

on the funds of the Poor-law administration and of our voluntary and municipal hospitals will amply recoup the expenditure involved.

I have necessarily in this brief sketch of my subject omitted many questions of importance. Nor can I more than allude to the importance of securing periodical returns from friendly societies and other sickness assurance societies to the medical officer of health; to the desirability of transference of the statistical work in connexion with notification from the Local Government Board to the General Register Office. Certain steps in this direction have been already taken at the suggestion of the Incorporated Society of Medical Officers of Health.

The science of medicine, including preventive medicine, makes no idle promise to extend human life beyond its natural complete term. It will—if the proper means to this end, some of them enumerated in my preceding remarks, are supplied—conduct all who live in accordance with the principles of preventive medicine in safety to the natural boundaries of their present being; it will enable them to escape the risks of early and middle life and to ensure that their

“Age is as the lusty winter,
Frosty, but kindly.”

To enable it to achieve this end not only is it necessary to improve the sanitary conditions of life in our cities from the standpoint of home, occupation, and municipal control, it is also necessary that every information capable of helping him in his work shall be given to the medical officer of health and his staff. He cannot make bricks without straw, he cannot forge his chain of preventive measures when half the links are missing. Possessed of this information and having secured the coöperation of an educated public he will be able to secure the maximum duration and the highest quality of life for every member of the community whose interests he guards.

Brighton.

EMBRYOLOGICAL ASPECTS AND ETIOLOGY OF CARCINOMA.

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AT a time when so much is being attempted in the investigation of the problem of the nature of cancer it may appear presumptuous on the part of an embryologist to express opinions and conclusions regarding this grave question. It has long been a subject of earnest research by physicians and pathologists who naturally are thoroughly familiar with actual facts and finds concerning carcinoma foreign to the embryologist. But hitherto the physician and the surgeon, the pathologist and the gynæcologist, have utterly failed to establish anything concerning the etiology of cancer, and without the intervention of the embryologist success may be as distant in the future as in the past.

As indicated by the above title, the present writing is intended to deal with aspects of carcinoma as they strike an embryologist, and not every embryologist but one particular investigator. At the outset it may be asked, “Is the etiology of carcinoma an embryological problem?” As the thing itself and its manifestations demonstrably fall within the province of the surgeon and the pathologist, for it confronts them almost daily, it is possibly not very clear why the problem of the nature of cancer should be an embryological one at all. It is a disease carrying with it death and destruction. On the other hand, the problems of the embryologist, as generally understood, treat not of disease but of the blossoming forth of life itself, of the phenomena which culminate in the appearance of new living beings. Death and decay would seem to be things of which from his researches the embryologist might be expected to obtain no practical knowledge. He is supposed to be concerned with “das Werden,” while “das Vergehen” is beyond the scope of his researches. Would that it were so! Unless he shut his eyes to plain facts “das Vergehen” in the midst of “das Werden”—death in budding life itself—is continually before him.

The conviction, impressed upon the writer's mind from 14 years devoted to the study of the mode of the development of the higher animals, the vertebrata, is that everywhere and at any point atrophy and death may be met with

in any individual life-history. Death and degeneration of cells, of organs, of organisms, of embryos themselves, are among the commonest phenomena under the eyes of the embryologist. His text-books, even his published researches, may be silent of these, for as a rule he believes himself to be solely concerned with the coming-into-being, and the opposite aspect, the decline of life, he leaves severely alone. It is not in his tacit opinion a theme of the science of embryology. This view of the problems of the science has for many years failed to commend itself to the writer and in his own researches he has endeavoured to take account of everything happening and capable of being observed during the developmental cycle, whether progressive or retrogressive.

