

The pathology of ante-natal life : an address delivered before the Glasgow Obstetrical and Gynaecological Society / by J. W. Ballantyne.

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THE PATHOLOGY OF ANTE-NATAL LIFE:

An Address

*DELIVERED BEFORE THE GLASGOW OBSTETRICAL
AND GYNÆCOLOGICAL SOCIETY.*

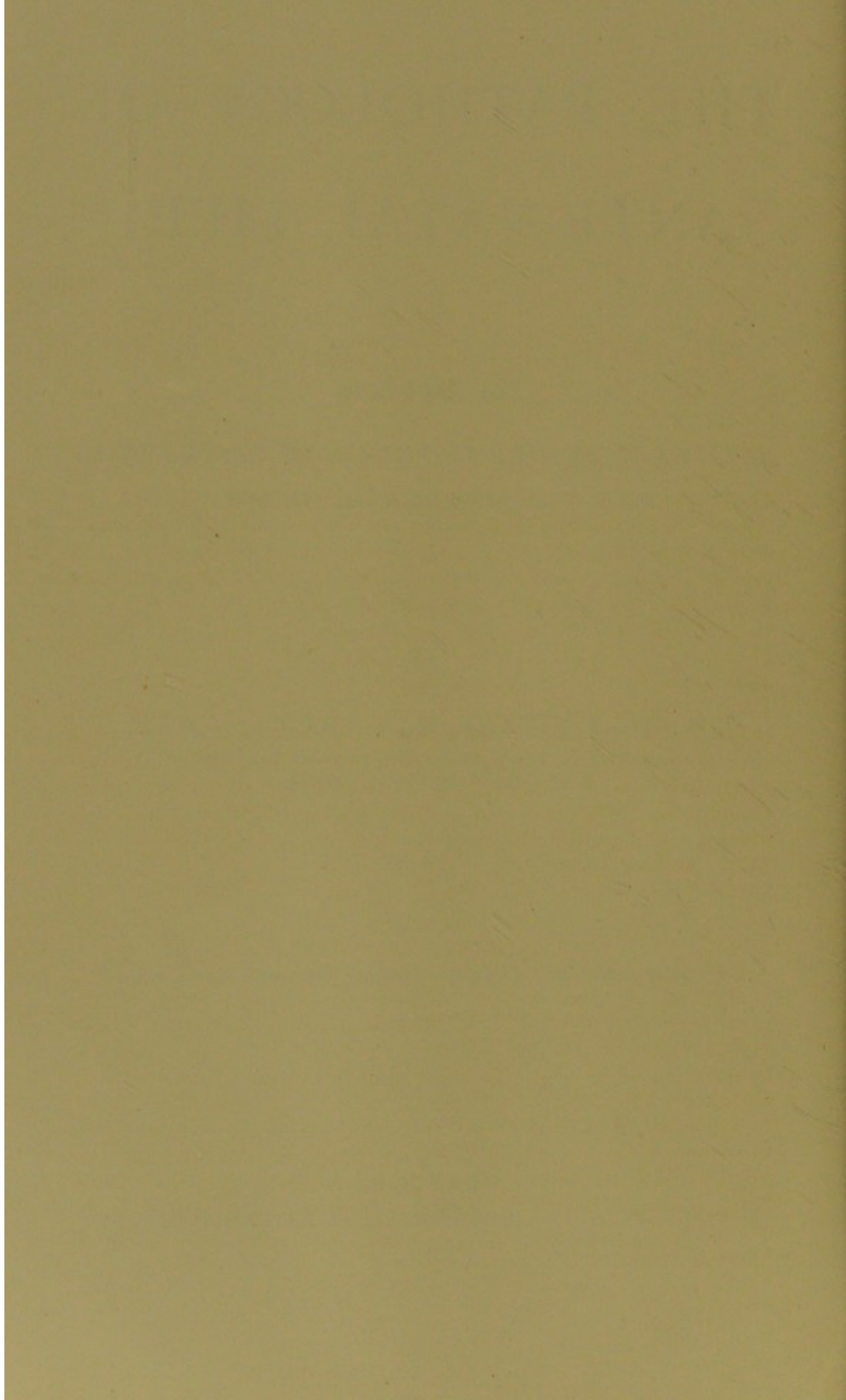
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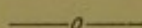
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THE PATHOLOGY OF ANTE-NATAL LIFE.¹



GENTLEMEN,—It is an inadequate and inaccurate view of the life of the individual which regards it as beginning with birth and ending at death. Theology teaches us that death does not end all; and no obstetrician can be in doubt that birth does not begin all. Birth does not mark a beginning, but a stage in life's progress. Birth is in one sense a beginning, it is the beginning of post-natal life; but the very words used imply that there has been an ante-natal life. Further, the post-natal is not independent of the ante-natal; on the contrary, it is largely the direct continuation and outcome of it. The life is unchanged, but the environment has been altered; birth marks the change from surroundings which are intra-uterine to those that are extra-uterine. The transition is abrupt and the surroundings are very unlike, nevertheless the life is continuous.

