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ON CANCER,

AS ILLUSTRATED IN

ICHTHYOSIS OF THE TONGUE AND ALLIED DISEASES RESULTING FROM PROLONGED LOCAL IRRITATION.

By JAMES F. GOODHART, M.D.

It may seem unnecessary, nay even prejudicial, to add to an already overstocked literature of new growths by enumerating individual opinions of a hypothetical nature as to the origin of tumours. This seeming unadvisability will not be diminished when we reflect upon the extreme complexity of the subject and that this complexity necessitates the consideration of such a multiplicity of details that it becomes almost impossible to give the requisite attention or, indeed, any at all to some points, and therefore to take estimate of all facts that bear upon the case. It is difficult to place oneself in that attitude of thought which shall allow amplitude enough to embrace all the contingencies upon which in any individual case "malignancy" depends. Yet if this be not done no adequate conception of *cancer*, using that term to signify all infiltrating growths, can be formed.

The prolonged debate on cancer during the last session of the Pathological Society was an apt illustration of this. Two contending armies came on to the field, the constitutionalists and the localists, each apparently prepared to fight out for convictions which admitted of no compromise. But as speaker

after speaker rose on this side and on that and used forcibly and well the points by which he was more especially impressed, thereby unearthing, I suppose, and playing upon strings of experience and thought with which others were familiar, but which lay at that time in buried memories, the one school apparently began to think that the doctrines of the other were after all not so very pernicious, nay that they even had some truth in them, and the opposing forces finished, as it seemed, by fraternizing on the field of battle. Reading through the report as published in the Society's 'Transactions' one cannot but be struck with this fact, that a comprehensive exposition of the cancerous process is to be obtained from the report of no one speech, but may be so by culling from all.

For instance, Mr. De Morgan devoted the length of his opening paper to showing that the facts are against the theory of the blood origin of cancer, and maintained the view that though local in its development there are general or constitutional conditions favouring its occurrence. In the course of this argument it was held that there is no genetic difference between malignant growths, and any other tumour whatever. "Admit that the elements of any tissue may take on independent action, and no line can be drawn between the mode of origin of the simplest and the most malignant of tumours." The discussion of these points was all important in framing some general notion of cancer, and on all of them I agree with the author of the paper; but for the complete picture of the features of malignancy something else is needed, and this Mr. De Morgan sees in the free mobility of the elements of certain tumours. Many will be inclined to disagree with him here, and in the debate in question Mr. Simon devoted his energies to showing that the mere wandering of cancer elements to parts distant from the primary tumour, and their overgrowth in their new habitat did not explain the facts as one saw them in these tumours. Mr. Simon thinks the essence of the specific force of "malignancy" is an impregnative or spermatic one, whereby the part primarily affected exercises on the tissues which receive its juices an influence which causes the latter "to fructify in conformity with its own deranged pattern." But then, again, holding these views, Mr. Simon still is able to see two fundamentally distinct classes of disease in cancerous

and non-cancerous tumours. With respect to the spermatic influence here mentioned, and also as to the distinctive nature of the two forms of tumour, Dr. Moxon agrees with Mr. Simon. I shall have more to say on this subject hereafter, but I would remark now that while agreeing with Mr. Simon and Dr. Moxon as to the essential feature of malignancy, I do not see that their view commits me to the adoption of the fundamentally different nature of it and "benignity." On the contrary, I hold with Mr. De Morgan that the two are genetically the same, and that both are the outcome of some common cause or causes.

After defining his idea of the nature of cancer Mr. Simon next proceeded to touch upon the relation of cancer to other diseases, and concluded by pointing out that he considers tubercle and syphilis to be processes analogous to cancer. On this question also something more will be said presently.

Mr. Hutchinson made a very valuable contribution to the discussion, and in so doing supported Mr. De Morgan, as it seems to me, in maintaining the oneness of the cancer process with that of any other tumour, by insisting on the occasional transmutation in hereditary transmission of one form of tumour into another. Though a pure localist in regard to the surgery of cancer, Mr. Hutchinson mentions this point in some remarks on what he considers its constitutional element. It is curious and interesting to note that the next speaker, Sir James Paget, adduces what would appear to be the very opposite of this in favour of the same constitutional element. Mr. Hutchinson says, that patients with warts on the body come of cancerous ancestors, having previously insisted that his definition of cancer was not limited by any histological structure. That proposition, I apprehend, might have its terms changed without altering its value, for if warts are related to cancers, why not lipomas and other forms of tumour? But Sir James Paget dwells upon the inconstancy of the transmission of cancer to any one part or tissue, upon the constancy of its seat in the same part or tissue as that of the ancestral tumour, when benign growths are inherited. These two opinions cannot be held together, for if the various forms of innocent growth are transmuted into those which are strictly malignant, a separate manner of inheritance for each cannot be

