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A WATCH BACKWARD IN EMBRYOLOGY

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Abstract:

The development of the embryo and eventually of the adult from the fertilized ovum is an extremely complicated process. The history of embryology is interesting and full of nebulous ideas, often tinged with religious beliefs; nor is this to be wondered at, for the coming into the world of a new human being is heavily charged with emotional and theological implications.

KEY WORDS:

embryology, fertilized ovum, seminal fluid, menstrual blood, placenta, egg.

INTRODUCTION:

The ancient Egyptians (3000 B.C.) appear to have learned the art of incubating eggs but seem to have shown little inquisitiveness about the facts of embryology; they believed, however, that the child was the product of the two parents, the germ existing in woman and the seed in man, to which the sun God, Aton, gave life and provided a soul (breath) at birth. Of the two, the father was genetically the important partner and the author of generation, while the mother only provided the nidus and nourishment for the foetus. This doctrine descended to the pre-classical Greeks; thus Apollo defended Orestes from the charge of matricide in the Eumenides of Aeschylus:

“She who is called the mother of the child
Is not its parent, but nurse of seed”

In early Greece, however, an attempt was made to account for the processes of development. The embryo, according to the Pythagorean philosopher, Empedocles of Agrigentum (c.500-c. 430 B.C.) was compounded of earth, air and water animated by the innate heat of the blood, while the Ionian teacher, Anaxagoras of Clazomenae (500-428 B.C.), held that it was moulded by fire, a view also advanced by Hippocrates of Cos (c. 460-375 B.C.), who taught that the embryonic parts were differentiated as they met with water or fire, some parts becoming condensed as the humidity disappeared to become bones and nerves. The embryo was nourished by maternal blood which coagulated to form flesh, the menstrual flow ceasing as it is used up on its way out; while air was supplied through the umbilical cord. And finally, when the demand for food exceeded the supply, the foetus was expelled from the womb or the chick from the egg.

Australian aborigines, believed that conceive of minute spirit-babies coming from afar in the East, so small as to be invisible to all but magicians and old woman, which look for kindly females, particularly those with large breasts ; when they find one they enter her body under the fingernail or through the loin or

A WATCH BACKWARD IN EMBRYOLOGY

the mouth to find a nidus for development and nourishment in the womb ; the entry of an injured spirit-baby results in the birth of a deformed child, of an animal or a monstrosity. In this scheme the mother has no genetic or biological responsibility for her child for she merely acts first as an incubator and then as a wet nurse ; while the share taken by the father is still less. To some Australian tribes his function is to open up the womb by the act of coitus so that the spirit can enter; to some East Indian and Polynesian peoples the semen blocks the exit of the uterus so that the menstrual flow is checked and the embryo nourished, an end satisfactorily and happily achieved only after much sexual intercourse.

The science of Embryology may be said to commence with Aristotle (c. 384-322 B.C.) whose studies covered the whole area of knowledge, though were quite unrelated to facts. Dissecting the egg and embryos of all kinds of animals, cold blooded, avian and mammalian, this great founder of many natural sciences gathered his observations in the five books of his (*On the generation of animals*), wherein he classified the animal kingdom according to embryological characteristics. The embryo, he contended was derived from menstrual blood to which the seminal fluid gave form, a concept which ascribed to the mother a more important role than hitherto. In the determination of form by the male, he considered that the semen played a role comparable to that of rennet in the coagulation of milk, separating the foetus from the liquid in which it lies, the whole being surrounded by membranes since the surface, like the skin of milk, solidifies on heating and cooling. He produced the first textbook of embryology on no other basis than his own tireless observations intermingled; it is true, with many incorrect deductions and much speculative philosophy. For 2,000 years thereafter little or nothing new was added to his clear but rigid teaching, and throughout the Dark and Middle Ages he remained the sole authority.