THE PERIODS OF LIFE—POST-NATAL.

By popular custom and with the consent of science, extra-uterine or post-natal life has been divided into periods. There is the period of old age with its terminus, death; there is the time of middle or adult life; there is youth; and there is childhood or infancy. Even in a strictly scientific sense, however, death is not really the terminus of life, for in many cases before that event has occurred the individual has thrown off a vital cell which impregnating another unit of life or being impregnated by it has carried on the existence of both.

¹ An address delivered before the Glasgow Obstetrical and Gynaecological Society, 23rd February, 1898.

Each individual organism consists then of a perishable part, which in point of size bulks largely, and of an imperishable part, microscopic in size but intensely vital in property. The imperishable part modern science has called the germ-plasm, and its imperishability is denominated its continuity. The same idea, however, was present in the mind of an exact thinker and a judicial writer of the old time when he said, speaking of Levi, that he was yet in the loins of his father (great-grandfather) Abraham when Melchisedec met him. Adult life is the epoch most largely concerned in reproduction; in infancy and childhood the most noteworthy incident is steady and continuous growth of the body; while in youth it is more especially the growth of one set of organs, the genital, that is conspicuous. At the same time while post-natal life may be divided into these periods, they must not be regarded as well defined or as absolutely distinct from each other. There are normal limits within which adult life may be prolonged or childhood shortened, and in a certain sense one part of the individual may be in one period and another part in another. Without crossing over the boundary into pathology it may be quite legitimate to describe a man as having the brain of a youth or of a child.

Extra-uterine is linked to intra-uterine life by the short period known as that of the new-born infant. Nevertheless, although it only lasts for about a month, most important physiological changes are going on in it. It is a time of metamorphosis: organs which during intra-uterine life have had little or no call put upon them are suddenly brought into functional activity, while many of those which have been physiologically active in foetal life begin to atrophy from disuse. The organism is adapting itself to its new environment.

ANTE-NATAL LIFE—PHYSIOLOGY.

Like post-natal life the ante-natal existence of the individual may be marked off into periods. These are the foetal, the embryonic, and the germinal epochs. During the first of these, the foetal period, the organism shows its vitality chiefly by growth along lines which have been already definitely laid down. In this respect it resembles the post-natal periods of infancy and youth. It is true that the intra-uterine environment has very distinctive and peculiar characters (the unborn infant exists in a fluid medium of practically constant temperature, it is protected to a large extent from traumatism

by the maternal structures, and it is shut in from the light); further, the foetus has several of its organs almost inactive and its most important and most active organ, the placenta, is extra-corporeal; nevertheless, the chief phenomenon of foetal life is growth, rapid and continuous, along lines already indicated. Within seven months, which is the length, roughly speaking, of foetal life in the human subject, the organism increases from a structure one inch in length to one measuring twenty inches, and its increase in weight is proportional.

During embryonic life, which may be regarded as beginning with the differentiation of the three layers of the blastoderm and ending about the end of the second month, a very different process is going on. There is growth as in the foetal period; it is not, however, simple increase but evolution or development that is the striking feature of the life of the embryo. The lines along which future growth is to take place are nearly all laid down in the embryonic period. The physiology of the embryo is development, that of the foetus is growth. As in the history of the rise of a great modern city there is record of a stage in which the main avenues of traffic are sketched out and natural obstacles overcome or utilised, to be followed by a period during which growth goes on along the lines of the plan, so in the story of ante-natal life there is the embryonic period, in which the cellular elements are arranged in groups to form organs, to be followed by the foetal, in which these organs simply increase in size, and by their activity lead to the growth of the whole organism.

About germinal life in the human subject we know little, but it may be regarded as the period which ends in the mysterious phenomena of germ and sperm maturation, of the expulsion of the polar globules from the ovum, and of the atrophy of the female element of the sperm-cell, and of the impregnation of the ovum by the spermatozoon, with the resulting formation of the morula mass. Prior to impregnation the ova and spermatozoa have simply led the life of specialised cells in the body, the former in the female, the latter in the male. Doubtless they have been impressed to a certain extent with the individuality of the organism, with what may be called the peculiarities of its vitality. Further, these cells are the descendants of others which have in their turn been component parts of other organisms which have also had their individuality. So in the earliest epoch of ante-natal life, just as in the later epoch of post-natal existence, we find ourselves confronted by the continuity of vital action; the individual is the link which enables the vitality to be continuous.

