well be combined. Discussing the size of the unit of health administration, he said this might easily be made too large. Perfect co-operation could be arranged between a central city with highly equipped hospitals and medical experts and the surrounding county units—a form of co-operation which it should be the duty of the Government to encourage.

Dr. H. S. BEADLES (Romford), representing the Poor Law Commission Committee of the Association, stated that unification, and not merely co-ordination, of all health services was already the settled policy of the Association, but such unification must begin at the centre, the Government departments concerned, and local health committees must not be the committees as now known. They must be strengthened by the co-option of representatives of the medical profession nominated by the local practitioners on the lines of the present Insurance Committees, with an Advisory Medical Committee.

Dr. H. SCURFIELD (late M.O.H., Sheffield) favoured experiments in the direction of unification by means of co-operation, as had already been done in Aberdeen, Gloucestershire, Essex, and Cardiff, so as to achieve a single public medical and nursing service with the consequent saving of time and money. He agreed with Professor Collis that the factory health service was a special one, and advocated closer co-operation between this service and the local public health department.

Dr. D. MCKAIL (Glasgow) expressed the view that all the confusion that had arisen was the result of ignoring the general practitioner. He thought that no one should be admitted into the ranks of the public health service without

at least three years' experience of the "rough and tumble" of general practice.

Dr. E. H. SNELL (M.O.H., Coventry) said it took the allied armies during the great war some three years to discover that success could only be achieved under a unified command. When the public health service learned the same lesson it would achieve the same result.

Dr. W. A. LETHEM (Ministry of Health) emphasized the necessity of a general training in public health work of junior members of the service. The need for this would be increased by any further unification of such services. Difficulty had already been experienced in certain towns on the retirement of the chief official, when it had been found that the subordinates, who were familiar only with the work of one subdepartment, were not qualified to take his place. As the scope of preventive medicine widened it would become increasingly difficult to find men capable of looking upon public health work as a whole, unless an effort was made to train the junior members of the personnel.

Dr. A. S. M. MACGREGOR, in a brief reply, said he thought there was no doubt that the balance of opinion had been in favour of unification. He was himself convinced that some form of amalgamation of existing services was necessary and inevitable, but he could not agree that the factories should be included in any such scheme. In Glasgow a number of factories had already made their own provision for health services, and he was satisfied that this was the right line of development. He believed that the only alternative to a State medical service was "general practice" on a higher plane than had been known in the past.

GROWTH IN ITS PATHOLOGICAL RELATIONS.*

BY

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THE cells of the body having attained during foetal life their destined characteristics of form and function, according to those of the organs of which they form component parts, lose to a varying degree their powers of reproduction. Some tissue cells have lost that power before birth, some retain it as long as life lasts; but, in general, the earlier the time at which complete differentiation of form and specialization of function have occurred, the less these powers can afterwards be displayed. At no time can we say that any normal cell, however undifferentiated, has an unlimited potentiality of proliferation; its bounds and its destiny are set before it by natural factors, of which we have only the vaguest and most imperfect notions. From its behaviour in normal circumstances we are not entitled to assume that it had more than rigidly restricted powers of reproduction, but by our observations of the phenomena of repair we can be certain that some cells at least have a hidden reserve of power, and by cultivating normal tissue cells in suitable nutritive media outside of the body we can demonstrate that they are actually endowed with limitless reproductive powers, which, in whatever way they are controlled, are not exhibited in the living composite organism. Not every kind of tissue cell has been cultivated so far, but since we have succeeded in growing such early and severely specialized cells as those of cardiac muscle, and have seen these cells exhibit their characteristic physiological property of rhythmical contraction, we may safely assume that all kinds of tissue cells have this potentiality. This autonomy is not lawless: each kind gives birth only to cells of the same class and characters; they remain in close communion with each other; they tend to arrange themselves in the pattern that prevailed in the organ from which their ancestors were removed; but when such a colony, accustomed for many generations to its independence, is returned to the animal

body the unrestricted power vanishes at once. It has been claimed that by employing certain agents, which we have used to induce malignant change in body cells, the cultivated cells can so be affected that their reproductive powers will not be restrained even in the environment of the living body, but the claim has not been corroborated. However that be, it is now beyond doubt that tissue cells have inherent powers of limitless growth, and that these powers are kept in check by some inhibitory factor in the body.

