LECTURES ON CYSTIC TUMOURS OF THE JAWS, AND ON THE ETIOLOGY OF TUMOURS.

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LECTURE II.—ON SOME POINTS IN THE ETIOLOGY, GENERAL CHARACTERS AND RELATIONS OF TUMOURS.

THE term, tumour, formerly employed in the wide sense indicated by the signification of the word, a swelling, is now exclusively applied to the various overgrowths of parts of the nature of new formations, the origin and increase of which is unattended by the course of events known as inflammation.

From the hypertrophies and inflammatory new formations, true tumours are chiefly distinguished by the diversity from the type of the normal tissues which they exhibit in their structure and relation to surrounding parts. Possessing in the highest degree a proliferative capability, they grow as a general rule continuously, with slight power of development, and without serving any purpose or utility in the economy. A true tumour may therefore be shortly defined as an atypical new formation not correlated with or adapted to the surrounding parts, and the causation of which cannot be solely referred to an ordinary inflammatory or reparative process.

In order more completely to comprehend the special characters of true tumours, let us briefly compare them with the other overgrowths of parts.

Taking the more common examples of hypertrophy, as of the voluntary muscles, the heart, urinary bladder, and kidney, we find that the overgrowth in each case is the result either of increased exercise of the part or the necessity of greater power. The hypertrophy in all cases serves a definite purpose, and adapts the organ to the emergencies occasioned by disease or stress of work; and "to whatever extent it may proceed, the part will maintain its normal form and structure." A familiar example of the contrast between a physiological hypertrophy and a tumour, is an hypertrophy of the uterus, and a myo-fibroma occurring within its walls. The enlargement of the uterus takes place throughout the entire organ, and the newly formed muscular fibres preserve their normal order and arrangement; whereas the tumour affects only a small, and, even from the commencement of its growth, a distinctly circumscribed area; the muscular fibres are arranged irregularly, often interlacing, and are intermixed with a large quantity of fibrous tissue. Again, the hypertrophy of the uterus has a direct purpose, either the expulsion of a foetus or of a pedunculated fibroid, as the case may be; and the organ subsides to the normal size after its accomplishment. The tumour, on the other hand, is characterised by its continuous and purposeless increase.

Some tumours are atypical in their form and relation to surrounding parts rather than in their minute structure. For example, the fatty tumours are indistinguishable in their minute structure from the normal accumulations of fat, yet they present a remarkable diversity in type from the rest of the adipose tissue in their peculiar and characteristic shape, and in their isolation by a capsule.

The excess of growth observed in the hypertrophies of limbs and various organs, is distinguished from tumour-formations, in that it is abnormal in the amount rather than in the kind of tissue produced. The part or organ maintains its natural form, but on a larger scale; and, in its minute structure, the component elements preserve closely their normal type and relative position. These distinctions, although of general application, lose much of their force when applied to some forms of tumour, which occupy an intermediate position between the hypertrophies and new formations. Among these, are the fatty outgrowths described by Sir B. Brodie, which have "no distinct boundary; you cannot say where the natural adipose structure ends, and the morbid growth begins." They most commonly occur beneath the chin and symmetrically placed on each side of the back of the neck, and are sometimes amenable to treatment.

When we turn to the malformations by excess, difficulties are met

with in distinction and classification, which we shall find in the highest degree suggestive in considering the causal relation of the anomalies and variations to which the body is liable. It is none the less difficult to draw a sharp line of separation between the tumours and inflammatory new formations, in fact, Cohnheim* states that it is only by means of their etiology or causation that they can be sharply and precisely divided.

It is not easy, for example, to distinguish with the naked eye some flat over-growths of bone or osteophytes from a heaping up of callus, and with the microscope this is impossible; there is even a strong resemblance in general architecture as seen under the microscope, between the tissue of growing and incompletely formed callus and that of an osteo-sarcoma.

There are, however, some other less distinctly marked characters by which the inflammatory new formations may be distinguished from the true tumours. The inflammatory process is capable of producing the common connective tissues, as fibrous tissue, fibro-cartilage, and bone, and even epithelium, as is seen in the production of the ordinary verrucae and condylomata; but its potentiality does not extend to the production of many of the higher forms of tissue, such as muscle, gland, and brain-tissues, which form the constituents of some tumours.

Again, the inflammatory new formation ceases on the subsidence of the cause which gave rise to it, and then may become reabsorbed. Or, if conservative in its action, and formed for the repair of some injury, it tends to assume a higher type of organisation, conforming in its structure to that of the surrounding parts.

But, just as gradations exist between the tumours and the hypertrophies, so are forms also observed intermediate between the tumours and the inflammatory new formations. By what means other than their causation are we capable of determining to which group keloid belongs, or the fibrous tumours in the lobules of the ears following irritation from the wearing of ear-rings? Both of these new formations of connective tissue tend continuously to increase, and both may recur locally after removal.

