curve gradually falls until the copper value is reached. This suggests that besides α - β glucose, disaccharides or other substances with a polarimeter: copper reduction ratio greater than that of α - β glucose are present in the blood of diabetic persons. We suggest that α - β glucose cannot be directly stored or utilized, but that an enzyme is responsible for the conversion of α - β glucose into γ glucose. We picture the change:

The absence or inactivation of this enzyme is suggested as the direct cause of diabetes mellitus.

Macleod and his co-workers³ have recently shown that injection of "insulin" into depancreatized dogs causes a decrease in the blood sugar. Determinations of the respiratory quotient showed that sugar was being utilized as long as the administration of insulin was maintained. Similar results were obtained by the injection of insulin into persons suffering from diabetes mellitus. We suggest that the effect of the insulin is to activate the enzyme responsible for the conversion of α - β glucose $\longrightarrow$ γ glucose. If this view be correct, examination of the blood sugar of diabetics after injection of insulin should show that the nature of the sugar approximates to that of normal persons.

We have investigated the action of tissue extracts on the rotatory powers of glucose and fructose. We have confirmed the observations of Hewitt and Pryde⁴ that extracts of the intestinal mucous membrane are inactive. The liver would appear to contain the enzyme. That another factor is concerned is shown by the fact that the enzyme is almost inactive in the absence of an extract of pancreas. The extracts of pancreas which we have recently used are preparations of "insulin" obtained by Collip's method.⁴ Similar activation of the enzyme is obtained.

Solutions of glucose or fructose when incubated at 37° C. with very small amounts of insulin and liver extract in a jacketed polarimeter tube have their rotations altered in a downward and upward direction respectively. In view of the fact that our insulin preparations invariably contain phosphorus, it is noteworthy that addition of phosphate accelerates the reaction to a degree not obtained by the use of other salts. Phosphate buffers have therefore been employed. Boiled liver extract is inactive, whereas insulin would appear to be thermostable in this respect. Our insulin preparations were tested for activity on rabbits.

The degree of alteration in rotatory power may be seen from the following examples:

Glucose.		Fructose.	
First reading ...	1.70° R.	First reading ...	177.92°
Lowest reading ...	1.47° R.	Highest reading ...	178.30°

The solutions contained 15 c.cm. of an arbitrary glucose or fructose solution, 2 c.cm. phosphate buffer, 1 c.cm. 0.1 M. KCl, 1 c.cm. weak insulin solution, 0.3 c.cm. liver extract.

Without phosphate—

Glucose.		Fructose.	
First reading ...	1.32° R.	First reading ...	178.60°
Lowest reading ...	1.30° R.	Highest reading ...	178.61°

The enzyme would appear to be slowly inactivated under these conditions. The unstable nature of the sugar formed is shown by the fact that after the maximum change has occurred the rotation tends to revert to the original value. Our experiments with the enzyme *in vitro* do not show a ratio copper reducing: polarimeter value equal to those observed in the case of blood sugar. It is difficult to convert any considerable amount of the sugar in our solutions into the reactive form, as this is not removed from the sphere of action. A stage would appear to be soon reached at which the reverse process attains a velocity equal to that of the original one.

The copper reducing power of the sugar solution at the beginning and end of the reaction is unaltered. The reaction is therefore different from that described by Levene and Mayer⁵ in connexion with muscle and pancreas extracts, in which the copper reducing power was lowered.

This method would seem to lend itself to the further purification of insulin. We have already found that the final product obtained by Collip's method is capable of being divided into two fractions, which differ markedly in their nature and activity as tested by the above method and on rabbits.

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THE VITAMIN CONTENT OF CERTAIN PROPRIETARY PREPARATIONS.

BY

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At the request of the BRITISH MEDICAL JOURNAL the writers have examined the vitamin content of certain of the best known of those proprietary preparations which are advertised in the medical press as containing vitamins. The following preparations were tested:

Metagen (Messrs. Parke, Davis, and Co.). The advertisements state that this is guaranteed to contain the three principal vitamins, and that it is "a concentrated product for therapeutic administration."

