The Annual Oration, ON FERTILIZATION IN RELATION TO PATHOLOGY,

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NOTHING which came under my observation in childhood left a deeper impression on my mind than the realization of the fact that the tadpoles, which swarmed in the ditch bordering my playground, came from the frog's spawn so conspicuous in that ditch in the early days of spring. Many events, apart from watching the conversion of the aquatic tadpole into the amphibious frog, quickened my interest in the phenomenon of reproduction, including the development of worms, moths, fishes, reptiles, birds, and mammals, and the whole subject has retained for me a peculiar fascination. It is scarcely appreciated by men to-day that the human ovum was not discovered until 1827; this discovery (one of the greatest man ever made about himself) we owe to von Baer. So far as man is concerned, the fundamental facts relating to the fertilization of the ovum are matters of inference, for no one has witnessed the union of a spermatozoon with a human ovum. Our knowledge of the development of spermatozoa (spermatogenesis) is founded, so far as mammals are concerned, mainly on observations made on the testes of rats. We know less of the development of the sperm than of ova, but no one denies that a new human being is the result of contact of an active mobile spermatozoon (microgamete) with a passive yolk-laden ovum (macrogamete). After these dissimilar gametes have met, the resulting body, known as the oöperm or zygote, begins to segment, and under favourable conditions produces an embryo.

It is worth bearing in mind that a spermatozoon is the most easily identified of all varieties of the epithelial cell, whereas the virgin human ovum has no specific characters; it is usually recognized by its situation in the reproductive tissues. Some years ago, as a matter of routine, I slit up many Fallopian tubes, removed in the operations of hysterectomy and ovariectomy, and scrutinized their contents with a microscope in the hope of detecting ova in them. I satisfied myself that the old idea of the regular shedding of a ripe ovum once a month by healthy women had no foundation in fact; ova are shed frequently, and it is probable that the Fallopian tubes of a mature woman are rarely without a ripe ovum. On one occasion, after removing a uterus containing fibroids, one of which obstructed the uterine end of a Fallopian tube, I found a recess in the tube lined with mucous membrane containing a number of cells, any one of which would pass for a ripe ovum. The difficulty of distinguishing a free ovum applied in this instance with great force. I do not know an absolute test.

Gametic Attraction.

Every thoughtful man must have asked himself the question, What is the power which leads a spermatozoon to an ovum? The usual description of fertilization leaves an impression on the mind that when environment is favourable, and the genital passages of the female contain spermatozoa, a meeting between an ovum and a spermatozoon is a casual affair. This is far from being the case: ova and spermatozoa are powerfully attracted to each other within short distances by some force of which we know very little, and which we may conveniently call *gametic attraction*. Observers who have studied the fertilization of eggs laid in water notice that when a mature ovum is brought into the vicinity of sperm, the spermatozoa are influenced by its presence to direct themselves towards it, and make energetic swimming efforts to reach it.

Gemmill in his description (1912) of the development of the starfish, *Solaster endeca*, describes the process of spawning. A female and a ripe male were in a tank, and whilst the female starfish was shedding ova, the male, resting near the side of the tank about 2 ft. distant, sent out thin streams of sperm. Although the eggs are much too large and opaque to allow the process of fertilization to be watched under the microscope, it could be readily seen that they attract the sperm strongly as soon as they are shed.

Botanists tell us that the spermatozooids of ferns are capable of spontaneous movements through water, and there is some influence in the neighbourhood of the egg cell which attracts these mobile spermatozooids. In the mature archegonium of mosses some of the cells in the canal leading to the egg cell yield cane sugar which, diffused in the water, exerts an attractive stimulus on the spermatozooids. It is probable that the movements by which spermatozooids approach the female organs are chemotactic. The following simple experiment, which I owe to Mr. J. B. Bergheim, is of the same class:

Take a full-blown flower of the beautiful orchid *Odontoglossum grande*, and with a pointed stick or pencil extract its pollinia in the manner described by Darwin. The pedicel carrying the pollinia sticks so firmly to the pencil by means of its adhesive disc that in half a minute it is

Fig. 1.—The pollinia and pedicel of the orchid, *Odontoglossum grande*. Immediately after extraction, and after the "act of depression."

difficult to detach it without damage, but if the pollinia, immediately after the act of depression, be brought in contact with the viscid stigmatic surface of another ripe flower of the same species, they instantly adhere and leave the stick without damage—indeed, in some instances the pollinia and the pedicel supporting them leave the pencil with alacrity. If the adhesive matter is allowed to harden firmly, then, when the pollinia are presented to the stigmatic surface, they become detached from the pedicel, which remains fixed to the stick.