Before passing to the consideration of pathology in these relations, I must point out that whilst ante-natal life is thus divisible into three periods, these are not sharply marked off from one another any more than are the epochs of post-natal life. One part of the organism may be yet in the embryonic stage while the others are in the foetal phase. An example of this is met with in the slower evolution of the limbs as compared with the trunk of the body and head, and probably no two parts pass out of the embryonic into the foetal condition at just the same time. To revert to the comparison I have already instituted, the progress of a city is not equal throughout, one part, *e.g.*, the suburbs, may be little more than planned when another, *e.g.*, the centre, is already built. Just as the first month of extra-uterine life, more than any other, is a time of metamorphosis and of transition, so the third month of intra-uterine life, more than any other, is characterised by readjustment and by change. Most of the organs pass at this time from the embryonic into the foetal state, just as in the first month of life most of them again pass from the foetal into the infantile condition. The bearing which this form of transition from one period to another has upon pathology will be soon made apparent.

Such, then, is a sketch of the periods into which ante-natal life may be divided—the foetal, the embryonic, and the germinal; but, so far, I have made reference only to the physiology of these epochs and not at all to their pathology. I have considered only the normal at first in order to simplify, as far as possible, the whole problem. Now, in the light of what has been already stated, we may with more profit discuss the incidence of the morbid. We shall find that the pathology of ante-natal life is closely bound up with its physiology.

ANTE-NATAL PATHOLOGY.

Post-natal and ante-natal life have this, at least, in common, that they are both subject to disease and death. As a French writer (Vernet) has expressed it, "*L'œuf fécondé jouit de la vie, sujet par conséquent aux maladies, à la mort;*" and I may roughly cast the same idea into verse as follows:—

The egg, impregnated, with vital ardour glows,
Subject thereby to maladies and death's destructive throes.

In the very springs of life there is the possibility of death; the ante-natal death-rate must be very high, and, I doubt not,

that all estimates which have been formed of it fall below the reality. Short of actual death, however, there is pathological change, and there is a morbid anatomy of intra-uterine life which has not up to the present time received the attention that it demands in view of the far-reaching effects it has on post-natal life. The pathology of ante-natal life is a subject which has been comparatively little studied; and the cause of this neglect has been not single but complex. The inherent difficulty of the research, the practical impossibility of exact diagnosis, the discouraging results of attempts at ante-natal therapeutics, the delayed progress of the study of ante-natal physiology, and the conflicting views regarding human embryology, have all played a part in discouraging investigations; but probably the most potent factor in delay has been the simple circumstance that the subject dealt with *ante-natal* affairs. The difficulties were not insurmountable; but investigators have been held back by the wide-spread belief that (so to say) the game was not worth the candle. The mercantile value, if I may so put it, of foetal life has been placed very low compared with that of the adult or of the child. In no country in the world save that in which the population is stationary or diminishing does the necessity of conserving and preserving foetal life obtrude itself upon the notice of the political economist or of the physician. The specialist in ante-natal disease, even in these days of specialism, is not wanted. Beyond all these reasons which have led the student to neglect the pathology of ante-natal life, I believe there lies yet another. There is, I think, a very prevalent notion that ante-natal pathology is not subject to the same laws as post-natal, that it cannot be regarded as similar to it—that it is, in fact, something apart, something mysterious. What I wish to try to show in this address is that in all probability *the causes of morbid processes are the same in post-natal and in ante-natal life*. That the effects produced by these causes differ markedly there is no gainsaying; but the differences are to be regarded as due to altered environmental conditions and to the peculiarities in the structure of the organism acted upon.

I do not suppose that anyone doubts that the same etiological factors in pathology are present in all the periods into which extra-uterine or post-natal life has been divided. The young, the aged, and the middle-aged are alike subject to the influence of injuries, of poisons, of microbes, and of parasites. It is true that at certain ages the individual is more liable to certain forms of disease and more or less free from others. It

is also to a small extent true that some diseases show certain slight differences in their manifestations according to the age of the person attacked by them—an example of this is found by contrasting the rheumatism of middle life with that of childhood—but manifestly these differences are not due to variations in the nature of the causes acting, but to alterations in the structure of the parts acted upon and in the environmental conditions. Peculiarities of this kind are specially evident in the diseases of the new-born infant, some of which have almost a pathology of their own, and it is precisely during this short period in extra-uterine life that the organisation of the body differs most from what it afterwards becomes. Such maladies as jaundice of the new-born, sclerema neonatorum, trismus neonatorum, and Winckel's disease owe their peculiar characters not to anything unusual in the causes which produce them, but rather to the fact that the causes are acting upon organs and tissues which are in a state of transition between the foetal and the infantile stage. It is probably partly on this account also that these causes produce such fatal results, for as everyone knows the mortality in the first days of life is truly appalling. Certainly the change from an intra-uterine to an extra-uterine existence must severely try the organism.

PATHOLOGY OF FŒTAL LIFE.

