INTRODUCTION TO GENERAL EMBRYOLOGY

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PREFACE

THIS book grew out of the material collected for thirteen broadcast talks on aspects on modern embryology delivered by the author in the spring of 1951 at the request of the *Université Radiophonique* of Paris.

For the French edition of 1952 the scripts were rearranged, filled out, and illustrated. The illustrations—diagrammatic only where the originals would have been too hard to grasp—were chosen to give an insight into various aspects of current research, and the legends were made full enough to be a source of information in themselves.

It was felt that this method of setting out the aims, methods, and principal discoveries of embryology might interest an English-speaking audience, and at the suggestion of Dr. David Newth a translation was undertaken by Mrs. Jean Medawar.

For this English edition the first nine chapters have been brought up to date; the remainder have been rewritten; and a new chapter devoted specially to mammals has been added. There are about twenty new illustrations, chosen and annotated in the same spirit as the originals.

This book is essentially selective and panoramic. From the great body of earlier material we have selected only those conclusions which have a bearing on modern research; and only the more important currents of modern research are mentioned, more weight being given to the dialectical working out of theories than to the facts themselves. The preface to the French edition referred to the need for paying rather detailed attention to certain recent concepts that were still in course of formulation. That is still true, particularly of the later chapters, which are deeply occupied with the practice and problems of present-day research, and which include certain perhaps original reflections of a constructive nature. I hope that some of my readers may be tempted to discuss some of these new ideas and even put them to the test of experiment.

Towards the end of his long and distinguished career, E. G. Conklin wrote: 'If we are ever to comprehend the nature of life, we must employ synthesis as well as analysis, for life is not to be found in individual atoms or molecules, or genes or chromosomes, but in the synthesis and organization of all of these' (*Ann. N.Y. Acad. Sci.*, 1951, p. 1282). This quotation exactly describes the spirit in which this little work has been written.

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I

WHY SHOULD ONE STUDY EMBRYOLOGY?

EACH one of us, according to his personal inclinations, has many reasons for taking an interest in embryonic development. The interest may have a purely practical basis, for all livestock breeding is founded on reproduction. The livestock breeder need often do no more than allow nature to take its course; however, artificial fertilization is used in fisheries, in order to protect the spawn, and distribute it at will, and this technique presupposes some knowledge of fertilization, and particularly of the sperm's length of life after its release. Again, the part played by artificial insemination in stock-breeding is well known: it needs a wide knowledge of sexual physiology to make the most of a good sire, or of a good breeder which can only bear a limited number of young in her lifetime. Studies have been made on the removal of recently fertilized ova from such specially endowed females, and their transplantation into the genital tracts of ordinary females, who thus function as nurses in the completest possible sense. These delicate operations require a thorough knowledge of the laws of heredity and development. Alternatively, this knowledge may be used for exactly the opposite purpose, to limit the spread of a harmful species, e.g. a parasite or its vector, for which purpose a study of the life-history is often necessary.

This brings us to the obvious medical interest of embryology. A knowledge of the stages of normal human development is indispensable for the proper understanding of the physiology of pregnancy and its pathological aberrations; for the treatment of sterility; in providing the most favourable conditions for the development of the embryo, and avoiding circumstances that may affect it adversely. It is necessary in order to be able to interpret and eventually to correct abnormalities, and to foresee, and if possible avoid, the production of imperfect offspring. The medical import of embryology does not end there. There are other, profounder reasons which concern the foundations of all scientific medicine. Anatomy is more readily learned and memorized if one can visualize how the tissues and organs have been formed. Even if one studies organogenesis in a rather superficial way, it can still clarify the complicated arrangement of the tissues, allowing one to distinguish the variant from the normal, and to interpret the variation. The histology—i.e. the microscopical anatomy—of almost every structure, whether the adrenal gland, blood, or nervous system, is equally illumined by a knowledge of development. Nor is it only anatomy among the fundamental sciences that benefits from a knowledge of embryological beginnings: the physiology of the heart should always take into account the way in which it has been formed, and its structure at the moment it begins to beat. The biochemist who studies the activity of adrenalin or insulin should not lose sight of the origin of the cells which manufacture them. Many similar examples could be drawn from realms as far apart as clinical medicine, pathological anatomy, immunology, and even surgery.

