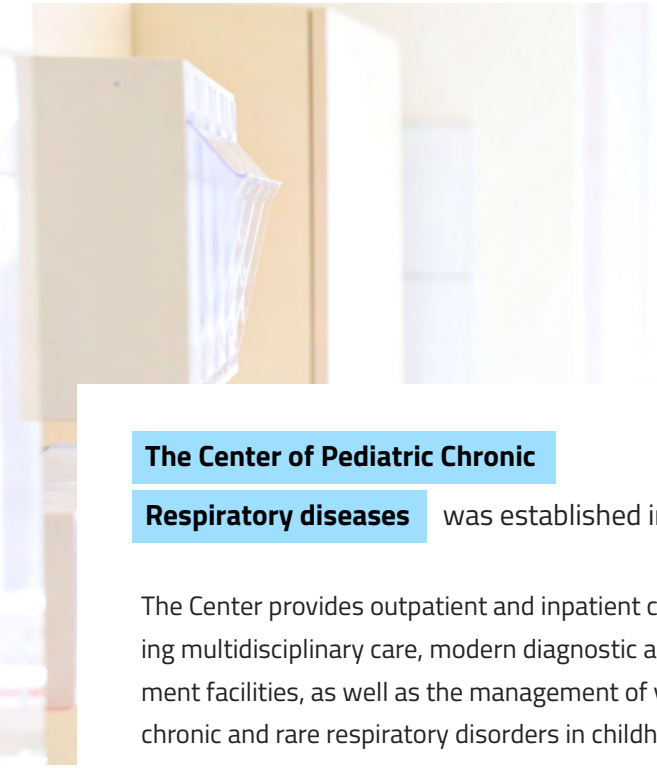

The Center of Pediatric Chronic Respiratory diseases was established in 2012.

The Center provides outpatient and inpatient care including multidisciplinary care, modern diagnostic and treatment facilities, as well as the management of various chronic and rare respiratory disorders in childhood.

Our team of paediatric pulmonologists offers expertise in diagnosis and treatment of asthma, recurrent respiratory infections, chronic cough, wheezing and respiratory failure, as well as rare pulmonary conditions, such as cystic fibrosis, non-cystic fibrosis bronchiectasis, primary ciliary dyskinesia, sleep-disordered breathing, congenital abnormalities of airway and lung development, lung diseases of prematurity and others.

The Center offers a wide range of diagnostic services, including spirometry and whole body plethysmography, methacholine and exercise challenge, exhaled and nasal nitric oxide testing, diffusion capacity and respiratory muscle pressure measurements, multibreath washout tests, baby body plethysmography, polysomnography, bronchoscopy, bronchoalveolar lavage, lung biopsies, sweat tests, genetic testing, high-resolution and magnetic resonance chest imaging, allergy testing, etc.

Specialists of the Center adjust home oxygen therapy and ventilation (either invasive or non-invasive) as well as provide longitudinal care and home ventilation support for children with chronic respiratory failure due to various conditions and reasons. The Center closely cooperate with the Adult Cystic Fibrosis Center, Pediatric Surgery, Neurology, Endocrinology and other departments of Kauno klinikos.

All paediatric pulmonology patients have access to our full multidisciplinary team, including nurses, nutritionists, physiotherapists, social workers and psychologists enabling us to provide comprehensive, patient and family-centered care to each child we take care of.

The Center of Pediatric Chronic Respiratory Diseases of Kauno klinikos is also a teaching center that actively participates in various national and international projects, registries and implements scientific programs in the field of rare pulmonary diseases. The Center has referred data to European Cystic Fibrosis Society Patient's Registry since 2018 and has been an associated national center in ERN LUNG – European Reference Network for Rare Respiratory Diseases since 2019.

