

Histology & Embryology Periodical

Department of Histology and Embryology Third Faculty of Medicine, Charles University in Prague

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Welcome!

Dear Students!

Welcome to the community of the Charles University in Prague, welcome to your first semester at the Third Faculty of Medicine, and welcome to our Department of Histology and Embryology!

We hope to match with your excitement at making such a great step in your life; starting a University, living probably for the first time away from your family, in a new place or a city.

As for our Department, during the first two semesters, we will support your study of the developing human, and micro- and nanoviews on human cells and tissues. We hope to present you with both facts and contexts, pieces of knowledge and often surprising connections.

Start with no hesitation, open your textbooks, prepare for each lecture and practical, ask questions, search for answers, and seek understanding!

Qualis principium, talis et clausula. (How you begin determines how you end)

Who is who?

At the Department of Histology & Embryology

Prof. MUDr. Josef Stingl, CSc.

The head of the Department of Histology & Embryology.

MUDr. Lucie Hubičková-Heringová, Ph.D.

lucie.hubickova@lf3.cuni.cz

A driving force of the Department of Histology & Embryology. You will find her in her office in the 3rd floor, room no. 326, or in the laboratory room no. 520.

See a short profile of Dr. Hubičková-Heringová in the October, 2014 issue of the Periodical:

http://www.lf3.cuni.cz/opencms/export/sites/www.l f3.cuni.cz/en/departments/histologie/hep/HEP-2014-04-en-2014-10-07.pdf

MUDr. Eva Maňáková, Ph.D.

eva.manakova@lf3.cuni.cz

Dr. Maňáková is the most experienced professional at the Department. You are welcome to get in touch with her whenever you get beyond the ordinary regarding histology, embryology and teratology.

See a short profile of Dr. Maňáková in the October, 2014 issue of the Periodical:

http://www.lf3.cuni.cz/opencms/export/sites/www.l f3.cuni.cz/en/departments/histologie/hep/HEP-2014-04-en-2014-10-07.pdf

MUDr. Tomáš Boráň

Tomas.boran@lf3.cuni.cz

An assistant employed both at the Department of Histology & Embryology 3rd Faculty of Medicine UK and at the State Institute for Drug Control, an institute neighboring to our Faculty.

See a short profile of Dr. Boráň in the December, 2014 issue:

http://www.lf3.cuni.cz/opencms/export/sites/www.l f3.cuni.cz/en/departments/histologie/hep/HEP-2014-06-en-2014-12-05.pdf

MUDr. Zdeňka Zemanová, CSc.

Zdenka.zemanová@lf3.cuni.cz

A counselor and a greatly experienced scientist.

For a professional and personal story of Dr. Zemanová, please see the December, 2014 issue: http://www.lf3.cuni.cz/opencms/export/sites/www.l f3.cuni.cz/en/departments/histologie/hep/HEP-2014-06-en-2014-12-05.pdf

Karen Vávrová

karen.vavrova@lf3.cuni.cz

An experienced and invaluable lab technician. Her office is in room n. 322.

A short profile of Karen Vávrová in an October, 2014 issue:<u>http://www.lf3.cuni.cz/opencms/export/sites/</u> www.lf3.cuni.cz/en/departments/histologie/hep/HE P-2014-04-en-2014-10-07.pdf

Michal Skala michal.skala@lf3.cuni.cz

The Sekretariate of the Department of Histology and Embryology, 3rd Faculty of Medicine UK.

See a short profile of Mr. Skala in an October, 2014 issue:

http://www.lf3.cuni.cz/opencms/export/sites/www.l f3.cuni.cz/en/departments/histologie/hep/HEP-2014-04-en-2014-10-07.pdf

MUDr. Klára Matoušková, MPH

klara.matouskova@lf3.cuni.cz

An editor of the Periodical of Histology and Embryology.

For a short profile of Dr. Matoušková, see an October, 2014 issue:

http://www.lf3.cuni.cz/opencms/export/sites/www.l f3.cuni.cz/en/departments/histologie/hep/HEP-2014-04-en-2014-10-07.pdf

REMINDER –I-

Please, wear your white coat during histology practicals as you do for other subjects of the Modules.