The Aristotelian view that the menstrual blood constituted the substance of the foetus has been widespread. In ancient Hindu medicine it was taught by Charaka and Susruta (500 B.C.) and is said to account for the belief still held in certain parts of India today that a girl should go from her father's house to her husband's before she starts to menstruate. Those early Indian writers also compared the formation of the embryo with the clotting of milk, an analogy which crept into Biblical writings. Thus Job ; " Hast thou not poured me out as milk and curdled me like cheese ; and again, in the Apocrypha ; " And in the womb of a mother was I moulded into flesh, being compacted in blood of the seed of man and pleasure that came with sleep. The Jewish Talmudic Commentators believed that the generative process was shared. From the white semen the Talmudists believed that the bones, the brain and the white of the eyes were derived, from the red menstrual flow the flesh, the blood, the hair and the iris.

The Alexandrian School which carried on the Greek tradition from 330 to 30 B.C. added little to embryological knowledge, accepting without protest the classical teaching embodied in Aristotelian doctrine.

Herophilus of Chaleedon (c. 344-280 B.C.), the greatest of its teachers, described the ovaries and fallopian tubes, while although his writings are lost, it would seem that Erasistratos of Chios (c. 300-260) studied the growth of the embryo. The most brilliant and authoritative of the Roman writer' Claudius Galenus (Galen) of Pergamoss (130-200 A.D.) described the amnion, the allantois and the placenta and gave an extraordinarily accurate description of the umbilical and foetal circulations including the ducts arteriosus, the ducts venosus and the foramen ovale. He divided into four stages : a seminal stage when it remained unformed, a stage wherein the three main organs (tria principa- the heart, liver and brain) are generated a stage wherein all the other organs are mapped out, and a final stage when all parts differentiate.

On the whole, however, from the Alexandrian School or the writings of Galen nothing new of note emerged and for some 14 centuries the teaching of Aristotle as interpreted by Galen was venerated as established doctrine to deny which was sacrilege. Even in the reawakening of science after the Dark Ages had passed, only a few incidental observations were made without any attempt at the formation of a comprehensive philosophy by such observers as Albertus Magnus (1206-80) of Cologne and Bollstadt, or, with his extraordinary insight, by Leonardo Da Vinci (1452-1519) in his delightful drawings.

The ancestor of these was Leonardo da Vinci (1432-1519). Leonardo's embryology is contained in the third volume of his notebooks (*Quaderni d'Anatomia*) that remained unknown until early 1900. His dissection of the pregnant uterus and its membranes are beautifully depicted. He was acquainted with amnios and chorion, and he knew that the umbilical cord only contained vessels. Concerning the foetus, he writes: The veins of the child do not ramify in the substance of the uterus of its mother but in the placenta, which takes the place of a shirt in the interior of the uterus which it coats and to which it is connected but not unite. The child lies in the uterus surrounded with water, because heavy things weigh less in water than in air and the less so the more viscous and greasy the water is.

Leonardo was the first embryologist to make quantitative observations on embryonic growth; he defined, for instance, the length of a fully-grown embryo as one braccio (one arm) and noticed that the liver is relatively much larger in the foetus than in the grown-up man. He also observed that the human body grows daily far more when in the womb of its mother than after birth. The application of the concept of

A WATCH BACKWARD IN EMBRYOLOGY

change in weight and size with time was thus first made by Leonardo more than one hundred years before William Harvey.

After Leonardo three great embryologists were born: Ulisse Aldrovandi and Cesare Aranzio in Bologna and Girolamo Fabrizio d'Aquapendente (nr. Viterbo). They were distinguished anatomists and left beautiful and accurate drawings and descriptions of the human embryo and of embryos of several other species as well. Aristotle's ideas begun to be critically discussed and some rejected, but the new theories were often erroneous, confusing and quite fantastic. The religious and social ideas of the age, together with the lack of any experimental methods, techniques and instruments to verify their theories produced the scientific thought of these embryologists.

Aldrovandi (1522-1605) was the first biologist since Aristotle to open the eggs of hens regularly during their incubation period, and to describe in details the stages of its development. From then on chick's egg became the most studied object by embryologists of those centuries. In his *Ornithologiae*, published in 1599, Aldrovandi set out to describe all the known kinds of birds. The book is sumptuously illustrated, but there is only one picture of embryological interest, namely, a chick in the act of hatching.

