

Epigenesis versus preformation: first chapter of the Russian embryological research

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"The history of [embryonic, ATM] development sheds a true light on the study of organic bodies. At each moment, it is constantly finding uses, and all ideas which we have about the interrelations of organic bodies are subject to the influence of our accomplishments on the history of development".

K. E. von Baer (1888).¹⁾

"There are, it should be recognized, many forms of democratic organization. Science constitutes one. It is a subtle structure in which without formal elections, the dominant views establish themselves in forms organized to give a hearing to dissent. These views prevail because of their power to persuade, and not because of the power of those who hold them."

J. Polanyi (1997).

Background

In the last three decades or so, developmental biology has come into its own as a major integrative tool used by researchers in such leading scientific areas as developmental and molecular genetics, molecular evolution, cell biology, neurobiology, genetic

engineering, where massive amounts of embryological data are also screened for biotechnological and biomedical purposes.

There is a long history of interest in the mechanisms by which a single cell, a fertilized egg, gives rise to a complete adult organism containing millions of cells with very different specialized structure and functions. The theoretical explanations that have been offered have varied down the centuries but, with few exceptions, they share a common theme. There has always been an intimate relationship between embryology and philosophy. Of course, there has been a shift of emphasis throughout the long period of theoretical embryological speculations. Nevertheless, some basic views, although not stated in quite modern form, can be traced to Aristotle.

The origin of embryology is traditionally associated with the name of the famous metaphysicist and naturalist, Aristotle. He was the first to define a basic problem which dominated embryology until the beginning of the 20 century. Here, it is appropriate to cite the corresponding paragraph from "The Triumph of the Embryo" by L. Wolpert (1993): "...Do, Aristotle asked, all the parts of the embryo come into existence together, or do they appear in succession? Is everything preformed from the beginning, or is development more like the knitting of a fisherman's net? He thus defined the preformation/epigenesis controversy"... Aristotle favored the knitting metaphor, which he termed "epigenesis."

¹⁾ Cited from the Russian edition: Baer (1953)

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Fig. 1. The St. Petersburg Academy of Sciences and the Kunstkammer (Cabinet of Curios). Colored print by G. Kachalov after the drawing by M. Makhaev (1753).

The contrary imaginative idea, i.e., the theory of preformation, supposes that all embryos have existed since the creation of the world. The advocates of preformation believed that germ cells (spermatozoa or oocytes) contained a miniature individual with all the parts of the adult. This view predominated in embryology up to the middle of the 18th century. The Swiss naturalist Charles Bonnet loosely interpreted the theory of preformation; for him this idea was "one of the greatest triumphs of rational over sensual conviction" (see Wolpert, 1993). However, as J. Gurdon (1997) noted: "...even Bonnet did not fully believe his theory because it implied, when taken to its logical conclusion, that Eve must have had 27 million embryos in her ovaries. And preformation was eventually discredited by the eighteen-century German embryologist Kaspar Friedrich Wolff, who observed that in both plants and animals specialized organs arise from unspecialized tissue." It is important to note that in the past it has been so difficult to determine the facts of embryology that we have not thought much about the process by which successful scientists convert facts into understanding.²⁾

Before retracing the contributions of famous Russian embryologists, namely K. E. von Baer and C. H. Pander, to the theory of epigenesis, I would like to briefly focus on the outstanding figure of K.F. Wolff. Although several modern historians consider him a representative of the German embryological school, I see him as a forerunner of Russian embryology as well. His life story collaborates this. Kaspar Friedrich Wolff (1734-1794) was born in Germany where he started his research on anatomy and embryology. The most important result of his activity in the field was his dissertation entitled: "*Theoria Generationis*" which was published in Germany in 1759. In the manuscript, K.F. Wolff develops

epigenetic views on embryonic development. German scientific circles at the time showed ill-will towards his work. As a result, Wolff could not find a job in German universities and was obliged to emigrate.