The manifestations of life present themselves under the headings of either form and structure or function. Embryological research deals largely with form and structure or, more exactly, with the coming-about of these. And as, according to the testimony of pathologists, cancer, when it appears, is something new to the organism, a neoplasm, a foreign thing, not growing and functioning after the manner of the individual containing it, increasing by cell-division after unknown laws which appear to defy all law, carrying with it widespread destruction only comparable to that dealt out by some parasites, the phenomena of cancer would have analogies at least to many such lying within the domain of the embryologist. Cancer is something with a beginning, it increases like a developing embryonic germ by cell-division, it invades territory at first foreign to it, and it only differs from a parasitic organism in the fact that its mode of reproduction is what may be defined as asexual. And thus, because as a rule its cycle is limited to the individual harbouring it, carcinoma is something with for itself an indefinite life-cycle which is only bounded by the life of its host but which cannot be directly carried over by germs or fertilized gametes to another organism.¹ That the resemblance between the life-cycle of a cancer and that of a metazoan organism should be incomplete is natural, for the former is an abnormal product and it is in the nature of such to differ in some or other important details from the typical or normal.

The problem of the nature of cancer has long been before the writer in his investigations—in fact, ever since he learnt from the researches of Wilms² and others that it had been occasionally encountered along with those curious tumours, the dermoid cysts of ovary or testis, the “embryomas” or rudimentary embryos of Wilms. The latter speaks of this occasional connexion of the two—it has, according to Wilms, been observed some nine times—as a remarkable fact (p. 86) in that in an organism of one or two years of age the development of carcinoma can happen. As this relates to the presumed age of the embryoma and not to that of the individual harbouring the latter, the validity of the conclusion is not apparent. On his part the writer must reject it. For the past two years from time to time in researches upon the germ-cells observations have been made³ which appeared to have bearings upon the nature of carcinoma. This period may not seem a long one, but beyond it lie the investigations of other 12 years, without which the standpoint of to-day would be an impossibility. If, therefore, no study of cancers underlies the present writing, the approach of the problem is not a sudden one, but it has been preceded by prolonged observation and, moreover, animal life is the same, whether it be that of a hydroid polype upon a shell of the sea-shore or that of a cancer within an individual of the human race.

The immediate cause of the present writing was as follows. In a recent paper dealing with the understudy theory of heredity in an altogether different connexion a few comments have been written upon the mode of growth exhibited by certain organisms and a comparison drawn between this and the pernicious growth of the human chorion in certain cases.⁴

¹ It has, however, been shown by Hanau and Wehr to be possible to transplant cancer from one individual—e.g., the dog—to another.

² Max Wilms: Ueber die Dermoidcysten und Teratome, &c., Deutsches Archiv für Klinische Medizin, Band 55, 1895, p. 1-108, 3 Pl. And also Martin: Die Krankheiten der Eierstöcke, &c., Leipzig, 1899, pp. 576-614.

³ Ibid.

⁴ The passage in question is as follows: “It should be mentioned that de Vries and Weismann have already noted the resemblance in mode of growth between the sporophyte and the colonial hydrozoa. Many of the latter also possess the indefinite unrestricted power of growth so characteristic of the sporophyte of the higher plants. As a rule, the asexual generations of the higher metazoa do not exhibit this faculty. They rarely obtain a chance of showing it, for it is their usual fate to undergo early suppression by the sexual generation.

And it was not until long after the proof had been returned that it was seen how in this comparison the key to the problem of the nature of cancer had been given away. If the pernicious growth of the chorion be in reality carcinomatous, and it is recognised⁵ as such by pathologists under the names of malignant placenta, deciduoma, chorion-epithelioma, or destructive placental polyp,⁶ the cause of cancer is clear as the light of day. And it has seemed desirable to offer the present essay in order that at least a warning note might thereby be uttered and an earnest attempt made to point to the futility of investigation in the direction of a cul-de-sac, such as the probable one of cancer as due to unicellular organisms. In the following the facts concerning carcinoma, as established by pathological research, such as those given in the latest edition of Ziegler's "Pathologie," will be taken for granted. It will be assumed that at the basis there is morphologically but one form of cancer, no matter how different it may appear to be in diverse localities. A cancer of the skin is naturally different from one of the stomach or liver, for it grows and increases under other conditions. Ziegler for one adduces reasons against the supposed origin of cancer from some effects of unicellular organisms, and to his objections something more can be added. It is not in the nature of parasitic maladies to lead to cellular increase, such as is characteristic of cancer, and while the phenomena of destruction possibly present themselves prominently to the surgeon and the pathologist, those of indefinite unrestricted cellular increase and multiplication most impress the embryologist. And if the source of cancer to be brought out in the course of the following be the true one any further cause is a superfluity.