Giulio Cesare Aranzio (1530-1589) published in 1564 a rather important book of embryology, *De Humano Foetu libellus*. He was the first to argue that the function of the placenta (jedor uteri) was to purify the blood supply to the foetus and that the maternal and foetal blood vessels are not connected. He discovered the vessel that connects the umbilical vein to the inferior vena cava and that brings his name.

Girolamo Fabrizio d'Aquapendente (1533-1619) professor of Anatomy in Padua was probably the most important embryologist of this age. In his famous books *De Formatione Ovi et Pulli Pennatorum* and *De Formato Foetu* of 1604, however, he introduced a number of grave mistakes and misleading theories. One of his mistakes was that the heart of the foetus has no proper function, but beats only in order to preserve its own life. Moreover, he exhumed the Aristotle's theory that the male semen plays but a secondary role in the generation of the embryo, by activating the egg through the *aura seminalis* but without contacting it. Fabrizio was a good comparative embryologist and it is upon this ground that he deserves praise: his plates were far better than anything before and for a long time afterwards. He dissected embryos of man, hen, rabbit, guinea-pig, mouse, dog, cat, sheep, pig, horse, ox, goat, deer, dogfish and viper, a comparative study which had certainly never been made previously. Fabrizio must also be remembered as teacher of the great William Harvey, who spent five years in Padua attending anatomy lessons by Fabrizio.

Gabriele Falloppia (1523-1562), born in Modena and professor of anatomy in Ferrara, Pisa and Padua, must be mentioned as discoverer of the uterine tube, the female reproductive organ which bears his name, but his service to embryology was only indirect. Two other scientists of this age who left embryological studies of some importance were Girolamo Cardano (1501-1576) and Costantino Varolio (1543-1575). Cardano's main thesis was about the origin of chick's embryo from the egg, one of the most debated subjects of that time. He attempted to mediate two theories by Aristotle and Hippocrates by maintaining that the limbs of the embryo derived from the yolk, while the rest of the body came from the white. Varolio was professor of Anatomy at Bologna and Rome. He treated of the formation of the embryo in a book appeared in 1551, but quite inadequately. He had certainly opened hen's egg and described the fourth-day embryo as *forma minini faseoli* (in the shape of a very small bean).

Even when biology was becoming rationalized and even in the School of Padua where successive professors of genius- Andreas Vesalius (1514-64), Gabriel Fallopio (1523-62), and Hieronymus Fabricius Ab Aquapendente (1537-1619)- interested themselves particularly in the subject and made detailed observations on the anatomy of the uterus, the placenta and the embryo, no revolutionary concepts appeared. The only real originality was shown by Volcher Coiter (1534-1600), a pupil of Fallopio who gave an excellent account of the reproductive tract of the hen and wrote a minute study of the developing chick. It was not until the middle of the 17th century that embryology may be said to have emerged as a modern science. William Harvey's classical work, *Exercitationes de generatione* (1651) in which, studying the embryo of the deer and the developing egg of the chick, he demonstrated the similarity between the two and concluded that the embryos of mammals were of the same nature as the eggs of birds; from this he enunciated and the placenta and gave an extraordinarily accurate description of the umbilical and foetal circulations including the ducts arteriosus, the ducts venosus and the foramen ovale. He divided into four stages : a seminal stage when it remained unformed, a stage wherein the three main organs (*tria principa*- the heart, liver and brain) are generated a stage wherein all the other organs are mapped out, and a final stage when all parts differentiate.

Moreover, the sequence of the events of embryogenesis must be looked at in the perspective that it was not until the year 1677 that Van Leeuwenhoek discovered spermatozoa, not until 1827 than Von Baer described the mammalian ovum, and not until 1843 that Martin Barry observed the penetration of the former into the latter. Embryology as science dates back little more than one hundred fifty years.