substantiated. And in truth to Sir James Paget's own most striking illustration exception might well be taken by the histologist, for after laying more stress on the constancy of transmission to tissue than to a definite part in innocent tumours, and the reverse in those of a malignant nature, a case is given where a lady dying with cancer of the breast transmitted to ten of her offspring (children and grandchildren) cancer, which affected in one the stomach, in another the uterus, and in others the breast, axillary glands, or rectum. With the exception of the axillary glands all the instances given were probably cases of disease commencing in epithelial structures, and so far were affections of a single tissue; and even in the exceptional case of disease in the axillary glands, the *onus probandi* would rest upon him who adhered to the opinion that the primary disease originated in the glands, rather than upon one, who without other proof, thought it more probable that the case might have been one, such as Sir James Paget has himself described,[1] of some apparently insignificant local disease about the nipple or elsewhere originating a secondary cancer in the axilla. But I cannot help thinking that this difference in the manner of inheritance of cancers and innocent tumours would almost disappear on a closer investigation of cases. I mean to say that the habit of thought has been so much to regard non-malignant tumours as one thing and cancers as another, that when inquiring into the hereditary tendency of a patient, the cancerous tumour in the family has been remembered, and not the lump of fat, the warts and moles, the uterine fibroids, and so on. The one is made much of and whispered in bated breath as some sort of stigma on the family, in the same way as, but to a less degree than, insanity, because the public educated by the doctors have been long taught, and I am far from saying erroneously so, that cancer is hereditary; while the other, if it has ever come under the doctor's eye, and the chances are that it never has, has been made light of as a harmless thing, and no more is thought or heard of it in nine cases out of ten. Without some close investigation of this particular point Sir James Paget's distinction between tumours is not, I think, altogether to be relied upon; or rather its apparently overbearing strength in

[1] "On Disease of the Mammary Areola preceding Cancer of the Mammary Gland," 'St. Bart. Hosp. Reports,' vol. x, 1874.

comparison with the only occasional occurrence of transmutation is greatly reduced. Sir James works out other points which may be called clinical rather than anatomical, all to show the prominence which should, he thinks, be given to the constitutional element; but while he puts that in the fore front he agrees with Mr. De Morgan and Mr. Hutchinson in the general conclusion that cancer is a disease which is both local and constitutional.

Dr. Moxon, on the other hand, wished to drop the term constitutional as only confusing the whole subject, and substituting the term *general* proceeded to inquire whether the general condition precedes and causes the local, or the local precedes and causes the general. He thought of those two issues both could not be true, and calling himself a pure localist endeavoured to prove that all that had hitherto spoken on the constitutional side of the question were really defenders of the localists' position. Though I am unable to see the objection to the word constitutional or that the term general is the more fitted to the subject, I cannot but agree with the arguments and facts which Dr. Moxon brought forward as bearing on the local origin of cancer. The most important one seems to me to be that in which he corroborated from his own observations, and the experience is surely not a singular one to any one accustomed to examine tumours histologically, the existence of a spermatic influence as exhibited by cancer-cells: in this, indeed, lies the essence of cancer. Dr. Creighton speaking later and giving some conclusions resulting from some observations made also spoke to the same point.

Many other issues were opened up in the discussion, upon which the limits of this paper forbid my entering, but it may just be mentioned that Mr. Arnott in a short and admirable speech touched upon some very important points in the history of cancer, when he alluded to the influence of position in reference to the malignancy of certain tumours. There can be no doubt that the position of a tumour must be taken into account in attempting to estimate the various causes which have ended in producing that *tumour*. I say a tumour advisedly because, besides favouring rapidity of growth and by consequence a wider and wider divergence from the original cell function and form, position, leading to modifications as it must do of the

warmth, moisture, blood supply, and many other things, will explain the first commencement of any tumour, and not especially of a cancerous one.

With this discussion on cancer still fresh in memory, and with the illustrations it affords of the improbability of one mind, unless it be by way of summarising the opinions of others, attaining to a complete exposition of the subject, it will not be expected that I should deal with "malignancy" in all its aspects, and I prefer to place myself with those who, by working out some one idea, may thus, perhaps, add something to the sum total of our knowledge. I therefore propose to continue a plan, adopted in a previous volume of the Reports, of taking a subject, in that case follicular disease of the scalp, and examining it with especial reference to its bearings on the general pathology of tumours. In the present case ichthyosis of the tongue will be taken as a text, and upon one or two points in connection with its origin and progress the subsequent remarks will be founded. There is no necessity to confine ourselves exclusively to ichthyosis of the tongue, since other regions would supply suitable examples of chronic irritation followed by cancer.

The cases of ichthyosis that I have examined are but two in number, but inasmuch as my own description tallies mostly with that of observers who have examined other specimens, the smallness of my experience will not matter. They were both obtained from patients under the care of Mr. Henry Morris. Both, one a man of fifty, the other of fifty-four, had had syphilis. In one the disease had existed for nine or ten years, the syphilis having occurred seven years before that; in the other it had lasted ten years, syphilis being probably contracted eighteen years before. Epithelioma followed in both cases. The naked-eye appearances of the disease were those of a thick white and hard coating in patches over the whole dorsum of the tongue; and in some cases it has been seen on the inside of the cheeks.

The first case showed to the naked eye a local warty excrescence, a millimètre in height or rather more, and on a vertical section, it was seen to be made up of a number of vertically set papillæ of somewhat fusiform shape and ragged surface. The thickness of the whole plaque set in the

surrounding mucous membrane was two millimètres. The epithelial coat of the tongue around the diseased spot was thick, though less so than the part more manifestly abnormal.

Examining the parts microscopically the mucous coat wherever examined appeared to be thickened first and chiefly in its epithelial coating; and, secondly, in its corium or subepithelial fibrous tissue. The epithelial coat was not at all places alike; in some it existed as an even layer, though one of increased thickness merely varied by the papillary eminences; in others it dipped down deeply into the subjacent fibrous coat, and was surrounded by a small cell growth, which spread freely in the deeper parts, and in this instance the two forms of cell, the epithelial and the smaller cell, had no obvious relation to each other. The vertically set papillæ mentioned just now as giving the patch the warty appearance were due to two conditions, both dependent upon an excess of the horny layer of epithelium proper to the surface: on the one hand, the true papillæ were coated with too many layers, and on the other the interpapillary depressions were clogged with an excess of similar elements. The rete Malpighii I suppose to be over active in forming cells to replenish the wear and tear at the surface, and the supply being greater than the demand, the excess, passing into the horny state, is pressed from all sides into the interpapillary troughs. The young cells, forced into the grooves between the papillæ, become welded together or moulded by the pressure to the form of the channel, and are gradually extruded as a mould on the surface.