Maltoline (the Maltine Manufacturing Co., Ltd.). The advertisements state: "Maltoline is therefore rich in three well-known vitamins, and is recommended as a nutritive to those who are unable to take or digest cod-liver oil"; and also that "Maltoline . . . satisfactorily takes the place of cod-liver oil."

Roboleine (Messrs. Oppenheimer, Son, and Co., Ltd.). The advertisements state: "The 'A.B.C.' of Diet. Because it is very rich in the vitamins 'A,' 'B,' and 'C' there is no tonic food more serviceable in wasting diseases"; and the statement is also made that it "supersedes cod-liver oil."

Virol (Virol, Ltd.). The advertisements state that one of the "essential points in the diet of growth" is that "the food must contain those food accessory substances known as vitamins, but the presence of vitamins is not sufficient in itself," and that "Virol as it reaches the public contains the vitamins."

Vitmar (Messrs. Callard and Co.). The advertisements state: "Biological tests prove that vitmar contains vitamins in abundance."

Mellin's Food (Mellin's Food, Ltd.). The advertisements state: "Vitamins. Those elusive principles of food which are essential to nutrition are present in Mellin's food when mixed for use as directed according to the age of the infant."

The specimens of these foods tested were all bought in the open market. Most of them claim to contain all three vitamins. Vitamins A and B are rapidly destroyed by certain chemical processes, and therefore their concentration or purification is a matter of extreme difficulty, but it is not difficult to prepare them in an unconcentrated form, in which they will keep for a prolonged period. Vitamin C is much more unstable; so far as we can ascertain it has not been concentrated, and it is difficult even to preserve it in a crude form. Dried orange and lemon juice are indeed the only known preparations in which this vitamin can be preserved for prolonged periods.

We have therefore only tested the above preparations for the presence of vitamins A and B, and have not tested for the presence of vitamin C, for it is reasonable to assume that any methods for the concentration or preservation of vitamins which fail in the case of vitamins A and B will be even less successful in the case of vitamin C.

The presence of vitamin A was determined as follows: Young rats (weight about 50 grams) were fed upon a diet which was free from vitamin A, but otherwise adequate. The rats consumed from 16 to 20 grams of food (moist weight) daily. On this diet they soon ceased to grow, and then a known amount of the substance to be tested was given to the rat before its basal diet each morning, or added to a small amount of the diet which was consumed before the rest of the basal diet was given. The minimal amount of the substance which contained sufficient vitamin A to produce growth in young rats was thus determined.

The presence of vitamin B was also determined by experiments upon rats. In this case young rats were fed upon a diet free from vitamin B but otherwise adequate. This diet soon caused arrest of growth, and the vitamin B content of the proprietary preparations was determined by finding the minimal quantity of the various preparations required to produce growth.

The course of the experiments made with metagen is shown in the accompanying figure. The curves marked A I show the effect of feeding 0.15 gram of metagen daily to rats on a diet devoid of vitamin A; this produced growth in one rat and failed to do so in two others; this result is termed "doubtful

TABLE I.—Vitamin Content of Proprietary Preparations as determined by their Power to Produce Normal Growth in Young Rats (weight about 100 grams) living on a Diet free from the Vitamin under consideration.

Proprietary Preparation.	Vitamin A Tests.		Vitamin B Tests.	
	Dose of Preparation which failed to produce Regular Growth.	Dose of Preparation which produced Normal Growth.	Dose of Preparation which failed to produce Regular Growth.	Dose of Preparation which produced Normal Growth.
Metagen...	Gram. 0.15 (D)	Gram. 0.3	Gram. 0.15 (Ir)	Gram. 0.3
Maltoline ...	1.0 (N)	—	0.5 (N)	1.0
Roboleine ...	0.5 (N)	1.0	0.2 (Ir)	0.5
Vitrol ...	0.2 (D)	0.5	0.1 (N)	0.5
Vitmar ...	0.2 (N)	0.5	0.2 (Ir)	0.5
Mellin's Food ...	0.2 (N)	0.5	0.5 (Ir)	1.0
Common Food Substances.				
Milk (summer feed)...	—	2 to 5 c.cm.	—	8 c.cm.
Butter (summer feed)	—	0.2 gm.	—	—
Cod-liver oil ...	—	0.003 gm.	—	—
Wheat germ ...	—	—	—	0.2 gm.
Yeast ¹ ...	—	—	—	0.2 gm.

