Johann Friedrich Meckel the Younger (1781–1833)

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On the occasion of the 200th anniversary of the birthday of Johann Friedrich Meckel the Younger (1781–1833) it is appropriate to examine his contributions to the field of clinical genetics. Special emphasis is given to his laws of "diversity" and "reduction." These deal respectively with the evolutionary and developmental differences between organisms and the reasons for similarities in development of parts of an organism and the parts of different organisms. Meckel is an important pioneer of modern clinical teratology because he did not restrict his studies to normal development, but rather concentrated on its aberrations in his reflections on the history of development.

Key words: comparative anatomy, history of development, teratology, genetics, medical history

INTRODUCTION

In preparing this historical address in honor of Meckel, I found the following sentence by John Opitz in his excellent lectures, "Recent Topics in Clinical Genetics" [1981]: "It is to these scholars—predecessors of immortal memory . . . that we clinical geneticists must pay respectful and humble homage, for without their giant intellectual and practical accomplishments our newest branch of medicine would still be considered an unaffordable luxury dealing mostly with esoterica. . . ."

This comment catches our attention because it is precisely the position in which a medical historian finds himself so frequently. He is regarded as the advocate and researcher of topics which appear to be of little relevance to contemporary problems. His results are at best accompanied by friendly, scientific applause. Yet they are hardly ever considered a necessary contribution to present-day questions. In contrast to this presentist approach, we have been searching for quite some time for a different,

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broader, position. In my country the medical historian is not a member of the Department of History, but of the Faculty of Medicine. In my opinion the history of medicine is not a historical discipline but rather a science to be applied to medical treatment: its aim is to make a contribution to the foundations of a correct evaluation of present-day problems and future needs through methodologically accurate studies of the past [Seidler, 1979].

The need for a short presentation of my own position appeared important to me because the search for the motivation to occupy oneself today with a scientist like Johann Friedrich Meckel can provide some additional dimensions. In order to understand his personality and his work, we will not only have to devote ourselves to his time and place, to those influential critical thinkers of his epoch, but we shall also have to examine his contributions to elemental problems in the theory and practice of medicine. The geneticist of today—and this too was pointed out by John Opitz [1981]—"will in time stamp the practice of modern medicine and shape its future more firmly than war, infections and nutritional disease ever did in the past." I would like to add that for our geneticists to accomplish this task they must be acquainted with the important ideas of their predecessors, their utopias, aporias, and dilemmas that were a part of their, and now are a part of our, problems.

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The lifetime of Johann Friedrich Meckel the Younger covers an epoch in which the emergence of new values and structures and disappearance of old ones determined everyday life to the same degree. I use the words "everyday life" deliberately, because a person who was born in 1781 and died in 1833 experienced in this half-century a great number of major crises in social and intellectual traditions, and also in those areas involving basic forms of man's existence. In his comparatively short lifespan of 52 years. Meckel was exposed to convulsive political ideas stemming from the French Revolution, to the rise and fall of Napoleon I, and after that to political developments connected with the Restoration. Intellectually, he experienced the climax of philosophy of the Age of the Enlightenment, the rise to glory and fall of German idealism, and the romantic philosophy of nature. He participated in the emergence of natural science as the foundation of a new medicine, and he was looked upon for quite some time as one of its protagonists [Clark, 1969; Glass et al, 1968; Nagel, 1944]. His famous and great contemporaries, Lamarck, Cuvier, and Goethe, preceded him by only a year or so in death (Lamarck in 1829, Goethe and Cuvier in 1832). For a long time, for reasons still to be discussed, hardly anyone took notice of him. To sum up: in his life we find in a highly concentrated form a confrontation of those questions which center quintessentially on man's existence. Even today we are still far from having understood or mastered the importance of those questions. Every examination of this period of history, commencing in the nineteenth century, is still an encounter with ourselves, with many elements still active and unanswered within us. Ouite a few philosophers and historians have even gone so far as to state that until now not one of the great problems confronted by the era under consideration has received a valid and credible answer of historical importance.

