But for the *post-mortem* examination, death might have been attributed to an extraordinary susceptibility to nitrous oxide poisoning.

I wish to thank Dr. Douglas Bigland for kindly giving me the notes of the case.

REFERENCES.

- Aschoff, L.: *Pathologische Anatomie*, Jena, 1921, p. 301.
 David, O.: *Zeit. f. klin. Med.*, 1912, lxxiv, 404.
 Glynn, E. E.: *Quart. Journ. Med.*, 1913, vi, 391.
 Glynn, E. E., and Digby, Lettice: *Med. Res. Council Special Report No. 79*, 1923.
 Glynn, E. E., and Dun, R. C.: *Lancet*, 1923, i, 1302.
 Henderson, Vandell: *BRITISH MEDICAL JOURNAL*, January 9th, 1926, p. 43.
 McGowan, J. P., and McNeil, C.: *Journ. Path. and Bact.*, Camb., 1913, xvii, 412.
 Osler, W., and McCrae, T.: *A System of Medicine*, Lond., 1907, ii, 561.
 Wilson, J. St. G., and Glynn, E. E.: *Lancet*, 1926, i, 392.

A NEW SYSTEM OF TREATMENT OF DIABETES MELLITUS.

BY

HENRI CHABANIER, M.D., D.Sc. PARIS,
 DIRECTOR OF LABORATORIES IN THE FACULTY OF MEDICINE OF PARIS;
 AND

W. S. C. COPEMAN, M.B., M.R.C.P. LOND.,
 LATELY ASSISTANT STRANGER IN THE FACULTY OF MEDICINE OF PARIS.

THE following is an outline account of a method of treatment which, although not claimed as a cure for diabetes, has been employed in over 160 cases of varying degrees of severity with considerable success since 1923.¹

If insulin be administered in large doses before the two principal meals of the day, over unbroken periods, it has been observed that a certain summation of effect can be obtained. That the actual basal trouble is diminished in intensity is shown by the progressive lowering of the "ketonic threshold value"²—the point at which ketonuria appears when a patient is placed on a diet containing a known quantity of protein and fat and no carbohydrate. This value is expressed as the patient's blood sugar content at this moment, and is a direct method of expressing the intensity of the basal factor at any given period.

This action of insulin can be pushed to such an extent that the patient may be transformed, metabolically speaking, into a normal person whilst under its influence; this condition being capable, in favourable cases, of persisting for variable periods after the cessation of injections. This experience led to the idea that treatment might be attempted in the form of "series" of injections, somewhat in the same way that syphilitic courses are arranged. The results which have been obtained appear to justify the adoption of this method of treatment, at any rate in a majority of cases.

Advantage is, further, taken of the fact that the patient is temporarily transformed into a normal individual to increase considerably the ingestion of carbohydrate which can, under the influence of the large doses of insulin administered (80 units per twenty-four hours), be easily tolerated and utilized to improve the general condition and resistance of the patient. It is found that in spite of the fact that, in certain instances, the regime is increased to almost normal proportions, the urine becomes sugar-free, and the blood sugar falls to the region of the normal in a short time.

It is considered that every case of diabetes mellitus presents two essential elements: (a) a basal, or metabolic, element; (b) a renal element.³ The former consists in the defective power of the tissues to consume glucose in normal ratio to their blood sugar content—for quantitatively this consumption is often found to be equal to the normal. The renal element is a phenomenon similar to that observed in cases of "renal glycosuria," but with the basal element superimposed.

These two elements may be combined in varying proportions, the preponderance, or otherwise, of the renal element tending to determine the clinical type of the disease (*D. gras*, or *D. maigre*). This being so, it is found advisable, when fixing the initial regime of a diabetic patient, to estimate approximately the intensity of this renal factor, since it is found experimentally that in any given case the time taken for the glycosuria to become normal is in inverse ratio to the importance of the renal diabetic

element. This is estimated very simply by comparing the blood sugar of the patient taken whilst fasting with his twenty-four hourly output of urinary sugar. If the difference is considerable, the renal element is said to be pronounced, and the carbohydrate content of the diet is modified somewhat in consequence, in order to allow of the glycosuria becoming normal in a minimum of time. It is seldom, however, found necessary to reduce it below a daily ration of about 100 grams, whilst if the renal element is found to be of moderate importance only, a ration of between 150 and 250 grams may be allowed from the start.

The insulin "series" is then commenced, the injections being given twice a day by the intramuscular route, generally into the buttock, and before the principal meals of the day in which most of the carbohydrate is massed. Hospital out-patients bring with them the 150 grams of milk which is specially introduced into their regime for the purpose, and which they drink immediately after the injection, by this means avoiding the risk of hypoglycaemic accidents which might otherwise intervene before they could reach their homes. Accidents of this nature, it may be mentioned, have been observed in only 7 cases amongst the 50,000 or so injections given between 1923 and 1925.