The conclusions are based chiefly, but not entirely, upon researches in elasmobranch fishes⁷ and to any but vertebrate embryologists there might appear to be no warrant for applying results obtained in animals so low down in the scale to man himself. But the broad outlines, the laws, and even most of the details of the development are the same in man as in the fishes, and the life-cycle of the former can be interpreted in terms of that of the latter. The starting-point goes back more than two years to the beginning of researches upon the germ-cells, and with these to the earlier work of Wilms upon the embryomas. The results of the work and of previous necessary inquiries dating as long ago as 1889 cannot be given at all in detail here. A general survey of the chief conclusions will be found in "Heredity and the Epicycle of the Germ-cells."⁸ The cause of cancer is really known but not recognised. Failure to perceive the true nature of carcinoma has hitherto been due to one simple fact: the views generally, nay universally, held and taught regarding the course of the cycle of development from egg to egg are erroneous.

Were an embryologist of to-day asked what in outline was the cycle of development in one of the higher forms, say a fish, chick, or mammal, he would probably be amazed at the question. "The hen lays the egg, the latter gives birth to a new hen," and so, as Kleinenberg once remarked of something else, under the eyes of the delighted and astonished spectator the cycle is completed. This supposed cycle has never really been witnessed—for the very good reason that it does not exist. The hen neither produces the egg nor is it the chief nor even the immediate task of the latter to give rise to a new hen. As the establishment of this and of the true life-cycle have filled in the working hours of the writer during more than a dozen years it may be obvious that the production of the evidences must be beyond the limits of this short paper. At the moment a pretty big book would be required to hold them all. Indeed, no attempt will be made to prove here what the true life-cycle is and wherein its details lie; the results of previous work will be assumed and for fuller information the reader may be referred to the series of memoirs whose titles are appended.

When, as happens sometimes in cases of abortion in the human subject, the embryo is got rid of prior to the critical period, or, at any rate, before the asexual generation has here been suppressed, the latter may go on growing indefinitely if left in the uterus. I refer, of course, to the unrestricted and pernicious growth of the chorion when left in the womb after an abortion." (Transactions of the Botanical Society of Edinburgh, 1902, p. 140-141.)

⁵ The carcinomatous character of the pernicious growth of the chorion was first clearly recognised by Professor Marchand in 1895.

⁶ Ziegler: Allgemeine Pathologie, vol. i., p. 483, 10. Auflage, 1901.

⁷ Also upon researches in mammalian development, especially upon the trophoblast (larva or phorozoön), allantoic placenta, critical period, and span of gestation.

⁸ Biologisches Centralblatt, 1902.