At the end of 1766, the St.-Petersburg Academy of Sciences invited him to fill a post of academician in the Department of Anatomy. In the spring of the following year, the 33 year old Russian academician Wolff settled in St. Petersburg where he lived for the next 27 years working in the field of embryology, teratology and anatomy. In 1768-69 he published his observations on digestive tract (intestine) formation in chick embryos³⁾, and concluded that the results obtained testify to the theory of epigenesis: "I believe that the proper understanding of the intestinal development will eliminate any remaining doubts about the reality of epigenesis.... I believe that it is proved that the intestine gradually develops [dur-

ing embryogenesis, ATM]. The idea that it does pre-exist in a latent form only to be discovered later, at a certain period [of development, ATM], is wrong" (cited from Blyakher, 1962).

From then on, Wolff's scientific career was mainly associated with the St. Petersburg Academy of Sciences. Prof. K. Sander, in the special issue of *The International Journal of Developmental Biology* dedicated to developmental biology in Germany, also refers to this fact and points out the great influence of Wolff's epigenetic ideas on the founders of the Russian embryological School, C.H. Pander and K.E. von Baer: "... Wolff, of German origin, did much of his later work at the Russian emperor's academy in St. Petersburg. After Russia and the German States had freed themselves from Napoleon's sway some sixty years later, two youngsters from the German-speaking gentry of Russia's Baltic provinces took over the lead in descriptive embryology. Christian Heinrich Pander, working at Würzburg, provided a thorough description of the developing chick embryo, including the three layers from which the body derives. This work attracted the attention of his friend, Karl Ernst von Baer who, as a professor at Königsberg and St. Petersburg, was to become the doyen of 19th century embryology, and a leading exponent of several other disciplines as well" (Sander, 1996).

The discoveries made by K.F. Wolff were ahead of his time and were misunderstood by his contemporaries. Later, his successor, academician K.E. von Baer (1836), noted: "...A study is recognized not only by its advantages over other researches but also by its timeliness. After extensive work, our academician Wolff discovered the law of organic transformation. Unfortunately, at the time it could not be tested and it was ignored by Science. Only half a century later, others, with much less effort, would win laurels in the same field..... and Wolff's contribution would finally be exalted."

Founders of Russian embryology

A brief look at the history of Russian biological science in the 19th century shows that as an organization that was determined to

²⁾ The selection of materials from extensive sources as well as their interpretation is my own responsibility.

³⁾ Wolff, C.F. "De formatione interstinatorum praecipue... observationes in ovis incubatis institute." *Novi Comment. Acad. Scientiarum. Petropolitanae.* 1768, 12, 1769; 13.



Fig. 2. Christian Heinrich Pander (1794-1865).

meet the challenges posed in this era, the St. Petersburg Academy of Sciences (see Fig. 1) had become an important part of the Russian and international embryological research. Two Russian academicians, C. H. Pander and K.E. von Baer were with the Academy for a long period of time, accumulating expertise in the areas of descriptive and comparative embryology, anatomy, and physiology. This was the birth of Russian embryology.

At that time, the most effective strategy for fostering the advancement of knowledge in the field of developmental biology was to investigate (at the morphological or micro-anatomical level) the embryological processes which are relatively stable over a wide range of external (i.e., laboratory) conditions. Therefore, chick embryos became the favorite object of descriptive embryological research.

Christian Heinrich Pander (1794-1865) (Fig. 2) was the first who was able to trace chick formation from several embryonic tissue sheets later named "germ layers". On the basis of the results obtained, he concluded that the walls of body cavities are formed from serous layer, while digestive canal (intestine), mesentery and blood vessels are developed from mucous and vascular layers, correspondingly. Moreover, he confirmed Wolff's observations on the process of intestine tube formation in chick embryos (see, Dettlaff, 1953). It should be noted that his schemes of chick embryos at different stages of development (Pander, 1817, 1818)⁴⁾ are surprisingly similar to current descriptions (Fig. 3).

If in the second half of the 18th century, major advances in the ways, in which embryonic development is described, are usually

associated with K.F. Wolff, then in the 19th century the leading role belongs by right to Karl Ernst (Maksimovitch) von Baer (1792-1876) (Fig. 4) who made important discoveries in this field.

He was born in Piep (Estonia) and, after graduating from university, started his career as zoologist and embryologist. For sixteen years he worked as professor of Anatomy at the University of Königsberg. In 1834, he settled down in the St. Petersburg Academy of Sciences, where he worked for nearly 30 years and published more than 400 manuscripts.