Much stress was formerly laid on the independence of tumours of the nutritive and physiological processes of the body generally. In some instances, this is strikingly manifested, as in the case quoted by Sir James Paget, in which fatty tumours of considerable size were found in the mesentery of a patient "from whom, in the extreme emaciation of phthisis, nearly all the fat was removed".†

Some other observations, however, point equally strongly in an opposite direction. I met with a case in which an encapsuled adenoma of the breast was filled with milk having a normal appearance and microscopic characters. The tumour was removed shortly after lactation, and the breast itself contained no milk; so that I think, there can be no doubt of the milk being formed within the adenoma itself. Virchow records a similar case. I have also observed a mucus-secreting goblet-cells lining the gland-tubes of a mucous polypus of the rectum.

The well-known fact that the multiple exostoses and enchondromata of bones cease to increase at the period of cessation of the growth of the bones, indicates that their nutritive activity is closely bound with that of the osseous tissue. The acceleration of the growth of uterine and ovarian tumours which, Leopold‡ observes, occurs during pregnancy, is another instance of the influence of a physiological stimulus upon the growth of tumours.

A distinct relation, can be shown to exist between the physiological and nutritive conditions of the different organs at certain periods, and their liability to tumour-formations and even with the variety of tumour occurring at each particular period.

In investigating the pathogeny of tumours, each organ must, therefore be taken as a separate unit, and considered in relation to its own life-history, as well as with the nutritive condition of the body generally, as indicated by age. For it is superfluous to remark, that the period of most active development and of greatest functional activity, as well as of commencing atrophy and degeneration, varies according to the purpose which each organ or tissue serves in the economy. This is especially exemplified at the period of puberty, when an immense acceleration is given to the development of the genital and allied organs; and to the skin, as shown by the growth of hair at various parts of the body. With this developmental activity, the appearance of certain tumours is coincident.

The dermoid cysts of the skin, Lücke§ observes, nearly always first

* *Allgemeine Pathologie* p. 631.

† Paget, *Op. cit.*, p. 378.

‡ Leopold, *Experimentelle Untersuchungen über die Aetiologie der Geschwülste*, Virchow's Archiv, Band xxxv, p. 318, 1881.

§ Pitha's and Billroth's *Handbuch*, Band ii, Alth 1, p. 127.

excite attention by their rapid increase at the period of puberty, although their rudiments are probably formed during embryonic life, by an involution of the epiblast. Multiple warts on the skin sometimes, according to the same author, appear in women at puberty.

The adenomata of the breast are concurrent in their appearance with the accelerated development and awakening of functional activity in that organ, being almost invariably observed between puberty and the age of thirty years. They often show themselves after the functional activity of the generative organs has been stimulated by marriage, or during the first pregnancy.* According to Thomas,† cystic adenoma of the ovary shows itself during the period of the most vigorous activity in the sexual organs; and, from the statistics of Chereau and Lee, it is shown to be most common between the ages of seventeen and eighteen and forty. The onset of symptoms of this disease, at a later period than the appearance of adenoma of the breast, is probably in a great measure explained by the situation of the affected organs rendering the detection of the disease at an earlier period most improbable. Myo-fibromata of the uterus, according to Leopold‡ never have been seen before puberty; while, on the other hand, Bayle estimated that, of all women dying beyond thirty-five years of age, 20 per cent. were thus affected.§

These facts, I think, distinctly indicate that the appearance of the highly organised or innocent tumours is, as a rule, coincident with the development and greatest functional activity in these organs. In fatty tumours, it might be thought are an exception to this rule, because they most often are observed in middle age. But their origin may be referred with much probability to an earlier period of life, for Cohnheim has found small fatty tumours many times in fetuses. They, therefore, may remain unnoticed until growth is brought about in association with the accumulation of adipose tissue throughout the body occurring chiefly in middle age.

Turning to the bones, the period of active growth of which is entirely different from the organs just considered, we find that the innocent tumours appear, as a general rule, at an early age. The multiple enchondromata are occasionally congenital. Both these and the multiple exostoses are generally met with in early life, and are said invariably to occur before puberty.

The sarcomata of bones are, on the contrary, met with at a later period. In a table of sixty-three cases of central tumours of bones, collected by Mr. Butlin,|| only two occurred before the age of sixteen, and one of these was in a child aged five years. Of the sixty-three cases, forty, that is, over three-fifths, occurred between the ages of sixteen and forty years.

In the table of fifty-six cases of subperiosteal tumours, there was a gradually increasing frequency from sixteen years upwards. Of the fifty-six cases, forty-three, or nearly four-fifths, occurred between the ages of sixteen and forty, inclusive.

Of the total number of one hundred and nineteen cases, seventenths occurred between the ages of sixteen and forty years. It must be remembered in connection with these figures, that the union of the epiphyses to the diaphyses, in the long bones, commences at fifteen or sixteen years of age, and ceases at twenty-five.

