DEVELOPMENTAL ANATOMY

A TEXTBOOK AND LABORATORY MANUAL OF EMBRYOLOGY

By

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To

WEBSTER CHESTER

PROFESSOR OF BIOLOGY, COLBY COLLEGE

An inspiring teacher, scholarly scientist and true friend of youth
who laid my biological foundations, tendered encouragement
and help in mastering early difficulties and
pointed the way to greater
opportunities

THIS VOLUME

is inscribed with a deep sense of admiration
and gratitude

PREFACE TO THE FOURTH EDITION

It has been a policy, shared with me by the publisher, not to bring out revisions of this text until something could be offered beyond what might be effected through minor improvements. Thus, the second and third editions appeared at intervals of six and four years, respectively, and each represented thorough tasks of rewriting, rather than selective revision. In those two editions 616 new drawings were introduced. Now, after another six-year interval, the fourth edition is offered as essentially a new book. This has required more than two years of concentrated effort, and the replanning and rewriting have been so drastic that only fragments, at most, of previously existing pages have been salvaged and re-utilized. The extensiveness and intensiveness of the revision involve equally the text proper and the laboratory manual.

Among the new features are 540 drawings, which raise the present total to 1385. In addition, nearly 200 of the earlier illustrations have been altered and improved in various ways. Seven new summarizing tables supplement those already present. The laboratory section has been strengthened both in text and in illustration for the better study of the chick and 10 mm. pig embryos, whereas most of the material on the 6 mm. pig, apparently little used, has been dropped. New standards of age have been adopted for human embryos of the first five weeks; these are in accordance with the precise information on the monkey made available by the Carnegie Laboratory of Embryology. Such time-standards are more reliable than any other information yet at hand, since the purely human data are highly contradictory and confusing.

Many important studies have appeared during the six-year period since the publication of the previous edition; in some instances this newer information has made obsolete certain traditional views, while it has modified others profoundly. An attempt to cover the world literature in embryology has at least been pursued with diligence and it is hoped that the presentation given reflects accurately the current status and trends of this science. As before, superscripts interspersed throughout the text agree with the numbered entries in bibliographies at the end of each chapter; in this way the reader may readily check the authorities responsible for new or controversial interpretations and find key sources of more comprehensive bibliographies. In some instances recent contributions with comprehensive literature reviews have been given preference in citation over more weighty, but older, researches.

The human subject naturally provides the principal focus on which the interests of medical students and mankind in general center. Since, moreover, the human embryo is a quite typical mammalian form and since more detailed information on it now exists than on any other species, apology is scarcely necessary for placing man in the embryological spotlight. Unless the context clearly indicates the contrary, the reader may assume that the developmental story as set forth in the pages which follow is an account of his own pre- and postnatal history.

The writer will appreciate critical comments and suggestions from any reader, since the sampling of reader-opinion is a necessary step toward further betterment in the direction of majority desire.

L. B. AREY.

CHICAGO, ILLINOIS.

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PART I. GENERAL DEVELOPMENT

CHAPTER I

INTRODUCTION

The Nature of Embryology.—Originally 'embryology' was a term restricted to the events of prenatal development. Only gradually was it realized that developmental processes continue long after birth. With the steady accumulation of data pertaining to the stages of development and their behavior, it has proved convenient to subdivide the several aspects of embryology into two divisions. One branch traces the formative history of animals from germ cell to adult. It paints the progressive panorama of change that cells, tissues, organs, and the body as a whole undergo in attaining their final states. These unified descriptions of advancing form, structure and relations can be designated by the term '*developmental anatomy*.' The other division of embryology attempts to explain on the basis of experiment the way in which development works. How seemingly mysterious happenings can be resolved into familiar physico-chemical phenomena; how parts interact in determining, regulating, coördinating and integrating the evolving embryo; how fetal physiology makes its beginnings; all these, and more, constitute '*experimental embryology*.' To include an analysis of experimental development in the present book would double its size. Hence the interested reader must look to special works (p. 15) for enlightenment on these topics. Yet, in so far as is practicable, the general functional aspects of development will be given consideration in the chapters that follow.

