Though the table is self-explanatory, it is necessary to emphasize that while the period elapsing between the rise of blood pressure and the onset of albuminuria varied between eleven and eighty-nine days, in only four of the cases was there during that time any symptom to draw attention to the fact that the patient was abnormal. The importance of routine estimation of blood pressure is evident; for there can be no doubt that it provides, in many cases at least, an earlier indication of the presence of toxæmia than does examination of the urine. It is noteworthy, too, that sometimes the blood pressure rises slightly at a comparatively early stage of pregnancy, any other demonstrable abnormality being absent, only to subside and remain at a normal level for some weeks. When this occurs it will usually be found that a more permanent rise takes place later, followed in due course by albuminuria. This was so in cases 547/31, 989/30, 1073/31, and 554/31 (see last column of table). It seems as if there is in these cases a curious instability of the blood pressure, and in this connexion one calls to mind the statement of Elwyn that there is an increased irritability of the vegetative nervous system in pregnancy, and that this leads to a greater tendency to vaso-constriction. At any rate, there seems good reason to believe that a temporary slight rise in blood pressure in the earlier stages of pregnancy may be taken as a warning of possible trouble later.

SUMMARY

1. It is shown that in the toxæmia of later pregnancy a rise of blood pressure often precedes by a prolonged period the onset of albuminuria.

2. During the interval between the rise in blood pressure and the appearance of albuminuria (varying in the

reported cases from eleven to eighty-nine days), there are usually no symptoms or signs to suggest that the patient is in any way abnormal.

3. There is some evidence that there may be, in the earlier stages of the pregnancy of patients who later develop toxæmia, a temporary elevation of the blood pressure, which soon subsides, and which may be an expression of increased neuro-muscular irritability and of a greater tendency to vaso-constriction in such patients.

4. The importance, for the timely diagnosis of toxæmias of pregnancy, of routine estimations of blood pressure is emphasized. When these are made, treatment can be commenced at a very early period, with the obvious advantage of minimizing the risk of eclampsia and of chronic nephritis.

5. The term "albuminuria of pregnancy" is a bad one, and is no doubt responsible for much of the permanent kidney damage that has in the past been a sequel of the toxæmia of late pregnancy. Its use has pushed unduly into the foreground the albuminuria, which is really a late symptom, and has therefore tended to obscure the early hyperpiesis, and has thus been the cause of dangerous delay in diagnosis and treatment.

BIBLIOGRAPHY

- Bennett, T. Izod: *Nephritis, its Problems and Treatment*. Oxford University Press, 1929, p. 51.
 Elwyn, Herman: *Nephritis*. Macmillan, New York, 1926.
 Fishberg, A. M.: *Hypertension and Nephritis*, second edition. Baillière, Tindall and Cox, London, 1931, p. 598.
 Koch, F.: *Zeit. f. klin. Med.*, 1925, cii, 182.
 Mahomed, F. A.: *British Medical Journal*, 1874, i, 585.
 Riegel, F.: *Zeit. f. klin. Med.*, 1884, vii, 260.
 Steiner, B.: *Klin. Woch.*, 1928, vii, 665.
 Theobald, G. W.: *Journ. Obstet. and Gynaecol. British Empire*, 1929, xxxvi, 803.

SYNTHALIN IN THE TREATMENT OF DIABETES

BY

A. P. THOMSON, M.C., M.D., F.R.C.P.

PHYSICIAN TO THE HOSPITAL

R. J. GITTINS, M.C., M.D., M.R.C.P.

CLINICAL ASSISTANT IN THE DIABETIC CLINIC

AND

GARFIELD THOMAS, M.Sc.

BIOCHEMIST TO THE HOSPITAL

(From the Diabetic Clinic of the General Hospital, Birmingham)

In November, 1926, a paper was published from the late Professor Minkowski's clinic in the University of Breslau by Frank, Nothmann, and Wagner¹ entitled "Synthetically prepared substances with an action similar to that of insulin on normal and diabetic subjects," in which the authors stated that their work had been undertaken in the erroneous belief that tetany following parathyroidectomy was associated with hypoglycaemia, and with the knowledge that other work had suggested that tetany in children was connected with guanidine poisoning.