During foetal life, as distinguished from embryonic, the organism is subject to diseases. Morbid causes acting upon the foetus produce diseases in it. More than ten years' study of the problems of ante-natal pathology has led me to the conclusion that the foetus is liable to the same diseases as the infant, the child, and the adult. It enjoys a partial immunity from the attacks of certain parasites which produce skin diseases in extra-uterine life, and it is to some extent protected from external violence by the maternal structures and the liquor amnii. On the other hand it is apt to be affected with certain maladies in a peculiarly aggravated form, and it is exposed to one gross traumatism, parturition. Nevertheless it is, I believe, true that the morbid causes which act upon the foetus are identical with those which are effective in later life. The peculiarities of foetal maladies are largely due to the peculiarities of foetal environment and of foetal physiology. Some illustrations of this may be given.

Foetal ichthyosis of the grave type is a disease in which the

thickening of the epidermis is of so marked a kind that it has on this account been asserted by some that it is not the same malady as the ichthyosis of extra-uterine life. The probable explanation, however, seems to be that the intra-uterine environment permits the continuance of life with a degree of cutaneous morbid change which would render post-natal existence impossible. As a matter of fact infants with advanced foetal ichthyosis rarely survive their birth by many hours—the horny epidermic plates surrounding the mouth make suckling impossible, and the interference with the cutaneous functions leads to congestion of the internal organs and especially to inflammatory states of the lungs and kidneys. Probably also the enormous epidermic proliferation may be connected in some way with the existence of that peculiarly foetal and transient structure, the epitrichium. General foetal dropsy, also, is a disease, or rather a symptom of several diseases, which reaches an altogether unprecedented degree of development *in utero*. With marked and deforming general anasarca, and with much fluid in the cavities of the peritoneum, pleura, pericardium, and cerebral ventricles, the foetus is still able to drag on in the uterus an existence which lasts till birth, even until birth at the full time. This peculiarity of foetal diseases I, some years ago, dubbed their “potential mortality.” The foetal environment and mode of life permit the existence of an amount of disease quite incompatible with the maintenance of extra-uterine life—the foetus is potentially dead, it will die as soon as it is born. Further, the fact that certain organs in the foetus are almost or quite quiescent, *e.g.*, the lungs, makes it possible for them to be seriously altered in structure without being affected in function; as soon, however, as birth occurs a sudden call is made upon these organs, and at once their potential morbidity becomes real. Truly, in many cases, it may be said that the cause of death is birth. Many other instances of this peculiarity of foetal disease might be given, such as occurs in foetal ascites, hydronephrosis and cystic kidney, and in foetal endocarditis; but these must suffice.

Foetal maladies differ not only in degree but also in character from those occurring after birth. Examples of this are found in foetal small-pox and foetal typhoid. At the time of birth the variolous eruption may show itself in the papular, pustular, or cicatricial form, according as the disease had existed a longer or a shorter time before labour supervenes. The face is frequently almost free of the eruption; the pustules resemble those met with on mucous surfaces rather

than on the skin in extra-uterine life; there is a less degree of suppuration; crusts are seldom formed; and the resulting cicatrices are feebly marked. These peculiar characters of foetal variola find their explanation in the fact that *in utero* the skin is kept moist by the liquor amnii, and is not under the influence of light and the atmospheric air. In foetal typhoid fever it is rare to find the characteristic intestinal lesions, a circumstance which may be due to the comparatively quiescent condition of the bowel in ante-natal life, or to the infection of the foetus by the way of the placenta, instead of by the mouth and stomach. In post-natal life it is uncommon to meet with cases of typhoid without intestinal lesions, although such do occur; in the ante-natal state it is rare to find cases with them. This leads me to advert for a minute or two to the relation of the placental economy to foetal diseases.

The fact that the unborn infant is brought into intimate and peculiar relations with the chemico-vital processes of the mother by means of the placenta is, at the same time, an advantage and a disadvantage. It is on account of this parasitic dependence that the foetus is able to continue an intra-uterine existence with several of its viscera in a far advanced stage of disease; but it is also on this account that it is exposed to fevers and microbic conditions affecting the mother, and to morbid alterations of her blood. We do not yet fully understand the mechanism which regulates the transmission of diseases from mother to foetus, but it would seem that under apparently similar conditions (*e.g.*, in twins) the infection may or may not pass through the placenta, and it is apparently necessary to believe that hæmorrhage in the placenta is not a *sine qua non* in the cases in which germs or their products traverse the afterbirth. Recent investigations on the structure of the amnion and on the liquor amnii suggest that possibly infection may occasionally find its way from the maternal blood through the amniotic fluid to the mouth and stomach of the foetus. *In utero* also, as in after life, the same law of individuality may hold good which brings it about that a certain percentage of organisms, placed under apparently identical conditions of risk of infection, escapes it. The placenta, therefore, is not an unmixed boon to the foetus; but, further, it may become an immediate and pressing danger. It is, in its foetal portion, an organ of the foetus although an extra-corporeal one; it is also the most vulnerable of the organs with which it is supplied. It results from this that placental lesions very quickly endanger the

life of the unborn; and everyone knows the frequency with which such are followed by the premature termination of pregnancy.