From a further examination of these tables, it is seen that, as regards the central tumours, not only those bones of which the sum of growth is greatest are most frequently affected with sarcoma; but also that the parts of bones, in which growth last ceases,** are, to a remarkable degree, liable to the disease. This is observed in the lower epiphysis of the femur, and upper epiphyses of the tibia and humerus. Of seventeen central tumours of the femur, ten were situated in the lower epiphysis; of thirteen in the tibia, eleven originated in the upper epiphysis; and of eight affecting the humerus, all but one were in the upper epiphysis.

These facts may, perhaps, be taken to indicate that the longer continuation of growth in these parts, after the cessation of the period of most active growth in the skeleton generally, renders them much more liable to sarcoma, and possibly connects the manifestation of the tendency to tumour formation with a decline of nutritive activity in the part, such as is observed in the breast during the cancerous age. And, further, the coincidence previously pointed out in the period when sarcomata of bones begin to appear in large numbers, and in that of the union of the epiphyses may show also, that the imperfect nature of the tissue of the sarcomata depends in part on

the period of their occurrence, viz., during the decline in the activity, and after the cessation of growth in the bones.

But how are we to explain the occurrence of cancer at a much later period than sarcoma, since the conditions favourable to the development of both depend on a diminished formative and nutritive activity in the affected part? An answer is found when the difference in the function of the two structures is borne in mind. After the cessation of growth, it may be supposed that the nutritive power of the connective tissues is, under ordinary circumstances, only sufficient for their maintenance, and of a much lower degree than in the epithelial structures. These are constantly thrown off, or used up in secretion, when they are replaced by a constant succession of newly formed cells. This is also shown by the earlier atrophy of the connective tissue in advancing age, upon which Thiersch strongly insists.

The generative organs in the female are the first epithelial structures to become atrophied, for the obvious reason that they are no longer of utility after the period of child-bearing. And it is in these organs that we find cancer first manifesting itself. Numerous statistics show that cancer of the breast is by far most common between the ages of forty and fifty. In two tables given by Sir J. Paget,* the far larger proportion of cases was observed between 40, or 45, and 50 years, when they decreased in frequency. The more recent statistics of von Winiwarter† and Oldekop,‡ refer the maximum of cases to a slightly earlier age. The former computes the average age at which cancer of the breast occurs as 45.3 years. Of 108 cases of cancer of a closely allied organ, the uterus treated by Scanzoni,§ a greatly prepondering maximum was obtained between 40 and 45 years; the disease, like scirrhus cancer of the breast, being very rare before 30 years. If, however, we take a structure, such as the epithelium of the tongue, mouth, and œsophagus, which may be supposed, on the grounds already given, to maintain its nutritive activity longer than that of the breast or uterus, we find that cancer is most common in the decades between 50 and 70. Of 70 cases of cancer of the tongue collected by Mr. Butlin,|| only 11 occurred before the age of 50, and of 57 cases of cancer of the œsophagus, only eight before 50. Of 31 cases of cancer of the kidney collected by Walshe, the maximum number occurred after the age of 50. The facts just stated are strongly supported by the statistical table of von Winiwarter, comparing the periods of greatest frequency of cancers in some different localities. The breast stands first, and is followed by cancer of the face, cancer of the mucous membrane of the mouth and œsophagus being last by many years.¶

It has long ago been pointed out that cancer is essentially a disease of degeneracy. Perhaps a nearer approach to truth is made in very broadly stating that, in the majority of cases, the origin of the innocent tumours corresponds to the periods of more active development, or, in some instances, of greatest functional activity in the particular organs; while the formation of the malignant tumours tends to occur during the decline of developmental activity (in the sarcomata), or subsequently to the completion of development (in the cancers), and extends throughout succeeding years. With the advance of life, the frequency of sarcoma decreases after the fortieth year, but the tendency to cancer increases until the sixth decennium, when it also diminishes.

It is needless to remark that exceptions to this broad statement are met with; and especially in a few tumours, either congenital, or occurring in childhood. They are nearly always sarcomata, the eye, kidney, and testicle being affected most commonly, and rarely the bones. The early occurrence of these tumours may, perhaps, be referred, in some instances, to a tendency observable in hereditary variations to appear at an earlier age in the offspring than in the parent; and, in others, to some peculiarity in the formation and development of the part.

We pass on now to consider one of the many debatable points with regard to tumours, and especially cancer, viz., heredity. The facts range themselves in two classes; 1, those derived from statistics; and 2, those observed in individual cases. The statistics at hand solely refer to cancer.

Probably the most reliable statistics of the heredity of cancer are those obtained by Mr. W. Marrant Baker from Sir James Paget's note-books,** which included hospital and private patients, in the proportion of about two-fifths hospital to three-fifths private.

* Laucke, *op. cit.*, p. 281.

† Thomas, *Diseases of Women*, p. 673.

‡ *Op. cit.*

§ Thomas, *op. cit.*, p. 507.

|| H. T. Butlin, *Sarcoma and Carcinoma*, p. 110, 1882.