Although the most striking changes in the development of man and mammals occur while the young (first called an *embryo* and later a *fetus*) is still inside its mother's womb, yet development by no means ceases at birth. Birth is a mere incident in the whole developmental program, which occurs when the new individual is sufficiently advanced to cope with conditions of life in the external world. Some vertebrates, such as fishes and amphibia, are capable of an active and independent existence at very immature stages; these free-living animals, with most of their development still before them, are called larvæ. The human newborn, although far more complete anatomically than such larvæ, is utterly dependent for food and care; many years of infancy and childhood must elapse before it becomes self-maintaining in human society. During all this time postnatal development continues; indeed, the altered conditions at birth itself induce changes that modify the body profoundly. Throughout the entire growth period, with its uneven but steadily slowing growth rate, come the completion of some organs and a gradual remolding of the shape of the body and its parts. Only at about the age of twenty-five are the last of these progressive changes complete, whereupon an individual becomes truly adult. The mature person remains in relatively prime condition until the regressive processes, which start slowly but advance steadily, begin to dominate; then the organs and the organism as a whole 'age,' or undergo a senescence, which inevitably terminates in death.

All vertebrate (*i.e.*, backboned) animals are organized upon a common anatomical plan, and even many of their structural details are comparable though superficially disguised. Similarly, their fundamental mode of development is essentially identical, although in the end 'higher' groups naturally progress to greater complexities than 'lower' ones. The chief variations that do occur are caused by such secondary modifying factors as the crowding yolk-content of the egg, or by adaptations to a course of development inside or outside the mother's body. While the comparative viewpoint is indispensable for gaining a broad understanding of embryology, it has been of special importance in supplying missing pages of the human developmental story and in interpreting otherwise perplexing conditions. The extent of this reliance on related forms will be appreciated when it is stated that the youngest human embryos known are already embedded in the uterus and possess their three primary germ layers. Indeed, even invertebrate stages have been useful in clarifying the earliest phases of development.

The Method of Study.—The progress of development is ascertained partly by observing entire embryos and dissections in proper age-sequence, and even more profitably by the microscopical study of stained sections. When sections are arranged in the same progressive order as cut, they furnish an orderly series in which the changing appearances from level to level can be traced and reconstructed either as mental images or physical models. Besides the dimensions of *length* and *breadth*, as in ordinary sections, a third measure, *depth*, must be visualized. Still a fourth dimension, *time*, enters since it is necessary also to correlate the degree of development of any part with respect both to associated organs and to the condition of the embryo as a whole. Thus, in a sense, embryology becomes a four-dimensional study.

The Value of Embryology.—A general conception of how man and other animals develop from a single cell by orderly and logical processes should share in the cultural background of every educated mind. From the theoretical side embryology is the key that helps unlock the secrets of heredity, the determination of sex and organic evolution. To the medical student, embryology is of primary importance because it supplies a comprehensive and rational explanation of the intricate arrangements of human anatomy. The body does not just happen to be arranged as it is. Each end-result in structure is preceded by a definite, developmental course of events; when these go awry or stop short of completion, they are readily explainable. Embryology is able to interpret such rudimentary structures, variations, anomalies and 'monstrous' conditions, as well as to throw light on the origin of certain tumors and other pathological changes in the tissues. For these reasons it is essential to sound surgical training. Furthermore, obstetrics is basically merely applied embryology.

Historical.—Several centuries before our era, Aristotle wrote the first book on Embryology. It was a mighty compendium of observation and argument, so far in advance of his age that only relatively recently have men outdistanced him. For nearly two thousand years after Aristotle almost nothing of significance was added. Although Aristotle discovered many astonishing facts and followed the general development of the chick day by day, he naturally fell into error on things about which he had to speculate. Thus he credited the popular belief that slime and decaying matter are capable of producing living animals, and he described the human embryo as organizing out of the mother's activated menstrual blood. Such origins were disproved by Redi (1668), although the death blow to the persistent belief of the spontaneous generation of microscopic animalcules and bacteria was dealt only in 1864 by Pasteur.

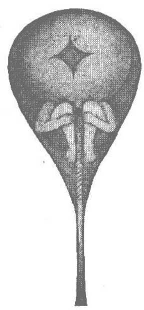

FIG. 1.—Human sperm cell, containing a miniature organism, according to Hartsoeker (1694).

