Histology & Embryology Periodical

Department of Histology and Embryology

Third Faculty of Medicine, Charles University in Prague

Volume 2, Issue 6

May 2015

In this issue:

What´s up…

May, the month named for Maia, the eldest of the seven Pleiades and mother to Hermes, a god of transitions and boundaries, and the conductor of souls to the underworld. May he bring you good luck in your transition to the next semester.

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Finis coronat opus

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There is one more course left to finish the module "Cellular Basis of Medicine". In our last course, course six, "Connective tissue; Blood and Immunity", we will address the organs and cells of the remaining, fourth type of tissue, the connective tissue.

The course includes lectures and practicals on different types of bone and cartilage as specialized forms of connective tissue, and ossification. The lessons on blood and lymphatic system will teach you mainly about different types of cells, their origin and the lineage of development.

Barriers & Phagocytosis are an essential part of the body's immunity, therefore make sure to brush up on what you learned earlier in the Module.

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Week 10
Practicals: Epithelia as a part of immunity, phagocytosis

Week 11
Lectures:
Connective Tissue
Cartilage, Bone and Ossification
Morphology and Development of Blood, and Immunity Cells
Practicals:
Connective Tissue

Week 12:
Lectures:
Components of Blood Plasma and their Function
Practicals:
Cartilage and bone

Week 13
Practicals:
Morphology of Blood Elements

Week 14
Lecture:
Tissues and Organs of the Immune System
Practicals:
Morphology of the Lymphatic tissue

Week 15
Lecture:
Special Methods of Histology to distinguish cells and tissues
Practical:
Review– tissues

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Students‘ Scientific Symposium

The ever more popular event of the 3rd Medical Faculty will be held on Tuesday, **May 19**, 2015. Come to listen to your fellow students, discuss the hot topics, or check on the posters! The Symposium will open with a short ceremonial speech at 9,45 am, the honorary lecture by a distinguished parasitologist **prof. Julius Lukeš** will start at 10am. http://www.paru.cas.cz/en/staff/Julius-Lukes-r1r/
All classes will be cancelled beginning 9,30 am to encourage the students to attend the Symposium!

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TEDx Charles University

You might have heard about TED talks already, however the TED organization, www.ted.com includes a global program called TEDx, x standing for independently organized event. The second year of **TEDx Charles University** takes place at the Faculty of Social Science (FSV), Economical Institute in **June 25, 2015**.
http://tedxcharlesuniversity.fsv.cuni.cz/.

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To give you an idea what TED talks look like, watch for example one of the videos below;

Nadine Burke is a pediatrician living in San Francisco. She presents that many person' s **childhood trauma** is not something one simply gets over as he/she grows up. As a medical

professional to be, listen how childhood trauma affects physical health across lifetime; https://www.ted.com/talks/nadine_burke_harris_how_childhood_trauma_affects_health_across_a_lifetime

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You might appreciate this! **Amy Cuddy** advices you practice so called **„power posing“** before an

examination or any public presentation to increase your testosteron levels and decrease the corticosteroids in blood. In other words, Dr. Cuddy's research suggests that just two minutes of e.g. „hurray pose“ improves your self-confidence and reduces stress level. Moreover, this „faking“ your confidence has more than an immediate effect. It turnes out that i.e. „power posing“ is a way to possibly become a bolder and more positive person.

https://www.ted.com/talks/amy_cuddy_your_body_language_shapes_who_you_are

*

The most popular TED video is one of the presentations by **Ken Robinson**. In his talk from 2006, sir Robinson advocates an idea that **creativity** deserves the same respect and support as academical knowledge. Does schooling kills creativity? http://www.ted.com/talks/ken_robinson_says_schools_kill_creativity

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Individual microscope practices

Mondays and Wednesdays
(Wed, May 13 is the Rector's Day, the individual practical falls on the next day, Thursday, May 14)

3,15 – 4,45pm
Room no 319.

One of your lecturers will be present during the hours to consult regarding histology or embryology issue.

Individual consultations are possible. Please, get in touch with your tutor.

Placenta;
The Cytokine Producing Organ

There is still not much known about the nature of occurrences in placenta during the relatively short period of its existence. The research on cytokines produced by placenta is yet another important milestone in our understanding this amazing organ.