Handle histology slides with extreme care as quality slides are:

- ✤ Expensive
- Precious (to acquire an appropriate tissue is a tall order)
- Unique (histology slides are all hand made, most of them right behind the door next to your microscopy room)
- Difficult to make (lab technicians who can make a nice histology slide are a rare kind, and it takes time, in fact a lots of time!)
- Fragile!



Figure 1 Robert Hooke's microscope, from *Micrographia* published in 1665.

What's up?

Study Programme General Medicine Module Cellular Basis of Medicine Course 1: Cell Structure

In weeks 1 and 2 you have learned about methods used in the science of histology, about basic cell types and started to become familiar with seeing structures in electonograms.

Week 3 and 4 Revisions and self-study October 21 Dean's day

Week 5

Two lectures: Epithelia and Specialized methods in Histology October 28 Public holiday (in 1918 the new republic of Czechoslovakia was created)

Week 6 A written test Course 1: Cell Structure

REMINDER -- II-

Workbooks:

- Accessible and printable from the website Curricular Database (if you still need your copy Michal Skala at the Secretariate will happily print one out for you).
- A completed workbook is a part of your semestral credits.
- Workbooks are meant to help you <u>in the course</u> of a semester, during practicals and self-studies.

REMINDER -III-

Microscope self-study in room n. 318

Wednesdays 3,15 - 4,45 pm (see your schedule for changes in weeks 4, 5 and 6 regarding the public holiday October 28)

You can borrow a set of slides and use the time to study microscopic images, compare them, discuss with a senior student present and ready to assist and consult with you.

Make sure you start using the self-study opportunity right from the beginning. There might not be enough microscopes for all students eager to study the week before their examinations at the end of semester!

"You can observe a lot by just watching"

Yogi Berra

News..

25th International ENTIS Meeting at the 3rd Faculty of Medicine, CU



From September 17 to 20, 2015 the 3rd Faculty of Medicine, Charles University in Prague hosted a conference of the European Network of

Teratology Information Services. It was the 25th anniversary meeting of members of this eminent organization founded in 1990 in Milan, Italy.

What does ENTIS stand for?

European Network of Teratology Information Services.

What is teratology?

Teratology is the study of developmental birth defects; structural, functional or physiological.

The examples of birth defects vary wide, from relatively innocent such as low birth weight or risk of obesity to serious e.g. congenital malformation of limbs, cleft of upper lip and/or palate, or various metabolic developmental disorders and disturbed function of protein receptors.

Considerations in teratology include environmental exposures and birth defects, developmental and reproductive toxicology, exposure type and level during varying stages of pregnancy, drugs and birth defects, genetic influence of birth defects, maternal health and nutritional influence on birth defects, and birth defects prevention.

A teratogen is an agent such as a drug, chemical, virus, pollutant or even a physical factor such as fever, which interferes with the normal development of the embryo or fetus.

What is TIS (teratology information service)?

TIS is a service providing information about risks posed by exposure to drugs or other exogenous agents to the healthy development of an individual during pregnancy and lactation.

What is ENTIS?

ENTIS is an international organization of teratology information services founded in May, 1990. ENTIS has nineteen members, among them twelve European countries, two south-American countries, and Australia, Japan, Russia, Turkey and Israel.

The general objective of ENTIS is to coordinate and collaborate with other TISs, and to collect and evaluate data in order to contribute to the primary prevention of birth defects and developmental disorders.

Birth defects caused by teratogens are preventable, therefore the main task of each TIS is to recognize and to detect risk factors with the objective of preventing birth defects.

What is CZTIS?

Czech Teratology Information Service (CZTIS) was founded in 1996 by Prof. Richard Jelínek, and associated with the Department of Histology and Embryology of the 3rd Faculty of Medicine, Charles University. Beginning the year CZTIS was established, it has been a member of ENTIS.

During its' entire existence, CZTIS has been an invaluable source of information about risk of exposure to possible or actual teratogens. CZTIS counsels medical professional about individual cases with exposure to drugs and other exogenous agents during pregnancy with respect to the risk of reproductive toxicity. The information provided is based on current scientific data, collected and analyzed.