With regard to the changes noticed in the papillæ by others I may state I have not been able to see any of the colossal papillæ described by Mr. Hulke in his original cases, though some of the pseudo-papillæ came somewhat near to his definition. Neither has it been possible to satisfy myself as to the presence of wasted papillæ as described by Mr. Fairlie Clarke. No doubt the conditions which are sufficient to form the pseudo-papillæ in this disease would also be likely to damage the true papillæ, and lead to their wasting; but though so probable, the certainty of such an occurrence seems hard to prove, since shrunken papillæ are very easily made by shaving just the outside of the cone, and it is, of course, impossible to cut through the centre of each papilla. Further, the inter-

papillary depressions being filled up by epithelium the papillæ become less prominent. The deeper fibrous structure of the mucosa is very thick, the vessels being both large and numerous; and the thickening is especially noticeable in connection with a horizontal band of fibrous tissue, which is to be found frequently in healthy tongues, running through the corium in a perfectly horizontal plane, that is to say, not following the undulations of the papillæ. In one of the cases upon which these remarks are based, and in several cases of epithelioma, a thickening of this horizontal band has been one of the most marked features of the disease, both to the naked eye and under the microscope. The muscular fibres of the tongue have not been found to be diseased.

Both cases terminated in epithelioma, characterised by an infiltration of the corium and intermuscular tissues with a small nuclear growth, and in one, though not as a marked feature, by the budding processes of the mucous layer of epithelium, which are looked upon as characteristic of cancer.

If it were to the purpose to discuss the appropriateness of the term ichthyosis of the tongue I should dwell longer on the changes noticed in the epithelial structures in this disease, but as it seems to me to be a matter of indifference what name is adopted, I shall only remark that changes such as I have described appear to be almost identical with those figured by Dr. Fagge[1] in a case of ichthyosis of the skin, and by Dr. Tilbury Fox from Kohn. Shortly, then, the disease may be described as a chronic overgrowth of the epithelial structures of the tongue, which ends in an infection or infiltration of the neighbouring structures.

I shall dwell chiefly upon three points—

Its prolonged duration,

Its incurability,

Its constant termination in epithelioma.

In a discussion which occurred on this disease at a late meeting of the Medico-Chirurgical Society some difference of opinion was expressed as to the second of these three points. Mr. Acton stated that in psoriasis of the tongue, a very common result of syphilis, he did not find the treatment so difficult as had been described, adding, perhaps this was

[1] 'Guy's Hospital Reports,' 1870, vol. xv, p. 315.

because he saw the cases in an early stage. Nearly, if not all, the other speakers agreed as to its incurability, and M. Debove and Mr. Fairlie Clarke, who have, I think, given the most comprehensive analysis of cases, also come to the same conclusion on the whole, though the former gentleman remarks that he has seen some cases which, after a treatment of months, were so much better that with more prolonged treatment they would probably have got well. M. Bazin is also reported to have seen several cases of cure.

Now, the disease is one of overgrowth of the epithelial layers of the tongue associated with a fibrous thickening of the deeper parts, *i. e.*, of the basement membrane, and corium. It cannot, I think, be shown from any specimens which have yet been examined, which of these two states, epithelial growth or fibrous growth, starts first. It seems probable that sometimes the primary change is epithelial, sometimes fibrous. The disease might very well be produced in either way, but when the relative stability of the two layers is considered, and it is remembered how quick is the reaction to stimulation in the direction of overgrowth, which takes place in epithelium, which is, in fact, one of its functions, there is much in favour of ichthyosis or psoriasis of the tongue originating more commonly in the epithelium; it is probable that the stimulus, whether it acts primarily on nerve, capillary, or cell, will produce as its resultant a multiplication of cells in the epithelial layers prior to causing changes in other parts. If so, we shall not be wrong in saying that in its early stages this disease is closely allied to catarrhal states of mucous membranes, and, from its insidious onset, to catarrhal states of but little intensity. If it were more severe at its onset the disease would earlier attract notice, but in many cases it goes on for years, and then comes under treatment in the confirmed state. Supposing that we had to do with it in the early stages we might fairly expect that it would be amenable to treatment, and I am disposed to accept in this light the statements of those who aver that the disease is by no means incurable. They have come across the early stage. Hospital surgeons, on the other hand, mostly get the advanced stages, or is it not rather that they do not call anything ichthyosis or buccal psoriasis till it puts on the advanced features? Then they say

it is incurable. Assuming then that it has been curable at its commencement, what has happened between the curable stage and the incurable? What are the conditions which determine incurability in chronic inflammations of the skin and mucous membranes?