Embryology has done medical science still another service in the formulation of many ideas upon which are founded our conception of living matter, and particularly of cell structure. This is not to claim that the cell theory emerged from the study of development, nor the distinction between cytoplasm and nucleus, nor even the discovery of karyokinesis—that extraordinary ceremony which regulates the majority of cellular divisions; but once these landmarks had been passed, the reproductive cells proved such excellent experimental material that the fundamental laws could be rapidly deduced from the mass of information they provided. It was by following the divisions of the sperm mother cells that Flemming worked out his classical analysis of the phases of mitosis (see Fig. 35). It was while examining the eggs of the internal parasite *Ascaris* that Edouard Van Beneden discovered, about 1880, that the formation of reproductive cells or gametes necessarily entails a special behaviour of the chromosomes, known as reduction division. It was by cytological studies on spermatogenesis and oogenesis, the very earliest stages of development, that Van Beneden, Rabl, and Boveri recognized that, although alternately visible and invisible, the chromosomes were permanent entities in the nucleus. It has been through researches of this type that we have gradually built up our knowledge of chromosome structure, and of some of the complex relationships between nucleus and cytoplasm.

These very general reasons for taking an interest in the study of development extend beyond medicine into the domain of biological science. It is, then, as living beings, seeking a better understanding of ourselves, that we should approach the facts of development and their meaning; for it is of the nature of life—a never-to-be-forgotten truism—that all living beings are perishable.

The definition of life, usually regarded as a dangerous undertaking, is not, in my opinion, such a very risky affair. It emerges[1] from our recognition of the existence of three categories of activity in one and the same system: assimilation, autonomy, and reproduction. For without the capacity to assimilate to itself substances external to it, and the power to refashion them into its own molecular fabric, a living system must progressively lose its individuality; unless it can command a certain autonomy it cannot make good its normal wear and tear. These two requisites alone involve such delicate and complicated arrangements that their permanence is inconceivable. Sooner or later reproduction must supervene, an event which must distribute newly formed elements which will be exempt from the dissolution that inevitably awaits their parents. It must reconstruct the system with its properties of assimilation and autonomy intact, without failing to provide for the formation of gametes which can inaugurate the next cycle. In fact, the reproductive elements, whether they are eggs or sperms, as in the majority of cases, or units of asexual reproduction, may be said to epitomize the vital functions. From the moment we feel an interest in this reproductive process, we are drawn into an investigation of the whole course of development. It ensures that a series of mortal individuals is marshalled into a lineage which is enduring in the sense that every living species may be traced finally back to the beginnings of life. The fact that so many lines can be distinguished is because their respective descendants copy so faithfully the pattern of features which were

[1] This description does not exclude the biochemical and enzymatic aspects of vital activity, which Bertalanffy has discussed.

characteristic of their forbears. There is thus a close bond uniting the study of development with the science of heredity. During the course of the present century this science came to be christened genetics, and acquired a true autonomy, with its own particular problems and techniques. It is none the less an offshoot and an extension of embryology and, so regarded, it ranks as a genuinely explanatory science. At the present time, embryology reserves the right to consider as its own the whole field of general inheritance, and the analysis of those factors which cause the offspring to reproduce the general characteristics of their stock.

Again, the moment we reflect upon the fundamental manifestations of life we are struck by the prodigious variety of different creatures, and we are faced by the problem of evolution. It is not difficult to formulate the problem clearly, in the light of the principle that has just helped us, of that trio of properties so evidently inseparable from any vital activity. If the essence of reproduction is to copy the type exactly, to improve it should be even better. That is what evolution does, mainly through sexual reproduction, which provides a series of situations highly favourable to the production of heritable variations. The gametes are the agents which ensure both the continuity and the progress of the line, at the cost of innumerable set-backs, but still with astonishing success. It would be too much to say that the study of development alone can give us an understanding of evolution, but it has proved a source of enlightenment in the past, and will certainly continue to be so in the future.