The organ of placenta forms in a matter of weeks to last, ideally, more than 37 and less than 42 weeks. During that time placenta function as a vital connection between the developing individual and her/his mother. In humans, the precursor cells of placenta can be seen between day three and four following fertilization. These are the cells of trophoblast, the outer layer of blastocyst. It takes twelve or thirteen weeks (up to the end of the first trimester) and number of morphogenetic processes to form the complete organ of placenta.

However, placenta expands and matures throughout the entire time of gestation. There are three distinct periods in the development of placenta. In the first period, the trophoblast undertakes a series of critical growth that eventually lead to the formation of villous and extravillous structures. In the second period the placenta anchors in the chorion and remodels the adjacent spiral arteries of the uterus into low-resistance vessels. During the second half the second period and the entire third period the placenta undergoes massive angiogenesis, vascularization and the villi growth. This third period occurs predominantly in the vascular endothelium for the most part [1]

The major functions of placenta include;

- Metabolism i.e. synthesis of glycogen, cholesterol and fatty acids
- Transportation and exchange, e.g. gases, nutrients and waste products
- Endocrine and paracrine function, i.e. synthesis and secretion of substances important during pregnancy
- Immunity and immunosuppression, including a limited but still existent function of a barrier between the embryo and mother

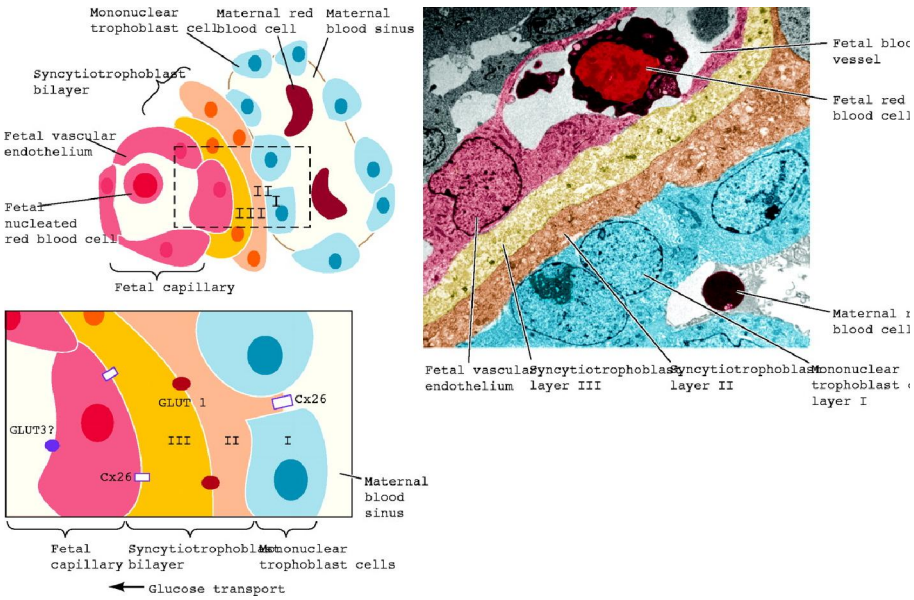

Fig. 1 **Interaction between trilaminar trophoblast layer and blood spaces within the labyrinth** *Left*: the trilaminar trophoblast layer consists of a bilayer of syncytiotrophoblast cells (layers II and III) that surround the fetal blood vessel endothelium and a mononuclear layer of trophoblast cells (layer I) that lines maternal blood sinusoids. Nutrients such as glucose must be transported through four cell layers to get from the maternal blood space into fetal blood vessels. Cx26 and GLUT1 have been shown to aid in the transport of glucose. *Right*: an electron micrograph of the trilaminar layer of labyrinth trophoblast cells that separate the maternal and fetal blood spaces.[2]

[1] Kaufman, P., Mayhew, T.M., Charnock-Johnes, D.S. *Aspects of human fetoplacental vasculogenesis and angiogenesis.II. Changes during normal pregnancy.* Plancenta, 2004.**25** (4), pp.114-126.

