The Mackenzie Davidson Lecture

ON

THE INFLUENCE OF RADIOLOGY UPON
OUR CONCEPTIONS OF DISEASE.

BY

SIR THOMAS HORDER, Bt., M.D., F.R.C.P.,
PHYSICIAN TO ST. BARTHOLOMEW'S HOSPITAL.

THE Mackenzie Davidson Lecture commemorates annually the life and work of a distinguished pioneer in the field of radiology. It was thought by those who founded the lecture that it was an additional and an appropriate tribute to the memory of the man they sought to honour, who combined a true scientific spirit with the exercise of the healing art, that the lecturer should be alternately a pure scientist and a member of some branch of the medical profession. This, rather than any merit of my own, explains why the honour and the obligation of delivering the lecture have fallen to me. I am here to carry on, however unworthily, the tradition which you have established, and I follow haltingly in the footsteps of such distinguished men as Professors Rutherford, Halliburton, and George, and Drs. Aston and Kaye. This explanation will, I am sure, entitle me to your indulgence.

As a physician it has been my privilege to be very closely associated with the students and exponents of radiology ever since the science had its birth. I have therefore had full opportunities of watching its progress, from the small beginnings of the nineties to the great developments of the present time. I am probably more indebted to my colleagues in this branch of our profession for help and guidance in diagnosis, and for treatment of my patients, than to any other single branch, not excluding the pathologists and the surgeons. I only say this to emphasize my interest in radiology. But this close association and its practical results are not the subject of my lecture. Neither is it a consideration of all those individual diagnostic and therapeutic achievements of which the radiologist may well be proud, and upon which physicians become so dependent in the ordinary pursuit of their daily practice. I wish to deal with a larger aspect of the subject, and to mark down some of the ways in which, as the result of these almost breathless strides that your science has taken, our ideas about certain diseases have changed.

In the first place, let us consider just where radiology stands in relation to other parts of the scheme of medical study. In our conception of the nature and extent of disease processes clinical medicine is capable of contributing admirably clear pictures as the result of careful examination of the surface of the body. And by the exercise of the trained hand and ear we are able to elicit physical signs of lesions lying beneath the surface. But for ocular demonstration of any disease process which affects deeper structures we are dependent upon three methods: there is the experience of the *post-mortem* room, there is the brief and limited observation afforded by surgical operations, and there is the valuable help given by *x* rays. Of the enormous value of the *post-mortem* room in controlling our imaginations and in teaching us the gross and the minute structural changes produced by disease I need say nothing more. I am, however, tempted to utter an exhortation to radiologists amongst others to remember what a bed-rock of fact is provided by this fundamental institution in the science of medicine, and what a salutary control it exercises over the natural tendency of the human mind to dogmatize. In reference to operations may I, in passing, share the lament of Sir James Mackenzie that hitherto so little has been done by way of systematic study when the living abdomen is opened and when the thoracic or when the cranial contents are exposed to view—proceedings that are becoming more and more common now that the surgery of the chest and skull is receiving more careful attention? But in the *post-mortem* study of disease, the great element of *function* is missing; and

observations during operations upon the living are necessarily very limited so long as the procedures are, as needs must, so rapid, and the surgeon, acting in the patient's best interest, guards so jealously the wound which constantly invites infection. Neither of these deterrents applies to the third process; the radiologist is able in many cases to study both structure and function, he has ample time for his observations, and he can submit these to such of his colleagues as are competent to offer suggestions and interpretations resulting from their own special experience of disease in other fields.

Against these obvious advantages we have to set the disadvantage that the radiologist's observations are much more difficult, and therefore his interpretations of what he sees are much more liable to error. He deals with shadows rather than with substances, and this fact alone places a serious limit, if not to the range of his methods, at least to the rate of his progress. Despite this and other obstacles, radiology is probably at the present time the branch of medical science which is most responsible for changing our views in regard to disease processes in a number of directions, confirming some important hypotheses, eliminating others, and suggesting new lines of thought. So far as time and your patience allow I will touch upon a few of these things.

FOCAL SEPSIS.