In 1827 he found the ovum in the ovary of dogs; previously none other had been able to detect mature unfertilized eggs (oocytes) in mammalian ovaries. In the paper "*De ovi mammalian et hominis genesi*", he notes: "By curiosity, I opened one of the follicles and, using a scalpel tip, took a very small sample; I could clearly observe it and noted that it was surrounded by mucus. When I put it under microscope, I was dumb-founded because I detected as ovum identical to the ova which I had already observed into oviducts. It was so evident that even a blind man could not disclaim this". By then, Baer had already started to analyze ovaries in rabbits, pigs and humans and describe human egg and the structure of Graafian follicle (Fig. 5). Baer developed Pander's ideas about germ layers and investigated more precisely their fates during embryonic development. Particularly, he was able to demonstrate that: "cutaneous" layer was transformed into superficial epidermis and the central nervous system; "muscular" layer formed muscles, skeleton and supporting tissues; "vascular" layer gave rise to blood vessels and mesenteries; and that the internal "covering" of the digestive tract

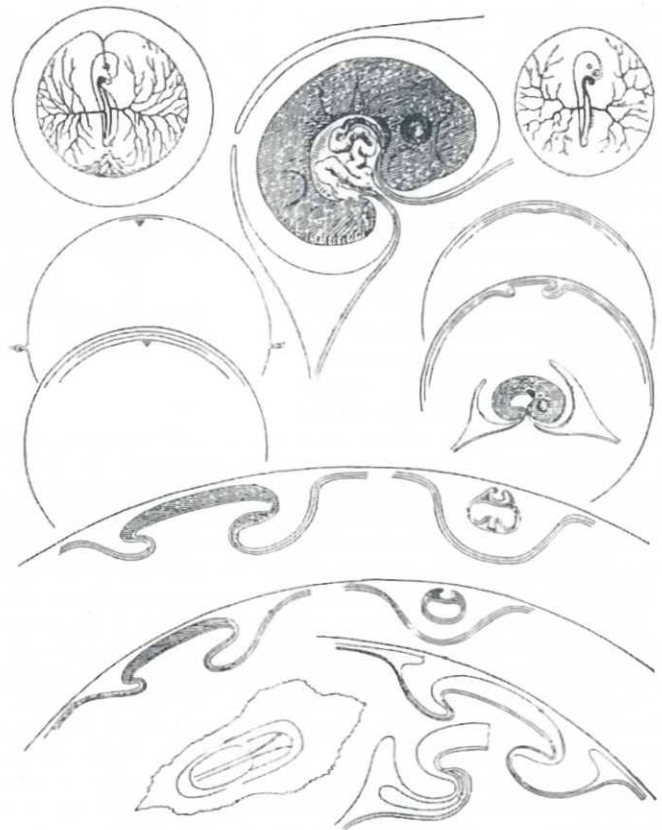


Fig. 3. Schemes of chick embryo development. (After C. Pander, cited by Blyakher, 1962).

⁴⁾Pander, Chr. "Dissertatio...sistens historiam metamorphoseos, quam ovum incubatum prioribus quinque diebus subit." Wirceburgi, 1817; Pander, Chr. "Entwicklung des Kuchels." Isis. 1818. S. 512, cited from Blyakher, 1962.



Fig. 4. Karl Ernst (Maksimovitch) von Baer (1792-1876)



Fig. 5. Baer's Table IV of the Figures 1-27 (from Baer, 1953).

(1) Scheme of vertebrate body plan. (From pp. 88-89). *a* and *b*, "brain" (brain and medulla) plate; *f*, "butcher's" plate; *g*, skin; *fg*, spinal plate; *fh*, abdominal plate; *ik*, mesentery plate; *k*, vascular layer; *l*, cutaneous mucous layer; *kl*, gut plate. (2) Flatness vertebrate animal which consists of the plates but not of the tubes. (Vertical section, p. 89). (3) More flatness vertebrate animal which consists of the plate including the following layers: (from bottom to top), cutaneous mucous layer, vascular layer, "butcher's" layer, skin layer, and brain plate (pp. 89-90). (4-6) Schemes of avian embryo (transversal sections). *a*, animal layer (black); *b*, yolk-sac, vegetal layer (orange); vascular layer (red); cutaneous mucous layer (yellow); *c*, cutaneous umbilical cord; *c'*, intestine umbilical cord. (7) Avian embryo. (Vertical section, pp. 91-94).