Throughout life, in normal physiological conditions, we have tissue cells that are constantly being lost and replaced, and others that in post-foetal existence remain constant, fixed in number, and irreplaceable. The squamous epithelium of the surface and of cavities in communication with it, and the glandular epithelium of the intestinal tube, as well as of certain gland structures, are examples of the former, whilst ganglionic nerve cells serve as a good example of the other extreme. It is true that cells of the former class are quite highly differentiated in form and in function, but bearing in mind that in certain conditions in adult life a glandular epithelial cell may assume the characters of a squamous epithelial cell, though the converse is more doubtful, we may say that the specialization is not absolutely rigid. In physiological replacement the activity is confined to the one tissue, and adjacent tissue cells do not participate, nor is the replacement out of uniformity with the original plan. Whether the connective tissues are normally in this state of continual renovation, or fixed and unchanging, is a question that, in the nature of things, cannot be determined.

In reparative processes following loss by wounds or degenerative lesions the active proliferation of connective tissue cells is such a predominant feature that the regenerative powers of other tissue cells are for the most part masked and overwhelmed; but still it may be said that the latter exhibit the property in inverse relation to the degree of their specialization. At one extreme the epithelial tissues display considerable powers of proliferative regeneration, and at the other the reproduction of such rigidly specialized cells as cardiac muscle and nerve cells is wholly suppressed. There are signs that ordinary striped muscle cells make a feeble attempt at repair, but it can hardly be claimed that they actually multiply. When the injurious

* The opening paper of a discussion in the Section of Pathology and Bacteriology at the Annual Meeting of the British Medical Association at Edinburgh, 1927.

action is repeatedly inflicted—that is, when it becomes a question of irritation—the stimulus induces an exaggerated repair, and the multiplication of cells is excessive. This hyperplasia in the ordinary course of events is temporary, as, owing to the subsequent maturation of the connective tissue cells, with the consequent devascularization, a shrinkage to or below the original limit occurs. That the proliferation of cells should cease when the defect is made good is no less mysterious to us than that they should commence to multiply to fill the gap. In the same process are exhibited the inherent capacity of cells to multiply and the restraint exerted upon them when the original plan has been restored. Sometimes the inhibition is late in coming into operation, as in the case of keloid formation, but the phenomenon of arrest is always evident. As we pass to tumour formations the less do we see exerted this repression of an inherent power in the cells, until in the extreme degree of malignancy the restraint on cell proliferation is almost entirely removed.

The boundaries between reparative growth, hyperplasia, and neoplasia are impossible to define—in fact, a tumour is a localized hyperplasia; nor is there any strict separation possible between benign and malignant growths as a whole. The words “benign” and “malignant” are clinical terms, and though they can often be related to histological appearances in tumours, yet the relationship is by no means invariably close. The gradation of the various processes suggests a difference of degree rather than any qualitative distinction; in short, the cell in neoplasia acquires no altogether new capacity compared with the cell in reparative regeneration. It will follow from this that tumours can only arise from such cells as can regenerate, and the frequency with which cells take part in neoplastic processes will be inversely related to their degree of specialization. But at once we are confronted with the fact that tumours are found composed of cells which do not multiply in adult life. The work of Cohnheim, by laying particular stress on these exceptional tumours, and by referring all tumours to the same origin as he quite rightly attributed to them, has given them an undue prominence. If cardiac and voluntary muscle cells, ganglionic nerve cells, and cartilage cells do not regenerate in post-foetal life, we must either give up our contention or fall back on the explanation that tumours composed of these cells have arisen from them when they were still in an embryonic and less highly differentiated state. In the latter case we may imagine with Cohnheim that such cells were cut off from communion with their kind which went to form useful organs, that they lay dormant with their proper destiny thwarted and their innate powers of reproduction still preserved until such time as some unknown stimulus unloosed them.