One of the most helpful conceptions in modern times in connexion with the pathogenesis of disease is that known as *focal sepsis*. We may say with confidence that the doctrine of focal sepsis has passed out of the realm of mere hypothesis and has become, in many instances, an established fact. The various clinical manifestations which we group together under the generic term "*fibrositis*" form some of the most common expressions of focal sepsis. True it is, there is still a considerable divergence of opinion as to the relative degree to which the microbic and the metabolic factors operate in the production of this condition; but it is demonstrable again and again that in many instances of this morbid process there is close association with a septic focus, drainage of which leads to cure of the disease without any other form of treatment. Radiology has given great help in establishing the truth of this doctrine. In the diagnosis of sinus infection, for example, it has enabled us to visualize the morbid condition of an antrum or of some other accessory nasal cavity; in mastoid infection the same experience often obtains; whereas in connexion with dental sepsis it has become our chief standby for exact knowledge wherewith to establish the diagnosis. Bacteriological researches led us some fifteen years ago to the conception of chronic toxic processes set up by sub-infection of certain tissues by streptococci of comparatively feeble virulence. We theorized about these processes, and were led to the idea that in some way or other these streptococci colonized in (amongst others) the periodontal tissues very frequently, and thus constituted a form of focal sepsis which gave rise to fibrositis as well as to several other pathological effects. Then came the revelations of dental radiography, and the progressively clearer and clearer views which we were given of the state of the periodontal membrane. At once our theory was confirmed: we had ocular demonstration of a chronic, painless, sclerosing inflammation, without pus formation, yet capable of causing all manner of remote disturbances, sometimes as trivial as housemaids' knee and sometimes as lethal as ulcerating endocarditis. The specific focal lesion caused by salivary streptococci was exposed, and we found ourselves justified in having sent out patients to their dentists with a statement of our doubts, only to receive too often the familiar assurance that "there was no pyorrhoea." Such assurance nowadays gives us no more comfort of mind than it gives the patient comfort of body, for we know that teeth may be firm and gums dry, yet *x*-ray examination may reveal a thickened membrane and apical abscesses—adequate causes for toxæmia and a chain of resultant troubles. I may perhaps be forgiven for quoting from a paper which I read before the Odontological Society in 1914, where I was dealing with this question:

"The pathological process going on at the root of the dead tooth, leading to sclerosis of the tissues hereabouts, is exactly similar to that which is taking place in the joint structures, the

muscular fasciae, and the sheaths of the nerve-trunks. There may be very little suppuration throughout all this pathological change accompanying the chronic streptococcal infection; quite often there is no suppuration at all. To the naked eye there is nothing to see that indicates infection, unless it be the dense fibrosis. All the same, a sterile platinum loop, applied to the adherent sac as the dental surgeon holds the tooth in his forceps, and bringing away a mere droplet of blood, as it seems, is capable of giving, when smeared over an agar slope, a copious and pure culture of streptococcus. This question of suppuration has been the bugbear of many practitioners for a long time past, and even now underlies many fallacies connected with our ideas of infective processes. 'No suppuration, no infection' is a rough and ready rule, than which no graver error was ever conceived. There are two conditions in which, as modern bacteriology has taught us, suppuration may be quite absent, though micro-organisms, ordinarily pyogenic, are saturating the tissues with their toxins, and are directly leading to serious diseases: (a) The first condition is one in which the infection is a fulminating one, the micro-organism unusually virulent, and the tissues are overpowered before their resistance can show itself. (b) The second condition is one in which the micro-organism is one of feeble virulence, of long-standing action, and the tissue response to the prolonged infection is constructive rather than destructive. It is this latter condition which is present in so many cases of dead teeth, the roots of which are infected by *Streptococcus salivarius*.

Even to-day this old notion that infection, and even gross infection, together with severe toxæmia, cannot exist without suppuration, has not died out. The confirmation of the fact given by radiography has been overwhelming, and the influence of such confirmation has been wide spreading.

I need only mention the chronically inflamed appendix and the chronically inflamed gall bladder as other instances of focal sepsis established frequently by radiography. In the case of the gall bladder I have little doubt that by improvement in technique we shall soon be able to establish the diagnosis of chronic sepsis in addition to mere concretions.

RADIOLOGY OF THE HOLLOW VISCERA.

Let me turn now to a very different subject. The influence of radiological investigations upon our knowledge of the anatomical relations and upon the motor functions of the hollow viscera, both in health and in disease, has been epoch-making. Physiology owes no less than pathology to these investigations; indeed, it is scarcely an exaggeration to say that the whole of our present conception of the neuromuscular mechanism of the alimentary canal is the result of x-ray revelations. Granted that a study of the shadows cast by the opaque meal give us one aspect only of this complex mechanism, it still remains that this is the only precise and consistent set of visible phenomena at present available to us in this connexion. And the study of these phenomena has advanced and clarified our ideas to an astonishing degree. When we remember the notions we were taught, and were ourselves accustomed to teach, concerning the physiology of the stomach movements, for example, and what we now know as the result of studying the x-ray screen, the recollection almost brings the blush to the cheek. Whether we really had any exact knowledge at all on the matter I cannot now remember: no doubt that redoubtable Canadian, Alexis St. Martin, with his exposed stomach and its zealous observer, had a lot to answer for; the unfortunate incident was probably given a much heavier load than it could be expected reasonably to carry. To-day we stand upon much surer ground. The "lie" of the stomach and transverse colon, the position of the caecum, the appendix, and the hepatic and splenic flexures are now matters of common knowledge. The variations, too, in the positions of these organs, variations which are not incompatible with good health, despite all the gloomy forebodings of the advocates of colo- and caeco-pexy—we are familiar with these, and they find us for the most part unconcerned, though the knowledge of them is apt to leave their owners much perturbed. We are passing through the stage of incrimination on the score of disease to that of tolerance on the score of variability in individuals, and we may yet arrive at the stage of indifference on the score of a changed conception of the standard of health—all as the result of greater familiarity with the facts as they steadily accumulate from large numbers of radiographic records. In other words, the same thing is happening with regard to our ideas about the hollow viscera as has happened with regard to our ideas about the kidneys. Even moderate degrees of nephropotosis