As New Year's eve of 1799 became dawn of 1800, an extraordinary conjunction of great minds gathered at the Court of Weimar to weigh the challenge of the new century. After the masquerade (the decor having been designed by Goethe) had come

to an end, Goethe, Schiller, and Schelling withdrew to a small chamber to share some champagne. Their conversation became increasingly animated as a young witness, Henrik Steffens, reported [Steffens, 1840]. The three were preoccupied, as was their age, with questions of nature and mind, evolution and perfection. All three of them were searching for that new individual, as embodied in Schiller's words: "The most mature son of the age, free through reason, strong through law, noble through meekness, rich through treasures of nature, and master over nature."

Goethe, who coined the term "morphology," had reached the peak of his creative power and had provided biologists with many fruitful avenues to explore in their search for an ideal typology [Steiner, 1949; Uschmann, 1939; Radl, 1905]. Most notably he stressed developmental processes in his work on the metamorphosis of plants in 1790 [Meyer-Abich, 1963]. Schelling, the third member of this New Year's eve gathering, had declared nature to be the philosophical starting point for all laws of mind [Schelling, 1799]. Still germinal was his precept that medical science should be raised to the level of a "general science of organic nature." He worked this out more fully in 1802 in his lectures "On the Study of Medicine and the Science of Organic Nature."

These three noble minds were united that night in their concept of a new anthropology, a doctrine of the new man. That mature individual, on the threshold of the nineteenth century, attempted to attain a scientific understanding of his own nature. A deeper understanding of the physical, psychological, and social structure of this new individual would encompass the close relationship between nature and mind, reason and reality, evolution and perfection, thus making man the ultimate architect of his world. Such fundamental analysis, offered that New Year's eve by these three great scholars, had a profound impact upon our culture. As their ideas were reworked by Hegel, Marx, and Nietzsche, they came to affect and inspire natural scientists up to the present day [Schipperges, 1970]. We shall return to this theme later, but now we must turn to Johann Friedrich Meckel. In that New Year 1800, the 19-year-old Meckel was honored by a verse inscription in the family guest book: "In your friendship I found harmony, the pure product of nature" [Beneke, 1934].

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It is not only interesting but vital from the point of view of the history of genetics to gain a deeper understanding of Meckel's intellectual structure. We recall that the Meckel family produced five renowned anatomists in four generations [Berner, 1963; Meader, 1937/8]. For one hundred years they made essential contributions in science and they were at the center in research and teaching in German universities. Johann Friedrich was named after his grandfather (1724–1774). This "elder" is still remembered for his important contributions to our knowledge of the sphenopalatine ganglion (described in 1747) and the maxillary ganglion (1771). As a student of the famous Albrecht von Haller (1708–1777), this grandfather (Fig. 1) laid the foundation for a distinguished family career in anatomical science. He charted the direction for generations to come by starting a private anatomical collection at his home in Halle. This later became very famous in medical and scientific circles.

Johann the Elder's oldest son was Philipp Theodor Meckel (1755–1803), who was brought up in this academic atmosphere and schooled in anatomy against his will. However, after completing his training under the most brilliant European scientists



Fig. 1 Meckel's grandfather, Johann Friedrich Meckel the Elder (1724–1774), and founder of the Meckel dynasty.

Fig. 2. A) The younger Meckel at about 15 years; B) Meckel as an adult.

Fig. 3. Johann Christian Reil (1759–1813), one of the most dominant of early influences on Meckel and his later collaborator.

and physicians of his time, he, like his father, became professor of anatomy and surgical obstetrics in Halle. He too would enhance its high reputation.

His son, Johann Friedrich the Younger (Fig 2A,B) blossomed in this atmosphere. He greatly admired his grandfather, whom he always called "avus." At home he enjoyed the tutorship of his father, now recognized as one of the greatest anatomists of his day. From childhood he was acquainted with the most brilliant scholars at the University at a time when it was very active. Among these visitors were Kurt Sprengel (1776–1833), a renowned botanist and historian of medicine, and Johann Christian Reil (1759–1813), the well known physiologist and clinician (Fig. 3). Reil became strongly influential on and later would collaborate with Johann.