Let us examine these disturbing tumours more closely. Cardiac muscle tumours are the rarest of all tumours; they are composed of peculiar cells which here and there display the characteristic striation in parts; they are small in size; they are accidental *post-mortem* findings; they have no malignant characters; and they are doubtless congenital. A peculiar feature of striped muscle tumours which are also pathological curiosities is that they are found mostly in situations where voluntary muscle does not normally exist, and then generally in association with other aberrant tissues, and it has been held that they originate from smooth muscle and not from striated muscle. At any rate, we have no satisfactory evidence of the formation of such tumours from adult striated muscle, and it is generally agreed that they originate from embryonic remains. Rare, too, are tumours composed of nerve cells. Such tumours seldom show malignant characters, and they make their appearance evident at an early age. They are undoubtedly congenital. The retinal neuroma, on the other hand, which betrays its presence in early infancy, is highly malignant. Sometimes it is bilateral and sometimes familial. It is derived from one of the most highly specialized classes of cells in the body, but everything points to its origin before birth. These examples will serve to show that we must suppose a retention of embryonic proliferative properties to explain certain exceptional tumours, but it is as easy to believe that they started as tumours when the parent cells were not rigidly specialized as that they arose in later life from

segregated cells that had lain dormant and docile for years. No one will deny that there are segregations of cells cut off in development and that they are by no means infrequent, but that these isolated communities are more prone than normal adult tissues to neoplasia is open to doubt. Still, experiments on the production of cancer have proved to us that it is possible so to change the nature of epithelial cells that while they may remain for a long time unaltered in microscopical appearance or in behaviour, they will subsequently flare up in malignant proliferation. There is thus experimental evidence that may be adduced in support of Cohnheim's contention. The tendency to explain morbid growths as originating from embryological faults is less pronounced now than formerly. For example, cartilage is a tissue which seldom if ever regenerates, and yet chondromata are not uncommon, and while we must admit a developmental fault in the case of the echondroses, yet for the true chondromata and for the mixed cartilaginous tumours another explanation is feasible. It is probable that the connective tissue cell may form collagen or elastic fibres, or a myxomatous, cartilaginous, or osseous matrix in different circumstances. In pure chondromata the very frequent association of myxomatous and cartilaginous areas is very suggestive, and still more is this the case in the mixed tumours. When we reflect that osseous tissue may be found in arteries and can be produced in them experimentally by painting the vessel with such substances as silver nitrate, and, above all, when a sarcoma can be produced by tar injections in rats which will show areas of cartilage and bone, we have no option but to believe that the connective tissue cell is not unalterably fixed in adult life and may exhibit rather surprising metaplasia.

The reproductive power of cells, as has been said, is in inverse ratio to their degree of specialization; but this is not invariably the case. The cells of the mammary gland multiply in preparation for their most highly specialized function—lactation; and probably also in response to the stimulus of the ovarian hormone. Malignant neoplasia rarely occurs in the male gland, which is not highly differentiated in function. It is remarkable that when mice are inbred for the development of strains with a high incidence of mammary carcinoma, the spontaneous tumours occur only in the females, and if the females are spayed during the first few months mammary tumours do not appear in them. Thus a less functionally specialized epithelium is less prone to neoplasia than one more highly developed—an exception to the general rule. What the ordinary function of the mammary gland may be is unknown: the secretion of milk is certainly a very evident function, but, after all, it is only occasionally that it is called forth. Malignant tumours of the breast are almost as common in barren women as they are in those who have suckled children.

On the other hand, the degree of malignancy in a tumour corresponds with the degree to which the constituent cells lose their functional properties. In the intestinal tract, for example, the secretion of mucin is one, though perhaps not the chief, of the functional activities of the epithelial cells; but in carcinomata arising from these cells it can be shown, by appropriate staining, that this function is very greatly diminished and in extreme cases may be entirely suppressed. The instances might be multiplied, but here again there are apparent exceptions to the rule. In melanotic cancers the intense production of melanin is characteristic, and though in parts of such tumours, indeed sometimes in whole metastatic nodules, the melanin may be largely wanting, and though the impression of abundance may be due mainly to the mass of tissue, yet individual cells would seem to be as densely crowded with the black granules as any normal chromatophore. Despite the great amount of investigation that has been done in the chemistry of malignant cells, there is little or nothing to suggest any qualitative distinction from normal cells, the differences being for the most part quantitative and inconstant. While recognizing exceptions, we may say that the exercise of the reproductive power of the cells is maintained at the expense of their other properties.

