POST - ALCOHOLIC HYPOGLYCAEMIA

A CLINICAL AND PATHOLOGICAL STUDY

A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF MEDICINE

by

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CONTENTS

INTRODUCTION

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For a number of years a history of sudden onset of coma, followed later by death, was noted amongst Africans at King Edward VIII hospital, Durban. Necropsy, where performed, revealed no cause in many of these patients. In 1957 after cerebrospinal fluid had been examined in some of the cases it was seen that the only abnormality present was a low cerebrospinal sugar. Hypoglycaemia was suspected and blood sugar estimation confirmed it. Further investigation failed to reveal the cause of the hypoglycaemia and in some cases because of a 'flat' glucose tolerance curve organic hyperinsulinism was suspected. In one case total pancreatectomy was performed but thorough macroscopical and histological investigation failed to reveal a tumour or hyperplasia, and the patient subsequently suffered from diabetes (Joubert, 1958). In August 1958, I admitted an African female patient, of 26 years, to the ward in coma. Because she was smelling distinctly of alcohol and yet clinical examination revealed no abnormality, I thought she was suffering from severe alcoholic intoxication. Later in the day her level of consciousness had worsened and a blood sugar estimation, performed amongst other tests, was found to be 37 mgms%. Administration of 50% intravenous dextrose solution resulted in an immediate recovery of consciousness. History, then obtained from the patient, revealed that she had been drinking heavily on the day before admission and that she had reawakened in hospital. She had previously been quite well. I was reminded of a similar case I had

seen while a house surgeon at Groote Schuur Hospital, Cape Town. There a Coloured male, smelling of stale alcohol and in coma, was admitted in the morning for observation to exclude internal head injury. By the afternoon the patient had not improved and because he looked mildly dehydrated, I gave him 5% intravenous dextrose saline. A little later I found him, to my surprise, sitting up in bed and wanting to be discharged.

As a result of this experience, I decided to watch for further cases of hypoglycaemia that followed excess alcohol, and a patient was later admitted to the hospital. I wondered, therefore, whether ethyl alcohol, a substance added to their alcohol, or a substance formed in the production of African alcoholic brews, might not be the cause of some cases of spontaneous hypoglycaemia.

Subsequent to reporting my ideas to Professor E. B. Adams, Professor of Medicine, Professor J. Wainwright, Professor of Pathology, and Dr. S. M. Joubert, head of the sub-department of biochemistry at the Medical School, Natal University, I commenced an investigation at the beginning of 1960, on all cases of hypoglycaemia admitted to King Edward VIII Hospital. (See appendix). In order that cases were not missed, the staff were encouraged to send a blood sugar estimation from all patients admitted in coma. During the initial survey it was found that there were four major groups of spontaneous hypoglycaemia amongst the African at the hospital :-

(1) The largest group consisted of cases of hypoglycaemia following the intake of excess alcohol. (Neame and Joubert, 1961).

(2) The second group consisted of cases of hypoglycaemia that occurred after the intake of herbal medicines. In these patients, who usually died, necropsy revealed acute zonal necrosis of the liver and, in most, acute tubular necrosis of the kidneys. (Neame & Pillay, 1964).

(3) A third group was associated with kwashiorkor and the diagnosis was usually obvious.

(4) The last group consisted of the well known causes of spontaneous hypoglycaemia and included a number of cases of cirrhosis of the liver and hepatic carcinoma.

In this thesis I will deal with a clinico-pathological study of patients, both African and Indian, who were admitted to King Edward VIII Hospital in hypoglycaemic coma following the intake of alcohol. It will include the initial group studied in 1960, as it was during this period that I came to the conclusion that ethyl alcohol was almost certainly the cause of the hypoglycaemic coma.

SURVEY OF LITERATURE

ON

POST - ALCOHOLIC HYPOGLYCAEMIA

SURVEY OF THE LITERATURE

The first report on post-alcoholic hypoglycaemia was published by Brown and Harvey in 1941. They reported on six patients who had been drinking a liquor known as "smoke", which contained certain additives (methyl alcohol, gasoline and ethyl acetate). A second report soon followed, in 1942, from Tucker and Porter who reported four cases. These authors suspected their patients had been drinking a denatured alcohol known as "solox", the composition of which was the same as that of "smoke". In both these reports the denatured alcohol was regarded as responsible for the hypoglycaemia.

Bottura et al., in 1949, were the first writers to note hypoglycaemic coma after the ingestion of ethyl alcohol. They reported eleven cases from Brazil and thought the hypoglycaemia was related to ethyl alcohol. Neves et al., (also from Brazil) reported twenty cases in 1950. They were the first to note post-alcoholic hypoglycaemia in non-alcoholics with normal livers. In addition they reported the first case in a child.

In 1957 Hammack noted seven cases amongst patients that had been admitted in "solox intoxication". In 1958 Hed mentioned two adult cases, when studying carbohydrate metabolism in chronic alcoholics, and Peluffo (1958) described two cases in Uruguayan children.

Three further reports of post-alcoholic hypoglycaemia, in children, were reported in 1960 and 1961. Jeune et al., (1960) and Weill and Gorouben (1960) each mentioned a case from France, while Cummins (1961) reported two cases in North America.

Neame and Joubert (1961) reported the findings in twenty-three patients admitted in post-alcoholic hypoglycaemia in South Africa. They noted glycogen depletion, on liver biopsy, during the hypoglycaemic coma and they suggested the mechanism of the post-alcoholic hypoglycaemia was due to a failure of gluconeogenesis during the period of glycogen depletion. Neame and Joubert (1963) subsequently reported a case in an African child.

In 1962 Teelucksingh and Symonds reported five cases of hypoglycaemia in children after the intake of rum. In the same year abstracts appeared on the production of hypoglycaemia by ethyl alcohol in normal adult volunteers and in patients previously admitted in hypoglycaemic coma after imbibing alcohol. (Field et al., 1962; Freinkel et al., 1962). Both these groups subsequently described their work in detail. (Field et al., 1963; Freinkel et al., 1963). Field et al., (1963) produced alcoholic hypoglycaemia in one patient, who had previously been admitted in alcoholic hypoglycaemia, and in five normal volunteers after a 44 hour fast. Freinkel et al., (1963) described their investigations and the experimental production of alcoholic hypoglycaemia in nine patients previously admitted in alcoholic hypoglycaemia. The aetiological role of ethyl alcohol was thus proved but the precise mechanism remained undetermined.

In 1963 and 1964 a number of cases of alcoholic hypoglycaemia were reported. Fredericks and Lazor (1963) described a case in a chronic alcoholic in North America. Roche et al., (1963) and Arnould et al., (1964) reported cases from France. Ramon Guerra et al., referred to four cases in Uruguay and also produced hypoglycaemia in two children after administering ethyl alcohol. The first British case was described by Marks and Medd (1964) who subsequently reproduced the hypoglycaemia by administering ethyl alcohol to the patient. Duckworth and Cooper (1964) mentioned a case in an African in Johannesburg, when describing accidental hypothermia in the Bantu. They said post-alcoholic hypoglycaemia was fairly common in the Bantu population in Johannesburg. Two further American cases were described by Kahil et al., (1964) and Gumpel and Kaufman (1964).

PATIENTS STUDIED

PATIENTS STUDIED

In order to select the patients for the investigation, four criteria were used :

1. A clinical presentation suggestive or compatible with hypoglycaemia.
2. The disappearance of these signs after administration of 50% dextrose by the intravenous route.
3. A low blood sugar (below 51 mg%, Folin-Wu) on admission.
4. A history of imbibing alcohol before the hypoglycaemic episode.

The second criteria was not satisfied in a few patients where treatment was either not given, or, because of prolonged hypoglycaemia, they did not recover consciousness (though even in these patients there was usually some sign of clinical improvement).

The fourth criteria was satisfied only after treatment with intravenous dextrose solution, when a history was taken, and thus many patients, who were seen initially, were subsequently not included in the investigation.

Ultimately 52 patients were studied. These consisted of 46 Africans (28 males, 18 females) and 6 Indians (2 males, 4 females). Two patients (Cases 10/60 and 2/62) were admitted in hypoglycaemic coma on two separate occasions following the intake of alcohol. The ages of the patients varied from 4 years to 70 years, and amongst the patients were 3 children (Cases 21/60, 5/61, 8/61). Fig. 1 shows the age distribution of the patients, and Fig. 2 their race and sex.

FIG. 1. AGE DISTRIBUTION OF PATIENTS

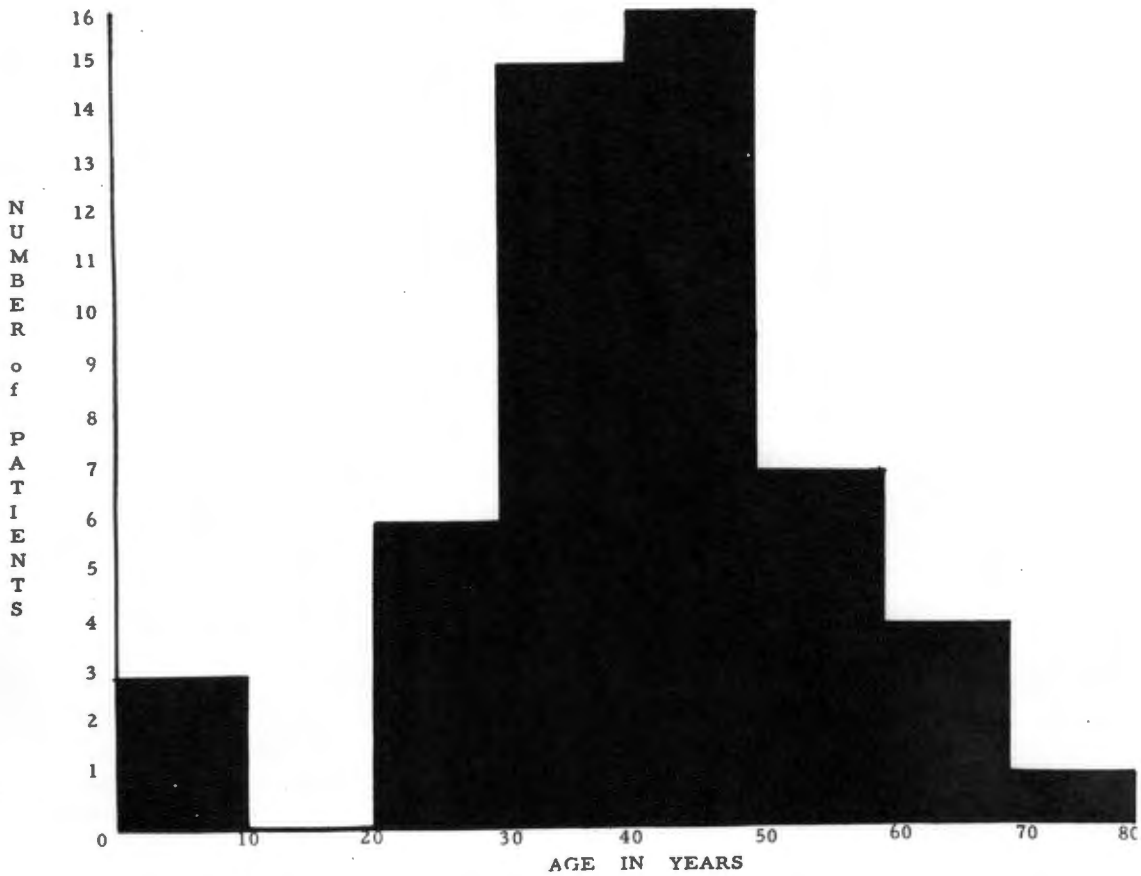
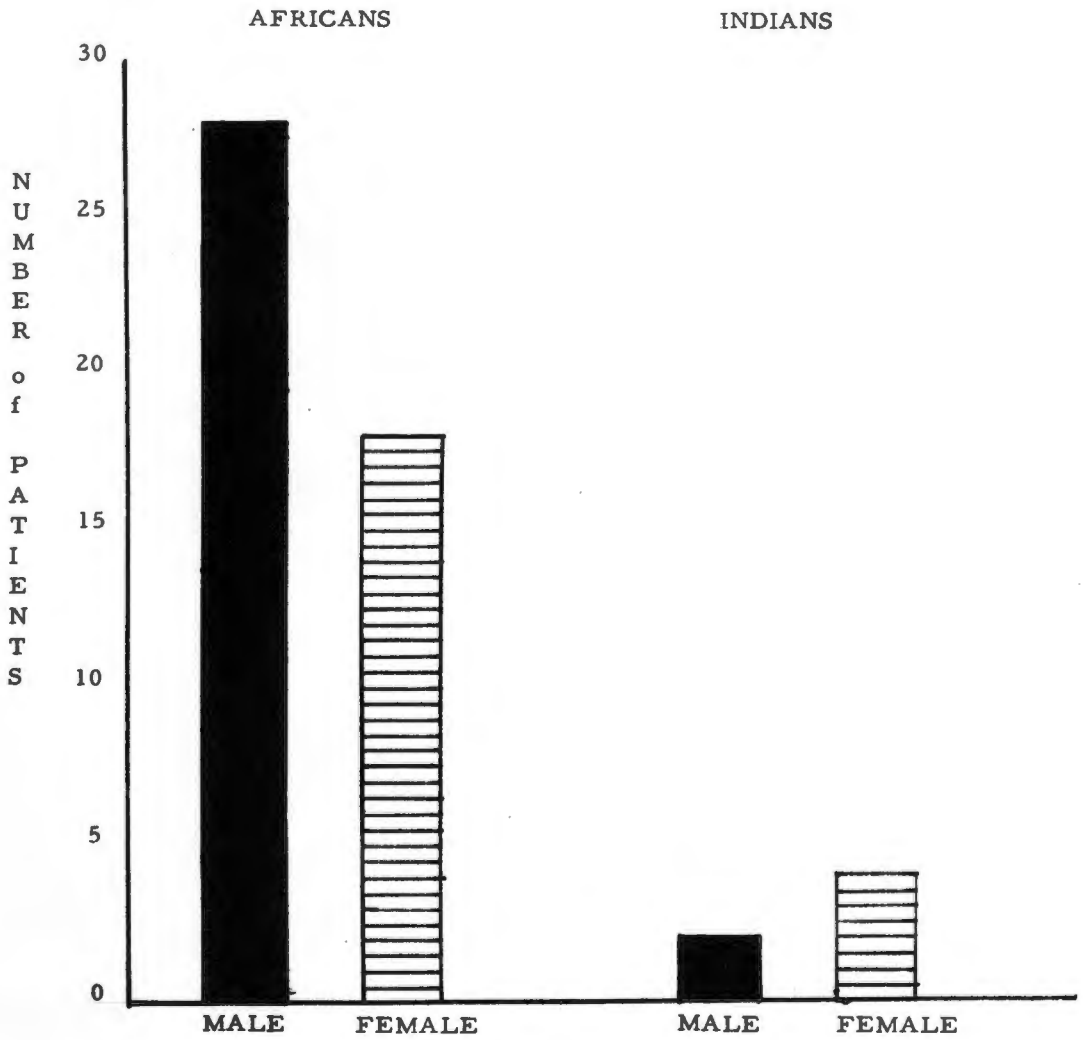


FIG. 2. RACE AND SEX OF PATIENTS



METHOD OF INVESTIGATION

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All patients were admitted as emergency admissions from the out-patient department. Initially the hypoglycaemia was discovered by biochemical means when a low blood sugar was found. As the hospital doctors became aware of the frequency of the hypoglycaemia and its association with alcohol, the diagnosis was often suspected in the out-patient department, or on admission to the ward. Usually I was informed immediately and was thus able to see the patients soon after hospitalisation. In this way a more detailed study was possible. In addition I became a voluntary resident at the hospital for three months in 1960 and was able to see the patients on admission, at night.

Following admission to the ward, whenever possible, initial histories were obtained from accompanying relatives. After clinical examination, blood was withdrawn for haematological and biochemical investigation. Where the diagnosis of hypoglycaemia was suspected, 50% intravenous dextrose solution was administered immediately after the blood had been withdrawn, and a more detailed history was taken once the patients were fully orientated. The patients were kept in hospital and repeat clinical examinations and laboratory investigations were done. All specimens were collected by myself and I visited the patients daily. Liver biopsy was performed on 37 patients.

There was no special metabolic unit available and

investigation was undertaken in the general medical wards of King Edward VIII hospital where all patients received a full diversified hospital diet during their hospitalisation. Seventeen of the patients were investigated in the professorial medical unit at the hospital, where at the time, fewer patients were admitted and control was easier. Each of the patients was thoroughly re-examined by the ward medical staff.

The histories were taken carefully and certain set questions were asked from every patient. In addition various members of the nursing staff, and for a time, Sister C. Majola, of the department of social medicine, checked histories. This was necessary because of language difficulties and also to find out whether the patients were giving accurate histories.

Laboratory investigations were done in the routine laboratories at King Edward VIII hospital, or at the biochemistry laboratory at Natal University Medical School. Because of this, investigations were kept as simple as possible and the methods performed were the standard methods already used. Reliable technologists were used to perform the tests and the results were controlled by myself, Dr. S. M. Joubert and his senior laboratory staff.

The technical methods are described in the appendix.

PART I

CLINICAL AND PATHOLOGICAL INVESTIGATION

CLINICAL FINDINGS

CLINICAL FINDINGS

Details of the findings of each case are supplied in the appendix. A summary of the clinical findings, related to alcoholic hypoglycaemia, will now follow.

History

No previous attacks of hypoglycaemia

In only two patients was there a definite history of more than one hypoglycaemic episode. Both these patients, chronic alcoholics, (Cases 10/60 and 2/62) were admitted to King Edward VIII Hospital on two occasions in hypoglycaemic coma, following an alcoholic debauch. One patient (Case 5/63) thought she had a similar episode after alcohol, at home, the year before, but she had recovered without treatment. In the remainder there was nothing to suggest a previous attack of hypoglycaemia, and it seemed, therefore, that the hypoglycaemic coma was an isolated occurrence.

Association of the hypoglycaemic coma with the intake of alcohol

Every patient had taken alcohol prior to their hypoglycaemic episode. In 44 patients, a history of an alcoholic debauch on the day or days preceding admission was obtained. In 3 children (Cases 21/60, 5/61 and 8/61) and in 2 adults (Cases 8/62 and 4/63) there was a history of intake of alcohol on the day of hospitalisation. Three patients (Cases 12/60, 2/62 and 4/62), though possessing a stale alcoholic odour on their breath, were unable to remember whether they had been drinking prior to admission or not. Most patients

imbibed alcohol at the weekends - Friday night, Saturday and Sunday - and were admitted during the weekend or on Monday. Table I shows the days on which the patients were admitted and there is little doubt that the majority were admitted following drinking at the weekends.

Fourteen of the patients awoke on the morning after their alcoholic bout and subsequently lost consciousness. From these patients it was possible to discover the interval between the end of the alcoholic bout and the onset of the hypoglycaemic coma, and it varied from 5 - 15 hours. The lucid interval between awakening and the onset of coma varied from minutes to 7 hours. These patients remained in hypoglycaemic coma from 2 to 11 hours before treatment was administered. (Table 2). The remaining patients were admitted in coma 5 to 24 hours after retiring to bed intoxicated.

Quantity of alcohol imbibed

It was not always possible to make an accurate estimate of the quantity of alcohol imbibed by the patients. Where the patient had been drinking in a group, he usually had been imbibing from the same container as the rest of them. The patients, however, were usually severely intoxicated after drinking and there is little doubt that large quantities of alcohol were imbibed by the adult patients on the day or days before hospitalisation.

TABLE I. DAY OF ADMISSION

AFRICAN PATIENTS

Day:	Sat.	Sun.	Mon.	Tues.	Wed.	Thurs.	Fri.
Case Nos :	22/60, 23/60, 4/61, 6/61, 10/61	2/60, 7/60, 9/60, 12/60, 17/60, 1/61, 9/61, 1/62, 7/62, 10/62, 12/62, 13/62.	1/60, 4/60, 5/60, 15/60, 18/60, 20/60, 3/61, 5/61*, 8/61*, 11/61, 4/62, 15/62, 2/63.	8/60, 13/60, 14/60, 19/60, 14/62, 1/63** 3/63	3/60, 11/60, 8/62, 4/63, 5/63.	3/62, 9/62,	21/60*, 7/6
Total:	5	12	13	7	5	2	2

* Children

** Admitted during New Year holidays

INDIAN PATIENTS

Day	Sat.	Sun.	Mon.	Tues.	Wed.	Thurs.	Fri.
Case Nos:	6/62	2/62*. ?10/60*	10/60*, 16/60, 2/61, 2/62*.		5/62		
Total:	1	2	4		1		

* Admitted on two occasions.

* TABLE 2

Case No.	Period between end of Alcoholic bout and onset of hypoglycaemia (hours)	Lucid Interval	Duration of hypoglycaemia (hours)
2/60	12 - 13	Minutes	11
3/60	7	Minutes	4
7/60	12	Minutes	10
17/60	12	Minutes	2
18/60	12 - 13	±2 hours	8
22/60	12	15 minutes	$2\frac{1}{2}$
9/61	12	Minutes	3
10/61	15	$\frac{1}{2}$ hour	$2\frac{1}{2}$
3/62	12	± $\frac{1}{2}$ hour	7 - 8
5/62	12	Minutes	8
7/62	15	7 hours	$2\frac{1}{2}$
15/62	15	1 hour	3
4/63	5 - 6	Minutes	8
5/63	12	Minutes	4

Type of alcohol imbibed

Table 3 shows the type of alcohol imbibed by the patients and the list includes Zulu beer, shimeyane, gavine, cane spirit, brandy, gin and wine. Of the last group, 12 had drunk a mixture of African brews, and 4 (Cases 9/60, 18/60, 1/63 and 2/63) African brews together with commercially produced ethyl alcohol (gin, brandy, wine and cane spirit). It can be seen that 7 patients had only taken commercially produced ethyl alcohol prior to their hypoglycaemic coma. The type of alcohol taken by 3 patients (Cases 12/60, 2/62 and 4/62) was not known.

Table 4 gives the ingredients of the African liquors imbibed. The ingredients mentioned were obtained by questioning numbers of Africans, who produced the liquor. The percentage alcohol content figures were obtained from Dr. I. Robertson (1960).

No toxic additives

Every patient was asked whether he had added any substances to his liquor. After careful interrogation it was found that none of them had done so. In addition 17 of the patients had imbibed their alcohol with others. None of the latter were admitted to King Edward VIII Hospital in hypoglycaemic coma.

Fasting prior to the intake of alcohol

In those patients where a positive history could be obtained in regard to their food intake during the period prior to their

TABLE 3.

Type of Alcohol imbibed *

	Zulu beer	Shimeyane	Gavine	Cane spirit	Gin	Brandy	Mixture of type
Number of Cases	10	6	10	5	1	1	16
Case Numbers	4/60, 15/60 17/60, ?21/60, 4/61, 6/61, 7/61, 9/61, 11/61, 7/62,	7/60, 8/60, 14/60, 3/62, 10/62, 14/62,	2/60, 11/60, 13/60, 1/61, 5/61, ?8/61, 10/61, 8/62, 9/62, 4/63.	10/60, 20/60, 2/61, 5/62, 6/62.	23/60,	16/60,	1/60, 3/60, 5/60 9/60, 18/60, 19/60, 22/60, 3/61, 1/62, 12/62, 13/62, 15/62, 1/63, 2/63, 3/63, 5/63

* Unknown(cases 12/60, 2/62, 4/62).

TABLE 4. ZULU BREWS AND DISTILLATE*

	Zulu beer	Shimeyane	Gavine
Ingredients	Mealie meal Corn malt Water	Brown bread Brown sugar Corn malt Yeast Water	Distillate of Shimeyane
Alcohol content (%)	± 3	3 - 6	30 - 50
Time taken in preparation:	4 - 5 days	24 hours	

*Table from Lancet 2:893, 1961.
(Neame, P. B. & Joubert, S. M.)

drinking alcohol, the majority (30) had either not eaten or only taken a little food on the day on which they had imbibed. Nine had eaten a meal before or during their ingestion of alcohol. A few patients were unable to remember if they had eaten or not. Table 5 shows the food intake prior to the ingestion of alcohol.

Carbohydrate ingested in the alcohol

Though most of the patients had not eaten prior to drinking, many had taken substantial quantities of carbohydrate in their alcoholic beverages (Zulu beer and shimeyane). Table 6 shows the number of patients who had taken no food prior to drinking but had ingested large amounts of carbohydrate in their alcohol.

Lack of food intake following the ingestion of alcohol

All patients were in alcoholic coma for a certain period of time and during it there was no intake of food. In those patients who had a lucid interval, between awakening from the alcoholic coma and developing hypoglycaemia, the period without food was estimated between 5 and 15 hours. In the majority it was 12 hours or more. (Table 2).

Exclusion of hypoglycaemic agents

None of the patients had been given insulin, tablets or herbal medicines before their admission.

Dietary histories

The dietary history of the African patients consisted of

TABLE 5. Food intake prior to ingestion of alcohol.

	No or minimal food on the day of alcohol ingestion	A meal before or during alcohol ingestion	No history available
Number of cases	30	9	13
Case Nos.	2/60, 3/60, 4/60, 8/60, 13/60, 15/60, 16/60, 19/60, 20/60, 21/60, 22/60, 23/60, 2/61, 4/61, 5/61, 6/61, 7/61, 8/61, 9/61, 7/62, 8/62, 9/62, 10/62, 12/62, 13/62, 14/62, 15/62, 2/63, 3/63, 4/63	1/60, 9/60, 18/60, 3/61, 10/61, 1/62, 3/62, 6/62, 1/63.	5/60, 7/60, 10/60, 11/60, 12/60, 14/60, 17/60, 1/61, 11/61, 2/62, 4/62, 5/62, 5/63.

TABLE 6.

	Substantial quantities of carbohydrate in their alcohol (Zulu beer, shimeyane).	Ingestion of gavine or commercial ethyl alcohol
Number of cases	18	12
Case Numbers	3/60, 4/60, 8/60, 15/60, 19/60, 21/60, 22/60, 4/61, 6/61, 7/61, 9/61, 7/62, 10/62, 12/62, 13/62, 14/62, 15/62, 3/63.	2/60, 13/60, 16/60, 20/60, 23/60, 2/61, 5/61, 8/61, 8/62, 9/62, 2/63, 4/63.

mealie meal porridge, 'putu' (thick porridge), samp, bread and tea. Vegetables were eaten occasionally and meat, if taken at all, was about twice a week. Four of the patients, including two children (Cases 21/60, and 8/61) received good diets. One of the adults (Case 3/62) lived on his own plot, where he grew vegetables, and the other (Case 9/61) worked at King Edward VIII hospital where he was fed adequately at the compound. The Indian patients received poor diets. This was the result of chronic alcoholism in 4 and poverty in 2 patients (Cases 16/60 and 2/61).

Alcohol habits

The alcohol habits of 22 of the patients were published in 1961, (Neame and Joubert, 1961), but these results have been reassessed. The assessment of the alcohol habits of the patients was largely influenced by the work of Keller (1960). However there does not appear to be any adequate definition of alcoholism; certainly no indication of the exact limits to which the term refers (Jellinek, 1946; Seeley, 1959; Marconi, 1959; Keller, 1960 and Lancet 1961). I divided the patients into three groups : chronic alcoholics, weekend drinkers, and non-alcoholics. The last group, which included three children, consisted of patients who normally did not imbibe alcohol or had an occasional drink. The first group were heavy drinkers, who suffered from "loss of control" over alcohol, who usually drank daily, and who suffered ill effects in health and in personal relationships as the result of excess alcohol. Most of them

however, did not show any obvious desire for alcohol during their hospitalisation. Heavy weekend drinking appeared to be part of a social-behaviour pattern of the African patient in Durban, during prohibition, and it seemed to be a common experience in the lives of many Africans who could not be classified as chronic alcoholics. I therefore classified patients who only drank heavily in the weekends, into a separate group. Table 7 shows the alcohol habits of the patients.

TABLE 7.

ALCOHOLIC HABITS OF THE PATIENTS *

	Chronic Alcoholics	Weekend Drinkers	Non-Alcoholics
	25	18	6
Case Numbers	3/60 4/60	1/60 2/60	15/60 20/60
	5/60 8/60	7/60 16/60	21/60** 2/61
	9/60 10/60	18/60 22/60	5/61** 8/61**
	11/60 12/60	1/61 4/61	
	? 14/60 ?17/60	? 9/61 ?10/61	
	19/60 ?23/60	11/61 1/62	
	3/61 6/61	3/62 4/62	
	7/61 2/62	7/62 10/62	
	5/62 6/62	15/62 1/63	
	? 12/62 13/62		
	? 14/62 2/63		
	3/63 4/63		
	? 5/63		

* 3 Patients (Cases 13/60, 8/62 and 9/62) were not assessed.

** Children

Chronic alcoholics "Loss of control" over alcohol. Heavy drinking, often daily, regardless of its effects on the health and personal relations of the patient.

Weekend drinkers Heavy drinkers in the weekends; appeared to be part of the social behaviour pattern of the African drinker in Durban.

Non-alcoholic

Examination

All patients were admitted in coma, semi-coma, or stupor.

Alcohol on breath:

A smell of stale alcohol on the breath, on admission, was noted in 30 of the patients, who are shown in Table 8.

Body temperature:

The temperature was taken on admission in 23 patients. As can be seen from Table 9, many temperatures were in the subnormal range.

Sweating was noted in 3 patients (Cases 10/60, 17/60 and 9/61).

Pulse rate:

Table 10 shows the pulse rate, on admission, in 37 of the patients. In three of the patients (Cases 9/60, 12/60 and 1/61) the pulse was not palpable and the heart rate was less than 30 per minute. In the majority the pulse rate was normal or slightly raised.

Blood pressure:

Table 11 gives the blood pressure on admission in 36 patients. In three patients (Cases 9/60, 12/60 and 1/61) the blood pressure was unrecordable. It can be seen that in the majority of patients the blood pressure was in the normal range. In a few it was temporarily raised or lowered.

TABLE 8. ALCOHOLIC ODOUR

Number of Cases			30			
Case Numbers	1/60	5/60	9/60	11/60	12/60	13/60
	14/60	16/60	17/60	18/60	23/60	2/61
	3/61	4/61	5/61	6/61	7/61	8/61
	9/61	10/61	2/62	3/62	4/62	5/62
	6/62	12/62	13/62	1/63	2/63	5/63

TABLE 9.

Temp. °F.	94.5	95.1-96	96.1-97	97.1-98	98.1-99	99.1-100	100.1
Number of Cases	1	4	7	9	1	1	0
Case Numbers	14/62	8/60	12/60	3/60	2/61	1/63	
		13/60	16/60	11/60			
		1/61	6/61	14/60			
		6/62	9/61	18/60			
			11/61	5/61			
			5/62	10/61			
			15/62	13/62			
				2/63			
				3/63			

TABLE 10.

Pulse Rate	0-50	50-69	70-85	86-100	101-120	121-150
Number of Cases	4	2	10	12	7	2
Case Numbers	9/60	1/60	2/60	3/60	7/60	5/62
	12/60	18/60	4/60	8/60	14/60	3/63
	1/61		5/60	10/60	21/60	
	17/60		13/60	11/60	3/61	
			15/60	19/60	4/61	
			16/60	23/60	8/61	
			22/60	2/61	11/61	
			9/61	10/61		
			13/62	6/62		
			15/62	14/62		
				1/63		
				2/63		

TABLE 11.

Systolic Blood Pressure	0-50	55-75	80-95	100-140	145-160	165-180	185-240
Number of Cases	3	1	1	19	4	5	3
Case Numbers	9/60	23/60	4/60	3/60, 5/60.	14/60	2/60	1/60
	12/60			8/60, 10/60.	16/60	13/60	7/60
	1/61			11/60, 15/60.	6/61	11/61	10/61
				18/60, 19/60.	13/62	5/62	
				20/60, 22/60.		3/63	
				2/61, 3/61.			
				4/61, 9/61.			
				6/62, 14/62.			
				15/62, 1/63.			
				2/63.			

Respiration :

Respiration was normal, stertorous, or slow and shallow. Two patients were breathing at five (Case 9/60) and six (Case 12/60) per minute.

Central nervous system:

Forty-nine of the patients were either in coma or in semi-coma. The remaining three were stuporose (Cases 1/60, 14/60, 18/60). In one there was mental confusion, aggressiveness and incoherent speech (Case 14/60), while in another there was mild stupor, disorientation and slurred speech (Case 1/60). Three patients (Cases 9/60, 12/60 and 1/61) were moribund on admission and had impalpable pulses, unrecordable blood pressure, a heart rate of 30 or less per minute, and slow shallow or stertorous breathing. In many patients bizarre involvement of the central nervous system was found. Eight patients had generalised convulsions (Cases ?7/60, 18/60, 19/60, 21/60, 1/61, 7/61, 15/62, and 2/63), and one (Case 2/60) clonic contraction of the lower limbs. Symptoms found in other cases were upper motor neurone facial palsy (Case 16/60), hemiparesis (Case 12/60), conjugate deviation of the eyes (Cases 12/60 and 16/60), trismus (Case 7/60), spasticity, hypotonia, abnormal deep reflexes (increased or absent), clonus, and extensor plantar reflexes (both bilateral and unilateral).

Signs of liver disease:

There was no evidence of gross liver disease in any patients. Petechial haemorrhages, spider naevi, ascites, splenomegaly,

haematemesis were not found. In 24 patients the liver was palpable and firm, but in none was it grossly enlarged. (Table 12). In only 4 patients was the liver tender. (Cases 13/60, 20/60, 7/62 and 13/62).

TABLE 12. LIVER PALPABLE ON OR DURING ADMISSION

Number of Cases			24*			
Case Numbers	1/60,	2/60,	3/60,	5/60,	7/60,	8/60,
	9/60,	10/60,	13/60,	17/60,	20/60,	23/60,
	3/61,	11/61,	7/62,	10/62,	12/62,	13/62,
	14/62,	15/62,	2/63,	3/63,	4/63,	5/63.

*Tender liver in 4 cases (Cases 13/60, 20/60, 7/62, 13/62).

Endocrine disturbance:

Except in one patient (Case 15/62) who showed marked pigmentation of his skin and buccal mucosa, none of the other patients had clinical evidence of Addison's disease or hypopituitarism. Almost all patients claimed they had been well before their episode of hypoglycaemia. There was no evidence of gonadal hypofunction or of hypothyroidism in any of the patients where specific investigation was undertaken. (See appendix).

Nutrition:

The assessment of nutrition was largely based on the general appearance of the patients on admission, on evidence of vitamin deficiencies (FAO/WHO report, 1951), and on the general condition of the patient on discharge from hospital. Haemoglobin and

serum proteins were done, though an interpretation of the latter in Africans is difficult. Nutrition was finally assessed as "poor, fair or good", and was a clinical assessment. Patients with "poor nutrition" showed obvious evidence of malnutrition and pellagra was found in eight of them. The group with "fair nutrition" were assessed as showing satisfactory nutrition and were comparable with the nutritional state of the average patient admitted to hospital. On the other hand their diets consisted largely of mealie meal porridge, thick porridge (putu), samp, bread and tea with vegetables and meat occasionally. Two patients, both children, with "good nutrition" looked well nourished and their dietary habits were good.

Table 13 shows the nutritional state of the patients.

Diagnoses on Admission

Diagnoses of the out-patient or ward officers included spontaneous hypoglycaemia, alcoholic coma, cerebrovascular accident, internal head injury, hepatic coma, grand mal epilepsy, post-epileptic state and undiagnosed coma. (Table 14).

Treatment

All patients, except one, were treated by intravenous administration of 15-100 ml 50% dextrose solution. Forty-one regained consciousness but three of them (Cases 23/60, 13/62

TABLE 13 NUTRITIONAL STATE OF PATIENTS

	Nutrition		
	POOR	FAIR	GOOD
	25	25	2
Case Nos.	3/60*, 4/60, 5/60 8/60*, 9/60*, 10/60, 11/60, 12/60, 14/60, 17/60*, 19/60*, 20/60, 23/60, 3/61, 6/61*, 7/61, 2/62, 4/62, 5/62, 6/62, 10/62, 13/62,* 2/63, 3/63*, 5/63.	1/60, 2/60, 7/60, ?13/60, 15/60, 16/60, 18/60, 22/60, 1/61, 2/61, 4/61, 5/61, 9/61, 10/61, 11/61, 1/62, 3/62, 7/62, 8/62, 9/62, 12/62, 14/62, 15/62, 1/63, 4/63.	21/60, 8/61.

* Patients with pellagra.

TABLE 14.

DIAGNOSES ON ADMISSION*

	Alcoholic coma	Cerebro-vascular accident	Head injury	Hepatic coma	Epilepsy	Post-epileptic state	Undiagnosed coma	Hypoglycaemia	Post-alcoholic hypoglycaemia
Number:	11	10	2	2	3	3	15	13	36

* Diagnoses of Out-Patient and Ward Officers

and 2/63) were still inebriated. In the remainder, though there was improvement in their level of consciousness, abnormal mental states were present for varying periods. The untreated patient (Case 15/60) died a few hours after admission. Only one patient (Case 2/63) lapsed into hypoglycaemic coma after dextrose therapy. This occurred three hours after administration of 15 ml 50% intravenous dextrose solution.

Two patients (Cases 13/62 and 2/63) were initially given 10 gms sodium pyruvate intravenously but there was no response. Both responded immediately to 15-20 ml 50% intravenous dextrose solution administered thirty minutes later.

Complications

Two children (Cases 21/60 and 8/61) and one adult (second admission) (Case 2/62) died within twenty hours of hospitalisation without regaining consciousness, despite treatment with intravenous dextrose solution. Eight patients (Cases 7/60, 11/60, 12/60, 17/60, 19/60, 1/61, 11/61, 1/62) despite initial improvement in their level of consciousness, remained mentally abnormal for varying periods. One patient (Case 11/60) was unable to speak for about 24 hours; (it was later ascertained that he had a period of motor aphasia for about twelve hours and loss of memory before that). Another patient (Case 19/60) was mentally dull for twenty-four hours and suffered from slurred speech for four days before complete recovery took place.

Case 11/61 was disorientated for three days and had slurred speech for four. Case 12/60 remained mentally abnormal and was able to say only a few words until her death from bronchopneumonia eighteen days later. The others remained confused for 12-24 hours before complete recovery took place. In all it was considered to be the result of prolonged hypoglycaemia. Three patients (Cases 8/60, 10/60 and 2/62) developed delirium tremens two days after admission, and a further two (cases 13/62 and 2/63) were considered to be suffering from alcoholic psychoses. Two patients (Cases 7/60 and 1/62) were thought to be suffering from aspiration pneumonia, and one patient (Case 12/62) developed lobar pneumonia and died four days after admission. Six patients (Cases 5/60, 14/60, 22/60, 3/61, 5/62 and 10/62) had pulmonary tuberculosis, the fifth had an associated pneumothorax, and the last developed miliary tuberculosis with meningitis. A further three patients (Cases 20/60, 15/62 and 5/63) had apical scarring on chest X-ray. One patient (Case 1/60) developed acute pancreatitis and it was considered to be the result of his alcoholic debauch.

