was always due to metastatic disease in the thorax. Widespread local recurrences after radium treatment are very uncommon, and they do not ever appear to be attributable to the treatment. Finally, a number of patients have been encouraged to undergo treatment only because they were to be spared the mutilation entailed by surgery. Patients have sometimes said and written to me most moving things in this connexion, and I have no doubt that if conservative treatment were to be commonly practised it would finally have the result of bringing more patients to the benefits of early treatment, and so improve the end-results.

Some Disadvantages

Against these advantages of conservative treatment must be set certain disadvantages. There is, for example, the difficulty of the interpretation of results. I have already mentioned the possibility of there being a residual tumour after treatment by radium alone, and the difficulty of knowing whether this contains active carcinoma or not. In addition to this there is the post-irradiation fibrosis which is apt to appear as long as two years after treatment in the positions where the irradiation has been most intense. It is particularly liable to occur on the inner wall of the axilla, and many of my patients have fibrous lumps in that situation which would unquestionably be diagnosed as recurrent cancer by inexperienced observers. Needless excisions of these lumps and long experience have enabled me to distinguish confidently between fibrosis and recurrence, but it is clear that they introduce real difficulty in the way of widespread adoption of the method. Eighteen months ago I treated a lady for a very early cancer of the breast, and subsequently she returned to South America. Events then took place which greatly alarmed the surgeons in Brazil, and afterwards in Baltimore, though I feel sure in my own mind that the patient did not have a recurrence of carcinoma.

Another disadvantage of the conservative method is the increased liability to neuralgia or "rheumatic" pains in the treated areas. It is true that every woman who has had a cancer of the breast is likely to exaggerate slight pains into worse ones because she always thinks that pain indicates recurrence. Nevertheless, the treated areas do certainly remain for some time more likely to give rise to pain than an operation scar, and the patients are to that extent more conscious of their past experiences. I have never encountered among my patients a true brachial neuritis due to placing needles too close to the brachial nerve trunks. I have seen it produced, however, in another clinic, and it must be remembered that radium needles are dangerous weapons if used with insufficient skill (but so, it may be answered, is a scalpel or almost any of the instruments we are accustomed to use in surgery). Post-irradiation fibrosis may also affect the pectoral muscle and produce some degree of limitation of movement. This is greater when the position of the disease in the breast or axilla necessitates placing a large dose of radium over and under the border of the pectoral muscle. In treating early disease this is not necessary, and the resulting limitation of movement is negligible.

Conclusions

The foregoing account of a clinical investigation, which has now extended over fourteen years, seems to me to show that the treatment of carcinoma of the breast may justifiably be made much more conservative

than it usually is, provided that the necessary facilities for irradiation are available. Statistics appear to demonstrate that a definite improvement can be obtained in the most favourable group of patients by judicious use of interstitial radium alone, or of radium combined with very conservative surgery. The rapid improvement in x-ray technique now taking place suggests that x rays may perhaps be used as an alternative to radium according to circumstances. The treatment here advocated is, however, conservative rather than purely radiological, and details of the technique will no doubt undergo further modification. The general trend of surgery in the treatment of cancer is away from the very extensive operations formerly in vogue, and I believe that this may be found to be true of the future treatment of cancer of the breast. My own results with conservative methods encourage me to proceed in that belief.

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TUMOURS OF BONE* RESPONSIBILITIES OF THE PATHOLOGIST

BY

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(WITH SPECIAL PLATE)

This is the second occasion within a year on which radiologists, surgeons, and pathologists have met to discuss the same, or very much the same, problem. At the Royal Society of Medicine meeting in January it was urged by the radiologist and by the pathologist that "the closest co-operation must exist between the clinician, pathologist, and radiologist." As I understand it co-operation in diagnosis means nothing more nor less than a fair co-ordination of responsibility, with a spice of mutual understanding and good will. Therefore I should like to summarize at this meeting the responsibilities, as I see them, which rest upon the pathologist in respect of tumours of bone.