I may mention two, not as exhausting the number, but as being perhaps of most importance. They are an altered habit on the part of the cells of the membrane and the formation of new tissue. The word habit is not, perhaps, the fittest that could be used, but still it may be retained to express what I mean. A habit may be defined to be an automatic action resulting from repeatedly occurring stimulation. For instance, a hysterical girl takes to vomiting, and she vomits for weeks and weeks till the doctor and she are heartily tired of each other, and the friends are weary of both. It is obvious that the condition to be remedied at the end of that time is not the same as it stood at the beginning; the nerve-centre, over-readily stimulated, or stimulated with over-intensity in the first instance, has been so repeatedly made to react in like manner that in the end the apparatus has worked too perfectly and the one pole has answered to the other on the slightest provocation. To put it figuratively, the train has run along the main line and has failed to answer to the points set to conduct it to the siding. The stimulus has passed so often along certain channels, and the centre has so often responded by discharges in another equally constant route that the well trod path has become the easiest, and no diffusion of force takes place to surrounding parts which have the lower sensori-motor centres under control. And where lies the difficulty in curing such a case? Why, of course, in opening up again the old road and diverting part of the traffic. The main road has to be rendered somewhat less passable, so that the surrounding parts may become aware of its being used and exact their toll in kind.

This illustration holds good in regard to the subject of cell growth. Though we may, not perhaps be, I do not say are not, dealing with nervous impressions leading to action, and may possibly be dealing directly with altered states of nutrition in cells unassociated directly with the nervous system, yet the fact remains the same that in cell life

certain definite stimulation leads to certain activity, which may under healthy conditions lead to general hypertrophy and, as I think, if continued, eventually to tumour. The more frequent the one (stimulation), the more immediate the response of the other, and ultimately a response which is elicited without anything like the intensity of stimulus which called it at first into existence.

The nerve-cell accustomed to let off steam in the form of nervous discharge passes thus on to so-called functional aberrations and insanity. The epithelial cell with which we are now more especially concerned uses up its force in its function of cell growth and displays its aberrations in the method of formation of those cells and in the form of its progeny. But the insanity of the one and the growth of the other are equivalent expressions of a like force; and the tendencies of both are difficult of correction for the same reason, viz. that they both react to such trivial excitants that they are beyond control.

It may be remarked in passing that here lies the explanation of the rarity of tumours of nerve substance. They are almost unknown; neuromata, that is to say, new growths of nerve elements and not of connective tissue, are described by Cornil and Ranvier, but it has fallen to the lot of but few to see such. It is easy to see, why their rarity is so great. If it be true that an electrical or allied discharge is the functional endowment of nerve cells, they must needs much more readily manifest disturbance in the direction of their accustomed habit than in that of proliferation to which they are unaccustomed; and *vice versâ*, the epithelial cell, since it cannot become insane, must needs germinate.

But we further know that what is a mere acquired habit in one generation may become a fixed, or inherited, or constitutional predisposition in another. Take, for instance, the case of Dr. Brown-Séquard's guinea-pigs, mentioned by Mr. De Morgan in his opening speech on Cancer, and also quoted by Dr. Carpenter in his 'Mental Physiology,' p. 371. Dr. Brown-Séquard "discovered that after a particular lesion of the spinal cord of guinea-pigs a slight pinching of the skin of the face would throw the animal into a kind of epileptic convulsion." Further, "when these epileptic guinea-pigs bred

together, their offspring showed the same predisposition without having been themselves subjected to any lesion whatever; whilst no such tendency showed itself in any of the large number of young which were bred by the same accurate observer from parents that had not thus been operated on. Now, if a habit requiring often the co-ordination of complex muscular actions and surrounding conditions favorable to its manifestation can be perpetuated in a single generation, much more likely is it that that habit will be transmitted when the conditions are all simplified, as in the case of the direct transmission of likeness from the parent cell to its progeny. But we will discuss a little further this question of constitutional predisposition of an epithelial cell. The routine of animal life is constant within certain limits, that is, there are certain fixed times for the attainment of maturity, for the reproduction of the parent form, and for decline. Is it otherwise with the elementary unit than with the complex organism of many units? A single cell has its cycle. It, like more complicated beings, is set to a certain rhythm. Now, what happens in the case of the ichthyotic tongue? This rhythm surely is altogether disturbed, and cells, as we can see, are produced at an unwonted rate. This stage of excitement is prolonged, and, as a matter of necessity, one of two results must happen; either the cell must *grow to*, to use an expression of Dr. Carpenter's, the altered requirements, *i. e.* adapt itself to those requirements, or it must cease to exist. The acquired state being constant is perpetuated and a new race of elements comes into existence, whose cycle is different from that of its healthy progenitors.

Nerve force was used just now as a parallel and illustrative case to that of cell growth. Let us again make use of it. There is good evidence to show that in the long course of years or generations a race of madmen or criminals may be produced. It is not to be supposed that insanity in the majority of cases—it is, no doubt, in some—is a sudden explosion which repeats itself, rather is it often as true a process of education as any of the higher consistent intellectual operations. It is the gradual specialisation of nerve force in particular grooves, the intensification of the slighter forms of abnormal nervous action which ultimately culminates in madness or

criminality. In the same way the altered processes of cell life will not stop after one generation if the surrounding conditions which started the process be kept up; the primary variation must gradually become more marked. Then when investigating such a disease as ichthyosis of the tongue, in its advanced condition, how many generations of cells have passed by and left their mark upon the coming race? Who can tell? And of what is it so true that "one day is as a thousand years" as of cellular life, when compared with the fabric of a body so complicated as that of one of the higher animals?

With regard to the natural history of plants or animals we now accept it as a recognised fact that in the reproduction of the species there is a tendency to the gradual formation of varieties which by a process of natural selection are liable to be perpetuated. Can we subscribe to these facts in the complex organism and refuse to apply them to the constituent elements of that organism? If the whole varies, its parts will vary, and if the parts vary, then I apprehend there will probably be some such process among the cell elements of our bodies which may be called the "survival of the fittest." The cell varies under existing conditions, because those conditions have been favorable to variation; the varieties must needs, therefore, be the most adapted to the position, they may be said to be abreast of their age; and thus, as in highly organised beings, the variations will be perpetuated. Are not the conditions identical in the lowly and in the highly organised?