Mortality

Six patients died. These included the untreated patient (Case 15/60), the three patients (Cases 21/60, 8/61 and 2/62) who died within twenty hours of admission, despite intravenous dextrose administration, and two (Cases 12/60 and 12/62), who died from pneumonia.

COMMENT ON CLINICAL FINDINGS

The differential diagnosis of this form of hypoglycaemic coma and the relationship between alcohol and hypoglycaemia will be described in later sections.

The clinical features related to hypoglycaemia are well known (Harris 1924, Gittler, 1962). Bizarre neurological signs, abnormal mental states (Tedstrom, 1934; Moersch and Kernohan 1938; Himwich, 1942), alterations in pulse rate, blood pressure, and respiration, seen amongst the patients, have all been described and need no elaboration (Wauchope 1933; Loeb 1946; Conn and Seltzer 1955; Kornfield 1955). Subnormal temperature is also well known (Wauchope 1933; Brown and Harvey 1941). The clinical findings described in hypothermia can be similar to those found in hypoglycaemia (Duguid et al., 1961; Rosin and Exton-Smith, 1964; McNicol and Smith, 1964), and it is suggested that in all patients with hypothermia a blood sugar estimation should be performed, amongst other investigations. (Duckworth and Cooper, 1964). However patients with signs of hypothermia have temperatures below $90^{\circ}F$, whereas patients in hypoglycaemic coma tend to have temperatures above this level. (One cannot be certain that the mercury column of the thermometer was always shaken to hypothermic values). It must also be remembered that hypothermia can be a clue in the diagnosis of asymptomatic hypoglycaemia (Kedes and Field, 1964).

Sweating, a common finding in hypoglycaemic states, was noted in only three patients in this series. However, when hypoglycaemia is protracted, as in these cases, signs of adrenalin response are usually not present and neurological manifestations dominate the clinical picture (Conn and Seltzer, 1955; Gittler, 1962).

In regard to therapy, the response to the administration of sugar was usually dramatic with the neurological disturbances swiftly disappearing. However, occasionally, following protracted hypoglycaemia - and particularly in the children (Case 21/60 and 8/61) - persistence of neurological disturbance, or even death, occurred. (Fazekas et al., 1951; Conn and Seltzer 1955).

Difficulties were encountered in the assessment of the alcoholic habits of the patients. As already stated, there does not appear to be any adequate definition of chronic alcoholism, and there is certainly no indication of the exact limits to which the term refers (Marconi, 1959). "Loss of control", manifested by the inability of the alcoholic to control either the start of drinking or its termination, has been used as the important criterion. However it is not always easy to be sure if loss of control over alcohol exists. This was particularly the case in some of the African patients reported here. Those defined as "chronic alcoholics" had undoubtedly lost control over alcohol. Those defined as "weekend drinkers" did not appear to have lost control - they did not drink during the week. Other investigators would possibly have reached

different conclusions in the assessment of some of them. However, as will be stressed in the section on 'pathogenesis', this study has shown that alcoholic hypoglycaemia can occur in both chronic alcoholics and non-alcoholics (children).

There were also difficulties in assessing the nutritional state of some of the patients. Despite the criteria, already mentioned, (vitamin deficiency, general condition on admission and discharge from hospital) one is naturally influenced by one's medical background, and by the frequency with which certain mild deficiencies are found in the group as a whole. (FAO/WHO report, 1951). The final assessment of nutrition might be less influenced by certain factors which would be regarded as important if assessed by other workers (U.S. Army, Manual for nutrition surveys, 1957). However, regardless of these difficulties, what is important is the fact that alcoholic hypoglycaemia was found in patients with both 'poor' and 'good' nutrition. It apparently occurred more often in those on imbalanced diets or with poor nutrition, but this association may well be fortuitous. The problem will be discussed in a later section.

SUMMARY OF CLINICAL FINDINGS

1. The patients gave no history of previous hypoglycaemic episodes.

2. Every patient had taken alcohol prior to the onset of hypoglycaemia. In 5 patients the alcohol was taken on the day of admission, and in 44 patients on the preceding day or days. The adult patients had taken large amounts of alcohol.

3. The onset of hypoglycaemia occurred between 5 and 15 hours after the end of the alcoholic bout, in the patients who had a lucid interval.

4. The period of hypoglycaemic coma ranged between 2 and 11 hours.

5. 7 patients had been drinking commercially produced ethyl alcohol, the remainder, African brews and distillate or a mixture of different liquors.

6. There was no evidence that toxic substances were added to the alcohol.

7. None of the patients had taken hypoglycaemic agents before their alcoholic bout.

8. 30 patients had taken no, or minimal, food before

drinking their alcohol. 9 had eaten a meal before or during the intake of alcohol. A few patients were unable to remember whether they had eaten or not.

9. Despite the fact that 30 patients had taken little or no food before the ingestion of alcohol, 18 of them had substantial quantities of carbohydrate in their alcohol.

10. There was lack of food intake following the ingestion of alcohol and it was estimated between 5 and 15 hours, usually 12 hours or more.

11. The dietary histories were poor and the diet taken consisted mainly of maize products.

12. 25 patients were considered to be chronic alcoholics, 18 weekend drinkers and 6 non-alcoholics. 3 patients were not assessed.

13. On examination, on admission, all patients were in coma, semi-coma or stupor. An odour of stale alcohol was noted on 30 patients. A subnormal temperature was a common finding. Alterations in pulse rate, blood pressure and respiration, and abnormal neurological signs, were found.

14. Gross liver disease was absent.

15. One patient showed evidence of Addison's disease. In the remainder there was no obvious clinical endocrine disturbance.

16. Nutrition was assessed as 'poor' in 25 patients, as 'fair' in 25 patients, and as 'good' in 2 patients.

17. Diagnoses on admission, treatment, complications and mortality were listed.

18. The clinical findings are briefly discussed.

BIOCHEMICAL FINDINGS

BIOCHEMICAL INVESTIGATIONS

Certain investigations were undertaken. These included blood-glucose ("true" blood-sugar), blood alcohol, total serum bilirubin, alkaline phosphatase activity, serum glutamic-oxaloacetic-acid-transaminase (S.G.O.T.), prothrombin index, routine urine examination, urinary urobilin and bilirubin, urinary steroid excretion, serum amylase, serum electrolytes, blood urea, serum proteins, and four-hour glucose tolerance tests. Details of the methods used are supplied in the appendix.

Blood sugar

Table 15 lists the individual blood sugar concentration of the patients, and Fig. 3 gives the frequency distribution of these results. It can be seen that the levels varied between 9 and 47 mg% and that the diagnosis of hypoglycaemia was not in doubt. There was no correlation between the blood sugar level and the severity of hypoglycaemic symptoms. (Wauchope, 1933). Case 1/61 had a blood sugar of 47 mg%, on admission, and yet he was moribund with an impalpable pulse, an unrecordable blood pressure, a heart rate of under 30 per minute, and stertorous respiration. Though confused on recovery, he responded immediately to 50 ml 50% intravenous dextrose solution.

Blood Alcohol

The blood alcohol (volatile reducing substances) done on

TABLE 15.

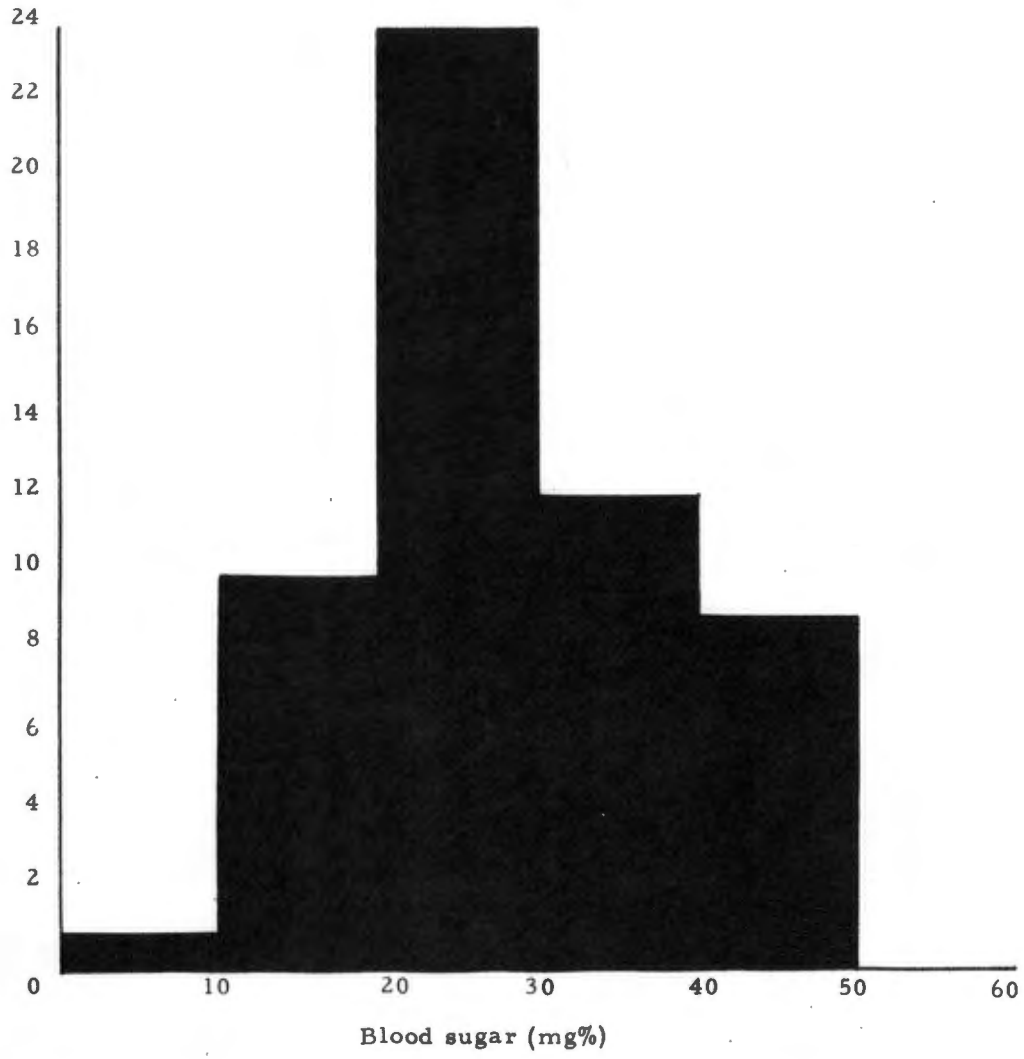
BLOOD SUGARS (mg per 100 ml) ON ADMISSION

Case No.	Blood Sugar	Case No.	Blood Sugar	Case No.	Blood Sugar	Case No.	Blood Sugar
1/60	28	15/60	36	5/61	19	7/62	30
2/60	35	16/60	26	6/61	25	8/62	21
3/60	25	17/60	33	7/61	25	9/62	25
4/60	28	18/60	43	8/61	16	10/62	20
5/60	44	19/60	23	9/61	43	12/62	38
7/60	25	20/60	23	10/61	18	13/62	47
8/60	13	21/60	24	11/61	17	14/62	15
9/60	9	22/60	20	1/62	29	15/62	30
10/60	(a) 27 (b) 20	23/60	47	2/62	(a) 46 (b) 31	1/63	22
11/60	20	1/61	47	3/62	35	2/63	15
12/60	25	2/61	27	4/62	19	3/63	38
13/60	20	3/61	28	5/62	14	4/63	34
14/60	39	4/61	34	6/62	21	5/63	18

(a) = 1st admission

(b) = 2nd admission

FIG. 3. BLOOD SUGAR (mg%).



13 patients, are shown in Table 16. It is clear that they were either within normal limits (normal 0-20 mg%) or, if raised, not anywhere near the levels found in alcoholic coma (+ 300 mg%). In other words it was usually a post-alcoholic hypoglycaemia. In addition the duration of the hypoglycaemic coma evidently did not depend on the blood alcohol level (Bottura et al., 1949).

TABLE 16.

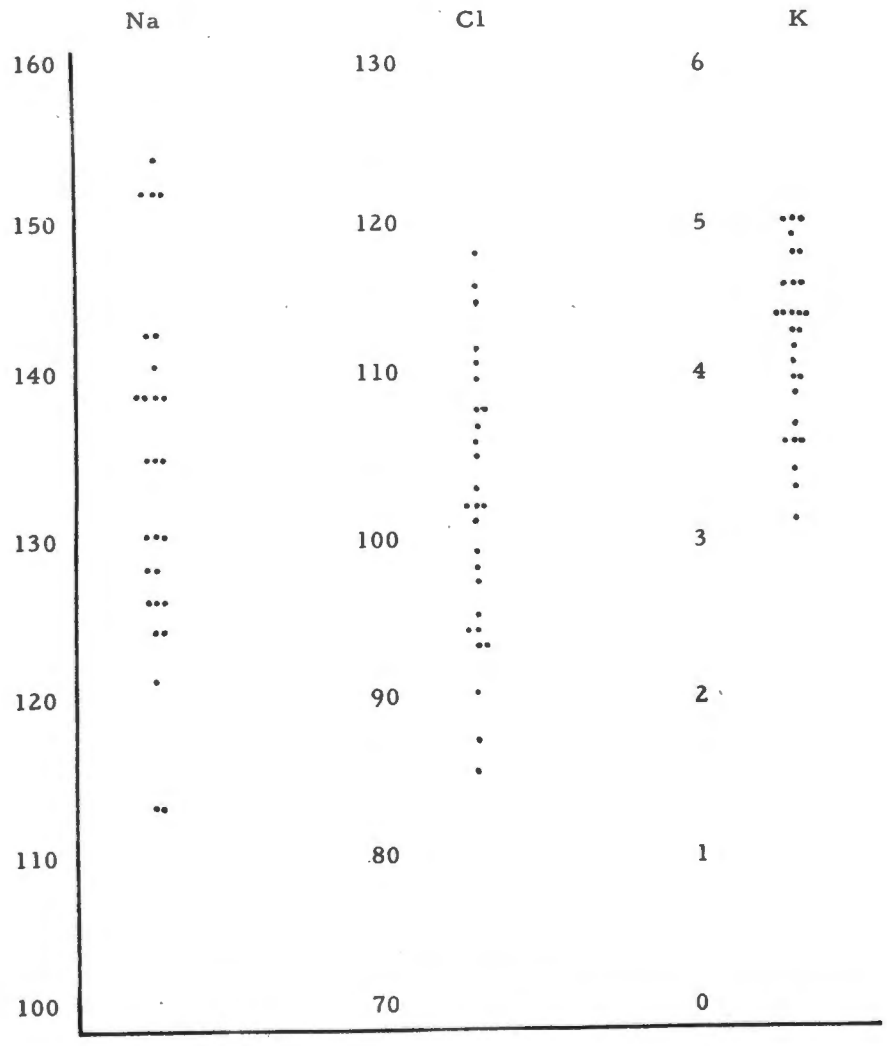
Case No.	Blood Alcohol (V.R.S.) mg%	Case No.	Blood Alcohol (V.R.S.) mg%
11/60	6	19/60	28
12/60	17	20/60	20
13/60	76	4/61	75
14/60	11	5/61	14
16/60	11	11/61	3
17/60	12	2/63	70
		3/63	0

Serum electrolytes

Serum electrolytes were done on 28 patients on admission. Fig. 4 shows these results. The results did not aid in the diagnosis of the cause of the hypoglycaemia. The serum sodium and chloride showed considerable variation. It is known that ethyl alcohol can cause acidosis (Westerfield, 1955). In addition, many of the patients might have vomited, and they had been in alcoholic and hypoglycaemic coma for a prolonged period. There was a low potassium level in a number of patients. It is known that alcohol

FIG. 4. SERUM ELECTROLYTES ON ADMISSION

Meq/l.



can lead to a low potassium level via stimulation of the adrenals (Klingman et al., 1959). Other factors were probably involved in my cases.

Blood Urea

A blood urea was performed on 44 patients and almost all were in the normal range. Table 17 shows the individual results and Fig. 5 the frequency distribution of the results.

Liver function tests

Because tests related to serum proteins are difficult to interpret in African patients (Joubert et al., 1959), tests were confined to estimation of the serum glutamic oxaloacetic acid transaminase activity (S. G. O. T.), serum bilirubin, alkaline phosphatase, prothrombin index and urinary urobilin and bilirubin. Table 18 shows the liver function tests on admission. From these results there is evidence of liver dysfunction.

As results obtained, on admission, in a group of patients reflect a scatter pattern of the disease process at various stages of development, daily examinations were carried out in order to follow the progress of the disease. Fig. 6 shows the S. G. O. T. activities during the first fourteen days of admission. It can be seen that the transaminase level was raised (normal 7-40 units), in most, during the first week of hospitalisation. The maximum level varied from 40-550 units per ml., and was usually obtained during the first four days of admission. In 19 patients the maximum transaminase activity was present on the day of admission. (Table 19). It returned to normal within two to sixteen days.

TABLE 17 BLOOD UREA (mg%)

Case No.	Blood Urea	Case No.	Blood Urea	Case No.	Blood Urea
1/60	43	18/60	35	1/62	39
2/60	50	19/60	33	2/62	20
3/60	33	20/60	24	4/62	38
4/60	23	22/60	20	5/62	31
5/60	22	23/60	29	6/62	40
7/60	37	1/61	20	7/62	34
8/60	31	2/61	24	8/62	37
9/60	31	3/61	47	10/62	31
10/60	37	4/61	12	13/62	27
11/60	40	5/61	41	14/62	40
12/60	31	6/61	18	15/62	24
13/60	35	7/61	25	2/63	20
14/60	36	9/61	17	3/63	48
16/60	40	11/61	30	4/63	37
17/60	33	10/61	32		

FIG. 5. BLOOD UREA (mg%)

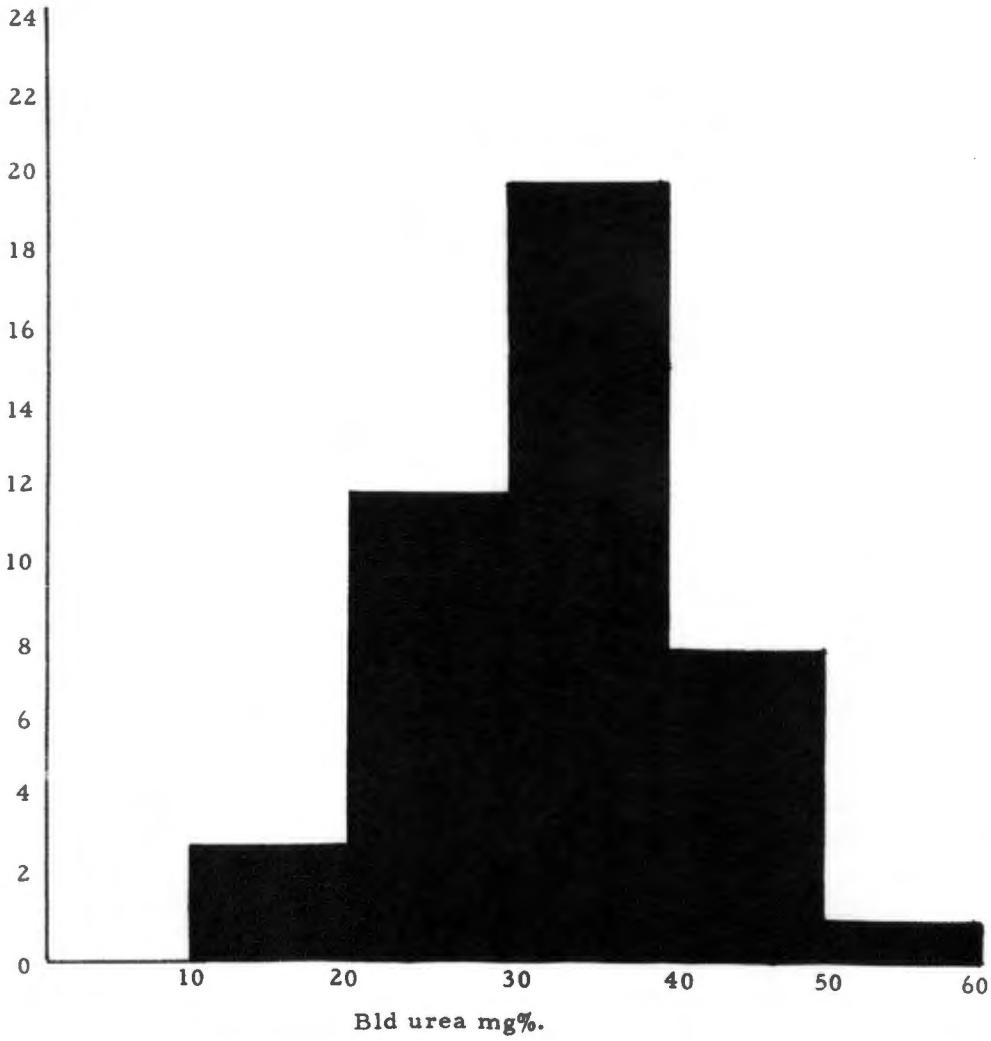


TABLE 18

LIVER FUNCTION TESTS ON ADMISSION*

Case No.	T	B	A.P.	P.I.	U	Case No.	T	B	A.P.	P.I.	U
4/60	98	1.5	22	74	+	10/61	58	0.6	5	70	Nil
9/60	148	0.8	4	57	Nil	11/62	150	0.5	7	100	
10/60		4.3	12	78	+	1/62	86	0.6	9	73	Nil
11/60		0.5	11	72	Nil	3/62	40	1.0	6	80	+
12/60	56	1.5	8	88	Nil	4/62	180	0.9	10	100	Nil
14/60	200	0.7	15	82	Nil	5/62	72	1.0	11	97	Nil
16/60	38	0.8		100	Nil	6/62	30	1.1	12	100	Trace
17/60	150	0.8			Nil	12/62	110	2.5	13	100	
19/60	550	0.4	15	35	Nil	13/62	120	0.8	6	52	Trace
20/60	28	0.8	12	92	++	14/62	20	0.8	9		
22/60	186	1.2	7	78	Nil	15/62	90	0.7		100	
23/60	336	0.4	7	91	Nil	1/63	40	0.2	6	100	
2/61	110	0.9	5	78	Nil	2/63	160	1.3	20	78	Nil
4/61	164	0.3	9	100	Nil	3/63	70	0.4	6	95	Trace
5/61	92	0.8	30		Nil	5/63	110	0.9	5		

*Urinary Bilirubin was negative in all cases except in case 10/60.

T = S.G.O.T. in Karmen units (Normal 7-40 units).

B = Serum bilirubin (mg/100 ml) (Normal 0.2-0.8 mg%).

A.P = Alkaline phosphatase (King Armstrong units) (Normal 3-12 K.A. unit; Children 10-20 K.A. unit).

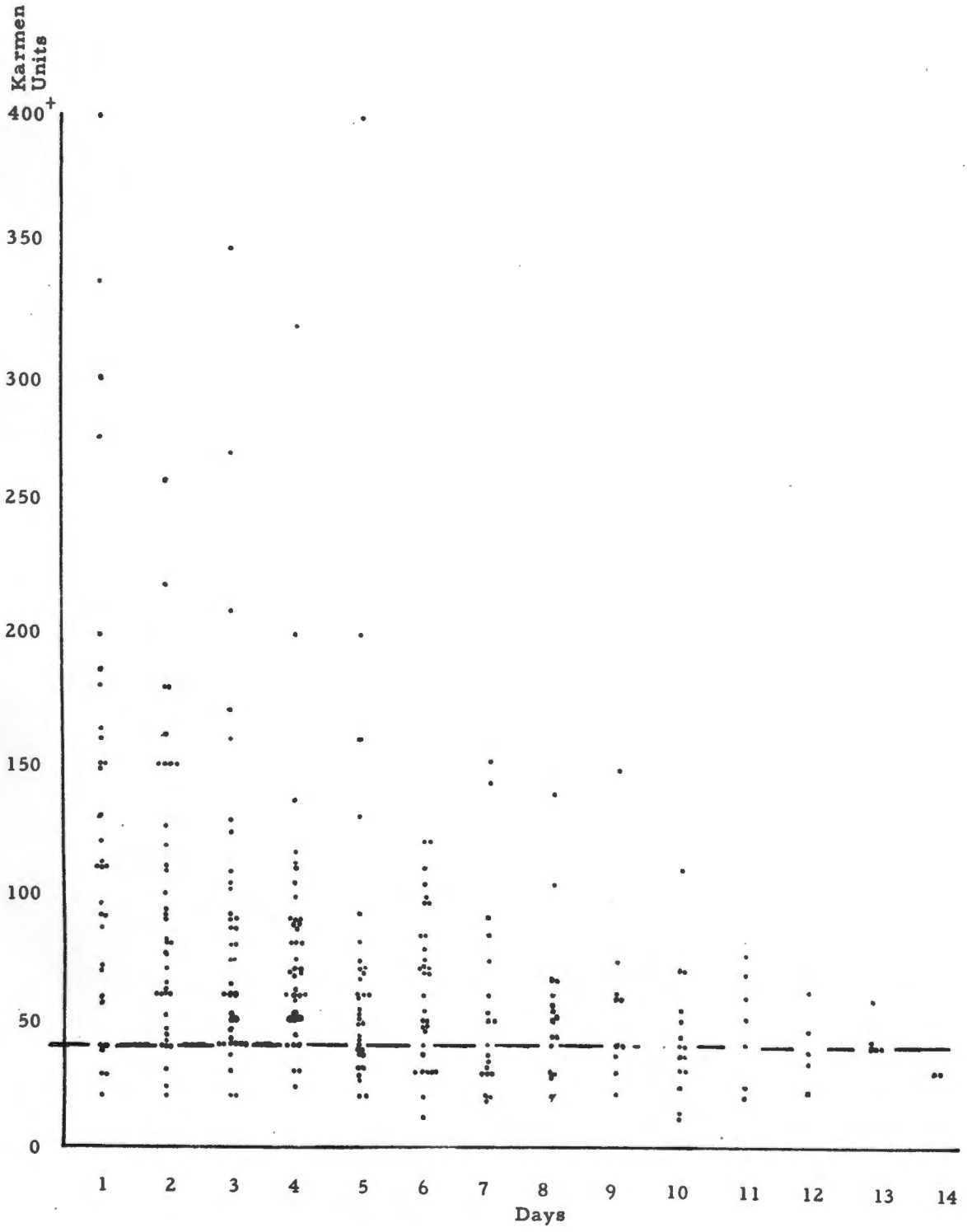
U = Urinary urobilin.

P.I = prothrombin index.

TABLE 19. DAY ON WHICH MAXIMUM TRANSAMINASE ACTIVITY (S.G.O.T.) WAS OBTAINED

Days	1	2	3	4	5	6	7	8	9	10
Number of Cases	19	7	4	10	4	1	1	0	0	0

FIG. 6. DAILY S. G. O. T. ACTIVITIES



The serum bilirubin was raised above normal (0.2-0.8 mg%) in thirty out of forty-five patients where frequent tests were performed. The level varied from 0.9 - 2.5 mg%, except in Case 10/60, where the level was 4.3 mg%. The maximum total bilirubin obtained from the patients is shown in Fig. 7 and Table 20.

The alkaline phosphatase activity was between 5 and 14 King-Armstrong units in 38 patients. In a further 9 patients it ranged between 15 and 30 K.A. units.

The urinary bilirubin was negative in all patients, except Case 10/60, where the test was done. The urinary urobilin was increased in 42 patients.

Table 21 shows S.G.O.T. activities, together with the total serum bilirubin, alkaline phosphatase and urinary urobilin. On the evidence of these results the liver disorder is a mild and transient hepatogenous jaundice. There was evidence of hepatic disturbance in 42 patients, where serial tests were performed.

Elevated transaminase activity can be indicative of hepatocellular injury (Molander et al., 1955; Wroblewski and La Due, 1956; Madsen et al., 1958; Pryse-Davies and Wilkinson, 1958). The results, here, when following the progression of the disease, suggest that there has been an acute onset of mild liver injury followed by recovery during hospitalisation. Bang et al., (1958), Hed (1959) and Madsen et al., (1959) have found elevated transaminase activity in chronic alcoholics, after acute alcoholic intoxication, while Green et al., (1963) have found similar findings

FIG. 7. MAXIMUM TOTAL SERUM BILIRUBIN

mg %

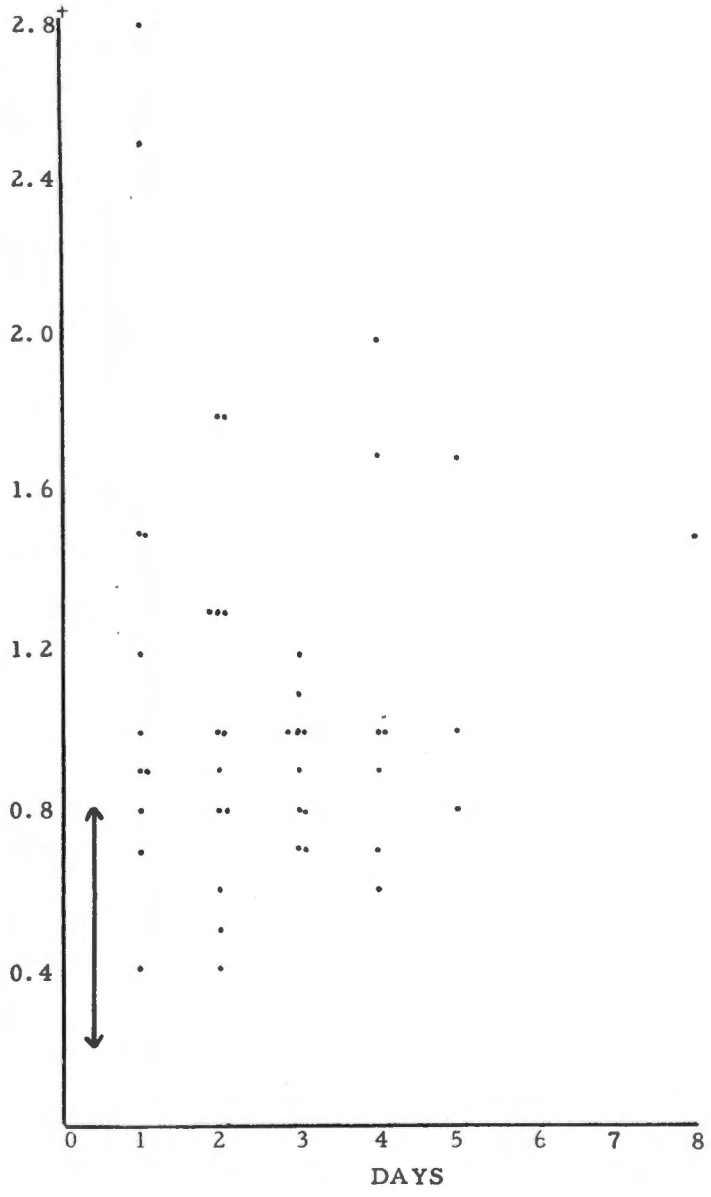


TABLE 20. MAXIMUM TOTAL SERUM BILIRUBIN OBTAINED (mg %).

Case No.	Maximum Bilirubin	Day of Test	Case No.	Maximum Bilirubin	Day of Test	Case No.	Maximum Bilirubin	Day of Test
1/60	1.5	8	1/61	0.7	3	6/62	1.7	4
4/60	1.5	1	2/61	1.0	2	7/62	1.3	2
5/60	1.0	3	3/61	1.0	5	8/62	0.9	3
9/60	1.1	3	4/61	1.0	2	9/62	1.2	3
10/60	4.3	1	5/61	0.8	2	10/62	0.7	3
11/60	1.3	2	6/61	0.8	3	12/62	2.5	1
12/60	1.5	1	7/61	0.9	1	13/62	0.9	4
13/60	2.0	4	9/61	0.8	5	14/62	1.3	2
14/60	1.2	1	10/61	0.5	2	15/62	0.7	1
16/60	0.9	2	11/61	0.8	3	1/63	1.0	4
17/60	0.8	1	1/62	1.0	4	2/63	1.8	2
18/60	0.6	2						
19/60	0.4	1	2/62	1.7	5	3/63	0.8	2
20/60	0.4	2	3/62	1.0	3	4/63	1.8	2
22/60	0.7	4	4/62	1.0	3	5/63	0.9	1
23/60	0.6	4	5/62	1.0	1			

TABLE 21

S.G.O.T., Serum bilirubin, serum alkaline phosphotase, and urinary urobilin

Case No:	11/60				14/60				1/62				2/63				4/63			
Days:	T	B	A.P.	U	T	B	A.P.	U	T	B	A.P.	U	T	B	A.P.	U	T	B	A.P.	U
1	..	0.5	11	Nil.	200	0.7	15	Nil.	86	0.6	9	Nil.	160	1.3	20	Nil.	..	..	..	..
2	60	1.3	..	Nil.	126	0.8	..	Nil.	60	0.5	10	Nil.	110	1.8	18	Trace	150	1.8	7	..
3	104	1.6	..	++	102	1.2	..	+	..	..	..	Nil.	90	1.6	16	++	128	0.9	9	..
4	110	0.5	..	Nil.	40	0.4	2	+++	112	1.0	8	+	200	1.3	17	++	86	0.7	7	trac
5	70	0.5	..	Nil.	32	0.5	..	+++	38	0.9	7	+++	200	1.0	17	+++	..	..	..	trac
6	78	0.3	4	Nil.	20	0.2	..	+++	50	0.9	8	trace	110	1.2	14	+++	120	0.4	9	trac
7	..	..	..	..	18	0.2	..	++	34	1.2	8	trace	..	..	..		144	..	..	Nil.
8	44	..	..	..	..	..	..	++	..	..	..	..	138	0.8	16	++	..	..	..	..

T = S.G.O.T.

B = Serum bilirubin

A.P = Serum alkaline phosphatase

U = Urobilin

Nil = Not increased

in acute alcoholic hepatitis. It seems, therefore, that the liver disorder reported here, was the result of excess alcohol. As there were no accompanying clinical signs, such as anorexia, nausea, vomiting, jaundice or abdominal pain (Beckett et al., 1961, 1962; Green et al., 1963), except in Case 10/60, it was a subclinical alcoholic hepatitis. It is of interest that similar hepatocellular injury was found in a child (Case 5/61) after excess alcohol. Chronic alcoholism could not have been a predisposing factor in its production.

Fasting blood sugars

Fasting blood sugars were performed on 33 patients after 15 hours fasting, and varied between 54 and 100 mg%. The hypoglycaemia was thus disimilar from organic hyperinsulinism and hepatogenous hypoglycaemia where low blood sugars are frequently found, after fasting. It should be emphasised, however, that hypoglycaemia does not always occur after a short period of fasting in the above states. (Conn and Seltzer, 1955).

Glucose tolerance tests

Oral glucose tests were performed on 32 of the patients after approximately a week or more of hospitalisation, during which they received a full mixed diet. The patients were fasted overnight and then given 50 g glucose orally after a fasting sugar (capillary blood) had been taken. Where possible the test was a four hour test and the patient was observed to see whether hypoglycaemic symptoms developed. In no patient was there evidence of hypoglycaemia

during the four hours of observation and the curves did not resemble any of the typical curves ascribed to the more common diseases that produce hypoglycaemia. (Conn and Seltzer, 1955; Gittler, 1962).

In general there were mild abnormalities, some of the curves not returning to fasting levels at two hours. In a number of the initial patients the curves might have been affected by the transient hepatogenous jaundice but most of the patients had their glucose tolerance test performed after a longer period of hospitalisation. Some of the results are shown in Table 22, and the overall picture in Fig. 8. It can be seen that the levels after 15 hours fasting are normal.

TABLE 22. GLUCOSE TOLERANCE TESTS

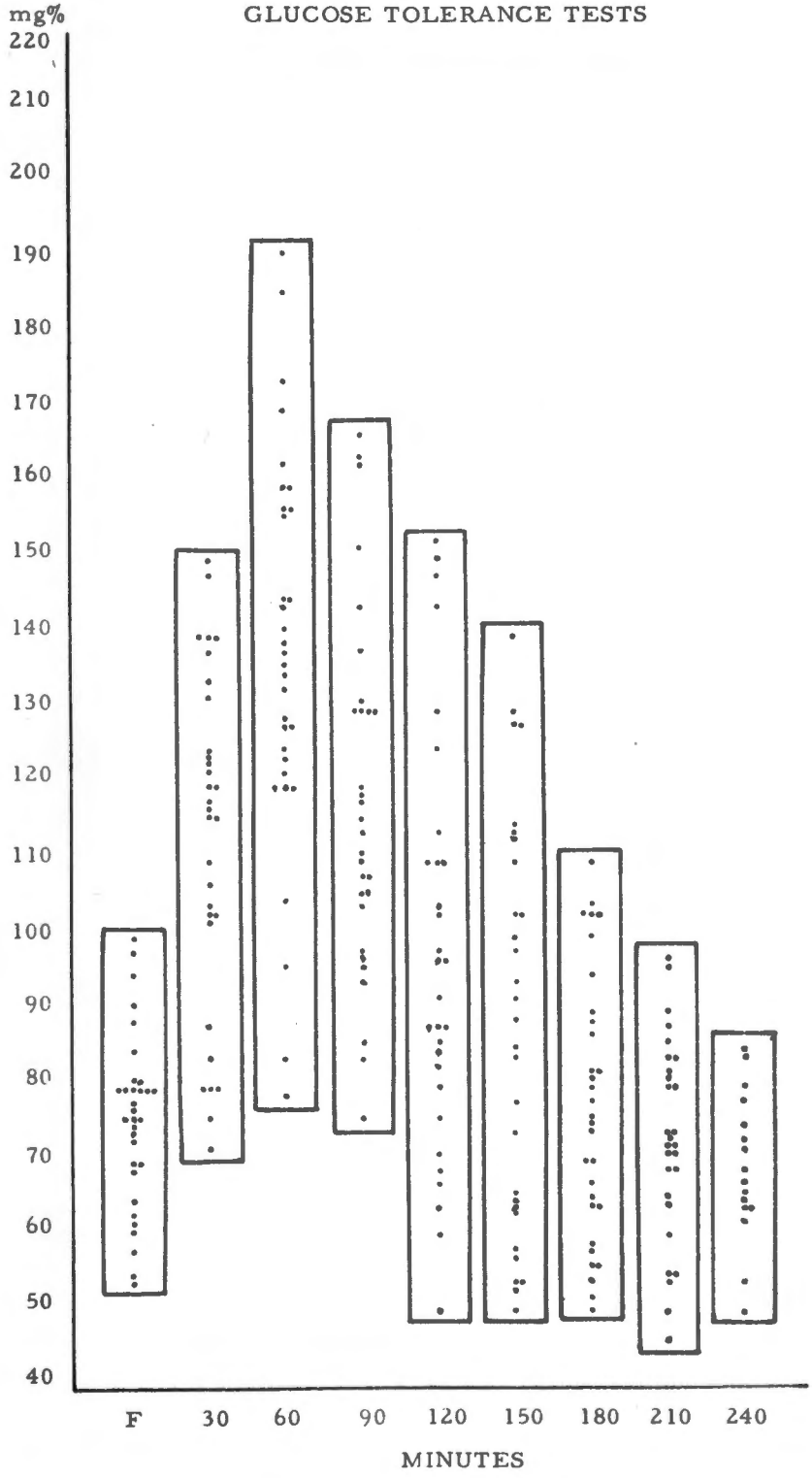
Cases	F	½	1	1½	2	2½	3	3½	4 hours
1/60	81	125	144	138	125	113	81	69	
7/60	77	134	145	170	153	140	103	71	75
13/60	85	123	141	116	97	78	78	82	85
20/60	63	70	90	90	74	55	45	49	63
11/61	75	138	122	97	69	64	67	69	72
6/62	80	124	124	126	110	110	110	84	84
13/62	89	150	139	106	97	103	103	97	64
3/63	76	118	145	130	110	88	75	81	69
4/63	80	140	160	167	150	114	87	73	54

Urinary steroid excretion

In 34 patients 24 hour urine specimens were collected, to be tested for 17-oxosteroid (17-ketosteroid) and total glucocorticoid excretion. Urine collection was commenced

FIG. 8.