¶ See Table of C. Länger. *Deutsche Zeitschr. für. Chir.*, Band x.

* *Op. cit.*, p. 635.

† *Ueber die Statistik der Carcinome.*

‡ Langenbeck's *Archiv*, Band xxiv, s. 691.

§ Thomas, *op. cit.*, p. 558.

|| *Op. cit.*, p. 158.

** *Op. cit.*, p. 265.

** *Medico-Chirurgical Transactions*, vol. xlv, p. 380.

In 322 cancerous patients, there were 78, or nearly one-fourth, who were aware of cancer in other members of their families.* The term cancerous is here used in the old sense, to signify any malignant tumour.

Lebert, from 102 complete observations, computed the number of cases of cancer in which a hereditary history can be obtained as one in seven; Sir J. Paget places it as high as one in three.

Mr. Harrison Cripps, in an ingenious article† seeks to prove that cancer is not hereditary. If cancer be hereditary, then the percentage of deaths from cancer in the parents of cancerous persons should be greater than among the population generally. Mr. Cripps, therefore, compares the death-rate from cancer in the parents of cancerous patients included in Mr. Baker's table, with the death-rate of adults from cancer in the United Kingdom. The comparison shows that there is only a slight difference in the death-rate in the two cases; and Mr. Cripps draw the natural conclusion that cancer is not hereditary; or, as he puts it, "that cancer in the parent in no way increases the liability of the offspring to suffer from the same disease." This result is so completely at variance with facts derived from individual cases, that I think there must be some sources of error, among which the following may be pointed out. In the first place, the Registrar-General's returns cannot be considered the most accurate data on this point; and, secondly, by taking only the parents of the cancerous patients, the evidence of a family tendency to cancer derived from its existence in near relations is completely excluded; for the tendency may be transmitted from a grandparent to a grandchild, the parents being unaffected; while some of the brothers or sisters of the parent or their children may exhibit the family predisposition.

The proportion of cases in which there is a hereditary history of cancers is diminished by the fact, which Sir James Paget has pointed out, that many of the parents may never have manifested the cancerous disposition which is in themselves, having died from some other cause before reaching the period of life most liable to cancer; and, in many cases, a parent may have died of a cancer, the true cause of death being unknown to the child, who becomes afterwards the subject of cancer.

We now turn from statistics—which must be regarded in the highest degree unsatisfactory—to individual instances, of which that recorded by Broca‡ is probably the most remarkable. Of twenty-six individuals, the descendants of Madame L., to the third generation, fifteen died of cancer. Broca computes the influence of hereditary tendency to cancer in this family in the following manner: calculating the death-rate from cancer in France as at most 4 per cent. in persons over 30, therefore, of twenty-six persons over 30 taken at random, a slight proportion over one would be cancerous; but, in the twenty-six descendants of Madame L., fifteen died of cancer; therefore the influence of heredity multiplied the chances of cancer by fifteen.

In regard to the heredity of cancer, the opinion of Sir James Paget must have, even from the nature of his practice alone, the greatest weight. He says, "every year's experience in practice among persons whose family histories are known, makes me more sure that inheritance is the great power in the production of all diseases which are not of distinctly external origin, and, among these, of cancer."¶

The hereditary character of certain innocent tumours is most clearly determined, and more especially of the multiple exostoses. Marle met a case in which he traced the disease through three generations. Sir James Paget gives a case in which a son and his father were affected. "None of this man's ancestors, nor any other of his children, had similar growths, but four cousins, children of his mother's sisters, had as many of them as himself." This last instance is interesting, as it shows that evidences of transmitted tendencies, if absent in direct ancestors, must be sought for among relations of a corresponding generation. Virchow and Otto Weber have each observed cases of enchondromata transmitted through three generations. An instance of hereditary adenoma of the breast came under Broca's observation; a woman and her three daughters were all the subjects of tumours of this description.

I know a young gentleman who has several adenomata of the cutaneous glands scattered beneath the skin of various parts of the body.|| A brother, his father, and a paternal aunt, had similar tumours bc.

neath the skin. Cases have been observed in which the common wen or sebaceous cyst on the head was hereditary. Glioma has been observed in many members of the same family; viz., in four children out of a family of seven, and in four children of the same mother. Moles and naevi are also hereditary, and this, in some instances, extends to their site.

These facts, if they show nothing further, at least prove that the disposition to tumour-formation, however originating, is distinctly hereditary in certain cases; but it is as impossible to say how far heredity extends, as, on the other hand, to fix a limit to a tendency to reversion in these abnormalities.

There appears to be no fixed rule of transmission of tumours to any particular part or organ; but the same variety of morbid growth usually appears in the offspring, although perhaps in a different part.