Shortly after Harvey (1651) and Malpighi (1673) had published their fundamental studies on the developmental stages of the chick embryo, as seen with simple lenses, Leeuwenhoek reported the discovery of the human spermatozoön in 1677. At this period it was generally believed either that fully formed animals exist in miniature in the egg, needing only the stimulus of the spermatozoön to initiate development, or that similarly preformed bodies, male and female, constitute the spermatozoa and merely enlarge within the ovum (Fig. 1). To be consistent this doctrine of *preformation* had to admit that all future generations were likewise encased, one inside the sex cells of the other, like so many Chinese boxes. Serious computations were even made as to the probable number of progeny thus present in the ovary of Mother Eve, at the exhaustion of which the human race would end! In recent years certain features of the preformational point of view have been reintroduced into biology, but in a far more subtle form than the original doctrine taught. It is now conceded that the chromosomes contain in their genes the determiners of hereditary constitution. Moreover, a regional organization of the egg may be recognized wherein certain areas correspond to rather definite parts of the future embryo (Fig. 28). This early segregation of formative stuffs is called *prelocalization*.

The preformation theory was strongly combated by Wolff (1759) who, like Harvey before him, saw the organs of the early chick embryo differentiate gradually from simple, unspecialized beginnings. This teaching, known as *epigenesis*, was proved correct when von Baer discovered the mammalian ovum in 1827 and later demonstrated the three primary germ layers from which all embryos and their constituent parts develop. For these and other far-reaching studies von Baer has justly been honored as the 'father of modern embryology'; through him the origins of the principal organs were determined and the science of embryology made comparative.

Schleiden and Schwann proved the cell to be the structural unit of the organism in 1839, and about twenty years later the ovum and spermatozoön were recognized as true cells. Hertwig, in 1875, was the first to observe and appreciate the events of fertilization. Since then it has become axiomatic that every multicellular organism develops from a single, fertilized egg ('*omne vivum ex ovo*'). The present epoch was made possible when Balfour (1880) reviewed, digested and made accessible the earlier scattered facts. Throughout this modern period two lines of endeavor have been notable. One is direct observation and description, naturally the earliest in the field. Of special interest has been the attempt to present a well-rounded account of human development, first led by His and Keibel in Europe and by Minot and Mall in America. The other field of activity is the experimental attack on developmental problems, as exemplified by Roux and Spemann in Europe and by Morgan and Harrison in this country.

GENERAL FEATURES OF DEVELOPMENT

A multicellular embryo begins life as a fertilized (*i.e.*, activated) egg. Further development depends upon: (1) growth (*cell proliferation*); (2) cell movements, which lead to the production of body form (*morphogenesis*); (3) cell specialization, which through changes in shape, structure and function produce tissues (*histogenesis*); (4) tissue combination, to set apart definite organs (*organogenesis*); and (5) functional adaptation and correlation, to produce a working organism (*integration*).

The fertilized egg straightway becomes a ball of cells, which soon organizes into three sheets known as the primary germ layers. From these the tissues, organs and body rapidly emerge in ways to be described later in considerable detail. At the end of the developmental period the adult body may be many billions of times bulkier and heavier than the original egg. The final number of cells produced is beyond adequate comprehension; in man there are 25 million millions of red blood corpuscles alone. Even more impressive are the subtle cellular specializations and adaptations that characterize the component tissues and organs.

Developmental Processes.—It seems like a long span from the egg to the trillions of cells that comprise the completed body of man, yet this prodigious final number can be attained quite readily by repeated cell division. So rapid is the doubling process that some 45 generations (2^{45}) of mitoses are sufficient. Of course, this theoretical product is not realized in any such mathematically precise fashion, since some cells

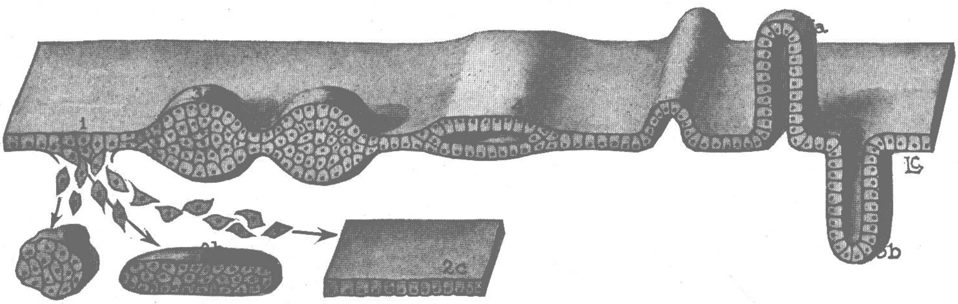

FIG. 2.—Stereogram illustrating the developmental processes. Numbered as in the text.

multiply much faster than others. Along with cell proliferation and growth goes the imbibing of water, so that in the early weeks of its development the embryo is nearly 98 per cent. fluid. It could be shown that such free use of water is highly advantageous to a growing organism. Following on the heels of imbibition go cell differentiation and various other processes, some of which require mention here.