In a short time it was supplemented by the studies of Marchello Malpighi (1628-94), with the use of

A WATCH BACKWARD IN EMBRYOLOGY

the simple microscope which he introduced, studied the development of the chick embryo during the first few hours after incubation. Thereby he was able to describe the neural groove, the optic vesicles, the aortic arch and the somites and can justly be credited with inaugurating the science of embryological histology. Fifty years later the full potentialities of this technique were finally realized by the great French surgeon Antoine Maitre Jan (1650-1730) who introduced fixatives hardening his embryos in distilled spirits of vinegar so that they could be accurately dissected and sectioned. In 1674 in his work, "De respiration in utero et ovo", he showed by ingenious experiment that the umbilical arteries of the placenta aerated the foetal tissues by "nitro-aerial particles" in the same way as the pulmonary vessels acted in the adult. These observations were extended to biochemical embryology by Hermann Boerhaave (1668-1738). The culmination of early embryological physiology may be said to have been achieved by Albrecht Vonhaller (1708-77).

Some insisted that the preformed individual was present in the male sperm, a view held by Van Leeuwenhoek (1632-1723) who, looking at unfixed specimens through his imperfect lenses with the aid of a flickering candle, first observed spermatozoa (1678) with the microscope which he evolved, and supported by scientists of the calibre of J. Von Leibniz (1646-1716) and Hermann Boerhaave (1732). The Dutch microscopist, Nicolas Hartsoeker (1656-1725), indeed published pictures of the performed men ("homuneuli") which he saw with the eye of faith in the spermatozoa.

The imaginative flights of authors of this time were well indicated by the publication of Theodorus Kerkringius of Amsterdam. His observation of a foetus tethered by the umbilical cord standing nonchalantly in the uterus 15 days after conception and the skeleton of a child conceived 3 weeks previously.

Von Pander (1817) claimed that the development of the various organs of chick embryo could be traced from three primary tissue layers, themselves characterized by fixity and specificity; from the outermost there developed the skin and nervous tissue, from the middle layer the muscles, skeleton and excretory system, and from the innermost the alimentary canal. Karl Ernst Von Baer (1792-1876), a native of Esthonia first saw the mammalian ovum in 1827, elaborated this theory at length, broadening its base by the examination of more varied material and adding a fourth layer which gave rise to the blood vessels (1827-28).

The workers who elucidated the morphological changes in the developing embryo, were, Martin Rathke (1793-1860) of Dorpat, Rudolf Albert Von Kolliker (1817-1905) of Wirzburg and Wilhelm His (1831-1904) of Leipzig, were among the most prominent for instead of hypothesis they looked on to facts.

The third period in the history of Embryological thought, in which it broke with the traditions of its purely morphological predecessor may be said to have been introduced to an experimental by Haeckel (1869). The experimental approach was enthusiastically taken up by his pupil, Wilhelm Roux (1850-1924), occupied chairs at Innsbruck and subsequently at Halle, in a long series of extended and original researches which were destined to lift embryology beyond the stage of anatomical description into that of experiment, and thus to elucidate the mechanics of development (1885-1912). The question "How?" now gave place to that of "why?" Working on amphibian embryos he came to the conclusion that the development of the egg was determined by mechanical forces within it. A massing of the cytoplasm fixed the point of entry of the sperm, the line of entry of the sperm determined the plane of cleavage and therefore the median plane in an animal with bilateral symmetry, the fates of all parts being determined at the onset of development.

Hans Driesch (1867-1941) showed that in the seaurchin all the cells within the egg up to the fourth or fifth division could, if separated, generate complete embryos; he thus introduced the physiological concept of "prospective potency" to indicate the several possible fates of the early cells (1894). This work introduced the organizer concept largely developed by the German Nobel prize winner, Hans Spemann (1869-1941) of Freiburg and his pupils who, in a long series of experiments showed that chemical substances elaborated within the egg initiated and controlled the later development of the embryo (1912-43). Later work, particularly the tissue culture and microsurgical grafting experiments exploited by R.G. Harrison (1918-21) in the United States, showed the advisability of supplementing this simple explanation by 'the field concept' whereby the developing organism is regarded as a unitary structure wherein the whole and its various constituent part are dynamically interrelated and are continually reacting to each other and to their environment.

CONCLUSION

It must be admitted, however, that it is impossible in the present state of our knowledge to decide whether these generalizing concepts of the organizer, the field, and the gradient contain the whole truth or whether they are skirting the periphery rather than penetrating the kernel of a difficult subject; possibly they are merely aspects of a more all embracing process the nature of which we do not yet understand.

A WATCH BACKWARD IN EMBRYOLOGY

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