1. Correlation of Radiography with Pathology

After every amputation of a limb for a bone tumour, and during every post-mortem examination of a subject in which there is a deep-seated or inaccessible bone tumour, the pathologist should bisect the bone containing the lesion at right angles to the plane of the best radiograph available or in such other plane as will best facilitate the interpretation of the radiographs. This is better done, of course, after consultation with the radiologist. Next the pathologist must determine the histological structure or classification of the growth. And then the radiologist and the pathologist together, with the surgeon if he is interested, should correlate the macroscopical and microscopical appearances of the growth with the radiographs. I need hardly say that the radiographs must be recent if the correlation is to possess any degree of accuracy. If no recent radiographs

* Read in opening a discussion at a joint meeting of the Sections of Pathology, Bacteriology, and Immunology, and of Radiology, at the Annual Meeting of the British Medical Association, Belfast, 1937.

are available it is desirable to take fresh radiographs after amputation, or post mortem, as the case may be, before the specimen is interfered with. In this connexion I have much pleasure in expressing my warmest thanks to my radiological colleagues in the Royal Victoria Hospital—Drs. Beath and Montgomery—for their inexhaustible kindness and help. For the purposes of correlating radiography with pathology there is no technical procedure which can approach the preparation of giant sections of the whole tumour, or segments thereof, approximately 4 in. by 3 in., if the tumour is very large. These sections, mounted and stained on a clean quarter-plate, can then be projected on a screen by means of the epidiascope. Three examples are illustrated: (1) an osteogenic sarcoma of the tibia, invading the knee-joint; (2) an osteolytic sarcoma (Geschickter) of the femur; and (3) a Ewing sarcoma of the upper end of the tibia following irradiation (positive radiodiagnostic test). In passing I may say that the application of the radiodiagnostic test in any surgically accessible and radio-apparent bone lesion of doubtful nature always fills me with alarm. The lesion in this case was a Ewing sarcoma, which had been regarded clinically as a Brodie's abscess. Eventually a biopsy was done and the diagnosis was returned within twenty-four hours. The patient, aged 21, serving in the Royal Irish Fusiliers, refused amputation, and intensive irradiation was instituted immediately. The local result was good, but meanwhile a swelling slowly appeared above the knee. Amputation was performed a month later, and then it was discovered that the supra-condylar pouch of the knee-joint was filled with tumour tissue. The Ewing tumour is very generally admitted to be the most radiosensitive of all bone sarcomas without exception; and yet in this case extension occurred during radiation treatment. The patient died five months later with widespread metastases in his skull, sternum, and other bones. In my opinion the radiodiagnostic test is apt to postpone amputation until it is too late.

I have no doubt that careful correlation of radiography with pathology is practised to a greater or less extent in all the larger centres, but the subject is important enough to bear repetition. Also it has the great merit of being above and beyond criticism and controversy.

2. Biopsy

When we turn, however, to the second responsibility or function of the pathologist—namely, to the diagnosis of bone tumours by biopsy—we discover a violent clash of opinion. In some centres, of which the Royal Victoria Hospital in Belfast is one, an "open" biopsy is carried out as a routine procedure in every doubtful but accessible lesion of bone before any major mutilating operation is undertaken. In other centres radiologists, surgeons, and pathologists are opposed, root and branch, to the procedure of biopsy on the grounds that it is dangerous, unreliable and often misleading, and unnecessary. If they are right it is evident that the practice of the Royal Victoria Hospital is not only wrong but dangerously wrong; if they are right we cannot mend our ways too soon.

Arguments for and against Biopsy

Our first requirement is to discover the essential facts upon which we can all agree, whatever our creed. We can surely agree that the diagnosis of a bone sarcoma is a matter of urgency—of greater urgency perhaps than in any other malignant tumour. According to the statistics of the American Registry of Bone Sarcoma the "five-

year-cure" rate does not exceed one in seven. In other words, radical treatment in America has been delayed beyond the time of dissemination of the growth in six cases out of seven. We have no comparable statistics in this country, and, for all that we know, our results may be worse than the American ones. Evidently we must diagnose bone sarcoma earlier and earlier before we can expect any significant improvement in the prognosis following radical treatment such as amputation or wide resection. We must diagnose it, in short, before the surgeon can diagnose it, on clinical examination alone.

There are only two more precise diagnostic procedures which need to be considered in the present state of our knowledge—namely, radiography and biopsy. The radiodiagnostic test is omitted deliberately. Radiography takes precedence in the procedure of diagnosis and should never be omitted. If the radiograph is convincing enough radical treatment must be carried out with the least possible delay. If the radiograph is not quite convincing—and in the early stages sarcoma can be confused readily with tubercle or with a Brodie's abscess, so that the stakes are a limb against a life—what are we to do? We can either perform a biopsy at once or we can wait for a month or for three months, or even longer, until the radiographic diagnosis is unmistakable. Our choice of procedure must undoubtedly be compelled by the relative merits of serial radiography and of biopsy in respect of (a) danger to the patient or risk of dissemination of viable tumour cells, (b) reliability, and (c) necessity, because these are the three respects in which biopsy is challenged and often condemned.