were at one time regarded as signs of a morbid state, capable of explaining most of the functional disabilities met with in the neurasthenic, and not excluding, in the opinion of some, even grave forms of psychosis. The dropped organ was supported by pads, was "stitched up," was even removed. To-day none of these treatments is considered necessary; the most that we do is to advise some sort of general abdominal support. Enteroptosis, its significance and its treatment, would seem to be passing through the same phases. But just as a kidney may be fixed in an aberrant and in an awkward position, justifying surgical treatment, so, no doubt, a caecum may be tied down in the pelvis, be incapable of emptying itself and may justify a surgical procedure to restore its function. But this difference—between mere ptosis from lack of tone and support on the one hand, and mechanical handicap from fixation on the other hand—constitutes the very essence of the matter, and it is a difference which radiography, and that alone, is able to distinguish in any given case.

But it is not only in the matter of the mere "lie" of the hollow viscera, and the presence or absence of fixation, that radiography has given us such clear ideas; a good many points connected with the motor function of these organs have also been established. I do not propose to deal in detail with the series of events that is now recognized as constituting the normal diorama of the passage of the opaque meal through the alimentary canal, though this is probably the most illuminating discovery of all. But I wish to refer to a few points in which radiography is still giving great assistance to our ideas and enabling us to understand more clearly the nature of some of the problems presented to us by the patient. To put my conclusions first and discuss them briefly afterwards, I would say that x-ray investigations of the alimentary tract seem to me to indicate that although there is a general average of results which may conveniently be taken as representing normal functions, there are many variations within this general average to which it is very important not to attach too much pathological significance. (1) These variations are as between individual and individual and they are probably part of the personal equations of the particular subjects examined, as much as are their facial expression, their gait, and their speech. But our experience of the posture and movements of the hollow viscera is a new experience—it is little more than half a generation old—whereas our experience of face and gait and speech is very old. No wonder that we lack unanimity in our views as to what is normal and what is abnormal. There being no rigid standard of health in this particular respect, it is not to be wondered at that our interpretations of what we see differ so much. Up till the present I doubt if we can say much more of large numbers of opaque meal skiagrams than that they are all of them representations of the alimentary tract of genus Homo, and that they do not reveal any evidence of gross structural defects.

How can we, by means of radiology, get further along this particular line? I suggest that one hopeful way is by departing somewhat from the fixed routine at present employed. There is surely room for some play of the imagination and some experimentation with the method. It was a great advance when the radiologist began to supplement his stereotyped methods of examination by varying the posture of his patient; it was a still greater advance when he began to combine palpation of the abdomen with the use of the fluorescent screen. Such combined methods were, I believe, almost resented by certain clinicians, who thought their own sphere of activity was being thereby invaded; but such resentment, though inevitable, was justly disregarded. I am not one of those who regard the radiologist as a mechanic, or as a photographer, though I am aware that some radiologists aim at little else. There is no reason why the radiologist should not be a clinician in spirit, indeed there is every reason why he should be, for to divorce clinical medicine and radiology is to impoverish both. This leads me to say that I think a closer co-operation between the clinician and the radiologist, and more exchange of views, are desirable factors in the advance of knowledge of the diagnosis and treatment of those diseases which have points of interest to them both.

Such co-operation might easily result in new methods of combined radiographic and clinical investigation as well as in more consistent results from radio-active treatment.

I have said that I think the ideal radiologist should be a clinician in spirit, and I have inferred at the beginning of my remarks that he is a pathologist in spirit also. But I think it very important that he should know the limits of his method, or rather that he should not strain his method past its possibilities in his interpretation of results. If he does this he is no longer giving us the valuable help of his technique and of his powers of observation—he is theorizing. Let me illustrate by reading the conclusions of a report upon the opaque meal examination of a patient whom I saw a week ago. They read as follows:

"The elongation of the pelvic colon and the kink of the iliac colon constitute the primary abnormalities in the alimentary tract. There is pronounced catarrh shown by increased sacculatation of the caecum, ascending and transverse colon, and by persistent narrowing from tonic spasm of the latter portions of the transverse colon and of the descending, iliac, and pelvic colon. The appendix is also catarrhal. The ileo-caecal valve is incompetent. The terminal coil of the ileum is hypertrophied. There is spasm at the ileo-caecal entrance. There is delay in the stomach, but no organic disease or mechanical abnormalities of the stomach or duodenum.

"The severe catarrh of the large intestine and the iliac stasis due to spasm at the ileo-caecal entrance lead to profound toxæmia."