What daily life must have been like in a family of scholars toward the close of the eighteenth century when fathers could force their sons—successfully—against their will to supreme achievements must be left to psychological analysis, or today perhaps psycho-history. The awareness of being a link in a strong chain, of representing history and having a responsibility toward it, can without doubt be considered an important element in his later decision to devote his life to discovering the secrets of human development.

In 1950, Owsei Temkin, the noted historian of medicine at Johns Hopkins, published an important article in which he pointed out that *Entwicklungsgeschichte*, literally the history of development, became an integral part of embryology as well as historical consciousness around 1800. He explained that "in Germany around 1800, a concept was formulated, in which the ages of man were for the first time reviewed as a 'historical' sequence from conception to death. In the formation of this concept, embryology on the one hand and true history on the other played a decisive role, both influencing each other. It was the idea of ontogenetic development in particular that linked the philosophy of nature and of history."

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These formative intellectual influences on Meckel must be kept in mind as we examine his life and work. The path that was evidently predestined for him ran its course. In 1797 at the age of 16 he went to St. Petersburg with his father, who had been summoned to deliver Czarina Maria Feodorovna's child. In the following year Johann Friedrich began to study medicine and to write his dissertation. The thesis topic, "On Malformations of the Heart," was suggested by his father. The private anatomical collection in the family, and one which Johann Friedrich would enlarge in his lifetime, contained adequate examples for research. Before taking his state examination, he spent the last two terms as a student at Göttingen. There he studied with Johann Friedrich Blumenbach (1752–1840) (Fig. 4A,B). Blumenbach was a pioneer in the field of comparative anatomy in Germany. Meckel emphasized that it was his mentor there who directed him to a life-work in comparative anatomy and physiology.

In 1803, having completed his studies, Meckel was in Vienna when word reached him of his father's death. The 21-year-old became heir to all the outer and inner responsibilities represented by a third generation Meckel. In 1805 their common friend and Johann's teacher, Johann Christian Reil, arranged an associate professorship for him at Halle. Prior to this he was able to travel more widely. In Paris he came under the influence of Georges Cuvier (1768–1832), the most notable life scientist of his time in France. Cuvier, a formidable zoologist and comparative anatomist, was approaching the height of his career. Cuvier reinforced Blumenbach's influence on Meckel. Later when Meckel was declared to be the "German Cuvier" it



Fig. 4. A) Meckel's teacher, the renowned Johann Friedrich Blumenbach (1752–1840) of Göttingen; B) Title page of Blumenbach's most important contributions: *The Institutions of Physiology*.

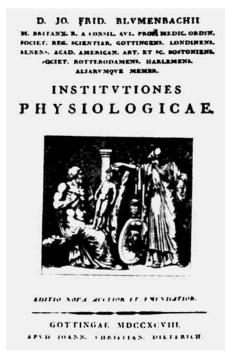
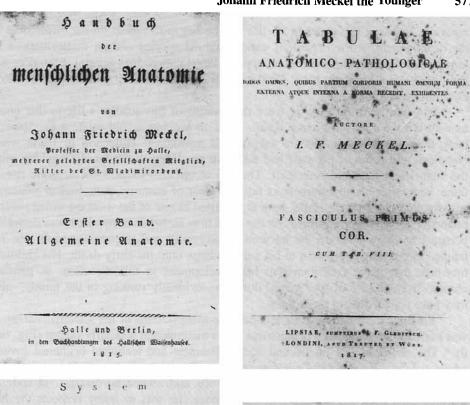




Fig. 5. Title page of the Froriep-Meckel translation of the Cuvier-Dumeril *Leçons d'Anatomie Comparée*.