(a) Risk of Dissemination of Tumour Cells

Biopsy is attended by the risk of dissemination of viable tumour cells because the surgeon must divide many of the vascular channels of the growth in procuring the specimen for examination. Serial radiography, because it postpones amputation or resection for a variable period, is attended by a risk of the same kind. No one can determine directly which of the two risks is the greater because each individual case of bone sarcoma in man is an uncontrollable experiment. If, however, secondary growths make their appearance at any time after the execution of a biopsy, the unfortunate biopsy is invariably incriminated by the opponents of the procedure, whereas if secondary growths appear after serial radiography or the radiodiagnostic test, without the intrusion of a biopsy, such secondary growths are regarded piously as an act of God. This conclusion is merely a stultification of reasoning, and, as I hope to show, may not be altogether just to our Maker.

Before we can reasonably proceed to a critical analysis of the risks attending biopsy and serial radiography respectively in the diagnosis of bone sarcoma we must close certain gaps in our knowledge of what might be called the biological behaviour of malignant tumours of bone. For example, we all know that these tumours are peculiarly liable to metastasize, but we can merely do our best to interpret the reason. It is scarcely possible, even if it were prudent, to make experimental observations on any bone sarcoma directly. Fortunately for our immediate purpose Nature carries out an appropriate experiment which is not uncommonly observed. This natural experiment takes the form of an intrinsic tumour of the brain growing within the bony shell provided by the cranium. Such a tumour may be present for months or for years, for all that we know, and may be symptomless so long as its growth can be compensated by adjustment of the

cerebrospinal fluid. As the growth proceeds beyond this point the hydrostatic pressure of the whole cranial contents gradually rises, affecting tumour and healthy brain tissue alike. This increased pressure is evidenced by flattening of the cerebral convolutions post mortem. The gradual and natural increase of pressure attending the gradual growth of the tumour is subject to a more sudden increase, irregularly from time to time, owing to the occurrence of haemorrhages into the growth. Indeed, occasionally a single large and fatal haemorrhage may occur into an astrocytoma which has been previously symptomless. A malignant tumour of bone, either endosteal or periosteal, is growing under mechanical restraint from a very early stage of its development, and it is a fair conclusion that its hydrostatic pressure will be higher than that of another sarcoma growing in soft tissues. We all know that haemorrhages are liable to occur into the substance of a bone sarcoma under natural conditions. Each of these haemorrhages must be attended by a further focal, perhaps momentary, rise of hydrostatic pressure whereby tumour cells could be propelled actively into the gaping vascular channel which had been the source of the haemorrhage. In my opinion the hydrostatic pressure which we cannot see under the microscope is a far more important factor in the dissemination of viable tumour cells in a bone sarcoma than the rich vascularity of the growth which we can see. This conception is not put forward as a scientific fact, because the physical problems involved are so highly complex; it is advanced as a reasonable hypothesis.

We have to apply this hypothesis not to one but to two alternative surgical procedures in the execution of a biopsy. First, there is the modern or "improved" method (Hoffman, 1931), which consists in the puncture of the bone sarcoma by a wide-bore needle attached to a 20 c.cm. syringe; the tumour tissue is "cored out" and "strong suction is made" (Coley, 1935). There can be no doubt at all that haemorrhage will occur into the growth following such interference and that the hydrostatic pressure will rise according to the volume of the haemorrhage. This method is described as "75 per cent. reliable," and is merely asserted to be safe. According to my view it would be better described as "100 per cent. dangerous."

The second or alternative method is the simple old-fashioned one of incising the periosteum or, it may be, the cortex of the bone over the bone sarcoma more or less freely and always gently. Decompression should occur gradually. After a short interval to ensure that the hydrostatic pressure shall have fallen a representative portion of the growth is excised with a sharp knife. Blood escapes more or less copiously into the wound, but *not* into the substance of the growth. Thus a rise of hydrostatic pressure is avoided. According to my view this method should be as nearly as possible "safe."