[2] Watson, E., D., Cross, J., C. *Development of Structures and Transport Functions in the Mouse Placenta.*

Recently, many research papers have focused on the physiological processes governed by complex **cytokine** interactions. Cytokines make up a large group of small proteins with a signaling function. The first of the now large family of cytokines, interferon alpha, was discovered in 1957 and soon the research pointed out many immune cells producing cytokines, e.g. macrophages, B and T lymphocytes, NK cells or mastocytes in a response to external stimuli of stress, injury or infection. However, it became increasingly apparent that cytokines are synthesized by a much broader range of cells, including stromal cells such as fibroblasts or endothelial cells. The year 1994 marked the discovery of leptin, the first of the family of adipokines i.e. cytokine products of adipose tissue. It was just a matter of time before placenta would be examined for cytokine synthesis. Due to the most recent research, we have learned that placenta synthetizes practically all now known cytokines. [3]

There are three different types of cells in placenta that synthesize cytokines; Hofbauer cells, trophoblast cells and the cells of vascular endothelium.

Placenta is not a mere producer of cytokines, it is also the target of their effect. To demonstrate the significance of cytokines in the placental activity, here we describe three cases of placenta-cytokines interaction;

Preterm labor is a serious complication of in about 10% of births (the number was 11.7% in the USA in 2009[4], the number in Europe is usually somewhat smaller). The underlying mechanisms of the beginning of labor is still largely unknown however recently the role of cytokines was studied. In several studies a higher concentration of interleukins (IL), e.g. IL6, IL12[5] or IL1alpha via regulation of a gene for IL8[6] was determined as a signal for the start of contractions before week 37 of pregnancy. In another study, a research team of Dr. Mitchell at the University of Queensland and University of Auckland emphasize the importance of epigenetic regulation of cytokine production in placenta. An inhibition of DNA methylation and deacetylation of histones appear to modulate the placenta cytokine production[7]. It is the shift in the fine balance between pro- and anti-inflammatory cytokines that appears to cause the clinical picture of a preterm birth.

A successful pregnancy is a fine task for the woman's body, requiring a specific form of immunosuppression. On one hand, immunosuppression needs to protect the fetus, which resembles a semiallogenic graft, on the other, such suppression should not be compromising for the mother. There are several types of T lymphocytes, and one of them are so called T-helpers, Th lymphocytes. There are also several subtypes of Th lymphocytes depending on what type of cytokine they synthetize. In his review article, Dr. Sykes et al. point out that it has been known for a while that a bias from the Th1 cytokine profile towards the Th2 profile contributes towards successful maintaining of pregnancy. Also, long has been studied the shift of Th1 to Th2 cytokines in

Physiology, Jun 2005. **20** (3) 180-193; DOI: 10.1152/physiol.00001.2005

[3] Bowen, J.,M., Chamley, L., Mechell, M.D., Keelan, J., A. Cytokines of the placenta and extra-placental membranes; biosynthesis, secretion and roles in establishment of pregnancy in women. Placenta 2002, 23. Pp. 239-256.

[4] Martin JA, Hamilton BE, Ventura SJ, Osterman MJ, Kirmeyer S, Mathews TJ *et al.* Births: final data for 2009. *Natl Vital Stat Rep* 2011; **60**: 1–70.

[5] Arababadi, M.,K. et al. Cytokines in Preterm Delivery. LabMedicine 2012. 43. Pp. 27-30. doi: 10.1309/LMY9ILPGSETU2CO0.

[6] Khanjani, S., Vasso Terzidou, Mark R. Johnson, and Phillip R. Bennett, "NFκB and AP-1 Drive Human Myometrial IL8 Expression," Mediators of Inflammation, vol. 2012, Article ID 504952, 8 pages, 2012. doi:10.1155/2012/504952

[7] Mitchell, M., D., Ponnampalam, A., P., Rice, G., E. *Epigenetic regulation of cytokine production in human amnion and villous placenta*. Mediators of Inflammation, 2012. Article ID 159709. Doi: 10.1155/2012/159709.

relationship with pregnancy loss and preeclampsia, and the role of infection and inflammation in preterm labor. In the review the researchers provide an evidence for an aberrant Th1 vs Th2 cytokine profile associated with premature labor. Based on the thorough review they conclude that there is a potential use of Th1 vs Th2 balance in screening as well as prophylactic therapeutic measures for the prevention of preterm labor and associated adverse outcomes. [8]