The changes which follow the pollination of the *odontoglossum* are represented in Fig. 2. They are worth

Fig. 2.—The essential sexual organs of *O. grande*. A, Before pollination. B, Seven days after pollination. C, Lateral view of the ovary one month later.

following. The ripe sexual parts are shown at A; after receiving a pollinium they gradually approximate, B; the petals and the labellum quickly fade, and a few weeks later the ovary is enlarged, C. The ovary continues to

increase in size, and five months later has the appearance shown in Fig. 3.

Fig. 3.—A, The ovary of *O. grande* five months after pollination. B, The shrunken remains of the rostellum. The seeds require nine months for ripening.

If we knew the force which impels the spermatozoon to seek an ovum many facts would be plain in pathology. We should know how the embryo of the guinea-worm recognizes its host the water flea (*Cyclops*), and the embryo of the liver fluke, the pond snail. A hundred similar examples could be adduced from the natural history of parasites.

The selective power possessed by the embryo of the liver fluke (*Fasciola hepatica*) for the pond snail (*Lymnaea truncatula*) has been graphically described by Thomas.

Fig. 4.—An embryo fluke engaged in boring into the tissues of a pond snail—x 500. (After Thomas.)

If it is not successful in finding one it dies in eight hours.

Whatever this remarkable force may be, it has a human interest, for it is doubtless the same influence which leads some men to prefer brunettes and other blondes. If we understood it, perhaps we should be able to explain why some blondes of delicate form and feature are fascinated by men of the type of Hercules and Vulcan, such as wrestlers, boxers, and blacksmiths, resisting the importunities of suitors possessing the attributes of Adonis.

The exquisite description furnished by Thomas of the manner in which the young fluke desperately hunts for a pond snail, is an admirable example of knowledge obtained by observation. Whenever reasoning is uncontrolled by facts, imagination is apt to be riotous. An extraordinary example of the perfervid speculation is contained in the Sardinian Report on Cretinism (Turin, 1848), for the reporters seriously urge that a cretin may be due to

sexual connexion between a man and a woman when one or both are drunk. The idea of an encounter between a jovial spermatozoon and a drunken ovum in the Fallopian alley is something peculiarly comic.

Although the idea of sex cells being influenced by the drunkenness of the individuals to which they belong sounds odd, there is no absurdity in the belief that morbid conditions of the parents influence egg and sperm. Those who have made prolonged and careful study concerning the possible causes of those malformations covered by the general term "monstrosities" are unanimous in the belief that the general health of the parents influences the physical development of the offspring. A careful consideration of the facts also justifies the opinion that the union of gametes in a malign environment is often expressed by a malformed embryo. Experimental teratology not only supports this conclusion, but adds trauma as a cause of monstrosity. The observations of those biologists who have studied vegetable teratology offer testimony in the same direction.

Parasitic Castration.

A good example of disturbed metabolism leading to changes in the sexual glands, and in the secondary sexual characters, is that known as parasitic castration, discovered

Fig. 5.—The spider crab (male) with large chelipedes, small abdomen, and the large copulatory styles.

in 1887 by Giard. This matter has been particularly studied in the spider crab *Inachus* and in the hermit crab. The facts are briefly these:

The male *inachus* (Fig. 5) is furnished with long and swollen chelipedes; the abdomen is small and furnished with a pair of copulatory styles. In the female (Fig. 6) the chelae are small and narrow, but she has a larger abdomen, which is trough-shaped and carries four pairs of ovigerous appendages. These crabs often harbour *Sacculina neglecta*, a peculiar barnacle which has taken to live parasitically on the crab. When the sacculina is hatched it swims near the surface of the sea and becomes transformed into the well-known Cypris larva. After living for a time a free existence, it seeks out a crab and fixes itself by means of hooks to a hair on the crab and penetrates its base. The larva then discards its appendages and as a small mass of undifferentiated cells enters the crab's body, and reaches the space round the intestine usually near the stomach and proceeds to throw out roots in all directions. When first discovered, *sacculina*, being so unlike a crustacean, was regarded as a tumour by one naturalist and as a worm by another.