Its influence on medicine and livestock breeding, its discovery and constant enlargement of ideas fundamentally important to our understanding of the basic structure of cells and organisms, its explanation of general inheritance, the interpretation of evolution—these are reasons enough to justify the study of development. There is a last reason, even more important than the others, but possibly even too ambitious. If we are in any degree able to apply our intelligence to the examination of our own origins, that is because the germ or fertilized egg from which each one of us stems has, in a sense, known how to construct the superb instrument which we make use of in doing so. A well-furnished mind certainly owes much to teaching, to example, and to society, but the essentials—the ability to perceive, remember, discriminate, compare, and judge—are all inborn. Every year tens of thousands of human minds, by virtue of their own ontogeny, inherit all the immense possibilities of intellectual development. Every day millions of nervous systems, in all ranks of the animal kingdom, become capable of activities which, whether instinctive, reflex, or conscious, are at any rate co-ordinated efficiently and adapted generally to the control of a certain living space. What is the meaning of this perpetual unfolding of psychical activity, at all its levels? That it is largely a consequence of development, with all its overtones of heredity and evolution, cannot be doubted. But what is the meaning of this relationship? To what extent does it explain the psyche and the deeper laws of development? That such a disturbing question can be asked shows that the origin of life has a significance which enters deeply into the province of philosophy.

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II

A SHORT HISTORY OF EMBRYOLOGY

In spite of their interest, we cannot here touch on the earliest attempts, made in classical antiquity and since the Renaissance, to study and interpret embryonic life. Until the middle of the eighteenth century these interpretations were extremely confused, partly because in many familiar animals reproduction was obviously brought about by eggs, whereas in mammals the foetus developed internally, so that its origins could only be guessed at. Again, because of the lack of optical equipment, or the misuse of that which was available, the function of the semen or sperm was ignored. For the same reason, the spherical bodies discovered in the ovaries by the Dutchman Regnier de Graef, in 1672, were thought to be the real ova, whereas in reality they were merely the receptacles of the ova, which are themselves of microscopical size. It is rather touching, today, to read in these old anatomical works the careful discussion of the case for or against the participation of these 'ovarian vesicles' in the formation of the human embryo, and to find the right conclusion reached, though on purely logical grounds and without any evidence from direct observation. Indeed, in those days, when there were so many avenues to explore, the study of development could not monopolize the attention of the great naturalists. Professor Guyénot's magnificent work on the *Sciences of Life in the 17th and 18th Centuries* gives some idea of the variety of their researches.

From these early and often confused beginnings, however, a formulation of the problems of development begins to emerge, though at first hampered by the dilemma of epigenesis or preformation. Following Malpighi, the preformationists believed that everything necessary to the future organism was contained in miniature within the germ, and required only to be unfolded. For epigenesists such as William Harvey everything arose gradually as development proceeded. The problem became more complicated when Leeuwenhoek in 1677 discovered the existence of 'sperm animalcules'. There then arose 'ovists' and 'animalculists', particularly in the preformationist camp; but most of them were, by modern standards, mere visionaries. In practice one belief or the other was upheld as much from prejudice still coloured by scholasticism as upon the grounds of direct observation. They were often biased and unconvincing, or even full of gross errors. The solution of the problem needed above all a technique, a method of analysis, and a material that lent itself to close examination. These conditions were fulfilled in the middle of the eighteenth century by G. F. Wolff, working on the egg of the domestic fowl. His drawings, published from 1759 onwards, still appear strikingly correct to us today. After observing the dramatic changes which in the course of two or three days transform the germinal disc of the new-laid egg into a well-defined embryo, the German naturalist declared for epigenesis. Wolff was, incidentally, one of the first investigators to pay particular attention to the development of the organs themselves, in the process which we nowadays call morphogenesis. So too did the Swiss naturalist Albrecht von Haller, but although he was the author of some admirable observations, he remained faithful to the ideas of preformation.