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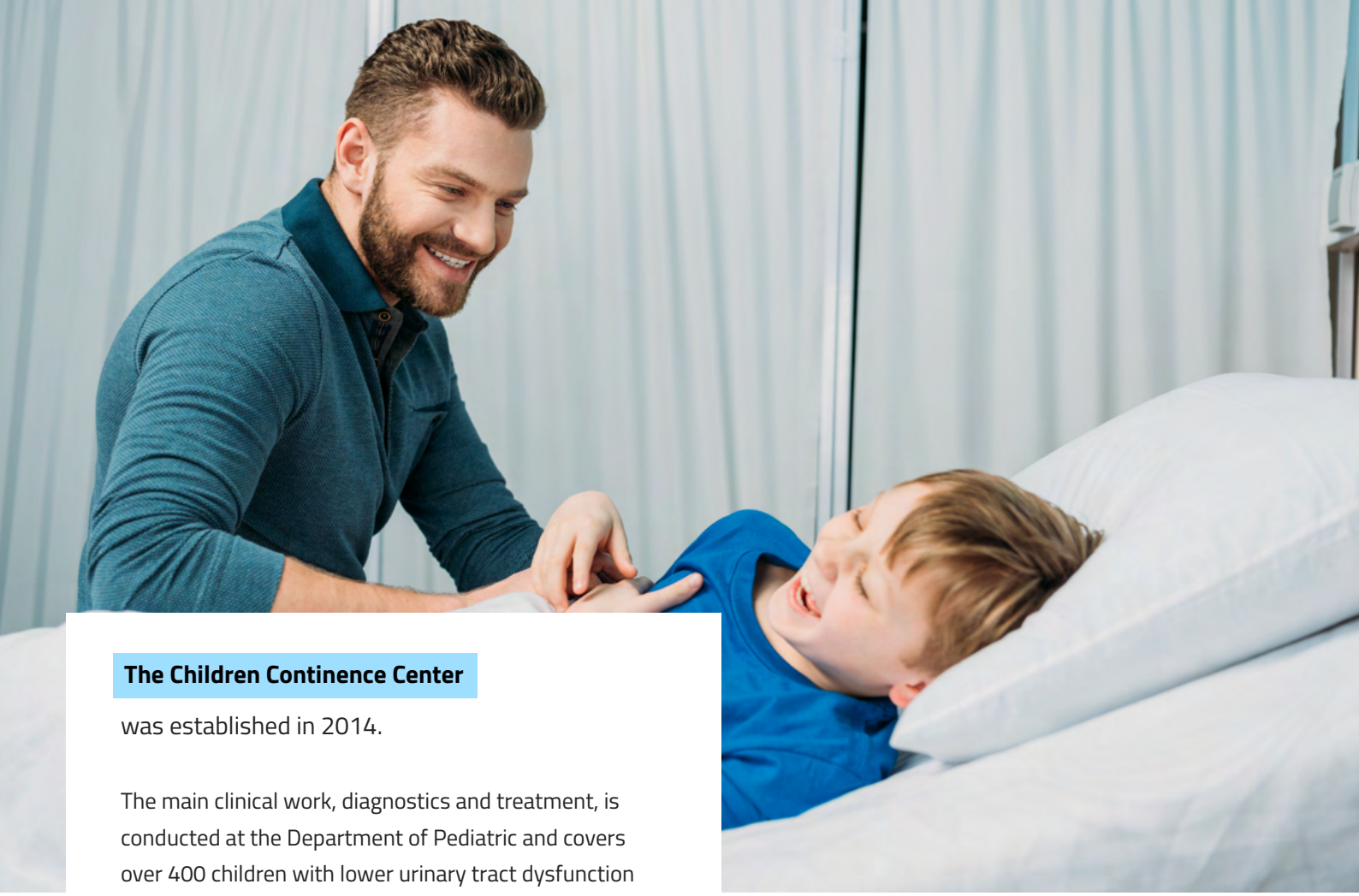

The Children Continence Center

was established in 2014.

The main clinical work, diagnostics and treatment, is conducted at the Department of Pediatric and covers over 400 children with lower urinary tract dysfunction (100-150 new cases each year) and 70 children with rare voiding continence problems (over 5-10 new cases each year).

The aim of the Center is to initiate, form and implement high-quality and timely diagnostics and treatment and rehabilitation of children with lower urinary tract dysfunction by coordinating and integrating the activities of the units participating in the Center. The Center closely collaborates with the Pediatric Surgery Department, Department of Neurosurgery, Department of Neurology, Department of Nephrology, Department of Radiology, Rehabilitation Department, Psychiatric Department. The Centre also cooperates with one of the leading children continence centres in Utrecht, the Netherlands.

The Center provides clinical expertise in the management of congenital and acquired lower urinary tract dysfunction abnormalities. Invasive and non-invasive urodynamic studies are performed. Modern computer “Biofeedback” procedures are performed for patients with voiding dysfunction.

At the Center, a team of highly qualified specialists treats and monitors patients with lower urinary tract dysfunction; a special outpatient room for consultations and follow up of such patients is established.

The Children Continence Center at Kauno klinikos is also a teaching center that actively participates in teaching doctors and patients about children continence problems.

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The Center of Rare Skin Diseases

has been an accredited member of the European Reference Network for Rare Skin Diseases (ERN-SKIN) since 2016.

Participation in ERN-Skin provides an opportunity to accomplish the care for rare and complex skin diseases that require special investigations and treatment, also to carry out educational and research activities in the field of rare skin diseases. The Department of Skin and Venereal Diseases (DSVD) of Kauno klinikos coordinates the activity of the Center of Rare Skin Diseases (CRSD) (https://www.kaunoklinikos.lt/contacts/clinical-departments-/skin-and-venereal-diseases/). It provides specialized secondary and tertiary dermatovenereological health care services from digital dermoscopy and siascopy, high-frequency ultrasound, skin biopsy, skin patch tests for contact allergens, direct microscopy examinations of skin and mucous membranes to cryotherapy or dermatosurgery. The healthcare (individual diagnostic procedures, treatment and follow-up) of patients with rare skin diseases is organized by the multidisciplinary team, which consists of highly qualified dermatologists, nursing personnel, experts assigned to this area (dermatopathologist, clinical pharmacologist, clinical geneticist, allergologist and clinical immunologist, surgeon, other specialists). If necessary, consultations with international experts from ERN-Skin are arranged on Clinical Patient Management System (CPMS) https://cpms.ern-net.eu/login/.