Deciding for these reasons to investigate the effect on the blood sugar of animals of injections of guanidine, Frank and his colleagues found that they produced very severe hypoglycaemia and convulsions indistinguishable in character from those which are known to follow heavy doses of insulin, but with the remarkable difference that animals convulsed by guanidine could not be rescued by intravenous injections of glucose. The next step was the endeavour to modify the chemical structure of guanidine in such a way as to eliminate its toxicity and retain its hypoglycaemic power. The original paper claimed that this had been successfully done, and that the new guanidine derivatives, which were called synthalins, not only

had an action indistinguishable from insulin, but also retained their potency when administered by the mouth.

The experimental evidence described in support of this contention was very strong, and may be briefly summarized as follows:

1. Animals convulsed by the synthalin administered by injection could be rescued by glucose intravenously.

2. After total extirpation of the pancreas from dogs the resulting high blood sugar could be reduced by synthalin, and in dogs rendered diabetic by partial extirpation both hyperglycaemia and glycosuria could be controlled.

3. After intra-arterial injection of synthalin a dog had less sugar in the blood of the femoral vein than in that of the artery.

4. Controlled cases of human diabetes were recorded, in which on fixed diets the glycosuria diminished by 40 to 50 grams daily when synthalin was taken by the mouth.

5. Acid bodies in the urine of diabetics diminished after the use of synthalin, and this suggested that more sugar was used as the result of the administration of the drug.

No detailed account of their clinical results was given at the time, but it was stated that the general results in seventy cases were good, and, in addition, the claim was made that two cases previously refractory to insulin had been successfully treated, one of which was complicated by pulmonary tuberculosis.

Towards the end of 1926 the action of synthalin was discussed by the Association of German Physicians,² and there was fairly general agreement on the following points:

1. It was not advisable to use synthalin in severe acute cases or in children.

2. The most suitable type of case was the milder diabetic with a total of about 30 to 40 grams of sugar in the daily urine on a fair diet.

3. Previous long insulin treatment, while not a final contraindication, seemed, in some way unknown, to make a patient refractory to synthalin. Transfer from insulin had to be slowly and carefully carried out.

4. Synthalin was slower in action than insulin, but its effect was more prolonged.
5. The effect on the blood sugar was not as striking as that of insulin.
6. Alimentary complications—vomiting, diarrhoea, loss of appetite, and depression—were sometimes severe.

On the whole, there could be no doubt, after reading the report of the discussion, that the opinion of the majority of the German physicians who had used the drug was distinctly favourable, and their experience extended over large numbers of cases.

A curious position had by this time arisen. In Germany a new drug was being widely used in the treatment of diabetes, particularly of the milder varieties, and in the rest of Europe and in America the method had not been investigated at all extensively—this was due to the fact that in their original paper Frank and his colleagues had not disclosed the method of preparation of synthalin. When one of us visited Breslau a little later he was told that this unusual departure from established medical practice was due to the fact that the cost of the very extensive research had been borne by Messrs. Kahlbaum, the manufacturing chemists of Berlin, on the understanding that if anything useful emerged from it they should have the right to place the synthetic product on the market before its method of preparation was disclosed. Dr. Aschoff, of the firm of Kahlbaum, was good enough to give us a supply of synthalin for clinical use; a certain amount had also been sent into England to the Medical Research Council early in 1927. A little later the precise chemical formula of synthalin was published, and its preparation was found to present no great difficulty.

In our first series of twenty-eight cases treated with synthalin (none of which are included in the detailed analysis set out later in this paper) no fewer than fifteen appeared to be benefited by the drug, and it was therefore with some surprise that we read the report of the physicians³ who had undertaken to investigate the matter at the request of the Medical Research Council, for their conclusions, with one or two exceptions, were distinctly at variance with the favourable opinion formed by the German Association of Physicians, to which reference has already been made. The explanation of this discrepancy seemed to us to be that the report of the Medical Research Council was based on very few cases, of which a considerable proportion were obviously unsuitable for synthalin in the light of German experience, and the period of observation of them for various reasons had been short. We therefore decided to continue to use synthalin cautiously, and we were encouraged in this course by the subsequent appearance of papers which disclosed a more favourable view of the drug than that of the Medical Research Council report.

In 1929 a further investigation of thirteen cases satisfied us that synthalin was of real value in the treatment of certain types of diabetic patients, and we have therefore used it more extensively in the last two years, mainly in the diabetic clinic at the General Hospital, Birmingham.