What a subject for Darwin would be the cells of a cancer, if only they were tangible; how the immortal pigeon would be completely eclipsed, while the hungry pathologist would be filled with food, if only we could observe the variation of tumours under judicious cultivation.

This is no mere fanciful idea. I cannot but think that this is really one of the points of view from which tumours in general must be considered as well as from others, and that there is reason for the belief that the growth of a tumour is to be looked upon, not as a mere retrograde or degenerate change, but as a process of evolution in cell or tissue; that by the perpetuation of certain states through generations and generations of cells a process of natural selection goes on, and variations, not necessarily of form only, but also of function, are intensified:

and it seems to me not improbable that a malignant or cancerous tumour may be, paradox as it might at first sight appear, an instance of the survival of the fittest.

To call cancer a process of degeneration is surely, in many cases, a misnomer; it is only a degeneration in respect of its fatal termination, otherwise it is often, nay generally, found to be existing under conditions of the body which betoken anything but decay. All who have had much experience in such diseases agree that malignant growths are more especially prone to occur in people of very good, if not robust, appearance; that they grow exceedingly rapidly when they appear in young life, and on the other hand in very old people they may often be found to exhibit very little activity; that those parts are especially liable to attack which are subject to periodical nutritional disturbances and excitement, while injuries to the body generally are repaired just as well when cancer is present in some part of that body as when the patient is, *quoad* cancer, sound.

But what has all this to do with my argument? I was discussing, it will be remembered, the question of the influence constitutional predisposition in a cell would have in rendering ichthyosis incurable. The observations just made are pertinent to that issue thus:—Supposing that a gardener had a certain variety of plant which he for some reason or other thought it unadvisable to propagate from, or that a bird-fancier attempting to make permanent and intensify some particular shade of plumage found the tint becoming less pleasing in each succeeding generation. Neither the one nor the other would attempt to deal with the variety in the individual; he would either destroy it as worthless or take care that the condition should not be perpetuated by the oversight of pairing and so on. Would he not seek to eradicate the bad vein by dealing not with the result but with the cause, not with the variety itself but with the conditions under which the variety was produced? and if not so, then he would try to work back again by careful mating in successive generations, or through the action of what is known as reversion. Regarding ichthyosis in the same way, we talk of its incurability, and even question whether it is so or no. Incurable? Of course it is, on the very face of it. And why? Because it is a disease which is the result of, perhaps, years of altered action in the epithelial structures.

To relieve that, either the conditions which led to the first aberration of cell growth must be altered, and so a fresh stock reared up, or, by keeping the surface perfectly free from all excitement or stimulation, we must allow of a gradual process of reversion to the primordial type of cell; and it is easy to see how the disease may be perfectly and easily curable in the early stage, while it is more than incurable in the later, for it is on the high road towards an evolution, which is most dangerous to patients so suffering.

The second condition which has been named as having an adverse influence on the curability of such an affection as ichthyosis is the formation of new tissue. There is no need to dwell long on this. Cell growth from whatever cause, if increased beyond the normal, will demand and obtain increased supplies of blood. The latter will, again, in its turn, stimulate to increased activity in cell life. Let this go on for years, as is the case in ichthyosis, and what must inevitably result? Nothing more nor less than a great thickening of the tissue. Again then, one of the chief abnormalities in the disease, without which there would be much difficulty in recognising it, is the very thing which is one of the chief causes of its intractability. It may be said that without the thickening of the corium we hardly know ichthyosis, nevertheless, this thickening would not seem to be absolutely essential to the disease. Were it not present the affection would probably be quite amenable to treatment, but with it, how can it be cured? How is the temporary excess of nutrition to be controlled which the necessities of the part have made a permanent excess? How is the cell germination to be kept under which is constantly tending to draw more blood to the part? Obviously, if at all, only by a most gradual process. It would not be altogether useless to dwell longer on this by showing how important it is in all chronic diseases to bear in mind that in proportion to the duration of the malady will, in all probability, be the length of time required for the cure. That this is so, is often forgotten at the time when a conviction of its truth would infuse perseverance and vigour into the treatment, and, perhaps, determine the ultimate recovery of the patient. But this, though an interesting point enough, must not detain us.

Ichthyosis in its most pronounced states is very similar,

though brought about, perhaps, in a different way, to elephantiasis Arabum of the leg. They both have an enormous growth of new fibrous tissue extending from the corium into the deeper structures, into the areolar tissue in the case of elephantiasis, amongst the muscular bundles in that of the tongue, and they both have blood-vessels supplying the new tissue out of all proportion to the size of the normal ones. Those who have examined any cases of elephantiasis cannot fail to have been struck with the immense vessels running in the diseased parts. It is exactly the same in the case of ichthyosis of the tongue. Both are alike incurable.

Of the disease called elephantiasis Arabum we know but little, except in its results. It is a remarkable disease which has this interesting property, that it would seem to link together the class of hypertrophies with tumours. Of its cause we are ignorant, but this we know, that in some cases of old ulcer of the leg, that is to say, chronic inflammation of the skin, the surrounding tissues put on exactly the same appearance. In contrasting this with ichthyosis of the tongue it will then not be unfair to assume that if a precisely similar state, so far as can be seen, can be produced in the one part by an inflammatory condition, it may be so in the other. In this light I am disposed to regard ichthyosis of the tongue, and at the same time I would extend the definition of chronic inflammation by saying, that by it I understand not merely the fully-developed condition, but the whole number of slight gradations which obtain under excitants of varying severity, from the very slightest excess of cell growth through all the degrees of catarrh up to that intensity, which is manifested by infiltration of the involved tissues with inflammatory cells. With the more pronounced states of inflammation there is no difficulty in dealing; they can and do produce a state similar to ichthyosis, and therefore it cannot be doubted that all causes which lead to such an inflammatory condition, whether it be prolonged irritation from rough teeth, syphilis leading to cracks and fissures, or any ulcers brought about by other states, are liable to produce ichthyosis, provided always such a state is sufficiently prolonged in time, and at no period excites an inflammation which goes beyond that point of intensity within which the organisation of the inflammatory product can be secured.