25th ENTIS Meeting was an inspiring gathering of health care professionals focused, besides their own specialization, on teratology. The topics presented included diabetes in pregnancy, neurodevelopmental origin of ADHD and autism, risks of gestational use of antidepressants or epigenetic changes as one of the mechanisms of teratogenesis.

The next ENTIS meeting, will be held early June, 2016 in Berlin, Germany.



Figure 2 Brandenburg Gate, the neoclassicist icon of Berlin.

... and more news.

The Lancet: Adapting to migration as a planetary force

The current migration crisis in Europe divides public opinion across the nations involved. There are discussions about future of Europe, its' culture and religion, and demographic changes. Much less is heard about individual refugees. To narrow the complicated topic to health concerns; how do they feel? How does any particular person feel? Does he suffer from cough? Does the girl doubled over in pain have a stomach ache, diarrhea? Is that old man cold, hypothermic? Does anybody check on the pregnant woman? Is she hydrated? How about people with high blood pressure? Diabetes? Depression? When scratched or injured, are they vaccinated against tetanus?

The Lancet, in its' editorial from September 12, 2015¹, is greatly critical of big health care organizations such as the Academy of Medical Sciences, the World Medical Association or the Royal College of Paediatrics and Child Health. The journal criticizes them for their weak or non-existent voice regarding health care for those who left their homes, migrating. The Lancet believes that there is a moral obligation for health professionals to speak on this issue. Regarding a large study on health and climate change published in this journal in June 2015², The Lancet reminds us that [political] conflict is a major factor

¹ The Lancet. Editorial: *Adapting to migration as a planetary force*. Sept. 12, 2015. 386, 9998. DOI:

http://dx.doi.org/10.1016/S0140-6736(15)00190-7. Available from:

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)00190-7/fulltext?rss=yes

 $^{^{\}rm 2}\,$ Watts, N. et. al. Health and climate change: policy responses to protect public

healthhttp://www.thelancet.com/journals/lancet/article/PIIS0140 -6736(15)60854-6/fulltext

that "undermines the capacity of populations to cope with climate change, leading to greater displacement than might have been the case in a more stable environment".



On the other hand, The Lancet respects the WHO response "grounded in the basic principles of humanity". In her Statement from September 2, 2015 the WHO Regional

director for Europe, Dr. Zsuzsanna Jakab points out that adequate standards of care for refugees and migrants are "fundamental for protecting and promoting their human rights"³. She emphasizes that there is no "systemic association" between migration and the importation of infectious diseases, and that

the risk that an exotic infectious agents such as Ebola virus or Middle East respiratory coronavirus (MERS) will be imported into Europe is extremely low. Dr. Jakab assures that Europe is well prepared, that there is no reason for panic, we should only remain vigilant and "focus on

ensuring that each and every person on the mover has full access to a hospitable environment and,

when needed, to high-quality health care without discrimination on the basis of gender, age, religion, nationality or race. This is the safest way to ensure that the resident population is not unnecessarily exposed to imported infectious agents." Last but not least, the WHO Regional director states that migrants and refugees are not a homogenous group therefore their needs are diverse, and that health is a state of complete physical, mental and social well-being, therefore the social determinants of health such as "education, employment social security and housing" have considerable impact on health. Besides the words of support, the WHO Regional Office for Europe provides "technical and onsite assistance to affected countries", also advice on planning and health personnel training, as well as delivery of "emergency kits, each covering the needs of a population of 10 000 for 3 months".

In a similar spirit of vigilance, but not panic, the chief medical officer of the Czech Republic, Dr. Vladimír Valenta commented: "There is always room for concerns however the current level of sanitary



Figure 3 Migration is not a new phenomenon. Human migration routes from 100 000 to 10 000 years ago. Photo: National Geographic.

standards, preventive and medical systems reassures us that we can respond to the problem [migration]" he says in June, a local medical 2015 for magazine. Dr. Valenta made a follow-up statement for the Ministry of Health of the Czech Republic in September, 2015

indicating that there has been no change in the epidemiologic situation since his previous

assessment in June⁴. After all, as mentioned by Tomas Cikrt, former Minister of Health, there has been several thousands of migrants in the country so far, however the travel business brought 8 million tourists just in one year⁵, Over 200 thousand tourist