ACTION OF SYNTHALIN

It has already been definitely established in several researches⁴ that synthalin brings about a decrease in the blood sugar of normal and diabetic subjects. Just as insulin causes an increase before a decrease in blood sugar,⁵ so synthalin first induces a transient hyperglycaemia and then a more lasting hypoglycaemia.⁶

There is general agreement that synthalin increases the respiratory quotient⁷; some authors report that the oxygen consumption decreases,⁸ others find an increase in the oxygen consumption.⁹ In this connexion it is important

to record that synthalin administration causes an increase in blood lactic acid.¹⁰

Glycogen stores of the liver and muscles are found to be diminished by synthalin.¹¹ Bodo and Marks discovered that if an animal be killed when it has the transient synthalin hyperglycaemia its liver contains no more than a trace of glycogen. In considering this it must be remembered that doses of 20 to 90 units of insulin in a day have been reported¹² to cause an immediate decrease of 30 to 85 per cent. of liver glycogen.

Simola (*loc. cit.*) made the interesting discovery that after synthalin administration there is in most, but not all, cases a fall in blood inorganic phosphate accompanying the fall in blood sugar. If a poisonous dose of synthalin be given there is a sharp rise in blood inorganic phosphate. Bodo and Marks found that when synthalin hypoglycaemia has been produced in an animal, restoration of the sugar to normal level or higher failed to resuscitate the animal. Even before a definite hypoglycaemia had set in adrenaline in doses which would normally produce a large and prolonged rise in blood sugar, failed to have any such effect. From their observations they conclude—and Dale¹³ agrees with them—that synthalin, in doses big enough to produce hypoglycaemia, damages the liver. If, then, the action of synthalin depends upon its damaging the liver, one may expect the mechanism of the lowering of blood sugar to be the same as that operating in the production of hypoglycaemia in poisoning of the liver by chloroform or by phosphorus,¹⁴ or that following complete extirpation of the liver.¹⁵

On the other hand, the fact that an animal made hypoglycaemic by synthalin cannot be resuscitated by administration of sugar probably indicates that, whatever damage may be done to the liver by a large dose of synthalin, the condition is not necessarily to be compared with that resulting from complete extirpation of the liver, for Mann and McGrath (*loc. cit.*) showed that the moribund animal (hypoglycaemic as a result of removal of the liver) is, in a minute or less, brought back to its normal appearance by the intravenous injection of glucose. It would therefore appear that an overdose of synthalin may produce hypoglycaemia, and it may also yield another result in that the animal is so badly damaged (poisoned) that, even though the lack of sugar is made good, the other trouble is so great that the animal dies.

Those authors who have reported the decrease in glycogen stores of the muscles and liver, and the marked damage to the liver after synthalin administration, have worked with doses which, in comparison with the quantities used in therapeutics, are enormous. Attention has already been drawn to the work of Simola, in which it is shown that the effect of synthalin in small doses differs from that in large doses. Liu and Krüger¹⁶ have shown that intravenous administration of small doses of synthalin often causes a temporary rise in blood pH, while large doses cause a fall in pH. Whereas Bodo and Marks, using large doses of synthalin, have reported decreased oxygen consumption, it is significant that Calvert (*loc. cit.*) and Karr, Schumann, and Petty (*loc. cit.*), working with normal and diabetic human beings, have noted, after synthalin, an increase not only in the respiratory quotient, but also in the oxygen consumption.

Therefore it might well be that for synthalin there is a therapeutic dose and a toxic dose, and that the therapeutic dose exerts its action without damaging the liver. Of this no definite proof is offered, but the purpose of this communication is to show that synthalin can be administered in doses large enough to produce a definite decrease in blood sugar, and that this dosage may be kept up for a considerable time without the appearance of toxic symptoms.

ANALYSIS OF RESULTS

Our patients attend the clinic periodically, the majority coming every one or two months, and on each occasion the blood sugar is estimated. In assessing the value of synthalin we have noted the clinical effects and also the effect on the blood sugar level. In many cases we have records of patients' blood sugar readings while on a steady diet and before synthalin was administered; we are thus in a position to compare such readings with those later while the patients were on the same diet, but taking synthalin regularly for short or long periods.

As far as possible, the effect of the treatment on the blood sugar was determined by comparing the *mean* of readings before administration of the drug was commenced with the mean of the readings while taking it. Owing to the quite large fluctuations in blood sugar level so commonly met with in diabetic patients, this method is more reliable than relying on single estimations while the patient is off or on synthalin.