Such differences of opinion between the views of distinguished contemporaries need not astonish us unduly, for divergences of the same sort have continued up to the present day. It took long to realize that the ideas of preformation and epigenesis were not mutually exclusive but *complementary*. In order to analyse a particular phenomenon in ontogeny we must always decide to what degree it has been foreshadowed in an earlier structure of the system under investigation, or, conversely, to what extent it may be a modification attributable to the influence of factors external to that system. The theoretical legacy for which we are indebted to the embryologists of the seventeenth and eighteenth centuries is to think of embryological events from alternative angles, in terms of *both* preformation and epigenesis.

In the course of the nineteenth century three fairly well-defined trends emerge from an ever-growing body of research; though intimately connected, each is dominated by the influence of a strong personality. They are the result of a general quickening of scientific thought, even more of the great improvement of optical and chemical techniques, but above all of the bracing wind of evolutionary thought, which animated all the sciences devoted to the study of life.

In the first phase there was little more than a continued pursuit of the lines of investigation already opened by the earlier embryologists, particularly by Wolff and Haller. This thankless task found many devotees. One figure, however, dominates the scene by his single-minded devotion, the importance of his discoveries, and the compass of his work—Karl Ernst von Baer, Professor at Königsberg and St. Petersburg, who has often been called the father of modern embryology. It is to him that we owe the discovery of the true mammalian egg and the descriptive analysis of the membranes which make up the embryonic annexa in higher vertebrates or amniotes.

From the middle of the nineteenth century onwards embryology received a great impetus from the success of Darwinism. It became of great importance to understand the development of the most diverse groups, in order to disentangle their ancestry and relationships. Ernst Haeckel, the Jena zoologist, maintained this momentum by giving emphasis to the law of recapitulation in development, which the Frenchman Serres had first formulated in 1842. The skill with which Haeckel propagated new ideas—the monistic doctrine which he propounded and ardently defended, his bold theory that the Metazoa took origin from a hypothetical ancestor called the *gastraea*—certainly did much to strengthen and enrich descriptive embryology.

On the other hand, a contribution no less decisive in this advance was the improvement of the technique of section cutting, which is essential for studying the internal anatomy of embryos. The invention of paraffin embedding, the use of precise microtomes, and the invention of staining techniques opened an almost endless field of research.

However, the 'historical' interpretation of development, as a legacy from more or less remote or even doubtful ancestors, was not enough for the more daring spirits. Some pioneers had the originality, which may seem commonplace enough today, to envisage development as a series of present, tangible episodes, susceptible to causal analysis. They tried simple experiments, and achieved a certain measure of success. Wilhelm Roux, a young anatomist from Halle who entered this field about 1880, was the most prominent of these pioneers. He grasped the importance of researches bearing on *Entwicklungsmechanik*, and founded a journal, still flourishing today, to publish research on 'the mechanics of development'. We shall return later to these early experiments and their significance: what concerns us now is the entry of the experimental method into embryology. In this connexion, Roux's energy was of capital importance, not only in Germany, but in every laboratory where biologists and anatomists had become aware of the need for such an approach.

Embryological research has widened and increased in complexity during the present century. It is not necessary at this point to fill in the landscape, for the chapters which follow will call attention to outstanding workers and their contributions. We shall now only touch on their principal interests, the places where they were able to carry out their work, and the directions which their work took.

At the end of the last century centres of research sprang up in most of the university towns of Europe and America, and to a lesser extent over the rest of the world. Departments of embryology arose in zoological, anatomical, and histological laboratories, and sometimes also in veterinary schools. Each of these disciplines has plenty of reason to concern itself with development, as we have already seen.

