Brit. J. Psychiat. (1964), 110, 228–232

Alcohol-induced Hypoglycaemia

By VINCENT MARKS and W. E. MEDD

The clinical manifestations that may result from abuse of alcohol are numerous. Profound, sometimes fatal, hypoglycaemia, first described a little over 20 years ago (Brown and Harvey, 1941), is among them although as far as we are aware, not previously described in this country. This may be due partly to differences in drinking habits here and abroad where "bootleg" liquor is more readily available, and partly to failure to recognize this complication of alcohol. Many cases of alcohol induced hypoglycaemia may well go undiagnosed, alcoholaemia alone being held responsible for bizarre behaviour or alteration in consciousness following the drinking of alcohol-containing beverages. In some cases, a patient brought into the casualty department with a provisional diagnosis of "drunkenness" is found to have a low blood sugar and the diagnosis hastily altered to the more socially acceptable one of "hypoglycaemia", but without the cause of the hypoglycaemia ever being determined.

A 35-year-old man was admitted to Kingston Hospital on 30 July, 1962. He was brought in by the police who observed him wandering in the street apparently drunk. His behaviour, sleepiness and slurred speech, when seen in casualty, were consistent with this diagnosis, but his breath did not smell of alcohol. He said that he had taken an overdose of sleeping tablets: however, the aspirated stomach contents and a sample of blood taken on admission did not contain barbiturates and later he denied any knowledge of his previous statement. Unfortunately, blood alcohol was not estimated*.

He had been an in-patient in a mental hospital on several occasions during the past five years where a diagnosis of psychopathic personality and chronic alcoholism had been made. He first began drinking excessively at the age of 22. This increased when his wife left him five years ago. He was admitted to hospital in November, 1961 and discharged in March, 1962 after a course of apomorphine aversion treatment interspersed with a course of modified insulin therapy. Fasting blood sugar taken before insulin therapy was commenced was 95 mg./100 ml.

For about three months after his discharge he abstained from alcohol, but he relapsed early in July of this year after attempting unsuccessfully to effect a reconciliation with his wife. He re-entered hospital but stayed only a week. It appears probable that thenceforth he spent most or all of his money on drink. He was unemployed and received National Assistance. On the morning preceding his admission to Kingston Hospital, he had attended an interview for work, where he was observed to be bedraggled and unkempt, though not obviously intoxicated. Some eight hours later he was brought into Kingston Hospital in the condition already described.

During the night, about 30 hours after admission, he was observed to have attacks in which he was unrousable, his breathing stertorous and his limbs rigid with occasional clonus. His pupils were unreactive to light and the plantar responses extensor. Hypoglycaemia was suspected and confirmed by finding a blood sugar, measured by a non-specific ferricyanide method, of 50 mg./100 ml. Intravenous glucose produced immediate, but temporary, return of consciousness. During the next two days he periodically lapsed into coma from which he could be roused only with increasing difficulty by intravenous glucose. His skin was bathed in sweat. The blood sugar was 22 mg./100 ml. during one episode. Glucose given continuously by intubation maintained normoglycaemia and

* He was admitted to the ward for observation.

TABLE I

Results of Liver Function Tests Soon After Admission and After Clinical Recovery

	August 2, 1962	August 14, 1962
Thymol turbidity	—	<1 unit
Cholesterol	105 mg.	210 mg.
Total bilirubin	<0·5 mg.	<0·5 mg.
Alkaline phosphatase	26 K.A. units	8·0 K.A. units
Total protein	6·1 g.	6·1 g.
Total albumin	—	4·2 g.
Total globulin	—	1·9 g.
S.G.O.T.	42 (S.F. units)	28 (S.F. units)
S.G.P.T.	19 (S.F. units)	19 (S.F. units)
Electrophoresis	Normal	Normal
Bromsulphthalein (retention at 45 minutes)	6%	7%

Liver biopsy: Sections showed no histological abnormality; moderate glycogen content

by the end of the second day he showed clinical signs of improvement. Glucose administration was then stopped and the blood sugar measured at intervals during the next 48 hours without food. There was no return to hypoglycaemic levels. This made a diagnosis of hypoglycaemia due to insulinoma or to hepatic insufficiency unlikely, especially in view of the comparatively mild abnormalities in the liver function tests (Table I). In addition, an aspiration liver biopsy showed no histological abnormality and sections stained with P.A.S. before and after diastase showed moderate glycogen content. Results of other laboratory tests are shown in Table II.