This invasion has extraordinary effects on the male crab, for it ceases to moult, the chelae diminish in size, the abdomen broadens, ovigerous appendages appear and cause

it to assume the external characters of a female crab. At one time, in consequence of these changes, it was supposed that sacculina only attacked female crabs. In the presence of the parasite the generative organs undergo degeneration and disintegration. The sequel is even more remarkable, for when the parasitic barnacle leaves its host the crab recovers, and, in the case of the male crab which has assumed female characters, the testis not only regenerates but becomes a true hermaphrodite gland capable of producing ova and spermatozoa. These remarkable changes have been especially studied by Geoffrey Smith.

It will at once occur to many that these observations have some bearing on the peculiar alterations of plumage seen in pheasants, peacocks, ducks, and chaffinches, in which the hen moults and, without obvious reasons, assumes the resplendent plumage, more or less complete, of the cock. Such birds are known as cock-feathered hens, and the change of plumage was supposed to depend on atrophy of the ovary. We know nothing concerning its cause, although many clever observers, including Hunter and Darwin, have considered it.

The changes which occur in the testis of a spider crab infested with sacculina, whereby it becomes converted into a hermaphrodite gonad, is a matter of great interest. The history of our own bodies teaches us that at an early

Fig. 6.—Spider crab (female). The chelipedes are small and the abdomen broad. The ovigerous appendages are shown free on one side, and on the other with eggs upon them.

stage the human embryo is hermaphrodite. When the gonad is an ovary the sexual organs assume the female type; when the testis predominates the male type prevails. At the very threshold of our practical acquaintance with human anatomy we learn that vestiges of the male reproductive organs are present in the female, and many vestiges of the special female organs exist in the male; some are present in the gonad itself, whether it be an ovary or a testicle. It is an interesting fact that in the male spider crab the testis, under the influence of parasitism, can produce ova. Although there is an enormous distance between crustaceans and man, these observations do bear on those rare instances in which dermoids arise in the testicle, for these remarkable tumours in men and in horses, though usually described as testicular, really arise, as I have often pointed out, in the ovarian vestiges known as the rete testis.

Ovarian Dermoids.

Apart from observations relating to "parasitic castration," some useful investigations have been carried out in the last twenty years which throw some light on the curious tumours known as ovarian dermoids. In 1880 I saw for the first time an ovarian cyst containing hair, grease, and teeth. I have removed a great many since, but my interest in them persists. Thirty years ago all tumours containing cutaneous structures growing in divers

parts of the body were called dermoid cysts; I soon recognized that such tumours were sufficiently important to form a group. Dermoids which arose in the ovary differed in so many particulars from those found in other parts of the body as to demand a genus to themselves. Whilst investigating the structures in ovarian dermoids I found and described the bodies now familiarly known as "ovarian mammae," and exhibited a series of cysts containing them to the Pathological Society in 1888. About ten years afterwards Wilms published his investigations on dermoids, which modified current views on these tumours, for he showed that the curious nipple-like processes and mammary structures, which he named embryonal rudiments, were important elements. Every dermoid, or embryoma, as it is now called, consists of a cyst and an embryonal rudiment. The wall of the cyst is of fibrous tissue, and at one part of its inner wall presents a skin-covered surface beset with hair; the embryonal rudiment appears as a nipple-shaped process projecting from the skin-covered surface. Its size varies greatly, for often it is so inconspicuous as to be easily overlooked, or it may be big enough to strike the eye of the least observant. The cavity which contains the embryonal rudiment is filled with oil, grease, or lumps of suet mixed with hair and epithelium shed from the cutaneous surface. Some embryonal rudiments are more complex, and contain such organs as a thyroid gland, fibrous or osseous capsules lined with pia mater and filled with nerve tissue.

On two occasions an organ like an eye has been found with a cornea, an anterior chamber, and a cavity lined with the conspicuous black uveal tissue (Baumgarten, Frankland, and Cleland). Organs obvious to the meanest intelligence are bones, cartilage, and teeth; less obvious than these is mucous membrane such as occurs in the intestine (Frank, Shattock, and Williamson).