In CRSD of Kauno klinikos, the specialized care for patients with rare skin diseases is provided:

- evaluation of clinical outcomes and follow up of patients with hidradenitis suppurativa, autoimmune bullous diseases, genodermatoses according to ERN-Skin recommendations;
- immunohistochemical skin investigations (IV collagen, inflammatory phenotyping), direct skin immunofluorescence (IGA, IGG, C3, fibrinogen, etc.);
- immunological tests for the diagnosis of autoimmune bullous diseases (detection of antibodies: anti-BP180, anti-BP-230, anti-desmoglein 1, anti-desmoglein 3, anti-envoplakin, anti-collagen VII);
- next generation sequencing analysis for congenital epidermolysis bullosa, ichthyosis, etc.;
- high frequency ultrasound and thermography of skin and subcutaneous tissue for assessment and monitoring the severity of hidradenitis suppurativa;
- complex management of the patients with hidradenitis suppurativa and other rare skin diseases, biological therapy and photochemotherapy;
- specialized – both conservative or surgical management of chronic wounds, fistules.

Research projects ongoing in CRSD in the field of rare skin diseases:

Since 2019, clinical study phase III: indication – hidradenitis suppurativa.

Since 2019, prospective long-term follow-up study of epidemiological, clinical, instrumental, immunological and genetic markers in patients with hidradenitis suppurativa.

Since 2020, ERN-Skin multicenter prospective study "COVID-19 Infection and Rare Skin Diseases".

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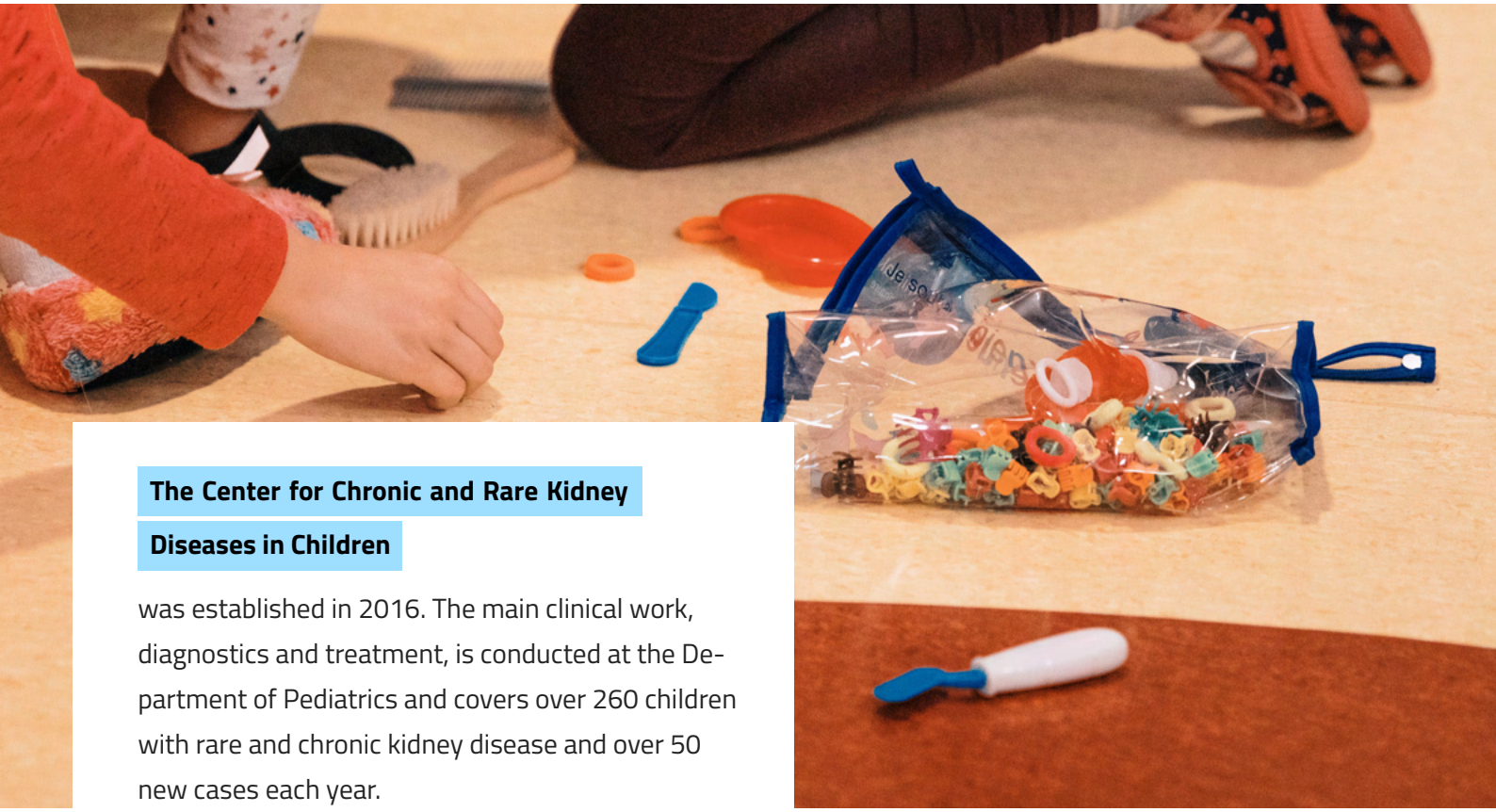