One last example of the significance of cytokines produced by placenta and cytokines targeting placenta, is a case of type II diabetes mellitus in pregnancy (gestational diabetes mellitus, GDM). Despite the great improvements in care to achieve adequate maternal glucose control, fetal hyperinsulinemia is quite common in GDM pregnancies[9]. GDM is a huge topic but what needs to be said in this short paragraph in an article about cytokines in GDM is that human placenta, as well as adipose tissue, synthetize adipokines. The main adipokines – cytokines produced by placenta include TNF α, leptin and resistin. Adipokines are the key players in insulin, and therefore, glucose regulation. There is a growing body of evidence that adipokines in placenta, particularly TNF-α, increase insulin resistance in pregnant women. The closer to the end of pregnancy, the more increase is observed. Some researcher even suggest that a cytokine TNF-α could also serve as a predictor of diabetes in pregnancy.[10]

Common Confusions In Histology

False: mucosa equals epithelium
True: mucosa usually consists of epithelium + *lamina propria (*and, in the digestive system, also *lamina muscularis mucosae)*

False: villi, crypts and microvilli are, more or less, all the same
True: First and foremost, the crypts of Lieberkűhn (Johann Nathanael Lieberkűhn, read his story in the Periodical from March 2014) take place in colon only. On the other hand, there are no villi in colon, only the microvilli just much less in number than in the small intestine.

Draw a picture, or two (or as many you need) to make sure you have a clear understanding of how villi and microvilli, and *plicae circulares of Kerckringi*, are explained in the small intestine.

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[8] Sykes, L., et al. *The Th1:Th2 Dichotomy of Pregnancy and Preterm Labor*. Mediators of Inflammation, 2012. Doi: 10.1155/2012/967629.

[9] Desoye, G., Hauguel-De Mouzon, S., *The Human Placenta in Gestational Diabetes Mellitus*. Diabetes Care, 2007. 30 (2), pp. 120-126.

[10] Kirwan, J., P. et al. TNF-alpha is a predictor of insulin resistance in human pregnancy. Diabetes 2002. 51, pp. 2207-2213.

Endocrine disruptors IV

Estimated Costs of Exposure to EDCs

The Endocrine Society published a press release in March, 2015 estimating that the cost of exposure to endocrine disrupting chemicals (EDCs) exceeds €150 billion annually in the 28 states of the European Union (EU)[11].

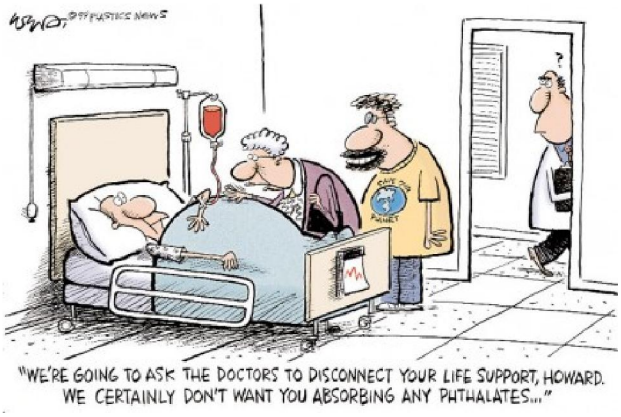
However, the number presents only "the tip on the iceberg" says Leonardo Trasande, MD, MPP, who led a team of eighteen researchers across eight countries in this initiative. The study took into account only three endocrine disruptors and five EDC related conditions. It was;

- DDE - related childhood overweight
- DDE - related adult diabetes mellitus
- BPA - related childhood obesity
- Phthalates - related adult overweight and obesity
- Phthalates - related adult diabetes mellitus

DDE (dichlorodiphenyldichlorethylen) is a breakdown product of one of the oldest and well known insecticide DDT. DDT is now banned in both, the EU and USA.

BPA (bisphenol A) is a synthetic compound that makes plastic clear and tough, and is used in consumers' products such as CDs and DVDs, as a coating in food and drink cans, plastic bottles and a variety of everyday products. BPA use is being reduced, particularly in baby products and banned in baby bottles and infant formula containers in the EU, USA and Canada.