(D)=Doubtful growth. (Ir)=Irregular growth. (N)=No growth.

growth" in Table I. In the figure, A II shows the effect of 0.3 gram of metagen on rats on a similar diet; regular growth resulted in all three cases; this is termed "normal growth." B I shows the effect of feeding 0.08 gram of metagen daily to

rats on a diet devoid of vitamin B; no growth resulted in three cases. B II shows the effect of 0.15 gram of metagen; this produced regular growth in one case and defective growth in two cases. This result is termed "irregular growth" in Table I. B III shows that 0.3 gram of metagen produced regular growth in three cases, and this is termed "normal growth."

The results obtained with the various preparations are summarized in Table I; this table also shows, for the sake of comparison, the vitamin content of certain common foods. The doses given in the table are as accurate as can be obtained in biological tests of this nature, but can only be considered as approximately correct.

The results recorded in Table I show that the preparations tested contained vitamins A and B, except maltoline, in which case the tests failed to show the presence of vitamin A in the quantities tested. A dose of 1 gram of maltoline, which is about 8 per cent. of the total diet (dry weight) of a rat, did not contain an active amount of vitamin A, and it seemed unnecessary to repeat the test on a higher dosage. A comparison between the vitamin content of the proprietary preparations and the vitamin content of those ordinary foods which are rich in vitamins shows that the former contain less vitamins than the latter. The vitamin A content of the proprietary foods was in all cases less than that of butter obtained from grass-fed cows, and less than one-hundredth that of active specimens of cod-liver oil. The vitamin B content of the proprietary foods was in all cases less than that of wheat germ or of yeast. The vitamin value of these foods as compared with that of milk from grass-fed cows is shown in Table II.

Mellin's food is not included in Table II as it is not given alone but is mixed with milk; if the food is mixed with milk in the proportion of a teaspoonful of food to two tablespoonfuls of milk the vitamin content (A and B) of the food will raise the vitamin content of the milk. The vitamin content of Mellin's food may therefore be sufficient to be of value in cases where an infant is being fed on milk which has a low vitamin content. As regards the other preparations, none of them can be said to contain a rich, abundant, or concentrated supply of vitamins. None of them can be considered to be a substitute for cod-liver oil as a source of Vitamin A, for in no case does the total daily adult dose of the proprietary food contain as much as one-tenth of the vitamin A

TABLE II.—*The Relative Value of Proprietary Foods and Milk as Sources of Vitamins.*

Proprietary Food.	Adult Dose.	Approximate Weight of Total Daily Adult Dose.	Amount of milk which provides approximately the same quantity of Vitamin as is contained in the daily adult dose of the proprietary foods.	
			Vitamin A.	Vitamin B.
		Gram.	Oz.	Oz.
Metagen ...	Two to five 5-grain capsules daily	1.6	1	1.5
Maltoline ...	One tablespoonful 3 times a day	45	8	13
Roboleine ...	Two teaspoonfuls 3 times a day	30	5.3	17
Virol ...	Two teaspoonfuls 3 times a day	30	11	17
Vitmar ...	Two teaspoonfuls 4 times a day	40	14	23

content of a teaspoonful of cod-liver oil. The present paper is of course solely concerned with the vitamin content of these preparations, and no opinion is expressed concerning their merits in any other respect. Whilst these experiments were in progress two papers appeared in America describing similar investigations.

Hess, Moore, and Calvin² investigated the content in vitamin B and C of metagen and vitamin (mastic). They concluded that "metagen as obtained on the open market contains no demonstrable amount of antiscorbutic substance (vitamin C), as shown by experiments on guinea-pigs." They also found that metagen contained less vitamin B than commercial yeast, as shown by its power to protect pigeons from polyneuritis.

McCollum and Simmonds³ measured the vitamin B content of six proprietary vitamin preparations advertised in the

United States; one preparation (Yeast Vitamin Harris) was found to contain a considerable quantity of vitamin B, but the others contained little or none of this vitamin.

Del⁴ found that half a capsule of metagen daily failed to maintain life in a guinea-pig on a scorbutic diet, although a dose of 0.5 c cm. orange juice daily had previously maintained the animal in normal health. This result agrees with the conclusions of Hess, Moore, and Calvin.