What has been said concerning the transmission of diseases through the placenta or liquor amnii to the foetus may be repeated with regard to the passage of poisons such as lead, arsenic, morphia, and alcohol. Less, however, is known regarding their action in producing foetal diseases, but this much can be affirmed that lead poisoning in the mother in pregnancy may be followed by the birth of an infant with paralytic and other symptoms of saturnism. The experiments of Porak go to show that the placenta may with certain poisons do what the liver accomplishes in later life, namely, store them up in its substance. It may thus prevent their passage to the foetus, but, in doing so, the placenta may have its own functions so far interfered with as to lead to abortion or premature labour.

During foetal life, then, the organism is subject, just as it is in later life, to the maladies which are caused by microbes and their toxins and by poisons, mineral and vegetable; it may also be affected by diseases which, in the absence of fuller knowledge, we must call idiopathic; and it may be wounded or bruised even inside the maternal protecting structures. Its pathology, therefore, agrees in its etiology with that of later life, but differs in some of its characters in accordance with the peculiarities of the environment. The foetus also may die *in utero*, and the well-known *post-mortem* changes, macerative in character rather than putrefactive, evidently owe their distinguishing characters to the intra-uterine surroundings which, in the great majority of cases, prevent the access of air to the dead tissues. It has sometimes been affirmed that death *in utero* was unaccompanied by rigor mortis; but I believe that this is not correct, and I have elsewhere¹ stated my reasons for this belief at considerable length. The rigor mortis which affects the foetus may differ in some of its features from that of the infant, *e. g.*, in the time of its onset and persistence and in its degree, but that it occurs is, I think, undoubted. In order to complete the summary of the morbid conditions which may develop in the foetal period of ante-natal life, it is necessary to state that probably every variety of neoplasm may be met with; but into this subject it is impossible here to enter, for it contains problems which would require an extended discussion.

¹ *Teratologia*, 1895, ii, p. 96.

PATHOLOGY OF EMBRYONIC LIFE.

Quite distinct from the pathology of the foetus is the pathology of the embryo. The morbid states which arise during embryonic life are so peculiar, so special, that it is no wonder that they have been placed by themselves in text-books of pathology and regarded as something apart. It is only now beginning to be recognised that the pathology of the embryo is after all a part of general pathology, and is subject to the same laws. In a word, *embryonic pathology is teratology*; and, as Duval¹ pithily puts it, teratology is truly a chapter, but also a very special chapter, of pathology ("La tératologie est donc bien un chapitre, mais un chapitre tout particulier, de la pathologie"). Let me indicate briefly what this great generalisation means.

It will be remembered that the life of the embryo consists in the evolution of the three layers of the blastoderm into the complex aggregate of organs and tissues which make up the body of the foetus. The embryo has no other functions than this—this is its one function. Now, when a morbid cause of any kind acts upon a foetal or adult organism it produces changes which interfere with its functions, *e.g.*, nutrition, respiration, excretion, and the like. In this way a disease is set up. When the same cause acts upon the embryo it interferes with its one function, the formation of organs. In this way a monstrosity, a malformation, or a structural anomaly is produced. In the one case the result is pathological, in the other it is teratological. Complete proof is not yet forthcoming, but I believe it will be furnished, showing that the causes of diseases are also the causes of monstrosities. The way in which these causes act is no doubt different, and the organism upon which they act and its surroundings are widely different; it is in this manner that the vast difference between the results, a disease and a monstrosity, is produced. We speak of pathogenesis in the one case, and of teratogenesis in the other; but the same ultimate causes, traumatism, toxines, microbes, poisons, lie behind both.

The experiments of Dareste, Panum, Warynski and Fol, Lombardini, and especially of Féré, have thrown much light upon the causes of monstrosities and their mode of action. The embryo chick is the organism in which it has been found most convenient, artificially, to produce monstrosities, although a certain number of observations has been made on

¹ M. Duval, *Boucharde's Traité de pathologie générale*, 1895, i, p. 164.

mammalian embryos. In the earlier experiments the means employed consisted in partially varnishing the eggs during incubation, in raising or lowering the normal temperature in the incubator, and in shaking the eggs or wounding their contents. By these measures it was found possible, constantly, to produce a certain percentage of chick monstrosities; but it was not very evident how the information thus obtained could be applied to the elucidation of human teratology. Far more valuable results have recently been obtained by Féré, who has experimented by injecting into the albumen of the egg at the beginning of incubation various substances known to be pathogenic when acting upon the adult or foetus. The results have been teratogenic.