The marine biological stations of the Mediterranean, English Channel, Atlantic, and Pacific coasts also played an important part. Among the most famous are those of Naples, Banyuls, Roscoff, Plymouth, Wood's Hole, and Pacific Grove. Embryologists have found that they offer splendid opportunities for studying marine species, and these stations have contributed much to the development of our science. For practical reasons it is exceptional for a university to devote a chair exclusively to embryology, but at least two institutes are devoted to it: at Baltimore, supported by the Carnegie Institute, and at Utrecht, the international Institute of Embryology which was founded with the help of a legacy from the famous embryologist Hubrecht.

From the beginning of the present century, research separated almost everywhere into the purely descriptive and into attempts at experimentation. The experiments were mostly of a mechanical or surgical kind, taking the form of delicate operations on eggs and embryos; sometimes they were of a chemical nature in that they involved modifications of the environment. In 1913 E. Fauré-Frémiet, by his memorable work on the egg of *Ascaris*, undertook the task of analysing the chemical composition of the egg, and of following, and so far as possible explaining, its subsequent modifications. Thus chemical embryology was born, and it has rightly enjoyed an increasing popularity. At about the same time, the American embryologist and cytologist T. H. Morgan began the experimental study of the role of the chromosomes in heredity, and so founded the science of genetics of Neo-Mendelism. After a fairly long period of almost independent expansion, genetics today is approaching closer and closer to embryology in its concern with the problems which they have in common.

In recent times, the classification of specialists has become more and more difficult; only a few are purely descriptive embryologists. They have nevertheless done admirable work—as for instance the late G. Streeter, for long the Director of the Carnegie Institute of Embryology; or in England, the late Professor J. P. Hill, who produced such remarkable studies on the early stages of various mammals. Pure experimentalists are equally rare: Hans Spemann, who won the Nobel Prize solely for his analysis of the results of delicate and complicated operations on embryos, was exceptional. So also is Professor R. G. Harrison, still actively engaged in research of world-wide repute. Most of the leading embryologists have recourse to simple observation, to surgical, chemical, or physical techniques and to genetical methods, according to the nature of the problem under investigation.

It is at the price of these concerted and continued efforts that our knowledge has gradually accumulated, following a rhythm which has varied with each problem. Spectacular discoveries are rare, and each important advance has its forerunners. The solution of difficult problems is approached by successive leaps, often separated by an interval of ten to twenty years which serves both for the overhauling of techniques, and for the recruitment of investigators better equipped for a task which becomes ever harder. In this way, slowly but surely, is being built the great anonymous endeavour which will one day become the theory of embryonic development.

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III

MODERN METHODS IN EMBRYOLOGY

It has become exceptional for an embryologist to be obliged to study one particular species rather than another. Such a thing only happens when it has become necessary to fill a gap in the literature or to prove some particular point. Generally speaking, research is inspired by the need to solve a special problem, and the material is chosen for its peculiar fitness for that purpose.

Nor are eggs necessarily the only subject of investigation. The elucidation of morphogenesis, the development of organs *de novo*, is our chief goal. Morphogenesis does not start only from the fertilized egg (or, where parthenogenesis is concerned, from the unfertilized egg): it is also to be seen in the asexual reproduction effected by various types of buds or spores; it is equally revealed in regeneration, where it begins from the cell mass or blastema which can be seen in sections through a cut surface of a whole organism such as a polyp or worm, or through the stump left after the removal of a limb or antenna in arthropods, or, again, through the base of an amputated limb or tail in amphibians.

Although they are of a specialized kind, these types of morphogenesis are important from several points of view, and sometimes clarify ideas which would otherwise be difficult to grasp.[1] No specialized technique is needed in studying them. It is enough to provide the conditions appropriate for the chosen material—to breed freshwater hydras or sponges for the study of asexual reproduction; to visit a marine laboratory to study the budding of tunicates or Polyzoa; or to carry out the necessary amputations on arthropods or on the amphibians that are capable of regeneration. The rest of the work proceeds as in other embryological studies.

[1] This is particularly true of the concepts of differential susceptibility, dominance, and physiological gradients introduced by C. M. Child, and of S. Spiegelman's (1945) concept of physiological competition.