The Center for Chronic and Rare Kidney Diseases in Children

was established in 2016. The main clinical work, diagnostics and treatment, is conducted at the Department of Pediatrics and covers over 260 children with rare and chronic kidney disease and over 50 new cases each year.

The aim of the Center is to initiate, form and implement high-quality and timely diagnostics and treatment and rehabilitation of children's chronic and rare kidney diseases in Kaunas County and the country by coordinating and integrating the activities of the units participating in the Center. The Center closely collaborates with the Pediatric Surgery Department, Department of Neurosurgery, Department of Neurology, Department of Nephrology, Department of Neonatology, Department of Radiology, Department of Genetics and Molecular Medicine, Pediatric Rehabilitation Department, Psychiatric Department.

The Center provides clinical expertise in management of congenital abnormalities of kidney and urinary tract, tubular diseases, renal calculi and nephrocalcinosis, various forms of glomerular disease, renal cystic diseases and ciliopathies. Renal biopsies are performed for the differential diagnosis of diseases affecting the kidney tissue.

Here the team of highly qualified specialists treats and monitors patients with chronic and rare kidney diseases, prepares them for renal replacement therapy-peritoneal dialysis, hemodialysis and kidney transplantation, and monitors patients after kidney transplantation at the Center. In indications, patients are consulted by a multidisciplinary team meeting.

The Center provides emergency nephrology care in acute renal failure for 24 hours, allowing patients to undergo all renal replacement therapy procedures: hemodialysis, peritoneal dialysis, haemofiltration and hemodiafiltration at any age, including newborns.

The Center for Chronic and Rare Kidney Diseases in Children at Kauno klinikos is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of chronic and rare renal diseases. Methodological recommendations for the diagnosis and treatment of chronic and rare kidney diseases in children are prepared.

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The Center for Rare Pediatric Cardiology Rheumatology Diseases

was established in 2016.

The Center for Rare Pediatric Cardiology Rheumatology Diseases at the Hospital of Lithuanian University of Health Sciences Kauno klinikos was established in 2016. The Center was established to improve access to medical services for children with rare cardiovascular and connective tissue diseases. The main task of the Center is to provide qualified, timely, multidisciplinary medical assistance, using various specialists in pediatric diseases and other specialists of Kauno klinikos, diagnosing and selecting treatment tactics, and referring children with rare connective tissue and cardiovascular diseases to adult specialists.

The Center closely collaborates with the Department of Cardiology, especially with the Unit of Cardiac Arrhythmias. The first radiofrequency ablation procedure for the child with arrhythmia in Lithuania was performed in 1991 at Kauno klinikos. Nowadays, the Center provides comprehensive multifactor evaluation and interventional treatment of rare and complex arrhythmic disorders for children.

The Center actively collaborates with the Department of Genetics and Molecular Medicine. Since 2019, the cardiogenetics program is available both at the diagnostic and research levels. The next generation sequencing enables analysis of up to 238 genes associated with familial cardiopathies (channelopathies, arrhythmias, cardiomyopathies).

The Center provides assistance in rare autoimmune and autoinflammatory connective tissue diseases, such as juvenile idiopathic arthritis, systemic lupus erythematosus, juvenile dermatomyositis, chronic multifocal osteomyelitis, vasculitis, and others. Experts in pediatric and adult rheumatology, ophthalmology, immunology, pathology, oncology and radiology take part in the multidisciplinary team for management of children with connective tissue diseases.

Every year the Center specialists diagnose about thirty new cases of rare rheumatic diseases for children. Most of them are treated with the biological therapy.

The Center for Rare Pediatric Cardiology Rheumatology Diseases at the Hospital of Lithuanian University of Health Sciences Kauno klinikos actively participates in national registries and implements scientific programs in the field of rare cardiovascular and rheumatic diseases.

