approximately at the corners of a four-inch square. The separation of the sources reduces the skin intensity and flattens the isodose lines, while only slightly reducing the intensity at a depth. In the upper and lower face of the container is a circular recess six inches in diameter, four holes in the bottom of which expose the radium. Into these recesses can be inserted lead plugs having various openings, which to some extent control the dimensions of the "radiant beam." The bomb can be tilted about one axis. The screenage, amounting to the equivalent of just over 1 mm. of platinum, consists of monel metal, brass, aluminium, and wood.

So far charts of the "radiant beam" have been obtained experimentally in air, but, for various technical reasons charts of the "radiant beam" in tissue are not yet available (Fig. 3).

The general procedure is as follows: The radium being withdrawn and the stretchers at the end of the room most distant from the "bomb," the patients are placed in position and moved to the "dummy," which is on the way to the radium. Here an idea of the best position can be obtained by inspection. The stretcher is then moved on until the same relative position at the actual radium is obtained, and close adjustment is effected. When both patients are adjusted the radium is put into the working position and the operator immediately leaves the room. Thus he receives the minimum of exposure to the radiation. A nurse who has to be in the room during the treatment places herself as far away from the radium as possible, and is further protected by a lead shield.

ENDARTERITIS OBLITERANS OF THE EXTREMITIES.

A DISEASE OF METABOLISM.

BY

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ENDARTERITIS obliterans of the extremities is nowadays found much more frequently than it was some years ago, because we are more on the look out for this disease, for which a precise method of exploration, based on the oscillographic examination, has been introduced. The frequency of the occurrence of this morbid condition raises important problems as to its physio-pathology and its treatment.

ETIOLOGY.

Following the modern conceptions of general pathology, endarteritis obliterans must be considered essentially a disease of metabolism. A series of external "causes," acting on an individual specially predisposed on account of deficiencies of his regulators of metabolism, determine metabolic disturbances bearing principally on the lipid metabolism—disturbances which, aided by certain localizing factors, result in the proliferation of the intima of the arteries of the extremities. In the etiology of endarteritis obliterans we have therefore to consider, not a unique cause, but a "constellation"* of external, constitutional, and localizing factors. The most important external factors are tobacco intoxication, infection, and emotional stress. The internal or constitutional factors are more important, and consist in constitutional inadequacies of certain "regulators of metabolism"—namely, of the pancreas, of the adrenals, and of the sympathetic nervous system—inadequacies which are found in certain families or races, as, for example, in Polish Jews. The factors which determine the localization of the metabolic disturbances on the arterial wall consist in infection of the arterial wall (from typhus, typhoid fever, syphilis, and perhaps from focal infection), and in constitutional metabolic deficiencies of the arterial wall, the arterial hypoplasias described by F. Parkes Weber.

* For nearly all morbid conditions, not only for endarteritis obliterans, we no longer look for "one cause," but for multiple etiological conditions—that is, for a constellation of etiological factors, to use the happy expression of Tendeloo.

It must be realized that the constellation of etiological factors can be described only in a general outline. Each individual patient has his own "structure" of constellation—that is, there are individual differences as to the proportionate importance and the mode of combination of the various factors constituting the etiological constellation.

Physio-pathological and Clinical Evolution of Endarteritis Obliterans.

Three phases or periods must be distinguished in the physio-pathological and clinical evolution of endarteritis obliterans of the extremities—a pre-arteritic phase of metabolic disturbances, a phase of incompletely obliterating arteritis, and a phase of thrombo-arteritis.

The Pre-arteritic Phase.—The features of the pre-arteritic phase can only be inferred by considering the metabolic disturbances which have been found in confirmed endarteritis, and which probably precede for many years the endarteritic localization. These disturbances bear on the lipid metabolism, as can be demonstrated by the occurrence of hypercholesterinaemia (J. Heitz) and the presence of cholesterol deposits in the endarteritic lesions. They are due to disturbed function of the pancreas, adrenals, and sympathetic system. The frequency of endarteritis obliterans in diabetes, and the results obtained by Vaguez and Yacoel with insulin in non-diabetic patients suffering from endarteritis obliterans, show the role of the pancreas, and the results of unilateral adrenalectomy in certain cases (Stulz and Stricker) allow us to admit the role of the adrenals.