³ Jakab, Zs. *Statement- Population movement is a challenge for refugees and migrants as well as for the receiving population*.[online] WHO/Europe, 2 Sept. 2015 (Cited Oct. 3, 2015). Available from: <u>http://www.euro.who.int/en/about-us/regional-director/speeches-and-presentations-by-year/2015/statement-population-movement-is-a-challenge-for-refugees-and-migrants-as-well-as-for-the-receiving-population#</u>

⁴ Tisková zpráva MZCR. Hlavní hygienik: Česká republika není aktuálně v souvislosti s migrací ohrožena nákazami. 4.9.2015 [online]. (Cited Sept. 29, 2015). Available from:

http://www.mzcr.cz/dokumenty/hlavni-hygienikceska-republikaneni-aktualne-v-souvislosti-s-migraci-ohrozena- 10740 1.html

⁵ Cikr, T. *Jaká jsou reálná rizika pro zdraví Čechů?* Zdravotnický deník, Sept. 15, 2015 [online]. (Cited Oct.2,2015). Available from:

came from China, a country with the highest year-onyear growth of multi-resistant tuberculosis. TB vaccine is no longer included in the recommended vaccination schedule in the Czech Republic.

There are also much greater possible health thread for the Czech population than fear of exotic viruses. The Lancet in 2013⁶ pointed out that the war in the eastern Ukraine has brought corruption in health care systems, and poor vaccine supply. That, combined with recent mistrust in immunization brings very possible risks for the Czech population as Ukraine immigrants are the most frequent and most successful permanent stay seekers.

The Lancet in September, 2015 however, speaks with a clear voice: "This is a today's crisis. Migration is not going away. It is going to be a major force shaping the 21^{st} century global society, as migration and climate change are inextricably entwined ... This is our current and future existence. We need to accept it – and address its human consequences"

http://www.zdravotnickydenik.cz/2015/09/jaka-jsou-realnarizika-migrace-pro-zdravi-cechu/

⁶ Holt, E.Ukraine at risk of polio outbreak. The Lancet, June 29, 2013, 381 (9885), p. 2244. DOI: <u>http://dx.doi.org/10.1016/S0140-6736(13)61469-5</u>. Available also from: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)61469-5/fulltext

Theme:

Genes, signaling molecules, proteins... and mechanical forces, too.

Few sights are as fascinating as the change of a mass of thousands of embryonic cells into a shape shared among all metazoans. Within a short period of time, the mass extends and narrows, and soon you see the head-to-tail body plan.



Figure 4

A time-lapse image composed out of 300 pictures taken during the development of zebrafish, 8.5 to 18.5 hours after fertilization. From the laboratory of Sean Megason, Harvard Medical School: https://www.youtube.com/watch?v=AAV5SiCoKKo

The process of elongation of the embryonic head-totail (anterior-posterior) body axis while the ventraldorsal axis narrows is named "convergent extension". Convergent extension is one of the elementary developmental processes. It is also a highly evolutionary conserved process, i.e. it happens in all studied multi-cellular organisms. Convergent extension takes place during gastrulation, neurulation, or in development of specific body organs such as heart tube or tubules in kidneys.

Scientists use various organisms to study early development. The animals most often studied are fruit flies (*Drosophila*)

melanogaster), zebrafish (Danio

rerio) or African



Figure 5 Danio rerio

claw frogs known as xenopus (*Xenopus laevis*), also chick embryos or laboratory mouse, *Mus musculus*.

The problem of anterior-posterior (AP) elongation, or convergent extension in general, while the motions in the mass of cells is seemingly chaotic pushing and pulling, has been studied by many teams, in many labs around the world over a few decades.



Figure 6 Eric Wieschaus in his lab at the University in Princeton, in 1978

One of them was a team of Erik Weischaus, an American developmental biologist, and Nobel Prize laureate, in 1995 for his, and co-laureates', discoveries concerning the genetic control of early embryonic development. Eric Wieshaus studies fruit flies embryos and their regulatory genes.