The analysis of this inherent reproductive power of tissue cells displayed physiologically, in repair, and in neoplasia,

presents problems of the first magnitude to all biological sciences, and is not the province of any one alone. It would seem as if the same principle were in action in the three phenomena, the resulting reaction being determined by the extent to which some inhibiting process was at work, and in the almost complete absence of definite knowledge of this growth principle the pathologist is thrown back on the study of the inhibitions, how they are removed or how they may be fortified. The older conception, of which Ribbert was an exponent, was that the inhibiting factors were purely environmental: if the restraint of the environment were weakened or removed the cells of a tissue would exhibit their innate property of unceasing multiplication. It has already been mentioned that by cultivating cells in suitable media outside the body this can be demonstrated, and that if these emancipated cells be returned to the animal body the process is arrested, and we might be tempted to conclude that the arresting force was exerted purely by the environment. But if the cells cultivated have been from a malignant tumour originally, the implant will go on increasing, and yet the environment in both cases is identical. From the impasse into which this has led us there are two ways of escape—either to assume that malignant cells have acquired an entirely new property not possessed in any degree by normal, reparatory, or benign tumour cells, or that they have developed in excessive abundance an already existing property. In the former case an easy explanation would be that in the cancer cells there is an extraneous agent, remaining always intracellular, which stimulates these cells to division and multiplies with them. This conception forms the basis of the parasitic theory, which has been rejuvenated by the strikingly original investigations of Gye and Barnard, and still more by their daring, and perhaps somewhat risky, conclusions. If we accept the other idea we shall have to conceive of a growth substance generated by the cells, capable of being stimulated to overproduction. In wound repair we may imagine that there is a transudation of growth substance in limited amount which not only stimulates the particular parenchymatous cells to reproduction but also stimulates the adjacent connective tissue. In neoplasia the stroma formation is even more essential. It is difficult to conceive any other means of local stimulus to connective tissue formation than the outpouring of some factor from the neoplastic cells. So far no one has been able to isolate this hypothetical growth substance, and the evidence for its existence is indirect and of doubtful validity. As is well known, animals may be "immunized" against transplanted cancer by previous treatment with red blood corpuscles, splenic tissue, and other unkillable tissues of the same species, and the only difference that can be detected in the phenomena that follow the inoculation of grafts in the refractory and the control animal is that in the former no stroma formation is evoked. Although it is impossible to find in the refractory animals any of the known serum antibodies, we may imagine that the immunizing treatment has induced the formation of an antagonistic substance which neutralizes the growth substance poured out by the cancerous cells. There is another experimental observation which supports the notion of the outpouring of growth substance. In the transplantation of certain strains of mammary carcinoma in mice and rats sarcomatous transformation of the stroma tends to occur. In ordinary cases the stroma introduced along with the parenchyma in grafts always dies and is replaced by new stroma furnished by the new host, but in these cases the stroma continues to proliferate. That the implication of epithelium of the same kind adjacent to a carcinoma is due to the same thing is much more dubious. But when all is said, we must confess that we have no explanation of the unerring transmission of the acquired property from cell to daughter cell. That growth may be temporarily arrested in malignant neoplasia, even for long years, is certain, but the cells so arrested do not lose their power. Heiman of the Crocker Research Laboratory has implanted a very active carcinoma into the midst of a slow-growing transplantable fibroma of the rat, and in this fibrous prison the carcinoma lives but does not increase, but if it is set free from its bonds, by the cutting up of

the composite tumour or by transplantation into a new host, it demonstrates its malignancy. Here the proliferation is quite arrested, it may be for long periods, but the malignant potentialities of the cells are not destroyed. Must we, then, conclude that there is a fundamental difference between the normal and the cancerous cell, and that the latter possesses some property quite foreign to the other, something extraneous? It is tempting to seek rest for our puzzled minds in such a belief; but when we face the fact that we can induce cells to become malignant by the use of certain carcinogenic agents long administered, and more especially the fact that we can biologically affect cells so that after a long period of normal quiescence they will break forth into malignant proliferation, we must reconcile ourselves to the troubled doubts that may lead us to clearer knowledge.