In the higher animals, the metazoa, what is termed direct development does not, and cannot, exist. It has been found that the cycle of animal development, even of the highest forms, resembles very closely that of a fern or flowering-plant. In the line from egg to egg there are two generations, an asexual form and one which, as it is the bearer of the sexual organs, is spoken of as the sexual generation. Under prevailing views of development the line of ancestry from generation to generation is exceedingly simple—too simple, indeed, to explain the facts, so simple that Nature could not adopt it in practice were she to make the trial. It may be represented thus: egg—embryo or sexual generation—egg—embryo, &c., the egg producing the embryo, the latter when mature forming from its own tissues new eggs. This is undoubtedly one of the most impossible conceptions which ever formed part of a science. The amended cycle of development and the course of heredity are as follows: egg—larva (phorozoön, or bearing animal, or asexual generation)—primitive germ-cell—primary germ-cells—secondary germ-cells—gametes, eggs, or sperms—fertilised egg. In the line of ancestry as given here—a line which apart from the larva is one of unicellular organisms—the embryo finds no place. It arises from one of the primary germ-cells whose number is always a definite one—2, 4, 8, 16, 32, &c.—and the rest enter the embryonic body to form its sexual products. A more detailed account of this cycle will be found in the memoir upon "Heredity and the Epicycle of the Germ-cells." The four important items in the cycle are: (1) the gametes, egg and sperm, by whose union a new cycle is initiated; (2) the first product of the zygote, the phorozoön, larva, or asexual generation; (3) the primary germ-cells destined for future generations; and (4)—only important to enable the completion of the cycle—the embryo or sexual generation.

Any and every primary germ-cell, if it develop or unfold as such, normally gives birth to an embryo, and, as elsewhere indicated, the embryomas of Wilms arise, and must do so, from persistent primary germ-cells. This unfolding of a primary germ-cell is equivalent to its landing in a cul-de-sac—its powers of growth and increase and its life are thereby limited. The contrast between this and the larva or phorozoön in these respects is very striking. The latter, like the corresponding generation in plants, often possesses indefinite unrestricted powers of growth in an apical fashion.⁹ In many animals there is only one apical region of growth in the larva; in the hydroid polypes there may be many such and Weismann and de Vries have already noted their powers of indefinite unrestricted growth. That which brings to a sharp and sudden close the growth of the phorozoön or larva, if there be but one growing point, is the cutting-off of this from the organism, its conversion into a primitive germ-cell, and the consequent formation of primary germ-cells from this. Normally, as already stated, the further development of a primary germ-cell results in an embryo, not in a larva.

Coming now to the primary germ-cells, upon which most of the observations of the past two years have been made, it has elsewhere been established that their number is always a member of the geometrical series: 2, 4, 8, 16, 32, &c., or 2 to the "n"th power, where "n" is one of the numerals 1, 2, 3, 4, 5, 6, &c., and that the greatest number of primary germ-cells in any embryo will be $2^n - 1$. Thus, the total number in the common dog-fish, scyllium canicula, is 128, in the male smooth skate, raja batis, 256, in the female 512, and the greatest number in the embryo of one of these 127 (in scyllium), 255 (in the male skate), and 511 (in the female skate). But for convenience and brevity, dealing with one

⁹ Of great but hitherto unrecognised importance in this direction are certain results of experimental embryology, such as those of Driesch, Morgan, and others upon echinoderms and of E. B. Wilson and others upon amphioxus, &c. (For a full account see E. B. Wilson's "The Cell," second edition, 1900, or Korschelt and Heider, "Lehrbuch der vergleichende Entwicklungsgeschichte, Allgemeiner Theil, Jena, Gustav Fischer, 1902.) Space does not permit of a description and discussion of these experiments. The general result is that in certain animals, if the cells of the early cleavage of the egg be separated, each of them will give rise to a diminutive larva, the size of this varying directly with the size of the original blastomere. These minute larvae are often but erroneously spoken of as "embryos." Though they may go on living for a considerable time no case is known in which an embryo with sexual organs arises upon such a larva, as, of course, would happen in a normal development. Allied to this latter circumstance is the fact that the invertebrate larvae obtained by embryologists by artificial fecundation never give rise to the sexual form, no matter how long they may be kept living in the laboratory. The writer has reared echinus-larvae for 15 days without the formation of a sea-urchin upon any one of them. Many other similar facts could be mentioned.

form only, say, the dog-fish (*pristiurus*), of the 127 primary germ-cells it never happens that all, or anything like all, reach the normal position, the germinal ridge, or nidus. Usually at the most from 90 to 100 of them arrive here, the remainder being found in all sorts of unusual places, where many of them degenerate.