FIRST GROUP (1929)

Number of patients, 13 (5 male, 8 female).

Average age, 58 years.

Average weight, 11½ stone.

Average dose of synthalin, 34 mg. daily.

Number of periods of synthalin treatment, 16.

Average length of period of synthalin treatment, 4½ months.

Diet: Twelve observations when the protein and fat of the diet was restricted (calories 1,900 to 2,200); four observations when protein and fat was unrestricted and carbohydrate from 80 to 160 grams.

Average blood sugar before institution of treatment, 246 mg. per 100 c.cm.

Result: In fourteen periods the blood sugar *fell* during period of synthalin treatment.

Average fall of blood sugar, 28.3 per cent. of original level.

In two periods the blood sugar *rose*, in both cases by 9 per cent.

Notes: During one of the two periods when the blood sugar rose, the carbohydrate content of the diet was considerably increased.

In another series of twenty-two periods of synthalin treatment the drug was commenced at the same time as dietetic treatment was instituted; these cases, therefore, did not provide comparable blood sugar readings off and on synthalin treatment. However, an average fall in the blood sugar of 31 per cent. of the original level was noted in sixteen periods; in six periods the average rise of blood sugar was 18 per cent. We also noted that, out of eighteen occasions on which synthalin treatment was stopped, on seventeen the blood sugar subsequently rose.

As we have already said, these results encouraged us to use synthalin more extensively, and we are now able to review another series of forty-seven cases. In several of these cases synthalin was commenced and stopped several times. The number of observations of the blood sugar and the period for which synthalin was or was not taken have been noted; where more than one blood sugar reading is available an average has been struck and compared with that after the change (on to or off synthalin). In a few cases, where a patient has been on or off the drug for a very long period, *all* the blood sugar readings before or after the change have not been included in the average, since there is a great liability for considerable fluctuations in the blood sugar level to occur over a period of some months. In such cases the mean of the two or three readings proximal to the change have been taken.

In assessing the effect of synthalin it must be remembered that the circumstances in which these outpatients attend naturally tend to obscure somewhat the full effect, because patients often allow their supply of synthalin to run out, perhaps some days, or even a week or two, before coming again. The blood sugar recorded

on this next attendance is taken as one after a period on synthalin, yet actually the effect of synthalin on the blood sugar may have disappeared by the time they are seen again. Furthermore, it is our practice to give synthalin for three days, with a rest on every fourth day; patients may return on a fourth day, and, though the effect of synthalin is considerably longer than that of insulin, its effects *may* be wearing off after twelve or more hours.

SECOND GROUP

Our usual dose has been 30 or 35 mg., as before, occasionally only 20 mg.

Number of patients, 47.

Number of changes of treatment—that is, on to or off synthalin—76 (without any material change in diet).

Number of blood sugar observations, 322.

SERIES A. In 35 patients, involving 41 changes,

By *adding* synthalin the blood sugar *fell*.

SERIES B. In 12 patients, involving 18 changes,

By *withdrawing* synthalin the blood sugar *rose*.

SERIES C. In 9 patients, involving 9 changes,

By *adding* synthalin the blood sugar *rose*.

SERIES D. In 7 patients, involving 8 changes,

By *withdrawing* synthalin the blood sugar *fell*.

From the blood sugar readings, therefore, it seems that synthalin was active in fifty-nine changes of treatment (on to or off synthalin), as against seventeen when it was inactive—that is, it appeared to be active in approximately 80 per cent.

Series A. Synthalin Active

Analysis of forty-one changes when synthalin was added and the blood sugar fell.

Average actual fall in blood sugar, 61 mg. per 100 c.cm.—that is, 35 per cent. of previous blood sugar level.

Average previous blood sugar level, 174 mg. per 100 c.cm.

Number of patients, 36 (7 male, 29 female).

Obese patients, 14; normal 8; thin, 14.

Ages: 40–60 years, 24; over 60 years, 12.

Type: mild (not requiring insulin at any time), 30; moderate (requiring up to 29 units insulin at some time), 6; severe (requiring 30 units or more), 0.

Total number of observations of blood sugar before change, 85—an average of 2.1 per change.

Total number of observations of blood sugar after change, 97—an average of 2.3 per change.

Total period on synthalin, 104 months—average 2.5 months per change.

Total period off synthalin, 71 months—average 1.7 months per change.

Average loss of weight, 1.7 lb.