The Center for Rare Pediatric Cardiology Rheumatology Diseases participates in the activities of the Adult Center for Rare and Complex Connective Tissue Diseases. Since 2020, the Center for Rare Pediatric Cardiology Rheumatology Diseases is a part of the National Center in ERN Re-CONNET – European Reference Network for Rare Connective Tissue Diseases.

Head of the Center:
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The Center for Rare Adult Kidney diseases

was established in 2017.

The main clinical work is organized and performed at the Department of Nephrology and comprises 15,000 – 16,000 outpatient appointments with more than 1,400 hospitalizations per year. The Department of Nephrology at Kauno klinikos is one of the largest nephrology centers in the Baltic States and provides specialized care for patients with kidney diseases, including clinical nephrology services, hemodialysis, peritoneal dialysis and kidney transplantation. The team of professionals working in the Center for Rare Adult Kidney diseases consists of five medical experts: three Professors and two Associate Professors. Units of Clinical Toxicology and Therapeutic Apheresis are included into the structure of the Department of Nephrology.

The Center closely collaborates with the Center of Rare Children's Chronic and Rare Kidney Diseases as well as other Departments of Kauno klinikos like the Department of Urology, the Department of Radiology, the Department of Genetics and Molecular Medicine and the National Center of Pathology.

Modern laboratory (immunological and biochemical blood markers – anti-PLA2R, anti-THSD7A, ADAMTS13, anti-MPO, anti-PR3, etc.) and instrumental tests (renal ultrasound and dopplerography, intravenous urograms, dynamic renal scintigraphy, renal computed tomography and/or angiography, renal magnetic resonance imaging and/or renal angiography) are available for the diagnosis of renal diseases. Native kidney biopsies are also a part of the diagnostic algorithm that are performed when necessary. In case of a suspected inherited kidney disease, patients are referred to a genetic counseling and testing.

Here are patients with primary and secondary glomerulopathies (glomerulonephritis, vasculitis, amyloidosis), tubulointerstitial diseases (myeloma nephropathy, acute and chronic interstitial nephritis of various etiologies), thrombotic microangiopathies and inherited kidney diseases (tuberous sclerosis complex, tubulopathies, Alport syndrome, Fabry disease, polycystosis, etc.) examined and treated at the Department of Nephrology. The diagnostic and management strategy is discussed during the meetings of medical experts, highly skilled nephrologists and physicians of other specialties.

The Center for Rare Adult Kidney diseases is also a teaching center that organizes local and national educational and practical activities.

Head of the Center:
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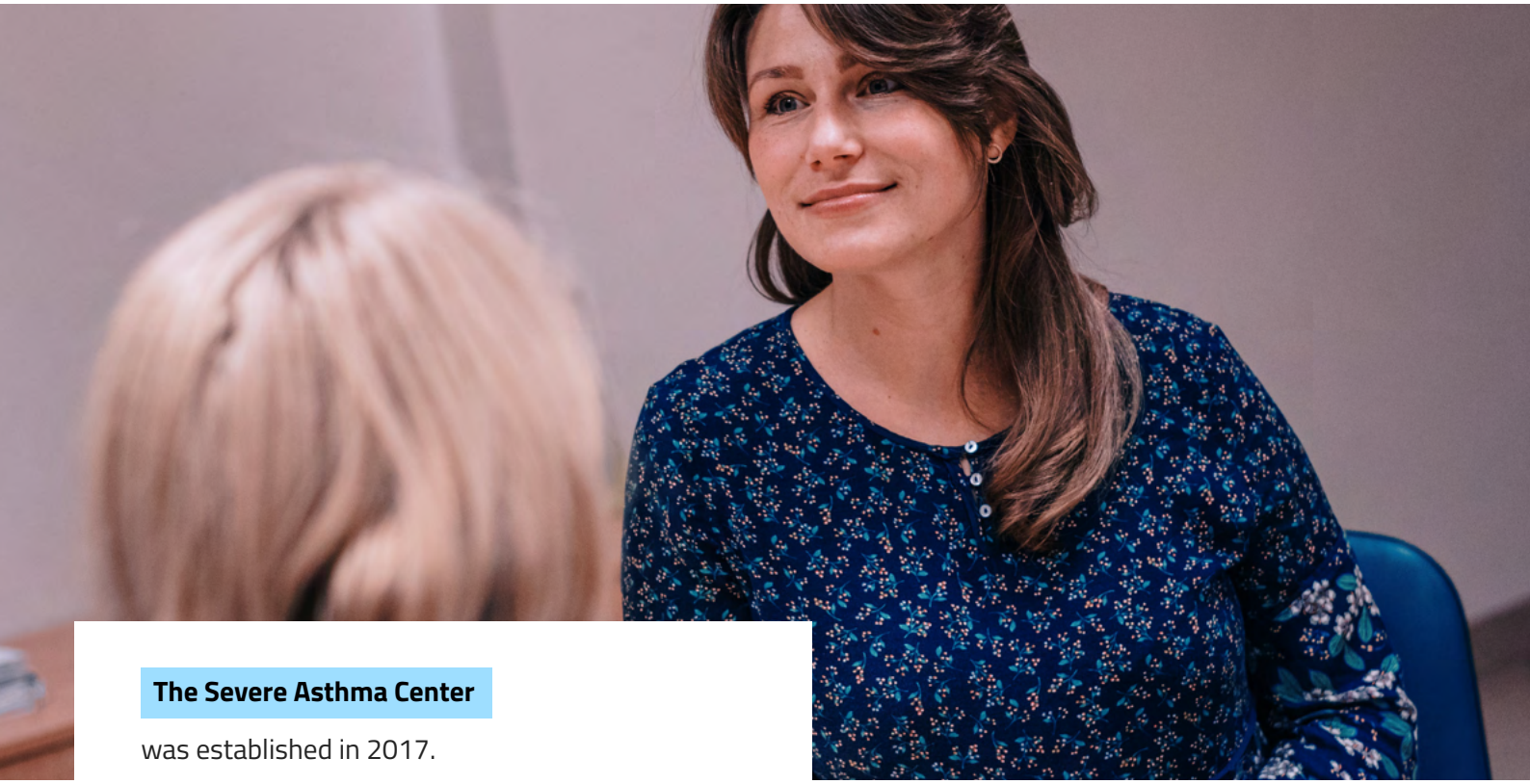