Now I should be the last to put a limit to the radioscopic method of demonstrating anything, whether it be "catarrh" or "toxæmia," but I am not aware that, up to date, either of these processes is amenable to the opaque meal method. Though I say it with less assurance, I am doubtful if "hypertrophy" is any more demonstrable than "catarrh." No doubt the argument is sound enough if we add to the radioscopic evidence the collateral facts elicited by clinical and clinico-pathological methods. But not otherwise. If forbearance be not exercised in these things and the radiologist really "lets himself go" he is apt to bring his science into disrepute. I have received reports of a much more committal kind than the one I have just read. It is by no means uncommon to be told that a child has active and extensive pulmonary tuberculosis because the hilum shadows are conspicuous, and the glands obviously enlarged, after some febrile illness. I have even been rung up on the telephone, so intent was the radiographer to let me know the seriousness of such a situation. I was able to assure him that the boy was already convalescing rapidly at the seaside. I am, of course, alive to the fallacy in these remarks: that the child might be suffering from pulmonary tuberculosis after all. But experience must be the final guide in such cases, and experience cautions us very definitely not to make exact diagnoses in the absence of clinical data. Why need we? There is no necessary parallelism between change in structure and change in function, and the essence of disease is a functional rather than an anatomical change. Radioscopy itself has helped us greatly in this conception. How many instances we see in which there are quite extensive bony changes in the hip-joints and in the spine, but little or no pain or other disability. On the other hand, how severe may be the symptoms of hip-joint disease, without any demonstrable change seen in the radiograms. One patient may have a large collection of gall stones and be in excellent health; another may have no actual concretions and yet be the subject of severe gall-bladder dyspepsia. These examples might easily be multiplied.

To return to the question of the opaque meal and its help in establishing variations in the position and in the functions of the hollow viscera. (2) Not only are these variations seen in skiagrams resulting from the examination of different healthy individuals, there are also variations, of no great moment considered pathologically, and yet of great physiological significance, in the same individual at different times and under different conditions. I have proof of this fact, and no doubt not a few others present have proof also. But as "repeat" investigations are not often undertaken the evidence is not so abundant as in the case of different individuals. Certain fortuitous observations, however, are pertinent. A radiological colleague of mine recently told me that he was on one occasion screening a nervous patient just after the opaque meal

had been swallowed. It was before the time of the fixed screen. In moving this upwards to get a view of the cardiac orifice, the top inadvertently struck the patient under the chin. It was immediately noticed that the stomach, which had previously been observed to lie in a good position, and to be actively motile, dropped suddenly a distance of several inches, and at the same time all active peristalsis ceased. This excellent demonstration of the sensitive response made by this organ to a sudden shock points a moral to the story that I am, by comparison, labouring in the telling. It is sometimes inevitable that, though no such physically painful stimulus as this takes place, the novel and somewhat alarming noises which occur during a radiosopic examination must have a somewhat similar effect. There is little doubt that when a patient says he has a sinking sensation in the abdomen the sensation is accompanied by a relative and temporary degree of gastroparesis; and I think it quite likely that, if we were able to screen a person during the play of various emotions, we should find that when his "heart was lifted up," and when his "heart sank within him," it is in reality not his heart but his stomach that changes its position in this manner, as the result of increased and of decreased tone respectively. I do not know if the cinematograph method has ever been applied to the transit of the opaque meal, but it is not at all unlikely that a series of pictures taken in this way would reveal many facts at present only guessed at, especially if the observations were made to cover some of the emotional states just referred to. If the stomach is so sensitive to emotions, to pain, and to reflex action through the special senses, it is not likely to be less sensitive to general fatigue. I think this may perhaps explain some of the discrepancies between the clinical examination of the stomach and the radiographic results. It was formerly not at all an uncommon experience of mine to conclude, as the result of my examination of a patient in the afternoon, that he had a dilated and atonic stomach, and to feel somewhat mystified when my radiological colleague demonstrated to me next morning that the organ was of a natural size and possessed of good motility. I now feel confident that it is the difference between afternoon and morning that accounts for the apparent disparity of the results, though I think that there are other factors which enter into the causation of the "splashing stomach" that is so common on the couch of our consulting rooms, and yet which so often finds no equivalent expression in the observations of the radiologist.

There are two or three further points in connexion with the important subject of enteroptosis where radiology has been illuminating in two senses of the word. One of these is the difference in level of the stomach, and especially of the colon, with posture. Radioscopic investigations certainly confirm the advice which we usually give patients suffering from this trouble to interrupt the erect posture of the greater part of the day by lying for a certain time in the semi-Trendelenburg position, for the difference of levels of the viscera in the two positions can be shown to be well worth the while. Again, examination during the wearing of a properly fitting support, such as special corsets which take their purchase from the hips and from the spine, proves that, in some cases at all events, the support really does assist in keeping the organs in better position. Lastly, it can be demonstrated that the effect of a walk which is not too fatiguing is to raise, and not to lower, the levels of the hollow viscera. For these demonstrations I am indebted to my friend Dr. Dudley Stone, whose skiagrams I hope to show you at the close of these remarks.

