Figs. 12 to 16 are examples of the Type I macropolyocyte. Its frequency in Addison's anaemia contrasts very sharply with the rarity in health and in infective conditions, and the cause of its appearance is not the same.

There are several possible causative factors. Polymorphs of normal size with hypersegmented nuclei accompany the Type I macropolyocyte in this disease, and the first thoughts are that there is some biochemical change in the plasma that prematurely ages the polymorph and alters its life-history; the second, that the mechanism for the elimination of old polymorphs is in abeyance. The third reasonable thesis may be advanced that the polymorph is inherently abnormal owing to a defect in its parent, the haemocytoblast, or in its environment. Possibly, too, there is a single biochemical defect that is responsible for all three conditions. The liver diet alters the polymorph picture in a few days. Macropolyocytes and polymorphs with hypersegmented nuclei disappear, and at the same time the morphologically and probably also chemically abnormal cells of the haemoglobiniferous series are replaced by cells of normal appearance.

2. The Type II or megakaryocyte type of macropolyocyte is found only in Addison's anaemia, and appears in blood films during serious relapses. Almost all the cases in which it has been found have had erythrocyte counts of less than 1,000,000 per c.mm., and before the era of liver treatment all died within a short time of its appearance. After death these large cells are found, as Gulland and Goodall (1925) pointed out, in the liver in association with islets of megaloblasts and in the pre-aortic lymph glands. Plate IV illustrates the variations in this type of cell. The cells are large, measuring up to 24 or more microns in diameter, and resemble the megakaryocyte of the marrow. The nucleus is gnarled and may be of the simple horseshoe type, or may have fourteen or more segments. The coarse cytoplasmic granules are not all oxyphil, but mixed with varying numbers of azurophil granules.

The cell does not resemble any embryonic or post-natal blood stream cell, nor is it an accurate replica of the megakaryocyte of the marrow. The life-history would appear similar to that of the polymorph in that it commences its circulatory existence with a single-lobed nucleus, which later becomes segmented. Its length of life we do not know, nor have we any means of calculating it. There is considerable doubt about its origin. It may be an expression of the abnormal reversion to embryonic type of the marrow haemocytoblast as are the haemoglobiniferous cells in Addison's anaemia. On the other hand, the cell may not arise in the marrow but originate in the mesenchyme descendants in the liver and haemolymph glands that have undergone abnormal myeloid metaplasia.

CONCLUSIONS.

1. The macropolyocyte found in health and in infections has no diagnostic nor prognostic significance, and is due to the accidental prolongation of the lifetime of a neutrophil polymorphonuclear leucocyte.

2. The causation of the appearance of the Type I macropolyocyte in Addison's anaemia is closely related with the factors responsible for the production of hypersegmentation in the nuclei of the polymorph. Whether the factor is a biochemical change in the environment or an inherent defect in its parent cell is not known.

3. The Type II or megakaryocyte type of macropolyocyte may have its origin in the marrow, or arise from the endothelium of the liver and haemolymph glands. In the first case it is the product of abnormal reversion of the haemopoietic tissue, and in the second of abnormal myeloid metaplasia.

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CANCER AND THE GENERAL PRACTITIONER.*

BY

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MANY of the papers on the subject of cancer might lead the casual reader to imagine that early diagnosis of this condition is never effected except by the writers of the papers in question, and that practitioners as a body fail signally in their duty to the community. It is often forgotten that the early diagnosis of a case of cancer demands the co-operation of an intelligent and alert patient, ready to seek immediate advice, with a doctor competent to appreciate minor departures from the normal and ready to give immediate advice. The patient, however, may be unobservant; or he may not bother, until it is far too late, about a condition which seems to him—usually because it is not painful—of little or no importance. Conversely, the doctor sometimes lets the patient down by making avoidable mistakes.

Generally, I think, mistakes arise from one of two causes: The first is imperfect examination, which may be the fault of the patient or the doctor. The patient, for various reasons, may refuse to be thoroughly examined, or the doctor may continue to prescribe for his patient without attempting any real examination. He may, for instance, give treatment for "piles" without examining the rectum, or give medicine for abdominal pain without inspecting the abdomen. The other fruitful source of error is want of thought—failure to attain, by a careful summing-up of symptoms, the clear perspective which would lead to an immediate diagnosis.

Unfortunately there is no royal road to a diagnosis of cancer—no short cut, as there is in the case of syphilis. But we have many valuable aids to diagnosis, both bedside and laboratory. In the former category are such instruments as the proctoscope, the sigmoidoscope, and the cystoscope, which are used far too rarely by practitioners,

though in many cases they are easy to use, easy to maintain, and most invaluable in the information they give.