was not simply because he translated five volumes of Cuvier's lectures (held 1799–1805; Fig. 5) or that he commented extensively upon them [qv Cuvier/Meckel, 1809–1810]. Rather, he earned that label because he focused precisely on those areas only lightly worked up by Cuvier. These germinal ideas became the basis of Meckel's own





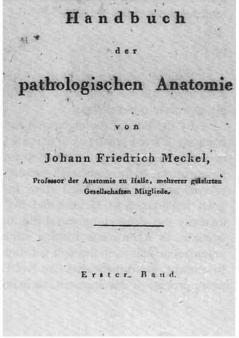


Fig. 6. Title pages of four of Meckel's own most important scholarly productions: A) The Handbook of Human Anatomy; B) The Anatomo-Pathological Tables; C) The System of Comparative Anatomy; D) Handbook of Pathological Anatomy.

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research. It was at this point in his life that he began to reflect on the differences in the development of the organs of various animal species and on malformations in terms of deviations from normal embryonic development [for general references see Fischer, 1945; Glenisher, 1964; Hintzsche, 1972; Meyer, 1939; Nordenskiöld, 1967; Oppenheimer, 1968].

It would be fascinating to trace the stations of this scholar's life in that enormously turbulent age in greater detail. Such an account would relate a hurried trip back from the Alps in 1805 to salvage his anatomical collection in Halle when Napoleon and some of his staff had taken up residence in the family dwelling after the victories at Jena and Auerstädt. The tale would also include his meteoric rise to fame: soon after his appointment as full professor of anatomy, pathological anatomy, surgery, and obstetrics at Halle, he was regarded as one of the most esteemed natural scientists in the academic world. At the same time he began to manifest less desirable personality characteristics: he became domineering and uncompromising. He remained in constant opposition to his surroundings until his early death. His childless marriage may have contributed to his development in this direction. A painful, chronic liver disease of four years' duration—evidently running in the family—also may have contributed to these traits.

Finally, we should have to delineate the main stations of his scientific career. It was marked by compulsive restlessness and a monumental scholarly output (Fig. 6a-d).* The abundance of intellectual accomplishment and technical brilliance invited admiration but also provoked mistrust and envy. It is certainly not a bold interpretation to call attention to a key fact: he raised no son and trained no disciple. In spite of massive pioneering contributions to his science, he was in many respects the last representative of it.

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Now let us turn to Meckel's work in two areas which still deserve closer scrutiny by today's geneticists. The first is his contribution to ontogeny, the second his approach to teratology.

By the turn of the eighteenth century, and strictly speaking well beyond that, opinions differed greatly as to the exact meaning of the term "development." Aristotle's epigenetic concept centered upon the gradual elaboration of greater diversity in an organism. In the eighteenth century, Caspar Friedrich Wolff (1733–1794; Fig. 7) revived and adumbrated this view. In his *Theoria Generationis* (1759)—a work of great importance to Meckel and his generation—Wolff was of the opinion that diversity was due to a universal life force. This life force effects and guides embryogenesis as it proceeds from a structureless onset to a progressive increase in organization and form through nutrition and growth [Aulie, 1961; Herrlinger, 1959]. In contrast, preformationists like Wolff's contemporaries Haller and Bonnet held that every process of development, including human, is predetermined in detail in either

^{*}Among which the following are the most important: The Froriep-Meckel translation of Cuvier's *Leçons d'Anatomie Comparée* in 4 volumes [1809–1810]; Meckel's *Beiträge zur vergleichenden Anatomie* in 2 volumes [1812–1818]; Meckel's *Tabulae anatomico-pathologicae* [1817–1826]; *Handbuch der menschlichen Anatomie* in 4 volumes [1815–1820]; and his *System der vergleichenden Anatomie* in 5 parts [1821–1831].



Fig. 7. Contemporary profile of Caspar Friedrich Wolff (1733-1794).

sperm or ovum as a purely mechanical process. It proceeds in the manner of insect larval embryogenesis [Bodemer, 1964].