The Period of Incompletely Obliterating Arteritis.—After a long period of purely metabolic disturbances the endarteritic lesion occurs, a lesion which is principally trophic—metabolic—although its localization may be aided by infection. The initial and principal phenomenon in this endarteritis consists in the proliferation of the intima—that is, in the multiplication and stratification of the cells of this arterial coat—and, more than that, in the neo-formation of connective tissue rich in cells. The lamina elastica interna is often divided; cholesterol deposits are frequent in the proliferating intima; calcium deposits are more tardive, and much less frequent. The involvement of the other coats of the artery is tardive, inconstant, and atypical. The proliferation of the intima causes a narrowing of the arterial lumen, and therefore a diminished irrigation of the limbs. In periods of rest or quiet movements this diminished irrigation is sufficient, but where there is a greater demand for blood, as in more active movements, the incompletely obliterated artery, instead of dilating as it normally does to increase the circulation, contracts spasmodically, and this vascular spasm is felt as pain of "intermittent claudication." Thus the symptoms manifested in this period do not depend on the arterial stenosis, but principally on the adjunction of an abnormal vascular reflex.

The Thrombo-arteritic and Thrombo-angiitic Phase.—This is the terminal phase of endarteritis obliterans, and may occur, as in young individuals, very early. Thrombosis adds itself to the clinical and pathological picture, and dominates it. This thrombosis may begin in a small artery, and extend much further upwards; it may occur also in the satellite veins, this being explained either by a concomitant phlebitis, or by the secondary disturbances of the venous outflow due to the insufficiency of the *vis a tergo*. In this thrombo-arteritic or thrombo-angiitic period of endarteritis obliterans collateral anastomoses develop to relieve the arterial obstruction.

The Place of Endarteritis Obliterans in Nosography.

Endarteritis obliterans is a special localization of atherosclerosis. In fact, in atherosclerosis the same constellation of etiological factors, and the same physio-pathological conditions (proliferation of the intima, disturbances in cholesterol metabolism, etc.), are found; and, on the other hand, there are cases which I described as polyarterial syndromes, in which endarteritis of the extremities coincides or alternates with coronaritis, and with endarteritis of the mesenteric arteries. The clinical and physio-pathological history of endarteritis obliterans is identical with that of the other localizations of atherosclerosis. In

athero-sclerotic coronaritis there is first a phase of metabolic troubles, then comes the endarterial localization with vasomotor disturbances, manifested clinically as angina pectoris, and later a thrombosis may occur, resulting in myocardial infarct. In athero-sclerosis of the mesenteric arteries there occurs also, after the prodromic obscure phase of metabolic troubles, the phase of incompletely obliterating endarteritis with vasomotor disturbances manifested by attacks of abdominal pain and constipation, and the terminal phase of thrombo-arteritis with intestinal infarct. The terms used point to that identity. Angina pectoris is often called intermittent claudication of the heart; the pain in mesenteric endarteritis is often described as abdominal angina, or as "dysbasia angio-sclerotica abdominalis" (Ortner). It would be well never to use these terms in clinical diagnosis, as they are liable to bring confusion, but to hold to the precise anatomical diagnosis of the syndrome—coronaritis, mesenteric arteritis, endarteritis obliterans of the extremities.

Thrombo-angiitis obliterans, or Buerger's disease, must not be considered as a special disease differing from endarteritis obliterans. The special etiological features, such as occurrence in young men, predominance in Polish Jews, are not sufficient to justify this absolute separation. Neither are the anatomical features described by Buerger absolutely specific. Arterial thrombosis occurs in endarteritis obliterans. Involvement of the veins with venous thrombosis is also found in endarteritis obliterans of the extremities, and is especially frequent in endarteritis of the mesenteric arteries.

The absence of calcium deposits or of cholesterol deposits in thrombo-angiitis is not absolutely demonstrated, and at all events is not sufficient to separate Buerger's disease from endarteritis obliterans. The giant cells described in the clot are found in all organizing thromboses. The argument put forward by the American authors—namely, that Buerger's disease is due to infection, whereas endarteritis is a trophic disease—is purely theoretical, because the exclusive role of infection in Buerger's disease is only hypothetical, whereas the trophic element is much more apparent. In Buerger's disease the same constellation of etiological factors, the same basic metabolic disturbances, the same clinical evolution, the same action of various therapeutic measures as in endarteritis obliterans, have been described. Endarteritis obliterans and Buerger's disease are therefore one and the same disease, and the most we can say is that on account of a special structure of the etiological constellation (predominance of certain racial constitutional factors) Buerger's disease is a special form of endarteritis obliterans.

Diabetic endarteritis obliterans is also a special form of endarteritis obliterans, and is simply characterized by the preponderance of the pancreatic element in the constellation of etiological factors.

This is the "synthetic" or "metabolic" conception of endarteritis obliterans. It is based on the modern physiopathological researches, is confirmed by the clinical observations of the polyarterial syndromes, and has the merit of offering a sound scientific basis for the treatment of this condition.

Importance of Early Diagnosis for Treatment.

