HYPOGLYCAEMIA: WITH NOTES ON TWO CASES.

BY

H. S. PEMBERTON, M.B., M.R.C.P.,

PHYSICIAN TO THE DAVID LEWIS NORTHERN HOSPITAL, LIVERPOOL;
CONSULTING PHYSICIAN, LIVERPOOL CANCER AND SKIN HOSPITAL.

THE sinking of the blood sugar level to a point at which symptoms appear may contribute to the clinical features of disease more largely than has perhaps been recognized. Whether hypoglycaemia denotes merely a fall below the normal fasting level or a fall associated with characteristic symptoms, it certainly occurs in many morbid or experimental conditions, some of which are set out below. It is of interest to speculate upon what part such a state plays in the symptomatology of the clinical counterparts to some of these conditions—for example, in Addison's disease or cholaemia. An examination of the literature makes it clear that hypoglycaemia may be associated with many diverse conditions, which I have attempted to classify as follows:

1. Hypoglycaemia follows the hyperglycaemia induced by glucose, fructose, galactose, starch, and adrenaline (Liefman and Stern,¹ Maclean and de Wesselow,² Frank,³ Foster⁴), but not after the hyperglycaemia of ether, which appears to be maintained (Pemberton and Cunningham⁵).

2. It also occurs in many lesions of the liver: such as removal in dogs (Mann and Magath⁶); parenchymatous changes caused by chloroform, salyarsan, and the fungus *Agaricus bulbosus* (Steinbrinck⁷), by phosphorus (Frank and Isaac⁸), and by hydrazine (Underhill⁹), and in the presumed circulatory changes which follow the intravenous injection of albumose and peptone in dogs (McGuigan and Ross¹⁰). In comment upon the statements of Steinbrinck, it may be pointed out that in the toxic jaundice of patients undergoing antisyphilitic treatment (arsenobenzol) Bailey and MacKay¹¹ found a normal fasting blood sugar; further, Joslin¹² states that the anaesthetic use of chloroform is accompanied by hyperglycaemia.

3. It may follow high section of the cord or sections of the nervous connexions of the adrenals (Falta¹³).

4. Various adrenal lesions are associated with hypoglycaemia: complete removal (Biery and Malloizel¹⁴); adrenal insufficiency (Mayer¹⁵); Addison's disease (Porges¹⁶).

5. It may occur in various states: such as alkalosis (Cambridge and Howard¹⁷); hypocalcaemia (Underhill,¹⁸ Cambridge and Howard¹⁹); following the intravenous injection of sodium bicarbonate, which also decreases adrenaline hyperglycaemia (Underhill²⁰).

6. Lastly, there are insulin and the insulin-like substances, all of which can produce hypoglycaemia. The insulin-like substances have been derived from clams, the cortical layer of oats, potatoes, rice, wheat, beet, and celery²¹; and recently Dubin and Corbitt²² have succeeded in separating the hypoglycaemia-producing principles from the hyperglycaemia-producing principles in cabbage, lettuce, celery, and spinach.

The symptoms of hypoglycaemia occur at varying levels of the blood sugar, so that the same level in different animals and individuals may be associated with different features. In dogs, Mann and Magath⁶ produced hypoglycaemic symptoms when the blood sugar had fallen to 45 mg. per cent. as a result of removal of the liver; in man, Banting, Campbell, and Fletcher²³ record a blood sugar of 52 mg. per cent., which was followed by uncontrollable hunger; Sevringhaus, Kirk, and Heath²⁴ state that symptoms appear at concentrations of 40 to 65 mg. per cent.; according to Macleod,²⁵ when the blood sugar reaches 75 mg. per cent. the patient experiences extreme hunger and a sense of fatigue; whilst in the case recorded below the venous blood sugar reached 48 mg. per cent. (and may possibly have fallen lower) without any marked symptoms being produced.

The fall in blood sugar, in causing symptoms which vary from slight vasomotor effects to convulsions comparable to those of toxic states, would appear to operate primarily upon pontine or medullary centres. Olmsted and Logan²⁶ found no symptoms in spinal cats even when the blood sugar had fallen below the convulsive level; whereas in decerebrate animals typical symptoms developed provided that the pituitary body had been removed. Dickson and others²⁷ suggest that, in insulin hypoglycaemia, abnormal metabolites appear; these bodies require oxidation, and thereby the respiratory centre is stimulated; they ascribe the muscular twitchings to cerebellar or mid-brain stimulation.