Abklc, embryo; *ce*, embryonic cover (including the 3rd area); *cm*, area vasculosa; *m*, border of the vascular layer (*vena terminalis*); *me*, area vitellaria. (8) Vertical section of turtle egg/embryo. (p. 207). *a*, spinal plate (transversal section); *b*, abdominal plate. (9) This figure must demonstrate that the abdominal plates originate from the arch ones. (p. 207). (10) Avian vascular system. (p. 178). *ab*, heart with five pares of arterial arches; *c*, head artery; *d*, vertebral arteries with a part of arterial root (plexus); *f*, bifurcation of aorta into umbilical arteries; *g*, anterior vertebral vein; *hi*, posterior vertebral vein; *h*, tail vein; *k*, transversal stem vein; *ll*, umbilical veins (the inferior veins of hind part of the body); *m*, vena cava; *n*, umbilical vein; *o*, common vein stem; *p*, vitelline artery. (11) There are no indications in the original text about this figure (the note of Prof. Shmidt who published in 1888 a legends to the table IV). (12) Ovary. (Transversal section). *abcd*, different yolk bodies. (13) Graafian follicle with egg. (High magnification, pp. 234, 238 and following pages). *a*, embryonic layer; *b*, peritoneum cover; *cd*, capsule; *e*, transparent cover; *g*, liquid; *h*, small bead. (14) Transformation of branchial vascular system into arteries in mammals. *a*, arterial stem; *bb'*, aortal plexus; *c*, art. carotis. (15 and 16) There are no indications in the text. (17) Twenty-one day old sheep embryo. (p. 466). (18) Brain formation and structure in mammals. (p. 280). *ab*, medulla oblongata; *bc*, mesencephalon; *de*, diencephalon and the 3rd ventricle; *ef*, forebrain. (19-27) Eggs with membranes. (Fig. 19-25: transversal sections; Fig. 26-27: longitudinal sections; p. 314). red, vascular membrane; yellow, mucous membrane; dark-yellow, yolk sac; orange, allantois; black, serous and external egg membrane covered by fibers (pp. 379 and following pages). (19) Avian egg. (Transversal section, p. 315). *a*, embryo; *b*, amnion; *c*, yolk stalk; *d*, yolk sac and allantois sectioned at the point "c"; *f*, external half of the allantois; *g*, internal half of the allantois; *h*, serous membrane; *i*, "hardening" egg albumin; *k*, shell membrane. (20) Rabbit egg. (p. 255). (21) Egg of predatory animal. (22) Pig egg. (p. 259, 324). (23) Human egg. (24) Scheme of formation of the amnion and serous membrane in mammals. (p. 255, 369). (25) There is no indication in the text. (26) Four week old pig embryo. (Longitudinal section, p. 332). (27) Pig egg. (p. 324).

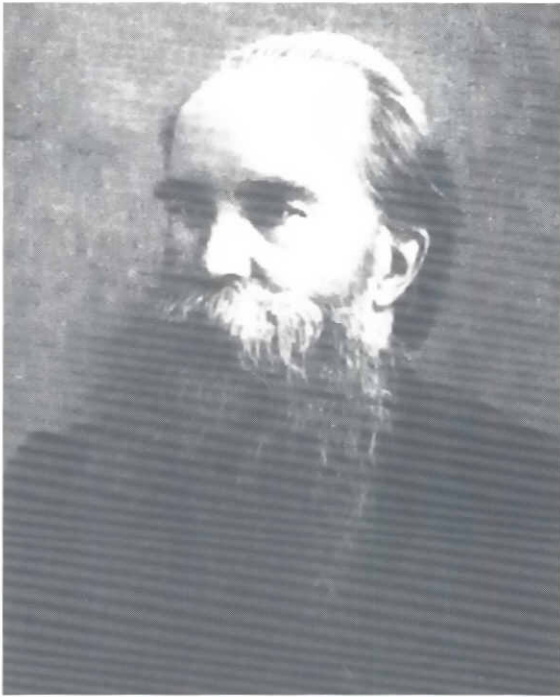


Fig. 6. Alexandr Onufrievitch Kowalevsky (1840-1901).