A diagnosis of alcohol-induced hypoglycaemia was considered. After a 40-hour fast, during which as on the previous occasion, there were only minor changes in the blood sugar, he was given 50 ml. of absolute alcohol diluted to an approximately 10 per cent. solution. The result is shown in Figure 1.

The blood alcohol, measured enzymatically (Harger, 1961), rose steeply to reach a maximum of 105 mg./100 ml. at 1 hour and fell gradually thereafter. The blood glucose,

TABLE II

E.S.R.	8 mm./hour
Haemoglobin	9·0 g./100 ml. (62%)
Red blood cells	$4·73 \times 10^6$/mm.^{3}
P.C.V.	33%
M.C.H.C.	27%
M.C.V.	70 μ^3
Serum iron	31 μg./100 ml.
Serum B_{12}	340 $\mu\mu$g./ml.
Plasma sodium	139 mEq/l.
Plasma chloride	105 mEq/l.
Plasma potassium	4·1 mEq/l.
Plasma bicarbonate	18·0 mEq/l.
Blood urea	22 mg./100 ml.
Urine 17 OHCS	9·2 mg./24 hour
Urine 17 KS	4·4 mg./24 hour
Metopirone test	Normal

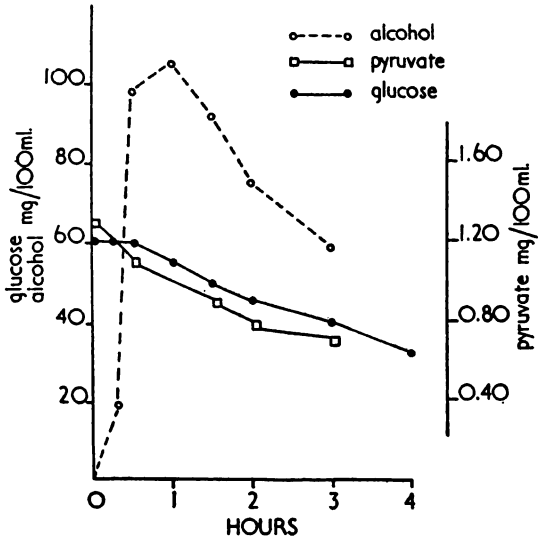

FIG. 1.—Effect of 50 ml. ethyl alcohol on blood glucose and pyruvate after the patient had been fasting for 40 hours.

https://doi.org/10.1192/bjp.110.465.228 Published online by Cambridge University Press

measured by glucose-oxidase, remained constant initially, but after 30 minutes began to fall progressively until, when the test was terminated after 4 hours, it was only 32 mg./100 ml. The blood pyruvate level followed the blood glucose concentration.

Tolbutamide and glucagon tests were carried out and the results shown in Figure 2. Both were normal.

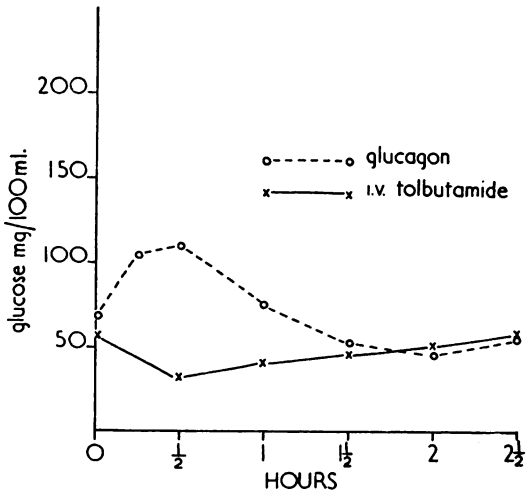

FIG. 2.—Result of glucagon (1 mg. i.m.) and tolbutamide (1 g. i.v.) tests carried out on different days while the patient was fasting.

Attempts to produce hypoglycaemia by alcohol on three further occasions were, with one exception, unsuccessful, despite the use of larger doses of alcohol to produce longer periods of alcoholaemia coupled, on one occasion, with prolonged fasting and repeated glucagon administration to deplete preformed hepatic glycogen scores.