The slighter forms of stimulation are much more difficult to deal with, for they cannot be proved, and from the position and function of the tongue are so frequent that they are normal to that organ. Still, no matter how slight the stimulant, if habitually in excess of the normal stability of the cells of the part, it will excite a response in the shape of increased cell-growth, and this in time will, if slowly, yet surely as the unequal balance is maintained, lead to further changes, and originate cellular elements, which in their round of life will be more and more aberrant from the primary form as the disease progresses. If so, then it is quite possible that such trifles as gastric disturbance, want of attention to the cleansing of the mouth after food, constitutional states, such as the arthritic, described by Bazin, and many others too numerous to mention, might all set an ichthyotic condition going, while subsequent surroundings might render it permanent.

It only remains to speak of our third point, viz., the constant termination of ichthyosis in epithelioma.

The microscopical difference between the two diseases, if they are two, is this, that in ichthyosis the normal structures though in excess are still in their proper relative positions, the one layer of skin succeeding the other in the proper order, the disease, in fact, falling under Sir James Paget's class of hypertrophies. In epithelioma the epithelial layers bud out in all directions into the deeper layers and appropriate and change the texture, and in many cases they so far lose their original appearance that they can no longer be called epithelium, but have been classed as "indifferent."

Now, if we can see the way from prolonged irritation of any part of the tongue to an ichthyotic state, and that without any special predisposition and merely by a process of evolution, and if too it can be shown, as all clinical facts do show, that ichthyosis, however produced, leads on most surely to epithelioma, it would almost seem as if we had acquired the key to one of the most intricate problems of pathological science, the true pathology of cancer. Or if we have not got as far as *that*, still we may be sanguine enough to hope that work in that direction may prove remunerative.

In endeavouring to explain the incurability of ichthyosis by a process of evolution, the individual cell only has been taken into

account, and its tendencies to variation. But if a certain cell varies in definite directions, is it not probable that a time in the history of its posterity will come when the family traditions and family likeness will be lost? To pursue a little further an analogous instance mentioned just now. "It is a matter of observation," says Dr. Maudsley, "that the criminal class constitutes a degenerate or morbid variety of mankind." "They are, it has been said, as distinctly marked off from the honest and well-bred operatives as black-faced sheep are from other breeds, so that an experienced detective officer or prison official could pick them out from any promiscuous assembly at church or market." And, again, they "herd together in our cities in a thieves' quarter, giving themselves up to intemperance, rioting, and debauchery, without regard to marriage ties, or the bars of consanguinity, and propagating a criminal population of degenerate beings." Does not this express the difference between ichthyosis and epithelioma? In the one we see, I think, the stages of the process, the gradual formation in a long course of years of a degenerate race of cells, in the other if we see not the steps, we see the result, a race of cells which has at last thrown off the restraints which were irksome to that mode of life, which interfered with the process of further development, and we see them, to speak figuratively, having discarded their moral obligations. In ichthyosis one makes a study of the individual cell, in epithelioma the cell must be examined as a member of a social community, and it is the disregard of the laws social in the cellular economy, which constitutes its malignancy. This, however, does not express the entire truth.

It is not the mere establishment of an *imperium in imperio*, as Mr. Hutchinson happily expressed it, that works the mischief, but that mischief must be measured by the power which the standard of revolt exercises upon the neighbouring cells. If they remain loyal, the tumour is not malignant. By their disaffection only do they make it malignant. This is in other words the doctrine of spermatism again. With Mr. Simon and Dr. Moxon I agree in entirety, that this is the cardinal feature of malignancy. By cancer I understand not a mere unlimited growth of cells of a peculiar kind which by very active growth insinuate themselves between the adjacent

tissues and so destroy them, but a process which shows a focus of cancer-cells, and a circumference far or near as the case may be, of healthy cells and between the one and the other all forms of cell intermediate. So that one can only come to the conclusion that the original cells of the normal structure are taking on the morbid activity, and growing into cancer-cells. This I have long held. But further, the spermatic influence may manifest itself in more than one way. Dr. Moxon dwelt upon the reproduction of the parent form in parts foreign to it, upon the presence of cylindrical epithelioma in the liver after a tumour in the rectum, or of bone in the lung after a bony tumour in the arm; but after all, these are the least common form of manifestation of secondary tumours. I should say that the secondary growths are on the whole more likely to put on the appearance of the cells of the part in which they *occur* than of those quite unlike them, and from which they have come: but even this latter case is no less an example of spermatism; a child may be quite unlike its parent in external form, and yet may react in the same way to external stimuli, that is, he may write like the parent or speak like the parent, or have the same habits of thought or aptitude for a particular avocation, or he may be of some characteristic temperament, explosive or otherwise, and so on; and in the same way the progeny of cancer and liver-cell, for example, will very likely not be typical cancer, but a form of growth not like the original, except in the manifestation of a certain function of morbid overgrowth of the cell-elements. But even this spermatism is no absolute test of cancer, since it is probably seen in normal states of cell-function. Of this the healing of an ulcer by skin-grafting seems to me an example. It is unlikely that the formation of skin for the closure of a large sore takes place entirely from the grafts that are placed upon it. It is much more probable that the graft exercises a spermatic influence on the granulations which it finds ready to receive it, and these form skin, because the normal *toned* cells have set them a good example. Or again, the formation of bone around transplanted periosteum surely does not all form from the bit of transplanted bone membrane, but that starts the process and the other cells follow suit; so that after all the malignancy of cancer rests not only in its spermatic influence, but in a certain altered rhythm of cell

life, characterised by great vitality or activity with the impregnative influence in great force.