There are two types of regulatory, body building, genes; the first type are "maternal effect genes" present in maternal oocyte while used by the embryo. The other type are "zygotic genes" produced and used by the embryo to control its' development in space and time.

As well as most of biologists in the 80' and 90' of the 20th century, Eric Wieshaus along with his colleague and a co-laureate of Nobel Prize in Medicine and Physiology in 1995, Christiane Nüsslein-Volhard, examined the genetic aspects of embryonic development. In fact, the role of genes, signaling molecules and proteins in development has taken center stage in the past several decades.

Times change, and so does the focus on aspects of embryonic development. The role of mechanical forces, long overshadowed by studies of genes and molecules, has reemerged after all. Scientists however have long appreciated the idea that mechanical forces are integral to creating form and shape. In 1984, an American embryologist John Phillipe Trinkaus published a book "Cells into Organs; The Forces that Shape the Embryo". In the book, he stated an obvious but long neglected fact that forces do shape embryos. A revival of studies on physical forces forming embryo is now underway. Moreover, labs are now armed with new tools for manipulating and imaging cells, and immense computing power, and scientists have much greater knowledge of tissues, cells and molecules.

Among other morphogenetic processes, the process of convergent extension has been recently studied from a perspective of mechanical forces. Jennifer Zallen launched her career in a team of Eric Wieschaus, and that is probably the reason behind her focus on *Drosophila* embryos. She has been exploring the role of mechanical forces in fruit flies early development for over a decade now. In her first published research, in *Developmental Cell* in 20067, she reported on an interesting observation; cells during embryonic convergent extension consistently join and exit pinwheel-like formation called rosettes.

Figure 7 Rosette windows. Church of St. Ludmila, Praha Vinohradzy.





Her hypothesis was simple: there are mechanical forces responsible for the rosette cohesion. Sure enough, in 2009 in a research article for

⁷ <u>Blankenship, J.T., Backovic, S.T., Sanny, J.S., Weitz, O., Zallen, J.A.</u> *Multicellular rosette formation links planar cell polarity to tissue morphogenesis.* Developmental Cell, October, 2006. 11 (4), pp.459-470. Doi: <u>http://dx.doi.org/10.1016/j.devcel.2006.09.007</u>

*Developmental Cell*⁸, she described the evidence that mechanical signals are equally essential for axis formation as chemical signaling. In other words, what looks like a chaotic pushing and pulling is in fact well organized mechanical signaling for the cells to elongate in an AP axis.



Figure 8 Tug-a-war, people or cells...

Three years later Jennifer Zallen discovered⁹ a biochemical cue of rosette formation in a molecule of tyrosin kinasis called Abl. Abl protein signals promoting cell-cell junctions (*zonula adherence*). Without the presence of Abl rosettes will not form, and the process of convergent extension will not make the embryo to elongate in an AP axis. In her latest published research Nature, in November 2014¹⁰, Jennifer Zallen described her discovery of positional receptors in Drosophila, receptors from a Toll family (Toll-2, Toll-6 a Toll-8). The receptors expressed in overlapping transverse stripes along the anterior-posterior axis (Fig.) act during convergent extension of the embryo.

Toll receptors, through their transcription factors *eve* and *runt*, pattern the location of myosin fibers inside the cells. That way the Toll receptors direct the myosin's contractile machinery, and orchestrate the mass elongation of the embryo in AP axis.

Figure 9 Toll receptors stained with different histochemical dyes patterning AP axis of *Drosophila* embryos. Photo: A.C.Paré, J.A.Zallen

	Allin
	200
	*3/4/10

Simultaneous disruption of transcription factors for Toll receptors leads to confusion in behavior and orientation of the embryonic cells. In that case, convergent extension, the underlying mechanism of elongation of the embryo in AP axis, is either flawed or missing completely.