Let us now try to compare and contrast the risks of an open biopsy (that is, one executed by free incision) with those arising from lapse of time occasioned by the requirements of serial radiography in the diagnosis of bone sarcoma. Every single malignant tumour in man is an uncontrollable experiment. The best that we can do is to study the operation of the factors of biopsy and of time in large-scale and adequately controlled experiments with malignant tumours in animals. Wood (1919) took 673 rats which had been inoculated with the Flexner-Jobling rat carcinoma—an adenocarcinoma which metastasizes readily to the regional lymph nodes and by way of the blood vessels to the lungs. These tumour-bearing

rats were divided into three groups. In the rats of Group I a portion of each tumour was excised aseptically (biopsy factor) and the skin sutured over the wound. Ten days later the remaining portions of these tumours and the intact tumours of the rats in Group II (biopsy and time "control") were excised (to prevent further dissemination from the primary site). The rats in Group III (time or serial radiography factor) were left untouched. All the animals in the three groups were killed approximately five weeks from the beginning of the experiment. The incidence of metastases in Groups I and II was 22.2 per cent. and 21.8 per cent. respectively. Thus the natural liability to metastases was *not* increased significantly by the procedure of open biopsy. The incidence of metastases in Group III was 32.2 per cent. Therefore in this particular rat carcinoma, under the experimental conditions stated, undisturbed growth for three to four weeks resulted in a considerably higher incidence of metastases than the procedure of biopsy followed ten days later by resection. Similar results were obtained with 384 rats implanted with the Crocker Fund rat sarcoma No. 10. It is not permissible to translate the results of these rat experiments directly to bone sarcoma as it occurs in man, because the biological behaviour of the rat and human tumours is so vastly different. For example, human bone sarcoma is more prone to metastasize.

We are now in a position to study the statistical analysis of bone sarcoma in man, with reference to survival, as carried out by the American Registry of Bone Sarcoma. It might be mentioned that the period of this survey preceded the introduction of the modern puncture method of biopsy.

Very briefly there are seventy-four "five-year cures" of osteogenic sarcoma. "It is interesting to note that twenty of the cases had some form of operative procedure on the tumour at periods of one day to five years prior to amputation. These operative procedures consisted of single or multiple biopsies, curettages, explorations, excisions, or resections" (Crowell, 1935).

These results have puzzled, not to say grieved, the opponents of the procedure of open biopsy. How have they received them? Their lament has echoed across the Atlantic from New York to London. And what has been the burden of their lament? "How many more would have been alive this day *if there had been no biopsy!*" Their lament comes from the very heart of their preconceived idea that an open biopsy is a highly dangerous, if not a lethal, procedure. Therefore it is all the more astonishing from their point of view that several of the patients survived more than one exploratory operation. It has been so often asserted as a fact that an open biopsy in bone sarcoma is a procedure highly dangerous to life that it is now very generally accepted as a fact, without a single vestige of proof. Indeed, there can be no scientific proof in this issue, because no man knows when dissemination of viable tumour cells occurs in bone sarcoma, except that it occurs early. Surely it is unnecessary to point out that the whole purpose of the American Registry of Bone Sarcoma will be defeated if the facts it brings to light are allowed to be overthrown by a preconceived idea—even if that preconceived idea is one precious to the hearts of many surgeons, many radiologists, and not a few pathologists.

Scanty as the figures are, they tell us that an *open* biopsy is not lethal. They suggest the possibility, in the light of Wood's experiment on rat sarcoma and rat carcinoma, that an open biopsy may not even be dangerous.

(b) Reliability of Biopsy as a Diagnostic Procedure

Every means has been used to discredit biopsy as a diagnostic procedure in bone tumours. It has been stated by some radiologists and by some surgeons that biopsy is "unreliable and often misleading." If there is any truth at all in that statement surely the radiologist, the surgeon, and the pathologist concerned should co-operate more closely to improve their joint efforts. It has been stated by some few radiologists that radiography is a more *conclusive* diagnostic procedure than biopsy! In considering the relative merits of radiography and biopsy in the diagnosis of lesions of bone, from the very outset we must avoid an elementary mistake which is too commonly made by the masters of radiology. It is not reasonable to match a pathological David with a radiological Goliath. For any fair test of the kind, deplorable as such a test must always be, we are bound to presume that the radiologist, the surgeon, and the pathologist participating in the test each knows his job. If these conditions are fulfilled it is merely absurd to continue the discussion, because the microscope is an instrument of infinitely greater precision than the radiographic machine. The microscopist will occasionally make false interpretations of his material if he is human: so also will the radiologist if he is not superhuman. The precision is a function of the instrument, not of the man. In stating these facts I do not disparage the magnificent achievements of radiography, but merely recall that, like every other science, including pathology, radiography has its limitations. One would not use a microscope to diagnose a simple fracture of the humerus, let us say, because that is the job of the radiographic machine. On the other hand, if the fracture were a pathological one the microscope might inform the radiographic machine that the real lesion was a secondary hypernephroma and direct it to the kidneys; the radiographic machine would inform the microscope which of the two kidneys was involved. In short, radiography and pathology (in the procedure of biopsy) are not rivals: the two sciences are complementary, one to the other.