In Meckel's formative years the sharp line between the opposing schools had blurred [Schopfer, 1945]. Four questions regarding the process of development, and thus of nature itself, had crystalized:

- 1. What is the methodological basis of a science of development?
- 2. What is the "nature" of the process of development? That is, what *really* takes place during development?
- 3. What is the nature of species? Is phylogenetic diversity apparent or real and does the resolution of this question require a biological or a historical approach?
- 4. What is the underlying reason for the entire process of development?

The last question in particular dominated discussions in the eighteenth century. The entrenched view of an omnipotent Creator still lingered on in the subconscious of some natural scientists. Increasingly sophisticated work in anatomy, chemistry, and physics yielded new data, but still an urgent question remained: what natural order was responsible for the integration of the whole? A certain life force, more or less teleologically conceived, regulated time and degree of individual development as well as environmental adaptation.

This concept also reinforced the idea of the "history of development." All species, including man, originated from a single process of development. The search for unities, similarities, and sequences in the development of the animal world dominated the biological efforts of Kielmeyer, Goethe, Cuvier, Etienne Geoffrey St. Hilaire, Lamarck, and many others.

For Meckel, two opposing laws of formation ruled the organic world: the law of diversity (*Mannigfaltigkeit*) and the law of unity (*Einheit*). The latter sometimes is

referred to as "the principle of reduction." The two laws can be understood only as being respectively under the influence of a form-inducing or a form-retarding power. They reflect processes that are permanently dynamic and even bipolar. The law of diversity (Handbook of Human Anatomy and Handbook of Comparative Anatomy) subsumes all characteristics that distinguish the various forms of life from one another. It includes not only innate characteristics that distinguish species from genera and higher groups, but also differing individual organs as they develop with age, habit, or heredity. The "law" attempts to determine the causes of the diversity of species and of the organs within an organism through the richness of findings of descriptive anatomy and embryology. It asks: what makes things different, ie, how does diversity arise during phylogeny and ontogeny? Thus is defined a broad field of descriptive anatomy that attempts to infer the causes of development of the manifold richness of nature. Each organism must proceed by stages through a more or less coherent sequence of development. As this process unfolds "the ability of the organism to be more or less determined and modified by the environment" is increased. Thus, evolution and developmental process are intertwined.

Comparative anatomy for Meckel embodied the "law" of reduction which attempts to discover the unifying principle and the cause of the "analogies" of structure within an organism and between related species from the findings of comparative anatomy. It asks: what makes parts of the body and of different animals similar in development, ie, (in modern terms) what is the genetic and evolutionary basis of homology? Meckel offered many examples, all directing attention to the developmental process: the lung of terrestrial mammals as it developed from the air bladder of the fish; similarities between male and female sexual organs; vermiform and arthropod segmentation and its analogous appearance in vertebrate metamerism. All lead to an inescapable conclusion: "Whole bodies are formed according to a similar plan; but this similarity may be obscured by variable regression or overdevelopment (predominance) of certain parts in different organisms; however, the basic similarity is never completely eliminated."

It was logical to search for analogies in the history of development. The idea that more highly organized animals pass through lower evolutionary stages during ontogeny had already been held by Aristotle. The same idea arose repeatedly in the eighteenth century. Its basic tenet referred to the similarity between the outer form of embryos during the very early stages of development. Meckel began his work at this point. He attempted to prove that the great diversity of organic forms is but a combination of variations on a single basic model. As he stated it: "The original form of all organisms is one and the same, and all organisms, the lowest as well as the highest, develop from this one form in such a manner that the latter pass through the permanent stages of the former by way of transient stages."