The number of elasmobranch embryos hitherto examined is several hundreds, belonging to different species, and in all these under a certain age no single embryo has been seen in which all the germ-cells present might be described as normally placed. The percentage of vagrant germ-cells varies; it is usually from 10 to 12 per cent. in *pristiurus* and from 25 to 30 per cent. in *raja batis*. The places where these occur are numerous, in the body-cavity, upon the somatopleure, on the subintestinal vein, in kidney-tubules, in the pericardium, in the liver, in any part of the gut-epithelium, especially in the rectum, in the skin, rarely in the head or gill-region, and practically always there are some in the immediate neighbourhood of the stomach in connexion with the yolk-stalk. Undoubtedly many of these germ-cells degenerate and few, if any, of the vagrant ones, after a certain early period, ever find their way to the germinal nidus. The embryomas of Wilms are to be regarded as products of such vagrant or of persistent (in ovary or testis) primary germ-cells. But—and this is remarkable—very many such vagrant germ-cells occur in places where embryomas are never encountered; thus in the immediate neighbourhood of the stomach, in the liver, in or under the skin, and in the rectum. In nearly every embryo one or more germ-cells may be found in the yolk-stalk in the immediate neighbourhood of the pylorus and also in the rectal epithelium.

It may therefore be suspected that if the germ-cells of many of these places—e.g., liver, pylorus, rectum, &c.—ever do develop they must give rise to some product not of the nature of an embryo, not an embryoma. It is not without interest that the common situations for the origin of cancer are the very ones in which vagrant germ-cells are usually met with—thus, in the rectum, near the pylorus (yolk-stalk), other parts of the gut, in the kidneys, in the skin, &c. Apparently cancer of the tongue, of the œsophagus, of the larynx, and of the mammary gland at the first glance form exceptions, but this is not really so. Tongue, œsophagus, and larynx are products in the higher forms of a metamorphosis of the gill-region; œsophagus and mammary glands are closely associated with the pericardium, where vagrant germ-cells (and sometimes embryomas as products of these) are often found. That cancer should arise in what embryologically are holes and corners, places where layers and folds come together, as in tongue and larynx, is readily explicable. Such vagrant germ-cells are intruders in the situations originally taken up by them, and it has often been remarked how they would appear to be hustled about from pillar to post when in the way until they land in some corner or other. Normally, if the paradox be allowable, the development of such a vagrant germ-cell should result in a more or less complete twin-embryo, but any gradation of this down to a very rudimentary embryo may be found in practice. Figured in Ziegler's "Pathologie" may be seen all sorts of steps, from complete identical twins, only abnormal in being united at some one point, through those more completely united, to others forming more or less complete embryos embedded within or projecting from a normal one, down to mere cysts or absolutely rudimentary embryos. No one has ever witnessed the development of such a rudimentary embryo or embryoma, and probably it never will be seen, but the connexion between them and vagrant or persistent (in ovary or testis) primary germ-cells is not less certain than that between an onion and the seed originally planted. In the same way the hypothesis that the vagrant primary germ-cells of certain regions, thus those of the neighbourhood of the stomach and of the rectum if they develop, give rise not to an embryo, but to a larva of indefinite unrestricted powers of growth, can never be converted into a fact by direct observation. It can only be inferred from the facts. But it is a very simple explanation of all the facts and its probability is increased by other considerations.

But why should such a vagrant germ-cell, when developing into a cancer, omit or skip the formation of an embryo and proceed with a different portion of the life-cycle? One reason is, perhaps, clear. It is that the further growth of a vagrant germ-cell or of its progeny to form a cancer takes place at a much later period than that at which its embryological development into a more or less complete

embryo should have happened. (The instances of cancer with embryomas, noted by Wilms, do not form exceptions.) Moreover, it must not be forgotten that we are dealing with pathological conditions, with phenomena, which in some glaring way do not conform with the normal. Cancer is an attribute of later sexual life or of old age. For this reason one is inclined to suppose that it is not immediately due to the further development of a vagrant germ-cell itself, that this latter first of all divides many times, as it would do if in the germinal nidus, and that it ultimately forms more or less normal forerunners of gametes, oocytes, or spermato-cytes. These would be in abnormal situations and under abnormal conditions and under some stimulus they would develop as though parthenogenetically but abnormally to form a larva.

