in the legs. The pathological process was confined to vessels supplying the leg muscles and the skin in two cases and to the leg muscles alone in one case. In each case the subsequent course of the disease was benign, in that there has been no evidence of visceral involvement and no clinical deterioration has appeared during the period of follow-up.

Case 3. Histological section of biopsy specimen from calf muscle.

The leg pains were always severe at the onset, and were aggravated by standing and walking. The histological and electromyographic changes of myopathy were always of mild degree, being secondary to the arterial changes—for example, in Case 3 the myopathy occurred only in proximity to involved arteries and the electromyogram was normal on several occasions. In primary polymyositis, where there are definite myopathic changes, muscle contractures occur at an early stage and electromyograms are definitely abnormal. Unlike polymyositis (and other forms of myopathy) leg pains in polyarteritis appear to be associated with active arteritic lesions and not with the relatively minor degree of associated muscle involvement which sometimes occurs. Possibly the pains are partially due to muscle ischaemia consequent on complete or partial arterial obliteration by endarterial thickening.

Generalized polyarteritis often presents with pain in muscles and around joints. Rose (personal communication) has stated that out of 111 cases of polyarteritis studied 14 had muscle pains as an initial manifestation, most often in the legs. Six of his patients had cutaneous polyarteritis of the legs, with or without muscle and joint pains, which remained as the only manifestation of disease for months or years. Rötstein and Good (1958) followed a case in which the manifestations were limited to skin and muscle for 11 years, and in reviewing the literature—including accounts by Lindberg (1931) and Boyd (1940)—they suggested that so long as the viscera are not affected the condition can be considered benign and eventual cessation of the active disease process may be anticipated. They stated that in such cases systemic steroid therapy does not appear to ameliorate the symptoms or the pathological process, and that prolonged high doses of systemic corticosteroids should be reserved for the severer forms of the disease, particularly when there is cardiorenal involvement. In one of our patients (Case 2) steroids had no beneficial effect on the symptoms, but in the others relatively small doses produced adequate clinical improvement.

Polyarteritis must therefore be considered as one possibility in patients presenting with leg pains at rest, on standing, or on walking (claudication). The conditions causing "muscular pain" most frequently encountered are perhaps polymyositis, vascular intermittent claudication, thrombophlebitis, and pain and tenderness referred from root pressure due to prolapsed intervertebral discs. "Vasculitis" is a non-specific term embracing a large variety of disorders (many not well understood) of the arteries and veins, ranging from self-limiting "allergic" arteritis through erythema nodosum, nodular panniculitis, localized nodular vasculitis, and finally to the full-blown picture of polyarteritis nodosa.

When polyarteritis is suspected a biopsy should be performed in order to establish the diagnosis, particularly as laboratory investigations may not be revealing in the early stages of the disease. When there are cutaneous manifestations a skin biopsy more often gives positive evidence than does a random muscle biopsy (unless, as is rarely the case, nodules can be discerned clinically because in a large proportion of cases—up to 87% according to Maxeiner (1952)—muscle biopsies do not reveal arteritic lesions in this condition.

I wish to thank Dr. E. J. Leiper and Dr. I. MacDougall, physicians to hospitals of the Harlow Group, for permission to report on two of these patients who were referred to me for consultation. Dr. J. H. Jacobs, of the North Middlesex Hospital, London, kindly gave permission to include the other patient. I also thank Dr. A. St.J. Dixon, of the Royal National Hospital for Rheumatic Diseases, Bath, for kindly reading the paper.

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Alcohol-induced Hypoglycaemia in Childhood

British Medical Journal, 1970, **1**, 278–280

Severe hypoglycaemia as a result of ingestion of alcohol in adults has been reported (Madison, 1968) and a similar condition is known to occur in childhood. It has been described in 12 children from different parts of the world, and three of them died. This article records an instance of this condition in a child and is the first to be described in this country. As there may have been a specific idiosyncrasy the effects of alcohol ingestion after an overnight fast on the blood levels of glucose, insulin, and cortisol, both in the affected child and in two sibs, have been studied.