Commenting on his former student groundbreaking research, Eric Wischaus compares the Toll patterning for myosin fibers and their subsequent contractions to imaginary dotted lines on a sheet of origami paper. The lines (Toll signaling) show where to fold and where to push (to contract myosin fibers) to get the final 3D structure (fruit fly embryo). The process is not much different in development: "Once you have a pattern, it gives you a way how to localize forces; then you can get form," he says. The idea that tissue remodeling and development results from coordinated action rather than from individual cells is getting more and more popular in the scientific world. Eric Wischaus explains; "We began thinking of the problem as a whole bunch of bricks. If you could understand how each brick behaved, you could put that all together and say how it leads to a whole organism. But over the past couple of years, we've become aware that maybe it's easier - or more useful or more correct - to realize that changes in morphology are bigger than single cells."11

⁸ Fernandez-Gonzalez, R., Simoes Sde, M., Röper, J.C., Eaton, S., Zallen, J.A. Myosin II dynamics are regulated by tension in intercalating cells. Developmental Cell, November, -2009. 17 (5), pp.736-43. Doi: 10.1016/j.devcel.2009.09.003.

⁹ Tamada, M., Farrell, D.L., Zallen, J.A. *Abl regulates planar* polarized junctional dynamics through β-catenin tyrosine phosphorylation. Developmental Cell, February, 2012. 22 (2), pp. 309-19. doi: 10.1016/j.devcel.2011.12.025.

¹⁰ Paré, A.C., Vichas, A., Fincher, Ch.T. Mirman, Z. Farrel, D.L., Mainieri, A. Zallen, J.A. A positional Toll receptor code directs convergent extension in Drosophila. Nature, Nov. 27, 2014. 515. pp. 523-527.

¹¹ Ehrenberg, R. *Show of Force*. HHMI bulletin, Spring 2015. Vol. 28 (2). Also available from: <u>http://www.hhmi.org/bulletin/spring-2015/show-force</u>

Vocabulary:

Convergent extension

Could be defined as concomitant tissue narrowing in one body axe and lengthening in another axe, perpendicular to the first one.

Examples include axis elongation, neurulation, and organ formation e.g. kidney tubules.

There are various underlying cellular mechanisms of convergent extension (John Wallingford from University of California in Berkley ¹² cites e.g. intercalation, oriented cell division, a change in cell shape via cytoskeletal myosin - see the article above).

Convergent extension is accomplished by different cellular mechanism in different organisms and tissues.

Gastrulation

- The formative process by which the three germ layers and axial orientation are established in an embryo.
- Marks the beginning of morphogenesis.
- In human development, gastrulation is the significant event occurring during the third week after fertilization.

(Look up online practically any video to understand gastrulation, the sooner the better!)

"It is not birth, marriage, or death, but gastrulation, which is truly the most important time in your life."

Lewis Wolpert

Neurulation

- A complex of processes involved in the formation of neural plate, neural folds and closure of the folds to form the neural tube.
- In human development, neurulation takes place from the third till the end of the fourth week after fertilization.

Eponyms

Lecturing halls of the 3rd Faculty of Medicine, Charles University in Prague.

"Nanos gigantum humeris insidentes"

Prof. MUDr. František Burian, DrSc. (1881-1965)

"There have been several Czech medical professionals during the 19th and 20th century we can be really proud of ... among the greatest of all was Prof. František Burian, a pioneer of a new field of medicine, plastic and reconstructive surgery..."¹³. With such words, Prof. Fara and doc. Tvrdek remembered 125th anniversary of birth of Prof. Burian.

Prof. Burian was born on September 17, 1881 in the Prague district of Mala Strana. In 1906 upon graduation from the Faculty of Medicine, he became an assistant at the Anatomy-Pathology Institute in Prague under the supervision of Prof. Hlava. And in 1908 he took an unpaid position as a surgeonassistant of Prof. Kukula.



Figure 10 Prof. Burian (the man on the right hand side in the front row) with his team, during the Balkan Wars.

During the Balkan Wars (1912-1913) Prof. Burian was a chief surgeon to the Bulgarian army. Only a few months after his return he was conscripted into the Austro-Hungarian army to serve in the World War I.

¹² Wallingford, J. B., Frazer, S.E., Harland, R.M. *Convergent extension: The Molecular Control of Polarized Cell Movement during Embryonic Development*. Developmental Cell, 2002. Vol. 3, pp. 695-706.