At the basis cancer is nothing more than the production abnormally of a phorozoön or larva within a sexual generation. Elsewhere analogues may be seen. In hermaphroditism we witness the conversion of the forerunners of male eggs (in what are really females) into sperms. In certain ferns abnormally upon the asexual generation or sporophyte what the botanists term "apogamy" is met with—i.e., the appearance of a new sporophyte upon the original one—the formation of a sexual generation or gametophyte and of sexual organs being skipped. It has been urged from a botanical side that comparison between apogamy in certain ferns and carcinoma in a mammal would not be justified, because the former was an abnormal condition. But we are dealing with abnormalities and not with normal occurrences of the life-cycle. If cancer be the abnormal production of a phorozoön or asexual generation by a vagrant germ-cell or its progeny, it may be asked why do not the other items of the life-cycle supervene? Why do not a primitive germ-cell, primary germ-cells, and embryo arise? Were this to happen the cycle, though commencing and being carried out under abnormal conditions, would revert to the normal, and from my experiences of abnormal development in various directions a reversion to the normal is always excluded. Were such an incipient carcinoma to form a primitive germ-cell, before the number of its apical or growing points had been increased, its portion of the cycle would thereby be brought to a close and it is in fact the omission of this which fosters and favours its indefinite unrestricted growth.

The etiology of carcinoma above suggested will be recognised as one whose nature indicates nothing favourable to its prevention or extermination. It may be said to explain completely its peculiarities and its hereditary character. But it is a despairing view. In this respect it is in only too close agreement with the experiences of physicians and surgeons. The one hopeful aspect is that in normal development at a certain period the embryo or sexual form is able in some way or other to suppress the asexual foundation upon which it arose and as a rule the victory of the former over the latter is complete.

As conceived here carcinoma would be a disease peculiar to mammals. For, as recognised by the writer some 10 years ago, in them the phorozoön or asexual generation has become parasitic in adaptation to uterine development. The possibility of carcinomatous development postulates uterine gestation at least for the normal life-span of the asexual generation—i.e., until what was termed the critical period. In fishes, such as the skate or dog-fish, neither a vagrant germ-cell nor its progeny could develop into a carcinoma, for the larval or asexual portion of the life-cycle is not passed as a parasite upon the parent (even in forms with apparent uterine development) but in sea-water; in other words, below the metatherian and eutherian mammals the phorozoön or larva is not adapted for a parasitic existence upon the parent organism and thus cannot become abnormally a parasite upon it. Carcinoma is not known below the mammals, the animal lowest in the scale in which it has been recorded being the short-headed phalanger, *belideus breviceps*.¹⁰ This disease is a sequel to uterine gestation. If the cycle of metazoan development really be that concluded by the writer, if his interpretation of the phenomena of mammalian development—which are not in the least based upon facts or factors noted in cancer but upon normal development here,—if these be correct the cause of carcinoma is not hypothetical at all but is actually known. More than one cause cannot be assumed and if one cause be shown all other explanations become superfluous. In certain cases in human development, when either no embryo arises within the chorion or

¹⁰ J. Bland-Sutton, *Evolution and Disease*, London, 1890, p. 247, Fig. 123. The case is one of cancer in the marsupial pouch.

when the embryo becomes aborted or dies prior to the suppression of the phorozoon or larva, the latter, the chorion, may go on growing indefinitely and may give rise to what pathologists and gynæcologists recognise as a form of cancer, placentoma, or chorion-epithelioma (Marchand). For years now I have recognised—and in homologising this structure with the larval skin of an amphibian Hubrecht has gone a long way in the like direction—that the human chorion represents the main portion or whole of the asexual generation or phorozoon here. In certain cases therefore we here witness the conversion of the chorion—i.e., of the asexual generation, or larva, into a malignant tumour, a carcinoma.