DISCUSSION.

Professor R. MUIR (Glasgow) said that the cellular proliferation underlying pathological growth constituted a fundamental question. No real explanation of it could be given; at present little more could be done than to analyse and classify the factors concerned in its occurrence. Apart from tumour growth, cellular proliferation was recognized to result (1) from breach of continuity, (2) from irritation, and (3) in the case of certain tissues, from excessive functional demands; cellular hypertrophy being followed by hyperplasia. Each of these must be further analysed. But there were other examples of proliferation which could not be placed under these headings, as, for example, the regenerative proliferation of erythroblasts after haemorrhage and the proliferation of myelocytes in leucocytosis. The question as to what extent definite substances acted as stimuli to proliferation was very important. The excessive growth of certain tissues in hypophyseal superactivity was a well recognized example of such an occurrence, but in connexion with tissue culture it had become a practice to speak of growth-promoting substances, stimuli, or trephones, and to explain the proliferation as the result of their action. It was very important to distinguish essential foodstuffs from true stimuli to growth. In the case of repair of wounds it had hitherto been customary to ascribe growth to the removal of the restraining effect of the adjacent cells. The proliferation occurred when the tissue balance was disturbed, and continued until it was restored. The question was whether the phenomena could be explained on the hypothesis of definite stimuli supplied by leucocytes or other cells. Tissue cultures were unsuitable for determining the matter, as in them the normal cell relationships were wanting, and the fact that embryonic juice promoted proliferation was not enough to show that it was effective by itself. An example was still needed to show that such stimuli could cause proliferation when the relationship of cells was not disturbed. It must be borne in mind also that repair in mammals was the representative of the more complicated process of regeneration in lower vertebrates, which latter in its turn was a reproduction of the phenomena of ontogeny. At present it did not appear justifiable or possible to explain the proliferative processes in repair as being the result of growth-promoting substances alone.

With regard to neoplastic proliferation, it was important to recognize, as regards conditions of occurrence, two types of tumour—namely, that which might result from irritation of previously normal tissues, and that which followed some disturbance of development. The question as to what extent tumours arose from displaced cells or "rests" was a separate matter, but the all-important fact was that there were various kinds of tumour—such as neuroblastomas and blastocytomas—which must arise from cells which had not reached the adult state and which were sometimes multipotent. The recent work on tumours of the central nervous system illustrated this in a striking way, as it appeared that a growth might originate at any stage in the differentiation of the original medulloblasts. Again, a simple hepatoma resulting from congenital abnormality might become malignant and give rise to metastases; in cirrhosis of the liver the compensatory hyperplasia of the liver cells might pass on to neoplastic proliferation, and,

again, malignant properties might appear. What might be called the life history in the two instances was widely different, while the end-result was the same. Any explanation of tumour growth brought forward must apply to the two types.