GLUCOSE TOLERANCE TESTS



as soon as possible after admission. In practice the first reliable 24 hour specimen was obtained after the first day of admission.

Table 23 shows the 17-oxosteroid and total glucocorticoid excretion in 33 patients during the first ten days following alcoholic hypoglycaemia. It is significant that 47% of the men, and 78% of the women have glucocorticoid excretions of 3 mg or less per 24 hours. In addition 65% of the men have a 17-oxosteroid excretion of less than 5 mg per 24 hours, and 64% of the women of less than 3 mg/24 hours. These findings indicate relative inactivity of the suprarenal cortex in the majority of the patients soon after admission, despite the fact that they varied in age, sex, nutritional status and general health background. Many of the patients had evidence of mild liver disease during this period, and it is known that patients with liver disease excrete less urinary steroids than do normal subjects (Brown et al., 1954). There are also reports that Africans show lower steroid excretion compared with Europeans (Whites) (Politzer and Tucker 1958). However there is no doubt that there was adrenal hypofunction in those patients that excreted minimal amounts of urinary steroids. Despite these low levels, there was no clinical evidence of endocrine disturbance, except in Case 15/62.

Table 24 shows A.C.T.H. response tests on nine patients who

TABLE 23.

17-Oxosteroid and Total Glucocorticoid excretion during the first ten days following alcoholic hypoglycaemia

Steroid Excretion	17-Oxosteroids				Total Glucocorticoids			
Mg/24 hrs	MEN (ages 23 - 70 yrs).		WOMEN (ages 26 - 65 yrs)		MEN (ages 21 - 70 yrs)		WOMEN (ages 26 - 65 yrs)	
<1.0	1	(5.9%)	4	(28.6%)	5	(26.3%)	5	(35.7%)
1. - 3	6	(35.3%)	5	(35.7%)	4	(21.0%)	6	(42.9%)
3. - 5	4	(23.5%)	3	(21.4%)	3	(15.7%)	0	
5. - 7	2	(11.8%)	0		2	(10.5%)	1	(7.1%)
7. -10	2	(11.8%)	1	(7.1%)	0		0	
10. -12	1	(5.9%)	1	(7.1%)	3	(15.7%)	0	
12. -15	1	(5.9%)	0		1	(5.3%)	1	(7.1%)
15. -19	0		0		1	(5.3%)	1	(7.1%)

TABLE 24

Results of A. C. T. H. stimulation on 17 - oxosteroid and total glucocorticoid excretion (mg/24 hours)

Case No.	Sex	Age	Day of hospitalisation on which A. C. T. H. commenced	Type of Steroid	Unstimulated steroid excretion	A. C. T. H. Stimulation and aftermath. Days 1	2	3	4	5	6
11/61	M	32	8	17-oxo	1.0	3.8*	8.1*	4.9	5.0		
				Total gluco	<1.0	9.6*	46.3*	58.9	<1.0	1.4	
8/62	M	21	4	17. oxo		17.0*	2.8*	17.3	4.1	3.4	2.8
				Total gluco	<1.0	19.4*	9.7*	32.1	10.7	5.0	<1.0
15/62**	M	58	8	17-oxo	3.3	3.6*	3.1*	2.2	2.0	2.7	2.7
				Total gluco	<1.0	<1.0*	<1.0*	<1.0	8.0	<1.0	3.3
6/62	F	65	12	17-oxo	<1.0	2.0*	1.3*	1.1	<1.0	<1.0	<1.0
				Total gluco	<1.0	2.2*	6.3*	10.2	<1.0	1.7	<1.0
10/62	F	30	12	17-oxo	<1.0	<1.0*	4.5*	5.5	2.2		
				Total gluco	<1.0	9.3	11.2*	6.9	<1.0		
13/62	F	60	18	17-oxo	0.8	9.1*	*	11.5*	9.8	Discharged	
				Total gluco	2.0	9.1*	*	10.5*	5.6	herself.	
3/63	F	40	18	17-oxo	3.1	7.8*	5.8*	5.2	1.8	2.2	4.6
				Total gluco	2.6	28.8*	45.9*	4.3	11.1	2.7	5.8
4/63	F	34	9	17-oxo	1.7	3.3*	25.5*	2.3	3.7	1.1	
				Total gluco	3.4	16.6*	23.2*	13.9	3.4	2.2	
5/63	F	35	9	17-oxo	3.1	6.7*	7.1*	4.6	1.8	0.8	
				Total gluco	1.1	1.5*	12.2*	24.2	9.1	18.1	

* Day on which ACTH given. ** Clinical Addison's Disease
*** 17-oxo = 17-oxosteroids. Total gluco = Total glucocorticoids

improvement takes place. However, factors such as improvement in nutrition during hospitalisation, and the known magnitude of day to day variations in urinary steroid excretion, may make it difficult to interpret the results.

A condition known as 'basal hypo-adrenal corticalism' has been described in patients with a low level of nutritional status. These patients have low urinary steroid excretion but respond well to corticotrophin. It has been supposed that the level of circulating corticotrophin is too low to maintain normal steroid excretion and not low enough to lead to cortical atrophy. sufficient to produce failure of response to corticotrophin (Prunty, 1956). It is possible that the five patients, reported above, who responded to corticotrophin, fell into this category.

Santisteban (1961), amongst others, (Forbes and Duncan, 1951; Smith, 1951) has shown that ethyl alcohol can act as a stressing agent in animals and that the stimulating effect on the adrenal cortex is probably by way of the pituitary. Santisteban (1961) also thought that an 'alarming' stimulus, such as that produced by a large dose of ethyl alcohol, could result in adrenal exhaustion and that repeated evocation might eventually lead to permanent changes in adrenal function. Kissin et al., (1959), after studying the 17-hydroxycorticoid excretions in alcoholics and non-alcoholics, concluded that chronic alcoholics basically had diminished adrenal cortical function secondary to liver damage. However, Smith (1949) inferred that alcoholics showed adrenal cortical hypofunction secondary to underactivity of the anterior pituitary gland. It does seem possible, therefore, that alcohol played a part in

initially showed low 24 hour urinary steroid excretion.* A. C. T. H. was given by I. M. route, using a gel preparation in such instances, or by intravenous infusion over eight hours, or a combination of both. Dosage by I. M. route was 100 units 12 hourly for four doses, and I. V. infusion contained 25 units. Only batches known to be active in stimulating the suprarenal were used.

In four patients (including an Addison's disease) the response to A. C. T. H. stimulation was subnormal. In the remaining patients, moderate to good responses occurred, and indicate normal adrenal function. In these patients it is probable that pituitary dysfunction was present and it is a pity that metopirone tests could not have been done at the time. It should be noted that in some of the patients there is apparent suprarenal exhaustion following A. C. T. H. stimulation.

There was no clinical evidence of adrenal or pituitary disease, except in Case 15/62, who was suffering from Addison's disease. The exact nature of the pituitary-adrenal disturbance is thus not certain. It might have anteceded the hypoglycaemic episode, been a consequence of the hypoglycaemia, or have been due to an action of alcohol on pituitary-adrenal function. It is reasonable to expect improved steroid excretion during recovery if the depressed pituitary-adrenal function was the result of one or other of the last two, provided the dysfunction was of a temporary nature. It will thus be necessary to repeat the examination of 24 hour urinary excretion during subsequent recovery in hospital to see if

* In 3 further patients (Cases 14/62, 1/63, 2/63), who showed normal total glucocorticoid excretion during the first ten days of hospitalisation, A. C. T. H. stimulation tests produced normal responses (see appendix).

causing endocrine dysfunction in some of my patients.

Serum Amylase

Table 25 shows the cases where serum amylase were done. The first patient (Case 1/60) developed acute pancreatitis soon after admission and it was attributed to his alcoholic debauch. (Owens and Howard, 1958). The subsequent patients did not show evidence of any abnormality and, after Case 14/60, it was decided that the investigation should be discontinued because it required time to perform and there was no indication that an abnormal result was associated with alcoholic hypoglycaemia.

TABLE 25. SERUM AMYLASE

Case No.	Day Test performed	Result *
1/60	6	192
	8	60
	10	16
	15	12
2/60	2	8
	3	8
3/60	1	8
4/60	1	8
5/60	2	4
6/60	1	12
7/60	1	4
8/60	1	8
9/60	3	16
10/60	3	4
11/60	1	8
13/60	2	8
14/60	5	8

* Wohlgemuth units. (N 3 - 10 units/ml).

Urine on admission

A routine urine was tested, on admission, in 13 cases. The only finding of interest was an acetonuria in 10. (Table 26). Acetonuria has been noted by other authors in patients admitted with alcoholic hypoglycaemia. (Tucker and Porter, 1942; Neves et al., 1950; Hammack, 1957; Weill and Gorouben, 1960), and it is probably related to the fasting state, and/or to ethyl alcohol (Forsander et al., 1965).

TABLE 26 ACETONE IN URINE ON ADMISSION*

Acetonuria	No Acetone	Trace	+	++	+++	++++
Case Numbers	8/60	20/60	4/60	6/61	2/63	4/61
	5/62		5/60			13/62
	5/63		9/60			14/62
			3/63			

* Results of routine urines, performed during admission, are given in the appendix with the case histories.

Serum proteins

These were measured colorimetrically by the biuret method (Weichselbaum, 1946), using an EEL colorimeter, and by serum electrophoresis (Joubert, 1959). Because of the difficulty in interpreting the levels in African patients, the results were not included with the liver function tests. (Joubert, 1959). Serum protein, by the biuret method, were done on 41 patients, and Table 27 shows the results. The patients (Cases 6/61, 10/62, 2/63) with a serum albumin under 2.1g% all showed evidence of poor nutrition. One of them had pellagra (Case 6/61) and one (Case 10/62) miliary tuberculosis. Of those patients with a serum albumin concentration between 2.1 and 2.5g%, five out of the nine were considered to be showing clinical evidence of poor nutrition.

Joubert et al., (1959) estimated the total proteins in Africans presenting for registration at the Durban Corporation employment centre. Ninety seven per cent of the Africans showed total proteins between 6.51 and 8.00 g%, and 3% between 6.25 and 6.50 g%. The majority of the patients, reported here, had similar total protein levels. The serum albumin concentrations of 100 Africans in Joubert's series (1959) varied from 2.79 to 4.10 g%. Twenty-nine of the forty-one patients, estimated here, showed concentrations between 2.6 and 4.1 g%. Thus, in general, the albumin levels were similar. Decreased mean albumin concentrations have been found in Africans, as compared with Europeans, by other investigators. (Arens & Brock, 1954; Bersohn et al., 1954).

TABLE 27 SERUM PROTEINS (g %)

	Serum Albumin					Serum Globulin				Total Proteins				
	1.0 - 2.0	2.1 - 2.5	2.6 - 3.0	3.1 - 4.0	4.1 - 5.0	2.0 - 3.0	3.1 - 4.0	4.1 - 5.0	5.1 - 6.0	4.0 - 5.0	5.1 - 6.0	6.1 - 7.0	7.1 - 8.2	8.3 - 9.0
Number of Cases:	3	9	9	19	1	3	27	8	3	4	7	14	15	1

SUMMARY OF BIOCHEMICAL FINDINGS

1. All patients had a blood sugar level below 48 mg%.

2. The blood alcohol levels were normal or slightly raised.

3. The blood urea was normal in most patients.

4. A mild and transient hepatogenous jaundice was found in 42 patients, where serial tests were done, and was considered to be due to ethyl alcohol.

5. The fasting blood sugar varied between 54 and 100 mg%. The glucose tolerance tests were normal or showed mild abnormalities, and did not resemble any of the typical curves ascribed to the more common diseases that produce hypoglycaemia.

6. In 33 patients, where urinary steroid excretions were performed within the first ten days of hospitalisation, the majority showed low excretions indicating inactivity of the suprarenal cortex. A. C. T. H. response tests, performed on nine patients, showed normal adrenal function in five, and subnormal response in four patients, including an Addison's disease. The exact nature of the pituitary-adrenal disturbance was not known. The nutritional state and the alcohol intake would have to be considered as possible factors.

7. Acetonuria was a common finding on admission, in those patients in which the test was done.

8. One patient, with acute pancreatitis, had a raised level of serum amylase.

HISTOLOGICAL FINDINGS

HISTOLOGICAL FINDINGS

Liver Biopsy

This was performed by the trans-abdominal route either by the Menghini technique, or with a Vim-Silverman needle.

Liver biopsies were performed on 37 patients. In one patient (Case 14/60) two biopsies were performed during hospitalisation, while another (Case 2/60) was biopsied on both admissions. It was not possible to report on four of the liver biopsies because insufficient tissue was obtained. Of the remainder, the liver biopsies were performed on six patients, on admission, on two patients on the first day, on five on the second day, on seven on the third day, on five on the fourth day, on three on the fifth day, on two on the seventh day, and on one each on the ninth, tenth, eleventh, twelfth and thirteenth days after admission. The specimens were fixed immediately in formalin, and absolute alcohol, and all were stained with haematoxylin and eosin. The majority of specimens were also stained by silver impregnation for reticulin, Weigert's iron haematoxylin Van Gieson's stain (W. H. V. G) for collagen, Perl's prussian blue reaction for haemosiderin, and with Best carmine and periodic-acid/Schiff (PAS) for glycogen. Staining for glycogen was controlled by a positive control and verified by saliva digestion. Fat staining was performed on 19 specimens with Sudan III and eleven specimens were stained with phosphotungstic acid haematoxylin (P. T. A. H.) for alcoholic hyalin (see appendix for

staining methods).

Each of the following was assessed separately; intralobular foci of degeneration and necrosis with or without inflammatory cell infiltration, alcoholic hyalin, the amount of fatty change (including both fatty vacuolation and fine intercellular change), the degree of fibrosis, the inflammatory cell infiltration in the portal tracts, the glycogen and haemosiderin content and the presence of bile thrombi and bile duct hyperplasia.

Foci of necrosis

Foci of necrosis were found in 20 specimens and were almost always accompanied by an inflammatory cell reaction consisting of neutrophils, monocytes and round cells in variable numbers. (Figs. 9, 10, 12). There was no correlation between the foci of necrosis and fatty change and in one case (Case 22/60), there was virtual absence of fat.

Alcoholic hyalin

Alcoholic hyalin was not noted in any sections (2 doubtful: Cases 5/62 and 2/62) but few were stained with phosphotungstic acid haematoxylin or other special stains.

Fatty change (lipohepatosis)

On haematoxylin and eosin section fatty change was absent in 1 case, mild in 4, moderate in 6, severe in 16, and extreme in 7 cases. In 19 cases, where tissue was stained with Sudan III, it was graded from 0 to 4 plus according to the proportion of cells containing fatty change, and was considered to be Gr. 1 (1 - <25%)

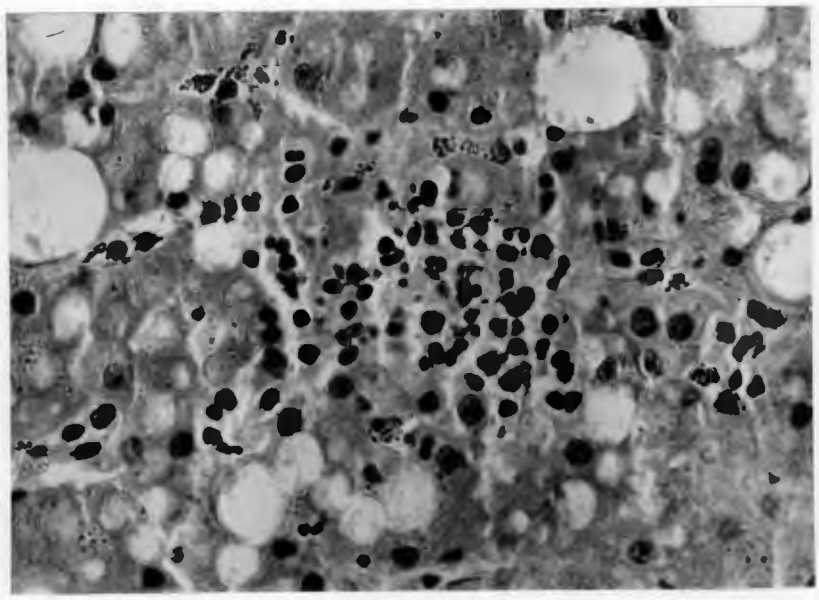


Fig. 9. Liver biopsy, Case 14/60. ? chronic alcoholic, shimeyane drinker. Typical focus of necrosis with inflammatory cell reaction; severe fatty change, gr. 4 (fibrosis grp.I; siderosis gr.4) H. & E.

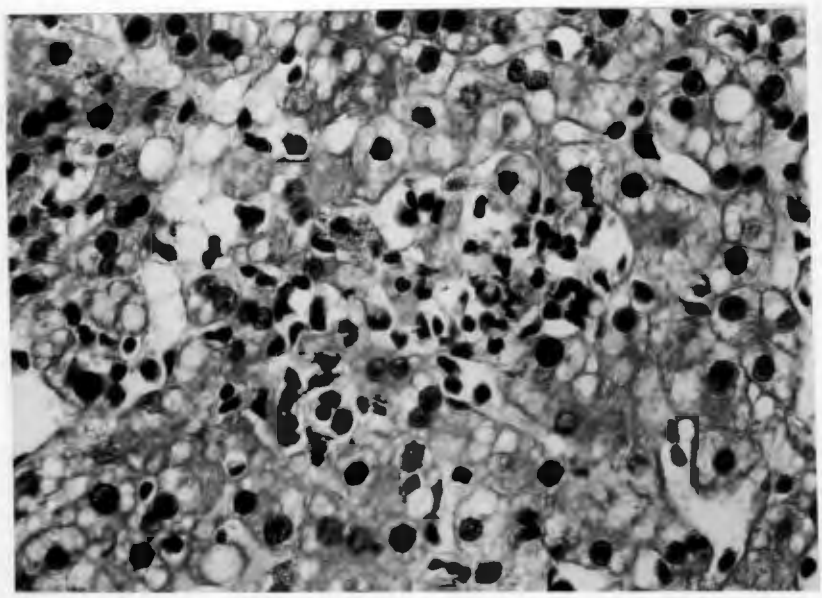


Fig. 10. Liver biopsy, Case 5/62, chronic alcoholic, cane spirit drinker. Focus of necrosis with inflammatory cell reaction; severe fatty change, gr. 4. (fibrosis grp.II, haemosiderin gr. 0) H. & E.

in 3 cases, Gr. 2 (25 - <50%) in 2 cases, Gr. 3 (50 - <75%) in 2 cases and Gr. 4 (75 - 100%) in 12. (Figs. 9, 10, 11).

Inflammatory cells in the portal tracts

Acute and/or chronic inflammatory cells were found in the portal tracts of almost all sections. This is a common finding in liver sections from Africans. (Davies, 1954; Higginson et al., 1957).

Fibrosis

This was classified according to Higginson et al., (1957) - Group I = Non-fibrotic liver; Group II = Slight portal fibrosis; Group III = Moderate portal fibrosis ('periportal fibrosis'); Group IV = Severe diffuse septal fibrosis (mild cirrhosis); and Group V = Severe cirrhosis. Group I was found in 11 cases; Group II in 10; Group III in 7. Group IV in 3, and Group V in 3. (Fig. 11).

Haemosiderin

This was graded according to Wainwright (1957), from grade 0-5. In gr. 0 haemosiderin was absent; in gr. 1 it was found in the Kupffer cells only; in gr. 2 in the parenchyma at the periphery of the lobules; in gr. 3 throughout the lobule; in gr. 4 clumps also in the portal tracts and parenchyma, and in gr. 5 more severely than in gr. 4. It was found to be grade 0 in five cases, grade 1 in two cases, grade 2 in four cases, grade 3 in six cases, grade 4 in eight cases, and grade 5 in the remainder (8). (Fig. 13).

Glycogen

It was graded from 0 to 4 plus according to the quantity of glycogen present. Six liver biopsies (Cases 14/60, 20/60, 23/60

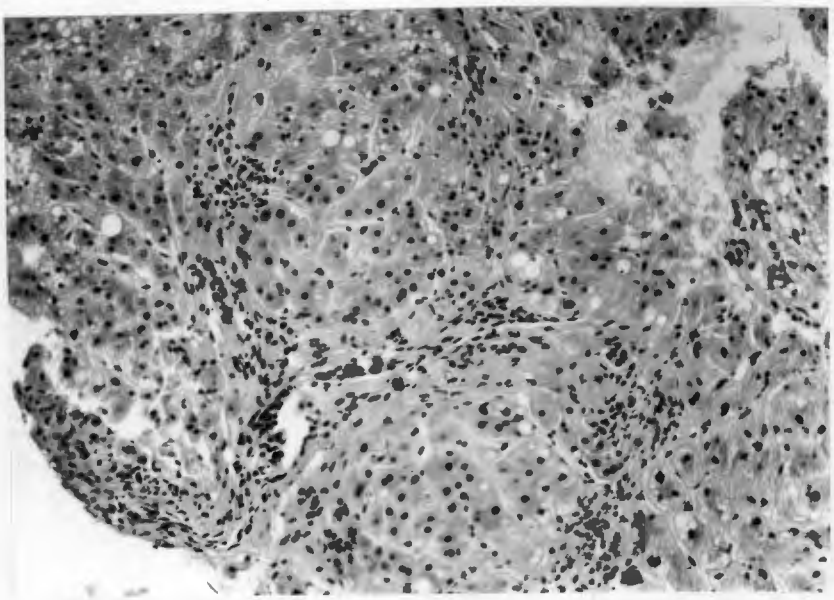


Fig. 11. Liver biopsy, Case 8/60, chronic alcoholic, heavy drinker 25 years. Cirrhosis with focus of necrosis (Fig. 12) and inflammatory cell reaction: severe fatty change. (Siderosis gr. 2) H. & E.

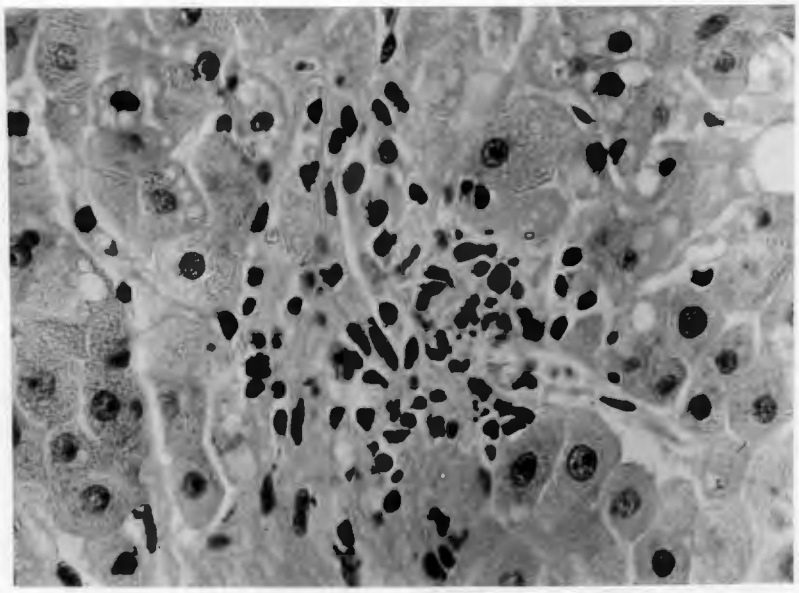


Fig. 12. Focus of hepatic necrosis from Fig. 11.

2/62, 6/62 and 2/63) taken on admission, showed complete absence of glycogen. (Figs. 13 and 14). In two cases (Cases 16/60 and 5/62), where liver biopsies were performed within $1\frac{1}{2}$ hours of admission, a moderate quantity of glycogen was found (gr. 1-2). In the remaining biopsies, glycogen varied from grade 1-4. (Figs. 15 and 16).

Bile thombi

These were not noted but were probably more difficult to assess because of large quantities of haemosiderin in our sections. Bile duct hyperplasia, accompanied by cirrhotic change, was noted in one case (12/62).

Most of the findings reported here, have been previously published. (Neame, 1964).
Table 28 summarises the findings and gives other relevant information.

Necropsy findings

Limited post-mortems were done on five of the six patients (Cases 12/60, 15/60, 21/60, 8/61 and 12/62) who died. In four there was bronchopneumonia (Cases 12/60, 15/60, 21/60 and 8/61), and in one lobar pneumonia (Case 12/62). Fatty liver was present in three cases (Cases 15/60, 8/61 and 12/62), and cirrhosis in one (Case 12/62). The adrenals, pituitary and pancreas were natural in all the patients.

COMMENT ON LIVER BIOPSY FINDINGS

Fatty liver was found in the majority of the patients on liver biopsy. Two factors may have played a part in the production of

ABSENCE OF GLYCOGEN ON ADMISSION

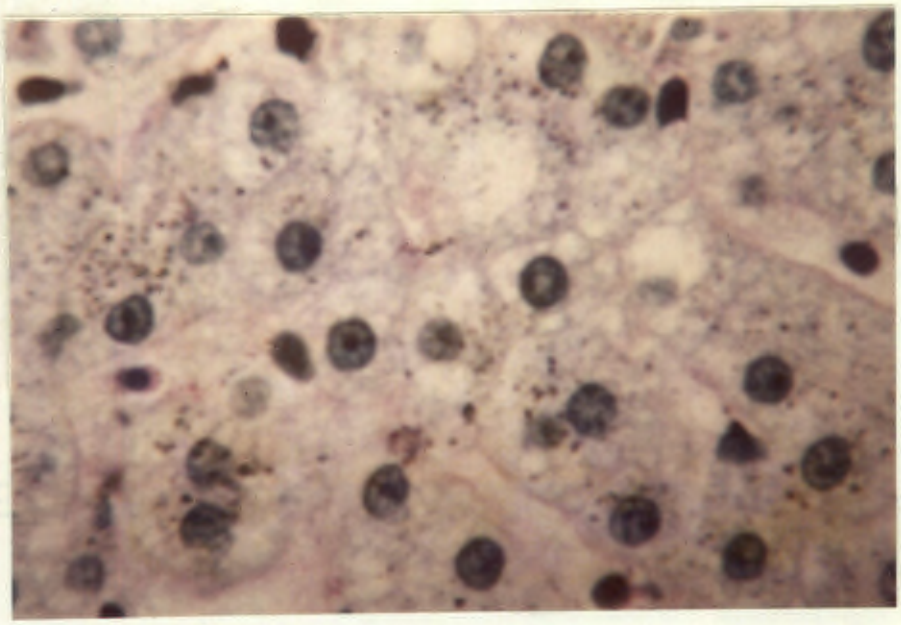


Fig. 13. Liver biopsy (Case 23/60) showing absence of glycogen. Haemosiderin can be seen.
[PAS STAIN]

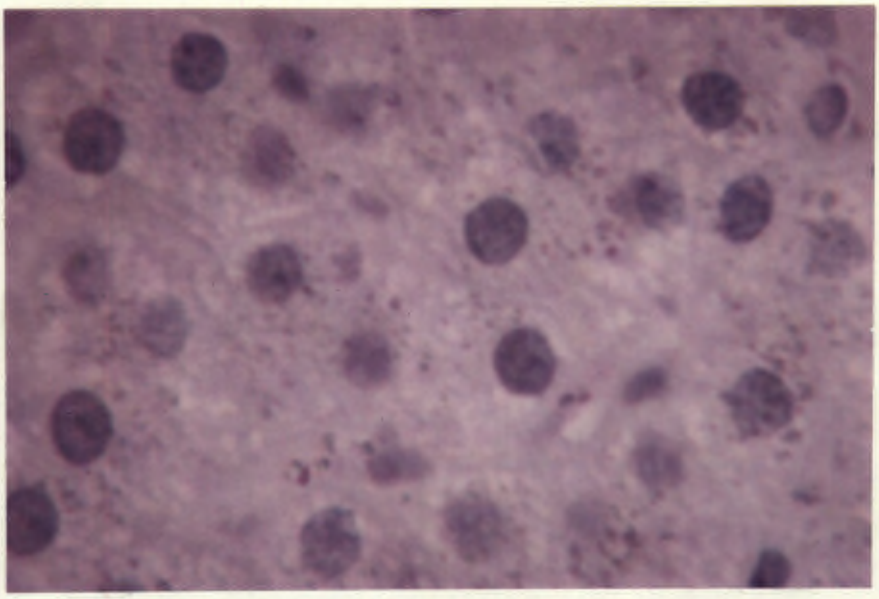


Fig. 14. Liver biopsy (Case 23/60) stained with Best Carmine. Note absence of glycogen.
[BEST CARMINE].

ABUNDANCE OF GLYCOGEN AFTER ADMISSION

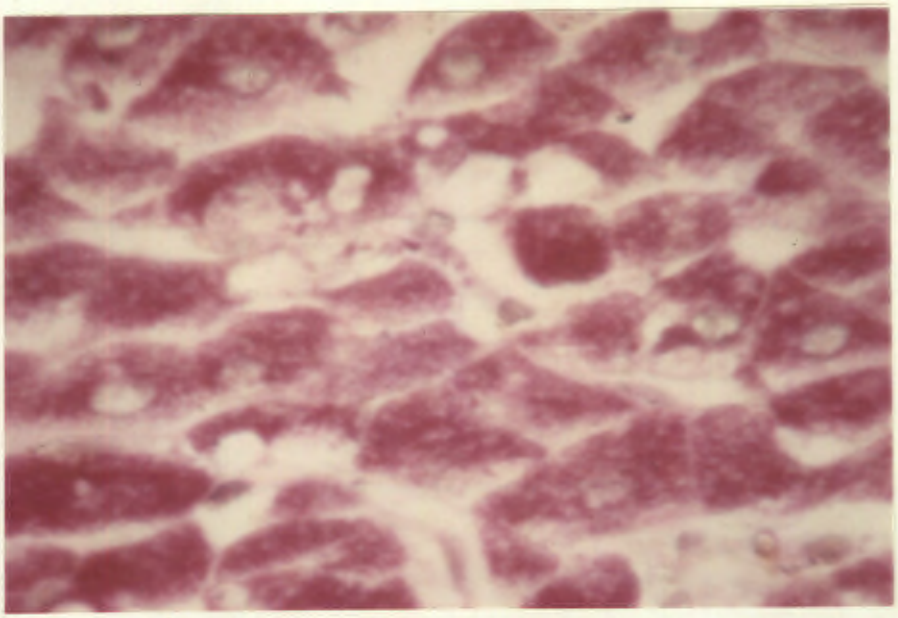


Fig. 15. Liver biopsy (Case 9/60) performed on the fifth day of hospitalisation, showing an abundance of glycogen, gr. 4. [PAS STAIN]

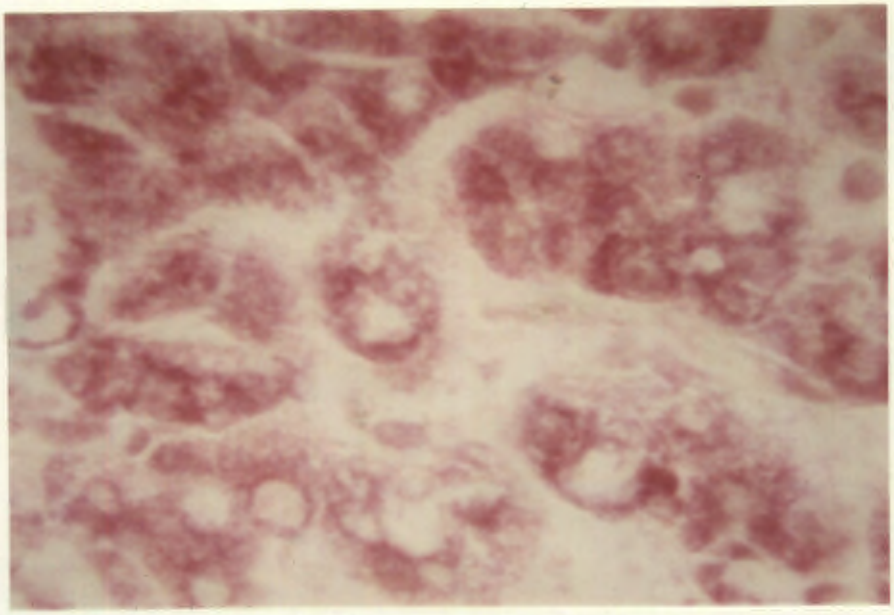


Fig. 16. Liver biopsy (Case 19/60), performed on the fourth day of hospitalisation, showing an abundance of glycogen, gr. 4. [BEST CARMINE]

TABLE 28

Case	Sex	Age	Alcoholic Habits[1]	Type of Alcohol taken[2]	Nutrition	Associated illness[3]	W.B.C. / C.MM.	Maximum S.G.O.T. Karmen U.	Day biopsy done	LIVER BIOPSY FINDINGS: Focal Necrosis	Alcoholic Hyaline	Glycogen Gr. 0-4	Fat H&E. Sud III	Fibrosis Grp.I-V	Siderosis Gr. 0-5
1/60	M	45	W.D.	Z.B.,S.	Fair	Acute Pancreatitis	7,000	460(5)[4]	3	+	Nil.*	4	Moderate	II	5
2/60	M	38	W.D.	G.	Fair		9,000	82(2)	4	+	Nil.	1	Moderate	III	2
3/60	M	24	C.A.	Z.B.,S.	Pellagra		10,000	96(1)	2	Nil.	Nil.	3	Severe	II	4
5/60	M	46	C.A.	S.,G.	Poor	P.T.B.	7,000	180(2)	5	Nil.	Nil.	2	Extreme	V	?
7/60	M	37	W.D.	S.	Fair	Aspiration Pneumonia	15,000	350(3)	3	+	Nil.	3	Severe	II	5
8/60	F	49	C.A.	S	Pellagra	D.T's	5,000	276(1)	2	+	Nil.	4	Severe	V	2
9/60	F	38	C.A.	S.B.,S.Gin.	Pellagra	P.U.O.	7,000	148(1)	5	+	Nil.*	4	Moderate	II	4
10/60	M	42	C.A.	--	--		--	--	10	Nil.	Nil.*	3	Moderate	III	4
11/60	M	23	C.A.	G.	Poor		19,000	110(5)	3	Nil.	Nil.	3	Severe	I	2
14/60	M	39	?C.A.	S.	Poor	P.T.B.	3,000	200(1)	A	Nil		0			
									5	+	Nil	3	Severe	I	4
16/60	F	49	W.D.	Brandy	Fair		8,000	50(5)	1	+	Nil.	2	Severe	I	3
17/60	M	45	?C.A.	Z.B.	Pellagra		9,000	150(1)	4	+	Nil.*	4	Moderate	IV	4
18/60	M	36	W.D.	Z.B. Brandy	Fair		9,000	44(2)	2	Nil.	Nil.	4	Severe	II	5
19/60	M	34	C.A.	Z.B.,G.	Pellagra		6,000	550(1)	4	+	Nil.	4	Severe	II	5
20/60	M	58	N.A.	Cane Spirit	Poor		20,000	50(4)	A	Nil	Nil	0	Severe	?V	4
22/60	M	50	W.D.	Z.B.,S.	Fair	P.T.B.	?	186(1)	4	+	Nil.	2	Nil	I	5
23/60	M	41	?C.A.	Gin	Poor		28,000	336(1)	A	Nil.	Nil.	0	Severe	III	5
1/62	M	50	W.D.	S.,G.	Fair	Aspiration Pneumonia	20,000	112(4)	12	Nil.	Nil.	3	Mild	III	4
2/62(a)	M	44	C.A.	?	Poor	D.T's	20,000	152(7)	3	+	Nil	3	Extreme	III	0
(b)	M	44	C.A.	?	Poor	Died	?	?	A	+	Nil.	0	Extreme	? IV	0
3/62	M	46	W.D.	S.	Fair		7,000	96(6)	13	Nil.	Nil.*	3	Mild	I	5
4/62	M	30	W.D.		Poor		10,000	180(1)	9	+	Nil.*	4	Mild	I	4
5/62	F	60	C.A.	Cane Spirit	Poor	P.T.B. Rt. Pneumothorax	12,000	194(4)	1	+	? Nil.*	1-2	Severe	II	0
6/62	F	65	C.A.	Cane Spirit	Poor	Fever	13,000	90(2)	A	Nil.	? Nil.	0	Extreme	III	0
10/62	F	30	W.D.	S.	Poor	Miliary T.B.	8,000	90(4)	11	+	Nil.	1	Extreme	II	3
12/62	M	36	?C.A.	Z.B.,G.	Fair	Lobar Pneumonia Died.	?	270(3)	2	?Miliary Kochs +	Nil.*	2	Severe	IV	5
13/62	F	60	C.A.	S.,G.	Pellagra	Alcoholic Psychosis	11,000	120(1)	3	Nil.	Nil.	4	Extreme	III	3
14/62	F	57	?C.A.	S.	Fair		4,000	60(2)	3	+	Nil.*	3	Severe	II	3
15/62	M	58	W.D.	Z.B.,G.	Fair		10,000	90(2)	3	Nil.	Nil.*	4	Mild	I	3
1/63	F	40	W.D.	G., ?	Fair		5,000	40(2)	2	Nil.	Nil.	4	Severe	I	0
2/63	M	35	C.A.	G., Wine Cane Spirit	Poor	Alcoholic Psychosis	?	200(4)	A	+	Nil.	0	Extreme	II	1
3/63	F	40	C.A.	Z.B.,G.	Pellagra		9,000	70(1)	4	+	Nil.	4	Moderate	I	2
4/63	F	34	C.A.	G.	Fair		7,000	150(2)	7	?+	Nil.*	1	Severe	I	1
5/63	F	35	?C.A.	S.,G.	Poor		8,000	110(1)	7	+	Nil.	3	Severe	I	3

1. Alcohol Habits - W.D. = Weekend Drinker; C.A.=Chronic Alcoholic; N.A. = Non-Alcoholic. 2. Z.B. = Zulu Beer; S = Shimeyane; G = Gavine.
3. P.T.B. = Pulmonary Tuberculosis; D.T's = Delirium Tremens; P.U.O. = Pyrexia of Unknown Origin. 4. Day after admission on which Test was done.
Nil. = Not observed. A = Admission. * = H. & E. and P.T.A.H. stains done.

the fatty liver; first excess intake of alcohol and, secondly, a poor dietary intake. The assessment of the importance of each is not possible but it seems likely that alcohol was the major factor in the production of the fatty livers in these patients. The quantities of fat were certainly greater than those seen in the average African liver at post mortem. Siderosis was common but this is well known in Southern Africa. (Wainwright 1957). It has been suggested that there is a relationship between excessive consumption of alcohol and development of iron overload (Charlton et al., 1964; Seftel et al., 1961).