developed from the "mucous" layer. As a result, he defined germ layers as early embryonic tissues from which all body structures are formed according to an orderly process and noted that each germ layer gives rise to a definite set of organs and tissues (Fig. 5). Studying chick embryos, he detected a "new" embryonic organ for the first time, i.e. spinal or backbone "cord" (notochord) (see Baer, 1828, 1836, 1953; Blyakher, 1955).

The results of detailed comparative investigations of embryonic development in different groups of vertebrates allowed him to formulate four generalizations:

- (1) In the embryonic development of any species, the general features of a large family of animals appear earlier than the species-specific ones;
- (2) during embryonic development, more specified characteristics appear later than the more general features;
- (3) embryos of a given species, instead of passing through the "adult-specific" stages of other (lower) animals, depart from these animals more and more at the advanced stages of development;

⁵¹ Although Baer did not declaim a natural evolutionary processes, he critically evaluates Darwin's theory and notes that it represents only a successful attempt to formulate a **doctrine** about the mode by which the evolution could be realized. Darwin's idea about the origin of *Homo Sapiens* from the monkey, Baer names "the greatest folly". On the basis of morphological, embryological, and paleontological results obtained at that time, Baer concludes that it would be impossible to trace the so-called "genealogical tree" of animal evolutionary history from a common hypothetical prototype as it has been postulated by Darwin's doctrine. In general, Baer considered the evolution as a selection of the so-called "predetermined natural systems" and noted that the heredity is one of the natural mechanisms of such a "purposeful predetermination". Modifications of Baer's view on the evolution have been developed by Russians scientists, N.Ya. Danilevsky, L.S. Berg and D.N. Sobolev (for details, see Lukina, 1978).

(4) the embryo of a higher animal "form" is never like a lower adult animal "form" but only like its early embryo (the so-called "*law of embryonic similarity*").

The value of Baer's theoretical advances and variety of the experimental results obtained by him cannot be fully analyzed in such a short review. Nevertheless, I wish to stress one aspect of his scientific activity which had a significant influence on the development of embryological research in Russia. I am referring to Baer's ideas on animal evolution and his studies in the field of comparative embryology.⁵¹ He applied the concept of vertebrate germ layers on the development of invertebrates. Studying the processes of embryonic development in sea urchins and crustacea, he wrote that the purpose of his study was to "...prove that metameric animals [like vertebrates, ATM] start their development with the formation of the primary streak since a similarity between these animals and vertebrates is settled" (cited from the Russian edition: Baer, 1953). However, Baer rejects Haeckel's ideas about recapitulation; he recognizes a certain similarity only between the *early embryos* of different animal groups. He criticizes the so-called "theory of parallelisms" and Haeckel's recapitulation doctrine and stresses that initially similar early embryos of various animal groups become more and more different in the course of their development. Moreover, he emphasized many times that it is possible to compare only early embryos from different animal groups, but not embryos of one type with the adults (or advanced embryos) from another. For this reason, Baer's "law of embryonic similarity" was also named the "*law of embryonic divergence*" (see, De Beer, 1930; Ivanova-Kazas, 1975, 1992; Dondua, 1994).

Nevertheless, a slightly modified theory of recapitulation was transferred from one text-book on embryology/developmental biology to another up to September of this year when the remark entitled: "Haeckel's embryos: Fraud rediscovered" was published in "Science" (Pennisi, 1997). It is noted in the article that: "...generations of biology students may have been misled by the drawing of embryos published 123 years ago by the German biologist Ernst Haeckel. They show vertebrate embryos of different animals passing through identical stages of development. But the