Phthalates are esters of phthalate acid, added into plastic products to increase the product's flexibility, transparency, longevity and durability. It is used in medical care products (e.g. tubes and tubing, gloves, pill coating), personal-care products (such as shampoos, deodorants, hair sprays, nail polishes) and some toys.



The five conditions related to only three EDCs makes, according to the authors of the study, less than 5% of the possible endocrine disruptors while the current number of chemicals suspect on endocrine disruption is close to one thousand[12]). The chemicals in this landmark study were chosen however based on the quality and amount of available evidence, points out Bruce Blumberg, professor of developmental and cell biology at the University of California, and co-author of the obesity and diabetes paper.

[11] The Endocrine Society, press release. *Estimated Cost of Endocrine-Disrupting Chemical Exposure Exceed € 150 Billion Annually in the EU*. March, 05 2015. [online]. Available at: http://www.endocrine.org/news-room/current-press-releases/estimated-costs-of-endocrine-disrupting-chemical-exposure-exceed-150-billion-annually-in-eu

[12] TEDX list of potential endocrine-disrupting chemicals. [online]. TEDX, 2015. [cited 5.5. 2015]. Available from: http://www.endocrinedisruption.org/endocrine-disruption/tedx-list-of-potential-endocrine-disruptors/chemicalsearch

Endocrine disruptor = an exogenous chemical or a mixture of chemicals, that interferes with any aspect of hormone action. [13]

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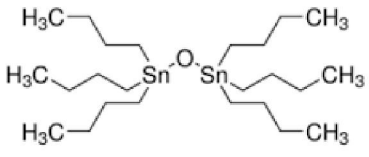
Regarding EDC related obesity, prof. Blumberg emphasizes that the current "obesity epidemics" cannot be attributed to the factors of the prevailing wisdoms such as too little exercise, too much food, known as "couch potato syndrome". Other factors of obesity must be taken into account such as; stress, inadequate sleep, genes developed to make the best in the times of scarcity, viruses and individual microbiome, but also prenatal nutritional experience (e.g. Southampton Studies, the study of Dutch Hungry Winter, or studies of maternal smoking). Recently, there is a growing body of evidence that a pre- or perinatal exposure to certain chemicals and synthetic compounds in the environment such as DDT and DDE, BPA, omnipresent phthalates, and also a chemical tributyltin, perform as obesogens.

Obesogen = a chemical inappropriately stimulating adipogenesis.



Fir.2 Tributyltin

Tributyltin (TBT) is a chemical used for over 40 years as a "bottom paint" of large boats, highly toxic for marine life, capable of impact development of many organisms and cause collapse of whole marine populations, banned in 2008 by the Rotterdam convention however still used illegally, remains in the ecosystem for up to 30 years. TBT was studies as a suspected obesogen. Besides others, TBT was found to induce adipogenesis in cell culture models, and if given prenatally, led to weight gain in F1 mice population in vivo. How does TBT do that? Hypothesis include changes in hormonal control of appetite and satiety, alteration of the ability of an adipocyte of process and store lipids and its´ ability to increase the number of adipocytes or preadipocytes. [14]

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The resulting economic analysis of the study takes into account the actual health care expenses and lost earning potential due to effects of exposure such as infertility and male reproductive dysfunctions, birth defects, obesity, diabetes, cardiovascular diseases, and neurobehavioral and learning disorders.

Somewhat surprising, even for many authors of the study was the fact that the biggest cost driver was the effect of EDCs on the nervous system. The study suggest that pesticides containing organophosphates cause a financial cost in dozens of billions Euro but more importantly, exposure to such pesticides means a loss of about 13 million IQ points throughout the population of the EU as well as almost 60 000 additional cases of intellectual disability each year.

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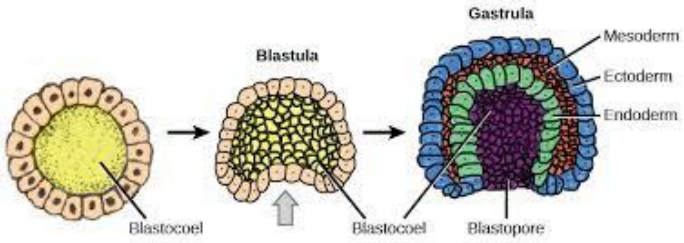
[13] Zoeller, R., T. et al. *Endocrine-Disrupting Chemicals and Public Health Protection: A Statement of Principles from The Endocrine Society*. *Endocrinology*, 2012. **153** (9), pp. 4097 – 4110.