The findings of importance in the liver biopsies were, first, the absence of cirrhosis, secondly, the glycogen depletion on biopsies taken on admission, and, thirdly, the presence of small foci of hepatic necrosis.

Only six biopsies showed evidence of cirrhosis. In the remainder there was a normal architectural pattern. Cirrhosis could, therefore, be excluded as the cause of the hypoglycaemia.

The finding of glycogen depletion in biopsies taken on admission, indicated that the hypoglycaemia occurred during a period of depletion of hepatic glycogen stores. That glycogen depletion is an essential factor in the production of the alcoholic hypoglycaemia will be shown during discussion of its pathogenesis. Where liver biopsies were taken within 90 minutes of administering small quantities of 50% dextrose solution, moderate quantities of glycogen were observed. Their livers, thus, had no difficulty in converting glucose to glycogen.

Small foci of hepatic necrosis were found on the liver biopsy

of 20 of the patients reported here. The foci were unassociated with cirrhosis in most cases, and there was no correlation between the hepatic necrosis and fatty change. (Volwiler et al., 1947; Neame, 1964). In addition, alcoholic hyalin was not found in association with the necrosis and its absence has also been noted by several others (Popper et al., 1955; Shorter and Baggenstoss, 1959; Beckett et al., 1961, 1962). (Table 28). It has been suggested that the presence of alcoholic hyalin might indicate a poor prognosis. (Rice and Yesner, 1960) but this was not a feature of our cases.

The lesion of focal hepatic necrosis has been noted in the livers of chronic alcoholics both cirrhotic and non-cirrhotic.† Mallory (1911) initially described a lesion in the chronic progressive alcoholic cirrhotic that he considered characteristic, and that consisted of a peculiar hyaline change ('alcoholic hyalin'). This change was often associated with polymorphonuclear and mononuclear cells and with hepatic necrosis. The hepatic necrosis has since been noted in chronic alcoholics without the hyaline change. The lesion has been related to preceding ethanol excess (Phillips and Davidson,

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† Mallory, 1911; Hall and Ophuls, 1925; Connor, 1938; Hall and Morgan, 1939; Volwiler and Jones, 1947; Volwiler et al., 1948; Davis and Culpepper, 1948; Chalmers et al., 1948; Buck, 1948; Siefe et al., 1950; Baggenstoss and Stauffer, 1952; Phillips and Davidson, 1954; Dubin, 1954; Popper et al., 1955; Gall, 1957; Davidson, 1958; Davidson and Popper, 1959; Shorter and Baggenstoss, 1959; Summerskill et al., 1960; Mallory, 1960; Tisdale and Klatskin, 1960; Beckett et al., 1961, 1962; Davidson and MacDonald, 1962, and Green et al., 1963.

1954; Gall, 1957; Beckett et al., 1961, 1962, and Green et al., 1963). Beckett et al. (1961, 1962), amongst others (Volwiler et al., 1948; Phillips and Davidson, 1954, and Green et al., 1963), described an accompanying symptom complex. This consisted of anorexia, nausea and vomiting, upper abdominal pain and fever with or without icterus.

In my patients the foci of hepatic necrosis were found, in association with a transient biochemical hepatitis, in chronic alcoholics and weekend drinkers, without accompanying clinical symptoms, after the intake of excess alcohol. On the above evidence there appears to be a relationship between the foci of necrosis and preceding acute alcoholic excess and the question arises whether alcohol was acting as a toxin in the production of the hepatic necrosis (Neame, 1964). Supportive evidence for the toxic action of ethyl alcohol has been given by Bang et al., (1958) and Hed (1959) who have shown that ethyl alcohol can cause increased S. G. O. T. activity in chronic alcoholics. Green et al., (1963) have also noted an increased S. G. O. T. activity and foci of hepatic necrosis after excess ethyl alcohol. They labelled their cases as "acute alcoholic hepatitis".

The possibility of toxic factors in the alcohol imbibed by my patients, had to be considered. There was, however, no clinical, biochemical or histological difference between those patients taking African liquor and those drinking commercially produced ethyl alcohol. Their livers might have been vulnerable to ethyl alcohol as a result of a poor dietary intake,

(Wahi, 1948; Schwarz, 1954; Madsen et al., 1959), but it is not possible to assess this factor with certainty. It seems that the foci of necrosis and the transient hepatitis were indicative of a subclinical alcoholic hepatitis. (Neame, 1964). The role of hepatic necrosis in the production of 'alcoholic' cirrhosis is a factor which requires further investigation.

There is little doubt that a close association exists between chronic alcoholism and cirrhosis, and evidence is now accumulating - both biochemical (Bang et al., 1958; Hed, 1959; Madsen et al., 1959; Green et al., 1963), and histological (Beckett et al., 1961, 1962) - that ethyl alcohol causes hepatic injury, acting directly or indirectly on the liver cells. One wonders, therefore, whether frequent episodes of hepatic necrosis in the chronic alcoholic, following frequent debauch, do not play a part in the production of 'alcoholic' cirrhosis. Features of post-necrotic cirrhosis have been observed in the alcoholic (Baggenstoss and Stauffer, 1952; MacDonald and Mallory, 1958; Klatskin, 1959; Popper et al., 1960; Rubin et al., 1962 and Green et al., 1963). However, one concept of the pathogenesis of 'alcoholic' cirrhosis is that chronic ingestion of alcohol leads to a type of dietary deficiency which results in fatty change in the liver, and that extreme fatty change is the precursor of cirrhosis. This theory results from a vast amount of experimental and clinical work which found that fatty change led to cirrhosis (Chaikoff et al., 1938; Hartroft, 1954); that fatty change resulted from the deficiency of certain dietary factors (Best et al., 1954); that malnutrition and fatty change were commonly found in 'alcoholic' cirrhosis, and that non-alcoholic cirrhosis was common in areas where dietary

deficiency occurred (Gillman and Gillman, 1944, 1945; Wahi, 1948). Far less emphasis has been placed on some of the inconsistencies in this theory (Dible, 1951; Gajdos, 1951; Klatskin, 1953, 1959, and Davidson and Popper, 1959), and on the role of hepatic necrosis in the aetiology of 'alcoholic' cirrhosis though hepatic necrosis is a common accompaniment of "progressive" (Hall and Ophüls, 1925; Hall and Morgan, 1939), and "active" alcoholic cirrhosis (Davidson, 1958). Dubin (1954) when discussing the paper of Hartroft (1954) stated that he believed the prime lesion in the pathogenesis of alcoholic cirrhosis was necrosis and not fatty metamorphosis, but he did not indicate the cause of the necrosis. Popper et al., (1955) in their paper on the transition of fatty liver into cirrhosis in alcoholic subjects, felt that the parenchymal necrosis might be even more important than the fatty change in the production of membranes and septums and they wondered whether the hepatic necrosis was the result of non-specific intercurrent infection. Gall (1957), Davidson and Popper (1959) and Shorter and Baggenstoss (1959), have related the parenchymal necrosis to cirrhosis. The last, (Shorter and Baggenstoss, 1959), felt that their observations possibly led to the conclusion that the parenchymal necrosis was of greater significance than the fatty change in the pathogenesis of permanent damage to the reticulin framework of the liver in the chronic alcoholic and the subsequent development of cirrhosis. They felt the aetiology of the necrosis was obscure. Becket et al., (1961, 1962) have suggested that the hepatic necrosis is the result of ethyl alcohol and it seems that the relationship between hepatic necrosis and excess ethyl alcohol and cirrhosis should be investigated

further. It certainly is of interest that in the patients reported here, foci of hepatic necrosis and a transient hepatitis were found after the intake of excess alcohol without accompanying clinical symptoms. Siefe et al., (1950) and Volwiler et al., (1947, 1948) have noted also the absence of clinical features in chronic alcoholics, with hepatic necrosis on liver biopsy.

SUMMARY OF HISTOLOGICAL FINDINGS

1. Liver biopsies were performed on 37 patients by the trans-abdominal route. Two patients were biopsied on two occasions. Six patients had their liver biopsy performed on admission.

2. Foci of necrosis, alcoholic hyalin, fatty change, inflammatory cells in the portal tracts, the degree of fibrosis, the glycogen and haemosiderin content and the presence of bile thrombi and bile duct hyperplasia, were assessed separately.

3. Fatty change and haemosiderin deposition were common findings on liver biopsy.

4. Cirrhosis was found in six biopsies and could be excluded as the cause of the hypoglycaemia.

5. Biopsies, taken on admission, showed that hypoglycaemia occurred during a period of glycogen depletion.

6. Small foci of hepatic necrosis were seen on 20 liver biopsies. The foci were unassociated with cirrhosis in most cases and there was no correlation with alcoholic hyalin or fatty change. The foci of necrosis were associated with the intake of excess alcohol and were unaccompanied

by clinical symptoms. It seemed that the hepatic necrosis and the transient (biochemical) hepatitis were indicative of a subclinical alcoholic hepatitis.

7. The possible relationship between the foci of necrosis, ethyl alcohol and 'alcoholic' cirrhosis were discussed.

8. Limited post mortem was done on five patients.

OTHER INVESTIGATIONS

HAEMATOLOGICAL FINDINGS

A haemoglobin and white blood count were performed on the first or second day of admission on 43 patients. The white blood count was under 11,000/cmm in 30 patients, and varied from 12,000 - 29,000/cmm in the remainder. The white blood counts in the patients on whom liver biopsies were done, are shown in Table 28. The haemoglobin was below 11 gms% in three patients (Cases 2/61, 10/62 and 1/63). Case 2/61 had an iron deficiency anaemia, and Case 10/62 a normochromic normocytic anaemia, associated with miliary tuberculosis. The cause of the anaemia in Case 1/63 was not elucidated.

CHEST X - RAYS

These were done on 30 patients. Six patients had pulmonary tuberculosis, (Cases 5/60, 14/60, 22/60, 3/61, 5/62 and 10/62), and three, fibrous scarring in the upper lobes (Cases 20/60, 15/62 and 5/63). Case 7/60 had irregular consolidation, and Case 12/62 a lobar pneumonia in the right upper lobe. The remaining patient had normal chest X-rays.

ELECTROCARDIOGRAPHY

This was done on the first nine patients, but as there was no evidence of acute myocardial injury to account for the elevated S. G. O. T. results in these patients, it was discontinued as an investigation. In the meantime it became obvious that the elevated transaminase was the result of hepatic injury.

PART II

ETHYL ALCOHOL AND HYPOGLYCAEMIA

ETHYL ALCOHOL AND HYPOGLYCAEMIA

In 1960 I suggested, after reviewing the initial cases, that ethyl alcohol was the cause of the hypoglycaemia (Neame and Joubert, 1961). Although, at the time, ethyl alcohol had not been shown, experimentally, to produce hypoglycaemia in man, there appeared to be sufficient indications to strongly suggest this possibility. It has since been shown that ethyl alcohol can produce hypoglycaemia in man. (Field et al., 1963; Freinkel et al., 1963). In this section I will give my reasons for suggesting that ethyl alcohol was the cause of the hypoglycaemia in the cases reported here, and also review the subsequent reports which have proved that ethyl alcohol can cause hypoglycaemia.

Exclusion of other causes of hypoglycaemia

Before suggesting that alcohol was the cause of the hypoglycaemia, it is necessary that the usual causes of hypoglycaemia should be excluded. Table 29 presents an aetiological classification of spontaneous hypoglycaemia from an article of Conn and Seltzer (1955). Although some additional causes of hypoglycaemia have since been added (Gittler, 1962) the table is quite adequate and was largely utilised in the differential diagnosis.

TABLE 29.

Aetiologic Classification of Spontaneous Hypoglycaemia *

1. Organic - recognizable anatomic lesion

   A. Hyperinsulinism
      1. Pancreatic islet cell adenoma
         a. Single
         b. Multiple
         c. Aberrant
         d. Associated with adenomas of other endocrine glands (parathyroid, anterior pituitary).
         e. Pancreatic islet cell "suspiciously malignant" adenoma (localized)
      2. Pancreatic islet cell carcinoma (with metastases)
      3. Generalized hypertrophy and hyperplasia of the islets of Langerhans

   B. Hepatic disease
      1. Ascending infectious cholangiolitis
      2. Toxic hepatitis
      3. Diffuse carcinomatosis
      4. Fatty degeneration or "fatty metamorphosis"
      5. Laennec's cirrhosis
      6. Viral hepatitis
      7. Chronic passive congestion in congestive heart failure
      8. Glycogenosis (von Gierke's disease)

   C. Anterior pituitary hypofunction
      1. Destructive lesions (chromophobe tumors, craniopharyngiomas)
      2. Atrophy and degeneration (Simmonds' disease)
      3. Surgical hypophysectomy
      4. "Pituitary myxedema"
         a. Thyroid hypofunction secondary to pituitary failure
         b. Pituitary failure secondary to myxedema
      5. Severe inanition
      6. Postoperative hypoglycaemia

D. Adrenocortical hypofunction
   1. Idiopathic cortical atrophy
   2. Des tructive infectious granuloma
   3. Destructive neoplasm
   4. Congenital adrenal hyperplasia

E. Fibromas and sarcomas

F. Central nervous system lesions (hypothalamus or brain stem; interference with nervous control of blood sugar).

II Functional - no recognized anatomic lesion, but explanable on basis of unusual somatic function

A. Hyperinsulinism (imbalance of the autonomic nervous system); "hypoglycemic fatigue; nervous hypoglycemia; functional hypoglycemia, reactive hypoglycemia.

B. Alimentary hyperinsulinism (rapid intestinal adsorption)
   1. After gastroenterostomy
   2. After partial or total gastric resection
   3. Hyperinsulinism of infancy (Staub-Traugott phenomenon)

D. "Idiopathic spontaneous hypoglycemia of infancy"

E. Renal glycosuria (severe degrees of low renal threshold for glucose)

F. Lactation

G. Severe continuous muscular work.

III Factitious (surreptitious insulin administration)

* Table from Conn, J. W. and Seltzer, H. S. Amer. J. Med. 19 : 460, 1955.

The majority of the causes of hypoglycaemia, shown in the table, are rare and seldom encountered. In addition, in most, the hypoglycaemia is largely overshadowed by the signs and symptoms of the main disease and the cause is, therefore, easily recognised. (Hastings - James, 1949; Conn and Seltzer, 1955; Kornfield, 1959 and Gittler, 1962).

Eighty to ninety percent of cases of hypoglycaemia, according to many investigators, are the result of three conditions: functional hyperinsulinism, organic hyperinsulinism and hepatogenous hypoglycaemia. (Conn & Seltzer, 1955; Kornfield, 1959 and Gittler, 1962). Functional hyperinsulinism is the most common cause of spontaneous hypoglycaemia, accounting for about 70% of all cases. (Conn and Seltzer, 1955).

Functional hyperinsulinism

This type of hypoglycaemia follows a meal and never occurs in the fasting state and, therefore, differs from the cases here, in which hypoglycaemia occurred after fasting (i.e. following a prolonged period of alcoholic intoxication during which there was no intake of food). In addition, deep coma occurred in most of the patients and this is not a feature of functional hyperinsulinism. (Conn and Seltzer, 1955). Finally, the oral glucose tolerance tests did not resemble those found in functional hyperinsulinism. There is, therefore, no doubt that my patients were not suffering from functional hyperinsulinism.

Organic hyperinsulinism

None of the patients showed a low blood sugar when fasted for 15 hours, (it is realised that prolonged fasting may be necessary to exclude some cases of organic hyperinsulinism) and in none was there a previous episode of hypoglycaemia, unassociated with alcohol, or a recurrence in hospital. In addition, though the glucose tolerance curve is not the most important diagnostic test in organic hyperinsulinism, the curves did not resemble those found in it. There seems to be no reason to suggest that the patients were suffering from organic hyperinsulinism. Freinkel et al., (1963) and Kahil et al., (1964) have shown that sustained hypoglycaemia can occur after intravenous tolbutamide in patients who have been in post-alcoholic hypoglycaemia. It therefore need not differentiate post-alcoholic hypoglycaemia from functioning islet cell tumours.

Hepatogenic hypoglycaemia

When hypoglycaemia occurs in liver disease, there is usually obvious evidence of derangement in liver function. (Aranow, 1946; Howard, 1955; Kornfield, 1959; Gittler, 1962). Although there was a transient hepatogenous jaundice in my patients, there was no evidence of gross liver disease on clinical examination, on liver biopsy, or at necropsy. In addition, there was no recurrence of hypoglycaemia after fasting and there had been no previous episodes of hypoglycaemia unassociated with alcohol. The patients, therefore, were not suffering from

hepatogenic hypoglycaemia.

Thus, the three major causes of hypoglycaemia could be excluded.

Adrenocortical and anterior pituitary hypofunction

In only one patient, Case 15/62, was there any clinical evidence of adrenal or pituitary dysfunction. Though many of the patients showed low urinary steroid excretion, it is rare for hypoglycaemia to occur in Addison's disease (Welty and Robertson, 1936; Anderson and Lyall, 1937; Rushton et al., 1940; Gittleson, 1956), or hypopituitarism (Sheehan and Summers, 1949; Howard, 1955) without other obvious signs of the disease. It seems, therefore, although there might have been a subtle pituitary - adrenal disturbance in some of my patients, there was no evidence that the hypoglycaemia was the result of a definite endocrine disorder.

Hypoglycaemia has been reported in association with severe inanition (Gounelle and Marche, 1946), but this could not have been the cause in the patients reported here. Factitious hypoglycaemia, due to insulin and other hypoglycaemic agents, such as tolbutamide and chlorpropamide, was also excluded as the cause.

Alcoholic hypoglycaemia

As shown above, the common causes of hypoglycaemia could

not be implicated. On the other hand in all the patients the hypoglycaemic episode was associated with preceding intake of alcohol. It seemed possible that ethyl alcohol or a toxic substance in the alcohol was the cause of the hypoglycaemia.

Toxic additives or impurities in the alcohol

Previous investigators (Brown and Harvey, 1941; Tucker and Porter, 1942; Bennett, 1953 and Hammack, 1957) had believed that toxic additives were responsible for the post-alcoholic hypoglycaemia. As the majority of my patients had been drinking "illicit" liquor owing to the liquor laws relating to Africans in South Africa at the time (these laws have now been removed), the possibility of toxic additives had to be considered. All patients were, therefore, questioned to find out whether they had added any substances to their alcohol. No such history was obtained from any patients and there did not seem to be any necessity for their withholding this information, as many had already admitted to drinking gavine and shimeyane. At the same time I tried to find out how the liquor had been prepared. No evidence was obtained that any of the substances used in the production of zulu beer or shimeyane were toxic and, in general, a standard method of producing them was noted. (Table 4). Gavine was made by distilling shimeyane and, as the methods were primitive, it was possible that the toxic substances were present in it. However, many of the patients had not imbibed gavine.

Some of the patients had been drinking in social groups. Whenever possible I tried to find out whether other members were

affected. No history was ever obtained that they were and as King Edward VIII Hospital was the hospital in Durban for admitting African and Indian emergencies, it seemed likely that if other members were affected, they would have been admitted to the hospital. On the few occasions when more than one case of hypoglycaemic coma, following the intake of alcohol, were admitted on the same day, the patients (Cases 4/60, 5/60, 22/60 and 23/60) were questioned and introduced to find out whether they had been drinking together. This had not occurred.

Thus, it seemed unlikely that toxic substances in the alcohol were the cause of the hypoglycaemia. In addition, as a number of the patients had only been drinking commercially produced ethyl alcohol (cane spirit, brandy, gin), it seemed that ethyl alcohol was the most likely cause. The fact that ethyl alcohol was associated with hypoglycaemia was confirmed when reviewing the literature. Certain South American writers (Bottura et al., 1949, Neves et al., 1950 and Peluffo et al., 1958) had also come to the conclusion that hypoglycaemia followed the intake of ethyl alcohol.

There was, therefore, evidence, from my own experience and from reports in the literature, that hypoglycaemia was associated with the intake of ethyl alcohol. Despite the fact that association and cause are often not one and the same, there were reports on the relationship between alcohol and carbohydrate metabolism which seemed to confirm that ethyl alcohol was the hypoglycaemic agent. The reports indicated that carbohydrate was utilised during the metabolism of alcohol, and that hepatic

glycogen depletion could follow the administration of ethyl alcohol. (Westerfield and Schulman, 1959). There therefore seemed to be not only an association between ethyl alcohol and hypoglycaemia but also a reason for its occurrence. This subject will be discussed in detail when the pathogenesis is described but, at this stage, I can state that the knowledge that carbohydrate was utilised during ethyl alcohol metabolism appeared to indicate to me that ethanol was the cause of the hypoglycaemia (Neame and Joubert, 1961).

Experimental production of alcoholic hypoglycaemia in animals

In September 1961, Clark et al., reported the production of hypoglycaemia in dogs, following ethyl alcohol. In actual fact, a Japanese worker, Matunaga, had produced hypoglycaemia in rabbits with ethyl alcohol in 1942. Subsequent work has shown that hypoglycaemia can easily be produced in animals by ethyl alcohol provided the liver has been depleted of its glycogen stores. This has been done by using lecithin (Matunaga, 1942), by fasting (Clark et al., 1961; Lochner and Madison, 1963), and by using oxythiamine (Wilson et al., 1962).

Experimental production of alcoholic hypoglycaemia in man

Field et al., (1962, 1963) and Freinkel et al., (1962, 1963), have proved, beyond doubt, that ethyl alcohol is a cause of hypoglycaemia in man. Both workers have produced hypoglycaemia with ethyl alcohol in normal adult volunteers, and in patients previously admitted in hypoglycaemic coma following excess alcohol. Likewise, in 1964, Marks and Medd produced

hypoglycaemia with ethyl alcohol in an adult patient who had previously been admitted in alcoholic hypoglycaemia. In addition, Ramon Guerra et al., (1963) claimed that they had produced alcoholic hypoglycaemia in two children. The exact mechanism, however, remains undetermined. I had tried to produce hypoglycaemia by administering ethyl alcohol to patients in 1960. Five patients (Cases 1/60, 2/60, 3/60, 14/60 and 18/60) were starved for 15 hours and then given 100 ml absolute alcohol half diluted with water. Hypoglycaemia was not produced and it seems, in view of the work of Field et al., (1963) and Freinkel et al., (1963) that the period of fasting prior to the test was too short. Efforts to prolong the period of fasting failed because of the lack of co-operation of the patients. The tests were ultimately discontinued because of inadequate facilities.

Comment on post-alcoholic hypoglycaemia

The above evidence indicates that the hypoglycaemia in the patients, reported here, was the result of ethyl alcohol.

Post-alcoholic hypoglycaemia has followed most types of ethyl alcohol, including beer (Bottura et al., 1949, Freinkel et al., 1963); cane spirit (Bottura et al., 1949, Neves et al., 1950; Peluffo et al., 1958); wine (Peluffo et al., 1958; Jeune et al., 1960; Weill and Gorouben, 1960); gin (Cummins, 1961; Freinkel et al., 1963); vodka (Eathorne, 1962); rum (Teelucksingh and Symonds, 1962); whiskey (Fredericks and Lazor, 1963, Freinkel et al., 1963) and brandy. It has also

followed the intake of cologne (Cummins, 1961), of mixtures of ethyl alcohol, methyl alcohol, gasoline and ethyl acetate, such as "smoke" and "solox", (Brown and Harvey, 1941, Tucker and Porter, 1942) and of liquor taken in Africa, such as zulu beer, shimeyane and gavine. It is apparent, therefore, that the intake of any type of ethyl alcohol can be followed by alcoholic hypoglycaemia.

Whenever a patient is admitted in coma, and has a history of taking alcohol, the possibility of post-alcoholic hypoglycaemia should be considered. This is important where the patients are known chronic alcoholics. In many of the latter cases, acute alcoholic intoxication could be diagnosed with disastrous results, particularly if insulin was administered in treatment of acute alcoholic coma (Bottura et al., 1949). The history, however, is often obtained only after recovery, when dextrose solution has been administered. A smell of stale alcohol on the breath is sometimes helpful. Where no history is obtained, the various manifestations of hypoglycaemia may be recognised. Bizarre neurological signs and abnormal mental states should always suggest the possibility of the diagnosis. (Neame and Joubert, 1961).

In those of my patients that had a lucid interval, the hypoglycaemia occurred 5 - 15 hours after the last drink. Bottura et al., (1949) estimated this period as 12 - 20 hours, and Tucker and Porter (1942) as 8 - 12 hours. The interval between the end of the ingestion of alcohol and the onset of hypoglycaemia appears to be of shorter duration in children (Jeune et al., 1960).

Although two of my patients had more than one attack of

hypoglycaemia after ethyl alcohol and a third had suffered a possible previous episode, the hypoglycaemia in the remainder was an isolated occurrence. One of the patients of Brown and Harvey (1941) had suffered a previous attack and a similar finding has been reported in the cases of Fredericks and Lazor (1963), Field et al (1963), Duckworth and Cooper (1964), Kahil et al., (1964) and Arnould et al., (1964). Considering the fact that most of the adult patients have been chronic alcoholics, it is odd that recurrent attacks have not been noted more frequently.

It is unusual for patients with alcoholic hypoglycaemia to lapse into coma after treatment with even small quantities of intravenous dextrose solution. However one of the patients (Case 2/63), reported here, did so. The recurrence of coma occurred about three hours after the administration of 15 ml of 50% intravenous dextrose solution. It is interesting that the patient had a blood alcohol of 70 mg% after the second period of hypoglycaemia. Pillay (1965) has seen two similar cases. He has recommended an intravenous glucose drip after the initial intravenous dextrose therapy in order to prevent the subsequent death that occurred in his two patients. Bottura et al., (1949), on the other hand, starved a few patients for 24 hours after administering small quantities of intravenous dextrose solution and noted a sustained therapeutic effect.

The finding that excess alcohol can lead to hypoglycaemia has important medicolegal consequences, especially as the symptoms and signs of hypoglycaemia can resemble those found in alcoholic

intoxication (Wauchope, 1933; Tedstrom, 1934; Moersch and Kernohan, 1938). It seems important that a blood sugar estimation, as well as a blood alcohol test, should be done in the latter patients. Arenstein (1962) suggested that a man, who he was defending in Durban, against driving a train under the influence of alcohol, was, in fact, suffering from hypoglycaemia. A blood sugar estimation had not been undertaken. One patient, (Case 10/62) was arrested by the police for drunkeness and was later found in hypoglycaemic coma in her cell. No blood alcohol had been taken and, as it was possible to argue that the patient had been in hypoglycaemia at the time, charges were withdrawn.

The prognosis of post-alcoholic hypoglycaemia in adult patients is good, even after relatively prolonged hypoglycaemia, provided treatment is undertaken. In children, however, delayed treatment often results in permanent damage to the central nervous system or in death.

Finally, it should be mentioned that nearly all the patients were sober, after recovery with intravenous dextrose therapy, and their blood alcohol levels, where performed, were usually within normal levels. Thus, from the clinical aspect, though the hypoglycaemia is the result of alcohol, the disease usually presents as a "post-alcoholic" hypoglycaemia. For this reason the term "post-alcoholic hypoglycaemia" has been used, rather than "alcoholic hypoglycaemia", as the title of this thesis. It indicates that the hypoglycaemia has followed the intake of alcohol and does not suggest that abnormal blood alcohol levels will be associated with the hypoglycaemia. The terms, however, are used synonymously.

SUMMARY

Ethyl alcohol was the cause of the hypoglycaemia in the patients reported here :-

i. The usual causes of hypoglycaemia could not be implicated.

ii In all there was a preceding history of alcohol intake.

iii Toxic factors in the alcohol could not be blamed.

Iv Some of the patients had only taken ethyl alcohol prior to their hypoglycaemic attack.

v The literature showed that carbohydrate was probably utilised during the metabolism of ethyl alcohol and that ethyl alcohol could cause depletion of hepatic glycogen.

vi Hypoglycaemia has been produced in animals with ethyl alcohol.

vii Hypoglycaemia has been produced in man with ethyl alcohol.

Comment is made on the clinical findings in post-alcoholic hypoglycaemia.

PART III

PATHOGENESIS OF POST-ALCOHOLIC HYPOGLYCAEMIA

ETHYL ALCOHOL AND CARBOHYDRATE METABOLISM

ETHYL ALCOHOL AND CARBOHYDRATE METABOLISM

Before discussing the mechanism of alcoholic hypoglycaemia, it seems imperative that the metabolism of ethyl alcohol and the relationship between ethyl alcohol and carbohydrate metabolism should be summarised. Without having a background of these facts it would not be possible to understand some of the factors which are possibly involved in the production of alcoholic hypoglycaemia.

Metabolism of ethyl alcohol*

Ethyl alcohol is metabolised almost completely in the animal organism, with only 10% or less being excreted in the expired air, urine, saliva and sweat (Goldberg, 1963). Alcohol is mainly metabolised in the liver and it is generally agreed that there are three main stages in this metabolic process. These include :-

1. The oxidation of alcohol to acetaldehyde.
2. The conversion of acetaldehyde to acetyl coenzyme A (CoA) either directly or via acetic acid, and
3. The combustion of acetyl CoA to carbon dioxide and water.

(Jacobsen, 1952; Westerfield, 1955, 1961; Goldberg, 1963)

* The terms "alcohol" and "ethyl alcohol" are used interchangeably in subsequent portions of this section.

Blood alcohol disappears along a straight line except at very low levels, when it disappears exponentially. (Jacobsen, 1952; Isselbacher and Greenberger, 1964).

The enzyme which carries out the oxidation of alcohol to acetaldehyde is alcohol dehydrogenase (A.D.H.) and in vivo this takes place in the liver. Alcohol dehydrogenase utilises DPN and is also dependent upon free SH groups in the protein for activity. The most important factor in determining the rate of alcohol metabolism appears to be the rate at which DPNH is oxidised to DPN, and the first step in alcohol oxidation is probably the slowest and consequently the rate limiting step in alcohol metabolism. (Jacobsen, 1952; Westerfield, 1943, 1955, 1961; Lundquist and Wolthers, 1958; Smith and Newman, 1959; Isselbacher and Greenberger, 1964).

According to Westerfield (1961) there are two possible methods by which DPNH can be reoxidised to DPN. Firstly, this could occur via the flavoprotein-cytochrome system. Secondly, by using some other substrate, such as pyruvate, as a hydrogen acceptor the DPNH could be oxidised. The latter reaction, a coupled oxidation - reduction between alcohol and pyruvate has been shown to occur in liver slices. (Leloir and Munoz, 1938). Westerfield (1943) showed that this reaction probably played a part in alcohol metabolism in vivo. However this coupled oxidation-reduction reaction would tend to be self-limiting as lactate would accumulate.

Once acetaldehyde is formed from ethyl alcohol it is converted to acetyl CoA but the exact mechanism is not known. It might or

might not occur via acetic acid (Westerfield, 1961).

The metabolism of acetyl CoA is through the citric acid cycle and alcohol is therefore ultimately burned to Co_2 and H_2O. The final step probably proceeds at all sites where energy from acetyl CoA is needed (Goldberg, 1963).

Carbohydrate and Alcohol Metabolism

A probable relationship between alcohol and carbohydrate metabolism has been considered for a number of years. In 1942 Westerfield et al., wrote : "there is a great deal of evidence that the metabolism of alcohol is favoured by the simultaneous metabolism of carbohydrate". Newman, in 1947, noted: "that some relationship between the rate of alcohol metabolism and carbohydrate metabolism has long been apparent". Jacobsen, in 1952, stated that "the experimental evidence puts it beyond doubt that there is some connection between carbohydrate and alcohol metabolism". The relationship can be divided under two main headings :

1. The effect of alcohol on carbohydrate metabolism,

and

2. The effect of carbohydrate and related substances on the rate of alcohol metabolism.

A brief review of this relationship is necessary as it might help to explain the mechanism of alcoholic hypoglycaemia. Not only has hypoglycaemia followed the intake of ethyl alcohol but, in addition, liver biopsies, performed on admission, have

shown glycogen depletion. It does seem possible that carbohydrate is utilised during the metabolism of alcohol, and, if this is so, it might be partly responsible for the production of hypoglycaemia by ethyl alcohol. Reviews on the subject of carbohydrate and alcohol metabolism have been given by Newman (1947), Jacobsen (1952) and Westerfield (1955). Stress has usually been placed on the effect of carbohydrate substances on alcohol metabolism. On the other hand, some of the effects of alcohol on carbohydrate metabolism are probably significant to the problem of alcoholic hypoglycaemia.

The effect of ethyl alcohol on hepatic glycogen stores

Though there was initial controversy over the effect of ethyl alcohol on the hepatic glycogen stores, later workers have generally agreed that ethyl alcohol can cause a reduction in liver glycogen. Regardless of its mechanism, the fact that ethanol can cause glycogen depletion is significant as it has been shown that alcoholic hypoglycaemia occurs during a period of depletion of hepatic glycogen. In addition, if the glycogen stores of the liver are reduced during or following the administration of alcohol, it does seem as if ethyl alcohol utilises or diverts carbohydrate during its metabolism.

Salant, in 1907, was one of the first investigators to show that ethyl alcohol caused glycogen depletion in experimental animals. He, as the result of the discordant results obtained by Nebelthau (1891) and Kruikoff (1902), administered alcohol

to rabbits. He came to the conclusion that large quantities of alcohol hastened the process by which glycogen was made to disappear from the liver, and that the depletion of hepatic glycogen occurred not during but following the alcoholic intoxication.

Newman et al., (1940), studied the effect of ethyl alcohol on isolated cats' livers when comparing the effect of propylene glycol, other glycols and alcohol on hepatic glycogen. They found that perfusion with ethyl alcohol caused the liver glycogen to decrease 45% as compared with a decrease of only 24% in control unpoisoned livers.

Tennent, in 1941, worked with rats. He found the administration of ethyl alcohol, in sufficiently large amounts (3g per kg) to rats, whose livers initially contained an abundance of glycogen, resulted in a decrease in the amount of glycogen in the liver. This decrease in liver glycogen was accompanied by a rise in blood sugar concentration and Tennent felt that the hepatic glycogen had been mobilised to supply the glucose.

In 1950, Forbes and Duncan found that ethyl alcohol caused a reduction in hepatic glycogen in both starved and unstarved rats. They emphasised that a moderate degree of chronic alcoholisation did not exert any definite effect on the level of glycogen in the liver, and that the reduction in hepatic glycogen only followed acute alcoholic intoxication.

Clark, Wilson and Hulpieu (Clark et al., 1961; Wilson et al., 1962) showed that ethanol lowered the liver glycogen in dogs. In

1962 they showed that an infusion of 1g/kg of ethanol reduced liver glycogen about 20% of its control level; from 13 to 2.5 mg/kg of wet weight of liver.

In 1963 Field et al., showed that there was significantly less glycogen in the livers of rabbits treated with ethanol than in controls.

Thus, it is generally agreed that ethyl alcohol can cause a depletion of hepatic glycogen in animals, and it probably takes place in man. It is significant to the problem of alcoholic hypoglycaemia for, if alcohol depletes the liver of glycogen, it does indicate that during a period of starvation the patient would be more prone to develop hypoglycaemia, if gluconeogenesis was inadequate. The mechanism of the glycogen depletion is not clear but it might be related to the effect of the alcohol on the adrenal medulla and/or to utilisation of carbohydrate during alcohol metabolism.

The effect of ethyl alcohol on the adrenal medulla and its relationship to glycogenolysis

Tennent (1941) has shown that the administration of alcohol to rats causes a rise in blood sugar level and a corresponding decrease in liver glycogen. He felt the hepatic glycogen had been mobilised to supply glucose. It is possible that an increased secretion of adrenaline after the ingestion of ethyl alcohol produces the glycogenolysis. Klingman and

Goodall (1957) have found increased urinary excretion of adrenaline, of medullary origin, after the administration of very large doses of alcohol to dogs. However moderate and small doses of alcohol to cats (Perman, 1960) and to normal subjects (Perman, 1958) have caused an increase in adrenaline output. Perman (1960) did not feel the increase in adrenaline was a reaction to stress and postulated other mechanisms.

A rise in blood sugar level, at the time when alcohol is consumed has been reported in humans by Vartia et al., (1960). This would correlate with the action of increased adrenaline secretion (Kalant, 1962). It appears, therefore, that depletion of hepatic glycogen, after alcohol ingestion, could result from glycogenolysis following stimulation of the adrenal medulla and increased adrenaline secretion. According to Perman (1960), Abelin et al., (1958) have suggested that the release of catecholamines by the body, after alcohol administration, forms a kind of defence mechanism whereby the body accelerates the disappearance of alcohol by increasing its oxidation.

The effect of carbohydrate and related substances on alcohol metabolism

Despite the fact that alcohol has a peculiarly constant rate of oxidation, according to most investigators, some substances have been shown, on occasion, to alter the rate of alcohol metabolism. These have included insulin, glucose, or insulin and glucose, pyruvate, alanine and fructose. In addition, the effect of fasting, and low and high carbohydrate diets, on the rate of alcohol

metabolism have been noted. Though there has been controversy, many investigators have shown that fasting lowers the rate of alcohol metabolism, (Leloir and Munoz, 1938; Mirsky, 1939; Smith and Newman, 1959), and that pyruvate and the other carbohydrate and related substances, mentioned above, increase the rate of alcohol oxidation. It does suggest that carbohydrate substances, or an intermediary in carbohydrate metabolism, can be utilised during the metabolism of alcohol, and it therefore might help to explain the depletion of glycogen produced by ethanol. The literature on this subject is now summarised.