On the successful occasion, 50 ml. of absolute alcohol was given after a 40-hour fast. Through the kindness of Dr. Kawerau at St. James's Hospital, Balham, we were able to analyse blood for glucose continuously on the Auto-Analyser. The fasting blood sugar was 67 mg./100 ml. After the first hour, during which the blood glucose remained constant save for a transient (20 minutes) rise, possibly produced by the small amount of sugar in the fruit juice used for flavouring, or by the alcohol itself (Forsander *et al.*, 1958), there was a persistent, regular fall in the blood sugar level. This reached its nadir after 14 hours when the blood glucose was 42 mg./100 ml. During the next 12 hours the blood sugar rose spontaneously almost to the initial level (62 mg./100 ml.) despite continued fasting, confirming that the fall in blood glucose after alcohol was not due to food deprivation alone.

During his stay in hospital, the patient improved markedly, both physically and mentally. He became reconciled with his wife. He was told and accepted that his recent severe illness had resulted from drinking and that even a small amount of alcohol might precipitate a further, possibly fatal episode.

DISCUSSION

Before proceeding to discuss the possible mechanisms of alcohol-induced hypoglycaemia, we felt it would be profitable briefly to mention some of the important clinical features of this syndrome revealed by analysis of the present case and those described in the literature (Brown and Harvey, 1941; Tucker and Porter, 1942; Peluffo *et al.*, 1958; Weill and Gorouben, 1960; Jeune *et al.*, 1960; Neame and Joubert, 1961; Cummins, 1961).

It occurs most commonly in poorly-nourished adults, generally some 6–36 hours after ingestion of alcohol. The amount of alcohol is not necessarily excessive and one or more meals may have been taken between the time of its ingestion and the development of hypoglycaemia. The symptoms of hypoglycaemia may be mistakenly attributed to acute alcoholic intoxication. However, in the former condition, unless hypoglycaemia has developed unusually rapidly, as may sometimes happen, the breath does not smell of alcohol and blood alcohol levels are low. The skin is frequently bathed in sweat and in some cases, paradoxically, this is associated with hypothermia. There is commonly a metabolic acidosis (Brown and Harvey, 1941; Cummins, 1961), which does not normally occur in other varieties of hypoglycaemia. The acidosis has been attributed to methanol, but this is probably incorrect as it also occurs in patients made hypoglycaemic by non-methanol containing liquors

and is a common accompaniment of acute alcoholic intoxication. The majority of patients recover immediately and completely with small doses of glucose intravenously, but a proportion, including our own patient, show delayed recovery despite continuous glucose administration. Some cases terminate fatally despite treatment (Cummins, 1961).

Why only a small percentage of those who over-indulge in alcohol develop hypoglycaemia and then only on some occasions, is obscure. Most investigators who have tried have been unable to reproduce hypoglycaemia with alcohol in their patients after recovery in hospital.

As most of the earlier cases reported from America were associated with the drinking of liquors containing in addition to ethanol, varying amounts of methanol, petrol and higher alcohols (Brown and Harvey, 1941; Tucker and Porter, 1942; Gadsen *et al.*, 1958) it has been contended that the contaminants and not ethyl alcohol itself were responsible for the hypoglycaemia. Our experience shows that hypoglycaemia can result from pure alcohol ingestion, and there is evidence to support this in the literature. The relationship between alcohol and hypoglycaemia is, however, still poorly understood.

Acute toxic hepatitis is a well recognized complication of alcoholic over-indulgence, (Beckett *et al.*, 1962) and it has not unjustifiably been suggested that this is the initial injury and ultimately responsible for the observed hypoglycaemia (Neame and Joubert, 1961). However, in most patients with post-alcoholic hypoglycaemia standard and more elaborate liver function tests reveal little or no disturbance, and liver biopsies show little deviation from normal. Conversely, even profound hepatic dysfunction from infective hepatitis or portal cirrhosis is rarely associated with hypoglycaemia.

Vartia *et al.* (1960) have shown that blood sugar levels are significantly lower during "hangover" than in normal fasting subjects. Excepting children, who seem to be particularly susceptible to the hypoglycaemic effects of alcohol, most cases of post-alcoholic hypoglycaemia have occurred in more or less chronically malnourished individuals who were often, though not invariably, chronic alcoholics. This suggests that the nutritional state is an important factor in determining whether hypoglycaemia develops after alcohol. This has been confirmed experimentally in animals by Clark *et al.* (1961) who found that ethyl alcohol produced hypoglycaemia in dogs, but only when food was refused or withheld.