Before leaving this matter of enteroptosis I wish to refer to one other point, partly because of its pathological interest and partly as a warning. It is common knowledge that we are often able, by a carefully devised programme of treatment properly carried out, to improve the health of the subjects of this condition very considerably, even to the extent of hearing them declare that they are "cured" of their symptoms. If now we examine them again radiosopically by the opaque meal method we find, in quite a number of cases, that the "lie" of the stomach and colon is practically unchanged. The moral is obvious: to the patients whose intelligence is able to hear the news we

explain that it was not the mere ptosis of their organs that caused their discomforts and their general inefficiency, but the associated nervous asthenia, and even more (as I myself think probable) the congestive state of these same organs. To the majority of such patients, however, it is wiser to avoid the repetition of the examination altogether—not a very difficult situation to negotiate in actual practice in view of the present cost of a complete opaque meal investigation. The experience that I have just recorded serves well to confirm the principle that many diseased conditions are complexes made up of anatomical defects, together with nervous, vascular, metabolic, and infective associations. Radiology shows us one part of the picture, and a very important part—still, only one part.

In the history of its progress radiology must, of necessity, have first concerned itself with gross structural points, both normal and abnormal. It was essential to get certain rough criteria established. The method has now passed this stage in most regions of the body, though not in all. It is now contributing help of a more important, though more subtle, kind: it is helping us to study function, again both normal and abnormal. It is helping us to realize more vividly the fact that for a long time the patient does not suffer from diseases but from a tendency to disease; that later, when disease is established, the dis-function is not a fixed state, but an ebb and flow. I should like to make it clear that to me this is the kind of help that seems of vital importance. I doubt very much if those radiologists who are striving after "standards" may not be missing some more important things—I do not speak of physical standards, but of health standards. One such radiologist friend of mine with whom I was discussing a case of mutual interest said recently, "I wish we had a standard measurement for the breadth of the mediastinal shadow." Comment is unnecessary, but that is the outlook which I regard as likely to stultify some of the great possibilities of his science in the near future.

RADIOLOGY IN DISEASES OF THE LYMPHATIC GLANDS.

Upon our knowledge of diseases of the lymphatic glands radiology has thrown a flood of light. The discovery of enlarged nodes by x-ray methods was for a time such a revelation that it not only gave confirmation to the view that tuberculosis of those glands was a very common disease, it led many radiologists to give quite unwarranted and pessimistic opinions concerning the patients examined by them—an error of judgement that even to-day is by no means rare. If I may add that it is also by no means rare for patients to be given possession of their own or their children's radiograms, it is readily seen how easy it is to construct, quite unwittingly, situations full of apprehension and alarm, but which can be avoided by a little care and tact on the part of the radiologist. With improvement in technique, the frequency with which shadows are demonstrated in the regions where glands are known to enlarge—such as the roots of the lungs—becomes greater year by year. It is no longer necessary that a node shall be calcified, or even caseous, to throw a shadow by modern radiological methods. The standards of health are therefore, in this respect, changing. On the one hand we realize more clearly than we formerly did that there is an ebb and flow in the size of lymph glands in the thorax as there is in superficial parts of the body that are open to palpation; to some extent, therefore, the significance of demonstrating enlarged glands in the former situation is not so serious as was once supposed. On the other hand radiology has opened our eyes to the fact that, in certain diseases of the lymph glands where we thought the lesions were confined to the superficial nodes, in many cases the intrathoracic nodes are enlarged also. An important example of this is lymphadenoma, where such a discovery at one and the same time increases the seriousness of our prognosis yet enables us to treat the disease much more promptly and effectively. In the not uncommon cases of this disease in which periodic pyrexia occurs, we were often quite in the dark as to where the specifically active process which led to the fever was going on. We watched the glands in the neck, axillae, groins—nothing occurred. We suspected the visceral lymphoid tissue, and we therefore kept the spleen and liver under close observation—still we had no clue. A good x-ray

picture solved the mystery by its revelation of the rise and fall in the breadth of the shadows in the hila of the lungs. No doubt in some of these cases we shall in the future, with improved methods, get similar demonstrations in regard to the abdominal lymph nodes in lymphadenoma. In the case of carcinoma of the breast a similar demonstration of the fact that the zone of lymphatic infiltration is more extensive than would otherwise be supposed is often given by radiological examination. And the significance of this finding is much the same as was seen to be the case in lymphadenoma: on the one hand our conception of carcinoma mammae as a disease has changed in that we now know it to be often a more extensive affair than was formerly supposed, and, on the other hand, we are able to set against this serious consideration knowledge that leads to much earlier and therefore more effective treatment.