The effect of insulin, or insulin and glucose, on alcohol metabolism

Many investigators have found an increase in alcohol metabolism following the administration of insulin and this effect appears to be more frequent after the administration of both insulin and glucose. The dosage of insulin, in dogs, has usually been about 1 unit/kg. Confirmatory evidence for an association between insulin and alcohol metabolism has been supplied by Clark et al., (1941) who showed a marked decrease in the rate of alcohol metabolism in dogs and cats after pancreatectomy. The mechanism of the increase in alcohol oxidation has been suggested to be the result of insulin increasing glucose oxidation, and this in turn supplying intermediates in carbohydrate metabolism, such as pyruvate, (Westerfield, 1955; Lundquist and Wolthers, 1958), which increase the first stage of alcohol metabolism, i.e., between ethyl alcohol and acetaldehyde.

However, many other writers have stated that they have found

no increase in alcohol oxidation after insulin; despite the fact that they have used similar animals and methods (Gregory et al., 1943), to workers who have shown an increased rate. (Newman and Cutting, 1948). Some investigators have used even higher doses of insulin and others have administered glucose, at the same time, without any effect. (Gregory et al., 1943). The results of various authors are summarised in Table 30.

Investigators have tried to explain the differences in the results. Widmark (1935) noted that he only saw the effect of insulin in dogs with a low metabolic rate and not in animals with a high metabolic rate. Newman and Cutting (1948), Jacobsen (1952) and Westerfield (1955) agreed with this observation, and Westerfield (1955) suggested that insulin plus glucose increased the amount of pyruvate available for the coupled oxidation-reduction reaction, and he felt the magnitude of this effect depended upon the extent to which the reaction was already taking place prior to its administration. However differences in results have been noted in both fed and fasting animals, and the subject remains controversial. (Kinard and Cox, 1958; Newman et al., 1959).

The effect of pyruvate on alcohol metabolism

That pyruvate accelerates alcohol metabolism has been shown by numerous investigators. It is probable that this increase in alcohol oxidation is the result of a coupled oxidation-reduction reaction between pyruvate and alcohol. In this reaction alcohol

TABLE 30

THE EFFECT OF INSULIN AND INSULIN PLUS GLUCOSE ON ALCOHOL METABOLISM

Authors	Species used	Fasting prior to test	Insulin Dosage	Insulin effect	Insulin plus glucose effect
Hirschfelder & Maxwell(1924)	Rabbit		4 units	-	
Supniewski (1926)	Rabbit		1 unit	+	
Harger & Hulpieu(1935)	Dog		1 unit/kg	-	-
Widmark(1935)	Dog		0.85-1.28 unit/kg	+	
Fleming & Reynolds(1935)	Man	Fasted	10 units	-	
Leloir & Munoz (1938)	Rat Liver Slices			-	
Godfarb et al. (1939)	Man		15 units or plus 25 g glucose I.V.	-	+
Clark et al. (1941)	Dog		1 unit/kg or plus 3g/kg glucose	+	+
Greenberg (1942)	Dog	10 hours	1 unit plus 3g/kg glucose		+
Gregory et al. (1943)	Dog	15 hours	1 unit/kg or plus 3g/kg glucose	-	-
Newman & Cutting (1948)	Dog		1 unit/kg	+ (2 out of 3 dogs)	
Clark & Hulpieu (1958)	Dog	16 hours	1 unit/kg or 2 units/kg plus dextrose	?	-
Kinard & Cox (1958)	Dog	Fasted overnight	1 unit/kg or plus 1g/kg glucose	-	-
Newman et al. (1959)	Dog	Fasted overnight	1 unit/kg x 2 at 3 hrs or plus 25g glucose	+	+
Loomis (1950)	Dog		1 unit/kg plus 2g/kg glucose	-	-

+ = Increase in Alcohol Oxidation
- = No increase in Alcohol Oxidation

is oxidised to acetaldehyde and pyruvate is reduced to lactate, and the reaction is dependent upon diphosphopyridine nucleotide (DPN) (Westerfield, 1943). This reaction was first suggested by Leloir and Munoz (1938), when noting increased alcohol oxidation in vitro, by using a liver slice technique, after the addition of pyruvate. Westerfield (1943) subsequently advanced this theory and showed, with in vivo experiments in dogs, both an increase in alcohol metabolism following pyruvate, and a utilisation of pyruvate during alcohol metabolism. In 1959, Smith and Newman showed that the DPN:DPNH ratios, which were markedly decreased during alcohol metabolism in fed and fasting rats, were increased after the administration of pyruvate or alanine, and this occurred particularly in fasting animals. At the same time the blood alcohol was lowered and the lactate increased. They attributed their results to the fact that the cytochrome system per se was probably not active enough to maintain a normal DPN:DPNH ratio and that a superimposed reduction of pyruvate to lactate maintained a higher ratio, thus speeding the rate of alcohol oxidation. They found the effects greater in fasting animals as compared to fed animals.

The acceleration of alcohol metabolism, however, is controversial and it has been disputed by a number of investigators. (Table 31). Hulpieu et al., (1948), stated that they believed pyruvate had no influence on the metabolism of alcohol since they were unable to demonstrate any change in the disappearance of alcohol from the blood due to pyruvate. Bartlett and Barnet (1949), using radio-active techniques, found that pyruvate caused a definite retardation in the rate of combustion of alcohol. The

TABLE 31

THE EFFECT OF SODIUM PYRUVATE ON ALCOHOL METABOLISM

Author	Animal used	Fasting prior to test	Dosage	Method of Administration	Effect on Alcohol Metabolism
Leloir & Munoz (1938)	Rat Liver Slices				+
Westerfield et al. (1942)	Dog	16-18 hours	5-10g x 2	Oral	+
Greenberg (1942)	Dog	10 hours	1g/kg	I. V. or by stomach tube	+
Westerfield et al. (1943)	Dog	fasted	25 ml. 10%	I. V.	+
Gregory et al. (1943)	Dog	15 hours	0. 5g/kg x 2	I. V. or by stomach tube	-
Berg et al. (1944)	Dog	fasted	50ml. 10% x 2	I. V.	+
Hulpieu et al. (1948)	Dog	Some 144 hours	15 g in 3. 5g doses	I. V.	-
Bartlett and Barnet (1949)	Rat		0. 5 mg x 2	Intraperitoneal	-
Kinard et al. (1951)	Dog	16 hours	10g in 125 ml H_2O	Stomach tube	-
Vitale et al. (1954)	Rat		20 mM/ kg	Intraperitoneal	-
Clark & Hulpieu (1958)	Dog	16 hours	0. 33g/kg per hour x 6 hours	I. V. infusion	-
Smith & Newman (1959)	Dog		6%	I. V. in alcohol infusion	-
	Rat	fed	200 mg	Intraperitoneal	+
		fasting	200 mg	Intraperitoneal	++

I. V. = Intravenous;
+ = Increased alcohol oxidation;
- = No increase or decreased alcohol oxidation.

writers emphasised that their experiments differed from those previously reported, and that alcohol or acetaldehyde dehydrogenase could have been accelerated without markedly affecting the total combustion of alcohol.

Westerfield (1955) attributed the inconsistent results to the fact that different species had been used for the experiments by various workers and that pyruvate was effective only when the initial rate of alcohol metabolism was less than maximal and could thus be increased to maximum levels. Jacobsen (1952) made a similar observation. Regardless the subject remains controversial.

The effect of alanine on alcohol metabolism

An increase in alcohol metabolism after alanine administration was first shown by Widmark in 1933. Subsequently it was shown in rabbits by Le Breton (1934), in rat liver slices by Leloir and Munoz (1938), in cats by Eggleton (1940), in dogs by Westerfield et al., (1942), and in dogs and rats by Smith and Newman in 1959.

The fact that alanine can exert an acceleration of alcohol metabolism has been attributed to the fact that pyruvate is formed in the organism from alanine by deamination (Westerfield, 1942; Newman 1947; Lundquist and Wolthers, 1958; and Smith and Newman, 1959). Westerfield et al., (1942) showed an increase of pyruvate and lactate in the blood after the administration of alanine, and they also noted that the effect of alanine was delayed in comparison with corresponding amounts of pyruvate.

Smith and Newman (1959) found that alanine caused an increase in alcohol oxidation in their dogs and yet pyruvate had no effect. Since the effect of alanine had been ascribed to the deamination of alanine to pyruvate they found this paradox difficult to explain. They postulated that the deamination of alanine produced a small steady supply of pyruvate, not enough to produce inhibition of lactic dehydrogenase which they felt probably occurred when pyruvate itself was administered. (Winer and Schwert, 1958). This latter statement possibly explains why, whereas the subject of the action of pyruvate, in the literature, is controversial, investigators have found alanine to increase alcohol metabolism.

The effect of fructose on alcohol metabolism

A number of investigators have shown that fructose increases alcohol metabolism (Pletscher et al., 1952; Lundquist and Wolthers, 1958 and Clark and Hulpieu, 1958). Westerfield (1955) suggested that it increased the amount of pyruvate available for the coupled oxidation-reduction reaction. Lundquist and Wolthers (1958) thought that fructose increased the first stage of alcohol metabolism by supplying glyceraldehyde, an intermediary product of fructose. Glyceraldehyde would cause the oxidation of the ADH-DPNH complex, which would then increase the overall reaction rate of the first stage of alcohol oxidation.

Comment on effect of carbohydrate and related substances on alcohol metabolism

A number of carbohydrate and related substances have

been shown, therefore, on occasions, to speed the rate of alcohol metabolism. The only mechanism by which the increase in alcohol oxidation occurs appears to be through some influence on the reoxidation of DPNH (Westerfield, 1961). This could involve pyruvate in a coupled oxidation-reduction reaction with alcohol, and alanine, fructose, glucose and insulin could work via this mechanism, by increasing the amount of pyruvate available. (Westerfield, 1955). In this reaction alcohol is oxidised to acetaldehyde and pyruvate is reduced to lactate, and the reaction is dependent upon disphosphopyridine nucleotide (DPN) (Westerfield, 1943). Could it therefore be in this way that carbohydrate is utilised during alcohol metabolism ? It does not seem that this reaction alone would cause the depletion of carbohydrate reserves, observed during alcohol metabolism, since it does not involve an irreversible utilisation of carbohydrate (Westerfield, 1943). However it could produce a temporary depletion in carbohydrate reserves and thus lower the blood sugar.

SUMMARY

A brief review of ethyl alcohol metabolism and the relationship between ethyl alcohol and carbohydrate metabolism is given. Ethanol was shown to cause a reduction in hepatic glycogen in animals. It was suggested that two factors could be involved in the production of the glycogen depletion: (1) glycogenolysis following the stimulation of the adrenal medulla by ethyl alcohol, and (2) an increased utilisation of carbohydrate during alcohol

metabolism. These effects of ethyl alcohol could be involved in the production of glycogen depletion seen in alcoholic hypoglycaemia.

ADDENDUM

In a recent article, Forsander et al., (1965) have shown, when studying the effects of ethyl alcohol on perfused rat livers of fed and fasting rats, that ethanol probably increases glycolysis. They have found a greater increase in glucose into the medium from perfused livers of fed rats after the addition of ethanol. With livers from starved rats there was no release of glucose but when ethanol was added a marked uptake of glucose from the medium occurred. A simultaneous release of glycolytic end products, lactate and pyruvate, was noted. They interpreted their findings to indicate increased glycolysis in ethanol perfused livers. This may prove to be the important mechanism by which the glycogen stores of the liver are depleted after the ingestion of ethyl alcohol.

SURVEY OF LITERATURE ON THE MECHANISM OF POST-ALCOHOLIC HYPOGLYCAEMIA

Survey of Literature on the mechanism of Post-alcoholic Hypoglycaemia

(a) Toxic additives :

The initial reports of post-alcoholic hypoglycaemia by Brown and Harvey (1941) and Tucker and Porter (1942), and the reports of Bennett (1953) and Hammack (1957) suggested that the hypoglycaemia was the result of toxic additives in the "smoke" and "solox" imbibed by their North American patients.

Brown and Harvey (1941), considered that, in all probability, in their cases the hypoglycaemia resulted from inhibition of gluconeogenesis, owing to the additives. They recognised that starvation, prior to the alcoholic bout, might have played a role. They also wondered whether a poisonous substance might not have caused an increased utilisation of carbohydrate with resulting hypoglycaemia during the period of glycogen depletion.

Tucker and Porter (1942) suggested that there had either been an inhibition of gluconeogenesis, or else a temporary generalised damage to liver function due to a toxic substance in the "solox" imbibed by their patients.

Bennett (1953) felt the exact mechanism was not known but suggested that decreased food intake during the alcoholic bout might have, in some way, reduced the blood glucose. He noted that

no significant hepatic dysfunction was demonstratable.

Hammack (1957) felt solox "smoke" intoxication was a relatively common cause of profound hypoglycaemia, but thought the cause was not known. He noted that there had been no evident hepatic disease but he wondered, when comparing the disease to vomiting sickness in Jamaica, whether glycogen depletion was not a contributory factor.

(b) Ethyl Alcohol :

Bottura et al., in 1949, were the first investigators to suggest that ethyl alcohol was the cause of the hypoglycaemia. Subsequently other investigators suggested that ethyl alcohol was the cause of the hypoglycaemia. Though the cause seemed probable at the time, the mechanism was difficult to explain.

Bottura et al., (1949) wondered whether the fatty liver, seen amongst their patients, was the cause of a low production of glucose and hence the hypoglycaemia. However they realised that it did not explain why a small quantity of glucose should produce permanent recovery, despite the fact that some of their patients fasted for 24 hours subsequent to treatment. They felt that there had been an inhibition of gluconeogenesis and they showed that this continued during relatively low blood alcohol levels, and thought, therefore, that it could not depend on the alcoholic intoxication. They emphasised that there had been a period of fasting following the alcoholic bout while the patients were intoxicated. Suprarenal or Hypophyseal deficiency was excluded on the fact that their patients did not return into hypoglycaemic

coma despite a period of fasting of 24 hours after administration of a small quantity of glucose.

Neves et al., (1950) emphasised that post-alcoholic hypoglycaemia could occur in patients that had normal livers. They thought there was an inhibition of gluconeogenesis but stated that it was unrelated to the blood alcohol level. They felt the fasting that followed the acute alcoholic intoxication aggravated the inhibition of gluconeogenesis.

Peluffo et al., (1958) postulated that the hypoglycaemia might be due to rapid liberation of insulin as a result of rapid absorption of alcohol by fasting patients.

Jeune et al., (1960) felt that the period of starvation, before and after the ingestion of alcohol, was involved, but thought that it could not explain why the hypoglycaemia followed shortly after it. The authors stated that, without understanding its mechanism, there was a severe attack on the hepatic cells resulting in inhibition of gluconeogenesis and glycogenolysis.

Weill and Gorouben (1960) suggested that alcohol had an inhibitory effect on the diencephalon which resulted in a fall in blood sugar, through the medium of the suprarenal medulla.

Cummins (1961) thought that alcohol could interfere with gluconeogenesis or inhibit glycogenolysis. He also noted that during the metabolism of alcohol glucose was utilised.

Neame and Joubert in 1961, suggested that three factors may have played a part in the production of hypoglycaemia in their

patients :

(1) A period of inadequate food intake;

(2) Increased utilisation of glycogen stores during the metabolism of ethyl alcohol, and

(3) Decreased glycogen synthesis during the utilisation of these stores.

They knew from liver biopsies performed on admission during the hypoglycaemic coma, that there was glycogen depletion, and thought that the period of deficient intake of food and, more important, the concomitant utilisation of carbohydrate during alcohol metabolism had caused it. They felt that the quantity of ethyl alcohol consumed would influence the ultimate amount of carbohydrate utilised. (Forsander, 1963). However, they realised that hepatic glycogen depletion alone could not be expected to cause the hypoglycaemia, and that there must, therefore, have been a transient failure of gluconeogenesis during the period of glycogen depletion. They suggested that the inhibition of gluconeogenesis might have resulted from a toxic action of ethyl alcohol on the hepatic cells, but felt that further study of adrenal function in their patients was necessary. In a further article in 1963, Neame and Joubert emphasised that some of their patients on whom adrenal function tests were done, had shown pituitary disturbance. They also noted that the lack of food intake during alcoholic intoxication should be included in the period of fasting prior to the hypoglycaemic attack.

Roche et al., (1963) felt that the utilisation of glucose by ethyl alcohol and its inhibition of gluconeogenesis resulted in the hypoglycaemia. They felt that chronic alcoholism, malnutrition

and fasting were important factors and probably reduced the body's glycogen reserves.

Field et al., (1963) produced hypoglycaemia with ethyl alcohol. After studying both clinical and experimental alcoholic hypoglycaemia in man and the effect of ethanol on man and animals, they stated that they considered an inhibition of gluconeogenesis to be primarily responsible for the hypoglycaemia, in conjunction with depletion of liver glycogen (as shown by lack of response to glucagon administration). They emphasised that a preceding period of fasting of about 40 hours was required to produce alcoholic hypoglycaemia. Furthermore, Field et al., (1963) noted that there was a rise in plasma free fatty acids. With increased blood insulin an increase would be expected and not a decrease. They felt, therefore, that the ethanol-induced hypoglycaemia was not mediated primarily by insulin. They observed decreased urea formation and thought the defect in gluconeogenesis was due to a defect in the oxidative deamination of amino-acids and not to the formation of amino-acids from protein breakdown. The mechanism by which ethanol inhibited urea production was not known. They speculated that it was a consequence of changes in DPN and DPNH levels in the liver, resulting from the metabolism of alcohol. They postulated that the resulting increased levels of DPNH lead to decreased glutamic dehydrogenase activity. They felt the decrease in this activity would result in decreased deamination of amino-acids and consequently to decreased conversion of amino-acids into glucose and glycogen -- in other words to decreased gluconeogenesis.

(Isselbacher and Greenberger, 1964).

Freinkel et al., (1963), after producing alcoholic hypoglycaemia, with ethyl alcohol, in patients that had already been admitted in this condition following an alcoholic debauch, concluded that a preceding fast was necessary to produce alcoholic hypoglycaemia. However, they were able to produce hypoglycaemia after an overnight fast in these patients, whereas, in normal subjects a minimum of two to three days fasting was necessary. They showed that the hypoglycaemia was not due to hyperinsulinism and, as a result of their findings with glucagon, concluded that there was glycogen depletion during alcoholic hypoglycaemia. They felt there was no acute hepatocellular toxicity in their patients. They thought that, despite possible diverse mechanisms, all of their patients (nine cases) displayed some limitation in their reserve for regulation of endogenous carbohydrate metabolism. All nine patients had responded with excessive lowering of the blood sugar or deficient counter regulation to at least one of the procedures that acutely (insulin, tolbutamide) or chronically (starvation) challenged the fasting equilibrium between endogenous glucose production and glucose utilisation.

SUMMARY

A survey of the literature on the mechanism of alcoholic hypoglycaemia in man is given.

FACTORS ASSOCIATED WITH POST - ALCOHOLIC HYPOGLYCAEMIA

Factors associated with Post-alcoholic hypoglycaemia

Incidence

It would not be possible from my findings to judge the incidence of the disease but, during a survey of hypoglycaemia in 1960, it was the commonest cause amongst adult African patients at King Edward VIII hospital (Neame and Joubert, 1961). In addition there was little doubt that it remained the most common cause during 1961 and 1962.

Age, Sex and racial incidence

The majority of adult patients with alcoholic hypoglycaemia, reported in the literature, have been males. Among my adult cases there were 29 males and 20 females.

My patients varied from 4 to 70 years and in the literature patients have ranged from 3 to 81 years. Considering the few cases of alcoholic hypoglycaemia reported, and the infrequency of children ingesting alcohol compared with adults, there appear to be a large number of cases reported in children (Table 32). One wonders, therefore, whether children are more prone than adults to develop hypoglycaemia after ingesting alcohol.

It would not be possible from my findings to judge the incidence of the disease amongst the various race groups in South

TABLE 32

ALCOHOLIC HYPOGLYCAEMIA IN CHILDREN

Author	Number of Cases	Ages (years)
Neves et al., (1950)	1	6
Hammack (1957)	1	4
Peluffo et al. (1958)	2	6, 4
Jeune et al. (1960)	1	$4\frac{1}{2}$
Weill & Gorouben (1960)	1	$3\frac{2}{3}$
Cummins (1961)	2	6, 3
Neame & Joubert (1961), (1963) and Thesis.	3	5, 4, 4
Teelucksingh & Symonds (1962)	5	4, 5, 3, 4, 4
Freinkel et al. (1963)	1	16
Ramon-Guerra et al. (1964)	2 ? 4	4, - 6
Arnould et al. (1964)	2	$3\frac{1}{2}$, 5

Africa as our hospital admitted only African and Indian patients. Duckworth and Cooper (1964) have found post-alcoholic hypoglycaemia fairly common amongst the African population in Johannesburg. It has been noted amongst two Coloured patients at Addington hospital in Durban (Eathorne, 1962).

Alcoholic hypoglycaemia undoubtedly has a world-wide distribution and the race and number of patients reported are shown in Table 33. Including the 52 patients reported here, I have been able to find 136 cases in the world literature. Of these, about one-sixth have been children.

Chronic alcoholism and alcoholic hypoglycaemia

Twenty-five of my patients were regarded as chronic alcoholics and six (including three children) as non-alcoholics. The remaining 18 patients were heavy weekend drinkers. Thus, from this series, it is possible to state that chronic alcoholism is not a necessary factor in the production of alcoholic hypoglycaemia. (Neame and Joubert, 1961, 1963). In the literature there are many well documented paediatric cases to confirm this fact. (Table 32). In addition Field et al., (1963) and Freinkel et al., (1963) have produced alcoholic hypoglycaemia in normal adults.

On the other hand the vast majority of adult patients described have been chronic alcoholics (Table 34). This is not surprising as an important factor in the production of alcoholic hypoglycaemia is an excessive intake of ethyl alcohol. This would be a common occurrence in the life of a chronic alcoholic. In addition, as will be

TABLE 33

RACE AND ALCOHOLIC HYPOGLYCAEMIA

Authors	Race	Number
Brown & Harvey (1941)	American	6
Tucker & Porter (1942)	American	4
Bottura et al., (1949)	Brazilian	11
Neves et al., (1950)	Brazilian	20
Hammack (1957)	American	7
Peluffo et al., (1958)	Uruguayan	2
Hed (1958)	Scandinavian	2
Jeune et al., (1960)	French	1
Weill & Gorouben (1960)	French	1
Cummins (1961)	American	2
Neame & Joubert (1961), (1963) and Thesis	South African (46 African, 6 Indian)	52
Teelucksingh & Symonds (1962)	Trinidadian	5
Fredericks & Lazor (1963)	American	1
Field et al., (1963)	American	1
Freinkel et al., (1963)	American	9
Roche et al., (1963)	French	1
Ramon-Guerra et al., (1963)	Uruguayan	4
Duckworth & Cooper (1964)	South African (African)	1
Marks & Medd (1964)	British	1
Kahil et al., (1964)	American	1
Gumpel & Kaufman (1964)	American	1
Arnould et al., (1964)	French	3

TABLE 34

CHRONIC ALCOHOLISM AND ALCOHOLIC HYPOGLYCAEMIA

Authors	Number of Adult Cases reported	Chronic Alcoholic	Non-Alcoholic
Brown & Harvey (1941)	6	6	
Tucker & Porter (1942)	4	4	
Bottura et al., (1949)	11	11	
Neves et al., (1950)	19	18	1
Hammack (1957)	5	"usually present"	?
Hed (1958)	2	2	
Neame & Joubert (1961) and Thesis	49	25	3*
Fredericks & Lazor (1963)	1	1	
Field et al., (1963)	1	1	
Freinkel et al., (1963)	8	8	
Roche et al., (1963)	1	1	
Marks & Medd (1964)	1	1	
Gumpel & Kaufman (1964)	1	1	
Kahil et al., (1964)	1	1	
Arnould et al., (1964)	1	1	

* Most of the remaining patients were regarded as "weekend drinkers".

discussed later, fasting is an important predisposing factor in the production of post-alcoholic hypoglycaemia and as chronic alcoholics often imbibe excessively without eating, hypoglycaemia can be expected to occur more commonly amongst them than amongst non-alcoholics.

Nutrition and alcoholic hypoglycaemia

Of the patients reported here 25 showed obvious signs of poor nutrition, 25 were of fair nutrition and 2 (children) were well nourished. From these results it can be said that poor nutrition is not an essential factor in the production of alcoholic hypoglycaemia in children but might be a factor in the adult patient. However, Hed (1958) stated that the "general condition was good in all his patients", while Duckworth and Cooper (1964) felt their patient was "well-nourished". In addition alcoholic hypoglycaemia has been produced in normal adult volunteers by Field et al., (1963) and Freinkel et al., (1963). It is apparent therefore that poor nutrition is not an essential factor for the production of alcoholic hypoglycaemia in adults.

However, the patients reported by Brown and Harvey, (1941), were from a low income level and on poor diets, while many of the other patients reported have been of poor nutrition. (Bottura et al., 1949; Neves et al., 1950; Hammack, 1957; Peluffo et al., 1958; Fredericks and Lazor, 1963; Gumpel and Kaufman, 1964; Kahil et al., 1964). One wonders, therefore, whether poor nutrition is not a predisposing factor. The fact that poor nutrition has been found in a number of patients suffering from alcoholic

hypoglycaemia is probably partly due to the association with chronic alcoholism and partly due to the fact that the poor often cannot afford to eat when they drink, and, as will be shown later, the fasting state predisposes to alcoholic hypoglycaemia.

Prior fasting and alcoholic hypoglycaemia

Thirty of the patients reported in this thesis, had fasted for a varying period of time prior to their drinking bout. In surveying the literature, prior fasting has been reported in many of the patients. (Table 35). As will be noted later, fasting before imbibing alcohol is an important predisposing factor in the production of experimental alcoholic hypoglycaemia. However, nine of my patients had eaten before or during their alcoholic bout and Teelucksingh and Symonds (1962) also noted that at least two of their five patients had not been fasting prior to the intake of alcohol. In addition some of the patients of Freinkel et al., (1963) had eaten full meals during the day on which they had imbibed. Thus a period of fasting prior to the alcoholic bout, though an important predisposing factor, is apparently not an essential factor for the production of clinical alcoholic hypoglycaemia.

Liver disease and alcoholic hypoglycaemia

Forty-two of my patients showed evidence of a transient hepatitis by biochemical investigations, and in 20 of these liver biopsy showed small foci of hepatic necrosis. As already described, the serum transaminase (S. G. O. T.), serum bilirubin

TABLE 35

PRIOR FASTING AND ALCOHOLIC HYPOGLYCAEMIA

Author	Number of Cases reported	Fasting	Non - Fasting
Brown & Harvey (1941)	6	6	
Tucker & Porter (1942)	4	? 4	
Bottura et al. (1949)	11	11	
Neves et al. (1950)	20	?	?
Hammack (1957)	6	"Majority"	?
Peluffo et al., (1958)	2	2	
Hed (1958)	2	?	?
Jeune et al., (1960)	1	1	
Weill & Gorouben (1960)	1	? 1	
Cummins (1961)	2	?	?
Neame & Joubert, (1961), (1963) & Thesis	52	30	9
Teelucksingh & Symonds (1962)	5	2	2, ? 1
Fredericks & Lazor (1963)	1	1	
Field et al., (1963)	1	1	
Freinkel et al., (1963)	9	? 6	3
Roche et al., (1963)	1	1	
Marks and Medd (1964)	1	?	?
Gumpel & Kaufman (1964)	1	? 1	
Kahil et al., (1964)	1	1	
Arnould et al., (1964)	3	3	

and the urinary urobilin usually showed maximum levels soon after admission and, in studying the progression of the disease, it became evident that there had been an acute liver injury followed by rapid improvement. It suggested that the acute transient hepatitis was the result of the acute alcoholic debauch preceding admission. As already noted a similar transient hepatitis (Green et al., 1963) and foci of necrosis, on liver biopsy, have been seen by others and have been ascribed to ethyl alcohol. (Phillips and Davidson, 1954; Gall, 1957; Beckett et al., 1961, 1962; Green et al., 1963). In these cases there was no accompanying hypoglycaemia. The question arises whether the transient hepatitis is involved in the production of the alcoholic hypoglycaemia, or whether it is merely an association, the hepatitis and the hypoglycaemia being related only by their common aetiology, ethyl alcohol.

In surveying the literature on alcoholic hypoglycaemia, the majority of writers have stated that liver disease was absent, or else there was a mild abnormality. In most cases, however, daily testing of the transaminases, serum bilirubin and urinary urobilin and bilirubin was not performed. Brown and Harvey (1941) noticed depressed liver function in one of their six patients. In two patients, amongst the four patients of Tucker and Porter (1942), in whom tests of liver function were done, there was questionable evidence of disease in one. The patients of Bottura et al., (1949) had fatty livers and they felt that the hepatic condition of their patients played a part in the production of the hypoglycaemia. Neves et al., (1950) also found fatty livers but they were of the opinion that the degenerative changes in the liver were not the

primary factor in the production of the hypoglycaemia; in fact they found normal livers in some of their patients. Hammack (1957) noted that there was no evidence of hepatic disease to account for the hypoglycaemia in his study. The two patients described by Hed (1958) had slight fatty livers but the serum bilirubin and serum proteins showed normal values. Jeune et al., (1960) observed no liver disease in their patient but they felt the site of action in the production of the hypoglycaemia was the liver. The patients of Fredericks and Lazor (1963) showed normal liver function tests and liver biopsy. Field et al., (1963) noted minimally deranged liver function tests in their patient. A few of the patients of Freinkel et al., (1963) showed slightly raised serum bilirubins and serum S.G.O.T. Gumpel and Kaufman (1964) noted no signs of liver disease other than hepatomegaly.

Thus, in general, most investigators have found little, if any, hepatic disturbance in their patients admitted in alcoholic hypoglycaemia. However, Clark et al., (1961) when producing alcoholic hypoglycaemia in dogs, noted fatty metamorphosis and foci of hepatic necrosis on histological examination of their livers. It is probable that the lesion was merely an association as they had been administering ethyl alcohol daily to their dogs for a prolonged period prior to the onset of the hypoglycaemic attack.

In summary it can be said that liver disease, as found in my patients, is not considered to be the cause of the alcoholic hypoglycaemia.

Pituitary - adrenal function and alcoholic hypoglycaemia

As noted previously, urinary steroid excretion was performed on 33 of my patients during the first ten days following alcoholic hypoglycaemia. In the majority there was evidence of inactivity of the suprarenal cortex. Patients in whom A. C. T. H. stimulation tests were done showed variable responses, but of the nine patients in whom the prestimulation values were low, five showed a good response indicating normal adrenal function, and probable pituitary dysfunction. In some of these patients a very low value followed the A. C. T. H. response test, apparently indicating adrenal exhaustion.

Of the patients suffering from alcoholic hypoglycaemia reported in the literature, very few have had adrenal function tests performed. Though no adrenal function tests were done, Tucker and Porter (1942) felt that the small stature of one of their patients, the flat glucose tolerance curves and the low metabolic rate were definitely suggestive of hypopituitarism. They thought it was likely that the patient had 'hypoglycaemic unresponsiveness' associated with anterior pituitary insufficiency, and that severe hypoglycaemia was precipitated by alcoholism and starvation. Bottura et al., (1949), on the other hand, felt that suprarenal or hypophyseal insufficiency could be excluded, as despite starvation of 24 hours duration of some of his patients, after treatment with a small quantity of intravenous glucose, the hypoglycaemia did not recur. In addition, clinical evidence of

endocrine disturbance has not been noted in the various reports in the literature.

Of the few patients reported in the literature, where 17-ketosteroid and 17-glucocorticoid excretions were done, at least one patient had a low 17 - hydroxycorticosteroid excretion (Field et al., 1963). (Table 36). Freinkel et al., (1963) concluded, from studies of basal steroid excretion and responsiveness to metopirone, that subtle disturbance in pituitary adrenal inter-relationships were displayed in two of their patients.

Further investigation of the steroid excretion in alcoholic hypoglycaemia is required.

Differences between clinical and experimental alcoholic hypoglycaemia

As noted previously, it has been shown that ethyl alcohol can cause hypoglycaemia in normal volunteers (Field et al, 1963, Freinkel et al., 1963) and in patients initially admitted in hypoglycaemia following a drinking bout (Field et al., 1963, Freinkel et al., 1963). Recognition of the clinical entity and the aetiological role of ethyl alcohol has, however, resulted in certain differences being noted between experimental and alcoholic hypoglycaemia.

The absolute requirement of a minimum period of starvation of about 40 hours before the hypoglycaemic response was elicited in normal volunteers (Field et al., 1963) is not

TABLE 36 URINARY STEROID EXCRETIONS

Author	Number of cases	Sex	Age	17-ketosteroids (mg/24 hours)	17-ketogenic steroids or 17-hydroxycorticosteroids (mg/24 hours)
Fredericks & Lazor (1963)	1	F	53	Normal	Normal *
Roche et al., (1963)	1	F	32	5.4	--
Field et al., (1963)	1	M	52	8.0	2.6
Freinkel et al., (1963)	2	M	60	5.4	10.4
		M	75	3.8	5.7
Marks & Medd (1964)	1	M	35	4.4	9.2
Arnould et al., (1964)	1	M	48	5.6	5.9

* Values not given

usually satisfied in the clinical form of the disease. In addition, contrary to experience in normal adults, the hypoglycaemic response was elicited after a shorter period of starvation in patients previously admitted in alcoholic hypoglycaemia. (Freinkel et al., 1963). Finally a few of the patients reported in the literature had eaten before or during their ingestion of alcohol, and consumption of alcoholic beverages containing substantial quantities of carbohydrate, preceded the hypoglycaemic episodes in a number of my cases.

A further discrepancy in the experimental and clinical varieties is the time factor. The experimental hypoglycaemic response follows within a few hours of the administration of alcohol, whereas in the clinical varieties, there appears to be a lag period of some 5 - 15 hours after the drinking bout, which may have been protracted.

The difference between the clinical and experimental forms of alcoholic hypoglycaemia requires further investigation.

Differences between adult and childhood cases of alcoholic hypoglycaemia

The number of childhood cases, reported in the literature, suggests that they are more prone than the adult to develop alcoholic hypoglycaemia. In addition, there seem to be certain differences in the presentation of adult and childhood cases. In children the onset of the hypoglycaemia after the ingestion of the alcohol, usually follows after a shorter period of time than seen

in adult cases. In addition, all the children have taken alcohol accidentally, usually when hungry, whereas the majority of adults have been chronic alcoholics. Finally the nutritional state of the children has usually been good in comparison with many of the adult cases. This latter difference is probably due to the association of adult cases with chronic alcoholism. A further difference is in prognosis. It is usual for the adult patient to survive the episode of alcoholic hypoglycaemia where treatment has been instituted. On the other hand,the child commonly dies or shows residual cerebral damage (post hypoglycaemic damage) if the hypoglycaemia is not treated soon after the onset of the hypoglycaemia.

SUMMARY

Various factors associated with alcoholic hypoglycaemia have been described. The exact incidence of the disease is not known but it is of a world wide distribution. It occurs amongst children and adults but the former seem to be more prone to develop the disease. Chronic alcoholism has been noted in the majority of adult cases but it is not a necessary factor. Likewise poor nutrition has been a common association in adult patients. It is possible that both chronic alcoholism and poor nutrition, though not essential factors, are predisposing factors. Prior fasting is a common occurrence before the onset of alcoholic hypoglycaemia and it seems to be an important predisposing factor in the clinical form of the disease. In experimental alcoholic hypoglycaemia in normal volunteers a period of starvation of at least 40 hours seems to be obligatory.

The presence, or not, of liver disease or pituitary-adrenal disturbance amongst the reported cases is discussed. Finally

possible differences between the experimental and clinical forms of the disease and between childhood and adult cases are mentioned.

MECHANISM OF POST -

ALCOHOLIC HYPOGLYCAEMIA

MECHANISM OF POST-ALCOHOLIC HYPOGLYCAEMIA

Two major factors should be considered in the mechanism of production of post-alcoholic hypoglycaemia. These are (1) hepatic glycogen depletion and (2) inadequate gluconeogenesis. The absence of liver glycogen during alcoholic hypoglycaemia is a definite occurrence while inadequate gluconeogenesis is a logical assumption. The exact mechanism, however, remains undetermined.

Glycogen depletion and alcoholic hypoglycaemia

The occurrence of hepatic glycogen depletion

That glycogen depletion occurs during alcoholic hypoglycaemia is shown by the finding of absence of glycogen on liver sections taken during the post-alcoholic hypoglycaemic coma, from indirect evidence of glucagon and adrenalin administration, and from the fact that there is decreased hepatic glucose output during the hypoglycaemia.

The absence of hepatic glycogen was proved by my finding no glycogen on six liver biopsies performed on admission. (Neame and Joubert, 1961). In addition, in producing alcoholic hypoglycaemia in dogs, Clark et al., (1961) and Wilson et al., (1962) noted depleted hepatic glycogen stores.

Indirect evidence of glycogen depletion has been supplied by Field et al., (1963) and Freinkel et al., (1963) who administered glucagon to their patients while in hypoglycaemic coma, and noted no increase in the blood sugar during the subsequent thirty minutes. In contrast, Field et al., (1963) exercised their patient during a 71 hour fast without supplying ethanol, and then administered 1 ml. glucagon to the patient, and produced a prompt rise in blood glucose. They also showed that ethanol was not inhibiting the hyperglycaemic response of glucagon, and therefore concluded that the failure of glucagon to raise the blood sugar during ethanol induced hypoglycaemia was consistent with a marked depletion of liver glycogen at the time of the hypoglycaemia.

Bottura et al., in 1949, gave one of their patients adrenalin during the hypoglycaemic coma and noted no alteration in the level of blood sugar. Clark et al., (1961) gave 25 microgram of epinephrine per kg to two dogs in alcoholic hypoglycaemia and thirty minutes later noted a minimal rise in their initial blood sugar levels. They interpreted their findings as evidence that the livers of their dogs were either depleted of glycogen, or else there was inhibition of glycogen release. Subsequently they showed, by direct examination of the liver, that the liver glycogen was lowest in the dogs that had received ethanol.