We have been contented in the past with an examination of these bodies by means of microscopic sections, but Shattock, in a brilliant investigation, has shown that when some of these embryonal rudiments are studied by dissection rather than by thin sections, organs may be identified in them. In one example he found nerve matter present in the form of a thin-walled sac; the inner wall of this sac was lined with columnar epithelium and the halves of a spinal cord lay on each side of it. This hydromyelic sac represented the dilated central canal (syringomyelia) of an imperfectly developed spinal cord. In another cyst he found a smooth-walled cavity containing a blind coil of gut possessing the structure of small intestine. I have often pointed out that nearly all the organs found in ovarian dermoids are of epiblastic origin. Organs such as lung, liver, and kidney have never been found. This serves to distinguish ovarian dermoids from the teratomatous representatives of conjoined twins.

The great principle underlying tumour formation conceived by Müller and established by Virchow postulates that every neoplasm, using this term in its strict pathological sense, arises from pre-existing tissue of the same structure, therefore we must seek a reason for the presence of tumours in the ovary containing teeth, skin, nerves, and intestine. The conclusion is plain—they are the products of a sex-cell or ovum. From the earliest observations on ovarian dermoids the idea that they were imperfect pregnancies took deep root in the minds of the men who examined them, and the discovery of parthenogenesis, or the development of an ovum without impregnation (von Siebold, 1856), provided a plausible theory.

Conjoined Twins.

Although the observers who described ovarian dermoids before the discovery of spermatozoa regarded them as "imperfect pregnancies," they were careful to point out that these tumours could not be the products of conception in the ordinary sense, for some of them occurred in infants. On examining the "indigested and deformed lump," known as an embryonal rudiment, we have difficulty in believing it to be an embryo, especially when it contains only an eye, or a fragment of spinal cord, or a few teeth connected with an orifice representing perhaps a mouth. All these odd imperfections can be paralleled by twins. It is not an uncommon event for an ovum to give origin to two embryos, and both may attain full development, make their entry into the world, and survive as independent individuals.

Occasionally the twin embryos develop equally, but are

partially joined together, and in this condition survive to the normal period of delivery. Many conjoined twins die in the course of being born, but a few escape with their lives, grow up, and in due course earn money for enterprising showmen as freaks. When twin embryos are conjoined it does not necessarily follow that each goes on to full development; occasionally one of them is represented by a shapeless mass attached to its brother or sister as the case may be. Matthews Duncan tells of a case in which a parasitic fetus of this kind was attached to the buttocks of a young man, occupied as a clerk, who spent the greater part of the day sitting on his sadly deformed twin brother. A shrunken parasitic fetus stuck on an otherwise well-formed individual recalls the delightful conception of Thackeray in the story of *The Rose and the Ring*, wherein the porter, Jenkins Gruffanuff, is transformed into a knocker on the front door for his rudeness to Fairy Blackstick.

Fig. 7.—A, Normal egg of the American salamander, showing the medullary folds. B, An egg with abnormal medullary folds from which the double-headed embryo C was formed. D, The adult form of the American salamander. (Figs. A B and C after Clark.)

Embryologists agree that conjoined twins are the product of a single egg. A strong body of circumstantial evidence of a most convincing kind can be adduced in support of this opinion. Moreover, the development of a double embryo from a single egg has been actually witnessed in the case of a batrachian. In the spring of 1879 Clark of Boston had in his aquarium 2,000 or 3,000 eggs of the American salamander, *Amblystoma punctatum*, for the purpose of studying their development. He found one with the medullary folds nearly completed, but they had not united at the cephalic end, and appeared to be much rounded at their anterior ends, instead of having the ordinary vague outlines; it was set apart for observation (Fig. 7). Each free portion of the medullary fold developed a perfect head, which, at first partly united, became gradually more so until they were connected throughout their length. Posterior to the heads were no signs of duplicity.

The development of double-headed embryos from single eggs is a frequent event in salmon hatcheries. An instructive series is shown in Fig. 8, comprising twins and bicephalous salmon fry in various stages of dichotomy, but all exhibiting a common feature, for in each the yolk sac is single.