It has been repeatedly pointed out that this statement anticipated by a century the "biogenetic law" formulated by Ernst Haeckel: ontogeny recapitulates phylogeny [Haeckel, 1870, 1874; Heberer, 1943; Zimmermann, 1953; Zündorf, 1943]. Because Meckel referred to this process as a law, not as an hypothesis, he indicated that he was firmly convinced that "higher animals in their development pass through stages which appear to be fixed for lower animals." Thus, an important principle of post-Darwinian biology, professed by his "bulldog" T.H. Huxley, derived from Meckel [Kohlbrügge, 1911]. Others, like Cuvier, Kielmeyer, and the great embryologist Karl Ernst von Baer (1792–1876), insisted that the major, more permanent characteristics of one animal group never appear in the embryonic form of another, higher group.

Later admirers of Meckel suggest that his mistaken conception would have been rectified automatically had he lived a decade longer. By then advances in cytology, microscopy, and population biology might have guided him. However, speculation is fruitless. Meckel had stretched the conceptual limits of his age to the limit and had exhausted all possibilities.

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We have yet to focus on Meckel's central interest in the embryo, the history of animal and human development. It was his aim to approach this subject utilizing normal embryogenesis and to examine with care abnormal development. As a result of this dual approach Meckel effected a significant change in anatomy and physiology. Vesalius, Harvey, Descartes, and many others had described normal development. They followed the regular form and the unbroken function of body and mind to fathom nature more clearly. Giovanni Battista Morgagni (1682-1772) sought to locate the source of disease in specific organs. He introduced methods of detailed examination into pathological anatomy and physiology. But Meckel no longer restricted his investigations to normal embryogenesis. He concentrated on aberrations, thus making a decisive contribution to medical science. Owen E. Clark, in the Osler Lecture at Yale University in 1967, stated that Meckel's work in descriptive teratology was "probably his most substantial and lasting scientific contribution." Yet all of the small group of biographers have traced Meckel's interest in congenital malformations back to his doctoral thesis. Once he commenced the study of malformations of the heart, he never deviated in his search for developmental anomalies.

Tradition in pathological anatomy had held that malformations were basically vagaries of nature which occurred sporadically and were usually unique. Meckel opposed these views with his conception that they were simple, primary variations of generative energy. The causes were not yet known but lay within the realm of scientific inquiry. Normal and abnormal processes were placed side by side as essential foundations of the origins of form. The boundaries between normal and abnormal processes, and this is of crucial importance, are removed and the causes are sought. Differences are investigated and recognized as a measure of existing developmental conditions. The interplay between diversity and reduction can be recognized now. Normal and abnormal development follow the same principles. If that be so then one can expect to find most malformations of higher animals to be present in some degree in sequences of development in lower animals.

Meckel recognized four basic types of abnormal development: insufficient generative energy, excessive generative energy, aberration of form and position; and finally Zwitterbildung. This last type includes twinning and ambiguous genitalia (Fig. 8A,B). In his Handbook of Pathological Anatomy [1814–1818], Meckel developed for the first time an extremely accurate system of human malformations, ranging from the anomalies of the placenta to the tiniest ramifications of the organ systems, detailing all gradations of known anomalies. Clark has drawn our attention to the similarities between Meckel's subclass of insufficient energy and the modern concept of developmental arrests. Particularly for these anomalies which involved multiple organ systems, Meckel postulated that the organism was structurally normal at conception and subsequently suffered an arrest in its development, resulting in absence or diminution in size of an organ or persistence of an embryonic condition (Fig. 9).



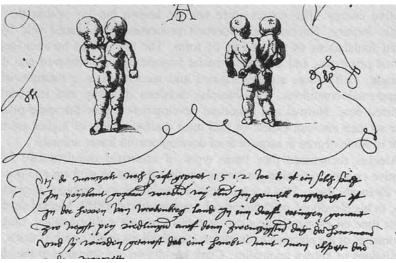


Fig. 8. Conjoined twins discussed by Meckel: A) The Hungarian pygopagus girls from 1724; B) the dicephalus tetrabrachius twins illustrated by Dürer in 1512.