The Severe Asthma Center

was established in 2017.

The work of the center is coordinated by the Department of Pulmonology – the most advanced Department in this field in Lithuania.

The aim of the Center is to initiate, form and implement high-quality and timely diagnosis and treatment of severe asthma by coordinating and integrating the activities of the units participating in the Center. The activities of the Severe Asthma Center take place in three directions: clinical practice, research and teaching.

The Department of Allergology and Clinical Immunology, the Department of Pediatrics, the Department of Ear, Nose and Throat diseases, the Department of Gastroenterology, the Department of Rehabilitation participate in the work of the Severe Asthma Center, performing the functions assigned to it. The Center also closely collaborates with the Department of Radiology, the Department of Cardiology and many others.

The Department of Pulmonology has Pulmonary Function Testing Unit, Interventional Pulmonology Unit, Sleep Laboratory. With the latest modern equipment, a wide range of lung functional tests (spirogram, bronchial inhalation provocation test with methacholine, allergen, exercise challenge test, gas diffusion test, plethysmography, respiratory muscle force measurement, exercise load tolerance test, sputum induction, etc.) are performed. The Bronchology Unit performs complex, wide-profile interventional procedures that, in some cases, delay or even replace the need for surgical procedures.

Severe asthma research projects are carried out in the Pulmonary Laboratory of the Department of Pulmonology. One of the main research areas of the laboratory – issues of etiology, pathogenesis, pathophysiology, diagnosis, treatment of chronic obstructive pulmonary diseases. Updating Lab equipment system for the growth of structural lung cells and the formation of combined cell cultures has been introduced.

The Severe asthma Center doctors have multidisciplinary teams meetings once a week were the cases of severe asthma are discussed. Severe asthma treatment with biologics has started since 2018. More than 100 asthma patients on biologics are followed up in the Severe Asthma Center. A “green corridor” has been created to improve the health care for patients with severe asthma. The Green Corridor helps patients reach a severe asthma specialist as quickly as possible.

The Severe Asthma Center at the Hospital of Lithuanian University of Health Sciences Kauno klinikos has joined the European Respiratory Society project SHARP CRC (Severe Heterogeneous Asthma Research collaboration, Patient-centered Clinical Research Collaboration). The head of the Severe Asthma Center is the national lead for this project. Participating in this project the Department of Pulmonology has joined European Severe Asthma register SHARP Central and carries out several research projects together with other European countries.