It is not only in relation to lymph nodes that our conception of carcinoma has changed as the result of radiological findings: the same remarks are applicable to the bones. We now know that osseous metastases are much more common than was thought to be the case before the era of radiology. The clinical picture presented by a woman who has undergone excision of the breast for cancer two, four, six, or even ten years ago, and who now complains of severe pain in the back, hips, or legs, due to cancerous infiltration of the bodies of the vertebrae, or of the pelvic bones, is all too familiar. Such cases were usually thought to be severe examples of fibrositis until one or more of the lesions led to local prominence or to spontaneous fracture. It is possible that such cases are more common to-day than formerly; it is even possible that they are relatively more common in patients who have had radical operations done for the primary growth; but it is certain that as the result of x-ray investigation we are able to diagnose them much earlier, and it is highly probable that many are brought to light to-day which would never be discovered at all. Further, it is not a very uncommon experience to find these tell-tale lesions overlooked in a good radiogram, even by the radiologist; and I think the reason is, either that he is not warned of the possibility of neoplastic disease, or because his attention is distracted from the infiltrations by some osteo-arthritis changes at the periphery of the vertebrae. I have recently dealt more fully with this subject of carcinomatosis in the Purvis oration. I pointed out there that in not a few of the cases the appearances may be equivocal. For there is a condition now and then met with in carcinoma in which good radiograms reveal a state of diffuse rarefaction of several of the bones, the nature of which is difficult to determine, and which is almost certainly different from the more localized deposits that I have just referred to. I regard this change as part of the general toxic or nutritional disturbance that occurs in carcinoma, and which leads eventually to the so-called malignant cachexia. It is sometimes asserted that malignant cachexia is due to secondary microbic infection of the growth; but this is probably only so in part; these bony changes go to show that there is something specific in the carcinomatous cachexia, for we have no knowledge of them in chronic pyogenic infections. I was interested to hear from my colleague, Dr. Gilbert Scott, that he had met with this same appearance, and that he felt sure it was not due to actual cancerous infiltration, however widespread this undoubtedly is at times. I purpose showing lantern slides, taken from skiagrams kindly lent to me by Dr. Gilbert Scott and by Dr. Robert Knox, which illustrates this condition. I find that this peculiar form of mollities has been noticed by one or two observers before, particularly by Roger Williams, but I have not come across any radiographic examples of it.

RADIOTHERAPY.

Thus far I have dealt only with some of the ways in which radiology has influenced our ideas of disease by revealing to us changes in structure and function that we previously knew nothing about or merely guessed at. I turn now to a few examples of modifications in our views of disease resulting from the experience of radiotherapy. And it is a natural transition from the radiographic aspects of carcinoma to which I have just referred to the radiotherapeutics of malignant disease. The surgical treatment

of malignant tumours has advanced very little during the past generation, and such advance as it has made is to be attributed almost entirely to advance in the means of diagnosis whereby operative procedures offer better hope of radical cure. The practice of aseptic methods once established, and the importance of the anaesthetist's contribution to the success of the operation once fully recognized, the limits of the surgeon's possibilities in this direction seemed to be reached. Handley's important work upon the lymphatic spread of cancer of the breast is now just twenty years old, Stiles's and Halstead's classical papers advocating widespread removal of infected tissues are ten years older. The work of these men has not been materially altered up till to-day. Perhaps the only important advance in the operative treatment of carcinoma during the past two decades is the abdomino-perineal operation for cancer of the rectum, for the present improved technique of which credit is to be given in this country to W. E. Miles. If we turn to the medical side of the question, and ask what advances the physician has made towards the treatment of malignant disease, we are met almost with silence. The evidence that the injection of the heavy metals materially benefits the subject of malignant disease is, I think, very slight, although I consider that they have a definite value when used in conjunction with radio-active treatment. The fact that various sorts of serums and antigens, even including Coley's fluid, have completely fallen into disuse, goes to show that in this field nothing is being accomplished. Certain ancillary helps, it is true, the physician can give, both to the surgeon and to the radiologist, but I know of nothing he does, any more than the surgeon, in the direction of therapeutics which affects our conception of the neoplastic process.

If we now turn to the sphere of the radiologist, we find an entirely different state of things. I am not to-day concerned with the results, still less with the methods, of treatment of malignant growths by x ray or by radium. But the bearing of such treatment upon our ideas of the course and even the pathogenesis of such growths is very close. It is fairly safe to predict that the many observations now in actual progress will very shortly yield important facts the knowledge of which will not only help to crystallize our ideas upon some of the causative factors, but will also enable us to control our remedies more hopefully. One great change in our ideas about cancer, or so it seems to me, as the result of radio-active treatment, is the abolition of the notion that there is anything necessarily and inevitably progressive about the disease. Once we have seen—as which of us here has not?—a patient's general condition of health restored, and his growth greatly reduced in size, by radio-active treatment, we can never again look upon cancer in quite the same light. It is true that, with our present limited knowledge, working in the dark to a large extent as we are, such restoration to health, and such resorption of the tumour, are but of temporary duration. But my point is this—that in such cases we have a demonstration of the fact that *cancer is controllable*, using a word that I regard as more applicable to diseases in general and more scientific in its connotation than the more popular word "cure." If we consider the matter for a moment, do we *cure* tuberculosis? We do not, but we are perhaps getting the disease slowly under control. We have certainly added nothing specific to our means of "cure" in this disease; we are even using specific methods less and less. Syphilis is more definitely controlled to-day than twenty years ago, but there are many cases that still resist curative treatment; syphilis of the central nervous system we are still almost powerless to deal with by any of our present methods. Ulcerating endocarditis we neither cure nor even control, and of certain forms of rheumatic infection of the heart unfortunately the same thing may be said.