In the latter category are tests for occult blood in the stools, or for free acid in the stomach. But it is most important to remember that these are only aids; they must never be considered apart from their context—the patient. We must guard ourselves against the danger of getting lost in a laboratory maze; above all, we must not attach undue importance to negative findings, especially to those of the x-ray examination. One often finds that both patient and doctor are lulled into a feeling of security by a radiologist's report that there is nothing abnormal to be seen, which is wrongly taken to mean that nothing abnormal is present.

The subject of early diagnosis embraces a consideration of the preventive treatment of cancer by the early detection and prompt treatment of conditions that we know to be precancerous. I still often see patients with warts of the lip and tongue, papillomas of the bladder, small rodent ulcers of the face, or small tumours of the breast, who have been told that they need not bother about them unless they become troublesome. By the time such things become troublesome they are troublesome indeed.

Periodical Medical Examination.

I will refer briefly to the controversial topic of periodical medical examinations, although why it should be controversial I cannot imagine. We all go to the dentist at regular intervals; we are all examined for life insurance from time to time; some of us have our drains inspected periodically; others have their electric wiring tested. It does not seem to me unreasonable, therefore, to carry this established principle to its logical conclusion and to undergo periodical medical inspection. I should like also to see much more intelligent and sustained instruction of our youth in the elements of physiology, for there can be no question that a more perfect knowledge on the part of the public of normal physiology would result in a quicker appreciation of any departure from the normal standard, and greater readiness to seek advice. At present people know far more of the anatomy and physiology of

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their cars than of their own bodies. They know whether or not the car is missing, or heating up, or knocking, and that such defects require immediate investigation and treatment; but to similar premonitory symptoms in their own bodies they attach no importance, and often fail to undergo an overhaul until complete breakdown has developed.

It is still believed by most surgeons that cancer is a strictly local disease in its early stages, and that if the growth can be completely removed or destroyed a good permanent result will be achieved. What are the local methods of treatment at our disposal? They are only two—operative removal and radium; and it is the anxious and by no means easy task of the practitioner to make or influence a final decision when the alternatives have been put before the patient.

RADIUM THERAPY.

The therapeutic action of radium and its mode of use depend upon the fact that it emits two kinds of rays which produce effects upon the cells and tissues of the body—*beta rays*, which are caustic and indiscriminate in their action, equally affecting every kind of tissue, and *gamma rays*, which are selective in their action, and affect cancer cells more easily than the normal tissues.

The caustic, indiscriminate, and, incidentally, the very superficial action of beta rays renders them unsuitable for therapeutic purposes, and as they are unable to pass through a thin sheet of platinum it is quite easy to cut them off entirely by enclosing the radium in a shell of platinum 0.5 mm. thick. The more powerful and selective gamma rays easily penetrate this amount of platinum, and as it is only these rays that we make use of, it is gamma-ray therapy that we really mean when we speak of radium therapy.

A fundamental feature of the gamma ray is its short radius of effective action; it is therefore necessary to place the radium in intimate contact with the part it is proposed to treat, and so has come about the use of the buried radium needle. Radium needles are hollow, provided with an eye, and vary in length and thickness according to the purpose for which they are to be used and the amount of radium it is proposed to put inside them. Suitably filled, they are threaded with silk or similar material, and embedded in and around the growth, which undergoes destruction, leaving the normal tissues unaffected. But this does not happen all at once, and we know now that there is an important time factor in radium treatment, the effects produced by a large quantity of radium acting for a short time being quite different from those produced by a relatively small quantity acting for a long time. The explanation would appear to be that in the main the gamma ray exercises its selective action upon cancer cells in the act of division. Not all the cells of a growth are undergoing this change at the same time; one cell may divide to-day and be destroyed in the process, while its next-door neighbour, which may not be due to divide for three or four days, will escape injury if the radium is not still in position. There has thus come about the gradual development of a technique involving the use of buried needles each containing no more than two or three milligrams of radium, but remaining in the tissues for a week or so at a time.

There is another important practical point in treatment that results from the selective action of radium upon the dividing—that is, the growing—cell. The main mass of a new growth is composed largely of adult cells which have lived their life, and will, in any event, ultimately die a more or less harmless death. It is at the growing edge of cancer that all the actively dividing cells are situated, and it is therefore the periphery, and not the centre, that matters. If we can control the periphery, the centre will often look after itself. Surround the growing edge with a barrage of radium needles and the whole growth melts away. There are, furthermore, wide variations in the reaction exhibited by different kinds of cancer, but we are beginning to recognize and understand them, and by examination of the tissue are able to form some sort of estimate as to its probable reaction to treatment.