The symptoms of hypoglycaemia quickly disappear when

the blood sugar again rises. Among substances which cause this rise Noble and Macleod²⁸ regard glucose as pre-eminent; other sugars, such as mannose, galactose, and laevulose, have a certain value, whilst the pentoses, cane-sugar, and lactose appear to be inert. Adrenaline would appear to act as a physiological antagonist in cases of insulin hypoglycaemia, whilst in other cases its antidoting action is probably due directly to glycogenolysis; so that its effect will vary according to the amount of glycogen present in the liver and muscles. In hypoglycaemic states with mild symptoms the polysaccharides themselves appear to be efficient, whilst in severe cases with convulsions all known antidoting agents seem to lose some of their usual potency. This statement may perhaps be illustrated by a description of two cases, one mild and one severe.

The first case was experimentally induced in a normal man by fasting for five hours, feeding with glucose, and

then, just as the normal hyperglycaemic curve was beginning to fall, exhibiting insulin. The lowest recorded level of blood sugar was 48 mg. per cent. (see chart), but as the preliminary vasomotor symptoms began before this, the level may have sunk lower still. Among the symptoms and signs infra-orbital oedema was of interest; it is perhaps comparable to similar oedema

observed in anaphylactic states and in one case of presumed adrenal insufficiency. The hunger, which all observers record, may be similar to that of hyperglycaemia, inasmuch as in both states the tissues would appear to be starved of glucose. Shortly after the last estimation of blood sugar a meal of bread and jam was taken; all the symptoms quickly disappeared, only to reappear an hour later in a milder form. This latter observation has also been made by Sevringhaus, Kirk, and Heath,²⁴ and would appear to be due to a secondary hypoglycaemia following a hyperglycaemia of the type recorded above. The second case, which was fatal, occurred in a man, aged 30, suffering from diabetes mellitus, who had been under my observation for two years; he also had pulmonary tuberculosis.

He was readmitted to hospital on March 29th, 1924, in a very poor condition—16 per cent. of glucose in his urine, a blood sugar of 0.357 mg. per cent., marked acidosis, and weighing 91 lb. As the table given below shows, a very definite improvement was obtained by April 4th, and on April 5th his diet and insulin dosage were both increased. On the night of April 6th, however, he became rigid with a marked opisthotonos, which lasted five minutes, after which he vomited; his temperature rose to 101° F. He was given 2 oz. of glucose by the mouth, after which he went to sleep. No more insulin was given, but his carbohydrate intake was again increased. On April 7th he was quiet, but early on the morning of April 8th he again became excited and threw his pillows about; 10 c.cm. of 5 per cent. glucose were given intravenously and glucose feeding by mouth was attempted; adrenaline was given hypodermically in 0.5 c.cm. doses every hour. By 8.45 a.m. he was in a flaccid, semi-comatose condition, temperature 100.6°, pulse 72, respirations 20; his skin was clammy, the eyeballs showed a pendular movement, and the corneal and abdominal reflexes were absent; the knee-jerks were present, and he exhibited double ankle clonus and plantar reflexes of the extensor type. Blood taken at 11.30 a.m. contained 27 mg. per cent. of glucose. At 1.15 p.m. the pulse was 108, and although the pendular movements of the eyeballs had ceased, ankle clonus and extensor toe were still present. He died a few minutes later.

Day.	Diet.	Blood Sugar.	CO ₂ (vols. per cent.).	Insulin.
April 2	Protein ... 60 grams Fat ... 30 " Carbohydrate 15 "	0.143 mg. per cent.	57	0.5 c.cm.
April 4	—	0.091 mg. per cent.	51	0.5 c.cm.
April 5	Protein ... 90 grams Fat ... 60 " Carbohydrate 30 "	—	—	1 c.cm.
April 7	—	—	—	None.
April 8	—	0.027 mg. per cent.	54	None.

No *post-mortem* examination was possible until the next day, when the following changes were found.

Lungs.—The right lung was studded with caseous tuberculous masses, some an inch in diameter. There were pleural adhesions at both apices.

Heart.—Weight 7 oz. No macroscopic changes were seen.

Liver and Pancreas.—No naked-eye changes were seen, but subsequent microscopic examination of the pancreas showed extensive fibrosis in which no islet tissue was visible. Other ductless glands showed no changes.

Glycogen Contents.—The amount of glycogen was determined in the heart, liver, and muscles by Pflüger's method rather more than twelve hours after death had taken place. Considering the glycogenolysis that must have taken place in this time and the fact that he was a severe diabetic, the figures of 0.014 per cent. for muscle, of 0.028 per cent. for myocardium, and of 0.04 per cent. for liver are perhaps suggestive of what happens to circulating glucose in insulin hypoglycaemia.

Brain.—This was definitely "wet"; the pia mater showed areas of milkiness, but there was no evidence of basal meningitis.

In making this record of the two cases I am greatly indebted to my colleague, Dr. L. Cunningham, with whom all the biochemical work was done; also to my late house-physician, Dr. A. J. Hawe, who made many of the observations in the fatal case.

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CONGENITAL CYSTIC DISEASE OF THE LUNGS.