The experiments recorded in the present paper show that in none of the cases examined have the manufacturers succeeded in concentrating vitamins on the commercial scale. This result was only to be expected, for the concentration of the two more stable vitamins (A and B) is a process of the greatest difficulty even on a laboratory scale, and in the case of the successful attempts the final yield of purified vitamin only represents a minute fraction of the total quantity of vitamins present in the raw material.

Our experiments confirm what other workers on vitamins have emphasized—namely, that under normal conditions of life an adequate supply of vitamins can be easily ensured by including in the diet a suitable amount of "protective foods," such as milk, butter, green vegetables, and fruit, and that no advantage is to be gained by trying to obtain these substances in the form of drugs.

Since the above article was written Bailey⁵ has reported that he tested the activity of more than twenty commercial vitamin preparations, and found that only in two or three was the vitamin B content higher than that of dry brewer's yeast; in several the vitamin B content was negligible.

Note.—The expenses of this research were defrayed by a grant from the British Medical Association.

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APITUITARISM AND THE ANENCEPHALIC SYNDROME.

BY

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THE subject of apituitarism and the anencephalic syndrome was brought to my notice by a leading article in the *BRITISH MEDICAL JOURNAL* of November 27th, 1920, which drew attention to the work of F. J. Browne, published in the *Edinburgh Medical Journal* (vol. xxv, page 296).

As a result of investigations in five instances of anencephalic foetus, Browne concluded that certain characteristic features of the condition were due to a failure of development or to destruction of the pituitary gland. In particular he directed attention to the large amount of subcutaneous fat, the hypoplasia of the thymus, suprarenal, and genital glands, and the shortness of the limb bones, and stated that these facts showed that the mother's internal secretions play little part in the metabolism of the foetus, which relied on its own glands. He also considered that the facts established formed an important confirmation of the functions of the pituitary glands.

I have examined four anencephalic foetuses, three preserved in the museum of the Adelaide Hospital, and one recent specimen placed at my disposal by Professor Wood Jones. In each of the four instances the anterior (pharyngeal) portion of the gland was found without much difficulty in its usual situation and resting on the body of the sphenoid. In none of the cases was any real attempt at the formation of a sella turcica apparent, though the gland was of a size approximating that in a normal full-time foetus.

In one instance a process of apparently neuroglial tissue, probably representing the pars nervosa, was found; and it is

noteworthy that this was the only one examined comparatively soon after delivery. In all, microscopic sections displayed a structure corresponding with the epithelial segment of the pituitary body—namely, strands of polygonal cells with somewhat granular protoplasm and rounded nuclei, separated by a loose connective tissue, in which were abundant thin-walled vessels. From the position and structure of these glands I have no doubt that they represent the epithelial portions of the pituitary.

[Dr. Barlow sent with his manuscript a microscopic section, which we have submitted to Professor S. G. Shattock, F.R.S., who confirms the view expressed, and has superintended the accompanying drawing (by Mr. J. Ford) of the author's specimen.]

A microscopic section of the pars anterior of the pituitary of an anencephalic foetus, exhibiting the normal glandular structure. The red blood cells in the plexus of capillaries are stained of a deep black (iron haematoxylin). 1/6 objective.

My observations make it appear probable that the gland has been in reality present in cases examined by others, but has not been distinguished from the vascular connective tissue covering the base of the skull.

As a result of the discovery of the anterior segment of the pituitary gland in four successive typical examples of the anencephalic syndrome, it may be concluded that the other features of the condition are certainly not due to apituitarism, and that any conception of the functions of the gland based on such an assumption is erroneous.

Details of the specimens examined are as follows:

1. Male, about the size of an average full-time foetus. Nothing representing vascular connective tissue. The eyes were moderately prominent and the orbital plates much foreshortened. No sella turcica was present, but resting on the body of the sphenoid was a small rounded moderately dark body. No stalk was apparent. Microscopic section showed glandular cells in strands separated by loose connective tissue containing many thin-walled blood vessels.

2. Male anencephalic foetus, normal full-time size. The eyes were prominent and orbital plates foreshortened. There was no