What other proof could be asked for? That this proof of the nature of cancer is not in agreement with accepted views of normal development cannot be set down to the fault of the writer. He holds, and has alone long maintained, such views to be false and unfounded in fact, and, moreover, it has been attempted to indicate the right way. The arguments and conclusions have been neither refuted nor confirmed, but have been ignored. But embryologists are living, and have long been existing therein, in a mental universe, where but a tithe of the facts observed are explicable under their views. Under the conception of development as an antithetic alternation of generations, especially as laid down in "Heredity and the Epicycle of the Germ-cells," all the known facts of development fit in, all are capable of easy and natural explanation. And the elucidation of the etiology of carcinoma follows as a natural corollary to the law of the developmental cycle. The embryologist and the pathologist may ignore and neglect the plain and palpable fact, but on no theory of direct development—a thing only existing for the metazoan animals in the human imagination—can any explanation whatever of the nature of carcinoma be advanced. The cause of this would long ago have been clearly recognised had some embryologist taken the trouble, as the writer has done during 14 years past, to trace out in full the details of the life-cycle of one of the higher metazoa from egg to egg. The idea of direct development, accepted within examination of the evidences, and the erroneous belief in the somatic origin of germ-cells have retarded the advance of knowledge to an extent difficult to estimate.

The nature of the argument employed in the present writing may be summarised as follows. Granted the facts of the origin, migrations, and history of the germ-cells of vertebrates, and assuming the course of the life-cycle to be that previously indicated, by hypothesis cancer is derived from vagrant primary germ-cells, which, instead of forming a more or less complete embryo or embryoma, skip this and give rise to a larva or phorozoon of indefinite unrestricted powers of growth. This is, of course, purely hypothetical, but it becomes the true explanation by the following facts. On the one hand, as my researches have shown, the hypothetical "verirrte Keime" or "lost germs" of pathologists not only exist but they are numerously represented and by things capable of abnormal development, the vagrant primary germ-cells. On the other hand, the carcinomatous nature of such an abnormal growth of a larva or phorozoon has been abundantly demonstrated by Marchand for the instances of the pernicious growth of the chorion, chorion-epithelioma. If such a chorion the representative more or less complete of the asexual generation, when robbed of its embryo or when it fails to form such, can—and this is established—give origin to a malignant carcinomatous tumour the nature of cancer is clear. The vagrant primary germ-cell is the seed, while its fruit, sometimes represented by an embryoma, may on occasion take the form of a carcinoma.

List of Memoirs upon the Metazoan Life-Cycle, 1889-1902.—1. The Early Development of *Lepidosteus Osseus*, Proceedings of the Royal Society of London, 1889. 2. The Transient Ganglion-Cells and their Nerves in *Raja Batis*, *Anatomischer Anzeiger*, 1892. 3. On a Supposed Law of Metazoan Development, *ibid.*, 1892. 4. On the Phenomena of Reproduction in Animals and Plants, on Antithetic Alternation of Generations, &c. (with J. A. Murray, B.Sc.), *Annals of Botany*, 1895, and *Anatomischer Anzeiger*, 1895. 5. The History of a Transient Nervous Apparatus in certain Ichthyopsida: An Account of the Development and Degeneration of Ganglion-cells and Nerve-fibres, Part I., *Raja batis*, with eight plates, *Zoologische Jahrbücher*, vol. viii., 1896. 6. Further Remarks upon the Phenomena of Reproduction in Animals and Plants, *Anatomischer Anzeiger*, 1896. 7. On Certain Problems of Vertebrate Embryology (The Critical Period, &c.), *Jena*, Gustav Fischer, 1896. 8. The Yolk-Sac, Yolk, and Merocytes in *Scyllium* and *Lepidosteus*, *Anatomischer Anzeiger*, 1896. 9. On the Disappearance of the Transient Nervous Apparatus in the Series: *Scyllium*, *Acanthias*, *Mustelus*, and *Torpedo*, *ibid.*, 1896. 10. The Span of Gestation and the Cause of Birth, *Jena*, Gustav Fischer, 1897. 11. The Birth Period of *Trichosurus vulpecula*, with one plate, *Zoologische Jahrbücher*, 1897. 12. The Morphological Continuity of the Germ-cells in *Raja batis*, *Anatomischer Anzeiger*, vol. xviii., 1900.