BY

SYDNEY SMITH, M.D., D.P.H.,

PRINCIPAL MEDICO-LEGAL EXPERT, EGYPTIAN GOVERNMENT.

A NEWLY born child was found dead in circumstances which suggested infanticide, and was submitted to me for examination.

The body was that of a child of about eight months' intrauterine age. It was free from marks of violence. Both lungs were in an apparently foetal condition and sank on being placed in water; both were in a state of advanced cystic degeneration (Fig. 1).

FIG. 1. Left Lung.

Cysts varying in size from a pea to the head of a pin were distributed throughout the whole of the lung tissue. The larger cysts were found towards the free surface. A number of cysts abutted on the pleura, but there were no pleural adhesions.

On microscopic examination no air cells or vesicles could be made out, the lungs being composed of unexpanded tissue and cysts. The cysts were smooth-walled and lined in certain cases with flattened cells. There was no trace of cubical epithelium lining the cavities nor of muscular or elastic fibres in the walls. Here and there the cavities were filled with a mucoid or colloid-looking material. Numbers of microscopic cysts could be observed immediately under the pleural surface. Numerous bronchi were seen filled with cast-off cubical and cylindrical epithelium and other debris. A certain amount of cellular infiltration could be observed around the bronchi and there were numerous small haemorrhagic foci in the lung tissue.

Cystic degeneration in both lungs of a newly born child is very rare, and the reason for its occurrence is rather obscure. Bronchiectasis occurring after birth is usually

attributed to weakening of the walls of the bronchi by disease, whereby they are unable to resist the air pressure in fits of coughing. Barty King considers that pleural adhesions also play an important part in producing the initial dilatation.

In this case air pressure cannot be considered, for the child had never breathed, nor were there any pleural adhesions, and the cause of the condition must be sought elsewhere.

In the developing lung the bronchioles terminate in a bulbous extremity into which groups of atria open. Groups of air cells or alveoli which form the air sacs open into these atria. The alveoli are not formed until about the sixth month of intrauterine life, and before respiration commences they are lined with cubical epithelium which gradually becomes flattened when respiration occurs.

In our specimen the microscopical state of the tissues indicates that the cysts have not been recently formed, and their origin from the alveoli cannot be admitted in view of the late development of the alveoli. They must therefore be due to dilatation of the atria, infundibula, or bronchioles.

The absence of columnar or cubical epithelium in even the smallest cysts and of any trace of muscular or elastic tissue in their walls tends to exclude an origin from bronchi or bronchioles. Such a condition is, however, found in ordinary bronchiectasis, where the pressure of the retained secretion causes flattening of the cubical or cylindrical epithelium, while the stretching causes atrophy and disappearance of the muscular fibres. It would be difficult, therefore, to be certain from the histological disposition of the tissues whether we are dealing with a dilated bronchus or a dilated infundibulum, but the appearance of the smaller cysts particularly does not resemble bronchial dilatation. The cysts are found immediately under the pleura, and as the terminations of the bronchioles do not abut on the pleural surface this tends to exclude an infundibular origin. The condition is therefore a congenital cystic degeneration of both lungs caused by the dilatation of the atria.

The presence of mucoid or colloid matter in many of the cysts indicates that secretion from their walls is fairly active, and if, as is suggested by the microscopical sections, there was some inflammation of the bronchioles which caused blocking of their lumen, this would account for the retention of the secretion and dilatation from the consequent pressure.

PNEUMOCOCCAL WOUND INFECTION:

NOTES ON TWO CASES.

BY

BERTRAM MUIR, M.B., B.S., F.R.C.S.,

HONORARY SURGEON, SHANTUNG ROAD HOSPITAL, SHANGHAI.

CASES of suppuration due to the pneumococcus in regions other than the upper and lower respiratory tracts and adjacent sinuses, the pericardium and peritoneum, the meninges, and the middle ear, are sufficiently rare to merit publication, especially when the infection is apparently primary and not blood-borne. Even the subcutaneous injection of a virulent pneumococcal culture in guinea-pigs causes death by septicaemia, with comparatively little local reaction, although a local abscess, with a characteristic fibrinous exudate, sometimes forms. The two cases here described were both "traversing" bullet wounds, and in both the primary infection appeared to be pneumococcal.

CASE I.—Pneumococcal Infection of Diffuse Traumatic Aneurysm of the Axilla.

A Chinese soldier, aged 35, was shot through the right sub-clavicular region in November, 1924. The bullet entered anteriorly and traversed the pectoralis major, injured the third part of the axillary artery, and passed out through the teres major muscle. A tense pulsating swelling immediately formed in the right axilla, and he lost the use of the right hand, although no sensory disturbance was noticed, and very little haemorrhage occurred from either wound. After a few weeks the swelling increased so much that he had to maintain the arm in a position of marked abduction.

Six weeks later the swelling became very painful, and the