The frequency of such malformation among salmon obtained in hatcheries probably depends on the artificial mode of fertilization. In relation to this it may be mentioned that in some experiments on cross-fertilization made by Gemmill on the eggs of starfishes, he found the ova of *Solaster endeca* strongly attractive to the spermatozoa of *S. papposa* and are fertilized by them; segmentation and development proceeded in some specimens, showing various abnormalities of growth.

It is possible to arrange a series of parasitic fetuses so rudimentary as to parallel the confused and ill-shaped "embryonal rudiments" so common in ovarian dermoids. Such a series and such a comparison make the conclusion irresistible that the embryonic rudiment, like the parasitic fetus, is the product of an ovum. The structure of the embryonal rudiment supports, in a measure, the opinion that it is an embryo arrested at an early stage of its development. The frequent presence of nerve tissue, neuro-epithelial elements, and ocular tissues is not surprising, because the neural tube from which the spinal

Fig. 8.—Twin salmon embryos from a hatchery, showing monstrous development with one common feature—the yolk sac for each monstrous form is single.

cord, brain, and ophthalmic cups are formed is an early and conspicuous structure in all mammalian embryos.

Traumatic Parthenogenesis.

At the outset I laid special emphasis on the fact that our knowledge of the fertilization of mammalian ova is derived from observation made on the eggs of low animal forms. We have been too long satisfied with the opinion that it is only the contact of a spermatozoon which will start an ovum on its extraordinary career of development, but there are other stimuli which will induce a mature ovum to segment. Loeb's experiments show that the mature eggs of starfishes can be made to develop by the addition of soda water to the sea water of the aquarium or by mere shaking (shock fertilization).

Professor Bataillon, Dean of the Faculty of Science, Dijon, has succeeded in inducing complete embryogenesis by puncturing the virgin eggs of frogs with exceedingly fine metal stylets. The eggs were obtained from the common grass frog, *Rana temporaria* (Fig. 9). The frogs were carefully washed in water saturated with bichlorides to prevent any accidental contamination with spermatozoa. The instruments were sterilized in a flame immediately

before use. The eggs after removal from the oviduct were placed in flat-bottomed receivers and covered with water at 15° C. Each egg was then punctured by a short stylet made of glass, manganin, or platinum, varying in thickness from 20 to 30 micromillimetres. A slight track in the egg marked the line of puncture. In making the puncture Bataillon aimed to get at the egg at a point excentric of

Fig. 9.—Eggs of the grass frog, *Rana temporaria*. (Natural size.)

the black hemisphere. The punctured eggs were covered with water and effected their rotation in forty-five minutes, so that the black spheres were uppermost as in normally fertilized eggs, whilst the virgin unpunctured eggs were disposed irregularly. Four hours later segmentation began in the eggs and proceeded as quickly, and in one-third of the punctured eggs as regularly, as in eggs normally fertilized, but arrest of development took place at all stages. In 10,000 eggs which he punctured three developed complete tadpoles (Fig. 10). Bataillon states that the

Fig. 10.—Three tadpoles produced by traumatic parthenogenesis. The tadpole near the top of the vase was the result of an experiment performed March 9th, 1910; it died June 18th, 1910, in consequence of shock due to changing it into a jar for the purpose of being photographed. (After Bataillon.)

critical period for a tadpole produced in this way is when the tail begins to regress. The consideration of these experiments must make us think that if the eggs of human beings were as big as those of the grass frog many problems in human embryology would be less misty than they are to-day.

The consideration of traumatic parthenogenesis would not be complete without reference to the conduct of the chromosomes in the cells of these segmenting eggs. All animal cells contain in their nuclei a definite number of chromosomes, and though the number varies in different species of animals, it is constant for a given species, but the number of chromosomes in an ovum during its maturation is reduced one half; they are also changed in character. A similar condition exists in the spermatozoon, but when the ovum and spermatozoon unite and form an oöperm or zygote the number of the chromosomes in the zygote equals that of the somatic cells. The significance of the change is not understood, but it has served as a

text for much vague speculation, especially in relation to sex and heredity.