Two groups of workers in America (Freinkel *et al.*, 1962; Field and Williams, 1962) have recently claimed that normal healthy subjects can be made hypoglycaemic by moderate doses (30–50 ml.) of alcohol provided they have fasted 47–72 hours beforehand; overnight fasting is said to be sufficient to elicit a hypoglycaemic effect within one hour and persisting for at least 3 hours in susceptible subjects. Field and Williams (1962) and Freinkel and his colleagues (1962) have presented evidence that alcohol exerts its hypoglycaemic effect by a specific inhibition of gluconeogenesis; reducing hepatic synthesis of glycogen from three carbon fragments (e.g. pyruvate) derived from the periphery. On the other hand, Coulthard (1958) concluded as a result of his own and published studies that alcohol does not lower blood sugar in normal subjects, even after prolonged fasting, but may on the contrary raise it. It appears probable that for hypoglycaemia to develop clinically a combination of factors including prolonged undernutrition, hypovitaminosis (Sinclair, 1953) and possibly magnesium deficiency (McCollister *et al.*, 1960) is necessary. Correction of these factors on admission to hospital might account for some of the difficulties experienced in reproducing the hypoglycaemic effect of alcohol experimentally on patients but premature termination of the experiments may also contribute.

Summary and Conclusions

A case of unconsciousness due to hypoglycaemia in an alcoholic male is described, and its relationship to alcohol ingestion confirmed. The syndrome of alcohol-induced hypoglycaemia is particularly liable to occur in chronic alcoholic subjects who also suffer from malnutrition. The blood glucose should

be measured in any patient who becomes unconscious, or fails to regain consciousness, after drinking alcohol. The possible mechanisms responsible for the hypoglycaemia and the difficulties attached to its subsequent experimental reproduction are discussed.

Acknowledgments

Our thanks are due to Drs. M. R. Brown, D. L. Monks and B. Moore-Smith for their clinical care of this patient and for establishing the presence of hypoglycaemia. We are also indebted to Dr. B. W. Meade for his advice and for much of the initial biochemical investigations and to Dr. Julius Merry and Dr. H. Palmer.

References

Beckett, A. G., Livingstone, A. V., and Hill, V. R. (1962). *Brit. med. J.*, *ii*, 580.

Brown, T. Mcp., and Harvey, A. M. (1941). *J. Amer. med. Ass.*, **117**, 12.

Clark, W. C., Wilson, J. E., and Hulpieu, H. R. (1961). *Quart. J. Stud. Alc.*, **22**, 365.

Coulthard, A. J. (1958). *J. Forens. Med.*, **5**, 185.

Cummins, L. H. (1961). *J. Pediat.*, **58**, 23.

Field, J. B., and Williams, H. E. (1962). *J. clin. Invest.*, **41**, 1357.

Forsander, O., Vartia, O. K., and Krusius, F. E. (1958). *Ann. Med. exp. Fenn.*, **36**, 416.

Freinkel, N., Singer, D. L., Gilbert, C. K., and Anderson, J. B. (1962). *J. clin. Invest.*, **41**, 1359.

Gadsen, R. H., Mellette, R. R., and Miller, W. C. (1958). *J. Amer. med. Ass.*, **168**, 1220.

Harger, R. N. (1961). *Toxicology* (Ed.: Stewart, C. P., and Stolman, A.), Vol. II. Academic Press.

Jeune, M., Cotte, J., and Nivelon, J. L. (1960). *Pediatrie.*, **15**, 664.

McCollister, R. J., Flink, E. B., and Doe, R. P. (1960). *J. lab. clin. Med.*, **55**, 98.

Neame, P. B., and Joubert, S. M. (1961). *Lancet*, **2**, 893.

Peluffo, E., Scolpini, V., Grezzi, J., and Tarallo, N. (1958). *Arch. Pediat. Urug.*, **29**, 24.

Sinclair, H. M. (1953). *Proc. Nutrition Soc.*, **14**, 107..

Tucker, H. St.G., and Porter, W. B. (1942). *Amer. J. med. Sci.*, **204**, 559.

Vartia, O. K., Forsander, O. A., and Krusius, F. E. (1960). *Quart. J. Stud. Alc.*, **21**, 597.

Weill, J., and Gorouben, J. C. (1960). *Bull. et Mem. Soc. med. Hôp. Paris*, **32**, 1270.

Vincent Marks, M.A., B.M., M.R.C.P.E., *Consultant Pathologist, Area Laboratory, West Park Hospital, Epsom, Surrey*

W. E. Medd, M.D., M.R.C.P., *Physician, Kingston General Hospital, Kingston-on-Thames, Surrey*