Radium therapy has, however, very definite limitations, chiefly arising from the fact that the action of radium is strictly local. We are all sometimes pressed to give radium treatment in cases with metastases when we know full well that the course of the disease cannot be influenced in any degree whatever. It is our duty to do what we can for our patients, not only physically, but mentally; but we also owe a duty to our own reputation, to our profession, and to the development of radium therapy. It would be the greatest disaster to the cause of radium surgery if the results following upon its reckless and uninstructed use were allowed to obscure the good results obtained in properly selected cases.

Cancer of the Cervix.

Radium scored its first regular and consistent successes in the treatment of cancer of the uterine cervix. At the Cancer Hospital many patients who have come into hospital on an ambulance—weak, emaciated, septic, and bleeding—with a growth of the cervix long past the stage of operation, have been enabled, after treatment by radium alone, to walk home, well and strong. The results of irradiation in cancer of the cervix are, in my judgement, such that radium can now compete on equal terms with surgery in the treatment of early and operable cases of this disease, and I believe that it is perfectly fair and proper to offer patients the choice of operative or radium treatment. Operation, even in the ablest hands, carries a fair mortality, and always involves removal of the ovaries and most of the vagina, but gives a good prospect of permanent freedom. Radium treatment, on the other hand, carries practically no mortality, involves no injury to ovaries or vagina, and gives a prospect of permanent freedom not quite so good perhaps as operation, but at any rate so good that the actual figures over a five-year period afford material for legitimate controversy between the protagonists of the two methods.

Cancer of the Buccal Cavity.

About the next site I want to consider there is no controversy at all. It is the tongue, and buccal cavity generally, and here, with epithelium which closely resembles that of the cervix uteri, the results are similar. All surgeons will agree that operations for cancer of the tongue are about the most disappointing they are called upon to perform. It is true that we have all had occasional successes, but my own were so few and far between that I came to dread the admission of these cases to my wards. You will understand, therefore, with what interest we watched the work of Regaud in Paris and Evans and Cade in this country, and how gladly we relinquished operative surgery and whole-heartedly adopted the radium needle technique for the treatment of these depressing cases. We have a long way to go yet, and much to learn, particularly in dealing with the secondary glands, but we have certainly reached a point where it may be said that the treatment of choice for cancer of the tongue, floor of mouth, cheeks, pillars of fauces, tonsil, pharynx, and larynx is radium.

Cancer of the Breast.

The radium treatment of breast cancer is still in the experimental stage. The operative treatment of early cancer of the breast gives excellent results, for the mortality is negligible, the mutilation is not important, and the ultimate results are good. What can radium offer in similar cases? The immediate results in many cases are apparently as good as those obtained by surgery; the primary growth shrivels up, the glands disappear, and, of course, the breast is not sacrificed. But we do not know yet how long this will last; the systematic treatment of early breast cancer by radium has not been practised long enough to enable us to form a clear opinion as to whether the primary growth or glands return, or whether distant metastases are more or less likely than after surgical operation. My own practice, therefore, is to operate upon early and suitable cases, but to use radium when the patients are old and feeble, when there is any intercurrent disease, or when—owing to extensive glandular involvement—there appears to be no good prospect of obtaining permanent cure by operation.

Cancer of the Rectum.

I think the position with regard to the rectum is very similar to that of the breast. I have seen a few very good results from radium treatment—that is to say, destruction of the growth without the disadvantage of a permanent colostomy. But these cases are so few in number, and the results of surgery in early cases are so good, that I still think it our duty to recommend surgical removal in suitable early cases, reserving radium for the more advanced cases, for the old and feeble, and for the very young; for I know of no case of cancer of the rectum under 30 years of age where operation has had any permanent success.

These examples exhaust the common kinds of cancer in which radium has had a real test, but it has been tried, and is being tried, in many other situations. Cancer of the stomach, cancer of the colon, and cancer of the head of the pancreas are examples that suggest themselves as suitable, and I have embedded radium in all these situations. The numbers are too few, however, and the time too short, to form any definite conclusion about results.

THE RESPONSIBILITY OF THE SURGEON.

Cases of this latter class lead to a consideration of the question as to who is to decide when radium should be applied, and who is to apply it. There is no possible doubt as to the answer; it must be the surgeon; for who else is competent to perform an exploratory laparotomy, to diagnose the nature, and estimate the extent and connexions of the growth, and embed radium needles suitably and effectively in such a way that they will do their work and then permit of safe withdrawal? In the past in this country radium has been chiefly entrusted to the care of roentgenologists, who from the very nature of their training and daily avocation have few opportunities of acquiring extended clinical experience or of familiarizing themselves with surgical technique. But now that the position of radium has been established in surgery many hospital authorities have put their stock of radium in charge of the surgical departments.