[14] Blumberg, B. *Endocrine Disrupting Chemicals and the Obesity Epidemic.* [online]. Webinar for The Colaborative for Health and the Environment. 28. 4. 2015. [citováno 2.5.2015] Available from: http://www.healthandenvironment.org/uploads/docs/BlumbergslidesApr282015.pdf

Repetitio mater studiorum…

… Gastrulation



Gastrula is a ….(1) layered embryonic disc formation.

Gastrulation is a transformation of a …. (2)into a gastrula.

Gastrulation is the beginning of an embryonic process called … (3).

Gastrulation occurs during the …. (4) week, in days … (5) of embryogenesis.

The three primary germ cell layers of gastrula are called; … (6 a, b, c)

Gastrulation in mammals is similar to that in birds with the formation of the primitive … (7) – the first morphologic sign of gastrulation - and ….(8) node, and the ingression of cells through the primitive … (9) to form the endoderm and the mesoderm.

Cells of mesoderm migrate out to form the blood vessels of the chorion and connect the chorion to the embryo through the …. (10).

Embryonic mesoderm gives rise to all muscles, (11) cells and the lining of … (11) vessels, and visceral smooth muscular linings of all body cavities, the ducts and organs of reproductive and excretory system, mesoderm is the source of all … (12) tissues including cartilage, bones, tendons, ligaments, dermis, and stroma of internal organs.

Embryonic endoderm is the source of epithelial linings of the …. (13) and …. (14) tracts, including the glands opening into the GIT tract and the glandular cells of associated organs such as the … (15) and … (16).

Embryonic ectoderm gives rise to the epidermis, nervous system, the eye, the inner ear, and, as crest cells, to many connective tissues of the head such as; (17).

Gastrulation is a phase early in the development of most animal embryos, during which the morphology of the embryo is dramatically restructured by a number of … (18) processes such as: (19).

*

Answers

1) Three
2) Blastocyst
3) Morphogenesis
4) Third
5) 14 to 16
6) Endoderm, Mesoderm and Ectoderm
7) Streak
8) Hensen's
9) Groove
10) Umbilical cord
11) Blood
12) Connective
13) Respiratory
14) Digestive
15) Liver
16) Pancreas
17) odontoblasts, dental papillae, the tracheal and laryngeal cartilage, the dermatocranium

(membranous bones, i.e. bones formed via intramembranous ossification e.g. cranial bones, bones of the *cingulum membri superioris*), pericytes and smooth muscle of branchial arteries and veins, connective tissue of head and neck glands (pituitary, salivary, lachrymal, thymus, thyroid) dermis and adipose tissue *calvae*, ventral neck and face, **endocrine cells** such as chromaffin cells of the adrenal medulla and parafollicular cells of the thyroid, sensory neurons and glia of the dorsal root ganglia and cephalic ganglia (VII and in part, V, IX, and X) in the **peripheral nervous system,** Schwann cells of all peripheral nerves, melanocytes and iris pigment cells, etc.

18) Morphogenetic

19) Cell Migration, Apoptosis, Proliferation....

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Repetitia in the previous issues:

March, 2014

... Epithelial tissues

April, 2014

... Male genital duct system

May, 2014

... Cells of the connective tissue

October, 2014

... Cilia

November, 2014

... *Apoptosis*

December, 2014

... Myoepithelial cells

February/March 2015

... Neuroglia cells

April 2015

... Female reproductive system

Common Confusions In Embryology

False: epidermis develops from dermatome
True: dermatome gives rise to the connective tissue of skin, and epidermis develops from ectoderm

False: mesoderm = mesenchyme
True: mesoderm is a germ layer of gastrula, mesenchyme is a derivative of mesoderm. In other words, mesenchyme is formed with proliferation of the cells of mesoderm. A typical example of mesenchyme derivative is the endothelium in vessels.