It has been ascertained that the chromosomes in the parthenogenetic larva of frogs are of the reduced type. This is a matter of interest, and probably explains the failure of Bataillon's method to produce complete frogs. It also helps us to understand the incompleteness and the unlikeness of the embryonal rudiment to a human fetus, in spite of the high standard occasionally attained by its component tissues. It is undeniable that the organs existing in ovarian dermoids are rarely of the same completeness as those of parasitic fetuses; the muscles even of a shapeless conglomerate twin sessile on the sacrum of its autosite will twitch when mechanically irritated, but no organ in an ovarian dermoid has ever been reported in a functional condition. This indicates the value of the spermatozoon for the production of a complete individual.

Epithelial Infection.

No surgeon will deny that the ovarian dermoid in its common form is the most benign tumour that attacks women, but it is not to be forgotten that the epithelial elements of such tumours often possess remarkable vitality, which is occasionally manifested in a curious way. At least half a dozen cases have been carefully reported where such a tumour has been burst by violence, and its pulqueous contents—hair, grease, and epithelium—spread far and wide through the abdominal cavity. (In one instance, described by Randall and Lawrence in 1908, the leakage occurred from a hole made in the procedure known as tapping.) Some of the epithelium engrafted itself on the peritoneum, so that in the course of an operation performed for the purpose of removing the tumour, the surgeon found the serous surface of the viscera and the omentum beset with nodules, many of them possessing a tuft of hair. These epithelial weeds, to use an agricultural term, differ from those secondary nodules which are such a common feature of cancerous infection of the peritoneum, for they remain as grafts upon the serous membrane, and do not penetrate the underlying tissue nor display the invasiveness which is such a marked feature of the cancerous nodule. This induced me to apply the term *epithelial infection* to this phenomenon. One of the earliest examples was described in 1867 by Moore; the specimen is preserved in the museum of the Middlesex Hospital.

I have satisfied myself that it is not an easy matter for dermal cells to engraft themselves on the peritoneum. These elements may be loose in the abdominal cavity for a long period and fail to become engrafted. Lucy recorded a striking case in which an ovarian dermoid leaked and distended a woman's belly with the usual sebaceous paste; her belly was so full that the mass pitted as if it were plastic clay when pressure was made upon it with the finger. At the operation he removed 11lb. of the pulqueous sticky stuff. In spite of this prolonged contact of such a large amount of epithelial material with the peritoneum there were only two grafts.

A critical study of cases in which this peculiar epithelial infection has occurred led me to express the opinion, in 1896, that the facts pointed in the direction of occasional malignancy, but a further study of this matter in the wards, *post-mortem* room, and laboratory convinced me that the innocency of these tumours could not be impeached with the scanty and unreliable evidence available at that time. I thought that the few examples which had been published where small dermoids were found on the peritoneum could be regarded as examples of epithelial infection.

Malignant Teratoma.

We know now beyond any doubt of a variety of the ovarian embryoma (or teratoma) in which malignancy is displayed in a very intense form. This tumour occurs in girls and young women as a solid or semi-solid mass, and rarely attracts attention until an increase in the size of the abdomen is noticed by the patient or her relatives. The tumour grows quickly, disseminates like cancer, recurs very rapidly after removal, and destroys life in a few weeks or months. No tumour is more deadly, not even a periosteal sarcoma of the femur, or of the humerus. These malignant ovarian teratomas consist of a hotch-potch of embryonic elements of various kinds, such as

epithelium, neuro-epithelium, pigmented retinal cells, enamel organs, dentine-papillae, skin, hair, cartilage, ganglia, and medullated nerves. These tissues occur in the nodules which grow throughout the abdomen, and in those which grow in the substance of the liver or the lungs. Details of at least fifty examples of the malignant ovarian teratoma are available for study; many of the tumours have been investigated by competent men.

The condition I had in my mind that led me in 1896 to express my belief in the innocency of the cystic variety of ovarian embryomas was the alleged occurrence of cancer in the embryonal rudiment, especially the ovarian mamma. Several surgeons interested in the pathology as well as in the surgery of ovarian tumours sent me occasionally descriptions and sections of specimens which they believed were examples of carcinoma arising in ovarian dermoids. In all the specimens submitted to me none would bear this interpretation, and my opinion has been supported by the subsequent histories of the patients. In 1897 Professor Yamagiva, of Tokio, described a cystic teratoma of the ovary containing a mamma, which he believed had become cancerous, but the evidence is by no means convincing. Since that date we have become familiar with a subtle form of cancer dissemination known as "implantation."

