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OUTLINES OF EMBRYOLOGY

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KAROLINUM

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Preface to the first edition

There exists nothing in the world without history – and we cannot understand the present status quo of anything not knowing its history. From this it appears that one cannot understand also the living organisms, their body organization and function without knowing their history. Biological history represents a process of development of the organ structures, i.e.an ontogenetic process, started by meeting of two parenteral germ cells, passing through the prenatal and postnatal period and ended by the death of an inividual.

Human biological history has, of course, two faces – an ontogenetic and a phylogenetic, which are both in mutual correspondence and influence each other. We should not forget that also the process started by our animal predecessors, which evolved to the modern human, is mirrored in our individual development. For this development, i.e. human ontogeny, the term embryology became common, even though it covers not only the fate of an embryo, but the whole prenatal developmental process. To understand embryology, we should be informed at least about the main stages of its developmental history.

The whole text has been divided in seven chapters. The first one is devoted to the history of embryology, the topic which was until now mostly neglected in the textbooks of embryology, but according to our opinion it can provide essential help to students in orienting within the explosive scientific development of the whole subject, esp. in the way of understanding cancerogenesis or modern efforts to improve the human fertility.

The developmental topics start in a chapter of general embryology, named here as progenesis. We have used that term, even though we know, that it has also been used to describe a shortening of the developmental processes, and can play an important role in evolution of some species. But we understand under that term the earliest developmental period, leading from fertilization to the formation of all three germ layers and neurulation.

The whole text cannot completely follow the time sequence of the too-complex processes of development and even though we know that also other systems in successive chapters are not fully appropriate, we have divided the organogenetic part according the anatomical systems to enable an easy orientation to the whole topic.

After the preembryomic period, which takes the first four weeks of development, the main body organs are laid down, followed by the real embryonic period in which the main anatomical systems are established. Starting from the 9^{th} week during the fetal period, growth and maturation bring the fetus to the birth of a newborn in the 40^{th} week, at which time the intrauterine development ends and the postnatal period of the new individual's development begins.

These “Outlines” are not intended to replace comprehensive textbooks of Embryology, but they should serve as a short summary of the knowledge which has been given by the teacher in the lecture hall. They are written in simplified English and they should help the international students at the time of their preparations for the examination of embryology in the second year of the pregraduate medicine curriculum. They can also serve as a first orientation to developmental problems for the colleagues of other branches of medicine or general biology.

The author would like to express many thanks to all those who helped him to prepare these “Outlines”. They include first of all his friends – colleagues from the Department of Histology and Embryology, Faculty of Medicine, Charles University in Pilsen, but also his students, who have listened to him, judged him, taught him and made his engagement meaningful.

Prof. Jaroslav Slípka, Dr. med., DSc.
Pilsen, 2010

Preface to the second edition

Embryology affects every person in the world. We all once were fertilized oocytes, zygotes, morulae and blastocysts. All of us managed to implant into the uterine mucosa while undergoing gastrulation. We all went through organogenesis. If you are interested in which processes are bedding these words, this book is for you. Just keep on reading.

In pregraduate course on medical embryology, the students are supposed to understand the basics of developmental processes that happen during the pregnancy. This starts with a sperm cell fertilizing an oocyte, and, if everything goes well, it leads to the birth of a newborn. Although we are not able to understand or explain all (or even the majority of) the processes during the prenatal development, our aim is to provide you with the most relevant information you should be aware of as healthcare professionals. Understanding embryology explains a lot on anatomical structure of the human body, including the variability of anatomical structures and organs found in every individual. Although this small book covers mostly the normal prenatal development, it may help you to understand also some developmental defects.

This textbook outlines the courses in embryology, taught to the international students of general and dental medicine in the second year of their pregraduate studies at the Charles University, Faculty of Medicine in Pilsen. The first edition was prepared in 2010 and modified in 2012 by Prof. Dr. Jaroslav Slípka, DSc (1926–2013), who was an enthusiastic and inspiring researcher and teacher at the Department of Histology and Embryology. The second edition was updated in 2018 to reflect some of the advances in teaching of embryology. Nevertheless, the illustrations and the concise concept of the book designed originally by prof. Slípka were kept. We recommend using this textbook for revising and summarizing the essential knowledge. For full color textbooks and atlases that are necessary for understanding the basics of human prenatal development, see the literature recommended. As the development of the human body reflects a number of more general principles common for various zoologicla taxons (placental mammals, amniotes, vertebrates, chordates, triblastics etc.), students interested in a more deeper understanding of the underlying processes are referred to literature on evolutionary biology.