Toxic symptoms: In only two cases were *mild* toxic symptoms observed; in one of these it is probable that a slight pain over the liver was due to causes other than synthalin.

In twenty-seven periods on synthalin the notes indicate that the general condition was good or satisfactory; in six periods it might be termed poor, though there were no specific symptoms. In the remainder there is no indication that there was any change clinically, though the blood sugar was lower.

Series B. Synthalin Active

Analysis of eighteen changes when synthalin was withdrawn and blood sugar rose.

Average total rise of blood sugar, 60 mg. per 100 c.cm.—that is, 42.5 per cent. of previous level while on synthalin.

Average previous blood sugar on synthalin, 141 mg. per 100 c.cm.

Number of patients, 12 (2 male, 10 female).

Obese patients, 7; thin, 5.

Type of case: mild, 10; moderate, 2; severe, 0.

Ages: 20–40 years, 1; 40–60 years, 8; over 60 years, 3.

Total observations of blood sugar before withdrawing synthalin, 43—an average of 2.4.

Total observations of blood sugar after withdrawing synthalin, 46—an average of 2.6.

Total period on synthalin before change, 64½ months—an average of 3.6 months.

Total period off synthalin, 68½ months—an average of 4 months.

Average loss of weight off synthalin, 0.6 lb.

Series C. Evidence of Synthalin being Inactive

Analysis of nine changes when synthalin was added and blood sugar rose.

Average total rise of blood sugar, 32 mg. per 100 c.cm. (15.5 per cent. of previous level).

Average previous level, 206 mg. per 100 c.cm.

Number of patients, 9 (2 male, 7 female).

Obese patients, 3; thin, 6.

Ages: 20-40 years, 1; 40-60 years, 5; over 60 years, 3.

Type: mild, 4; moderate, 4; severe, 1.

Total observations before adding synthalin, 11—an average of 1.2.

Total observations after adding synthalin, 13—an average of 1.4.

Total period off synthalin before change, 11 months—an average of 1½ months.

Total period on synthalin, 27 months—an average of 3 months.

Average gain in weight, 0.75 lb.

Notes: (a) The average total change in blood sugar was much less than in Series A and B, when synthalin appeared to be active. (b) It should be noted that moderate and severe cases totalled 5, approximately 56 per cent., whereas in the series when synthalin led to a reduction in blood sugar level the moderate cases were only 20 per cent. of the total.

Clinical: One case showed marked hyperpiesia, which appeared to account mainly for symptoms; this patient took insulin for a time later. One case was clinically well, and showed at other times a favourable response to synthalin. One patient reported feeling not so well when off synthalin, though synthalin did not constantly lower the blood sugar. One patient was a "bad dieter," and had symptoms suggestive of mild cholecystitis; she seemed better on synthalin, and at other times the blood sugar reacted favourably to the drug, with falls more marked than the rise included in this series. Two other cases later required insulin, one of which reacted favourably to synthalin on other occasions. One patient seems to be slowly deteriorating, and it appears that he will probably need insulin.

Series D

Analysis of eight changes when synthalin was withdrawn and the blood sugar fell.

Average total fall of blood sugar, 28.5 mg. per 100 c.cm. (10.25 per cent. of previous blood sugar level).

Average previous blood sugar level, 278 mg. per 100 c.cm.

Number of patients, 7 (2 male, 5 female).

Obese patients, 4; normal, 1; thin, 2.

Ages: 40-60 years, 4; over 60, 3.

Type: mild, 3; moderate, 4.

Total observations before adding synthalin, 19—an average of 2.4.

Total observations after adding synthalin, 8—an average of 1.

Total period on synthalin before change, 25½ months—an average of 3.2 months.

Total period off synthalin after change, 15 months—an average of 1.9 months.

Average loss of weight, 0.4 lb.

Notes: In this series when synthalin appears to be inactive it should be noted that, as in Series C, the moderate cases account for 57 per cent. Clinically, one patient, also in Series C, suffered with severe hyperpiesia. One patient was soon afterwards admitted as an in-patient suffering with ulcerative colitis; there was no reason to believe that this was due to synthalin, but the colitis may have disturbed the carbohydrate metabolism. Two patients reported as not being so well when off synthalin. Two later required insulin. In one patient delayed menstruation might possibly have disturbed the blood sugar level.