(c) Necessity of Biopsy and Summary

The one sure fact that we know about the biological behaviour of bone sarcoma is that it metastasizes early. Probably, but not certainly, dissemination of viable tumour cells has already occurred in most cases before a single radiograph can be convincing enough to justify any operation so radical as amputation or wide resection. Serial radiography and the radiodiagnostic test are dangerous by reason of delay in amputation. We know that an open biopsy in bone sarcoma is not lethal, and there is no direct proof that the procedure is dangerous—although it may be so in fact. On the other hand, there is experimental evidence in malignant tumours of the rat that a free biopsy is probably not dangerous at all, and certainly less dangerous than lapse of time. There is a faint hope, founded on a reasonable hypothesis, that decompression of the growth may minimize the risk of dissemination of viable tumour cells by lowering the hydrostatic pressure of the tumour tissue.

If these data are acceptable it seems to me that the following routine should be adopted as a logical procedure.

(1) In every surgically accessible and radio-apparent bone lesion which might *conceivably* be a bone sarcoma, by reason of radiographic appearances, site, age of patient, and symptoms, decompression by open operation should be carried out as soon as possible.

(2) During this open operation a piece of tissue large enough to be regarded as a fair sample of the lesion should be excised carefully for the purposes of microscopical diagnosis. If the pathological report is not conclusive another piece of tissue should be excised as before with the least possible delay.

(3a) If the lesion is proved to be a bone sarcoma, amputation or wide resection should be carried out immediately.

(3b) If, happily, the lesion is not bone sarcoma, other appropriate measures should be applied.

This broad statement of policy is submitted as a contribution towards a more enlightened procedure in the early diagnosis and early treatment of bone sarcoma.

I have to acknowledge with many thanks the helpful advice of my colleague Professor K. G. Emeléus, M.A., Ph.D., professor of experimental physics, Queen's University, with regard to the physical principles cited in the discussion. I have also much pleasure in thanking two of my technical assistants, Mr. D. Mehaffy and Mr. J. Davidson, for the willing help they have given me in preparing giant sections on my behalf.

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THORACOPLASTY WITH EXTRA-FASCIAL APICOLYSIS*

BY

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The so-called collapse therapy in pulmonary tuberculosis has been developed mainly on an empiric basis. As far as thoracoplasty is concerned this collapse therapy should first and foremost be a cavity therapy. Cases without cavities may heal without thoracoplasty. Infiltrations in other parts of the same lung or in the other lung may disappear after collapse of the cavity.

According to our present knowledge of collapse treatment three requirements have to be satisfied by a thoracoplasty: (1) It should cause a *complete* collapse of the cavity; (2) it should cause a *selective* collapse of the cavity; (3) the operative risk should be *small*, not above 1 to 3 per cent. mortality.

1. Complete collapse of the cavity should be carried out, because an open uncollapsed cavity represents a potential danger of spreading the disease. The so-called immobilization of the lung by thoracoplasty with incomplete collapse has never been shown to cure pulmonary tuberculosis in a large series of cases. Our follow-up examinations of thoracoplasty patients show that cases with persistent cavities (found by radiographs) after thoracoplasty always sooner or later produce positive sputum. In patients with positive sputum following thoracoplasty a cavity in the lung is usually demonstrable by radiographs.

2. A selective thoracoplasty should be performed for the following reasons. Before operation patients with pulmonary tuberculosis have a diminished respiratory function and therefore need to preserve healthy lung volume as much as possible. The disease may affect the other lung, which may also require collapse treatment. A too extensive collapse at the first operation may exclude bilateral treatment. An extensive thoracoplasty is more dangerous than a limited one (Morrison Davies, 1933):

3. In a chronic lesion like pulmonary tuberculosis a low mortality rate is essential. A high operative risk not only

* Read in opening a discussion in the Section of Tuberculosis at the Annual Meeting of the British Medical Association, Belfast, 1937.