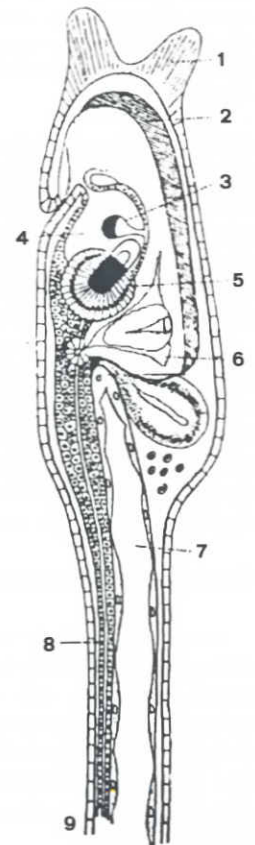


Fig. 7. Ascidian larva; lateral view. (After Kowalevsky, 1871, cited by Korschelt, 1936). 1, fixation organ; 2, endostyle; 3, statocyst; 4, cephalic vesicle; 5, eye; 6, pharynx; 7, notochord; 8, spinal cord; 9, tail.



to scientific journals while he was still in his teens; he wrote these papers frantically a few hours after he had trained his microscope on some bugs or beetles; the next day he would look at them again, and find that what he had been so certain of, was not quite the same now. Hastily he wrote to the editors of a scientific journal: "please, do not publish the manuscript I sent you yesterday. I find I have made a mistake". At other times, he became furious when his ideas were turned down by the editors. "The world does not appreciate me" he cried, and went to his room, ready to die."

Fig. 9. Development of *Solmundella* (Aeginopsis). (After Metchnikoff, 1886, cited by Ivanova-Kazas, 1975). 1-4, stages of development; 1, "multipolar immigration".

impression they give, that the embryos are exactly alike, is wrong". Dr. M. Richardson and his colleagues re-examined the embryos from the species which E. Haeckel studied and demonstrated that the embryos looked "surprisingly different". Moreover, "not only did Haeckel add or omit features,....but he also fudged the scale to exaggerate similarities among species, even when there were 10-fold differences in size" (see, Pennisi, 1997).

Thus, many years ago, it was already evident that Baer's theoretical concepts about embryonic development and animal evolution which contradicted the "recapitulation" model proposed by F. Muller, E. Haeckel and Ch. Darwin (see, Garstang, 1922), would continue to function as a basic retrospective view-point to serve us as long as developmental biology and evolution are studied (for instance, see Dondua, 1994).

Founders of Russian comparative embryology

In spite of pioneer studies by K.E. von Baer in comparative embryology, for a long time it was held that the formation of germ layers is specific only for vertebrate embryos. However, after comparative studies by academicians of the Petersburg Academy of Sciences, Alexandr Onufrievitch Kowalevsky (1840-1901) and Ilya (Elie) Ilyitch Metchnikoff (1845-1916), it was evident that embryonic development in all Metazoa is characterized by germ layer formation.

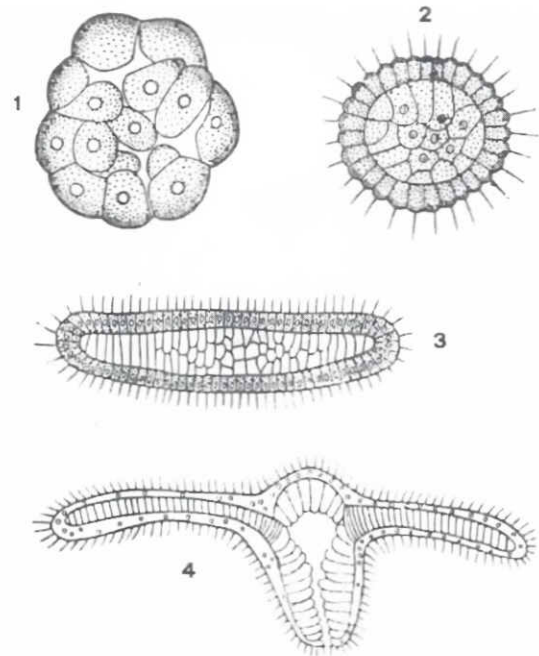


Fig. 8. Ilya (Elie) Ilyich Metchnikoff (1845-1916). Metchnikoff's major field of research was comparative embryology. Whenever he worked in laboratory, he tried to interpret the results obtained to make some important theoretical conclusions. As P. DeKruif noted (1926): "....Metchnikoff was always trying to get ahead of himself. He sent papers

In 1871 Kowalevsky (Fig. 6) wrote: "...If we now attempt to compare the development of the worms studied with the development of other animals, we would be especially amazed by the similarities between germ layers [of the worms, ATM] and vertebrates up to the minuscule details" (cited from Kowalevsky, 1951).