CASE HISTORY

A boy aged 2 years 7 months, appeared well to his father at 7.15 a.m. but was found to be drowsy by his mother two hours later. He had had nothing to eat since the previous evening. He was taken to hospital 45 minutes later, where he was found to be semiconscious, and was then transferred to the Queen Elizabeth Hospital for Children. On examination he was well nourished, drowsy, and continually falling asleep, though he could speak coherently when roused. He moved all his limbs spontaneously, the tendon reflexes were all present, and the plantar responses were flexor. His rectal temperature was 95·4°F. (35·2°C.). His mother denied that he had taken any medicine or drugs during the previous 24 hours. Despite her contention gastric lavage was carried out and a red liquid smelling strongly of wine was produced. The mother was not surprised, as the whole family took wine regularly with their meals. It transpired on further inquiry that the patient and his older sister had drunk about 500 ml. of Beaujolais between them at about 8.30 a.m. on the day of admission.

He remained sleepy but rousable until 1.30 p.m., when he began

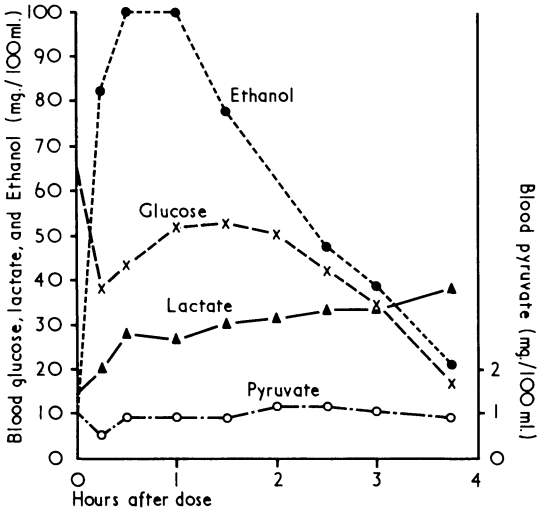
having continuous generalized convulsions. Sweating did not occur and he had a good colour. Because encephalitis and hypoglycaemia were considered as possible diagnoses a lumbar puncture was performed, and after taking venous blood for glucose estimation an injection of 40 ml. of 50% glucose was given, followed by an intravenous infusion of 20% glucose. He gained full consciousness dramatically within five minutes. The glucose level in the C.S.F. was low by Clinistix test, but zero by quantitative analysis, the fluid being otherwise normal. The blood also showed no detectable glucose level. Two hours after starting the intravenous infusion the blood glucose level was 297 mg./100 ml. He was fully recovered and ate a normal meal at 6 p.m., when infusion was discontinued.

He had had no serious illnesses, his milestones were normal and his general state of nutrition was satisfactory. He was first given a few drops of wine at the age of 3 months, and up to the time of his admission was given about 20 ml. of wine with his meal twice a week. His father, a waiter, was born in Italy and drank about 500 ml. of wine each day. His mother had on one occasion taken 9 fl. oz. (250 ml.) of vodka, without adverse effects. All the family appeared to have a good diet. There was no family history of any adverse effects of alcohol.

Laboratory Methods and Results

Blood alcohol was measured by gas chromatography, glucose by a specific oxidase method, pyruvate and lactate by an enzymatic assay, and plasma cortisol and insulin by immunoassay. For the tolerance tests pure ethanol was given well diluted with water, but in one sib it was given as wine. Fasting blood samples were taken at 15 minutes, half an hour, and thereafter every half-hour for three and a half to five hours after ingestion.

The blood glucose level remained unaltered when a test dose of 0·15 g. of alcohol per 1 kg. body weight was taken. The results with 0·75 g./kg. are shown in the Chart. Absorption of alcohol



Effect of alcohol ingestion (0·75 g/kg.) on blood glucose, lactate, and pyruvate. Note fall in blood glucose and rise in lactate.

was rapid, the blood level reaching 100 mg/100 ml. in 30 minutes, but falling quickly after the first hour. The blood glucose dropped sharply from a fasting level of 65 mg./100 ml. to 38 mg./100 ml. in 15 minutes, rising to 52 mg./100 ml. at one hour and falling again to 16 mg./100 ml. at three and three quarter hours at which time glucose was given. The blood lactate rose steadily from a normal fasting level to nearly three times its initial value, whereas the blood pyruvate, which was normal initially, fell sharply to about half the fasting value at 15 minutes, but rose again to its former level. The lactate/pyruvate ratio rose from a normal of about 14 to the high value of 40.