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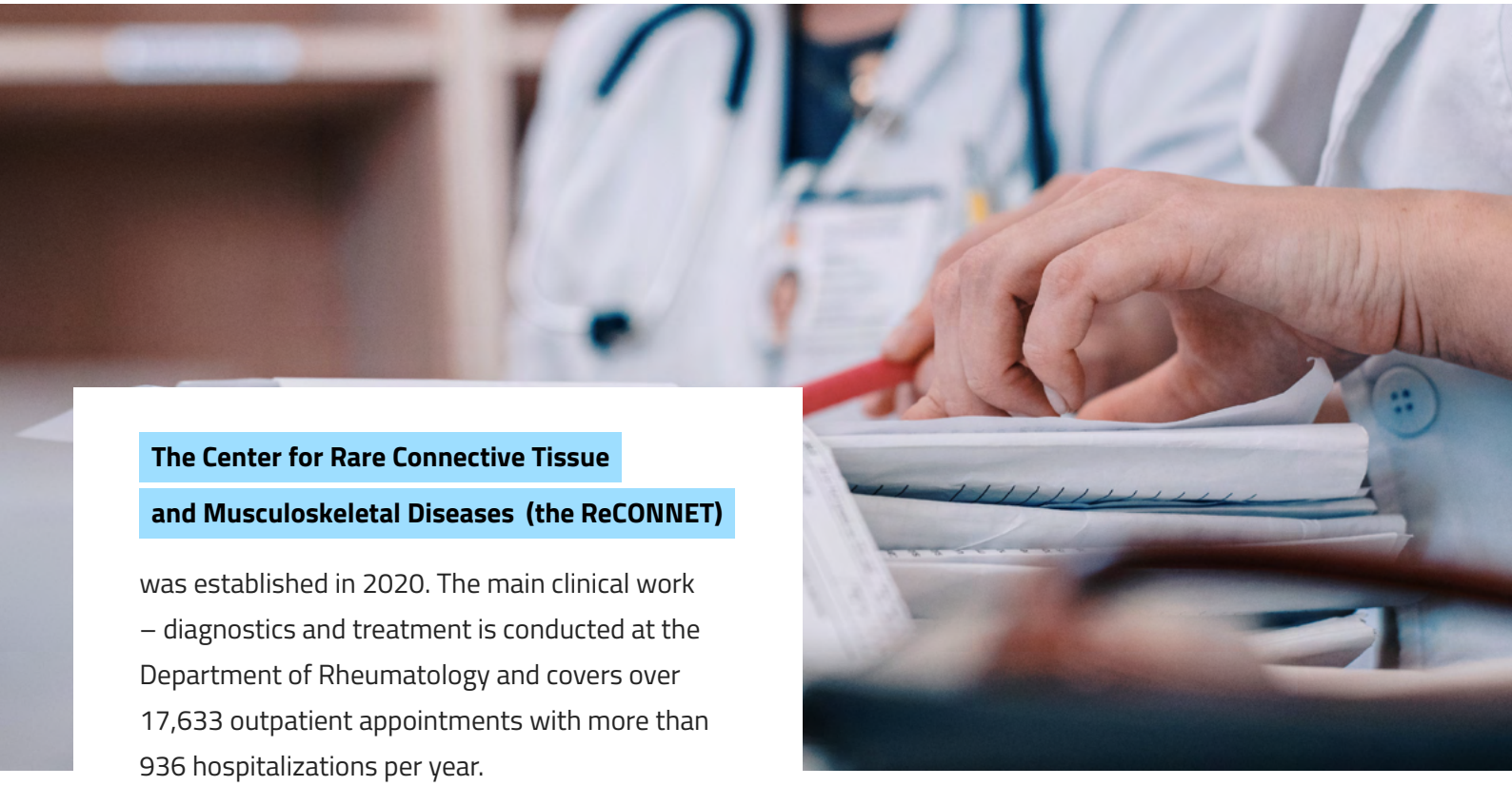

The Center for Rare Connective Tissue and Musculoskeletal Diseases (the ReCONNET)

was established in 2020. The main clinical work – diagnostics and treatment is conducted at the Department of Rheumatology and covers over 17,633 outpatient appointments with more than 936 hospitalizations per year.

The Center closely collaborates with others departments of the Hospital, especially with the Departments of Immunology, Genetics, Cardiology, Pulmonology, Nephrology, Pediatric, Pathology, etc.

The Center provides clinical expertise in management of different rare connective tissue diseases and vasculitidies, such as systemic sclerosis, mixed connective tissue disease, idiopathic inflammatory myopathies, IGG 4 related diseases, relapsing polychondritis, Sjogrens syndrome, systemic lupus erythematosus, antiphospholipid syndrome, undifferentiated connective tissue disease, granulomatosis et polyangitis, large cell vasculitis and many others.

The multidisciplinary team of professionals provides access to specialized medical, surgical and all kind of instrumental assessment and treatment of these disorders. A wide spectrum of instrumental, immunological and pathological assessments are available at the Center. The Center also provides a full range of rehabilitation and care for patients.

The Center for Rare Connective Tissue and Musculoskeletal diseases is also a teaching center that actively participates in national and international projects, registries and implements scientific programs in the field of rare connective tissue and Musculoskeletal diseases.

Since 2020, the Center is an associated national center in ERN ReCONNET– European Reference Network for Rare Connective Tissue Diseases and Musculoskeletal Diseases.

Head of the Center:
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The Epilepsy Center

The healthcare of adult and pediatric patients with rare, complex epilepsies is managed by the Epilepsy Center (EC) of Kauno klinikos.