Professor J. SHAW DUNN (Manchester) thought that in spite of greatly varying cellular structure there was much in common in the general biological aspect and behaviour of simple tumours, while the malignant forms, though derived on the one hand from connective tissue cells, on the other from epithelial, and differing in intimate architecture on that account, showed more features of similarity than of difference, and were clearly separable from other active proliferative processes of known causation. The whole group of tumours retained a certain uniformity of general idea, which was borne out by the not uncommon occurrence of linking forms and of simple growths which ultimately became malignant. It appeared reasonable to suppose that, if new growths had not a common cause, yet there must be in the genesis some general etiological principle which would link together this group of morbid activities, somewhat as the conception of organismal infection linked together the diverse group of bacterial diseases; but a review of the etiological factors known to be concerned in neoplasia showed little or no suggestion of any such unifying consideration. Recent experimental work with certain chemical substances had shown that tumour growth, often with malignant characters, could be induced after sufficiently prolonged application, and this not only provided a direct explanation of a limited number of human growths, the industrial cancers, but suggested a similar explanation of some tumours of the alimentary tract where the irritating agents were not definitely isolated. Pre-existing damage was another factor that in some way led to cancer formation. Cancer of the liver was very rare apart from hepatic cirrhosis, and it developed on the latter in at least 3 per cent. of cases. Cancer of the kidney was associated with pre-existing renal lesions. All were familiar with the development of epithelioma on scars. Again, the development of malignant tumours from simple tumours was not uncommon, and it was hardly possible to escape the conclusion that the more serious condition was predetermined in the earlier cellular activity however that, in its turn, might have been caused. The influence of true hereditary factors in the production of tumours was evident from the occurrence of such malignant forms as retinoblastoma, more simple tumours as angioma and neurofibroma, and simple tumours liable to become malignant, such as polyposis coli. In xeroderma pigmentosum the coincidence of two factors would appear to be necessary—an hereditary susceptibility; and the irritant action of the physical agency, sunlight. Whatever were the factors so diversely concerned the end-result was the same in all cases, and it was hardly legitimate to ignore the implications if an attempt was being made to discover any general etiological principle. The question as to whether this principle might be of the nature of a special type of organism had not been raised there, as there was no evidence available in relation to human or even mammalian growths which pointed definitely in that direction. The production of some tumours by external chemical agencies, and the predominant part played by true hereditary factors in the genesis of others, were facts which did not encourage belief in a specific organismal cause. The available data rather suggested that enlightenment must await a more complete knowledge of the conditions regulating cellular proliferation and the harmonious relationship between different kinds of cells in the tissues.

Professor E. H. KETTLER (Cardiff) believed that it was generally assumed that malignant and innocent tumours and simple hypertrophies were merely exaggerations of the normal physiological process of growth, but he thought that it might be doubted if these phenomena were really comparable, or even that all forms of malignant growths were examples of the same process. Was it justifiable to regard growth or enlargement as necessarily the same thing as cell multiplication? What was the difference, if any, between local and general growth? Even if these forms

of protoplasmic activity were fundamentally similar, it must be admitted that they might be due to several different causes. The power to grow might be latent, but it was inherent in all living matter, and might manifest itself at any time in response to an appropriate stimulus. It would scarcely seem necessary to seek for any further explanation of the ordered enlargement or growth of the developing individual than this inherent property of the cells, but even this form of growth was subject to controls. It might, for example, be inhibited or increased by the presence or absence of various hormones. The phenomenon, therefore, was not simply an example of the inevitable performance of an inherited function, whether spontaneous or in response to stimulation; in adult life this became even more apparent. A substance which stimulated cells to multiply was produced in the degeneration of cell protoplasm, and presumably the cellular proliferation by which the healing of wounds was brought about was due to its presence. Its action could be demonstrated *in vitro* by the technique of tissue culture, and its presence had also been shown in the intact malignant cell. The suggestion was that the malignant cell differed from the normal in that there existed within it the growth-promoting substance which normally was found only when cell protoplasm broke down. If this view was correct it was obvious that malignancy was not merely an exaggeration of the normal physiological process of growth, for the malignant cell had definitely acquired a new property. It was scarcely likely that the matter was so simple as this. The development of a malignant new growth appeared to be accompanied by a constitutional change, according to Murray's experiments, so that the other tissues of the body no longer reacted in the normal way to cancerogenic agents. Even in the simple healing of wounds the presence of some other controlling force besides the growth-stimulating substance seemed probable, for how otherwise could be explained the nice adjustment of the covering epithelium in the healing of superficial wounds?

Though it was necessary to guard against too wide an application of the results of tissue culture, some observations by the late Dr. Strangeways seemed highly significant; he had pointed out that the cell was at its most plastic and impressionable state during division, and had suggested that cell division was the process by which the cell could best reorganize its protoplasm so as to adapt itself to altered physiological conditions. If the cell was in a state of physiological equilibrium it remained quiescent or vegetative, but should this equilibrium be upset, usually by alterations in environment, it adapted itself by such a mingling and reorganization of its protoplasmic molecules as could only occur in the process of division. From this point of view, therefore, the growth or enlargement of a tissue might be the accidental result of a cellular proliferation which itself was purely protective.