Facts at present existing tend to show that, if organs especially predisposed to cancer be the seat of the disease, it will more commonly be transmitted to the same part in the same sex; and, in any case, the disease will be more likely to affect the same organ in persons of the same sex. Among sixty-one cases taken from Sir James Paget's note-book, Mr. Baker found that in twenty-seven the cancer in the offspring was in the same part as in that of the parent or grandparent; in thirty-four it was in a different part; but in the first-named group the breast and uterus were exclusively affected. Of the fourteen females who died with cancer in Broca's case, in nine the disease affected the breast, four the liver, and one the uterus; and in the only male who was cancerous the disease was situated in the stomach. Sibley met with a family in which a mother and five daughters had cancer of the left breast. Sir J. Paget observed cancer of the uterus in three generations—in a grandmother, mother, and daughter.

On the other hand, cases occur in which different organs are affected in almost each individual; but these are probably the exception, and the hereditary character of the tumours is open to doubt; perhaps the tendency may have been modified, in such instances, by a "cross" with a family predisposed to tumours in another part. In a case related by Sir James Paget, a lady had cancer of the stomach, her two daughters cancer of the breast; and, of eight grandchildren affected, in two the disease was situated in the breast, in two others in the uterus, and in the remaining four in the bladder, axillary glands, stomach, and rectum respectively. Warren saw cancer of the breast in a son, two daughters, and two grandchildren of a man who had epithelioma of the lip.

Very few facts* can be brought forward indicating a change or transmutation in the character of a tumour in transmission. Sir J. Paget records one in which the three daughters of a lady with scirrhus of the breast suffered removal of the breast for what was probably rapidly growing adeno-sarcoma.

The following case lately fell under my own observation. A female, aged 46, was admitted into St. Bartholomew's Hospital with a recurrent sarcoma of the breast. The following family history was obtained from her. A grandfather died with a tumour in the throat. Her father had a tumour removed from his cheek forty years before his death; it did not recur. A brother, then aged 46, had a tumour removed from his cheek when six years old. Her two sisters each had a tumour of the breast. One sister had a tumour, probably a sarcoma, of the left breast, of two years' duration; she was still living, but the tumour was rapidly growing, and her health was becoming affected. In the other sister, aged 48, a tumour had existed in the right breast for sixteen years, which was not growing, and she was still in excellent health; it is therefore most probable that this tumour was an adenoma.

From the instances of hereditary multiple exostoses, fibrous, fatty, and glandular tumours, and from the occurrence of transmitted cancers in different organs in individuals of the same family, the conclusion perhaps may be drawn, that a tendency to tumour-formation is sometimes diffused throughout a system of the body, such as the osseous, cutaneous, glandular, or epithelial, as the case may be; and that in cancer the morbid growth will be more likely to form in the organs most predisposed to cancer in each sex—viz., the breast and uterus in women, and the lips, tongue, or stomach in men.

A belief in the heredity of tumours does not necessarily imply an adhesion to the doctrine of their constitutional origin, premising that by the term constitutional a disease such as gout is signified, in which an error of assimilation or elimination leads to accumulation of urate of soda in the blood and its deposition in those parts, the nutritive condition of which is most favourable for its reception. It is true that when the cancer-elements, probably the nuclei of

* Von Winiwarter's statistics, as regards the influence of heredity, are open to the objection that the cases were drawn entirely from hospital patients, from whom an accurate and complete family history cannot be expected. Thus, in Mr. Baker's tables, the percentage of cases of cancerous inheritance was 37.4 among the private cases, against 17.9 among hospital patients.

† *St. Bartholomew's Hospital Reports*, vol. 14, p. 217.

‡ *Tumours*, vol. i, p. 155.

¶ *Clinical Lectures and Essays*.

|| *Trans. Path. Soc.*, vol. 33, p. 336.

* Mr. Hutchinson has, I believe, cited some other cases in his unpublished lectures delivered at the Royal College of Surgeons.

cancer-cells, have become mingled with the blood, they may in a similar manner be deposited in different organs. But the analogy does not reach further, for in gout, the origin of the disease is probably functional, not structural, and may be referred to a faulty action of one, or more probably a whole group of organs. Cancer and other tumours must be considered as local aberrations in the structure of the part affected. When looked at in this light, the transmissibility of cancer or tumours in general is no more surprising than that of any other structural peculiarity or disposition, such as form and feature, colour, or the still more remarkable inheritance of habits, gait, and mental disposition. Or, again, than of certain local diseases and malformations which have been shown to run in families, such as hydrocele, hernia, hare-lip, club-foot, and supernumerary digits. For we might just as well attribute the form of the nose, or the colour of the eyes or hair, to a constitutional cause as the formation of an exostosis, a fatty tumour, or even a cancer. Even if the tendency to abnormal growth be diffused throughout different parts of a whole system such as is observed in the multiple exostoses, enchondromata, or fibromata, it is still localised in the cellular elements of a certain tissue.