The senior surgeon of a large London hospital recently said publicly that he regarded the exploitation of radio-therapeutic methods as a menace to the effective treatment of cancer, asserting that he considered such efforts prevented patients from receiving the early benefits of radical surgical measures. Such an extraordinary indictment calls for some comment. If radiotherapy really did this I should agree with him. But of course it does not. No reputable

radiologist dreams of denying a patient with an operable malignant tumour the advantages of surgery; in every case the surgeon has the "first call"; and a firm conviction that in the treatment of malignant disease to remove the diseased organ cannot be more than a method *faute de mieux* does not, in the present stage of our knowledge, cause us to swerve from this invariable rule of practice. Unfortunately there are all too many cases in which, even at the earliest moment of the diagnosis, modern surgical technique is unavailable; the growth is so situated anatomically that it cannot be reached or is already disseminate. Appropriate material for the radio-therapist is therefore not lacking, though he is, by virtue of the rule already mentioned, denied the very sort of material with which he could probably do the best work. But even with this handicap it is possible to mark a steady change in the course of cancerous diseases as the result of the radiologist's efforts, and the outlook for sufferers from the dreaded scourge was never so hopeful as now. Many cancer patients live longer to-day, and live less painfully, both in body and mind, than ever before, and this is very largely on account of radio-active therapeutics.

Do these facts throw any clear light upon the etiology of cancer? Perhaps not. But the more successful application of radiotherapy to lymphadenoma is to me significant in this connexion. There are many similarities between these two diseases. If, as I think is not unlikely, the lymphadenomas are proved to be caused by a group of protozoal parasites, then the increasing success that we find attending the combined treatment of these affections by arsenic and x rays does seem to suggest that we should be premature in considering that cancer is not an infective disease as has been recently asserted, and asserted semi-officially, by some workers. But this is too large a question for the purpose of this lecture. Like many other questions connected with cancer, the answer can only come from concentrated labour and constructive thought. I am optimistic about combined methods of research—radiologist, clinician, and pathologist working in team fashion. Research combined with treatment is not popular with scientific advisory committees, but we must do our best to make it popular, and no doubt the more contributions it makes to knowledge, the less unpopular will it become. "Why," said a colleague to me recently, "why do they call it research when *they* put radium into a mouse, but not when *we* put it into a man?" No answer seems possible unless it be that the radiologist, the clinician, and the histologist are not considered to be capable of observation or experiment. Let us demonstrate that this is not true, and let those who disburse public funds help us to explore this fertile ground of research combined with treatment. I have often remarked that every piece of treatment properly devised and carried out is a piece of research. I am no prophet, but I hazard a prediction that the effective control of cancer will come by other means than by a direct attack upon the essential *materies morbi*, even if it does not come before we know what that *materies morbi* is. And I think that research combined with radiotherapy will have been a conspicuous factor in bringing the control about.

I must not stay to deal with other diseases in which our conceptions have been influenced by the experience of radio-therapy. In the leukaemias, in exophthalmic goitre, in various skin diseases, and to a less degree in several other fields, our ideas about pathology have been modified. I think the modifications would have been even more striking if the work had been more thoroughly controlled by combined clinical and histological methods. But there are, as I have said, hopeful signs that such control will be sought and will be given in the future.

CONCLUSION.

I am all too well aware that in this address I have brought coals to Newcastle. For a physician to talk to radiologists about a subject so special as theirs is must lead of necessity to not a few bizarre expressions and demonstrations of his own ignorance. But the point of view of one who is an outsider in all matters of radiological technique, and yet an insider in all matters of pathological interest, may not be without its suggestiveness to your minds. And surely it is pathology (I use the word in its

old and truest sense) that links together all our diverse interests. We must never lose sight of the essential *unity* of pathological processes. Though clinical medicine sees one aspect of a disease, and radiology another, and morbid anatomy a third, and parasitology a fourth, the disease is one and the same, and our best conception of it is obtained, not by undue insistence upon any one of these aspects, but by a proportionate mingling of the pictures presented by all. He who achieves the most complete conception of a disease in his mind is the most likely to envisage the appropriate treatment and get the best result. None of us can afford to neglect the facts elicited by the methods of others; indeed, our own methods will yield us more facts, and a clearer vision, in exact proportion as we allow them to be guided and controlled by the methods of others. It is of the utmost importance that we keep our minds alert and free from stereotyped ideas, yet bound always, fettered even, by the principles of science and reason, with a healthy scepticism withal—that saving grace so essential to the scientific mind. Let us remember that our present notions of diseases, even when we think them very complete, are probably extremely crude. We have already ample experience that this is so. Not only are they crude in respect of the extent and the complexity of the disease process, as instanced earlier in this address, but in respect of the course diseases run and their response to our efforts at treatment. The problems of pathology become more elusive and yet more fascinating the closer we study them. It is a glorious contribution to such study that you are making to-day by means of radiology, both in its diagnostic and in its therapeutic values. The memory of him in whose name we meet together to-day is, I feel sure, being well served by you who follow him. I wish to congratulate you upon the fine work with which you are supplementing his and other pioneer achievements, and I shall have justified myself if anything I have said serves to stimulate you to further efforts and yet greater results.