When the glycosuria has been *nil* during a minimum period of fifteen days, and if the blood sugar is within reasonable limits, the injections may be suspended, pending a return of the symptoms, which must be carefully watched for; a further "series" being commenced under the same conditions as the former on the slightest indication. In this way the free intervals between the series will be found gradually to increase, whilst the duration of the series can be progressively diminished to a minimum of about ten days, until a patient with a basal trouble of moderate severity, who has come under treatment early, may be enabled to go three months or so at a time without insulin. Longer than this it is not considered advisable to permit the patient to go, although it is occasionally quite possible—two patients, for instance, having actually been able to dispense with insulin for over a year without return of their symptoms. In the intervals between the "cures" the diet is modified merely to the extent necessary to maintain the glycosuria and blood sugar at the same level as they were whilst the patient was receiving insulin.

Indications.

It is considered that every case of diabetes mellitus presents an indication for treatment by insulin, however slight it be. Contrary to the classical conception of insulin as "a useful adjunct to diabetic treatment," insulin is here considered as the factor *par excellence* of the treatment, dietetic methods being only of secondary importance, and never insisted on to the degree which is at present usual; certainly never to the detriment of the patient's general condition.

In states of pre-coma and coma insulin is naturally indicated, although it is not considered to be by any means the best indication from the point of view of ultimate results, since so much damage is frequently sustained by essential viscera, such as the kidney or the heart, during the presence of a state of acidosis, that delayed collapse is frequent even after apparent cure.

In cases of mild diabetes of the type known clinically as "*gras*" it is considered that insulin treatment should be instituted even when the glycosuria can be controlled, as it generally can, by dietetic methods alone. This is particularly true in the presence of any of the ordinary diabetic complications, such as pruritus or carbuncle. It is in cases of severe diabetes (*maigre*), with acetoneuria, that this treatment finds its best indication, if the patients come under observation early,⁴ since in these cases a very real benefit will generally result from repeated "cures," at increasing intervals if this be found to be possible.

Results.

The immediate results of this system of treatment are estimated as the result of observations of (1) the ketonuria, (2) the glycosuria, (3) the general condition of the patient, and (4) his blood sugar content.

1. The effect on the condition of ketonuria, if present, is extremely marked. The ketone bodies of the urine result, it is generally believed, from the incomplete oxidiza-

tion of fatty acids, this incomplete oxidation resulting from (a) the inability of the body to utilize carbohydrate adequately, or (b) an insufficient supply of carbohydrates to enable the body to oxidize the fatty acids completely to their final products (Rübner and Zeller). In the former case the defect of metabolism is remedied by insulin, whilst the latter eventuality does not arise, owing to the high content of carbohydrate in the ration allowed.

2. The glycosuria can, in the average case, and in spite of the large amount of carbohydrate allowed, generally be abolished in a short time, any considerable "renal diabetic element" being compensated for as explained above.

3. The improvement in the general condition of the patient is considered, under this system, to be an even more important criterion of progress than a lowering of the blood sugar content, and is generally very noticeable; the first effect observed being usually a disappearance of the weakness and lassitude so characteristic of the diabetic. If the patient be weighed at the same time every morning the weight will nearly always be found to augment progressively; whilst the suppression of such symptoms as polyuria, polyphagia, and insomnia, together with the possibility of his leading a normally active life, generally has an important psychological as well as physical effect on the patient.

4. The blood sugar will always fall to a level approaching the normal, this being all that is considered absolutely necessary.

Of the remote effects of this treatment less can, naturally, be asserted, although the diabetic process appears in many cases to have been arrested for various periods—as, for example, in the case of the two patients mentioned above who were free from all symptoms for over a year, after several insulin "cures"; such cases, however, form a minority of the whole, the average free period being considerably shorter. Actually no case is allowed to go for more than about three months without receiving insulin, a new series being commenced automatically at the end of that period, whether any direct indication be present or not.

In certain cases, nearly always children, who have come under treatment late, it is found impossible to suspend the injections of insulin at all; these cases can, however, be brought to, and maintained in, a condition in which they can continue their normal lives and activities. The younger the patient the more necessary does it appear to start such a treatment early, and not to waste time on dietetic methods which seem, in most cases, to have little or no effect on the basal dietetic factor, but which merely suppress the symptom of glycosuria, and sometimes that of hyperglycaemia.

Finally, owing to the minimum of restrictions, both dietetic and otherwise, imposed on patients submitting to this regime, it is found to be easier to persuade them to continue on it over long periods than it would appear to be under some other methods of treatment.

REFERENCES.

- ¹ Chabanier, Lobo-Onell, and Lebert: *Étude de 160 cas de diabète traités par l'insuline*, *Acad. de Méd.*, March 24th, 1925. ² Copeman, W. S. C.: *Med. Press and Circular*, December 23rd and 30th, 1925, and January 6th, 1926. ³ Chabanier, H.: *Du rôle du rein dans le diabète*, Maloine et Cie, Paris, 1925. ⁴ Chabanier, H.: *Bull. de l'Acad. de Méd.* (séance du 24 mars), 1925.