The findings in the two sibs were similar, except that the lowest blood glucose levels were 38 and 39 mg./100 ml. In all the tests the lactic acidosis was accompanied by a fall in blood *p*H, which still, however, remained within the normal range. The standard bicarbonate ion concentration, which was usually low normal, fell below the normal level. The plasma bilirubin, aspartate aminotransferase, and alanine aminotransferase were also normal initially. In the patient there was no change in the transaminases after the test, but in both sibs the plasma aspartate aminotransferase was slightly increased. The urine did not contain glucose or protein before or after the test, but ketone bodies, which were absent initially, were afterwards present. The fasting level of insulin was usually about 1 μU./ml. and did not vary during the test. There was a response in the plasma cortisol, which rose from 19 to 29 μg./100 ml.

In the hope of preventing the inhibition of gluconeogenesis, ascorbic acid (0·2 g. intramuscularly) was given in one test at the same time as the alcohol was taken, with a further 0·1 g. injected two hours later. The changes in the blood glucose, lactate, and pyruvate were, however, similar to those when ascorbic acid was not given.

Discussion

Previously published reports of alcohol-induced hypoglycaemia in children have given only scanty clinical and biochemical details. Though both males and females have been affected, only 2 of 13 children were girls. The ages ranged from $2\frac{1}{2}$ to 6 years. All but two had convulsions three to four hours after ingestion of alcohol, but sometimes longer; this symptom therefore being commoner in children than in adults with the condition. In all but one, in whom sweating occurred, there were no symptoms due to adrenaline excess, such as dilated pupils, sweating, or tachycardia. Thus there were no clinical signs to suggest hypoglycaemia. In some cases where encephalitis was suspected (Tolis, 1965) treatment with glucose was delayed despite the low C.S.F. sugar, and death ensued. Of the nine children in whom the nutritional state was recorded eight were well nourished. In addition to the present patient four other patients were noted to have taken the alcohol after an overnight fast. In at least two of the three patients who did not respond to glucose there was a long delay in its administration, and all three died.

There is little information about the relation between alcohol and glucose levels in the blood. The former varied between 20 and 125 mg./100 ml., but as only one level was determined in each case the peak may not have been detected. Blood sugar was low in one, being only 15 mg./100 ml. The blood sugar response to a dose of alcohol was determined in one child (Jeune *et al.*, 1960) the highest blood alcohol attained over three hours being 200 mg./100 ml., while the blood sugar never fell below 75 mg./100 ml. There was no loss of consciousness and the only sign of intoxication was ataxia, the gait returning to normal four hours after the alcohol was taken.

The diagnosis of hypoglycaemia may be overlooked in these patients either because of lack of knowledge of the syndrome or because of the absence of a history that alcohol had been taken. The latter was the case in two of the patients described by Tolis (1965) and also in the present patient, in whom it would not have been suspected if gastric lavage had not been carried out. In the present case the long period of semiconsciousness before the onset of generalized convulsions suggested that the initial drowsiness was due to alcohol intoxication and that hypoglycaemia only supervened later. This is supported by the demonstration that hypoglycaemic levels are reached only several hours after the alcohol is taken. In one case of alcohol poisoning in a child (Dickerman *et al.*, 1968) neither convulsions nor hypoglycaemia supervened, though the blood level of alcohol was extremely high, indicating that it does not directly cause convulsions. Hypoglycaemia did not occur, presumably because glucose was given as early as one and half hours after the alcohol was taken.

In some cases hypoglycaemia may not be recognized because of the absence of signs of increased adrenaline secretion. It has been suggested that this is due to an insufficient stimulus to its secretion, either because of the gradual fall in blood glucose (Luft *et al.*, 1966) or because of initial overstimulation of the adrenal medullary secretion by alcohol, followed by its exhaustion (Perman, 1958).

Hypoglycaemia should be suspected in any unconscious or semiconscious child who has taken alcohol without food, even before convulsions have occurred. In such cases it is essential to monitor the blood glucose at intervals up to five hours after ingestion or to give intravenous glucose as a precautionary measure. The amount of alcohol need not be large, as our results show, and the alcohol contained in a small glass of wine may be sufficient.

The length of the preceding fast is an important factor, probably because of the reduction in liver glycogen. In normal adults a fast of 44-72 hours is necessary to induce alcohol hypoglycaemia (Arky and Freinkel, 1966), whereas in alcoholics and adults with diseases such as thyrotoxicosis, in which glycogen stores are depleted, an overnight fast is sufficient (Arky and Freinkel, 1966).