CONCLUSIONS

1. Used under the conditions outlined it appears that synthalin generally causes a moderate fall in the blood sugar level of adult out-patients with diabetes of mild or moderate severity, and that the general condition of such patients is improved by taking the drug.

2. Though we have used synthalin over long periods and in sufficiently large doses to produce a definite effect on the blood sugar in approximately 80 per cent. of sixty patients, we have found no evidence of toxicity, except in a few rare instances in which the toxic symptoms were only mild.

3. Our usual dosage has been 10 mg. three times daily after food for three consecutive days, with a "rest" on the fourth day.

4. We are not satisfied that synthalin B (the more recent product) has any material advantages over synthalin, which is the less expensive.

REFERENCES

- ¹ Frank, Nothmann, and Wagner: *Klin. Woch.*, 1929, No. 45.
- ² *Verhandlungen der Gesellschaft für Verdauungs und Stoffwechselkrankheiten*, 1927.
- ³ *Lancet*, 1927, ii, 649.
- ⁴ Calvert: *Lancet*, 1927, ii, 649.
- ⁵ Rathery, Kourilsky, and Laurent: *C. R. Soc. de Biol.*, 1930, ciii, 563.
- ⁶ Bodo and Marks: *Journ. Physiol.*, 1928, lxxv, 83; Boedeker and Junkersdorf: *Arch. Exp. Path. Pharm.*, 1928, cxxix, 354; Staub: *Zeit. f. klin. Med.*, 1928, cvii, 607.
- ⁷ Calvert: *Loc. cit.*; Karr, Schumann, and Petty: *Arch. Int. Med.*, 1929, xliii, 384; Bodo and Marks: *Loc. cit.*
- ⁸ Bodo and Marks: *Loc. cit.*
- ⁹ Karr, Schumann, and Petty: *Loc. cit.*
- ¹⁰ Simola: *Zeit. physiol. Chem.*, 1927, clxviii, 274; Bodo and Marks: *Loc. cit.*
- ¹¹ Bodo and Marks: *Loc. cit.*; Staub: *Loc. cit.*
- ¹² Rathery, Kourilsky, and Gilbert: *C. R. Soc. de Biol.*, 1930, ciii, 307.
- ¹³ Dale: *Proc. Roy. Soc. Med.*, 1927, xxi, 527.
- ¹⁴ Williamson and Mann: *Amer. Journ. Phys.*, 1923, lxxv, 267; Stander: *Bull. Johns Hopkins Hosp.*, 1924, xxxv, 46.
- ¹⁵ Mann and McGrath: *Arch. Int. Med.*, 1922, xxx, 73.
- ¹⁶ Liu and Krüger: *Zeit. Ges. Exp. Med.*, 1928, lxi, 780.

ACTIVITY OF COMMERCIAL PREPARATIONS
OF HOG'S STOMACH

BY

JOHN F. WILKINSON, M.D., M.Sc., Ph.D., F.I.C.

DIRECTOR OF THE DEPARTMENT OF CLINICAL INVESTIGATIONS AND
RESEARCH, UNIVERSITY OF MANCHESTER, AND MANCHESTER
ROYAL INFIRMARY; LECTURER IN SYSTEMATIC MEDICINE,
UNIVERSITY OF MANCHESTER

The increasing replacement of liver by hog's stomach in the treatment of pernicious anaemia^{1 2 3} makes it very important to ensure that the stomach preparations should be active and suitable for that purpose. During the last two years a large number of different preparations have become available, with the coincident possibility of unsuitable preparations being employed at grave risk to the patient. Obviously the palatability and ease of administration of a particular preparation is of no account if the preparation is inactive. As I have had occasion to examine one or two commercial preparations which were found to have an inadequate potency, it appeared advisable to investigate the activities of others. This was imperative, since the distribution of stomach preparations of uncertain value might continue and prove a potential danger to the class of patients concerned.

Of the sixteen preparations examined fourteen are in the form of powders (desiccated muscular or mucosal portions, or whole stomach), the other two being described as hog's stomach tissue "extracts." Their equivalence in fresh tissue is variously given by the manufacturers as four to seventy times the weight. Ten of these preparations are stated to be fat-free. The stomach preparations were supplied for clinical trial by the commercial houses which issue them, but a few samples were purchased in their original packages. Of some of the preparations further clinical samples were submitted by the suppliers after preliminary adverse reports, and it is believed that several active products have become available for general clinical use. Investigations showed that the commercial preparations