¹³ Fara, M. Tvrdek, M. Připomenutí výročí prof. Františka Buriana [online]. ACTA CHIRURGIAE ORTHOPAEDICAE ET

Prof. Burian led the surgical department of a backup hospital at Prague's Rudolfinum (nowadays a concert hall), and in 1916 became the head of an army hospital in Timisoara, (today's Romania).

After the War, with much experience, Prof. Burian began to engage in reconstructive and burn medicine in an effort to relieve wounded soldiers. He gradually developed techniques to transplant skin, bone, cartilage and tendons. He was among the first clinicians to promote the use of auto-transplants.

During his career, he became fascinated with corrections of congenital developmental defects, especially clefts. In 1939 Prof. Burian founded a Clinic of Plastic Surgery at the Royal Vinohrady Teaching Hospital.

In contrast to the norm of time, Prof. Burian was a major proponent of prudent operating, emphasizing a long term plan in surgical corrections of major defects. He produced extremely detailed therapy documentation including photographs before and after each surgery procedure, and the archive updated with his successors case documentation totals over 200 000 cases now. Prof. Burian was greatly considerate of his patients and, in cases of young patients with congenital defects, of the entire family. Those who remember Prof. Burian in person say there was no way a child would cry during his or his trainee's visiting!

Prof. Burian was an internationally accomplished pioneer of his field, plastic surgeons from around the world would come to his Institute for residency and, in turn, Burian was often invited to give lectures in many foreign countries.

Prof. Burian left a lasting legacy, and remains an inspiration for the next generations of medical professionals.

Burian histologist, embryologist and anatomist, and the founder

anatomist, and the founder of Czech experimental teratology.

Prof. Richard Jelínek was a

Prof. MUDr. Richard Jelínek, DrCs.

(October 8, 1934 – October 27, 2008)

He was the head of Department of Histology and Embryology of the 3rd Faculty of Medicine, Charles University in Prague for fifteen years.



Figure 11 Prof. MUDr. Richard Jelínek, DrCs.

Richard Jelínek was born on October 8, 1934 in Prague. As a medical student of the Faculty of Medicine, Charles University in Prague, he started working at the Institute of Anatomy under the leadership of Prof. Borovanský, later as an assistant to the professor, with specialization in neuroembryology and teratology of the central nervous system. At the Institute of Histology, Prague he became a close collaborator of Prof. Klika.

Following the Prague Spring and the occupation of Czechoslovakia in 1968, his associate professor degree was suspended causing him to take a position with the Czechoslovakian Academy of Sciences. There Prof. Jelínek became a leader of the Teratology Department of Professor František Burian's Plastic Surgery Laboratory.

Between 1990 and 1994 Prof. Jelínek was a director of the respected Institute of Experimental Medicine, Academy of Sciences, Czech Republic.

As a member of the WHO Commission on Environment he visited a number of countries around the world.

Between 1991 and 2006 Prof. Jelínek was the head of the Department of Histology and Embryology of the 3rd Faculty of Medicine, Charles University in Prague.

In 1996 Prof. Jelínek founded the Czech Teratology Information Service (CZTIS).

TRAUMATOLOGIAE CZECHOSL. 2007. 74, p. 426. (cited Oct. 8, 2015). Available from: http://www.achot.cz/detail.php?stat=145

Professor Richard Jelínek possessed many talents. When he had to decide what to study his major interests where mathematics, medicine and music. He chose medicine and math. After two semesters of both his interest shifted to medicine exclusively. But he did not forget his old love and studied math later in life in a course "Applied Logic" at the Philosophical Faculty, Charles University. And he didn't betray music either; played piano, recorder and guitar. He enjoyed singing and sang well.

As a medical student of the General Medicine Faculty, Charles University in Prague he became an assistant at the Anatomic Department. Prof. Borovanský influenced his professional interest in brain structure and embryology. During his eight semester of med school, he published his first piece of science. And then 300 more.

He put his last publication efforts into the Czech translations of a histology textbook by L. C. Junqueira et al.: Basic Histology in 1993 and embryology textbook by K. L. Moore, T. V. N. Persaud: The Developing Human in 2000. Those textbook translations were meant as an intrinsic debt repayment to his students for the twenty years he was forbidden to teach. All that as a consequence of his statement, proclaimed during a student happening on August 21, 1968, that the 200 000 Warsaw Pact troops and 2000 tanks invading Czechoslovakia was, in fact, an "act of aggression".