Madison (1968) stated that in general infants and children are liable to alcohol-induced hypoglycaemia. It is, however, possible that an inherited predisposition may exist in some children. To test this hypothesis alcohol tolerance tests after an overnight fast were performed on the patient, his two sibs, and two other children with suspected hypoglycaemia. All showed a fall in blood glucose, the lowest level of which occurred four to five hours after ingestion of alcohol, which was at that time usually below 20 mg./100 ml. A pronounced rise in blood lactate combined with an unchanged and even decreased pyruvate accompanied the fall in blood glucose in all cases. The similarity of the results in all five and the failure to detect disturbance of liver or renal function tend to exclude a specific inherited metabolic defect.

Insulin and Plasma Cortisol Levels.—In all cases the insulin level was normal initially and even fell a little during the test, despite the hypoglycaemia, proving that this was not due to increased insulin production. The pronounced rise in the plasma cortisol, a response similar to that seen in normal adults, indicates a normal adrenal cortical function, in contrast with the impairment found in alcoholics, in whom the plasma cortisol falls when they are given alcohol (Merry and Marks, 1969).

A fuller account of the biochemical findings will be published elsewhere.

We thank Dr. M. J. Wilmers for permission to study this case, Dr. Ann E. Robinson, of the London Hospital Forensic Laboratory, for the alcohol estimations, and Dr. E. Ann Burgess for her assistance.

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Acute Alcoholic Hypoglycaemia in Two 4-year-olds

British Medical Journal, 1970, **1,** 280

Hypoglycaemia is a well-recognized complication of alcohol poisoning in adults, and over 120 cases have been recorded since 1941. Hypoglycaemia as a result of alcohol ingestion by children, however, has been recorded on very few occasions (Peluffo *et al.,* 1958; Cummins, 1961; Ramon *et al.,* 1963). This paper describes the cases of two children who developed hypoglycaemic convulsions after alcohol ingestion.

CASE 1

A 4-year-old boy was admitted to hospital via the casualty department in July 1968. Three hours earlier he had consumed 540 ml. of sherry. He had vomited several times and had gradually become drowsy. On examination he was unconscious and did not respond to painful stimuli. There were no neurological signs and respiration was not depressed. His breath smelled strongly of alcohol. Gastric lavage was not performed.

Five hours after ingestion he developed six right-sided convulsions, each lasting two minutes, though by this time he was conscious but drowsy, the blood sugar was less than 25 mg./100 ml. and blood alcohol was 100 mg./100 ml. He was given 300 ml. of milk containing 30 g. of glucose by mouth. Within 10 minutes the convulsions ceased and full consciousness was regained. He then drank a further 300 ml. of milk containing 10 g. of glucose. The convulsions did not recur and there was no residual neurological deficit.

Next day he was his usual self, apart from a slight headache and symptoms suggestive of an alcoholic "hangover." Blood sugar levels were normal. He was discharged two days after admission.

CASE 2

A 4-year-old boy was admitted to hospital in October 1969. Four hours previously he had consumed approximately 400 ml. of gin. He had become drowsy over the next three hours and had convulsed for five minutes previous to admission.

On examination he was deeply unconscious and convulsing. His capillary blood sugar was less than 40 mg./100 ml. (Dextrostix), and in venous samples. Blood sugar was found to be 12 mg./100 ml. An intravenous drip of 10% dextrose was set up and 20 ml. of 50% dextrose was injected intravenously at once. The convulsions ceased and consciousness was regained within two minutes of this injection. Venous blood sugar levels were normal after four and eight hours. The intravenous 10% dextrose was then discontinued.

The boy behaved normally thereafter and physical examination was negative. Subsequent blood sugars and an oral glucose tolerance test were normal. He was discharged on the third day after admission.

COMMENT

It is now accepted that alcohol can produce hypoglycaemia in normal subjects, though the exact mechanism is not clear. In acute alcoholism islet cell response is normal, but there is thought to be a failure of normal glycogenolysis and gluconeogenesis.

In the two cases described here the convulsions developed within five hours of ingestion of the alcohol and were clearly due to hypoglycaemia. Prolonged and severe hypoglycaemia can be fatal (Cummins, 1961) or produce irreversible brain damage.

If a child thought to have ingested alcohol develops drowsiness, coma, convulsions, or bizarre central nervous system signs, blood sugar levels should be estimated and an immediate therapeutic trial of intravenous glucose is justified.

I wish to thank Dr. W. Henderson for assistance with this paper.

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