Both, embryology and histology bring along a host of new terms and new concepts. Learning from the microscopic slides and textbook pictures is often overwhelming. There is no better help than grabbing the old good crayons and draw, draw, and ... draw. By reproducing the confusing pictures and images, you achieve a better understanding to the matter, and what you understand you will also remember.

Eponyms

"Hodgkin's lymphoma"

Thomas Hodgkin (1798-1866)

"Humani nihil a se alienum putabit"

"Nothing humane was foreign to him"

an inscription on Hodgkin's grave in Jaffa, Israel

Thomas Hodgkin was a prominent man, a prominent pathologist of his times, a pioneer in preventive medicine. He led a productive professional life and despite of premature end of his scientific career his name will probably never be forgotten.

*

Thomas Hodgkin was born in 1798 into a Quaker family, in Pentonville, Middlesex County, England. His upbringing infused him with honesty, discipline and concern for the less fortunate from his early years, e.g. at age 21, he wrote an essay criticizing imperial behavior of colonists that led to the degradation of the North American Indians and other native people. [15]

Quakers; the official name is "Religious Society of Friends", a religious movement that broke of the Church of England in the mid-17th century. The only religious group that was awarded the Nobel Peace Prize (in 1947).

Young Thomas Hodgkin soon developed interest in science and served as apprentice in apothecary in the Guy's Hospital in central London. He continued his education as a medical student at the University in Edinburgh. While still a medical student school, in 1821-22, Hodgkin visited European medical centers in Italy and France.

In Paris, Hodgkin met **René Laennec**, the inventor of the stethoscope. Laennec taught him to use the instrument and Thomas Hodgkin brought the novelty to England.

Fig.3
René Laennec and the Stethoscope (Robert A. Thom, 1915-1979, American)

A stethoscope met in England with a general skepticism, and professors used it – membrane down - as a flower vase during lectures. However, Hodgkin's close friend and a colleague, **William Stroud** was one of those who believed in the new examination tool. Not only did he adopt it into his clinical practice, he improved it by adding a hose inventing the flexible stethoscope. Although the invention of flexible stethoscope is today credited to **Golding Bird**, Bird published his article on the tool in 1840 while Dr. Stroud has been using it since 1820'. When Dr. Bird learned about this fact, he fully and gentlemanly recognized it in his letter to the Editor of the Medical Gazette in 1841 (fig.4)

[15] Stone, M., J. *Thomas Hodgkin: medical immortal and uncompromising idealist*. BUMC Proceedings, 2005. **18**, pp. 368-375

To the Editor of the Medical Gazette.

Sir,
I venture to occupy a space in your valuable journal [...] to do justice to the talent and ingenuity of an excellent and much-esteemed physician, to whom I have through a private source lately learned that we are indebted for the first application of a flexible tube for the purpose of auscultation. I refer to Dr. Stroud. This gentleman, about twelve years ago, first suspected the possibility of hearing the sounds of the chest by means of a flexible tube, and on submitting this idea to positive experiment ([.....]) he was gratified by discovering that the respiratory murmur were distinctly audible; he was led to modify the length of the tube and to adapt a metallic ear-piece, and has constantly used this instrument since. Dr. Stroud gave an account of his contrivance, and presented instruments similarly constructed to several physicians [.....]. It is to be regretted that Dr. Stroud did not publish an account of this instrument. I first heard of the employment of the flexible tube [....] and it was not until the last week that I became acquainted with the real history of the contrivance [.....]
– I remain, sir,
Your obedient servant,

GOLDING BIRD

Wilmington Square, July 16, 1841

Fig.4 A letter of Golding Bird to the editor of the respectable London medical newspaper, Medical Gazzete from July, 1841

*

In **1823** Hodgkin graduated from the University of Edinburgh Medical School, and less than three years later, in **1825,** he was appointed a lecturer in morbid anatomy and curator to the newly established Pathology Museum at the Guy's Hospital Medical School. Such an assignment launched his career as an enthusiastic and notable pathologist. In about twelve years Thomas Hodgkin performed hundreds of autopsies, established a catalogue – so called Green book – of over 3000 specimens, among his many accomplishments he explained a regurgitation of aorta five years before Corrigan[16]. **1827** Hodgkin and **Joseph J. Lister** improved a microscope with achromatic lenses and described the biconcave shape of erythrocytes and striation of muscle tissue. They published a paper together, "*Notice of some microscopic observation of the blood and animal tissues"*, a paper called by some "the foundation of modern histology". [17]

In **1832** Thomas Hodgkin's scientific endeavors were topped with publishing a paper; "*On some Morbid Appearances of the Absorbent Glands and Spleen."* In the article he reported on clinical histories and *postmortem* findings of "seven patients with enlargement of lymph nodes and spleen but without inflammation or other significant pathological findings"[15].