The developing embryo acquires a progressively complex structure, the diverse steps in the production of which occur in orderly sequence. A number of component mechanical processes can be recognized which the embryo uses repeatedly in acquiring form and structure. The more important of these are the following (Fig. 2): (1) *cell migration;* (2) *cell aggregation,* forming (a) masses, (b) cords, and (c) sheets; (3) localized *differential growth,* resulting in (a) enlargements and (b) constrictions; (4) *delamination,* that is, the splitting of single sheets into separate layers; (5) *folding,* including circumscribed folds which produce (a) evaginations, or out-pocketings, and (b) invaginations, or in-pocketings.

The production of folds of all sorts, due to unequal rapidity of growth locally, is the chief factor utilized by the embryo in producing new organs and in molding its general form.

Organizers.—It can be demonstrated during development that various localized parts of an embryo, called *organizers*, exert definite, directive influences on neighboring parts. Two kinds of effects are produced, and true organizer material exhibits both. The first is a simple activation by one region that arouses or releases inherent developmental potentialities in an appropriate reacting field. Such 'induction' is due to some general, unspecific property of tissues, living or dead. This is shown by the capacity of the activating principle (apparently chemical; perhaps involving glycolysis) to survive such treatment as boiling or alcoholic fixation. But there is more to organizer action than the mere eliciting of activity in a field, without displaying any itself. A true organizer is also able to impose organization upon regions that come under its influence. That is, it instructs the region in a kind of differentiation that it otherwise would be incapable of displaying.

Two illustrations will perhaps make these matters clearer. If an ear vesicle from a frog embryo is transplanted under the flank it induces the formation of an extra limb there; but transplanted dead matter can accomplish the same result. On the other hand, an optic vesicle transplanted into an indifferent region, such as the belly skin, calls forth the differentiation of a lens in the overlying ectoderm (epidermis), just as occurs normally in the appropriate region of the ectoderm of the head.

Cell Division.—All cells arise from pre-existing cells by division. There are two methods of cell division—amitosis and mitosis. The details of these processes are described fully in textbooks of histology.

Amitosis.—A cell may divide 'directly' by the simple constriction and fission of its nucleus and cytoplasm. This rather infrequent process is called *amitosis*. Some think it occurs only in specialized cells or in cells approaching death.

Mitosis.—In the multiplication of typically active somatic cells, and in all germ cells, complicated changes take place in the nucleus. Since these changes give rise to thread-like structures developed out of the nuclear chromatin, the process is termed *mitosis* (*i.e.*, a thread) in contrast to amitosis (*i.e.*, no thread). The distinctive feature of mitosis is the production of a characteristic number of chromosome bodies, their growth into double structures, and the separation and accurate distribution of these components to the two daughter cells.

The Germ Layers.—The first important move toward organization in a young embryo establishes three superimposed, cellular plates, the *primary germ layers*. From their positions they are termed the *ectoderm* (outer skin), *mesoderm* (middle skin) and *entoderm* (inner skin) (Fig. 3 *A*). Since the ectoderm covers the body it is primarily protective in function, but it also gives origin to the nervous system and sense organs through which sensations are received from the outer world. The *entoderm*, on the other hand, lines the primitive digestive canal and is from the first nutritive; later it also becomes respiratory. The *mesoderm*, lying between the other two layers and later splitting into two sheets, naturally performs the functions of circulation, muscular movement, excretion and reproduction; it also gives rise to the skeletal structures which support the body. While all three germ layers produce definite sheets of cells known as *epithelia*, some of the mesoderm takes also the form of a diffuse meshwork of cells, the *mesenchyme* (Fig. 3 *B*). This is a filling-tissue whose own interspaces contain a watery gel. Nevertheless, the mesoderm is not the sole source of mesenchyme because both ectoderm and entoderm contribute as well, although in a much more limited degree.