We wish all our students might enjoy the insight into the prenatal development of human body. Welcome to the world of Embryology!

Zbyněk Tonar
Pilsen, 2018

I. History of embryology

We suppose that the first basic facts of human prenatal development were known already to the ancient Egyptians, who came in contact with various stages of fetuses and even embryos during the embalming of pregnant women. There exists also a whole list of observed malformations of human miscarriages, which was used for prediction of the future by Babylonian priests in ancient Mesopotamia 5,000 years ago.

The ancient humans tried to explain the accidental findings mostly as a result of the activity of supernatural powers and in that way, like most of the anthropological information, human development was mostly included as a part of the religious category.

The sacred scriptures of the Hindu religion in the second millennium B.C. describe their ideas on the developmental processes during pregnancy, which they considered to be a result of a junction of mother's blood and father's semen, but the Old-Indian priests also already had simple experience in heredity, and they provided instructions on choosing a wife to prevent heritable illnesses. The ancient Greeks also respected the importance of the environment during pregnancy and they recommended that the pregnant woman should be surrounded by beauty only, and during the wedding day the newly married couple should not drink wine.

These ideas were taken over in the ancient Greek science and the "father of medicine" *Hippocrates* (460–377 B.C.) had already compared human development with the development of the chick. But the first serious information on developmental processes was collected by *Aristotle* (384–322 B.C.) who proclaimed relatively correctly, that a human embryo originates from the material of both the mother and father. The mother provides only the raw material (postmenstrual discharge) and the man through his semen the organizing principle. Various organs are at first fashioned in a simplified way before becoming structurally and functionally complex. His epigenetic view on successive development of organs (e.g. the heart appears sooner than lungs) has influenced his successors and in several features corresponds to our contemporary knowledge.

An exceptional position among the ancient Greek scholars was occupied by *Galen* (130–201 B.C.), who in his anatomical studies also described the nourishment of the embryo, and his humoral theory influenced medicine throughout the whole Middle Ages.

The Romans added only a little to the basic theories of the Greeks and they adopted more or less the Greek views, like *Gaius Plinius Secundus (Pliny the Elder)* (23–79 A.D.), who in his large series of 37 books "Natural History" covered in an encyclopedic way the entire knowledge of nature at that time, also including medical information.

There was a big stagnation of scientific progress in Europe after the fall of the Roman Empire. But in Arab countries a new cultural power appeared in connection with the development of new religion formed by Mohammed in the 7th century. Even in the holy script of Islam – the Holy Qur'an – are mentions of the stages of the human, which starts from a small drop in the mother's womb into a form of a leech or "suspended thing" (embryo?) and finally in a "chewed substance" (somites?). It is interesting that *Mohammed* in his "sayings" (hadeeth) indicates relatively accurately the embryonic period, when he narrates that the body components should be shaped after 42 days and the "hearing, vision, skin, flesh and bones are created."

When Mohammed died (632 A.D.?) Islam had already spread throughout the whole of Arabia, Persia, Syria, Egypt, North Africa, and Spain. The Arabs grasped the cultural element of the conquered nations very quickly, and they built their own advanced culture which can be characterized as a perfect synthesis of Old-Indian, Persian, Greek and Roman science which they completed by their own contribution of experimental methods.

In that way, there emerged at the time of European cultural darkness, in the Islamic countries a sort of Arab Enlightenment Era, considered as the golden age of Arab culture within the 9th–13th centuries. Among the Persian and Arab scholars of that Era of Reason who paid attention to medicine and problems of human development *was Ibn Rhazes* (850–923) and *Ibn Sina – Avicenna* (980–1037), who based his work on Aristoteles and Galen and won by his "Canon of Medicine" fame at that time in the whole world. Another scholar was *Ibn Heitham* (965–1038), who denied the old view of the function of eye and proved that sight depends on the passage of light-rays through the eye. The next great man of science and esp. of medicine was *Ibn Rushd – Averroes* (1126–1198) whose principal work was in the form of commentaries on Aristotle's writings, which he further developed.