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A CASE OF DIFFICULT DIAGNOSIS WITH A RARE COMPLICATION.

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THE patient was a married woman, 37 years of age, well-developed and healthy, of a sensitive, highly-strung temperament, and with an excessive dread of pain and illness. No previous illness threw any light on the present attack. The family history was unimportant except as revealing the fact that two brothers and a cousin had died from enteric fever. The illness started, it was supposed, with a chill, but of this there was no proof. On Jan. 16th, 1902, having experienced for a day or two previously an ill-defined sense of malaise, she felt generally ill and was drowsy, shivery, and giddy. Headache was present, as was nausea which went on to vomiting. Cough, sore-throat, and coryza were absent. After three days in this condition she sought advice and was seen for the first time on Jan. 19th the fourth day of actual illness. The symptoms already mentioned were then present and in addition she felt weak, faint, and depressed. She had gastric pain and felt sick. She was constipated. The tongue showed a thin white fur which afterwards became thick, grey, and creamy. The pulse was 96, regular, but weak. The temperature in the early afternoon was 99.6° F. and it rose in the evening to 101°. She had slept badly. Some cases of influenza of the gastro-intestinal type had occurred in the household about this time and it was thought that the patient was suffering from the same complaint. For the next five days the course of illness corresponded well with the diagnosis that had been made. The morning and evening temperatures from the fourth day to the tenth day, and a four-hour chart from the tenth day to the sixteenth day, are appended. On Jan. 25th some tenderness in the right iliac region was complained of. It being now the tenth day of illness and the sixth of ascertained pyrexia the possibility of typhoid fever had to be entertained. A search for spots and splenic enlargement revealed nothing. The bowels had acted on this day in response to a gentle aperient and four yellowish stools had been passed, but otherwise constipation had been the rule. All precautions were, however, taken and the patient was placed on enteric diet. An examination for Widal's reaction was clearly desirable at this stage but the patient shrank from the discomfort of the trifling puncture and in her weak state it was not insisted on. On the 27th, the twelfth day of illness, the diagnosis was still in doubt. The onset, neither sudden nor insidious, had given no clear indication either way. The facial expression showed impatience rather than apathy. Hectic flush was absent. The pupils were of normal size. The tongue, though furred, was not parched. Abdominal tenderness was trivial. Constipation was present and meteorism was absent. The heart sounds showed increasing weakness of the heart muscle. The pulse, weak, occasionally irregular, of low tension, but not yet palpably dicrotic, varied from 96 in the morning to 120 in the evening. At this date it was too early to suggest typhoid myocarditis; the heart weakness fitted well with poisoning of the myocardium or of the vagus centre by the toxin of either disease. In other respects the patient on this day expressed herself as feeling much better and begged to be lifted for a few hours out of bed on to her couch. The wish was gratified to her great comfort and apparent benefit. At 7.30 P.M., while resting quietly, she was threatened with a sudden action of the bowels. In endeavouring to accommodate herself to the utensil she, forgetting previous warnings, actively co-operated with the nurse by raising her hips and trunk from the bed while in the dorsal position. She was immediately seized with abdominal pain, followed by pain in both legs from the middle of the thigh downwards. To this succeeded tingling in the legs and feet and soon afterwards numbness and coldness of the extremities. Examination shortly afterwards showed that the