Among many substances, which have been found to be teratogenic, may be mentioned the alcohols and isoalcohols, nicotine, the toxines of tubercle and diphtheria, mercury, atropine, hydrocyanic acid, and morphine. To a certain extent, also, the agents which are most pathogenic or most poisonous are also most teratogenic. The alcohols can be arranged in an ascending series according to their power of producing terata, beginning with ethylic alcohol and going on to methylic, propylic, butyric, and amylic. It may yet be found possible to group all the substances which act teratogenically in a series according to their relative virulence, and it will then be interesting to note whether those most powerful teratologically are also most effective pathologically. Certainly the alcohols which are most toxic are also most teratogenic.

While the ultimate causes of monstrosities are doubtless such agencies as have been referred to above, their mode of action presents very special and difficult problems for solution. During the embryonic period there seems to be good reason to believe that the amnion has a very important bearing upon these problems. It is the presence of the placenta which, to a large extent, impresses upon foetal pathology its peculiar characters; and in the same way it is the presence of the amnion that accounts for much that is distinctive in the pathology of the embryo. That the allantois and umbilical vesicle also play a part in producing malformations is, I believe, true; but it is specially the amnion that moulds the structural destiny of the embryo. The importance of the teratogenic rôle of the amnion has been fully demonstrated experimentally by Dareste and others. One of the earliest phenomenon in embryology is the development of the extra-embryonic somatopleure to form the amnion, and anything which interferes with

its evolution will cause disturbance in the growth of the embryo. It is probably on account of defective development of the head-and-tail folds that the terata with anencephaly, spina bifida, and sympodia are produced. The delayed separation of the amnion from the body of the embryo, as in cases of absence of the liquor amnii, will result in the action of pressure; and the effect of the pressure will be the arrest of development in the stage then reached. The rest of the organism not subject to this pressure will go on developing, and so, ultimately, an embryo will be produced with one part or several parts in a stage of evolution anterior to that reached by the rest. A temporary and transient phase has for part of the body become fixed and permanent. If one imagine a continuous photograph of the evolution changes in the organism, and if one further imagine that the changes in the head, thorax, abdomen, and limbs are represented by parallel photographic strips, then it is easy to understand that so long as the strips continue to move synchronously, as in a cinematograph, the picture of the phenomena will be normal and perfect. So soon, however, as one of the strips stops moving or slackens its rate of progress, something very abnormal, monstrous in fact, will be presented to the eye of the observer. The abdomen may be found in an early stage of evolution while the rest of the body has moved on into a later phase. In some such way exomphalos may be produced. The comparison is, at best, an imperfect one, for in teratology other factors come into play, and the continued evolution of the rest of the body will in time come partly to mask the part which has had its progress stopped, continued pressure will cause fusion of neighbouring developing parts, and so forth. An instance of this is found in the sireniform foetus in which amniotic pressure arrests the development of the tail end of the embryo and of the lower limbs, then causes rotation of the stunted limb-buds outwards and backwards, and finally leads to greater or less marked fusion into one limb of the originally separate ones.

While foetal pathology is concerned with diseases, and embryonic pathology with monstrosities, both the foetus and the embryo are subject to death. Here, again, the nature of the organism and its surroundings have much to do in determining the character of the morbid changes which result. Maceration is characteristic of foetal death; dissolution and mummification mark embryonic death. There is some reason to believe that although the foetus is dead yet its annexa may continue to live, and so there are also some grounds for supposing that the embryo may die, and the rest of the

blastodermic vesicle go on growing. Into the subject of the curious forms of abortion sac which are thus produced, Giacomini has entered, and while he has discovered many interesting facts, many questions still remain obscure. I have met with three cases, in two of which the abortion sac contained a nodular embryo of only 2 or 3 mms. in length, instead of one of 5 or 6 cms., while in the third sac the most minute examination revealed no embryo at all.

Just as the transition from foetal to infantile life is marked by a terrible mortality, so, I believe, the passage from the embryonic economy to the foetal is accompanied by a great destruction of embryos. Everyone knows how common is abortion at the second and third month; and, while several causes have been adduced to explain this, it is reasonable to suppose that the radical changes which mark the replacement of embryonic conditions by the foetal environment lead to embryonic death, and so to emptying of the uterus.

Now, while it is true that morbid causes produce diseases in the foetus and monstrosities in the embryo, it is not always possible to distinguish between what is a disease and what is a monstrosity. The reason is not difficult to find. The whole organism does not pass out of the embryonic into the foetal stage at the same time: one part or organ may be yet in the stage of construction, of evolution, when the part next to it has taken on its mature form, and has become functional. An instance of this is met with in the limb-buds, which are still embryonic when most of the internal organs are in the foetal state. A morbid cause, therefore, acting upon two parts of the organism may produce a disease in the one and a deformity in the other. This is one reason why the so-called foetal bone diseases and the malformations of the limbs are so difficult to understand. What we regard as peculiar bone diseases, and try vainly to classify with post-natal osseous lesions, may be really malformations; while more or less complete absence of the limbs or their rudimentary state may be either the results of disease or of arrested development.