From the discussion of the question of spermatism it is not far to turn to that of the relation of cancer to zymotic processes, and he who holds to the one will certainly in some sort acknowledge the existence of the other. The process of tuberculisation by generalisation from a single focus so nearly corresponds with that of the extension of cancer from its centre that it would seem a very nice distinction to define the difference betwixt the two.

We therefore rise hopefully from a somewhat hazy subject in the belief, to use Dr. Moxon's words, "that when the solution of the question comes" (viz., that of the nature of cancer, tubercle, syphilis, and specific fevers, and their various inter-relations), "some general law governing the whole must be discovered," and I further think that such general law must explain not merely the material phenomena of the tissue-cell, but be alike applicable to the functional phenomena of the nerve-cell. Whether these various processes are set going *ab extra* or not, I shall not now attempt to discuss, but the general bearing of the remarks that have been made, will, I think, make it plain, that in holding to the analogy between the discharge from a nerve-cell, and the germination of a tissue or gland-cell, we must also incline to the belief that the causes of their action are not dissimilar. And since we should hold that the various phenomena of abnormal nerve action, mania, convulsion, pain, &c., may be produced both by causes within the diseased part, such as habitual abnormal working of its machinery, and by causes *ab extra*, such as blood poisons and the like, so in the case of the phenomena exhibited by tumour-growth, in one person it might be decidedly *ab intra*—I do not say constitutional, it might be *ab intra* and yet not constitutional—in another quite as decidedly *ab extra*.

It is said by some that ichthyosis is merely a stage of epithelioma, but to that I think it may be responded that many cases of epithelioma do not show the characteristic changes. It is true that on comparing sections, the actual thickness of the parts superficial to the muscle in each may not differ, but while, in the case of ichthyosis, this is due to the growth of new tissue, in the case of epithelioma it has seemed to me rather due to atrophy

of the already existing muscular bundles or to their infiltration with cells than to the formation of organised fibre. At the same time I regard it as a stage of cell development whose natual cycle turns inevitably towards epithelioma, if the disease or the patient live long enough. It is, however, no necessary preliminary stage which all epitheliomas pass through.

These remarks have been chiefly confined to ichthyosis of the tongue, but other diseases would equally well illustrate the points for which it has served. Epithelioma of the lip and scrotum, for instance, are cases similar, but without, perhaps, such a prolonged pre-cancerous stage. Others are those of some cases of cancer at the pyloric end of the stomach originating in old ulceration, and probably as Dr. Fagge thinks, most cases of death from old obstructive jaundice due to gall-stones. With regard to the last-mentioned series, the frequency of the association of gall-stones with cancer of the liver and other parts has of course long been known, but I am not aware that anyone has hitherto pointed out that nearly all old cases of obstructive jaundice are associated with cancer of the obstructed duct. Dr. Fagge found from an examination of the records of Guy's Hospital that this was the case. It seems probable that, considering the frequency of jaundice due to gall-stones met with in practice, many of these cases are not those of gall-stones due to the obstruction of the cancer, but that they are actually cases of cancer consequent upon the chronic obstruction and its resulting local irritation. Dr. Wilks is also of the opinion that the irritation of gall-stones leads to cancer of the ducts.[1]

All these examples seem to me to illustrate the progress of a cancer, from its first starting in healthy cells to its final, though varying degree of malignancy; but there are others which setting out on the same road would seem to stop at the halfway house. Such are cases of keloid which starting as allied to, if not identical with, inflammatory processes ultimately become permanent and hold their own as tumours, and yet they are not malignant. Why not? Well, they may not have lived long enough before the surgeon cut them out or they occur at the wrong period of life, or some local or general condition is

[1] 'Path. Anatomy,' 1859, p. 338.

somewhat adverse to their perfect freedom of growth. Many such things would explain their non-malignancy, and I should be much more disposed to allow for some local or particular something which unknown had arrested the wheel before it had completed its revolution, the completed process being visible in other cases starting from apparently like causes, than to say that because the final stages were not attained, the earlier ones were in malignant and non-malignant tumours essentially different. Again, other cases are still more closely allied to inflammatory states, and further removed from the malignant. Of this class no more beautiful example could be given than that of Mr. Simon in his remarks in the discussion on cancer.[1] He removed a little fibroid tumour from the top of a lady's chest; she had had the disease removed before but it had come back again, and now in removing it the surrounding parts were widely cut into, and the edges brought together with three harelip pins. A few weeks after the tumour was growing again, and in addition each of the six pinholes was giving rise to a little fibroid growth of its own; yet these tumours all shrunk under the use of ice, and the lady, now approaching mid-life, has had no subsequent inconvenience. A somewhat similar case I saw two years ago under Mr. Bryant's care: a boy many months previously had torn his wrist with a rusty nail; an indurated ulcer formed which never healed, and for this he was admitted to the hospital. It was seared and treated in a variety of ways to get it well, but nothing short of excision was of any avail. It speedily got well after the latter procedure even though at the operation some of the material forming the sore was found to dip deep among the tendons and could not be extirpated.