A CASE OF PATENT DUCTUS ARTERIOSUS.

BY

WILLIAM GORDON, M.D., F.R.C.P.,
SENIOR PHYSICIAN TO THE ROYAL DEVON AND EXETER HOSPITAL.

THIS case, apart from its rarity, presents several features of interest.

A man, aged 31, a wine-merchant's cellarman since the war, a gymnasium instructor during the war, and a gardener before the war—all occupations involving heavy physical strain—has had gradually increasing shortness of breath for nine years, occasional short attacks of stabbing pain over the heart, mostly at night, for six years, and palpitation caused rather by worry than by exertion. He has never had rheumatic fever, scarlet fever, or syphilis, never had a severe blow on the thorax, never felt anything "give way" in his chest during an effort.

His heart is nearly normal in size, but a little dilated rightwards. The apex beat lies just inside the left mammary line—in the erect position it beats behind the sixth rib, but this is due

to cardiopneumosis, since, in the recumbent posture, it is found, as normally, in the fifth space; but the right margin of its dullness in the erect position is $1\frac{1}{2}$ inches to the right of the mid-line—that is, about an inch too far to the right. There is no excessive impulse anywhere and no thrill. In the second and third left intercostal spaces there can be made out, at least after exertion, Gerhardt's "ribbon dullness."¹ There is a loud, roaring, continuous murmur, lasting throughout the entire cardiac cycle, with marked systolic augmentation, loudest in the second left space by the sternum and over the adjoining sternal border, in the erect position. On recumbency the only noteworthy change in this murmur is a movement of its area of maximum loudness about $1\frac{1}{2}$ inches leftwards. The murmur rapidly lessens in loudness as one recedes from this maximum area, except downwards along the left sternal border and the adjoining third, fourth, and fifth spaces. But it is faintly heard over almost the whole chest, front and back. In the area of maximum loudness there is no audible second sound, but lower down, at the levels of the third, fourth, and fifth spaces, there is heard an accentuated and sometimes reduplicated second sound. Over the aortic cartilage and up the right carotid a clear second sound is audible, not reduplicated and nearly free from the continuous distant rumble of the murmur just described. At the sixth left space in the mammary line, in recumbency, the rumble is sometimes quite lost and then a second sound is clearly heard without reduplication or murmur. Fig. 1 shows most of these signs.

The pulse is regular, about 84, rather sudden but not collapsing, and pulsation is certainly more visible than usual in the neck up to the ears and at the elbow. The left pulse is slightly smaller than the right. Here are tracings of both pulses taken with the lowest pressure of a Dudgeon's sphygmograph; they do not suggest aortic regurgitation (Fig. 2). The blood pressure is low—110 systolic and 55 diastolic. The pulsus paradoxus, described by François-Franck,² is absent in this case.

FIG. 1.—E E=Outline of cardiac dullness in erect position. R R=Outline of cardiac dullness in recumbent position. Shaded area=area of murmur in erect position; unshaded area outside it=area of murmur in recumbent position. +=Spot where the second sound was free of all murmur. O=Spots where the second sound was nearly free of the distant murmur.

FIG. 2.

The respirations are quiet (20), the temperature constantly subnormal (I had him six weeks in hospital), there is no enlargement of spleen or liver, no sign of embolism, no haemorrhage, no daily changes in the murmur. Except for pyorrhoea (which has to be seen to) there is nothing else abnormal in any structure. There is no clubbing of fingers, no polycythaemia, but after exertion there is slight cyanosis of the fingers.

Diagnosis.

The murmur is, as Gibson of Edinburgh² first insisted, pathognomonic of patent ductus arteriosus—that is, a continuous murmur, with systolic augmentation, only dying out in the end of diastole; here I do not lose it at any point of the cardiac cycle. It has received the names of the "tunnel murmur" and the "machinery murmur." It is quite different from any other murmur with which I am acquainted. But it is said to be also produced by the opening of an aortic aneurysm into the pulmonary artery. The history of this case makes that diagnosis unlikely, and the x-ray examination definitely negatives it (Fig. 3).

Patent ductus arteriosus, then, accounts for the murmur. And in support of that diagnosis we find (1) the Gerhardt "ribbon dullness," (2) accentuated and divided second sound lower down, (3) unequal pulses (with, in this instance, low arterial tension, a feature not hitherto noted, I think, but likely to be common in this condition); some enlargement of the right heart, together with x-ray observation of dilatation and unusual pulsation of the pulmonary artery.

But it has been suggested that this might be a case of aortic regurgitation with an unusual dislocation of the murmur, because there is some visible pulsation in the neck. Apart from the facts that the murmur is absolutely different from any produced by aortic regurgitation and that such dislocation of an aortic murmur must be ex-