EC coordinates the activities of all the relevant hospital units involved in the care of epilepsy patients: adult and pediatric neurology, neurosurgery, psychiatry, neonatology, rehabilitation, radiology, genetics, laboratory medicine, intensive care, etc. The core unit of the EC is the Neurology Department, which provides secondary and tertiary level health service for neurological and pediatric neurological patients from Lithuania and abroad. The Epilepsy Center provides continuous care of epilepsy patients from newborn period to childhood and transition to adult epilepsy care.

All types of EEG recordings for epilepsy patients are available, including long-term video EEG monitoring, and invasive/intra-operative EEG recordings.

Epilepsy patients have access to modern radiological diagnostic equipment – CT, MRI, PET, SPECT.

The specialized functions covered by the different professionals within the Epilepsy Center team include:

- Clinical expertise, video EEG, video EEG monitoring 24/7, high resolution MRI, fMRI, PET, SPECT, neuropsychology.
- Department of Laboratory Medicine provides a comprehensive list of laboratory tests with accompanying competent consultative support related to rational use of tests, clinical interpretation of the results for diagnosis. Plasma levels of all antiepileptic medications and antidepressants are available in Lithuania.
- Genetic consultation, testing for genetic and hereditary metabolic diseases. Whole exome sequencing has been recently included. Safe and reliable preparation and storage of biological samples is ensured by the proper equipment. Whenever an investigation in need cannot be performed at Kauno klinikos, the samples are sent to outside certified laboratories (Centogene AG or Archimed Life Science GmbH). Safe shipping to outside partners is performed following the Regulation of Personal Data Protection.
- Epilepsy surgery (resective, palliative, gamma knife, vagus nerve stimulation).
- Ketogenic diet has been implemented for children with refractory epilepsy.

The staff of the Epilepsy Center takes an active part in policy-making (epileptology, child neurology and rare diseases in general) at the national level, participates in different working groups and legislation processes regarding diagnostics and treatment, rehabilitation, participates in clinical trials for children and adults with epilepsy and rare diseases, has experience with orphan products.

Since 2019, EC has become an affiliated partner of the European Reference Network for rare and complex epilepsies (EpiCARE).

Head of the Center:
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The Center for Rare Bone diseases

was established in 2020.

The main clinical work is conducted at several departments of the hospital. Diagnostic procedures are provided at the Department of Genetics and Molecular Medicine and the Department of Radiology. Various treatment modalities are provided at the Department of Children Surgery Pediatric Orthopedics-Traumatology division and the Department of Orthopedics.

The patients with rare bone disease are consulted at other departments of the hospital: Dental and Oral Pathology, Plastic and Reconstructive Surgery, Endocrinology, Pediatrics, Neurology, Neonatology, Neurosurgery, Rehabilitation, Pediatric Rehabilitation, Anaesthesiology, Laboratory Medicine, Obstetrics and Gynaecology, Ophthalmology, Maxillofacial Surgery, Nephrology, Rheumatology, Ophthalmology, Pulmonology, Otorhinolaryngology and others.

The Department of Radiology is the largest radiological diagnostic department in Lithuania with concentrated modern radiological diagnostic equipment: digital X-ray machines, 10 units of ultrasound diagnostic equipment, four CTs, three MRI (magnetic resonance imaging) machines, three gamma cameras, angiography and bone densitometry (DXA) devices. The Department of Radiology is a modern, broad-based unit with all modern methods of radiological investigation.

The main purpose of the Department is implementation of up-to-date science-based radiological methods for diagnosis and treatment of rare bone diseases.

The Department of Genetics and Molecular Medicine provides state of the art molecular diagnostic methods for patients with rare bone disorders. The department consist of Clinical Genetics division and Laboratory division. There are Cytogenetics laboratory, Molecular Genetics laboratory and Biochemical Genetics laboratory. The Molecular Genetics laboratory is equipped with different methods of PCR, sequencing, new generation sequencing machines and highly qualified personnel to ensure careful molecular diagnostics for rare bone diseases. Mass spectrometry method is also established at the Biochemical Genetics department.

Orthopedic surgeons take care of pediatric and adult patients and perform almost all required procedures for rare bone disorders. Modern management methods are provided for bone fragility disorders: telescopic intramedullary needles, synthetic bone replacement, etc. Personalised guides are used for the complex surgeries in order to diminish traumatism. Pediatric orthopedic surgeons are pioneers in using the Ponsee method in treating foot deformities and support the method in Lithuania.

The Center for Rare Bone diseases at the Hospital of Lithuanian University of Health Sciences Kauno klinikos is also a teaching center that provides education to students, residents and fellow colleagues about rare bone disorders. Members of the center also collaborate with foreign specialist to provide state of the art diagnostic and treatment options.

Since 2020, the Center has been an affiliated national member in ERN BOND, European Reference Network on rare bone diseases.

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