In examining the edge of this ulcer after its removal it was evident enough why it had not got well under less severe measures than the one ultimately adopted. The border showed nothing more than vascular and organising granulation tissue; the cellular growth had procured for itself a sufficient blood supply, and it was overgrowing even to the extent of gradual invasion of the parts around, and so the ulcer increased rather than diminished; but as it grew some sort of tissue was formed likewise, that is to say, the cellular elements still retained the

[1] 'Path. Soc. Trans.,' 1874, p. 306.

traditions of the parts and were still true to their primordial type; but I cannot see the necessity for anything more than the lapse of time to have produced in this case an infiltrating and recurrent tumour. Keloid-tumours are of much the same nature as the edge of this ulcer, and as is well known they not unfrequently become cancerous in the end.

From the consideration of cases such as these it is, that one is compelled to differ from those who think that there is always something of a constitutional nature in cancer. They show, I think, the possibility of the origin of cancer in a purely local cell stimulation; but then I must further say that, counting myself a localist, I am unable to see that localism and constitutionalism exclude each other. Sir James Paget has said[1] that fatty tumours, fibrous tumours, and cartilaginous tumours may be inherited, and Mr. Hutchinson[2] dwelt especially upon the fact that transmutation is sometimes observed in the hereditary transmission of the cancerous tendency, that is to say, that cancerous parents may produce children who shall be affected with warts, and more often that a malignant growth of one organ in the parent will be transmuted to malignant disease of another part in the child. Now, if this be so, if the warts in the child be the representative of a cancer in the parent, what becomes of the essential difference between the two forms of disease as insisted on by many? But I would add other facts to this, and say that warts always occur in young people, and further, it seems to me not unlikely that those much affected by warts in young life will die of cancer as they become older, putting aside, of course, the well-known cases where the warts continuing one of them becomes epitheliomatous; and further, though the simultaneous outbreak of several primary cancers in different parts is very rare, I think it is by no means uncommon to find a fibrous or a fatty tumour in one part, while a cancerous tumour occupies another.

All things considered, then, if there is not a general cancerous predisposition, and that there is not such I agree, still there is evidence in favour of a predisposition to the overgrowth of tissue and tumour formation in the body generally,

[1] 'Path. Soc. Trans.,' 1874, p. 318.

[2] Loc. cit., p. 312.

the locality being determined by local causes. But when once a tumour has formed, a process has been started which it is henceforward impossible to control, and which may, unless removed, evolve a cancer.

The unnatural mobility of the elements in cancer was very properly insisted on by Mr. Arnott and others as giving a thoroughly satisfactory explanation of the occurrence of secondary growths, and thus accounting for degrees of malignancy as found in various tumours; but that point need not be dilated upon here, because secondary tumours only exhibit the same form of malignancy as the primary growth ; and their presence is no test of malignancy, since many tumours infiltrate the surrounding structures and are truly malignant without showing any secondary nodules. They merely repeat the process which is to be observed in the primary growth.

To repeat then, while I hold with Mr. Simon and Dr. Moxon as to what should be considered the essence and the allies of cancer, I further hold, disagreeing with them, but agreeing in the main with Mr. De Morgan, that innocent and malignant tumours are not totally distinct. On the contrary, that new growths may all be placed on one scale, at the one end being placed inflammatory growths, at the other malignant growths, the intermediate degrees being many ; but that one and all are to be looked upon as so many steps in a process of evolution which culminates in malignancy.

And here I shall conclude. It has been my aim in this paper to treat of cancer as far as possible only from that point of view which would consider it as a direct process of cell variation, much as one might take note of the modifications of fungus spores when cultivated in soils of different composition. Not to make it unnecessarily long, I have mostly omitted the consideration of those conditions which exist in the surroundings of the cancer, that is to say, I have taken no thought of the *soil.* To do this would have necessitated the discussion of the reason of the selection of the various parts for its occurrence, of the influence of warmth and moisture, or "forcing" in causing exuberance of cell growths, and of many other details which can, I believe, only be taken note of, since they only occur, in individual cases. It is necessary to say thus much to explain the very one-sided view, as some may think, of cancer here

stated. It would not, however, be difficult to show that these other aspects all focus towards that conclusion as to the nature of cancer which I have drawn from one alone.

But faith without works is dead; therefore, with regard to the treatment of ichthyosis of the tongue and allied diseases, a living faith says, Extirpate at once in the *persistent* forms of the disease. Here is an affection which can be recognised before it has become cancerous; the very stage the surgeons are all on the look-out for, and which, facts show, will be succeeded by one of cancer. Surely then no waiting should be allowed. Cut out while there is yet time; but then not only so, but to the earlier stages of ichthyosis attention must be directed. I cannot but think that, if it could be seen at its onset, it would be amenable to less severe measures than that of the knife or écraseur, but causing as it does at first so little inconvenience to the patient, it is in many cases past cure by mild measures before it is recognised. The failure of early recognition is, of course, not at our door, but the remedy is, in the inculcation of the doctrine that local causes play a large and necessary part in the production of cancer. Did we but keep this plainly before ourselves and our patients, it is no unreasonable hope that external cancers might eventually disappear from our nosology just as chimney-sweeps' cancer would appear to be diminishing, now that the local irritant is less constant than it was. At any rate more good would seem to promise from a belief in the local than in the constitutional origin of cancer. For the latter doctrine has in it so much of mere fatalism that it is encouraging neither to the surgeon nor his patient.