Among Arab scholars were also authors who believed in a sort of an evolutionary development of the living organisms and even put humans on the top of their evolutionary ladder of animals (*Al Masudi*) so that it can be spoken of as a sort of "chain of being" or even about "Darwinists" of the 10th century. The Persian and Arab science influenced the whole of Europe and no wonder, that at the Universities, which were founded at the same time in Europe, the students were asked to study from the Latin translations of those Persian and Arab authors.

It was not until the European renaissance that the theories of Aristotle and Arab authors were further elaborated. A great personality of the early renaissance was *Leonardo da Vinci* (1452–1519), who among others continued the investigation of human body and its development. In Bologna *Volcher Coiter* (1534–1576) and *Ulisse Aldrovandi* (1552–1605) studied the development of chick from the beginning of incubation to hatching. They have been considered as the real founders of embryology.

The founder of scientific anatomy was *Andreas Vesalius* (1514–1564), the author of the first modern illustrated textbook of anatomy "De humani corporis fabrica libri septem". His successors in Padua were *Fallopius* (1514–1562), who described the female genital organs and placenta, and his pupil *Fabricius* (1537–1619) who examined the development of some animals and compared them with human embryos and fetuses.

He influenced one of his students in Padua, an Englishman *William Harvey* (1568–1657) who is more known as a discoverer of blood circulatory system, but he was also interested in problems of development and contrary to Aristotle was persuaded, that it is the egg only from which all life originates to produce more eggs. His motto was: "Omne vivum ex ovo".

Harvey was in contact with a much younger Czech scholar *Marcus Marci* (1595–1667) who as a distinguished scientist of the Prague University by his discoveries in physics. Through his work applying his research in optics to the study of developing embryos, he anticipated the much later theory of morphogenetic fields.

The primary importance of the egg for beginning of development was strongly proclaimed by *Malpighi* (1628–1694) who thought that he observed preexisting parts of the fetuses in the unincubated hen's egg. He was a representative of *preformation theory* in its "ovist" form. This "ovistic" theory assumes that the egg gives the starting material for the development and the male semen is only a trigger of the developmental process.

Other preformationists propagated an opposite source of embryonic primordium, namely the semen – i.e. the male is the bearer of the whole development. This "animalculist" theory arose on the basis of invention of the microscope in the 17th century. *Antony van Leeuwenhoek* (1632–1723) from Leiden and his student *Ham* were the first who, using a primitive microscope, could observe the human spermatozoon. They thought to see in the head of sperm a preformed individual – a so called *homunculus*.

In Italy, *Lazzaro Spallanzani* (1729–1799) performed experiments in regeneration of some organs of amphibians, and even experiments with fertilization, adding sperm to the eggs of various animals, but he never left his ovistic conviction of a preformed individual in the egg.

These primitive preformation views were corrected only during the 18th century by *Caspar Friedrich Wolff* (1734–1794) who in his "*Theoria generationis*" (1759) claims that development starts from living homogenous substance and proceeds by gradual, i.e. *epigenetic* differentiation of tissues and organs – as a result of "vis essentialis".

At that time *Jean Baptiste Lamarck* (1744–1829) presented his theory of evolution on the basis of adaptation of organisms to the environment and on formation of organs according their function, and on heredity of acquired features.Another distinguished medical celebrity at that time was *Jiří Prochaska* (1749–1820), who was a defender of the epigenetic idea and criticized Spallanzani's preformation. His main scientific contribution was his modern conception of the nervous reflex, but he was also interested in extrauterine nidation of embryo and described some human malformations.

A uniform creative plan of living structures was defended by *Johann Wolfgang Goethe* (1749–1832), a famous German poet and romantic natural philosopher who supported the idea of organ homology, such as that of the incisive bone in various mammals. Another example was his explanation of skull segmentation as a result of a conversion of cervical vertebrae.

The same uniform plane was considered by *Etienne Geoffroy Saint-Hilaire* (1772–1844). He studied birth defects, considered them as deviations of ontogeny and created the term *teratology*. He was persuaded that current organisms had developed from the extinct ones and contributed to the creation of a modern view of natural evolution – mainly in discussions with *George Cuvier* (1769–1832), who was an advocate of the "catastrophism" theory and a well-known founder of comparative anatomy.