Professor M. J. STEWART (Leeds) stated that a careful scrutiny of necropsies during many years for the presence of adrenal rests and epithelial heterotopias of the stomach had shown that such occurrences were by no means uncommon; that they were unduly predisposed to tumour formation, in comparison with other tissues, could not be conceded. It was a different matter, however, to maintain that Cohnheim's theory thereby failed. It had to be admitted that no direct proof of Cohnheim's hypothesis had as yet been forthcoming; in the nature of things it seemed doubtful if this would ever be attainable. Yet this hypothesis remained an attractive one, especially to explain the origin of teratomas in situations other than the sex glands. It was not suggested that the hypothesis alone was sufficient, but it might well cover a part of the truth; in addition some factor or factors must be predicated to account for the onset of proliferation. Most of all was some additional explanation necessary in respect of malignancy—such, for example, as Adami's "habit of growth theory." It had been maintained that the functioning cells of fully differentiated tissues were no longer capable of proliferation, and that all loss of tissue, whether by accident or from wear and tear, was made good by the multiplication of physiologically hypoplastic cells, these constituting the germinal and regenerative centres of the

tissues. That was merely a generalization from what must obviously occur in the maintenance, for example, of surface squamous epithelium, where proliferation was confined to the undifferentiated germinal layer. It did not seem a great step from such a conception to Cohnheim's theory of cell-rests in relation to cancer. That cancer cells were able to remain in the tissues for considerable periods without appreciable proliferation was clearly shown by the experiments quoted by the opener of the discussion and by the numerous instances on record of metastases remaining dormant and inactive over many years.

Professor J. LORRAIN SMITH (Edinburgh) said that while recent investigation of tumour growth had dealt chiefly with etiology, the progress made had revived the question of the nature of the process. The discussion of this aspect of the subject had long been familiar in the contrast drawn between tumour, hypertrophy, repair, and regeneration. More recently cytologists had taken up the study of cell differentiation, especially in relation to changes in cytoplasm. The application of biological methods to corresponding changes in tumour cells was a problem for future investigation. A certain approach to it had been made in Unna's study of skin cancer. Adopting as a basis of classification the architecture of the normal skin, he opened up a field of investigation. In the lower layers of the rete mucosum the cells maintained active division and afforded an example of continued growth. On division of the cells in these basal layers the growth of the skin depended. Two types of cell were produced—one which remained a basal cell with power of continuous division, and another which passed from the basal layer to become a prickly cell, finally receiving the form and composition of a surface squamous cell. With this differentiation the power of division was gradually lost. There was, therefore, a double product from the original division. The architecture of the skin resulted from the production and maintenance of the two types of cell. In the one type there was continued division originating new basal cells, and in the other there was differentiation in the direction of keratin scale formation, and the power of division was lost. The haemogenetic tissue afforded another clear example of biological architecture. The primitive blood cell in division, continuously maintained, produced cells which remained primitive blood cells, and, at the same time, cells to become gradually transformed into red corpuscles; these, like the squamous cells, had lost their power of division. In cancers of the skin, as Unna had shown, the normal architecture was disturbed in a considerable variety of ways. With this principle of interpretation as a guide he reached a classification of cancer of the skin according to the type of disturbance. Whatever might have been the result of recent work on etiology, it must be acknowledged that it had provided a new means of investigating experimentally the process of cancer growth in relation to the process which in the normal tissue resulted in its biological architecture.