It would be contrary to what we know of pathological states in post-natal life if we were to find sharply defined and clearly delimited morbid conditions in ante-natal existence. It is not with well-marked types but with the intermediate types, the connecting links, that difficulty is found in classification and in comprehension. This is true of both post- and ante-natal life. Over these difficult cases, however, I shall not linger, for what I wish in this paper to do is to lay down general principles rather than discuss individual instances.

Even in post-natal life some few parts of the body remain in an incompletely developed form for some years. A good example of this is found in the uterus, which does not take on its adult characters or begin to functionate till the period of puberty. If, as sometimes happens, the uterus retain its foetal or infantile form in adult life, the result produced is a malformation, and is usually described as such. In this sense there is, as it were, a projection of the embryonic state through the foetal into the post-natal. Cases such as the above, while they increase the apparent complexity of the problems of pathology, serve to emphasise the general principle that morbid causes acting upon embryonic states produce malformations or monstrosities, and that the same causes produce diseases when they influence fully formed organs and tissues.

PATHOLOGY OF GERMINAL LIFE.

Comparatively little is certainly known of the pathology of the germ, and what information we possess has been almost entirely gained from the study of the lower animals, and even of invertebrate organisms. The great phenomenon of germinal life is impregnation with its antecedent phenomena of maturation and polar extrusion, and its subsequent phenomena of nuclear division and the formation of the morula mass. It is, therefore, to be expected that morbid causes, acting during the germinal epoch, will manifest themselves in results determined by the physiological characters of germinal life. There will be a disturbance of the normal progress of the phenomena of impregnation and segmentation. Experiments upon such organisms as ascidians and echinodermata have shown that such morbid causes as quinine, chloral, and cold, stop karyokinesis, while partial destruction of the segmentation spheres led to the production of monstrous fractions of individuals ("monstres fractions d'individu"). These experimental investigations by Hertwig, Chabry and Roux, and others, prove that monstrosities of a very advanced type result from the action of pathological agencies (traumatic or toxic) during the segmentation of the ovum. It is difficult to draw any deductions therefrom regarding the human germ, for it is scarcely conceivable that such a rudimentary organism as the fraction of an ovum could continue to develop *in utero*; but the well-known placental parasites, which are really only portions of a foetus, are brought to the full term through the presence of a normal twin, and in them it may be legitimate to look for resemblances to the artificially produced ascidian fragments.

The phenomena of impregnation may also be interfered with, and the tendency of modern research is to regard the very interesting terata, known as double monsters, as due to such interference. What is known as polyspermy, or the entrance of more than one spermatozoon into the ovum, is now the most strongly supported theory of diplogensis. Further, it is possible that certain very rudimentary and puzzling structures, such as dermoid cysts and teratomata, may originate in absence of the normal male element in impregnation and in a consequent imperfect parthenogenetic development of the ovum.

The pathology of germinal life is, therefore, probably teratological in type, and so resembles the pathology of the embryo. At present it would be unprofitable to attempt to classify teratological productions according as they were developed in the germinal or embryonic epoch of ante-natal life. The only suggestion that may be hazarded is, that while monstrosities by defect are characteristic of embryonic pathology, monstrosities by excess (polysomatous terata) seem to be the special product of germinal pathology. Even this generalisation, however, is not very firmly based.

So far, however, as experimental teratogeny has gone it would seem that the same morbid causes (toxic, microbic, traumatic) are at work in the germinal as in the other epochs of ante-natal and post-natal life. In the meantime pathology must wait upon physiology, for we cannot expect to know much about morbid processes in the human germ till we know more of its physiology, and of that we are present wonderfully in the dark.

RECAPITULATION—ETIOLOGICAL UNITY.

So far, therefore, as our knowledge of the pathology of post-natal and ante-natal life has carried us, it would seem that the same morbid causes are in action in all the periods into which the existence of the organism has been divided. The etiological factors of post-natal pathology, such as microbes and their toxines, poisons, mineral and vegetable, and thermic and traumatic states, have been found to be also the causes of pathological developments in the foetus, embryo, and germ. It has further been shown that probably the most effective morbid agencies in post-natal life are also the most active before birth. The results of the action of these factors differ widely, but the differences can be explained by differ-

ences in environment and in the structure of the organisms acted upon. Teratology is thus brought into line with pathology, of which it is simply an obscure but not unimportant department; and teratogenesis is seen to be simply pathogenesis acting on an immature organism. There is a unity in morbid causes.