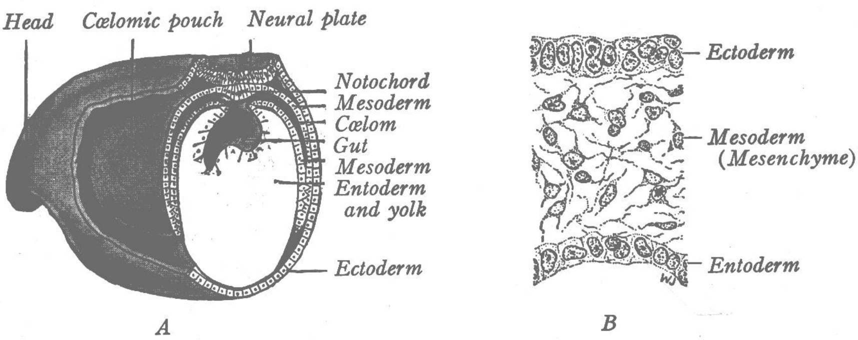

FIG. 3.—Germ layers of early embryos. *A*, Stereogram of the head end of an amphibian (Kingsley; × 15). *B*, Section of an early human embryo (× 400).

Derivatives of the Germ Layers.—For convenience of reference the origins of the various tissues and organs are arranged in the list tabulated on the next page.

The germ layers are not so absolutely specific in their potentialities as was once thought. For example, some skeletal elements and smooth muscle fibers come regularly from ectoderm; moreover, mesoderm can be made experimentally to produce either ectodermal or entodermal structures. Hence the germ layers possess more potentialities than they ordinarily show. In normal development these layers serve as sorting grounds through which the constituent parts of the embryo pass in a quite definite and rigid program of distribution. Yet it is important to understand that, when forced to do so, an embryo can modify or alter its method of distribution.

THE GERM-LAYER ORIGIN OF HUMAN ORGANS

Ectoderm	Mesoderm	Entoderm
1. Epidermis, including: Sweat glands. Sebaceous glands. Mammary glands. Hair; nails; lens. 2. Epithelium of: Retina; conjunctiva. Lacrimal gland and duct. External ear. Internal ear. Nasal cavity. Paranasal sinuses. Mouth, including: Enamel organs Taste buds. Oral glands. Hypophysis. Anus. Male urethra (distad). Amnion; chorion. 3. Nervous tissue, including: Neuroglia. Chromaffin tissue. 4. Smooth muscle of: Iris; sweat glands.	1. Smooth, cardiac and skeletal muscle. 2. Connective tissues; cartilage; bone. 3. Notochord. 4. Blood; bone marrow. 5. Lymphoid organs. 6. Suprarenal cortex. Epithelium of: 7. Pleura; pericardium; peritoneum. 8. Kidney; ureter· trigone of bladder? 9. Testis; epididymis; ductus deferens; seminal vesicle. 10. Ovary; uterine tube; uterus; vagina (part ?). 11. Blood vessels; lymphatics. 12. Joint cavities; bursæ; tendon sheaths. 13. Cavities of eye and cochlea.	Epithelium of: 1. Pharynx, including: Auditory tube. Tympanic cavity. Thyroid; tonsils. Thymus; parathyroids. 2. Respiratory tract (except nose). Larynx; trachea; lung. 3. Digestive tube, including: Intrinsic glands. Liver. Gall bladder; bile duct. Pancreas. Yolk sac; allantois. 4. Bladder (trigone?) 5. Vagina (all ?); vestibule. 6. Female urethra. Vestibular glands. 7. Male urethra (except distad). Prostate gland. Bulbo-urethral glands.

Histogenesis.—All of the cells of any particular germ layer are at first alike in structure, but they soon differentiate into specialized tissues, such as epithelium, connective tissue, muscle and nerve. Thus the bud that represents the primordial arm is composed originally of a single-layered sac of equivalent ectodermal cells, enclosing a central mass of diffuse mesenchyme. Gradually the ectodermal cells multiply, change their form and structure and give rise to the layers of the epidermis. By more profound structural changes the mesenchymal cells, as well, transform into the elements of connective tissue, cartilage, bone and muscle. Such aggregations of modified cells are termed *tissues*, while their differentiation from the unspecialized cells of the germ layers constitutes the process of *histogenesis*.

During histogenesis the structure and form of each tissue cell become adapted to the performance of some special function or functions. Cells that have once assumed the characteristics of a given tissue do not give rise to cells of any other type. In tissues like the epidermis certain basal cells retain their primitive embryonic characters throughout life, and by