LACRYMAL OBSTRUCTION: ITS NASAL ORIGIN AND INTRANASAL TREATMENT.*

BY

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THE exact pathology of lacrymal obstruction is still somewhat obscure. The part played by diseases or abnormalities of the nasal passages and accessory sinuses is considered to be more important than descending infections from the conjunctival sac. According to Kühnt, nasal diseases are responsible for 93.7 per cent. of cases of lacrymal obstruction, while a leading textbook on ophthalmology quotes as causes: inflammatory conditions of the nasal mucous membrane; simple catarrhal tuberculosis, and syphilis; ulcers of the nose, tuberculous, syphilitic, and lupoid; and nasal tumours, especially polypi blocking the lower orifice of the nasal duct. Brückner, although he regards nasal causes

as uncommon, admits that in the majority of cases diseases of the lacrymal apparatus are nasal in origin.

The purport of this paper is to report the results of an investigation into the nasal condition of 120 cases of lacrymal obstruction observed by me during the last four years through the kindness of my colleagues at the Manchester Eye Hospital.

Incidence.

The susceptibility of the female sex to lacrymal obstruction is a well known fact, and has, I believe, never been satisfactorily explained. In the present series 102 cases occurred in females and 18 in males.

The following table giving the age incidence of the disease shows that the greatest number of cases occurred between the ages of 30 and 60, but that of the three decades in this period the numbers of cases were practically equal.

1-10 years	...	...	...	...	...	4 cases
10-20	"	...	...	...	...	5 "
20-30	"	...	...	...	...	12 "
30-40	"	...	...	...	...	26 "
40-50	"	...	...	...	...	34 "
50-60	"	...	...	...	...	25 "
60-70	"	...	...	...	...	9 "
over 70	"	...	...	...	...	3 "

The oldest was 74 and the youngest 6 years. The shortest duration of symptoms, such as epiphora, was six months; the majority, however, had presented symptoms for two years or more.

Etiology.

Injury.—Any injury in the region of the inner canthus producing either a fracture of the infra-orbital margin or of the frontal process of the superior maxilla may mechanically obstruct lacrymal drainage. Similarly a chronic traumatic periostitis in the region of the lacrymal fossa following injury without fracture might be an etiological factor. A definite history of injury was obtained in only 5 cases (4.1 per cent.): 2 developed an abscess over the sac immediately following the injury, with subsequent epiphora, whilst 3 presented a definite scar, and in all the epiphora began immediately upon receipt of the injury.

Breadth and Width of Nose and Nasal Passages.—Whitnall has shown that the breadth of the lacrymal fossa varies with the shape of the skull, being wider in the brachycephalic and narrower in the dolichocephalic types. The lacrymal fossa is deepest at its base where it joins the naso-lacrymal canal, but Gérard has found that the canal is narrowest at the orbital opening, its lower end under the inferior turbinate body being wide and almost funnel-shaped. Moreover, the direction and inclination of the lacrymal passage is dependent upon the configuration of the facial skeleton, being influenced by the breadth of the bridge of the nose and of the nasal aperture, as also by the development of the maxillary sinuses. Testut showed that, seen in profile, the lacrymal fossa and canal slope gently backwards, forming an angle of 15 to 20 degrees with the frontal plane, while, viewed from in front, the fossa slopes outwards towards its lower end and the canal slopes inwards towards its nasal opening, together forming a curve the concavity of which is directed inwards, the summit being near the upper orifice of the canal—that is, the orbital opening. This lateral obliquity of the medial wall of the fossa is more marked in narrower noses. A narrow lacrymal fossa or an acutely curved lacrymal passage may more readily predispose to obstructive symptoms. The breadth of the nose and the width of the nasal passages were found to be distinctly narrow in only 13 cases (10.8 per cent.), and in only one of these was the epiphora bilateral. The intranasal prominence of the lacrymal groove was a distinct feature in all these cases. In 16 cases (13.3 per cent.) the nose and nasal passages were noted to be unusually wide, and the epiphora was bilateral in 6 cases. In none of the series was the size of the nasal passages dependent upon any deviation of the nasal septum.

Nasal Pressure Deformities and Reflex Neuroses.

Onodi considers that "the ostium of the nasal duct may be wholly or partially occluded by hypertrophy of the turbinates, by polypoid and papillary degeneration of the anterior end of the inferior turbinate, by foreign bodies, dental cysts, syphilitic and tuberculous lesions, etc." And

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