The diagnostic problem is very important, since most cases of endarteritis obliterans are diagnosed as rheumatism, sciatica, varices, flat-foot, etc. These errors will be avoided by bearing in mind the relative frequency of the arterial obstructions of the extremities at all ages and in all countries, and by exploring the circulation of the extremities with the oscillogram. The oscillogram method remains the most simple and the most precise diagnostic procedure, because radiology can give us results only in the rare cases in which calcium deposits exist in the arterial wall, and radiography after injection of lipiodol is much more difficult in its application, does not give more precise information than the oscillogram, and is not always innocuous.

In the intensive injection treatment of varices care must be taken not to mistake for real varices the venous dilations met with in cases of endarteritis obliterans, and which are provoked by the venous stasis frequent in this

condition. Injection treatment of such "varicose veins" may lead to disaster, as Sicard himself has pointed out, and this demonstrates the importance, for the internist and the surgeon, of a precise exploration of the arterial circulation of the limbs.

Treatment of the Etiological Factors.

Interdiction of smoking is necessary, and there is always a relief in the symptoms of patients who give up smoking. Syphilis must be looked for, and even, in doubtful cases, treatment with mercury or arsphenamine must be instituted. Active foci of naso-oral infection must be treated in consequence. In a disease which so largely affects the vegetative nervous system the role of careful psychotherapy need hardly be emphasized.

Treatment of the Basic Metabolic Disturbances.

The treatment of the basic metabolic disturbances constitutes the principal element in the treatment of endarteritis obliterans, and, provided an early diagnosis is made through the oscillogram exploration, gives striking results.

The most important method consists in the use of pancreatic preparations directed against the pancreatic element. Vaquez and Yacoel have shown the remarkable results of insulin treatment, and Dr. Quiserne of Bagnolles has made extensive use of pancreatic preparations in peripheral vascular diseases with very encouraging results.* Recent researches of Gley and Kisthinos have demonstrated in the pancreas a special substance, independent of insulin, but existing in insulin as an "impurity," and which has a definite vascular action.

Various protein shock preparations must be used after treatment with insulin has been tried. During these last four years I have used yatrien casein, which I prefer to the intravenous administration of T.A.B., advocated by Goodman and Gottesman—a method which may result in strong reactions. Lipiodol, which, on the advice of Professor Vaquez, I have used for many years, acts probably through the same mechanism of shock. There is, however, a special action of the iodine on the metabolic disturbances of the arteries, and that is why preparations such as lipiodol, tincture of iodine, and colloidal iodine are valuable as alternative methods.

Spas, the great modifiers of metabolism, show their action in endarteritis obliterans. I have seen remarkable results from Royat treatment, and although this spa acts principally on the vasomotor element, we cannot exclude a more general regularization of metabolism.

Adrenalectomy belongs also to these metabolic treatments. I have no personal experience of the effect of this method, but I cannot consider the published results as very encouraging.

The methods advocated—insulin, protein shock, lipiodol, spa treatment—very frequently bring about a striking amelioration of the subjective symptoms, and, what perhaps emphasizes their efficiency, an increase of the oscillogram index.

Treatment of the Circulatory Disturbances.

The second objective of the clinician in endarteritis obliterans consists in the diminution of the vascular spasm and the fostering of vaso-dilatation of the vessels of the limbs, so as to bring about as normal an arterial irrigation as possible. The effects of the various methods advocated, which will be used alternatively, must be followed with the oscillogram.

Among the pharmaceutical agents, the nitrites, aspirin, and acetylcholin will yield good results. Nitrites may be given either by the mouth or in the form of injections of sodium nitrite (twenty 1 c.cm. injections of a solution containing 0.01 sodium nitrite per c.cm.). Aspirin, although a banal drug, has real therapeutic effects, as Erb has shown, which are due to the central vaso-dilatory action of the salicylates (Wiechowski). Acetylcholin—in series of daily injections of 0.05 or 0.10—has been introduced in the treatment of this condition by Professor Villaret, and the reports of the French clinicians are very encouraging. Quinine also is used by certain physicians.

* Oral communication.

Among the physio-therapeutical methods, the simplest consists in the application of warm foot-baths, or radiant heat, but the best is diathermy (A. Wilson Gill, L. Newell Moss), which must always be applied. I have not seen any special results from x-ray applications, nor from galvanic foot-baths. Massage is strictly contraindicated, as also is any undue strain (exercise), because these can only accentuate the spasmodic condition. Balneotherapy is very important, and it is to the action on the vasomotor centres that must be attributed, in great part at least, the effects of Royat. Artificial carbon dioxide baths are not effective.

Among surgical methods Leriche's operation—arterial perisymphathectomy—which also enhances vaso-dilatation, has given some good results, but must be applied only in the last resort. Before its application a careful oscillographic exploration must be made, so as to determine that the artery is not completely obliterated, and also for the localization of the obliteration. Gangrene may be the result if these precautions are not taken.