Lochner and Madison (1963) showed, in dogs rendered hypoglycaemic after ethanol administration, that the hepatic glucose output fell from a mean control of 52.4 mg/min. to 6.6 mg/min.

at 120 minutes, suggesting that the hepatic glycogen stores were markedly depleted.

Thus, in summary, it can be said that there is sufficient evidence to show that there is a state of glycogen depletion during alcoholic hypoglycaemia. In addition, as will be shown later, there is little doubt that alcoholic hypoglycaemia cannot occur unless the hepatic glycogen stores have been depleted.

The pathogenesis of the glycogen depletion noted during alcoholic hypoglycaemia

The glycogen depletion found during alcoholic hypoglycaemia appears to be the result of three main processes :

(1) A period of fasting prior to the hypoglycaemic coma (Neame and Joubert 1961, 1963).

(2) A concomitant utilisation of carbohydrate during alcohol metabolism (Westerfield and Schulman, 1959; Neame and Joubert 1961).

(3) A stimulation of the adrenal medulla by ethyl alcohol with resulting glycogenolysis.

Period of Fasting:

The fasting can be divided into two main periods. Firstly, there can be a deficient intake of food preceding the ingestion of alcohol, and, secondly, as in all cases, a period of starvation during the alcoholic coma. Much emphasis has been placed on a period of fasting prior to the alcoholic bout in discussing the

mechanism of alcoholic hypoglycaemia (Field et al., 1963), and this antecedent period of fasting is definitely a most important factor in reducing the glycogen stores of the liver. However, not all of my patients (9 cases) or some in the literature (Teelucksingh and Symonds, 1962, and Freinkel et al., 1963), were fasting prior to their alcoholic bout, and yet hypoglycaemia followed. In addition, in 18 of my patients, substantial quantities of carbohydrate were present in their alcohol. What, therefore, is also of importance in producing the glycogen depletion, is a period of fasting following the alcoholic bout when the patient is in alcoholic coma. (Bottura, 1949; Neame and Joubert, 1963).

A concomitant utilisation of carbohydrate during alcohol metabolism :

As already shown, ethyl alcohol can cause glycogen depletion in experimental animals. In addition, in studying the metabolism of alcohol, there appears to be evidence to show that glycogen depletion results from a utilisation of carbohydrate during alcohol metabolism (Westerfield and Schulman, 1959). It is possible that this depletion is partly the result of increased glycolysis produced by ethyl alcohol (Forsander et al., 1965).

Glycogenolysis following adrenaline release:

As shown previously, ethyl alcohol can stimulate the adrenal medulla with resulting release in adrenaline. Glycogenolysis would follow. This effect might play a part in the depletion of liver glycogen seen in alcoholic hypoglycaemia.

The importance of glycogen depletion in the production of alcoholic hypoglycaemia

It seems from the production of alcoholic hypoglycaemia in both animals and man that hypoglycaemia has been produced only in those livers which were devoid of glycogen. Matunaga (1942) who produced hypoglycaemia in rabbits after administering alcohol, first depleted the liver of glycogen with infusions of emulsified lecithin. Clark et al., (1961) and Lochner and Madison (1963) produced hypoglycaemia in dogs with ethanol, after they had been fasting. Wilson et al., (1962) produced alcoholic hypoglycaemia in dogs and cats by first depleting the livers of glycogen with oxythiamine. They were unable to produce hypoglycaemia with oxythiamine or ethanol alone.

Most of the clinical reports on alcoholic hypoglycaemia have stressed the importance of a period of fasting prior to the alcoholic bout or starvation during the alcoholic coma. Field et al., (1963) produced alcoholic hypoglycaemia in normal volunteers after approximately 40 hours of fasting. Similar amounts of ethanol were ineffective after an over-night fast. However, Field et al., (1963) did not vary the amount of ethanol given, and it would have been interesting to see whether larger amounts of alcohol would have produced alcoholic hypoglycaemia after a lesser period of fasting. Forsander (1963) has shown that blood sugar values decrease in inverse proportion to the amount of alcohol that has been consumed. Freinkel et al., (1963) noted that alcoholic hypoglycaemia was more acute and pronounced in patients, previously

admitted in alcoholic hypoglycaemia, after a three day fast as compared with an over-night fast.

Thus glycogen depletion is an essential factor for the production of alcoholic hypoglycaemia. Without the onset of hepatic glycogen depletion it appears that alcoholic hypoglycaemia does not take place, but, on the other hand, glycogen depletion alone will not result in hypoglycaemia as gluconeogenesis would maintain the blood sugar. One must therefore postulate either an inhibition of gluconeogenesis or else an imbalance between the production and utilisation of glucose during the period of hepatic glycogen depletion, if hypoglycaemia is to result.

Inadequate gluconeogenesis and alcoholic hypoglycaemia

From the earliest reports (Brown and Harvey 1941; Tucker and Porter 1942) it seemed logical to hypothesise an interference with gluconeogenesis in order to explain the mechanism of post-alcoholic hypoglycaemia. The fact that the hypoglycaemic coma was found during or following a period of starvation indicated that the hypoglycaemia probably occurred after the glycogen stores of the liver had been depleted of glycogen. Now that it has been shown that there definitely is glycogen depletion during the alcoholic hypoglycaemia, (Neame and Joubert, 1961), this possibility requires thorough investigation. In the production of experimental alcoholic hypoglycaemia in dogs and cats, Wilson et al., (1962) concluded that two factors were involved: one a depletion of liver glycogen, and the other an inhibition of

gluconeogenesis. Lochner and Madison (1963) stated, after studying the hepatic glucose output in dogs rendered hypoglycaemic by alcohol, that their data indicated that ethanol had a profound effect on carbohydrate metabolism in the fasted animal, and that it was consonant with the view that alcohol impairs hepatic gluconeogenesis.

The exact mechanism is still not known but theoretically inhibition of gluconeogenesis could be produced either by interference with the activity of enzymes in the liver related to gluconeogenesis, or to disturbance of the hormonal (pituitary-adrenal) control of gluconeogenesis.

Insufficient work has been done on the adrenal-pituitary function in alcoholic hypoglycaemia, but there are indications that it may be disturbed, possibly only temporarily. Freinkel et al., (1963) have shown that the administration of cortisone will alter the metabolic response to alcohol in man, and that alcoholic hypoglycaemia could be prevented by its administration. In the patients reported in this thesis, on which steroid excretions were done, there is evidence of pituitary-adrenal disturbance in many of them and this is possibly of pituitary origin in most of them. Whether ethanol can cause a temporary pituitary dysfunction should be investigated.

It seems likely that disturbance in activity of an enzyme, or enzymes, in the liver, is a means by which gluconeogenesis is inhibited. As already mentioned, Field et al., (1963) have shown a decrease in urea formation after the administration of ethyl alcohol. They thought the defect in gluconeogenesis was due to a

defect in oxidative deamination of amino-acids and speculated that it was a consequence of changes in DPN and DPNH levels in the liver resulting from the metabolism of alcohol. They postulated that the resulting increased level of DPNH lead to decreased glutamic dehydrogenase, an important enzyme involved in the deamination of amino-acids. This consequently decreased the conversion of amino-acids into glucose and glycogen; in other words decreased gluconeogenesis. However, in diabetes mellitus, the liver cell is known to contain a high level of DPNH as a result of the increased long chain fatty acid oxidation (Wieland et al., 1961) and gluconeogenesis from amino-acids is greatly increased.

Lochner and Madison (1963) and Cohen et al., (1963) have attributed the effects of alcohol on glucose output to be the result of altered ratios of DPN and DPNH. Lochner and Madison (1963) showed that there was a marked reduction in hepatic glucose output in fasted dogs given ethanol. In addition ethanol was shown to block the capacity of α-ketoglutarate and glutamate (DPN dependent precursors of glucose) administration to elevate the blood glucose in these animals. They thought this supported the thesis that ethanol, by virtue of decreasing available hepatic DPN, interfered with gluconeogenesis, decreased hepatic glucose output and thereby produced hypoglycaemia. However Cahill (1964) felt it was difficult to ascribe diminished glucose synthesis solely from a change in this ratio, since DPN is necessary in certain reactions whereas DPNH is needed in others.

Imbalance between glucose production and utilisation in alcoholic hypoglycaemia

The onset of alcoholic hypoglycaemia may well be the result of imbalance between glucose production and utilisation during a period of hepatic glycogen depletion. Ethyl alcohol probably both decreases the production of glucose, by interfering with gluconeogenesis (Field et al., 1963; Lochner and Madison, 1963; Cohen et al., 1963), and increases the utilisation of glucose via glycolysis. (Forsander et al., 1965). The nett effect could be a low blood sugar or, in other words, hypoglycaemia. Other related and regulating factors in the production and utilisation of glucose might be involved and the mechanism of alcoholic hypoglycaemia need not be identical in each patient. The fact that the administration of cortisone prevented the onset of alcoholic hypoglycaemia (Freinkel et al., 1963) supports this hypothesis. The increased gluconeogenesis, that followed the administration of cortisone, presumably prevented the imbalance between production and utilisation of glucose. This theory might also account for the differences noted between clinical and experimental alcoholic hypoglycaemias, as these differences could be related to the various factors involved in the regulation of glucose homoeostasis. Many of the differences, however, seem to be due to the various ways in which the liver glycogen stores are depleted.

Finally, it should be noted that an increased level of ketones was present in many of the patients, where tests were performed

on admission. Ketones are known to have a hypoglycaemic action (Madison et al., 1964). The mechanism of this action is evidently via stimulation of the B cells of the pancreas. Increased insulin levels, however, have not been found in alcoholic hypoglycaemia (Freinkel et al., 1963; Lochner and Madison, 1963), though available techniques for the measurement of plasma insulin are not absolutely reliable. Field et al., (1963) found an increase in plasma free fatty acids instead of a decrease as seen with increased insulin. It does not seem likely, therefore, that the increase in ketones is involved in the aetiology of alcoholic hypoglycaemia.

SUMMARY

It was felt that two major factors should be considered in the mechanism of production of alcoholic hypoglycaemia. These were (1) hepatic glycogen depletion, and (2) inadequate gluconeogenesis.

The occurrence of glycogen depletion, its mechanism of production and its importance in the production of alcoholic hypoglycaemia were described.

Inhibition of gluconeogenesis was discussed. It was felt that this could result either from an interference with the activity of hepatic enzymes related to gluconeogenesis or from disturbance of the hormonal (pituitary-adrenal) control of gluconeogenesis. The role of each was mentioned. The relationship between

DPN - DPNH levels, following alcohol metabolism, in the inhibition of gluconeogenesis was considered.

It was felt that alcoholic hypoglycaemia could be the result of an imbalance between glucose production and utilisation and that ethyl alcohol, in particular, and other related and regulating factors could be involved in disturbing the balance. This theory could account for the differences seen in the experimental and clinical alcoholic hypoglycaemias.

The role of increased ketones in the production of hypoglycaemia was mentioned, but it was not thought to be involved in the aetiology of post-alcoholic hypoglycaemia.

SUMMARY OF THESIS

SUMMARY

Fifty-two patients with post-alcoholic hypoglycaemia have been studied. These patients represent the largest series documented to date.

The patients included 46 Africans (28 males, 18 females) and 6 Indians (2 males, 4 females). Their ages varied from 4 to 70 years.

Part I of the thesis gives the clinical, biochemical and histological findings from these patients.

All the patients had taken alcohol prior to the onset of the hypoglycaemia, which was an isolated episode in all but two patients. In 5 patients the alcohol was taken on the day of admission, and in 44 patients, on the preceding day or days. Large quantities of alcohol were imbibed by the adult patients. The majority had been drinking Zulu beer, shimeyane or gavine, but some had taken only commercially prepared ethyl alcohol (cane spirit, brandy etc.). There was no evidence that toxic substances had been added to their alcohol or that hypoglycaemic agents had been taken before their alcoholic bout. An interesting finding in 14 patients was the presence of a lucid interval between the end of their alcoholic intoxication and the onset of the hypoglycaemia. It

was possible to determine that the onset of the alcoholic hypoglycaemia occurred between 5 to 15 hours after the end of the last drink. The lucid interval ranged between minutes and seven hours.

Thirty patients had taken no, or minimal food before drinking their alcohol. Nine had eaten a meal before or during the intake of alcohol. In addition, in 18 of the 30 patients, the alcohol contained substantial quantities of carbohydrate.

There was lack of intake of food in all patients following the ingestion of alcohol and in those patients that had a lucid interval it was estimated between 5 and 15 hours, usually 12 hours or more.

The dietary histories were poor and the diet taken consisted mainly of maize products. Twenty-five patients were considered to be chronic alcoholics, 18 weekend drinkers and 6 non-alcoholics.

On examination, on admission, all patients were in coma, semicoma or stupor. An odour of stale alcohol was noted on 30 patients. A subnormal temperature was a common finding. Alterations in pulse rate, blood pressure and respirations, and abnormal neurological signs were found.

Gross liver disease was absent and only one patient

showed evidence of an endocrine disorder (Addison's disease). Nutrition was clinically assessed as 'poor' in 25 patients, 'fair' in 25 patients, and 'good' in 2 patients.

Diagnoses on admission, treatment, complications and mortality were listed.

All patients had a blood sugar level below 48 mg% and their blood alcohol levels were normal or slightly raised. A mild and transient hepatogenous jaundice was found in 42 patients where serial tests were done, and was considered to be due to ethyl alcohol.

Fasting blood sugars varied from 54 to 100 mg% and the glucose tolerance tests were normal or showed mild abnormalities. In 33 patients where urinary steroid excretions were performed within the first ten days of hospitalisation, the majority showed low excretions, indicating inactivity of the suprarenal cortex. A. C. T. H. response tests performed on nine patients showed normal adrenal function in five, and subnormal response in four patients, including an Addison's disease. The exact nature of the pituitary-adrenal disturbance was not known.

Acetonuria was a common finding, on admission, in the 13 patients on which the test was done. One patient, with acute pancreatitis had a raised level of serum amylase.

Liver biopsies were performed on 37 patients; on six patients on admission. Biopsies taken on admission showed that the hypoglycaemia occurred during a period of glycogen

depletion. Fatty change and haemosiderin deposition were common findings on liver biopsy. Small foci of hepatic necrosis were seen on 20 liver biopsies. The possible relationship between the foci of necrosis, ethyl alcohol and 'alcoholic' cirrhosis were discussed.

Part II of the thesis discusses the relationship between ethyl alcohol and the hypoglycaemia.

Ethyl alcohol was considered to be the cause of the hypoglycaemia. The differential diagnosis and the reasons for considering ethyl alcohol to be the cause of the hypoglycaemia are described. It was emphasised that whenever a patient is admitted in coma with a history of taking alcohol, the possibility of post-alcoholic hypoglycaemia should be suspected.

Part III of the thesis discusses the pathogenesis of post-alcoholic hypoglycaemia.

A brief review of ethyl alcohol metabolism and the relationship between ethyl alcohol and carbohydrate metabolism are described.

A survey of the literature on the mechanism of alcoholic hypoglycaemia is given.

Various factors associated with alcoholic hypoglycaemia are discussed. The incidence of post-alcoholic hypoglycaemia was not known but it was noted to have a world-wide

distribution. It occurred among children and adults but the former seemed to be more prone to develop the disease. Chronic alcoholism was noted in the majority of adult cases but it was not considered to be a necessary factor for the production of the alcoholic hypoglycaemia. Likewise poor nutrition was a common association in adult patients. It was thought possible that both chronic alcoholism and poor nutrition, though not essential, were predisposing factors. Prior fasting was a common occurrence before the onset of alcoholic hypoglycaemia and it seemed to be an important factor in the clinical form of the disease. In experimental alcoholic hypoglycaemia in normal volunteers, a period of starvation of at least 40 hours seemed to be obligatory.

The presence, or absence, of liver disease or pituitary-adrenal disturbance amongst the reported cases is discussed. The possible differences between experimental and clinical forms of alcoholic hypoglycaemia and between childhood and adult cases are mentioned.

The mechanism of post-alcoholic hypoglycaemia is discussed.

The writer felt two major factors should be considered in the mechanism of production of post-alcoholic hypoglycaemia. These were: (1) hepatic glycogen depletion, and (2) inadequate gluconeogenesis.

The occurrence of glycogen depletion, its possible mechanism of production and its importance in the production of alcoholic hypoglycaemia were described.

Inhibition of gluconeogenesis was discussed. It was felt that this must result either from interference with the activity of hepatic enzymes related to gluconeogenesis, or from disturbance of the hormonal (pituitary-adrenal) control of gluconeogenesis. The role of each was mentioned. The relationship between DPN - DPNH levels, following alcohol metabolism, in the inhibition of gluconeogenesis was considered.

It was felt that alcoholic hypoglycaemia might be the result of an imbalance between glucose production and utilisation and that ethyl alcohol, in particular, and other related and regulating factors could be involved in disturbing this balance. It was thought that this theory might account for some of the differences seen in the experimental and clinical hypoglycaemias, though most of the differences could probably be related to the various ways in which the liver was depleted of glycogen.

Increased ketones were not considered to be involved in the aetiology of post-alcoholic hypoglycaemia.

CONCLUSION

CONCLUSION

Investigations during the past few years have established post-alcoholic hypoglycaemia as a clinical entity. Ethyl alcohol has been established as the causative agent but the precise mechanism remains undetermined. It is hoped that this thesis will stimulate investigation into this problem - a problem that will require facilities, which were not available at King Edward VIII Hospital when this work was done.

In Africa thorough study of the adrenal and pituitary function in nourished and undernourished Africans is required.

In addition, the role of ethyl alcohol in the causation of foci of hepatic necrosis and, ultimately, cirrhosis should be investigated further.

A P P E N D I X

REPORT

to

Professor E. B. Adams, Professor J. Wainwright, and Dr. S. M. Joubert.

September, 1959.

SPONTANEOUS HYPOGLYCAEMIA in the AFRICAN

It seems fit that this problem should be investigated. Each year there have been a fair number of cases of unexplained spontaneous hypoglycaemia, some of which have recovered, following dextrose administration; others have died and, where post mortem examination has been done, certain interesting findings have been seen. With this in mind, possible causes and methods of investigations are to be put forward. There is little doubt that the investigation will require a fair amount of work, especially from the departments of biochemistry, medicine and histopathology.

Aetiological classification of spontaneous hypoglycaemia

(I) Organic:

(A) Hyperinsulinism
- (1) Pancreatic islet cell adenoma
- (2) Pancreatic islet cell carcinoma
- (3) Generalised hypertrophy and hyperplasia of the islets of Langerhans.

(B) Hepatic disease
- (1) Ascending infectious cholangiolitis
- (2) Toxic hepatitis
- (3) Diffuse carcinomatosis
- (4) Cirrhosis.
- (5) Fatty degeneration
- (6) Viral hepatitis
- (7) Chronic passive congestion in C.C.F.
- (8) Glycogenosis (von Gierke's disease).

(C) Anterior pituitary hypofunction
- Including severe inanition and post operative hypoglycaemia

(D) Adrenocortical hypofunction

(E) Fibromas and sarcomas

(F) C.N.S. lesions

(II) Functional :

(A) Functional hyperinsulinism

(B) Alimentary hyperinsulinism

(C) Hyperinsulinism of infancy

(D) Idiopathic hypoglycaemia of infancy

(E) Renal glycosuria

(F) Lactation

(G) SEVERE continuous muscular work

(III) Factitious (surreptitious insulin administration)

Classification mainly from S. hypoglycaemia - Conn J.W. & Seltzer S., Amer. J. Med. 19 July - Dec. 1955. P.460.

Hypoglycaemia can also be classified into fasting, stimulative, and those in which both phenomena are present - helpful clinically.

Aetiology of acute necrosis of liver

(I) Acute alcoholic poisoning
(2) Delayed chloroform poisoning, bromethol and other basal anaesthetics.
(3) Carbon tetrachloride
(4) Trinitrotoluene, tetrachlorethane, and other chemical solvents used in industry
(5) Arsenic
(6) Phosphorus
(7) Cinchopen
(8) Mushroom poisoning
(9) Infective hepatitis
(10) Gold.

Brief case histories:

Six cases of spontaneous hypoglycaemia, that have been admitted to wards at K.E.H., are to be briefly presented:

Case I.

History: The patient, an African female, 26 years, was admitted to K.E.H. on 27 August, 1958, at 11 a.m. in a comatose state. Her neighbour, who had brought her to hospital, said she had been called to see the patient at 4 a.m., that morning and had found her unconscious and frothing at the mouth.

O/E The patient was deeply comatose and her breath smelt of alcohol.

C.N.S. - no response to firm supra-orbital pressure. Pupils equal, some response to light, regular.

NIL ELSE OF NOTE.

SPECIAL INVESTIGATIONS

(I) Blood Sugar - 37 mgms %

(2) Bld urea - 24 mgms%.

(3) Urine - pH 6.5 alb +.

(4) Hb. 14.8 g%. W.B.C. - 7000/cmm.

COURSE AND MANAGEMENT

The patient recovered after glucose administration and was discharged fit on 30 August 1958.

Case 2.

History: The patient, an African female, 25 years, was admitted to K.E.H. on the 27 June 1959, at 8.30 a.m. in a comatose state. There was a history of a heavy alcoholic intake in the preceding few days.

O/E: Deeply comatose. B.P. 140/110.

C.N.S. All deep reflexes brisk. ? L hemiparesis.

SPECIAL INVESTIGATIONS

(1) Blood Sugar - 27 mgms %

(2) C.S.F. - clear colourless fluid. Cl - 760 mgms%.

Protein - 10 mgms %. Sugar - 35 mgms %. No cells.

COURSE AND MANAGEMENT

The patient recovered after glucose administration and was discharged on 29 June 1959.

Case 3.

History: The patient, an African male 45 years, was admitted to K.E.H. on 25 May 1959, at 7 p.m. in a comatose state. History, obtained from a relative, was that he had vomited on the day before admission, had a fit on the day of admission, followed by coma. There was no previous history of convulsions.

O/E Comatose, twitching of face. Reflexes not obtained. B.P. not recordable.

SPECIAL INVESTIGATIONS

(1) Blood Sugar - 21 mgms%.

DIED 26 MAY, 1959.

NECROPSY

Liver - acute centrilobular zonal necrosis

Kidney - lower nephron nephrosis ?

A number of young healthy looking adults admitted to K.E.H. with the diagnosis of 'hysteria' or 'stupor of unknown cause' have died and necropsy findings have shown acute zonal necrosis (centrilobular) of the liver and a renal lesion. Unfortunately a blood sugar was taken

in one case only (case 3). Some of them have followed intake of alcohol.

Case 4.

History: The patient, a male African child, 4 years, was admitted to K. E. H. on the 5 April, 1959 (6 a.m.) in a comatose state. The child had been taken to a beer party and at the end of which was found unconscious. Previously healthy.

O/E Comatose. Alcohol Breath++++

C. N. S. reflexes not obtained. Flaccid.

Bladder full +

SPECIAL INVESTIGATIONS

(1) Blood Sugar - 14 mgms % on admission.

(2) Blood urea - 54 mgms %.

(3) C. S. F. - N. A. D.

COURSE AND MANAGEMENT

Glucose solution was administered but there was no recovery of consciousness (Bld sugar 132 mgms%). The patient died at 8.30 a.m. 6th April, 1959, 26 hours after admission having never regained consciousness.

NECROPSY

Liver - congestion and slight fatty degeration.

Lung, spleen and kidney - congestion.

Heart muscle, small and large intestine - nil of note.

Possibly the lack of necropsy findings was due to the rapidity of death.

Case 5.

History: The patient, an African female 5 years old, was admitted to K. E. H. on 4 August 1959 in a stuporose state. Her father stated that she had developed diarrhoea the day before and he had taken her to a herbalist who prescribed "medicine". The child became progressively sleepy and started to vomit. She had no convulsions.

O/E: Stuporose child. No jaundice. Mildly dehydrated. Bradycardia. Liver 1 f. d. P. R. - loose yellow stool, no blood.

SPECIAL INVESTIGATIONS

(1) Blood sugar - 19 mgms%.

(2) Blood urea - 64 mgms % on admission.
46 mgms % next day.

COURSE AND MANAGEMENT

The patient recovered consciousness following glucose administration and after a slower recovery in general health was discharged on the 10th August 1959.

Case 6.

History: The patient, an African male 29 years, was admitted to K. E. H. on the 7th January 1959. He was restless, unco-operative and was unable to give a reliable account of himself. He claimed that a "friend" had given him some tea that morning following which he became ill.

O/E: Violent, strong, healthy-looking male. No jaundice. Nil else of note.

SPECIAL INVESTIGATIONS

(1) Blood Sugar - 70 mgms% on admission at 11 a.m.

6 mgms% at 6 p.m. on the same day.

8.1.59 29 mgms%

9.1.59 37 mgms%.

10.1.59 50 mgms%.

(2) Bld urea - 8.1.59 - 62 mgms%----------91 mgms% 10.1.59.

(3) Serum electrolytes:

Serum K - 8.5 m. equiv. % 10.1.59

Serum Na - 113 m.equiv. % " "

Serum Cl - 102 m.equiv. % " "

DIED 12.1.59 D.S.P.M.

CAUSES of SPONTANEOUS HYPOGLYCAEMIA seen in the AFRICAN at K.E.H.

(1) Terminal chronic liver disease - primary carcinoma of the liver, cirrhosis.

(2) Acute toxic degenerative liver disease - cases that have come to necropsy have shown acute centrilobular zonal necrosis of the liver and on occasions renal lesions resembling lower nephron nephrosis.

(3) Post alcoholic hypoglycaemia. Patients have recovered following glucose administration. This might be an earlier stage of 2.

(4) Paediatric cases :

(a) As for 2 and 3 above.

(b) Severe kwashiorkor.

(5) Pancreatic hyperinsulinism.

(6) Functional hyperinsulinism.

(7) Other causes.

Possible aetiological factors :

Cases that have shown acute degenerative lesions of the liver have probably presented as cases of hepatogenic hypoglycaemia, due to the action of a toxin on the liver. The African liver might be particularly susceptible to toxins, especially if he lacks certain protective protein factors in his diet. Many of the cases have been associated with alcohol. Whether alcohol is the causative factor or whether there is some added toxic factor is difficult to say. However, regardless of whether alcohol is a cause or not, there must be other toxins at work to account for cases 5 and 6.

If certain Africans do possess a functionally hyperactive pancreatic system as a result of longstanding, heavy carbohydrate intake - "compensatory hyperinsulinism" - would this not possibly predispose them towards spontaneous hypoglycaemia if any additional factor aggravated this situation - factors that would not lead to symptoms in the European ? Does alcohol for instance, stimulate insulin secretion ? Parasympathetic stimulation does. Or will alcohol stimulate a pancreatic system that is already functionally hyperactive ? Add to this lack of food intake during alcoholic coma. Could this combination result in the fall of the blood sugar into hypoglycaemic levels quite apart from the possibility of alcohol having a direct action on the liver itself ? Would this account for those cases that respond so well to glucose administration alone ? Are the cases that come to post mortem a further stage of this or are they possibly the result of an added toxin ?

Traditionally Potassium dichromate has been put forward as the cause of these hypoglycaemic episodes. Post mortem results,

toxological examination performed on the liver on a few occasions, and the literature on potassium dichromate poisoning seem to be very much against it. So for the moment lets put it aside.

Certainly, as far as alcohol is concerned, the patient's age, apparent health, and history have suggested that alcohol, a substance added to the alcohol, or a substance formed in the production of alcoholic brews may be the cause in some cases of spontaneous hypoglycaemia in the African. An investigation of this nature will always reveal something of interest.

METHODS of INVESTIGATION

The problem requires investigation by biochemical, clinical and pathological means.

The following could be investigated :

(1) A series of fasting blood sugar estimations and glucose tolerance curves should be obtained to try and obtain normals and variations.

(2) Full investigation of cases of spontaneous hypoglycaemia admitted to K. E. H.

(3) The administration of alcohol to grp. 2 prior to discharge to see whether it is possible to reproduce hypoglycaemia - variations of diets, fasting etc.

(4) Reaction of the blood sugar levels in Africans following the administration of alcohol should be investigated - effects of various diets etc.

CLINICAL INVESTIGATION:

(1) A full and adequate history. ? previous intake of alcohol. ? past attacks of hypoglycaemia. ? at what time of day did attacks occur etc.

(2) Complete physical examination. Exclusion of other causes of spontaneous hypoglycaemia.

SPECIAL INVESTIGATIONS:

(a) Fasting blood sugar.

(b) Liver function tests

- (i) Serum transaminase.
- (ii) Serum bilirubin.
- (iii) Alkaline phosphatase.
- (iv) Prothrombin index.

(c) Serum amylase.

(d) Bld urea and serum electrolytes.

(e) Bld alcohol.

(f) Analysis immediate catheter specimen of urine for alcohol and toxins.

(g) Aspiration of stomach contents ? analysis.

(h) Liver biopsy.

(i) Urine - Routine.

(j) Urinary steroid excretion.

(k) Glucose tolerance test.

(l) Necropsy.

CASE HISTORIES

QUESTIONS TO PATIENTS

Despite asking the following questions it was not always possible to get a direct answer to the question. This was due to difficulties in interpretation and sometimes to lack of understanding, or to failure to remember accurately the circumstances prior to admission. Time relationships were often a difficult problem. However, despite these difficulties, it is felt that the histories that follow are accurate. Careful cross-checking with members of the nursing staff, the house physicians, and, initially, with Sister C. Majola, of the department of social medicine, was undertaken, and a reasonably close correlation was noted.

Questions :-

1. Had the patient taken alcohol prior to admission?
2. When had he taken alcohol ?
3. What type of alcohol had he imbibed ?
4. How much alcohol had he imbibed ?
5. Was he drunk when he had finished drinking ?
6. Time relationships ?

7. Had he been awake before awakening in hospital ?

8. Had he added substance to his alcohol ?

9. Had the alcohol been prepared in the usual way ? How ?

10. What had the patient eaten on the day on which he drank and on the previous day ?

11. Had the patient had a similar episode to that which resulted in his admission to hospital ?

12. Had the patient been in coma unrelated to alcohol ?

13. Did the patient suffer from convulsions ?

14. Had the patient taken herbs, injections or medicine (tablets) before admission to hospital ?

15. Had the patient been well prior to this illness ?

16. Dietary habits - Breakfast; Lunch; Supper, and meals at any other time ?

17. Alcohol habits.

18. Social history.

CASE 1/60

O.K. AFRICAN MALE, 45 years

Admitted 1.2.60, at 10.10 a.m. Discharged 25.2.60

OUT-PATIENT DEPARTMENT

He was brought to the hospital by a relative who said the patient had taken some alcohol the night before and was found to be unconscious that morning. On examination he was semicomatous; alcoholic odour on breath; bradycardia; tender epigastrium; no focal central nervous system signs. A diagnosis of ? alcoholic coma was made.

WARD

No further history was available.

Examination: Resists examination. Groaning and frothing at the mouth. Mumbling slurred speech. No anaemia, jaundice or lymphadenopathy.

C.V.S. Pulse 68 per minute, full volume, regular. B.P. 190/95. J.V.P. = O. Heart sounds closed.

R/S Trachea central. Chest clear.

Abd. Not distended.
Hepatomegaly two fd.
No splenomegaly.
No free fluid. Bowel sounds present.

C.N.S. Stuporose. Resists examination. Mumbles to himself, groaning. Unable to answer questions.
No signs of head injury.
No neck rigidity or Kernigs sign.

Reflexes:

	R.	L.
Triceps	++	++
Biceps	++	++
Supinator	++	++
Knee	--	--
Ankle	--	--
Plantars	↓	?

No obvious cranial nerve lesion or paresis.
Pupils equal and react to light.
Incontinent of urine.

Diagnosis: ? Cause of Coma.

IMMEDIATE SPECIAL INVESTIGATIONS

Blood sugar 28 mg%; blood urea 43 mg%.

TREATMENT

50 ml 50% intravenous dextrose solution was administered and the patient responded immediately.

Diagnosis: Hypoglycaemia ? cause.

HISTORY FROM PATIENT

On the day before admission (Sunday) the patient, after a luncheon consisting of samp, beans and meat, went to a party where he drank a quarter of a large golden syrup tin of Zulu beer with four other people. He then drank shimeyane from a 2 lb jam tin with one other person. He was drunk after drinking the shimeyane. He left the party at 6.30 p.m. and went straight to bed, as he was too drunk to be able to prepare any food. He awakened during the night at about midnight but remembered nothing till awakening in hospital the next day.

Special Interrogation: He had been quite well till this episode. He had never had a similar attack nor had he lost consciousness previously or had convulsions (unrelated to alcohol). He had not taken herbal medicines, had injections or taken tablets. Nothing else of note.

Alcohol habits: He was a heavy weekend drinker and usually drank Zulu beer. He did not add toxic substances to his alcohol.

Dietary habits:
- Breakfast: Mealie meal porridge and tea.
- Lunch: Brown bread during the week when at work; samp and potatoes in the weekends.
- Supper: Samp and meat occasionally.

Social history: Married. One child (12-15 year old boy). Works at a factory during the week.

Subsequent history: As far as he could discover all the other people with whom he drank were well.

SPECIAL INVESTIGATIONS:

1.2.60 See above.

3.2.60 Hb. 16.4g%. W.B.C., 7,000/cmm. P.C.V. 48 (%mms)
E.S.R. 41 mm/hr.
Routine urine. Albumen +. Nothing else of note.

6.2.60 Serum amylase 192 W units. Chest X-ray - N.A.D.

8.2.60 Serum amylase 60 W. units.
Serum albumin 3.3g%.
Serum globulin 4.9g%.
Total protein 8.2g%.
Thymol turbidity 4 units.
Glucose tolerance test: Fasting 81 mg%, ½ hour 125 mg%, 1 hour 144 mg%, 1½ hours 138 mg%, 2 hours 125 mg%, 2½ hours 113 mg%, 3 hours 81 mg%, 3½ hours 69 mg%.

9.2.60 E.C.G. - N.A.D.

10.2.60 Serum amylase 16 W units.

15.2.60 Serum amylase 12 W units.

23.2.60 Alcohol test - See text p.63.

24.2.60 S.G.O.T. 50 K units.

25.2.60 S.G.O.T. 42 K units.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver Biopsy
3.2.60	3	172					86	Done
4.2.60	4		1.3	14				
5.2.60	5	460						
8.2.60	8	50	1.5	10				
10.2.60	10	40						
12.2.60	12	62	0.8					
15.2.60	15	56			++	Nil.		
17.2.60	17	48			Nil.	Nil.		
19.2.60	19	24						

Liver Biopsy: This was performed on 3.2.60. Section of liver showed a focus of parenchymal necrosis accompanied by an inflammatory cell infiltration, consisting mainly of round cells and mononuclears, but neutrophils were also noted. Moderate fatty vacuolation, mainly periportal, and a generalised fine intercellular change was noted.

Alcoholic hyalin was not observed. The portal triads showed oedema and an infiltration with chronic, and a few acute inflammatory cells. Slight portal fibrosis (grp. II) was present. Intercellular haemosiderin was noted throughout the parenchyma while clumps of haemosiderin were present in the portal triads and in the lobules (gr. 5). No bile thrombi or bile duct hyperplasia were observed. Large quantities of glycogen were present (gr. 4).

[STAINS used: Haematoxylin and eosin, silver impregnation for reticulin, Weigert's iron haematoxylin Van Gieson, Prussian blue reaction and Best carmine].

Course and management:

The patient developed severe epigastric pain on 3. 2. 60 and was found to be suffering from acute pancreatitis.

Assessment of alcohol habits: Weekend drinker.
Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Spontaneous hypoglycaemia following the intake of alcohol.

(2) ? Transient hepatitis.

(3) Acute pancreatitis following excess alcohol.

CASE 2/60

F. T. AFRICAN MALE, 38 years

Admitted 7. 2. 60. at 4. 50 p. m. Discharged 19. 2. 60.

OUT-PATIENT DEPARTMENT

Found in coma by friend. Admitted as an undiagnosed coma.

WARD

The patient had been found in coma by a friend at 6. a. m. on the day of admission. He had thought the patient was drunk but as his condition did not improve, brought him to hospital that afternoon.

Examination: Unconscious; stertorous breathing, apyrexial. Psoriasis on arms and legs and abdomen.

C. V. S. J. V. P. = O. Pulse 76 per minute. B. P. 180/120. Heart normal.

R/S Trachea central. Rhonchi both lung fields.

Abd. Nil abnormal detected.

C. N. S. Comatose. Clonic contractions of lower limbs. Pupils equal in size, dilated and respond to light. Hypertonia of all limbs (spastic).

Reflexes:

	R	L
Biceps	++	++
Triceps	++	++
Supinator	++	++
Knee	++	++
Ankle	++	++
Plantars	↑	↑

Bilateral ankle clonus
Cranial nerves - appear normal.
No neck rigidity.
No signs of injury.

Diagnosis: ? Post-alcoholic hypoglycaemia.

IMMEDIATE SPECIAL INVESTIGATIONS:

Blood sugar 35 mg%, blood urea 50 mg%.

TREATMENT:

75 ml 50% intravenous dextrose solution administered with immediate recovery of consciousness.

Diagnosis: Hypoglycaemia ? post alcoholic.

HISTORY FROM PATIENT:

The patient had worked till 1 p.m. on the day before admission (Saturday) and had then proceeded to Fynlands where he drank half a pint of gavine between 2 and 3 p.m., with three friends. By the time he left he was very drunk. The mixture was very potent and "burned all the way down". He arrived home at 5 p.m. fell on his bed and awoke at about 6 a.m. on the following day. He felt very weak on awakening. He drank water and vomited. He then began to wash his shirt, felt weaker, began to shake and remembered no more. He reawoke in hospital and found that he had bitten his tongue during the day. He had eaten breakfast consisting of tea and 2 teaspoonfuls of sugar on the Saturday but had not eaten lunch. On Friday night he had eaten meat and rice.

Special interrogation: He had been quite well prior to to the episode and had never had a similar attack of unconsciousness before and he had never had a previous fit. He had not taken herbs, tablets or had injections prior to the attack.

Alcohol habits: Drank every weekend, usually kaffir beer or brandy, but occasionally gavine.

Dietary habits: Breakfast: Mielie meal porridge and sugar (no milk).
Lunch: Bread and tea.
Supper: Rice curry. Meat four times per week.

Social history: Unmarried. He worked at the station as a porter.

Subsequent history: As far as he could discover all the the other people with whom he drank were well.

SPECIAL INVESTIGATIONS:

7.2.60 See above.

8.2.60 Hb 19.3g% (132%); P.C.V. 52 (mms%); W.B.C. 8000/cmm; E.S.R. 15 mms/hr.
Total proteins 8.2g%, S. Albumin 3.8g%, S. globulin 4.4g%, A:G Ratio 0.9 - 1.