Hunterian Lecture

ON

CANCER OF THE CERVIX.

(With Special Plate.)

DELIVERED BEFORE THE ROYAL COLLEGE OF SURGEONS,
JANUARY 25TH, 1924,

BY

SIDNEY FORSDIKE, B.S., F.R.C.S., M.D.

(Abridged.)

ETIOLOGY OF CANCER.

MODERN methods of experimental research have resulted in the production of cancer in animals at will. This result, together with Drew's observations upon the culture of tissues and tumours *in vitro*, are notable steps in the solution of the secret of cancer. Already theories which have held sway for generations have been demolished. The vague conception of tissue tension is no longer tenable, and the behaviour of malignant and benign cells during growth *in vitro* shows conclusively that Hansemann's theory of anaplasia is unfounded, whereas it confirms the view that tumour formation ensues upon chronic irritation. The production of tar cancer shows that there is a variable latent period between the application of the irritant and the appearance of the new growth, from which some interesting conclusions follow. A close study of cancer in human beings frequently fails to disclose recent evidence of tissue irritation; nevertheless, the irritant may have produced cell changes which are not histologically recognizable at the time, but long after the irritant has ceased to act the tissues exhibit malignant change. This is borne out by Leitch's experiments with tar cancer. He noted that, even though he stopped the application of tar before there was any sign of malignant change, warts appeared in due course and malignant evolution took place.

Furthermore, it has been shown that tumours which are

apparently benign may develop into malignant growths, and that injury, which of itself is not capable of producing cancer, will greatly accelerate the development of cancer after the application of a suitable irritant. Finally, there is the important fact established by Murray, that mice which have developed tar cancer will not develop a second tumour despite continued irritation, which observation offers an explanation of the rarity of multiple carcinomata in man. It shows that the mouse acquires immunity to the growth of further tumours, which is also borne out by the observation that certain inoculated tumours, after a period of growth, came to a standstill and were finally absorbed. Attempts to reinoculate the same mice with the same tumour completely failed, and they showed greater resistance than normal mice to other tumours. Bashford and Murray have shown that this resistance is of the nature of an active immunity.

Proemial Conditions.

I agree with Lenthal Cheate that this description is more exact than precancerous or precursory. Erosions, fissures, lacerations, and chronic cervicitis are described as fore-runners of cancer of the cervix, but as one or more of these lesions are invariably present in parous women, and as 90 per cent. of this disease occurs in that group, the evidence is not too convincing. Since, however, experimental cancer is shown to be dependent upon irritation, it is possible that any of these lesions is an indication that the irritant is present, and where it happens upon favourable ground malignant growth ensues. I investigated a large number of uteri of some of the more prolific domesticated animals—the cow, sow, bitch, and cat—with the object of ascertaining whether any of these lesions could be found in them. The cervixes of the cow and sow are formed of a rosette of protuberant cervical mucosa, and it was not possible to detect by naked-eye examination whether minor tears and lacerations were present or not; but in none of the organs examined was there any gross lesion, and on microscopic examination there was no evidence of cervicitis. In the cat and bitch the cervix has a less complicated structure and is therefore more satisfactory for examination. No evidence of laceration or chronic inflammatory lesion was found. Professor Wooldridge informs me that carcinoma of the uterus is exceedingly rare in any animal; nevertheless, it is of interest to note the rarity of both types of lesion which are so frequently associated in cancer of the cervix in women.

Erosions.—There is suggestive evidence that the papillary erosion stands in some sort of relation to cancer; four cases of interest have been under my observation.

One had been an in-patient for chronic cervicitis with a papillary erosion. She came under my observation nine months later with an extensive carcinoma of the cervix.

Another was treated similarly and a piece removed for section, which showed no malignant change; fifteen months later she came under observation with an inoperable growth of the cervix.

A third was regarded as an erosion, but as it bled a little more than usual she was entered for admission, with a view to exploration. She escaped observation for five months, and then returned with an inoperable cancer.

The fourth had been treated as a cervicitis, and seven months later came under my care with advanced cancer.

There is another type of lesion of which I have met three cases in all, and for want of a better description it may be called the "bleeding cervix."

Bleeding Cervix.—The whole cervix is soft and spongy, dark red in colour, bleeds persistently when swabbed, and a probe sinks into its substance. The haemorrhage resembles that which takes place from the surface of a granulating wound—numerous minute drops of blood ooze out, run together and form a stream. It differs from the haemorrhage of the papillary erosion, for that ceases at once with a little pressure, but this persists and may require a gauze plug to enable the patient to get home.

In one of these cases the bleeding persisted daily for a week, and I finally amputated the cervix. This patient died twelve months later from carcinoma of the stump of the cervix.

A second became malignant, and I removed the uterus.

The third is now under observation, and as the microscopic examination did not justify the radical operation I treated her with radium. The microscopic appearances are those of angioma. The deep part of the section shows evidence of cervicitis; the epithelium is squamous and shows no evidence of proliferation, the striking feature being the number of blood vessels in the section.