Fig. 5: Hodgkin's disease watercolor drawing by Robert Carswell in 1828, this was case 7 in Hodgkin's paper.

33 years later, in **1865**, Samuel Wilks rediscovered the pathology independently of Hodgkin and described it with a greater precision. However, when he learned about his predecessor Wilks wrote a detailed article on the pathology, named it in the title **"Hodgkin's disease"** thereby provided Thomas Hodgkin with immortality.

It is a curious fact that Thomas Hodgkin obviously did not use a microscope to describe the pathology of the disease while it is known that he had experience with microscopes (e.g. his works together with Joseph Lister). However, others did study microscopic images of different tissues of patients diagnosed with Hodgkin disease. Among them Carl Sternberg in 1898 and Dorothy Reed four years later. **Reed-Sternberg cells** (fig. 7) are usually clones from B-lymphocytes,

[16] Hodgkin, T. *On the retrovestion onf the valves of the aorta.* London Medical Gazette, 1829. **3**, pp. 433-442.

[17] Bracegirdle, B. A *History of Microtechnique*. 2nd ed. Lincolnwood, IL. Science Heritage Ltd. 1986.p. 27.

giant cells with multiple nucleus, looking like "owl's eyes" (fig.6). The cells are a necessary but not sufficient indication in the diagnosis of Hodgkin disease; among the Reed-Sternberg cells there has to be so called milieu of a reactive cellular infiltrate present consisting of cells such as lymphocytes, plasma cell, eosinophils and neutrophils.

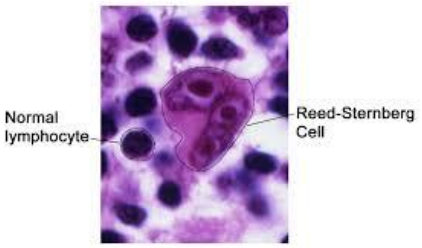

Fig. 6 Reed-Sternberg cell

The year **1837** marked the end of Hodgkin's scientific life. Thomas Hodgkin, the prominent and brilliant British pathologist, resigned all his positions at the Guy's Hospital and withdrew from London medical circles. There were probably several reasons for that, one of them his criticism of Benjamin Harrison, Jr., the administrator of Guy's Hospital and his factual employer. Hodgkin disapproved him as a board member of the Hudson's Bay Company which exploited the American Indians, traded alcohol and guns for fur making large profits. [18] However, Dr. Hodgkin did swallow the pill of disappointment and begin to study ethnology, geography and, a new science then, anthropology.

He became a full time personal physician to his close friend Moses Montefiore; a successful financier and philanthropist, knighted by Queen Victoria for his good works. They travelled the world, helping underprivileged and oppressed people. Thomas Hodgkin lectured on sanitary measures and maintaining of the physical fitness, stressed the importance of adequate oxygen, bathing and warned against excessive alcohol and tobacco use and occupational dust exposure, advocated the protection of child laborers and importance of education. During one such visit in Palestine in 1866, Thomas Hodgkin contracted a dysenteric-like disease and died.

The malignancy described with his name, Hodgkin's lymphoma, is nowadays curable with a combination of chemotherapeutical drugs. However, the name of Thomas Hodgkin will not disappear from the lecture halls of medical schools and hallways of hematology clinics yet for a while, as the etiology of this fascinating disease is still unclear.

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Good Luck with you Exams
And Have an Enjoyable Summer!

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[18] Kass, A.M., Kass, E.H. *Perfecting the World. The Life and Times of Dr. Thomas Hodgkin, 1798-1866*. Boston: Harcourt-Brace Jovanovich, 1988.