Implantation Cancer.

When a woman is attacked by cancer in the gastrointestinal tract, gall bladder, breast, or Fallopian tube, the cancerous cells permeate the adjacent tissues and are shed into the belly cavity; these cells, floating in the peritoneal fluid, are dispersed throughout the abdominal cavity. If the woman be so unlucky as to have an ovarian cyst or a dermoid in her pelvis, some of the cells will be deposited on the cyst wall, and some of them grow and form blocks of secondary cancer. I exhibited and described several specimens of implantation cancer to the Society in 1910. Large numbers of cancerous cells which are shed into the abdominal cavity perish, for the peritoneum exercises a defending or prophylactic power against such marauders; but the ovaries are more easily colonized, as they lack a peritoneal investment.

This new knowledge concerning the deposition of cancerous cells on normal ovaries as well as on ovarian cysts is of importance, because it renders previous records relating to specimens of primary ovarian cancer of no account. In future descriptions it will be essential for the recorders to furnish evidence that there was no primary cancerous focus in the stomach, big intestine, gall bladder, breast, or Fallopian tubes. A very small primary cancerous focus in the colon, though it has produced a big block of cancer in an ovarian cyst, will sometimes elude the surgeon's fingers and eyes in the course of an operation. Such small contracting cancers later cause intestinal obstruction, and are found in the course of a colotomy, or at a *post-mortem* examination, weeks or months after an ovariectomy.

In considering primary cancer of the ovary and in ovarian dermoids we have to clear away old records and begin anew. The distinction between a cystic ovarian embryoma and a malignant teratoma is as sharp as the difference between a simple chondroma and a chondrifying sarcoma, but there are, as in other genera of tumours (except lipomas) described as innocent, gradation forms by which we pass from species of undoubted innocency to others of the most pronounced malignancy.

Every surgeon has pondered often and long on that common feature of cancer known as "dissemination," wherein the histologic peculiarities of the primary tumour are reproduced in the secondary nodules; but the nodules due to the dissemination of malignant teratomas contain such structures as hair, skin, nervous tissue and embryonic teeth. These can only come from the activity of a developing ovum. We know that microparasites can stimulate growth in epithelial cells, and it is possible that benign ovarian dermoids and malignant teratomas express variations in the effects produced by minute agents, which are able to provoke segmentation in mature ovarian ova, though in a more subtle way than Bataillon's styles.

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THE INFLUENCE OF AGE AND TYPE OF PATIENT UPON THE COURSE AND TREATMENT OF APPENDICITIS.*

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So much has been written about appendicitis, and the disease in all its aspects has been so carefully studied, that it would seem that there can be little left for us to learn. So common is it amongst all classes of society that every medical practitioner must frequently meet with it, and has ample opportunity of acquiring a practical as well as a theoretical knowledge of its clinical manifestations. I speak advisedly when I state that of all the acute abdominal diseases appendicitis is most promptly and most accurately diagnosed. We early recognize the disease, we are alive to its dangers, we are familiar with the signs which call for urgent surgical interference, and we continue to lose a certain percentage of our patients. That this is not due to the operative risk of simple removal of the appendix is certain, for Sir Frederick Treves has recorded 1,000 cases of appendicectomy for chronic appendicitis without a death, and in the past five years nearly 400 patients, whose ages ranged from 4 to 69, have been operated upon at the Queen's Hospital, Birmingham, during a quiescent period without a single fatality. These hospital statistics are of special value, in that they represent the work of no particular surgeon, but of several, and are free from the suspicion that any attempt has been made to improve the statistical results by submitting only those cases to operation which were likely to do well.

It is generally agreed that almost equally good results would follow removal of the appendix within the first twenty-four hours of onset of an attack of appendicitis, and ideally this is undoubtedly the best treatment. There are, however, practical difficulties in the way of operating upon many cases at this early stage. It is often difficult at such short notice to get a surgeon and make the necessary preparations, and the surroundings of the patient are often very unsuitable for an operation. The difficulties are not, however, except in rare instances, so great as to prevent operation were it certain that such is absolutely necessary. It is this doubt as to the necessity for operation at all that is responsible for the delay. That many patients recover under expectant treatment is perfectly

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