The arguments supporting the doctrine that cancer is the result of a constitutional diathesis, or "the local manifestation of certain specific morbid states of the blood," chiefly rested on the frequent recurrences of malignant tumours after removal, and their tendency to multiply by dissemination throughout the system. In the absence of evidence of the transmission of tumour-elements by the blood-vessels and lymphatic vessels, it was most natural to suppose that the primary and the secondary disease were the result of the same morbid condition of the blood. The true explanation was found by Virchow, who taught that the general dissemination of tumours was, as he termed it, a deuteropathic phenomenon, that is, secondary to the formation of the tumour itself, and "the result of the introduction into the circulation of elements derived from the existing tumour."

This doctrine was one of the chief steps towards the establishment of the local origin of tumours, which is now supported by the following facts.

1. All tumours are the prototype of the adult or embryonic condition of the tissue or organ in which they originate, or from which they are derived.
2. The secondary formations are a more or less exact imitation of the primary tumour, which could not well be the case unless some of its formative elements were directly transferred to the new locality. Further, such a transference is proved by the occurrence of tumour-emboli.
3. Malignant tumours do not invariably recur after removal.
4. There is no indication of the existence of a general nutritive disturbance known as cachexia, preceding the formation of the malignant tumours, which might be taken to indicate an abnormal condition of the blood.
5. Many distinctly localised abnormalities, such as moles, nævi, warts, etc., which are physiologically and structurally imperfect, are especially liable to tumour-formations.
6. The heredity of tumours is not at variance with the theory of their local origin.

A belief in the local origin of tumours has led to many attempts to explain their formation by accidental causes acting locally, such as injury and inflammation or irritation.

Statistics collected by Tanchou, Marc d'Espine, and Virchow himself, showing the greater frequency of cancer in the stomach, rectum, uterus, and in certain special parts of these organs, led to the foundation of the theory of irritation by Virchow. He observes "that all the organs covered with a soft surface, which are frequently in contact with foreign bodies, develop tumours more often than those which are enclosed in the interior of cavities". And he continues: "if one goes further, that the malady affects precisely most often those points which are the most exposed by their situation to bruising and irritation, such as the lips, œsophagus, orifices of the stomach, rectum, and os uteri."

An injury, irritation, or inflammation is not rarely the precursor of the manifestation of a cancer, and therefore any attempt to explain the origin of malignant tumours must also account for the manner in which these act as exciting causes. Of all the tumours, the epitheliomata most commonly originate in connection with some form of irritation. Among 34 persons affected with epithelioma, Sir James Paget found that 19 were aware of an injury or a previous morbid condition of the part. A similar history, though in a lesser proportion, is also obtainable from the subjects of other

forms of tumour. The statistics of F. Boll,* taken from 344 cases of cancer operated on in Langenbeck's clinic, show that in 42—viz., 12 per cent.—a traumatic cause preceded their formation. Oldekop found, among 250 cases of cancer of the breast in Esmarch's clinic, that in 18 only a history of injury was given; in 4 cases the cancer-formation immediately followed the injury; but in 36 cases the patient had been affected with inflammation of the breast. Calculating the percentage from 103 patients who had borne children, and were thus in a position to have acquired puerperal mastitis, he found that 34.9 per cent. of women with cancer of the breast had been affected with inflammation of the breast at some time previously.† It is true that the largest percentage from these last statistics still show a greatly preponderating proportion of cases in which no such exciting cause existed. For example, in Boll's statistics, these amount to 88 per cent. Any doubt, however, that may arise as to the influence of inflammation and irritation as occasional exciting causes of cancer, especially epithelioma, must be at once dispelled when particular instances are called to mind.

Soot or chimney-sweepers' cancer is the most familiar example; it is said to be much less common now than formerly, when boys were made to climb the chimneys. The loose and folded character of the skin of the scrotum, offering a surface to which the soot readily clings, and its liability to friction against garments, render this part the almost exclusive seat of the disease; but it also occurs on other parts of the body, for instance, the skin of the neck, or the back of the hand, as in the case of a gardener, related by Sir James Earle.‡

Epithelioma of the scrotum has also been observed in stokers and other mechanics whose skin becomes begrimed with coal-dust. Soot or coal has, however, no specific action, for I have seen an instance of the disease in a mason. The first effect of the irritation is shown by the appearance of a crop of warts, which do not differ from ordinary papillary growths. After existing sometimes for a long period, they become ulcerated, and then rapidly assume the characters of epithelioma.

Again, the great frequency of epithelioma of the lip and tongue in males has been generally ascribed to the prevalent habit among the lower orders of smoking short unwaxed clay pipes. Mr. Hutchinson§ found that, in 110 cases of epithelioma of the lower lip occurring in hospital patients, 106 were males, and four were females; of the females, two had contracted the habit of smoking. That the constant use of a clay-pipe is capable of producing an appreciable tissue-change, is shown in the lower lips of inveterate smokers of clay-pipes, where a whitish smooth patch, a slight callosity, or even a groove from atrophy, may be observed at a point shown to be that on which the pipe rested by the corresponding worn teeth.