In my view this is the right procedure, and surgeons who wish to keep in touch with modern developments must learn the principles and practice of radium therapy in exactly the same way as they would learn the use of a new instrument or any other new method of treatment of proved value. There is no need even to discuss the suggestion that a new class of specialist should be evolved—primarily a physicist—who must learn enough surgery to enable him to devise means of approach to growths in the less accessible situations. The "surgery of access" is everyday surgery, and the view that the use of radium should be confined to a special class is just as unreasonable as the suggestion that the use of potassium iodide should be confined to pharmacologists.

TREATMENT OF ADVANCED CASES.

In discussing the treatment of advanced cases of cancer—cases which, for various reasons, do not lend themselves to radical operation or to radium treatment—I would first refer to the role of palliative operations—operations, that is to say, which merely aim at increasing comfort and prolonging life. There is a whole range of such operations—gastrostomy, jejunostomy, colostomy, and cystostomy—all most valuable in their way, but all carrying grave drawbacks in their train, chief of which is the fact that they must be performed upon patients already doomed to die of their disease, and so have come to be associated in people's minds with a hopeless outlook. I find that this pessimism is not confined to the general public, but that practitioners as a whole share the common opinion, and, indeed, often add the weight of their influence in dissuading their patients from undergoing them.

I find it easy to understand this, for no one practitioner sees very many cases of the kind, and it is difficult enough for him to form a just estimate when he daily sees his case going steadily downhill. He is inclined to forget how much unhappier the patient would be without it, and how much,

on the average, such an operation does towards prolonging life and increasing comfort. One only sees the value of these operations in perspective when they are done for non-malignant conditions. For example, a gastrostomy done for simple stricture of the oesophagus is fully compatible with an active busy life. Similarly, jejunostomy performed for the treatment of chronic simple ulcers of the stomach too extensive for removal is an operation which has given brilliant results—so good, in fact, that I have lately tried the experiment of treating the smaller ulcers of the stomach by jejunostomy in preference to partial gastrectomy. I invariably perform it in all cases of cancer of the stomach too advanced for excision or for gastro-enterostomy. Pain is at once relieved, vomiting ceases, and nutrition is easily maintained by four-hourly feeds through the jejunostomy tube.

What other means are at our disposal for helping the later stages of cancer, and delaying its almost inevitable termination? I am afraid we must reluctantly admit that there is nothing at present which is likely to prove a universal cancer cure. We are therefore reduced to treating symptoms, and I would like to refer to a few points which are brought home to us by our experience in the incurable wards of the Cancer Hospital.

Unquestionably our most important duty is to relieve pain, and to this end there is nothing that takes the place of morphine. Very large doses will often be necessary, but it is worth remembering that cocaine and hyoscine are useful variants in cases where morphine has distressing after-effects, or is ineffective. Many painful conditions are much relieved by exposure to x rays. There is no doubt a psychic element as well, but our patients at the Cancer Hospital certainly get great help and comfort from their periodical visits to the x-ray department.

Surgical opportunities of dealing with severe pain are few and far between, but when they come the results may be dramatic. For instance, the division of the lingual nerve in cancer of the tongue, or, better still, the destruction of the third division of the trigeminal nerve by alcohol injection, gives immediate relief. Bolder measures involving such major surgical procedures as the division of the posterior spinal roots, or even a portion of the cord itself, have a smaller application than might be expected owing to the poor general condition of the patient by the time that they are indicated. The aspiration of fluid from the pleura or the abdomen is an obvious method of giving help, but I am not sure that it is generally done soon enough or repeated often enough.

Attempts to control discharge from sloughing surfaces afford scope for ingenuity in the use of antiseptics, but the value of any antiseptic is greatly increased if it can be applied in the form of a power-driven spray. The mouth sprays used by dentists and operated by compressed air are most useful for this purpose and thoroughly cleanse every crack and crevice on a sloughing surface. I should like to see compressed air laid on at every bed in a cancer ward. If discharge is largely derived from excessive mucus secretion, the value of belladonna should be remembered. It gives special help in pharyngeal cases where the presence of much frothy mucus is such a troublesome feature.

The question of deodorants must also claim attention, for however careful we may be in maintaining adequate ventilation, something of the kind is often necessary. In my experience the most valuable has proved to be essential oil of peppermint, which should be sprinkled on the dressings or the blankets. It is true that it only hides one unpleasant smell by a more powerful one, but at least it is recognized and understood, whereas the undisguised smell of advanced uterine or rectal cancer, of which happily the patient is often quite unconscious, brings the greatest misery and suffering to the relatives and friends.

In thinking of symptoms and their relief we must not forget the patient. Sunshine, real or artificial, and fresh air, are of just as much importance in cancer as in other wasting diseases, and I look forward to the time when such hospitals as my own will have branches in the country where the incurable cases may spend their last remaining months of life on sunny balconies in the open air, rather than in the confined wards of a London hospital.