His enormous academic achievements were not without the downside, such as too little time for his family. His daughters would enjoy daddy only once they were capable of prolonged bike trips, Spartan camping and long hikes on the most challenging mountain trails. Biking, Nordic skiing, swimming, basketball, fencing in the early years, and canoeing with the dachshund in the lap of his wife were his regular, lifelong recreational activities. Many students were puzzled when they caught sight of their respected professor wearing an admiral's cap.

Prof. Jelínek was a man of great character, hardworking and demanding hard work, with a good sense of humor and an ability to see a situation or a problem in context and from different perspectives. He was charming and graceful.

The Czech poet Karel Šiktanc in his book "Horoskopy" wrote a characteristic of people born in the sign of zodiac of Libra: "*I am made of wings. Of the spread out feathers*".

He was, indeed.

Ivana Jelínková In Prague, October 14th 2014

Prof. MUDr. Jiří Syllaba, DrCs. (1902-1997)

Prof. Jiří Syllaba was born into a family of Prof. Ladislav Syllaba, an excellent internist and personal doctor of the first Czechoslovakian president T. G. Masaryk.



Figure 12 Prof. MUDr. Jiří Syllaba, DrCs.

Like his father, the young

Syllaba also signed up for the Faculty of Medicine, Charles University in Prague. As a medical student, Jiří Syllaba witnessed the very first time when insulin was used to treat a patient with diabetes. The new exciting treatment for both diabetic patients and clinical doctors became Prof. Syllaba's lifelong passion and commitment.

Jiří Syllaba spent a year interning with Prof. Bancroft (a Nobel Prize nominee). He gained invaluable experience interning in the USA (1929), France (1934) and Austria (1935). Starting in 1931, Prof. Syllaba worked at the Royal Vinohrady Teaching Hospital with Prof. Pelnář.

Soon after the occupation of Czechoslovakia in 1938, the Nazis closed all Czech Universities. Prof. Syllaba still published and practiced medicine however joined the national resistance movement, too. Twice during the war he was imprisoned by the Gestapo, and in 1944 was sent to the Nazi concentration camp in the fortress of Terezín (Theresienstadt). Towards the end of the war and also after the liberation of Terezín, he was instrumental in eliminating an epidemic of typhus fever that broke out among prisoners.

In May 1945, prof. Syllaba became the Chief of the Department of Internal Medicine at the Royal Vinohrady Teaching Hospital (RVTH) in Prague. In the fifties, under his leadership, the newly-formed II. Department of Internal Medicine at the RVTH increasingly focused on diabetes related diseases.

Prof. Syllaba never became a member of the Communist Party, a fact that cause him considerable

trouble. After the Soviet occupation of Czechoslovakia in 1968, Prof. Syllaba was dismissed from his positions both in the hospital and at the Faculty as well, and was forced to take a job as a doctor at one of the Prague's minor health centers.

Shortly after the Velvet Revolution in November 1989, prof. Syllaba was rehabilitated and could be welcomed again at the Department of Internal Medicine he once founded.

In 1996, prof. Jiří Syllaba was made a Knight of Medicine, "*Eqnes ordinis medicorum bohemicorum*", by the Czech Medical Doctor's Chamber.



His entire life Prof. Syllaba was a dedicated member of Freemasonry. In the 1990s he contributed significantely to rebirth of Czech Freemasonry and later became a Master of his Lodge.

Prof. Syllaba had multiple natural endowments. Besides his many clinical and academic achievements, he had a great appreciation for art and was an accomplished painter. He also wrote two memoirs, and a collection of his own poems.

Prof. Jiří Syllaba died May 17, 1997. He was 95 years old.

The Internal Newsletter, Third Faculty of Medicine, Charles University in Prague. Editorial Board: MUDr. Klára Matoušková, MPH – editor <u>klara.matouskova@lf3.cuni.cz</u> MUDr. Lucie Hubičková-Heringová, Ph.D. MUDr. Eva Maňáková, Ph.D.

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