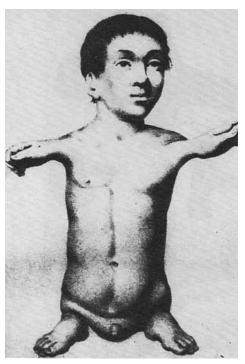


Fig. 9. Marco Catozzo, the "dwarf of Venice," described by Meckel in his *Handbook of Pathological Anatomy*.

Meckel pursues many interesting details of developmental anomalies. In a famous instance, he analyzes the *diverticulum ilei verum* or Meckel's diverticulum (Fig. 10). In another he sketches "Meckel's cartilage," first described in 1820; this structure develops at the beginning of the 2nd fetal month and is important in the formation of middle ear ossicles and the mandible.

Meckel's great researches apparently had little influence on immediately succeeding generations. He remained, strangely enough, a final representative of a fading tradition. His thorny personality and somewhat disorganized methods of research may have estranged some who would have built upon his contributions. The presentation of his findings was too deeply rooted in traditional terminology and ways of thinking to open an already visible gate to the new fields of research he had explored. He founded no school as did Johannes Müller, Rudolf Virchow, and Claude Bernard in the next generation.

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In closing, I would like to place Johann Friedrich Meckel in a broader contemporary perspective. He has not been sufficiently honored elsewhere in the world on this occasion of his two hundredth birthday. His achievements loom far larger now than at any point in history.

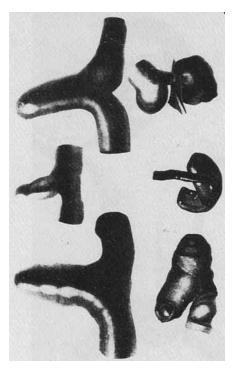


Fig. 10. Meckel's diverticulum, from the Tabulae anatomico-pathologicae [Leipzig, 1817].

He began systematically to study the history of development, including human embryogenesis, on the basis of malformations. That achievement transcends more than scientific progress in anatomy and embryology: he made man's fear of his own deformity, the freaks of nature, distortions, and crippled limbs, he made all that a fit subject for science. He must be regarded as one of those great representatives of the enlightenment era who sought the ideal, the new and better man. The aim of mankind is to improve, perfect if possible, the physical, psychological, and social status of all men. The force of nature married to the power of reason could lead to individual, social, and international harmony. Since Meckel, that which is inharmonious, aberrational—deformed—can only be elmiminated by reason and science.

It is peculiar that consideration of the new and better individual always appears to grow into utopian thinking as a century progresses and comes to its conclusion. The philosophical, scientific, and political conception of the new individual culminates in the programs of the enlightenment and revolutions at the end of the eighteenth century. At the end of the nineteenth, the ferment brewed by Darwin, Nietzsche, and Haeckel led some social Darwinians and racial theorists to proclaim the new individual of the dawning twentieth century. Such a new man was to be brought about by eliminating the deviants and the inferior. Fanatics put this horrifying doctrine into practice in Germany during the 1930s with disastrous consequences.

Today at the close of another century, geneticists in their counselling centers seek to advise ethically and accurately those mothers and fathers who face life and death situations for unborn embryos. Again we strive for the so-called better individual in our society. Many of the old fears of deformity still haunt us.

Johann Friedrich Meckel the Younger becomes, in an impressive manner, a model for the two sides of progressive knowledge. By making teratology the center of his thinking, he created the foundations for its objective understanding and at the same time for dealing more extensively with the problems of its subjective evaluation. Whether Meckel himself foresaw the implications of his genius is impossible to tell. I agree with Owen Clark: "For many scientists and most historians birth defects have retained their primitive horror."

We have returned to the beginning of this address. I am deliberately emphasizing John Opitz's statement that the real importance of genetics for the future of mankind is yet to begin. The historian of medicine must add that it is precisely those latest findings that are reviving in a dramatic manner the old historical dilemmas. It cannot yet be predicted what type of a relationship man will develop to his own living deformity at the end of the twentieth century, the scientific study of which had begun with Johann Friedrich Meckel, two hundred years ago.

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