Epithelioma of the lower lip is also met with in those much exposed to the weather, and a history of long continued and often repeated cracking of the part, from the moisture of the saliva, can usually be obtained; this is sometimes followed by the formation of a small wart, subsequently developing into epithelioma.

An epithelioma of the tongue is very commonly attributed by patients to the irritation of jagged teeth.

Epithelioma of the glans penis is almost invariably associated with congenital phimosis, and consequent irritation from retention of decomposed secretion.

An ordinary corn on the foot, or a callosity on the tongue, may, after existing some years, become warty, and develop epithelioma.

The long continued chronic inflammatory processes affecting the mucous membrane of the tongue very frequently give rise to epithelioma. The condition known as smooth-tongue commonly results in epithelioma; this affection is distinctly of a chronic inflammatory nature, and has been often attributed to excessive smoking and syphilis. Again, ichthyosis of the tongue possesses a similar and even stronger liability; for, among fifty-four cases of ichthyosis collected by Dr. Sangster¶, "30 per cent. eventuated in epithelioma after an average duration, in eight cases, of twenty-three years"; and, of

* *Die Princip. der Wachsthum*, Berlin, 1876.

† This proportion is probably somewhat too high, for it was not in all cases stated which breast had been inflamed. In von Winiwarter's cases, the number was lower—viz., 20 per cent.

‡ Pott's *Works*, ed. by Earle, vol. iii, p. 183, 1808.

§ "The Local Origin of Cancer," *Medical Times and Gazette*, 1881, p. 92.

¶ This has been also observed by von Winiwarter, who gives tables showing the very large proportion of persons affected with cancer of the lower lip, who either worked in the open air, or lived in the country; he estimates them as over 71 per cent.

¶ *Trans. Path. Soc.*, vol. xxxiii, p. 107.

forty-three cases of cancer of the tongue tabulated by von Winwarther, "psoriasis had preexisted in at least ten.*"

A simple ulceration of long standing may give rise to epithelioma; and Mr. Hutchinson has drawn attention to the fact that syphilitic ulcers of the tongue may become insensibly epitheliomatous, if allowed to remain unhealed.

Other instances of cancer following chronic inflammation are met with in the glandular organs and mucous membranes, such as the so-called eczema of the nipple, the association of which with cancer of the breast was pointed out by Sir James Paget,† who has also observed that chronic indurations of the breast sometimes become cancerous.

The statistics already quoted show that inflammation of the mamma is a common precursor of cancer. In rare cases, the irritation of calculi in the gall-bladder, kidney, and urinary bladder‡ may apparently excite the formation of a cancer.

Similar instances of tumour formation, in connection with an injury or chronic inflammation, are observed among the sarcomata, especially of the bones. A slight injury to a bone is occasionally followed by a rapidly growing sarcoma, sometimes exhibiting the heat and redness of inflammation; to these cases attention has recently been drawn, under the name of traumatic malignancy. And in most museums, specimens of sarcomata of bones may be found, which have developed after a fracture or a blow; cases of tumour formation in callus also have been recorded.§

Chronic inflammatory, and also some atrophic processes in bones, resembling mollities ossium, are occasionally associated with sarcoma.¶

Let us now turn to the microscopic appearances observed in cases of cancer, preceded by a chronic inflammatory, or "irritative" process, as it has been called. These show that the antecedent process is of a chronic inflammatory nature, and that the resulting hyperplasia passes insensibly into the tumour-formation.

A general thickening of the skin of the scrotum, and even of the perineum, may be observed in cases of chimney-sweeper's cancer; this is produced by thickening of the epithelium, and a slight indurating of its interpapillary processes into the corium, which is infiltrated with leucocytes. The changes in the earlier stage of ichthyosis of the tongue are also indicative of an inflammatory hypertrophy, consisting in a thickening of the superficial epithelium, and a slight elongation of the interpapillary processes, with infiltration of the submucous connective tissue, with abundance of leucocytes or indifferent cells. Such a slight hypertrophic ingrowth of epithelium, gradually increasing, leads to the formation of club-shaped or irregular processes of epithelium, dipping deeply into the submucous tissue, and containing "cell-nests." In both of these cases, a direct transition is observed, from the simple inflammatory hypertrophy of epithelium to the widely extending ingrowth constituting epithelioma; and it is quite impossible to say where the inflammatory process ends and the malignant disease commences, the latter being apparently the direct outcome of the former.

When the ingrowth of epithelium in these cases has attained a considerable extent, the epithelial cells undergo certain characteristic changes; they become enlarged, irregular in shape from mutual pressure, sometimes multinucleated, and numerous cell-nests make their appearance; the small cell-infiltration of the connective tissue increases, and the normal distinct boundary line between the epithelium and the subjacent tissue becomes blurred, the apices of the ingrowing epithelial columns gradually fading into the small cell-infiltration.