A.O. Kowalevsky was one of the few who applied the embryological approach to study evolution for the first time. At that time, the systematic position of tunicates was unclear, and they were usually placed to molluscs or to worms. Studying ascidian development, Kowalevsky detected swimming tail larvae similar to that of frogs (Fig. 5). After their settlement in substrate, ascidian larvae underwent metamorphosis: the tails were drawn into body cavity and degenerated, then adult organisms were formed from the so-called "trunk part". He also found that tunicate larvae formed their axis body structures (i.e., notochord, neural tube, etc.) in a manner typical to that of chordate animals. Therefore, he concluded that tunicates were similar to primitive chordates (Kowalevsky, 1871, 1951). Following Metchnikoff's ideas about the biological role of phagocytosis, Kowalevsky studied phagocyte-containing tissues in insect larvae and found that cells with phagocyte activity participate in the process of metamorphosis.

I.I. Metchnikoff (Fig. 8) was the other outstanding Russian biologist who tried to apply Baer's embryological ideas to evolution; he suggested that the evolution of multicellular organisms could be realized by changes in their embryonic development. In other

words, he thought that evolution consisted of the modification of embryos, but not of adults (for details, see Chernyak and Tauber, 1991).

His exacting scientific career involved combining comparative embryology with immunology, although he is often considered as an immunologist only. He was born in the Ukraine and started his scientific career as a zoologist. After graduating from the University of Kharkov (in two years instead of four), he studied zoology at various Universities in Russia, Italy, and Germany. In 1884, in Italy, at the laboratory of marine biology, he made the first observations of starfish larva cells characterized by phagocyte activity (he called these amoeba-like cells "phagocytes" from Greek terms meaning "devouring cells") that led him later to the discovery of the cell mechanisms of immunity. In 1908 Metchnikoff (together with Paul Ehrlich) received the Nobel Prize for physiology and medicine. His prize-winning discovery, the cell theory of immunity, marked the beginning of the immunology and played a significant role in immunobiological research at the time. When, owing to political and personal reasons, Metchnikoff emigrated from Russia, L. Pasteur invited him to Paris (to the Pasteur Institute) where Metchnikoff worked for 28 years and made great contributions to the field of cell immunity (for details, see Metchnikoff, 1921).

Metchnikoff always kept comparative embryological studies in sight which allowed him to achieve the highest success in science. Apart from his study on phagocytosis, Metchnikoff published many articles on the embryology of invertebrates. In the fifth edition (1997) of the excellent text-book on developmental biology by S. Gilbert, one can read (on p. 886) that: "...Metchnikoff attempted to make a phylogeny of all organisms on the basis of their germ layers, and he believed that all mesodermal cells could be characterized by their ability to phagocytize foreign substances. His discoveries in comparative embryology eventually allowed him to formulate the conceptual foundations of a new science, immunology".

In the second half of the 1800s, the so-called "gastrea" hypothesis by E. Haeckel dominated embryological and comparative studies. Metchnikoff modified Haeckel's hypothesis and introduced the concept of the colonial origin of Metazoa (the so-called "phagocitella" theory). In his writings Metchnikoff developed this theory and formulated the following generalizations: (1) the ancestors of Metazoa could be primitive Protozoa capable of rounding up and digesting organic substances; (2) intracellular digestion appeared earlier than extracellular; (3) the initial mechanisms of gastrulation are "mixed delamination" and "multipolar immigration" (see Fig. 9, Metchnikoff, 1886).

Studying sponge and starfish embryogenesis, Metchnikoff was able to detect the stage at which embryos consist of two germ layers only, namely: (1) external "covering" layer, and (2) internal sheet ("parenchyma" layer) containing amoeba-like cells. He suggested that this stage, which he called "the stage of phagocitella", represents the simplest form of embryonic organization. Amoeba-like cells from the internal layer of "phagocitella" were characterized by phagocyte activity and could form the mucous covering of the presumptive digestive tract, as well as the mesoderm at the next stage of development (i.e., at the gastrula stage).