HEREDITARY TENDENCIES.

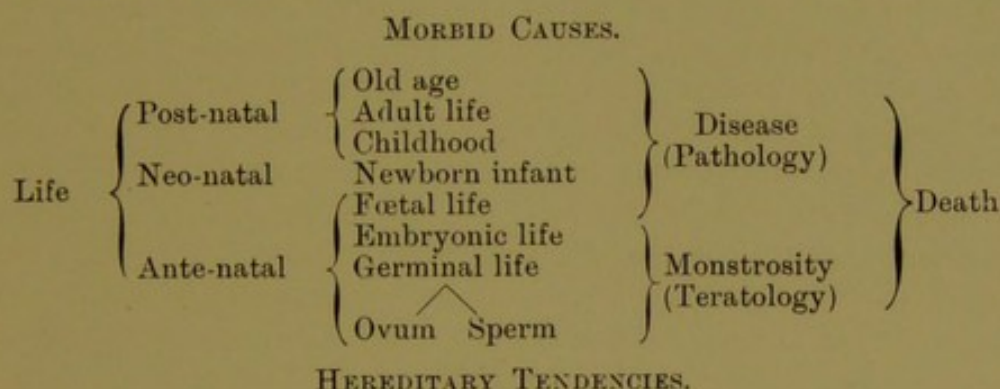
Manifestly this would be an incomplete sketch of ante-natal pathology if it contained no reference to hereditary tendencies. In addition to the external agencies, microbic and toxic, which determine disease in post-natal life, there is the predisposition to certain maladies, and the incomplete or complete immunity against others which heredity brings to the organism, and which gives to the organism its individuality. In ante-natal life, also, hereditary tendencies are evident both in the foetal and in the embryonic periods. Many foetal diseases, such as ichthyosis, general dropsy, foetal rickets, &c., are hereditary. In the nature of things it is seldom that direct heredity can be demonstrated, for, as has been explained, infants with such maladies rarely live, and therefore their progeny cannot be referred to; but that form of heredity known as family prevalence is very common in most foetal maladies. I have elsewhere¹ referred to many instances of this in congenital skin lesions, and have specially noted cases in which a woman had by one husband healthy children, and by a second spouse ichthyotic or dropsical infants. The sperm as well as the ovum may carry these tendencies.

In embryonic life, also, the same tendencies are met with, and I have recorded cases of the birth of two and even of three anencephalic foetuses in the same family. I have also met with polydactyly in several generations, and in several individuals in the same generation. One very interesting history I may give here. It was that of a woman showing a defective development of the muscles of one thumb; her first child had hydrocephalus and absence of one thumb, and her second foetus was anencephalic and had one thumb represented by a formless mass of skin-covered adipose tissue. Further, nothing is better known in the artificial production of monstrosities than the individuality of the germ, for no matter how strongly teratogenic the agency may be (*e. g.*, hydrocyanic acid), some organisms will escape its action and develop normally. I might extend and apply these observations to

¹ *Diseases and Deformities of the Foetus*, 1892-95, vols. i and ii.

germinal life, and refer to the heredity of twin-bearing, and so forth, but I must draw this already too long address to a close. Suffice it to say, that it is evident that in addition to morbid causes coming from without, we have to deal constantly with hereditary tendencies for or against pathological developments existing already in the organism. This is true of the pathology of all periods of life, ante-natal as well as post-natal; and the nett result is the health or disease, deformity or malformation, of the individual.

In a tabular form some of the chief conclusions which have emerged from this manner of regarding ante-natal pathology may now be given:—



HEREDITARY TENDENCIES.

In this communication I have refrained from touching upon any of the aspects of ante-natal pathology save those of its etiology. I have said nothing of the means of diagnosis of monstrosities and foetal disease before birth, although noteworthy advances have to be recorded in this relation; I have passed over the symptomatology and clinical history of such cases, and have referred not at all to their obstetric aspects; the prophylactic treatment of ante-natal malformations has been left unconsidered, as have also their medico-legal bearings. Nevertheless, all these aspects of the subject present problems of high interest; and with some of these I hope to deal in a series of six lectures to be delivered next session within the University of Edinburgh.

Gentlemen, I have tried to play the *rôle* of a guide, albeit a very inefficient one, in revealing to you some of the little known departments of ante-natal pathology. I have this qualification, at least, that I know some of the difficulties of the way, and some of the obstacles to be overcome. At best, I have given you but a glimpse of certain parts of the subject, and have through ignorance or imperfect acquaintance with

other parts had to keep silent; but if I have succeeded in rendering any portion more interesting or attractive, or in establishing ante-natal pathology in its rightful place, as a branch of general pathology, I shall have achieved a very large measure of the success I have hoped for. I have, in conclusion, to thank you heartily for the high honour you have paid me in inviting me to give this address.