9.2.60 Serum Amylase 8.0 W units.

10.2.60 Chest X-ray N.A.D. Bld urea 46 mg%. Serum electrophoresis. S. Albumin 3.3g%; S. globulins, α_1 0.6g%, α_2 1.1g%, β 1.3g%, γ 1.4g%.
Total proteins 7.7g%.

11.2.60 E.C.G. - N.A.D.

12.2.60 Glucose tolerance test: Fasting 62 mg%; half hour 88 mg%; 1 hour 163 mg%; 1½ hour 163 mg%; 2 hours 163 mg%; 2½ hours 88 mg%; 3 hours 63 mg%; 3½ hours 50 mg%; 4 hours 50 mg%; 4½ hours 50 mg%.

15.2.60 Alcohol test (see text P.63) Hypoglycaemia not produced.

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver Biopsy
8.2.60	2	82		11				
9.2.60	3	74					100	
10.2.60	4	58			+	Nil.		done.
11.2.60	5							
14.2.60	8				trace	Nil.		
15.2.60	9		0.9	11	+	Nil.		
16.2.60	10		0.8	9	Nil.	Nil.		

Liver Biopsy: This was performed on 10.2.60. Section of liver showed a focus of necrosis accompanied by an inflammatory cell reaction consisting of round cells and occasional neutrophils. No alcoholic hyalin was seen. Fatty vacuolation was not observed but moderate fine intercellular fatty change was noted. The portal triads showed oedema and numbers of chronic and acute inflammatory cells. An increase in fibrous tissue at the triads was noted; in places peripheral extension resembling periportal fibrosis (grp III). Haemosiderin was noted in the parenchyma at the periphery of the lobules (gr. 2). No bile thrombi or bile duct hyperplasia were noted. Glycogen was present in small quantities (gr. 1).

[STAINS used: haematoxylin and eosin, silver impregnation, Weigert's iron haematoxylin Van Gieson, Prussian blue reaction and Best carmine].

Course and Management:

On the 10.2.60 the liver was palpable 2 fd. The patient had an uneventful course in hospital. He wanted to return to work on 19.2.60 and he was discharged.

Assessment of alcohol habits: Weekend drinker.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS:

(1) Post alcoholic hypoglycaemia.

(2) ? mild hepatitis.

CASE 3/60

F.S. AFRICAN MALE, 24 years.

Admitted 10.2.60 at 3 p.m. Discharged 24.2.60.

OUT-PATIENT DEPARTMENT

The patient was known to have taken alcohol on the previous day and according to his brother became unconscious soon after awakening at 11 a.m. that morning. Coma ? hypoglycaemic.

WARD

History as above.

Examination:	Comatose. Pellagrinous skin. No anaemia, clubbing, cyanosis or lymphadenopathy. Temperature 98°F.
C.V.S.	Pulse 90 per minute. B.P. 120/90. Heart normal.
R/S	N.A.D.
Abd.	Liver 1½ fd. No free fluid. No splenomegaly.
C.N.S.	Comatose. Nil else.
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT:

Blood was taken for special investigations and 40 ml 50% intravenous dextrose solution was administered, with immediate recovery after 20 ml.

IMMEDIATE SPECIAL INVESTIGATIONS:

Bld sugar 25 mg%; bld urea 67 mg%; Hb 16.0g% (110%), W.B.C. 10,000/cmm.

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

The patient commenced drinking a mixture of kaffir beer and shimeyane - mixed in equal quantities - at 7 a.m. on the morning

of the day prior to admission. He drank half a large golden syrup tin full of this mixture. A friend arrived and they continued to drink shimeyane. They were both drunk at the end of it. The bout occurred prior to eating breakfast. The patient had eaten curried mutton and rice on the previous evening. He continued drinking and remained drunk all day, arriving home at 4 a.m. on the morning of admission. He awoke at 11 a.m. and felt drunk, (according to his brother he became unconscious soon after awakening), and later re-awakened in hospital.

Alcohol habits: The patient drank shimeyane daily and he was considered to be a chronic alcoholic by his brother.

Dietary habits: Breakfast: Mielie Rice.
Lunch: Mielie Rice.
Supper: Samp.

He ate curried mutton or fish occasionaly.

Social history: He did not work. He was unmarried.

Special interrogation: He had never had a similar attack previously. There was no history of fits. He had not taken herbs, tablets or had an injection.

Subsequent history: The friend who drank with him did not have a similar episode.

SPECIAL INVESTIGATIONS:

10.1.60 See above.
Serum amylase 8.0 W. units.

13.2.60 Bld urea 33 mg%.
Chest X-ray - N.A.D.

15.2.60 Total proteins 7.4g%; S. albumin 3.3g%; S. globulin 4.1g%; A:G ratio 0.8:1. S. Electrophoresis: S. albumin 2.6g%; S. globulin α_1 0.6g%, α_2 1.0g%, β 1.2g%, γ 1.4g%. Total protein 6.8g%.

16.2.60 Glucose tolerance test: Fasting 66 mg%; $\frac{1}{2}$ hour 92 mg%; 1 hr. 92 mg%; $1\frac{1}{2}$ hours 120 mg%; 2 hours 115 mg%; $2\frac{1}{2}$ hours 78 mg%; $3\frac{1}{2}$ hours 48 mg%.

19.2.60 Total protein 8.3g%; S. Albumin 3.8g%, S. globulin 4.5g%; A:G ratio 0.8:1.

20.2.60 E.C.G. N.A.D.

18.2.60 Alcohol test (see text P. 63.) Hypoglycaemia not produced.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
10. 2. 60	1	96			Nil	Nil		
11. 2. 60	2	64			Nil	Nil	74	Done
12. 2. 60	3							
13. 2. 60	4	68			+	Nil		
15. 2. 60	6	48		12	Trace	Nil	74	
17. 2. 60	8	54						
19. 2. 60	10	70		10	Nil	Nil		
20. 2. 60	11	68			Nil	Nil		
22. 2. 60	13	40						

Liver biopsy: This was performed on 11. 2. 60. Section of liver showed moderate fatty vacuolation but some fine intercellular fatty change was noted. No alcoholic hyalin or foci of necrosis were seen. Chronic inflammatory cells were noted in the portal triads, where an increase in portal fibrosis was observed (grp. II). Haemosiderin was present throughout the lobules with clumps being noted both in the parenchyma and at the portal tracts (gr. 4). No bile thrombi or bile duct hyperplasia were seen. Glycogen was present (gr. 3).

[STAINS used: haematoxylin and eosin; silver impregnation; Weigerts iron haematoxylin Van Gieson; Prussian blue reaction, and Best carmine].

Course and management: Uneventful course. The patient was given plebex 2 ml stat and daily His nutritional state had improved on discharge.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition (Pellagra).

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

(3) Pellagra.

(4) Chronic Alcoholic.

CASE 4/60

G. N. AFRICAN FEMALE, 50 years

Admitted 22. 2. 60, at 12.30 p.m. Discharged

OUT-PATIENT DEPARTMENT

According to relatives the patient was found unconscious that morning. She was known to be a heavy drinker. Coma ? Post-alcoholic hypoglycaemia.

WARD

No further history was available.

Examination:	Comatose; no anaemia.
C.V.S.	Pulse 80 per minute. B.P. 90/50. Heart normal.
R/S	Shallow breathing. Nothing else of note.
Abd.	No hepatomegaly or splenomegaly.
C.N.S.	Comatose. Nothing else of note.
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT:

Blood was taken for special investigations and then 20 ml 50% intravenous dextrose solution and 3 ml coramine were administered. The patient recovered consciousness immediately.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 28 mg%; blood urea 63 mg%; Hb 11.2g% (77%); W.B.C., 10,000/cmm; P.C.V. 36(MMS); M.C.H.C 31%; E.S.R. 41 mms/hr; Serum Na, 128 meq/l; serum K, 4.3 meq/l, serum Cl, 98 meq/l.

Diagnosis: Hypoglycaemia ? Post alcoholic.

HISTORY FROM PATIENT

Two days before admission the patient and two friends drank zulu beer from a large golden syrup tin. The following day (Sunday), at 10.00 a.m., she and a friend drank Zulu beer and she was drunk at

the end of it. At 11 a.m., after finishing the beer, she returned home, reaching it at 12.30 p.m. She remembers nothing else after that but was definitely drunk. On Friday the patient had eaten only porridge and on Saturday, porridge and bread at three meals. She had eaten breakfast (bread only) on Sunday.

Alcohol habits: She said she drank heavily at weekends but her relatives stated she was a chronic alcoholic.

Dietary habits: Breakfast: Mielie meal porridge, samp and tea.
Lunch: Porridge and beans.
Supper: Bread and tea.

Social history: Did not work.

Special interrogation: There was no history of fits or unconsciousness unrelated to alcohol. She had never had a similar episode. She had not taken herbal medicines, received injections or tablets. Otherwise nothing of note.

Subsequent history: As far as she could discover her friend, with whom she drank, did not have a similar attack.

SPECIAL INVESTIGATIONS:

22.2.60 See above.
Serum amylase 8.0 W. units.
Serum electrophoresis: S. Albumin 3.2g%; serum globulins, α_1 0.6g%; α_2 0.9g%; β 1.3g%, γ 2.3g%; Total proteins 8.3g%.
Routine urine: Acetone +. Nothing else of note.
23.2.60 P.I 79%.
24.2.60 E.C.G. - N.A.D.
26.2.60 Chest X-Ray - N.A.D.
29.2.60 Bld urea 23 mg%.
1.3.60 Glucose tolerance test: Fasting 58 mg%, $\frac{1}{2}$ hour 76 mg%, 1 hour 170 mg%, $1\frac{1}{2}$ hours 130 mg%, $2\frac{1}{2}$ hours 115 mg%, 3 hours 54 mg%, $3\frac{1}{2}$ hours 46 mg%, 4 hours 66 mg%.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver Biopsy
22.2.60	1		1.5	22	Nil.	Nil.	74	
23.2.60	2		0.9	24	+	Nil.	79	
24.2.60	3							
25.2.60	4	98	1.3	16				
26.2.60	5	160			+++	Nil.		
28.2.60	7							
29.2.60	8	50	0.8		Nil.	Nil.		
1.3.60	9	74						
4.3.60	12	38		7				

Liver biopsy: This was attempted but no tissue was obtained.

Course and management: The patient had an uneventful course in hospital.

Assessment of alcohol habits: Chronic alcoholic.
Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS:

(1) Post-alcohol hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Chronic alcoholic.

CASE 5/60

G.S. AFRICAN MALE, 46 years

Admitted 22. 2. 60, at 6 a.m. Discharged 17.3.60.

OUT-PATIENT DEPARTMENT

The patient was found in coma early in the morning of admission. He was known to have been drunk on the day before. A diagnosis of coma, ? cause was made.

WARD

No further history was available.

Examination:	Slight, thin, comatose man smelling of alcohol. Cold (subnormal temperature). No cyanosis, no signs of injury.
C.V.S.	Pulse 80 per minute, regular. B.P. 130/80. Heart sounds faint and closed.
R/S	Slow, shallow breathing. A few crepitations at both bases.
Abd.	Liver 3 fd. No splenomegaly. Nothing else of note.
C.N.S.	No neck stiffness. Extended hypertonia of lower limbs. Hypotonia of arms. All reflexes absent. Plantar reflexes absent.
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for glucose estimation and then 20 ml 50% intravenous dextrose solution and 2 ml coramine were administered. The patient recovered immediately but was talkative and unhibited - ? mildly inebriated.

IMMEDIATE SPECIAL INVESTIGATION

Blood sugar 44 mg%.

Diagnosis: Hypoglycaemia. ? Post-alcoholic.

HISTORY FROM PATIENT

The patient stated he had been drinking shimeyane and gavine on the day before admission (Sunday). He had lost consciousness and reawakened in hospital.

Alcohol habits : He drank heavily in the weekends, usually shimeyane or gavine, but usually the latter.

Special interrogation: He had never had a similar attack previously.

(An accurate history was not possible as the patient was gay and ? confabulating).

SPECIAL INVESTIGATIONS

22.2.60 See above.
Routine urine: Acetone +. Nothing else of note.
Hb, 11.0g% (76%), P.C.V. 36(mms)%, W.B.C. 7,000/cmm, E.S.R. 51 mms/hr., M.C.H.C. 30%; bld urea 22 mg%.

23.2.60 Serum amylase 4 W. units.
Serum electrophoresis: S. Albumin 1.5g%; S. globulins α_1 0.5g%, α_2 0.6g%, β 1.1g%, γ 2.9g%; Total proteins 6.6g%.

24.2.60 Chest X-ray - irregular consolidation at the right upper lobe ? small cavities. Also irregular consolidation in the right mid and lower zones. The changes are highly suggestive of pulmonary tuberculosis.

25.2.60 V.D.R.L. (slide) reactive 2 dilutions; Kolmer cardiolipin (W.R.) reactive 16 dilutions.

29.2.60 Sputum negative for A.F.B. Porphyrins not detected in urine.

1.3.60, 2.3.60, 3.3.60 Sputum negative for A.F.B.

4.3.60 Glucose tolerance test. Fasting 80 mg%, $\frac{1}{2}$ hour 80 mg%, 1 hour 136 mg%, $1\frac{1}{2}$ hours 152 mg%, 2 hours 148 mg%, $2\frac{1}{2}$ hours 128 mg%, 3 hours 64 mg %.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
22.2.60	1	130	0.8	15	+	Nil.		
23.2.60	2	180			+++	Nil.	79	
24.2.60	3	92	1.0	14	+++	Nil.		
25.2.60	4	66		15				
26.2.60	5	52						Done
29.2.60	8	30			Nil.	Nil.		
2.3.60	10	30						
10.3.60	18	24						

Liver Biopsy: This was performed on 26.2.60. Section of liver showed distortion of liver architecture as the result of severe cirrhosis (grp V). Extreme fatty vacuolation and fine intercellular fatty change were noted. No alcoholic hyaline or foci of parenchymal necrosis were observed. Glycogen was present (gr. 2) while no bile thrombi or bile duct hyperplasia were seen.

[Stains used: haematoxylin and eosin, Best carmine].

Course and Management:

The patient was given a course of penicillin after his Wasserman was found to be positive. Chest X-ray revealed pulmonary tuberculosis and he was transferred to a T.B. hospital, on 17.3.60.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Transient hepatitis ? alcoholic.

(3) Syphilis.

(4) Pulmonary tuberculosis.

CASE 6/60

Excluded from series.

CASE 7/60

P.B. AFRICAN MALE, 37 years.

Admitted 27.3.60 at 5.20 p.m. Discharged 20.4.60.

OUT-PATIENT DEPARTMENT

Coma ? hypoglycaemic.

WARD

A relative stated that the patient had been drinking shimeyane in the afternoon before admission and was drunk when he had finished it at about 7 p.m. On the morning of admission he awakened at about 7 a.m. and complained of abdominal pain. He gradually became weak and was unable to speak. He then lost consciousness. He had been perfectly well previously.

Examination:	Semicomatose. No anaemia or jaundice. Jaw stiff (trismus). Tongue bitten. No clubbing or lymphadenopathy. Cold. No sweating.
C.V.S.	Pulse 112 per minute, regular, good volume. B.P. 190/85. Heart normal.
R/S	Stertorous breathing. Chest clear.
Abd.	Hepatomegaly 1 fd. Nothing else of note.
C.N.S.	Semicomatose. No neck stiffness. No obvious cranial nerve lesion. Trismus. Hypertonia of all four limbs. Deep tendon reflexes appear normal. Plantar reflexes equivocal.
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT:

After taking blood for special investigations 70 ml intravenous dextrose was administered. The patient responded immediately but was violent and unable to speak.

IMMEDIATE SPECIAL INVESTIGATIONS

Blood sugar 25 mg%; bld urea 37 mg%; Serum electrolytes Na, 139 meq/l; K, 4.6 meq/l; Cl, 103 meq/l.

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

This was taken two days after admission when the mental state of the patient improved. He could not remember when he came to hospital or how he arrived there. He last remembered drinking shimeyane.

Alcohol habits: He was a heavy weekend drinker and had done this for a number of years. He did not add toxic substances to his liquor.

Dietary habits:
Breakfast: Porridge.
Lunch: Mielie meal porridge.
Supper: Mielie meal porridge and meat and vegetables occasionally.

Social history: Works as a bricklayer. Unmarried.

Special interrogation: He had never had a similar episode previously. He did not have fits. He had not taken herbs, tablets, or had an injection prior to admission.

SPECIAL INVESTIGATIONS:

27.3.60 See above. S. Amylase 4 W. units. Serum electrophoresis: S. Albumin 3.1g%; S. globulins α_1 0.8g%; α_2 1.1g%; β 1.7g%; γ 2.3g%; Total proteins 9.0g%.

28.3.60 Hb 16.4g% (112%), P.C.V. 53(mm)%, M.C.H.C. 31%, W.B.C. 15,000/cmm. Routine urine: occasional granular and hyaline casts on microscopy. Nil else of note.

29.3.60 Chest X-ray - Patchy irregular consolidation in right lower lobe.

31.3.60 E.C.G. - N.A.D.

8.4.60 Glucose tolerance test: Fasting 77 mg%, ½ hour 134 mg%, 1 hour 145 mg%, 1½ hours 170 mg%, 2 hours 153 mg%, 2½ hours 140 mg%, 3 hours 103 mg%, 3½ hours 71 mg %, 4 hours 75 mg%.

11.4.60 Hb 13.3g%, W.B.C. 11,000/cmm.

13.4.60 and 14.4.60. Sputum - No A.F.B. detected.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
27. 3. 60	1	300		9			83	
28. 3. 60	2	150		13	Nil.	Neg.		
29. 3. 60	3	350		12	Nil.	Neg.		Done
30. 3. 60	4	70			Nil.	Neg.		
31. 3. 60	5	74			Nil.	Neg.		
1. 4. 60	6	60			Nil.	Neg.		
4. 4. 60	9	40						
5. 4. 60	10				+++	Neg.		
6. 4. 60	11				+	Neg.		
7. 4. 60	12	34			+++	Neg.		
8. 4. 60	13	30			++	Neg.		
11. 4. 60	16				Nil.	Neg.		
12. 4. 60	17				Nil.	Neg.		

Liver biopsy:

This was performed on 29. 3. 60. Section of liver showed two small foci of necrosis accompanied by neutrophils and round cells. No alcoholic hyalin was observed. Numbers of acute and chronic cells were noted in the portal triads, which showed a slight increase in fibrous tissue (grp. II). A severe fine fatty change was observed throughout the parenchyma while fatty vacuolation was moderate. A heavy deposition of haemosiderin in the portal tracts and also throughout the parenchyma was present (gr. 5). Glycogen was noted (gr. 3). No bile thrombi or bile duct hyperplasia were observed.

[STAINS used: Haematoxylin and eosin, silver impregnation, Weigerts iron haematoxylin Van Gieson, Prussian blue reaction and Best's carmine].

Course and management:

The patient was unable to speak or understand on the first day after admission. On the following day he still was unable to speak but he could obey commands. On the third day after admission, speech had returned. Re-examination of his blood pressure after treatment showed B. P. of 130/80. On 1. 4. 60, a temperature of 100. 2°F was noted and examination of the chest showed evidence

of consolidation at the right base and apex, accompanied by crepitations. (Chest X-ray showed a patchy irregular consolidation). Penicillin was administered and the patient was discharged well on the 20.4.60.

Assessment of alcohol habits: Weekend drinker.

Assessment of nutrition : Fair nutrition.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Pneumonia ? aspiration.

CASE 8/60

N.S. AFRICAN FEMALE, 49 years

Admitted 29.3.60, at 11.35 a.m., discharged 14.4.60.

OUT-PATIENT DEPARTMENT

? Alcoholic coma.

WARD

A relative stated that the patient had drunk shimeyane all day on the day before admission. She had returned home at about 10 p.m. intoxicated and had not awakened on the morning of admission. She was a heavy drinker and drank daily.

Examination: Middle-aged, thin looking woman with pellagrinous dermatitis on her face and arms. Temperature subnormal - 96°F. Collapsed. No anaemia, jaundice or cyanosis. No clubbing, oedema or lymphadenopathy.

C.V.S. Pulse 100 per minute. B.P. 105/60. Heart normal.

R/S N.A.D.

Abd. Liver 1½ fd., hard, nobbly and non-tender. No splenomegaly and no free fluid.

C.N.S. Comatose. Nil else examined.

Diagnosis: ? Post alcoholic hypoglycaemia.
? Cirrhosis.
Pellagra.

TREATMENT

Because of her collapsed condition, intravenous dextrose solution was given before an adequate examination was made, but after blood had been withdrawn for special investigations, 60 ml 50% intravenous dextrose solution was administered and the patient recovered consciousness immediately.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 13 mg%; Serum electrolytes: Na, 141 meq/l, K, 4.4 meq/l, Cl, 118 meq/l; bld urea 31 mg%; hb 12.7g% (81%), P.C.V. 38 (mm), M.C.H.C. 33%, W.B.C. 5,000/cmm.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

The patient stated that she had drank heavily on the day before admission and had imbibed shimeyane with seven other people. She could not remember leaving the party and wondered how she had come to hospital. She drank daily but she had drunk more than usual on the day before admission. She had eaten mielie rice at 8 p.m. on the day before the debauch, but had no meal on the day of the party.

Alcohol habits: Heavy drinker. She usually drank shimeyane or zulu beer daily. She had been drinking for 25 years and heavily for 2 years. She did not add toxic substances to her alcohol.

Dietary habits: Mielie meal porridge and samp twice daily. Meat and vegetables twice a week.

Social history: She did not work.

Special interrogation: She had never had a similar episode previously. She did not have fits. She had not taken herbs or tablets, or had an injection before her admission.

Subsequent history: As far as her relatives could discover all the other people with whom she drank were well.

SPECIAL INVESTIGATIONS

29.3.60 See above.
Serum amylase 8 W units.
P.I. 74%.
E.C.G. - N.A.D.
Routine urine. Acetone nil, albumin trace
deposit occasional granular cast.
Serum electrophoresis: S.Albumin 1.9g%; S. globulins α_1 0.6g%; α_2 1.0g%, β 1.6g% γ 3.0g%. Total proteins 8.1g%.

30.3.60 P.I. 77%
Chest X-ray - N.A.D.
7.4.60 Glucose tolerance test: Fasting 80 mg%, ½ hour 170 mg%, 1 hour 156 mg%, 1½ hours 131 mg%, 2 hours 88 mg%, 2½ hours 57 mg%, 3 hours 76 mg%, 3½ hours 88 mg%, 4 hours 82 mg%.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
29.3.60	1	276		11	Nil.	Neg.	74	
30.3.60	2	150			Nil.	Neg.	74	Done
31.3.60	3	160			+	Neg.		
1.4.60	4	90			++	Neg.		
4.4.60	7	84			+	Neg.		
5.4.60	8				+	Neg.		
7.4.60	10	40		9	+	Neg.		
8.4.60	11				+	Neg.		
9.4.60	12				+	Neg.		
11.4.60	14	30			Nil.	Neg.		
12.4.60	15				Nil.	Neg.		

Liver biopsy:

This was performed on 30.3.60. Section of liver showed a severe portal cirrhosis (grp. V). Numerous inflammatory cells were present in the fibrous tissue and extension of the inflammatory cells into the surrounding tissue was also noted. Small foci of necrosis with an acute inflammatory cell reaction was also observed. Severe fatty change, both fatty vacuolation and fine intercellular fat, was present. Haemosiderin was noted in the periphery of the lobules (grade 2). No bile thrombi or bile duct proliferation were observed. Glycogen was present (gr. 4). Alcoholic hyalin was not observed. The features were compatible with "alcoholic" cirrhosis and hepatitis.

[STAINS used: Haematoxylin and eosin; silver impregnation (reticulin); Weigert's iron haematoxylin Van Gieson; Prussian blue reaction and Best carmine].

Course and management: Two days after admission the

patient suffered from delirium tremens. Paraldehyde was necessary. Three days later she was normal and the remainder of her hospitalisation was uneventful.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition (pellagra).

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Portal cirrhosis ("alcoholic").

(3) Alcoholic hepatitis.

(4) Pellagra.

(5) Delirium tremens.

CASE 9/60

M.G. AFRICAN FEMALE, 38 years.

Admitted 24.4.60 at 2.15 p.m. Discharged 21.5.60.

OUT-PATIENT DEPARTMENT

No history obtained. Admitted in coma ? cause.

WARD

No history available.

Examination:

Moribund patient. Just breathing at 5 breaths per minute. No pulse or blood pressure recordable. Subnormal temperature. Pellagrinous dermatitis. Heart sounds faint - rate 28 per minute. Stale alcoholic odour on breath. Ward urine: no sugar, acetone +.

Diagnosis: ? Post-alcoholic hypoglycaemia.

TREATMENT

As the patient was moribund, blood was taken from the femoral vein for special investigations and 30 ml intravenous 50% dextrose solution was given immediately afterwards. She became conscious but did not speak. A further 30 ml 50% intravenous dextrose solution and 1.5 ml methidrine were given. The patient became orientated.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 9 mg%; bld urea 31 mg%; serum electrolytes: Na, 121 meq/l, K, 4.3 meq/l.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

Examination of patient following therapy (15 minutes after resuscitation).

Still cold. Pellagrinous dermatitis of forearms and hands.

C.V.S. Pulse 96 per minute. B.P. 130/80.

Heart normal.

R/S Chest clear.

Abd. Liver and spleen not palpable.
No free fluid.

C.N.S. Coarse tremor.
Fully conscious and orientated. Nil else abnormal.

HISTORY FROM PATIENT

She had been drinking. She had commenced at 10 a.m. drinking Zulu beer and shimeyane with two other people after a breakfast consisting of mielie meal porridge. They had drunk from large golden syrup tins. After that she had shared gin with three other people and drank half a bottle. She did not know what had happened; whether she had finished drinking before becoming unconscious or not. She had re-awakened in hospital at 3.15 in the afternoon, but she was not sure whether it was the same day on which she had been drinking or the next day. She had eaten mielie meal porridge, a slice of white bread and a leg of chicken on the night prior to being drunk.

Alcohol habits: She was a heavy drinker, drinking on Friday night, Saturday and Sunday and often during the week. She had been drinking like this for eight years. She did not add toxic substances to her liquor.

Dietary habits: Breakfast: Mielie meal porridge, bread and tea.
Lunch: Samp, mielie rice, cabbage.
Supper: Mielie rice.

Social History: She had not worked for four years. She was supported by an aunt, who was a school teacher. Her husband had died in 1946 and she had two children (18 years and 9 years). Both were well.

Special interrogation: She had never had a similar episode. She did not suffer from convulsions. She had not taken herbal medicines, had injections, or taken tablets. She had been having pleuritic pain, malaise, fever and cough periodically over the previous year.

Subsequent history: As far as she could discover all the other people with whom she drank were well.

SPECIAL INVESTIGATIONS

24.4.60 See above. Bld sugar 47 mg% (6 hours after I.V. dextrose).
Hb 11.5g%, W.B.C. 7,000/cmm,
P.C.V. 35 (mms) M.C.H.C. 33%, P.I. 57%.
Routine urine: Acetone +, microscopy - approximately 10 leukocytes per H.P.F. Nil else of note.
Chest X-ray - N.A.D.

25.4.60 P.I. 61%.

26.4.60 P.I. 61%, Serum amylase 16 W units.

27.4.60 P.I. 92%.
Hb. 11.0g%, W.B.C. 7,000/cmm.
E.C.G. - N.A.D.

28.4.60 P.I. 100%.

29.4.60 S. electrophoresis: S. albumin 2.8g%; S. globulins, α_1 0.8g%, α_2 0.6g%, β 1.4g%, 2.8g%.
Total proteins 9.1g%. Pattern compatible with cirrhosis.

2.5.60 Glucose tolerance test: Fasting 76 mg%, $\frac{1}{2}$ hour 80 mg%, 1 hour 103 mg%, $1\frac{1}{2}$ hour 86 mg%, 2 hours 86 mg%, $2\frac{1}{2}$ hours 66 mg%, 3 hours 74 mg%, $3\frac{1}{2}$ hours 86 mg%, 4 hours 78 mg%.

6.5.60 Hb. 10.7g% (73%), W.B.C. 22,000/cmm (N, 89, L, 4, M, 7). P.C.V. 31 mm, M.C.H.C. 35%, E.S.R. 61 mm/hr.
S. Typhi 0 = 0; Brucella = 0; Proteins OXK = 0;
OX_{19} = 1/80; OX_2 = 1/80.
No malarial parasites.
Urine - N.A.D.

7.5.60 Chest - N.A.D.

9.5.60 Albumin 2.4g%; S. globulin 5.8g%.
A/G Ratio 0.4:1

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver Biopsy
24. 4. 60	1	148	0. 8	4	Nil.	Neg.	57	
25. 4. 60	2	94			Nil.	Neg.	61	
26. 4. 60	3	60	1. 1	13	trace	Neg.	61	
27. 4. 60	4	50	0. 7		++	Neg.	92	
28. 4. 60	5	36			++	Neg.	100	Done.
29. 4. 60	6		0. 5		trace	Neg.		
30. 4. 60	7	30	0. 6		trace	Neg.		
2. 5. 60	10	36	0. 2		Nil.	Neg.		
9. 5. 60	17	36	0. 5		Nil.	Neg.		

Liver Biopsy

This was performed on 28. 4. 60. Section of liver showed a focus of necrosis accompanied by infiltration with neutrophils and round cells. No alcoholic hyalin was noted. Moderate fatty vacuolation with mild fine fatty globulation was observed. The portal tracts were oedematous and a number of round cells and acute inflammatory cells were present, together with slight portal fibrosis (grp. II). Haemosiderin was noted in both the portal triads and parenchyma (gr. 4). Glycogen was prominent (gr. 4). No bile duct hyperplasia or bile thrombi were observed.

[STAINS used: Haematoxylin and eosin, silver impregnation, Weigert's iron haematoxylin Van Gieson, Prussian blue reaction, PAS and Best carmine].

Course and management: The patient was transferred to the professorial ward on 6. 5. 60, after developing a temperature of 102°F. accompanied by pleuritic pain on the left side of the chest. Examination revealed a pellagrinous dermatitis on her forearms and hands, and a hepatomegaly (2 fd), but nothing else. X-ray Chest, urine, agglutination tests for typhoid, brucella and Rickettsia were negative but her W. B. C. was 22, 000/cmm and her E. S. R. 61 mms/hr. A course of penicillin (I. M. U. crystalline 6 hourly for 1 week;) resulted in no improvement but following a course of sulphatriads (1 gm 4 hourly) she recovered. The cause of her fever was not elucidated.

Assessment of Alcoholic habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition (Pellagra).

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Pellagra.

(4) Pyrexia of unknown origin.

CASE 10/60

G. C. INDIAN MALE, 42 years

Admitted 2. 5. 60 at 6. 15 p. m. Discharged 18. 5. 60.

OUT-PATIENT DEPARTMENT

Deep coma. No neck rigidity. Pupils constricted. Reflexes brisk. Bilateral ankle clonus and Babinski. Coma ? cause.

WARD

The father of the patient said his son had taken cane spirit at 10 a. m. on the day before admission. He had been noisy until 5 p. m. when he had gone to sleep. He could not be awakened for supper and had been left to sleep. The following morning he had not awakened and he had been brought to hospital later in the day. He was a chronic alcoholic.

Examination: In deep coma. Cold extremities, sweating. Temperature subnormal. No anaemia, jaundice, clubbing or lymphadenopathy.

C. V. S. Pulse 100 per minute, regular and feeble.
B. P. 110/80. Heart normal.

R/S Trachea central.
Rhonchi and coarse crepitations L chest.

Abd. Liver 1 fd. No splenomegaly.
No masses or free fluid.
Bowel sounds present.

C. N. S. Deep coma.
No response to painful stimuli.
Corneal reflexes present.
Pupils dilated, equal and respond only sluggishly to light. (cf. O. P. D.)
No obvious cranial nerve lesion.
Hypertonic.

Reflexes:	R.	L.
Biceps	++	++
Triceps	++	++
Knee	++	++
Ankles	+	+
Plantar	↑	↑
Abdomen	+/+	+/+

Diagnosis: Coma ? hypoglycaemic.

TREATMENT

After blood had been taken for special investigations 75 ml 50% intravenous dextrose was administered. The patient awakened immediately, became very violent and developed a coarse tremor.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 27 mg%, bld urea 37 mg%, serum electrolytes: Na, 139 meq/l, K, 4.9 meq/l, Cl, 102 meq/l.

Diagnosis: Hypoglycaemia ? Post alcoholic.

HISTORY FROM PATIENT

This was not obtainable due to the mental state of the patient. The father said the patient drank heavily and daily. His diet was poor as he did not eat very often. He was married but he did not work.

SPECIAL INVESTIGATIONS

2.5.60 See above.
Hb 16.6g% (114%), P.C.V. 53% (mms), M.C.H.C. 31%,
W.B.C. 7,000/cmm., E.S.R. 2 mms/hr.
Bld sugar 215 mg% after dextrose solution.
Routine urine: Urobilin +, bilirubin ++.

3.5.60 S. Amylase 4 W units.

4.5.60 Hb. 16.0g% (110%), W.B.C. 8,000/cmm.
P.C.V. 48% (mms), M.C.H.C. 33%.

5.5.60 Total Protein 8.7g%, S. Albumin 3.7g%, S. globulin 5.0g%,
A:G Ratio 0.7:1.

6.5.60 Reticulocytes $<1.0\%$

11.5.60 Glucose tolerance test: Fasting 73 mg%, $\frac{1}{2}$ hour 132 mg%, 1 hour 191 mg%, $1\frac{1}{2}$ hours 96 mg%, 2 hours 50 mg%, $3\frac{1}{2}$ hours 64 mg%, 4 hours 73 mg%.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver Biopsy
2.5.60	1		4.3	12	+	++	78	
3.5.60	2						88	
4.5.60	3							
5.5.60	4		2.8	8	+++	Neg.	100	
6.5.60	5				++	Neg.		
7.5.60	6							
9.5.60	8	104	0.6		+	Neg.		
11.5.60	10	70			Nil.	Neg.		
12.5.60	11		0.3					
13.5.60	12				Nil.	Neg.		
14.5.60	13	42	0.5					
15.5.60	14				Nil.	Neg.		
16.5.60	15	40			Nil.	Neg.		

Liver biopsy: Not done.

Course and management: The patient developed delirium tremens on the second day after admission. He was mentally normal four days later after sedation. Otherwise his course was uneventful. There was marked improvement in his general condition on discharge.

Assessment of nutrition: Poor nutrition.

Assessment of alcohol habits: Chronic alcoholic.

Final diagnosis:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Delirium tremens.

SECOND ADMISSION

The patient was readmitted in December 1960, in hypoglycaemic coma, (bld sugar 20 mg%) following a spell of heavy drinking. He had stopped drinking for a month after his previous admission. A liver biopsy was performed ten days after admission.

Liver biopsy Performed on 21. 12. 60.

Section of liver showed moderate portal fibrosis (grp III). Moderate fatty vacuolation and fine intercellular change were noted (gr. 2). The portal tracts showed infiltration with numerous acute and numbers of chronic inflammatory cells. No definite foci of necrosis or alcoholic hyalin was noted. Glycogen was present (gr. 3). Haemosiderin was observed in the parenchyma and portal triads (gr. 4). No bile thrombi or bile duct hyperplasia were seen.

[STAINS used: Haematoxylin and eosin, silver impregnation, Weigert's iron haematoxylin Van Gieson, Prussian blue reaction, Sudan III and Best Carmine].

The notes of the second admission were mislaid.

CASE 11/60

Z.N. AFRICAN MALE, 23 years.

Admitted 11.5.60. at 12.35 p.m. Discharged 24.5.60.

OUT-PATIENT DEPARTMENT

In coma. Alcoholic odour on breath.

? gavine poisoning ? hypoglycaemic coma.

WARD

A cousin said the patient had drunk a large amount of gavine on the night before admission. He had vomited and had then fallen asleep. On the morning of admission the patient could not be awakened. He had been in good health prior to the drinking episode. There had been no history of injury.

Examination: Dehydrated. Temperature 98°F. No pallor cyanosis or jaundice. Odour of alcohol on his breath.

C.V.S. Pulse 100 per minute. B.P. 120/70. Heart sounds closed.

Abd. No hepatomegaly or splenomegaly.

C.N.S. Semi-comatose.
No obvious cranial nerve palsy.
Pupils react to light.
Generalised flaccidity.

Reflexes	R.	L.
Biceps	+	+
Triceps	+	+
Supinator	+	+
Knee	++	++
Ankle	+	+
Plantars	equivocal.	

Responds to supra-orbital pressure.

Diagnosis: ?Alcoholic poisoning ?? hypoglycaemia.

TREATMENT

Blood was first taken for special investigation and then 40 ml of 50% intravenous dextrose solution was administered. The patient regained consciousness but remained mentally abnormal.

IMMEDIATE SPECIAL INVESTIGATIONS

Blood sugar 20 mg%, serum electrolytes: Na 126 meq/l, Cl, 101 meq/l, CO_2 content 21.6 meq/l.

Diagnosis: ? Post-alcoholic hypoglycaemia.

HISTORY FROM PATIENT

No history was obtainable during the first two days because the patient was unable to answer questions. Once mentally normal he was unable to give a history other than that he was drinking before admission.

Alcohol habits: He was a heavy weekend drinker usually imbibing gavain. He did not drink on his own. He had been drinking for about seven years.

Dietary history: Breakfast: Mielie meal porridge.
Lunch: Samp and meat occasionally.
Supper: Porridge.

Social history: He had no job at the time of admission.

Special interrogation: He had never had a similar episode previously. He did not suffer from convulsions. He had not taken herbal medicines or tablets or had an injection prior to admission.

SPECIAL INVESTIGATIONS

11.5.60 See above.
Hb. 18.0g% (123%), P.C.V. 23(2 mms), M.C.H.C. 34%,
E.S.R. 4 mms/hr., W.B.C. 19,000/cmm (N86, L10, M4)
Platelets normal. Bld urea 40 mg%. S. amylase 8 W units.
Serum electrophoresis: S. Albumin 3.1g%, S. globulin α_1 1.1g%, α_2 1.2g%, β 1.2g%, γ 3.0g%, Total protein 9.6g%.

12.5.60 Routine urine N.A.D.

16. 5. 60 Chest X-ray. The heart and lungs appear normal. Glucose tolerance test: Fasting 61 mg%, ½ hour 72 mg%, 1 hour 79 mg%, 1½ hours 108 mg%, 2 hours 64 mg%, 2½ hours 54 mg%, 3 hours 64 mg%, 3½ hours 54 mg%.
S. Albumin 4.1g%, S. globulin 3.5g%, Total protein 7.6g% A:G ratio 1:2:1.