If to all these methods is added the scrupulous care of small wounds and excoriations of the lower limbs, a very effective treatment can be instituted in a disease which is relatively frequent, is met with in all countries and in all

rates, and has not, thanks to the possibility of an early recognition, the dark prognosis which was often attached to it.

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PERNICIOUS ANAEMIA.

PRELIMINARY REPORT ON THE RESULTS OBTAINED BY
TREATMENT WITH CERTAIN PREPARATIONS
OF STOMACH.*

BY

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THE unfailing regularity with which gastric achylia is encountered in pernicious anaemia has often been pointed out. Almost invariably the gastric secretion is deficient in hydrochloric acid and pepsin, even after the use of powerful gastric stimulants; in some hundred cases which I have examined only three exceptions were found.¹ That this achylia is of some significance has been pointed out by Castle,² who fed patients suffering from Addisonian anaemia with beef that had been predigested in a normal stomach, or with normal gastric juice *in vitro*, and obtained reticulocyte responses and increased erythrocyte counts comparable with those ordinarily seen after small doses of liver. He failed to obtain any improvement using beef (a) alone, (b) predigested with hydrochloric acid and commercial pepsin, or (c) incubated with 150 grams of mucous membrane of hog's stomach. The negative result in the latter case is somewhat surprising in view of the results described below.

These observations and the success of the liver therapy have suggested the hypothesis that pernicious anaemia might be a deficiency disease in which the gastric juice was unable to elaborate some necessary principle (normally formed in a healthy individual) from the proteins of the food. This substance is present in liver and kidney, as was originally shown by Murphy and Minot, and, in consequence, these organs can be readily administered in the treatment of the disease. Attempts to identify the active principle with certain vitamins and investigations upon the effects of various foodstuffs have been made by Elders,³ and Koessler, Maurer, and Loughlin⁴ among others.

The experiments described below were based upon a somewhat different view—namely, the possibility of pernicious anaemia being a type of deficiency disease, in which some factor of paramount importance was absent from the gastric juice. Despite some of the negative results obtained by Castle, it did not seem improbable that the stomach itself might be a potent source of the anti-

anaemic substance, and the complete lack of gastric enzymes suggested the importance of investigating this possibility more closely.

Action of Normal Gastric Juice.

It was decided in the first place to try the effect of normal gastric juice. This was obtained, as required, either with or without the use of histamine, and administered in a daily dose of 150 to 200 c.cm., given during meals to ensure its action upon the protein foodstuffs. Each individual sample of gastric juice was examined carefully beforehand for the presence of free hydrochloric acid and normal peptic activity to ensure that an active and fresh preparation was being used. All samples containing bile, or less than 0.036 per cent. free hydrochloric acid, were discarded.

The following case illustrates the type of response obtained in this group.

CASE I.

A male cotton operative, aged 59, was admitted to hospital complaining of weakness in the legs and lack of energy, so that he was unable to carry on his work. Apart from bacterial food poisoning in 1906, he had enjoyed perfect health until March, 1929, when he had an attack of influenza lasting for four weeks. Since that time he had had slight paraesthesias, more pronounced in the cold weather. These became gradually worse, so that, having ceased work, he had difficulty in using his limbs accurately. He had lost 14 lb. in weight in six months. His appetite was good and there was no history of indigestion, diarrhoea, nausea, vomiting, or marked flatulence. He had soreness of the tongue and gums in cold weather. More recently, he had had some slight pains in the lower abdomen, lasting for a few minutes only; his bowels were constipated.

The previous medical history contained nothing of note. As regards the family history, one sister had died at the age of 30 from an "anaemic wasting disease."

Examination.—The patient's teeth were artificial; there was nothing abnormal in the cardio-vascular, respiratory, alimentary, or genito-urinary systems. The knee-jerks and abdominal reflexes were exaggerated; no muscular wasting was present, but there was marked weakness in the limbs and some difficulty in walking. The blood Wassermann test was negative. A cytological examination showed: red blood cells 3,850,000 per c.mm., white blood cells 4,800; haemoglobin 100 per cent.; colour index 1.4; platelets normal; slight anisocytosis and poikilocytosis; no nucleated red cells or abnormal staining detected. Repeated fractional gastric analyses revealed complete achylia.

The case was diagnosed as one of early pernicious anaemia with subacute combined degeneration of the cord and achlorhydria syndrome.

Treatment.—No liver had been taken prior to admission, when he was given hydrochloric acid and commercial pepsin. After seven days this was discontinued and replaced by 150 to 200 c.cm. of normal fresh gastric juice once daily, taken with the midday meal. During the first week, while on acid and pepsin therapy, the patient's condition became worse. The reticulocyte count remained at the normal low level, while the red blood cells diminished by nearly 300,000; anisocytosis and poikilocytosis became

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