Metazoan embryonic "phagocitella" resembles a colony of some Protzoa formed by "external" flagellum-like cells and "internal" amoeba-like cells (for instance, in some species of genus *Volvox*, the individual cells forming hollow sphere colonies

are connected by cytoplasmic bridges so that their flagella propel the colony like a rolling ball, i.e., such colonies can swim). At that time and later, Metchnikoff and other zoologists were not able to detect any adult multicellular organisms like hypothetical "phagocitella" (see Ivanova-Kazas, 1975; Dondua, 1994). However, in spite of all this, Metchnikoff (1886) suggested that "phagocitella" embryonic state "is therefore entitled to be considered the prototype of multicellular beings". Modifications of this view on the origin of Metazoa have been suggested by Russian/Soviet scientists, Beklemishev (1944), Zavarsin (1945) and Ivanov (1968).

It is interesting to stress that Metchnikoff hypothetical "phagocitella" resembles the modern schemes of an ancestral bilateral animal. As E. Pennisi and W. Roush (1997) note: "With no fossil evidence to go on, biologists have typically pictured the last common ancestor of the vertebrates and invertebrates, which lived at least 540 million years ago, as a little more than a tube of cells with few distinguishing features beside perhaps a mouth and cilia for locomotion.

Metchnikoff was also attracted to the idea of discrete animal evolution, and he was among the first scientists who supported the synthesis of genetics and evolutionary research (see Mirzoyan, 1996). Therefore, he could not blindly follow Darwin's theory of evolution and criticized the role of the so-called "struggle for life" in the formation of species. For instance, in his review on "The Origin of the Species", 25 year old Metchnikoff wrote: "...I would like to say that a lot of Darwin's very important theses are unproved.... we must recognize the unfoundedness of principal aspects of his theory" (cited from Metchnikoff, 1950, p. 672).

Later, he many times critically evaluated several aspects of Darwin's doctrine. Here it is appropriate to cite the interesting paragraph from "Immune System Discovered" (Old News) by J. Risser: "When Ludmila (Metchnikoff's wife, ATM) died in 1872, Elie Metchnikoff was so upset that he tried to kill himself with morphine. Though he miscalculated the amount and merely slept. Waking up in his bedroom in the middle of the night, Metchnikoff immediately prepared a larger dose of drug. Before drinking it, however, he happened to glance out his bedroom window and found himself distracted by the sight of a cloud of mayflies swarming around a candle in a lantern. "These insects live only for a few hours!" he thought. "How can Darwin's theory of the survival of the fittest be applied to them?" So Metchnikoff decided not to kill himself in order to study this question.

Metchnikoff's contributions to comparative embryology, on the one hand, and to immunology and immunopathology, on the other, are well known. However, he also attempted to establish the general principles of biology and medicine (what we now call biomedicine). Moreover, he has convinced that theoretical basic science was capable of solving the current social problems of mankind: "...Only the theoretical study of natural history [i.e., natural sciences, ATM] can generate the correct approach to the understanding of the Truth and lead to the formation of a comprehensive outlook on the world order" (Metchnikoff, 1883, cited from Mirzoyan, 1996). Metchnikoff considered the development of purely theoretical approaches in natural sciences and especially biology to be essential to world progress. He used the quotation from the Bible that "a man does not live by bread alone" to illustrate "the unlimited curiosity about himself and his environment" as an essential characteristic of *Homo Sapiens*. This idea by the Nobel

prize winner Metchnikoff was well articulated by another Nobel prize winner, J. Polanyi, Professor of Toronto University. Polanyi proposes that "the science constitutes one form of democratic organization of societies" (see the second epigraph to this article). Currently, the world passively witnesses the precipitous decline of Russian science and, at the same time, hopes to create a democratic Russian society. It is appropriate to remind that these two processes are not compatible.

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⁶⁾ Citation of references is incomplete; only selected papers are listed (some of them are listed with my own translation of the titles). My apologies to all of those whose historical works about Russian embryology were not cited because of lack of time and space. The references are intended as a guide to further reading, and I have not been able to cite all of original or influential papers to illustrate antiquity.