The changes in mammae, affected with eczema of the nipple, are somewhat analogous to those observed in ichthyosis of the tongue. The superficial intractable ulceration of the nipple is, in the majority of cases, evidently inflammatory; and it is accompanied, as Mr. Butlin found, by a proliferation of the epithelium of the ducts, and infiltration of the tissue in their vicinity with indifferent cells. This proliferation of the cells lining the galactophorous ducts may, probably, be considered in some measure analogous to the overgrowth of superficial epithelium in ichthyosis. The subsequent changes are also similar, consisting in the projection of buds of epithelium from the walls of the ducts into the surrounding infiltrated connective tissue; these buds grow into tortuous columns, which constitute the cancerous new formation.

The formation of the cancer in these cases may perhaps be largely ascribed to the long continued nature of the irritative process, for it may be supposed that infinitely numerous successive generations of cells, formed under altered conditions as regards nutrition from excess of blood-supply, might gradually become changed in their nature, and endowed with a more active power of growth, together with the capacity of living in the connective tissues. It must also be remembered that the small cells, infiltrating the subjacent tissues, are identical with granulation-cells, and thus a granulation-tissue may be said to exist into which the epithelial cells grow. For an instance of the capability of epithelial cells to grow in granulation-tissue, I have only to refer you to skin grafting. The important fact, however, must not be lost sight of, that cancers following some inflammatory or hypertrophic process, offer no exception to the general rule in the age at which they occur; although the antecedent disease may have existed many years.

In the formation of tumours in connection with some irritation or inflammation, so many factors exist regarding the nature of which little is known, that it is only possible to speak in the most general terms of the part they severally take in the production of a tumour. Probably an abnormal constitution of, or tendency in, the tissues of the part exists in all cases; it manifests itself in the formation of a papilloma or in the occurrence of an inflammatory hypertrophy such as ichthyosis from slight exciting causes; or in the persistence of a chronic inflammatory process, such as eczema of the nipple or smooth tongue, the exciting cause of which is equally disproportionate to the result. And the tendency to tumour formation in imperfectly formed parts is obvious in cases of naevi, angiomas, moles, congenital warts, and in parts affected with congenital hypertrophy.

In proportion as the abnormal tendency is slighter will the exciting cause be more apparent; and in all cases the increased blood-supply resulting from the inflammation or irritation doubtless plays a most important part. The different manner in which the tissues of individuals react to irritations is well illustrated by Otto Weber.† He relates the case of a *post mortem* room porter, whose hands were covered with warts, and wherever he pricked himself in handling the corpses a fresh wart appeared; in another man, the same irritation led to the formation of numerous ulcers. A predisposition is even observed in the formation of the fibrous tumours in the lobules of the ears from the irritation of ear-rings, for they are usually symmetrical,* and have been observed in individuals of the same family.

The tendency to overgrowth of epithelium presumed to exist in the cases under consideration, and excited by increased blood-supply, may be roughly compared to the latent properties of the cells forming the adventitious buds in plants. These buds may be produced from any part of the cambium layer, no trace or rudiment of them having previously existed. After injuries to branches, new buds grow immediately below the severed extremity, their formation being probably due to an increased supply of sap to that part; and pollarded willows become immediately covered with buds. Irritation from parasites may also cause the formation of hundreds of buds. The analogy between the adventitious buds of plants and the growth of epitheliomata is rendered more striking by the fact, to which Sir James Paget‡ called our attention, that the tumours of plants are buds, which have become displaced inwards instead of growing outward into shoots. In precisely the same manner, the epitheliomata are produced by epithelial cells, which have grown inwards, instead of being pushed outwards, and developing, on the squamous epithelial surfaces, into a protective covering of laminated cells. The comparison may be carried still further. The cells of the cambium layer of plants doubtless possess a latent tendency to growth and higher differentiation, exhibiting itself, however, only on the application of a stimulus. In the same manner, the cells of an individual predisposed to cancer may be inferred to retain a latent tendency to growth above those of an individual not in the same manner susceptible, yet, as in the cambium layer of plants there may be no morphological differences. The same comparison will hold good for other varieties of tumours.

* *Chirurg. Erfahrungen und Untersuch.*, p. 285.

† See *Cat. St. Bart. Hosp. Museum*, Nos. 3264 to 3266.

‡ *Elemental Pathology*, p. 31.

* *Op. cit.*, p. 207.

† *St. Bartholomew's Hosp. Rep.*, vol. x, 1874.

‡ See *Trans. Path. Soc.* Vol. xxxii, p. 139.

§ See Lücke (*Op. cit.*, p. 62) and *Cat. St. Bart. Hosp. Museum*, No. 2454.

¶ See H. T. Butlin (*Op. cit.*, p. 106.)

A CURIOUS PROCLAMATION.—Some alarm has been caused in Burslem in consequence of the crier being employed by a chemist in the town to announce that a customer had by mistake been supplied with poison instead of magnesia. It is not yet known whether the person who made the purchase has been made aware of the mistake.