19. 5. 60 17 ketosteroids 6.5 mg/24 hours, glucocorticoids 18.9 mg/24 hours. 24 hour urinary volume 3,770 ml.

Date	Day	T	B	A.P.	U.	U.B.	P.I.	Liver biopsy
11. 5. 60	1		0.5	11	Nil.	Neg.	72	
12. 5. 60	2	60	1.3		Nil.	Neg.	89	
13. 5. 60	3	104	1.6		++	Neg.	89	Done.
14. 5. 60	4	110	0.5		Nil.	Neg.		
15. 5. 60	5	70	0.5		Nil.	Neg.		
16. 5. 60	6	78	0.3	4	Nil.	Neg.		
18. 5. 60	8	44						
19. 5. 60	9	30						
20. 5. 60	10				Nil.	Neg.		
21. 5. 60	11				Nil.	Neg.		

Liver biopsy:

This was performed on 13. 5. 60. Section of liver showed severe fatty vacuolation and fine intercellular fatty change. No alcoholic hyalin or foci of necrosis were seen. The portal triads were infiltrated by an occasional neutrophil or round cell and there was no increase in fibrous tissue (grp I). Haemosiderin was noted in the parenchyma at the periphery of the lobule (gr. 2). No bile thrombi or bile duct hyperplasia were observed. Glycogen was present (gr. 3).

[STAINS used: Haematoxylin and eosin, Weigert's iron haematoxylin Van Gieson, Prussian blue reaction and Best carmine].

Course and management:

The patient was unable to speak for about 24 to 30 hours after the dextrose therapy. It was later ascertained that he had had a period of motor aphasia for about twelve hours and loss of memory before that.

He was given no treatment and his remaining course in hospital was uneventful.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor.

FINAL DIAGNOSIS

(1) Post alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

CASE 12/60

M.M. AFRICAN FEMALE, 38 years.

Admitted 18.6.60 at 3.10 p.m. Died 6.7.60 at 8.20 p.m.

OUT-PATIENT DEPARTMENT

No history was available. The patient was admitted as an emergency in a state of collapse.

WARD

No further history was available.

Examination: Moribund. Poor nutrition.
? slight pallor of mucosa.
No cyanosis or jaundice.
? Alcoholic odour on her breath.
Subnormal temperature 97°F.

C.V.S. Radial pulses not palpable.
Femoral pulse present - bradycardia.
? L carotid pulse absent.
Heart rate 30 per minute.
Heart sounds closed.

R/S Deep, slow, gasping respiration - 6 per minute.

Abd. No liver or spleen palpable.
Soft, no guarding or rigidity.

C.N.S. Deep coma.
No neck stiffness. Pupils do not react to light.
No corneal reflexes. Conjugate deviation of eyes to left.
? Rt hemiparesis.

Deep tendon Reflexes: Present and equal.
Plantars: Equivocal R & L.

Diagnosis: ? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 40 ml 50%

dextrose solution was administered. A slight improvement in the level of consciousness, a loss of conjugate deviation of the eyes, and a response in pulse, blood pressure and respiration followed. She remained in semi-coma.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 25 mg%, bld urea 31 mg%, serum electrolytes; Na 113 meq/l, K, 4.4 meq/l, Cl, 94 meq/l, Bld alcohol (V.R.S.) 17 mg%.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM A FRIEND

The patient was a heavy drinker, imbibing large quantities of gavain daily. She had not had a similar episode previously.

SPECIAL INVESTIGATIONS

18.6.60	See above. Hb. 14.8g% (100%), P.C.V. 46(mms) W.B.C. 17,000/cmm. C.S.F. (after dextrose therapy). Protein 15 mg%, chlorides 700 mg%, sugar 96 mg%. Microscopy - N.A.D. Serum electrophoresis: S. Albumin 2.9g%; S. globulins α_1 0.8g%, α_2 1.1g%, β 0.9g%, γ 2.1g%. Total protein 7.8g%.
19.6.60	Bld sugar 162 mg%.
20.6.60	Hb 13.5g% (92%), W.B.C. - 15,000/cmm, P.C.V. 44(mms) M.C.H.C. 31%, E.S.R. 39 mms/hr. Bld sugar 77 mg%. Serum electrolytes: Na, 143 meq/l, K, 4.6 meq/l, Cl, 104 meq/l.
21.6.60	Serum electrolytes: Na, 130 meq/l, K, 3.3 meq/l, Cl, 114 meq/l.
22.6.60	Bld urea 42 mg%.
23.6.60	S. Albumin 2.3g%, S. globulin 3.4g%. Total protein 5.7g%. A:G Ratio: 0.7:1.
29.6.60	Serum electrolytes Na, 139 meq/l, K, 5.4 meq/l, Cl, 94 meq/l.
4.7.60	Serum electrolytes Na, 117 meq/l, K, 3.3 meq/l, Cl, 102 meq/l.

Date	Days	J	B	A. P.	U	U. B.	P. I.	Liver biopsy
18. 6. 60	1	56	1. 5	8				Not done.
19. 6. 60	2	52	0. 9					
20. 6. 60	3	40	1. 1				88%	
21. 6. 60	4	40	1. 0		Nil.	Neg.		
22. 6. 60	5	28						
23. 6. 60	6	12	0. 7					

Course and Management

The patient remained in semi coma until 20. 6. 60 when she looked round but was unable to speak or respond to sound. On 22. 6. 60 she responded to her name for the first time, and on 28. 6. 60 said her name was "Mary" and asked for Zulu beer. On 29. 6. 60 she deteriorated after developing bronchopneumonia and despite penicillin and terramycin, died on 6. 7. 60. Her mental state never improved beyond answering 'yes' or 'no'. She refused all food, except Zulu beer, and was given intravenous therapy.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

Necropsy Findings:

Histology: (1) Section of liver showed congestion and marked vascular leukocytosis. Severe fine intercellular fatty change was present while haemosiderin was noted throughout the lobules (gr. 3). There was no evidence of increased fibrous tissue, foci of necrosis, or alcoholic hyalin.

(2) Section of lung showed congestion, oedema, and bronchopneumonia.

(3) Section of spleen showed congestion and neutrophilia.

(4) Pituitary natural.

(5) The left adrenal showed a small focus of necrosis with acute inflammatory cell infiltration in the cortex.

(6) Sections of heart muscle, pancreas, thyroid and kidney showed no abnormality.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Bronchopneumonia with a small pyaemic abscess in the left adrenal.

CASE 13/60

K. S. AFRICAN FEMALE, 42 years.

Admitted 12. 7. 60 at 9. 10 a. m. Discharged 23. 7. 60

OUT-PATIENT DEPARTMENT

Admitted as ? post-epileptic state.

WARD

According to relatives the patient had been drinking gavine on the day before admission. She had retired to bed in the evening and her son had not been able to wake her on the following morning. She was cold, but sweating and he brought her to hospital.

Examination:	Semicomatose. No pallor. Fair nutrition. Temperature 95. 6°F. Stale alcoholic odour on her breath. No jaundice or lymphadenopathy.
C. V. S.	Pulse 84 per minute. B. P. 170/130. Heart sounds closed.
R/S	Chest clear.
Abd.	Liwer 1 fd, firm edge, hard and slightly tender. No splenomegaly.
C. N. S.	Comatose (not fully examined).
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 100 ml 50% I. V. dextrose solution was administered. The patient recovered consciousness immediately.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 20 mg%, bld urea 35 mg%. Bld alcohol (V. R. S.) 76 mg%.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

She had been drinking gavine on the day before admission and retired to bed in the evening slightly intoxicated. She had reawakened in hospital. She had not eaten on the day she drank.

Dietary history: Predominantly carbohydrate diet.

Alcohol habits: She had been drinking a lot in the weekends the six months prior to admission.

Special interrogation:

She had never had a similar attack previously.

SPECIAL INVESTIGATIONS

12.7.60 See above.
Hb. 15.3g%, P.C.V. 49(%) M.C.H.C. 31%,
W.B.C. 6,000/cmm.

13.7.60 S. Amylase 8 W units.

Routine urine - N.A.D.

Total protein 4.5g%, S. albumin 2.1g%,
S. globulin 2.4g%,
A:G ratio 0.9:1.

18.7.60 Glucose tolerance test:

Fasting 85 mg%, ½ hour 123 mg%,
1 hour 141 mg%, 1½ hours 116 mg%,
2 hours 97 mg%, 2½ hours 78 mg%,
3 hours 78 mg%, 3½ hours 82 mg%,
4 hours 85 mg%.

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
12.7.60	1				++	Neg.		Not done
13.7.60	2	150		12	+	Neg.		
14.7.60	3	90	1.0		+	Neg.		
15.7.60	4	90	2.0		+	Neg.		
16.7.60	5	32	0.8		++	Neg.		
18.7.60	7		0.8		Nil.	Neg.		
19.7.60	8	20	0.7		Nil.	Neg.		
20.7.60	9				Nil.	Neg.		
21.7.60	10				Nil.	Neg.		

Liver biopsy: Not done.

Course and Management: Uneventful course.

Assessment of alcohol habits: Not assessed.

Assessment of nutrition: ? Fair nutrition.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

CASE 14/60

W.M. AFRICAN MALE, 29 years

Admitted 16.8.60 at 6.40 p.m. Discharged.

OUT-PATIENT DEPARTMENT

The patient's brother stated that the patient had been drinking on the day before admission and that he had not awakened on that day. On examination he was stuporose, speaking occasionally, but irrational and confused. A diagnosis of ? alcoholic poisoning ? pre-hepatic coma was made.

WARD

The brother said that the patient had been drinking shimeyane over the whole weekend and on Monday (day before admission). He had gone to bed on Monday night slightly drunk but had not awakened in the morning. Though consciousness had improved slightly at 5 p.m. on the same evening he had decided to bring him to hospital.

Examination:	Patient aggressive, restless and mumbles a few incoherent words. Stuporose. Temperature 97.5°F. Furred tongue. Breath smells strongly of alcohol.
C.V.S.	Pulse 110 per minute. B.P. 150/100. Heart sounds closed.
R/S	Chest clear.
Abd.	Tender R.U.Q. No guarding. Genitals - N.A.D.
C.N.S.	Stuporose, aggressive and incoherent speech. No neck stiffness. No tremor. Pupils large equal and respond to light. Reflexes: Tendon jerks present and equal.

Abdominal	+ +	+ +
Cremasteric	+	+
Plantars	↓	↓

Diagnosis: ? alcoholic poisoning ? liver failure
?? hypoglycaemia.

TREATMENT

After blood had been taken for special investigations 25 ml 50% intravenous dextrose solution was administered. The patient's mental state improved immediately.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 39 mg%, bld alcohol (V.R.S.) 11 mg%, bld urea 36 mg%, serum electrolytes: Na, 135 meq/l, K, 4.6 meq/l, Cl, 94 meq/l, Hb 17.3g% (118%) W.B.C. 3,000/cmm.

Diagnosis: Post alcoholic hypoglycaemia.

HISTORY FROM PATIENT

The patient stated (17.8.60) that he had been drinking shimeyane on the day before admission and over the weekend. He could not remember the day of admission at all. He had thought he had awakened in hospital that morning (he thus had a period of amnesia after dextrose therapy).

Alcohol habits: He had taken alcohol for years but had been drinking heavily for months. He never drank gavine. He did not add toxic additives to his liquor.

Dietary habits: He ate mainly samp, bread and mielie meal porridge. He ate meat twice a week but did not take milk.

Social history: Unmarried and unemployed.

Special Interrogation: He had been reasonably well prior to this episode. He had never had a similar attack before. He did not have fits. He had not taken herbal medicines, had injections or taken tablets prior to admission.

SPECIAL INVESTIGATIONS

16. 8. 60 — See above.

17. 8. 60 — Hb 15.3g% (105%), P.C.V. 48% M.C.H.C. 32%, W.B.C. 5,000/cmm, E.S.R. 9 mms/hr. Serum electrophoresis: S. Albumin 2.7g%, S. globulins, α_1 0.5g%, α_2 1.0g%, β 1.5g%, γ 1.2g%. Total protein 7.8g%.

18. 8. 60 — Bld sugar 83 mg%. (Fasting).

19. 8. 60 — S. amylase 8 W units.

20. 8. 60 — Chest X-ray ; - "There is evidence of a bilateral patchy consolidation. Cardiomegaly is present. A loculated pleural effusion is noted along the left lung border."

22. 8. 60 — Hb. 15.3g% (103%), P.C.V. 45% (mms) M.C.H.C. 34%, W.B.C. 12,000/cmm.

23. 8. 60 — E.C.G. Left ventricular hypertrophy.

29. 8. 60 — Glucose tolerance test: Fasting 91 mg%, $\frac{1}{2}$ hour, 107 mg%, 1 hour 157 mg%, $1\frac{1}{2}$ hours 175 mg%, 2 hours 187 mg%, $2\frac{1}{2}$ hours 128 mg%, 3 hours 90 mg%, $3\frac{1}{2}$ hours 90 mg%.

Hb. 11.9g% (87%), P.C.V. 38% (mms) M.C.H.C. 31%, W.B.C. 9,000/cmm, E.S.R. 51 mms/hr.

30. 9. 60 — Alcohol test: Hypoglycaemia not produced (lowest bld sugar 76 mg%).

Date	Day	T	B	A.P.	U.	U.B.	P.I.	Liver biopsy
16.8.60	1	200	0.7	15	Nil.	Neg.	82	Done
17.8.60	2	126	0.8		Nil.	Neg.		
18.8.60	3	102	1.2		+	Neg.		
19.8.60	4	40	0.4	2	+++	Neg.		
20.8.60	5	32	0.5		+++	Neg.		Done
21.8.60	6	20	0.2		+++	Neg.		
22.8.60	7	18	0.2		++	Neg.		
24.8.60	9				++	Neg.		
25.8.60	10				++	Neg.		
26.8.60	11				++	Neg.		
27.8.60	12				++	Neg.		
29.8.60	13				++	Neg.	84	
30.8.60	14				trace	Neg.		
31.8.60	15				trace	Neg.		
2.9.60	17				Nil.	Neg.		
3.9.60	18				Nil.	Neg.		
4.9.60	19				Nil.	Neg.		
5.9.60	20				Nil.	Neg.		
6.9.60	21				Nil.	Neg.		

Liver biopsy: A liver biopsy was performed on admission, 16.8.60, prior to dextrose therapy. A small portion of liver was stained for glycogen with Best carmine and periodic acid / Schiff stains. Section showed a complete absence of glycogen. A second liver biopsy was performed on 20.8.60. Section of liver showed a moderate quantity of glycogen (gr.3). A focus of necrosis with acute inflammatory cells (Fig9) was noted. No alcoholic hyalin was present. Severe fatty vacuolation and moderate fine intercellular fatty change was observed (gr.4). The portal triads showed infiltration with numbers of acute and chronic inflammatory cells, but there was no increase in fibrous tissue (grp. 1). Haemosiderin was present in the cells throughout the lobule and small clumps were noted particularly at the portal triad (gr.4). No bile thrombi or bile duct hyperplasia were observed.

[STAINS used: Haematoxylin and eosin, Sudan III, Weigert's iron haematoxylin Van Gieson, Prussian blue reaction, Best carmine and periodic acid/Schiff].

COURSE AND MANAGEMENT

On 21. 8. 60 the patient developed a temperature of 102°F and bronchial breathing and crepitations in the chest. Chest X-ray showed bilateral patchy consolidation of the lungs and cardiomegaly. Courses of antibiotics were given, including chloromycetin, without improvement on Chest X-ray by 19. 9. 60. Sreptomycin and I. N. H. were then commenced as the diagnosis was considered to be tuberculosis and slow improvement occurred. He was well on discharge two months later.

Assessment of alcohol habits: ? Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) ? Chronic Alcoholic.

(4) Pulmonary tuberculosis.

CASE 15/60

L.S. AFRICAN MALE, 60 years

Admitted 19.9.60 at 12.25 p.m. Died 19.9.60 at 3.45 p.m.

OUT-PATIENT DEPARTMENT

Admitted as a cerebrovascular accident.

WARD

Relatives stated that the patient had been drinking Zulu beer on the day before admission in the morning. He had been talkative after drinking. At 1.30 p.m. he had felt weak and tired and had lapsed into unconsciousness. He had not eaten on that day. A private doctor had been called and he had thought that the patient had had a cerebrovascular accident. (The doctor's note stated that he had found a bilateral Babinski). He was admitted to hospital 24 hours later.

Alcohol habits: He drank in the weekends, but he was not a heavy drinker. Assessment: Non-Alcoholic.

Social history: He was married and worked at a factory.

Examination: Deeply comatose. Apyrexial. Fair nutrition. Irregular movements of right arm (twitching). No odour on his breath.

C.V.S. Pulse 70 per minute. B.P. 110/40. Heart normal.

R/S Crepitations and a few rhonchi heard bilaterally.

Abd. No hepatomegaly or splenomegaly.

C.N.S. Deep coma.
Pupils small and no response to light.
Fundi not visualised.

Deep tendon reflexes	R.	L.
Biceps	±	±
Triceps	±	±
Knee	—	—
Ankle	—	—

Plantar reflexes: No response.

Diagnosis: Coma ? cerebro-vascular accident
? bronchopneumonia.

TREATMENT:

Blood was taken for special investigations and 2 million units of crystalline pencillin was administered. No dextrose solution was given by the house physician. The patient died two hours after admission. The blood sugar, received later, was 36 mg%.

NECROPSY

This was performed 16 hours after death and apart from bronchopneumonic consolidation macroscopical examination was natural.

Histology:

(1) Section of liver showed a moderate fatty change (gr. 2). The portal triads were oedematous and numerous round cells were present. There was a slight increase in fibrous tissue. Haemosiderin was prominent in the parenchyma and at the portal triads (gr. 5). Glycogen was absent (gr. O). No foci of necrosis or alcoholic hyalin were noted.

[STAINS used: Haematoxylin and eosin (H & E), Sudan III, Best carmine, periodic acid/Schiff (PAS), Weigert's iron haematoxylin Van Gieson (W. H. V. G.) and Prussian blue reaction].

(2) The lungs showed oedema and bronchopneumonia.

(3) The kidneys, pancreas, adrenals, pituitary, heart muscle and brain cortex showed no abnormality.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.
(2) Bronchopneumonia.

CASE 16/60

M.S. INDIAN FEMALE, 49 years

Admitted 3.10.60 at 11.40 a.m. discharged 17.10.60.

OUT-PATIENT DEPARTMENT

No history was available. A smell of stale alcohol was noted on the breath. An abrasion was present on the forehead. She was admitted in coma ? internal head injury.

WARD

No history available; found in coma.

Examination:

Comatose.
Temperature 97°F. Abrasion on forehead.
Hydration fair. Nutrition fair. Smell of stale alcohol on her breath.
No jaundice, anaemia or cyanosis.

C.V.S. Pulse 80 per minute regular.

B.P. 160/120. Heart normal.

R/S Trachea central. Occasional scattered rhonchi.

Abd. Liver and spleen not palpable.

C.N.S. Comatose. No neck stiffness. Pinpoint pupils.
Conjugate deviation of eyes to L.
? Rt. facial nerve palsy.
Hypertonia in all limbs.

Reflexes:	R.	L.
Triceps	+++	+++
Biceps	+++	+++
Knee	+++	+++
Ankle	+++	+++
Plantars	↑	↑

Bilateral ankle clonus.

Diagnosis: ? Cerebro-vascular accident.
? Hypertensive encephalopathy.

IMMEDIATE SPECIAL INVESTIGATIONS

Blood was taken for special investigations and a lumbar puncture was performed. The cerebrospinal sugar was found to be 16 mg% without other abnormalities. No treatment was given until this result was received 1½ hours after admission.

Bld sugar 26 mg%, bld alcohol (V.R.S.) 11 mg%, serum electrolytes: Na, 130 meq/l, K, 4.4. meq/l, Cl, 108 meq/l, Bld urea 40 mg%, Hb 13.3g% (91%), P.C.V. 44 (mms), M.C.H.C. 30%, W.B.C. 8,000/cmm, E.S.R. 24 mms/hr.

C.S.F. Chlorides 740 mg%, protein 20 mg%, sugar 16 mg%, Microscopical N.A.D.

Routine urine PH 6.0, S.G. 1015, Acetone trace, micro. occasional hyaline and granular casts. Nil else of note.

TReatment

20 ml. 50% intravenous dextrose solution was administered and the patient immediately recovered consciousness.

HISTORY FROM PATIENT

The patient had taken brandy on the afternoon before admission. She had retired to bed drunk, at 6 p.m., and she had reawakened in hospital. She had been quite well previous to this. She had eaten breakfast at 8 a.m. on the day of admission.

Alcohol habits: She stated she only drank in the weekends and always brandy. She did not add toxic substances to her liquor.

Dietary habits:

Breakfast: Mielie meal porridge and milk.
Lunch: Not eaten.
Supper: Rice. Meat once per week.

Social history: She washed clothes and claimed she received three shillings a week. She had no relatives but was looked after by her next door neighbours. Her husband had died and left her the house. She rented out rooms.

Special interrogation: She had always been well and had never had a similar attack previously. She did not suffer from fits.

She had not taken herbs, had injections or medicine prior to the above episode.

SPECIAL INVESTIGATIONS

3. 10. 60	See above.
4. 10. 60	Serum electrophoresis. S. Albumin 2. 2g%. S. globulin α_1 0. 6g%, α_2 0. 9g%, β 1. 4g%, γ 3. 0g% Total protein 8. 1g%.
5. 10. 60	S. Albumin 2. 4g%, S. globulin 5. 6g% Total protein 8. 0g%, A/G Ratio 0. 4:1.
6. 10. 60	Bld urea 23 mg%.
13. 10. 60	Glucose tolerance test: Fasting 100 mg%, $\frac{1}{2}$ hour 116 mg%, 1 hour 157 mg%, $1\frac{1}{2}$ hours 144 mg%, 2 hours 144 mg%, $2\frac{1}{2}$ hours 130 mg%, 3 hours 102 mg%, $3\frac{1}{2}$ hours 86 mg%.
14. 10. 60	Chest X-ray: Small bilateral cervical ribs noted. Otherwise N. A. D.

Date	Days	T	B	A. P.	U.	U. B.	P. I.	Liver biopsy
3. 10. 60	1	38	0. 8	14	Nil	Neg.	100	Done
4. 10. 60	2	40	0. 9	9	trace	Neg.		
5. 10. 60	3	46	0. 6		Nil.	Neg.		
6. 10. 60	4	42	0. 7	8	Nil.	Neg.		
7. 10. 60	5	50	0. 4		trace	Neg.		
8. 10. 60	6	47	0. 4		Nil.	Neg.		
9. 10. 60	7	36	0. 4		Nil.	Neg.		
10. 10. 60	8	20	0. 6		Nil.	Neg.		
12. 10. 60	10	28	0. 6					
13. 10. 60	11		0. 5					

Liver Biopsy: This was performed on 3. 10. 60, $1\frac{1}{2}$ hours after receiving 20 ml 50% intravenous dextrose solution. Section of liver showed small foci of necrosis infiltrated with neutrophils. No alcoholic hyalin was noted. The portal triads showed infiltration with numbers of chronic and a few acute inflammatory cells but there was no increase in fibrous tissue (grp I). A severe fatty vacuolation,

particularly periportal, and a severe fine intercellular fatty change was noted (gr. 4). Haemosiderin was noted in the liver cells throughout the lobules (gr. 3). No bile thrombi or bile duct hyperplasia was observed. Glycogen was present (gr. 2).

[STAINS used: H & E, silver impregnation for reticulin, W. H. V. G., Sudan III, Best carmine and PAS].

Course and management:

The patient had an uneventful course during hospitalisation. No medication was supplied.

Assessment of alcohol habits:

Weekend drinker.

Assessment of nutrition:

Fair nutrition.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

CASE 17/60

M. N. AFRICAN MALE, 45 years.

Admitted 8. 10. 60. at 9. 55 a. m. Discharged 17. 11. 60.

OUT-PATIENT DEPARTMENT

No history available. Comatose, pellagrinous dermatitis, collapsed, smelling of alcohol, widely dilated pupils, stuporose, bradycardia (pulse 45 per minute), ? neck stiffness.

? cerebro-vascular accident ? acute alcoholic intoxication.

WARD

No history was available but as the patient was collapsed and smelling of stale alcohol 25 ml 50% intravenous dextrose solution was given, after blood had been taken for special investigation, in case the patient was in hypoglycaemic coma. There was an immediate improvement in consciousness. The patient was confused and unable to give a history.

Examination: (after dextrose therapy).

Thin, pellagrinous dermatitis. Lice $^{++}$
Cold, Sweating.
No anaemia, jaundice, clubbing, oedema cyanosis or lymphadenopathy.
Tongue - red and smooth.
Breath ? stale alcohol.

C. V. S. Pulse 88 per minute. B. P. 100/50. Heart normal.

R/S Coughing^{+}. Bilateral rhonchi.

Abd. Liver just felt but spleen not palpable.

C. N. S. Disorientated. No neck rigidity. Speech slurred.

Deep tendon reflexes absent.

Plantar reflexes equivocal.

Sensation N. A. D.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 33 mg%, bld alcohol (V.R.S.) 12 mg%, bld urea 25 mg%, serum electrolytes: Na, 135 meq/l, K, 3.7 meq/l, Cl 111 meq/l.

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

A history was obtained from the patient later in the day of admission, after he had become orientated. He had drunk Zulu beer on the day before admission, with friends, and he was intoxicated when he retired to bed at 8 p.m. that evening. He awoke on the day of admission at 8 a.m. and commenced to smoke. He reawakened in hospital. He thought he had eaten on the day he had imbibed but was not sure.

Alcohol habits: He had started drinking at the age of 18 years. He drank Zulu beer initially at the beer halls but over the two years prior to admission, with friends. He did not drink daily and at times stayed without liquor for 2 - 3 days. He rarely drank brandy. He often drank from morning till evening. He had not worked for two years and occupied most of his time drinking with friends. He had no money to buy liquor. He did not add toxic additives to his alcohol.

Dietary habits: His diet consisted mainly of mielie products.

Social history: He was married with two children aged 7 and 10 years (girl and boy). He stayed with his sister at Cato Manor and his family was at Bulwer. His sister had been the sole breadwinner for the family for the previous two years as he was unemployed.

Special interrogation: He had never had a similar attack previously. There was no history of fits. He had not taken herbal medicines, had injections or medicine prior to the episode.

Subsequent history: The friends with whom he drank apparently remained well.

SPECIAL INVESTIGATIONS

8. 10. 60	See above. Hb. 13. 2g% (90%), P. C. V. 42 (mms) M. C. H. C. 31%, W. B. C. 9000/cmm, E. S. R. 37 mms/hr. Serum electrophoresis: S. albumin 2. 0g%, S. globulins α_1 0. 9g%, α_2 1. 0g%, β 1. 1g%, γ 2. 9g%, Total protein 7. 9g%.
9. 10. 60	S. albumin 2. 4g%, S. globulin 5. 4g% Total protein 7. 8g% A. G. ratio 0. 5:1.
11. 10. 60	P. I. 100%.
13. 10. 60	Chest X-ray ; - N. A. D.
18. 10. 60	Glucose tolerance test: Fasting 63 mg%, $\frac{1}{2}$ hour 116 mg%, 1 hour 129 mg%, $1\frac{1}{2}$ hours 108 mg%, 2 hours 71 mg%, $2\frac{1}{2}$ hours 54 mg%, 3 hours 58 mg%, $3\frac{1}{2}$ hours 67 mg%, 4 hours 67 mg%.
20. 10. 60	V. D. R. L. (slide) Reactive 8 dilutions W. R. Reactive 16 dilutions
28. 10. 60	17 ketosteroids 11. 5 mg per 24 hours, glucocorticoids 3. 6 mg per 24 hours, urine volume 3, 440 ml.

Date	Days	T	B	A. P	U	U. B.	P. I.	Liver biopsy
8. 10. 60	1	150	0. 8		Nil	Neg.		
9. 10. 60	2	82	0. 8	15	Trace	Neg.		
10. 10. 60	3	74	0. 4		++	Neg.		
11. 10. 60	4	74	0. 4		++	Neg.	100	Done
12. 10. 60	5	66	0. 6	14	++	Neg.		
13. 10. 60	6	68	0. 4		+	Neg.		
14. 10. 60	7	40	0. 2		trace	Neg.		
15. 10. 60	8	60	0. 3		trace	Neg.		
16. 10. 60	9				Nil.	Neg.		
17. 10. 60	10	54	0. 3		Nil.	Neg.		
18. 10. 60	11	76	0. 3		Nil.	Neg.		
19. 10. 60	12	46			Nil.	Neg.		
20. 10. 60	13	58			Nil.	Neg.		
22. 10. 60	15	40						
24. 10. 60	17	30						

Liver biopsy:

This was performed on 11. 10. 60. Section of liver showed a number of foci of necrosis accompanied by neutrophilic and round cell infiltration. In some foci haemosiderin was noted. Alcoholic hyalin was not observed. The portal triads showed chronic and acute inflammatory cells, which were also present in fibrous septa that linked the triads and caused some lobular distortion (severe diffuse septal fibrosis) (grp IV). Moderate fatty vacuolation was noted but it was marked in the periportal zones (gr. 3). Haemosiderin was noted throughout the lobules while clumps of haemosiderin were present in the lobules and at the portal triads (gr. 4). No bile thrombi or bile duct hyperplasia were seen. Glycogen was present (gr. 4).

[STAINS used: H & E, silver impregnation, Sudan III, Best Carmine, Mallory's phosphotungstic acid/haematoxylin (P. T. A. H.)].

Course and management: There was improvement in his nutritional state on discharge. He was given plebex, 4 ml I-M. daily for 5 days and a good diet.

Assessment of alcohol habits:

? Chronic alcoholic.

Assessment of nutrition:

Poor nutrition (Pellagra).

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis

(3) Pellagra.

CASE 18/60

M. G. AFRICAN MALE, 36 years

Admitted 10. 10. 60 at 2. 25 p. m. Discharged 31. 10. 60

OUT-PATIENT DEPARTMENT

No history available. Semicomatose. Temperature 97. 6°F. Alcoholic odour on his breath. ? Acute alcoholic intoxication.

WARD

Stuporose. Said his name was Jeremiah Gamede. Unable to obtain anything else from him.

Examination:	Stuporose, coughing, temperature 97. 6°F. No anaemia or cyanosis ? clubbing.
C. V. S.	Pulse 60 per minute. B. P. 110/70. Heart sounds closed.
R/S	Trachea central. Chest clear.
Abd.	No hepatomegaly or splenomegaly. Genitals N. A. D.
C. N. S.	Cranial nerves apparently normal. Ears N. A. D. All limbs flaccid. Deep tendon reflexes present and equal. Plantars reflexes ↑↑ Responds rapidly to pain.
Diagnosis:	? Alcoholic intoxication ? Post-alcoholic hypoglycaemia.

TREATMENT

After taking blood for special investigations 35 ml 50% intravenous dextrose solution was administered. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 43 mg%, bld urea 35 mg%, Hb 15.1g% (103%), W.B.C. 9,000/cmm.

Diagnosis: Hypoglycaemia ? post alcoholic.

HISTORY FROM PATIENT

He said he had been drinking Zulu beer and brandy with a group of friends from 9 a.m. to 7 p.m. on the day before admission. He had then retired to bed, not having eaten lunch or supper though he had had breakfast of soup and samp. At 5 a.m. on the following morning he had awakened and had gone to work by bus, and had reached the factory at 6 a.m. when work began. At 6.35 a.m. while using a machine, he had felt giddy and had hot and cold flushes and cramp in the lower limbs. Within half an hour he had not been able to do a light job which the foreman had given him. He had then lost consciousness and convulsions had occurred. The employer had considered that the patient was drunk and he had been discharged from his job.

Alcohol habits: He participated in a social drinking group over the weekends. The group never visited Shebeens and most of them were teachers or clerks who had permits. He had commenced drinking at the age of 19 years. He had started by only taking Zulu beer but gradually went on to stronger drinks. On Saturdays and Sundays he drank the whole day with his friends, commencing at 9 or 10 a.m. and ending at 7 p.m. He drank Zulu beer, beer, gavine and European liquor. He only drank for pleasure in the weekends. He did not cause unhappiness at home or with his neighbours. He was never extremely drunk. He did not add toxic substances to his liquor.

Dietary habits: This consisted mainly of samp, curry and rice and milk. He had green vegetables two to three times a week and meat occasionally.

Social history: He worked in a factory earning £4.7.5 per week. His wife earned £3.4.0 per month and his brother, who stayed with him, £3.10.0 per month. He had two

children of 8 and 6 years (girl and boy). They spent 25 shillings perweek on food. After paying rent, they had £9. 14. 4 left over but most of it was used for furniture accounts.

Subsequent history: The friends with whom he had been drinking did not have similar episodes.

Special Interrogation: He had been quite well till his admission and had never had a similar episode. He had never had convulsions. He had not taken herbal medicines, had injections or taken medicine before his admission.

SPECIAL INVESTIGATIONS

10. 10.60 See above.

12. 10. 60 Total protein 7. 0g%, Serum albumin 3. 1g%, serum globulin 3. 9g%, A G Ratio 0. 8 1.
17-Ketosteroids 8, 2 mg/24 hours, total glucocorticoids 3. 4 mg/24 hours. Urinary volume 870 ml.

13. 10. 60 Chest X-ray - N. A. D.

17. 10. 60 Glucose tolerance test: Fasting 70 mg%, ½ hour 102 mg%, 1 hour 138 mg%, 1½ hours 130 mg%, 2 hours 110 mg%, 2½ hours 98 mg%, 3 hours 82 mg%, 3½ hours 71 mg%, 4 hours 65 mg%.

20. 10. 60 Alcohol test: 100 ml alcohol, as 200 ml 50% redistilled ethyl alcohol, was administered between 9. 15 - 10. 00 a. m. Bld sugar remained in 70-80 mg range in subsequent 4 hours (lowest level 71 mg%). The blood alcohol level reached 153 mg% (see text p 63). For subsequent liver function tests see table.

28. 10. 60 17-ketosteroids 12. 6 mg/24 hours, total glucocorticoids 7. 2 mg/24 hours, urinary volume 1800 ml.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
11.10.60	2	44	0.4	7	Nil.	Neg.	94	Done
12.10.60	3	40	0.6	6	+	Neg.		
13.10.60	4				Trace	Neg.		
14.10.60	5	26	0.4		Trace	Neg.		
15.10.60	6	40	0.2		Trace	Neg.		
16.10.60	7				Trace	Neg.		
17.10.60	8	28	0.2	7				
18.10.60	9	30	0.3		Nil.	Neg.		
19.10.60	10				Nil.	Neg.		
20.10.60	11	36						
Alcohol Test								
21.10.60	12	44						
22.10.60	13	50	0.2		Nil.	Neg.		
23.10.60	14	154	0.2		Nil.	Neg.		
24.10.60	15	66	0.2		Nil.	Neg.		
25.10.60	16	38	0.3		Nil.	Neg.		
26.10.60	17	50	0.4		Nil.	Neg.		
27.10.60	18	48	0.4		Nil.	Neg.		
28.10.60	19	34	0.4		Nil.	Neg.		

Liver Biopsy: This was performed on 11.10.60. Section showed no foci of necrosis or alcoholic hyalin. Fatty vacuoles were not observed but there was severe fine intercellular change. A number of acute and chronic inflammatory cells were noted in the portal triads, which showed a slight increase in fibrous tissue (grp II). Haemosiderin was present throughout the lobules and clumps were noted in the parenchyma and at the portal triads (gr. 5). No bile duct hyperplasia or bile thrombi were seen. Glycogen was present (gr. 4).

[STAINS used: H. & E., silver impregnation, W.H.V.G. Prussian blue reaction, Best carmine].

Course and Management: Uneventful course in hospital.

Assessment of alcohol habits: Weekend drinker.

Assessment of Nutrition: Poor nutrition.

FINAL DIAGNOSIS: (1) Post-alcoholic hypoglycaemia.
(2) Alcoholic Hepatitis.

CASE 19/60

F.M. AFRICAN MALE, 34 years.

Admitted 1.11.60 at 4.15 p.m. Discharged 19.11.60.

OUT-PATIENT DEPARTMENT

A relative stated that the patient had had ten seizures that day. A diagnosis of grand mal epilepsy was made.

WARD

According to the relative the patient had been drinking heavily on the night before admission, and he had lost consciousness. He had been incontinent and had vomited on three occasions. On the morning of admission he had begun to fit and had approximately ten seizures.

Examination:	In coma. Pellagrinous dermatitis.
C.V.S.	Pulse 90 per minute, regular. B.P. 120/70. Heart sounds closed.
R/S	Stertorous breathing. Numerous rhonchi posteriorly.
Abd.	Right paramedian scar. No hepatomegaly or splenomegaly. Genitals N.A.D.
C.N.S.	Comatose. No neck stiffness. Pupils small, equal and react to light. All limbs spastic. Deep tendon reflexes brisk and equal. Plantar reflexes ↓↓
Diagnosis	? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 70 ml intravenous 50% dextrose solution was administered. The patient regained consciousness but was confused and restless.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 23 mg%, bld urea 33 mg%, blood alcohol (V. R. S.) 28 mg%, Serum electrolytes: Na, 124 meq/l, K, 5.0 meq/l, Cl, 112 meq/l, prothrombin index 35%, Hb 14.8g% (100%), W. B. C. 6000/cmm.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

The patient remained confused until 5.00 p.m. the next day when he was able to give a vague history. Evidently he had been drinking heavily on the day before admission. He had been drinking gavine and Zulu beer on his own. He had not awakened on the following morning and he had found himself in hospital. He had eaten a little food on the day he had been drinking.

Alcohol habits: He drank gavine daily in large quantities. He did not add toxic substances to his liquor.

Dietary habits: Mainly mielie products but exact history difficult to obtain.

Social history: Unemployed. Unmarried. Sells gavine for a living.

Special Interrogation: He had never had a similar attack or fits previously. He had not taken herbal medicines or had injections prior to the above episode.

SPECIAL INVESTIGATIONS

1.11.60 See above.
Serum electrophoresis: S. albumin 2.3g%. S. globulins α_1 0.5g%, α_2 0.9g%, β 1.4g%, γ 2.6g%
Total proteins 7.7g%.

2.11.60 Serum proteins: Total proteins 7.8g%, S. albumin 3.0g%, S. globulin 4.8g%, A:G ratio 0.6:1.

6.11.60 Glucose tolerance test: Fasting 78 mg%, ½ hour 103 mg%, 1 hour 174 mg%, 1½ hours 119 mg%, 2 hours 103 mg%, 2½ hours 84 mg%, 3 hours 70 mg%.

9.11.60 17-ketosteroids 6.8 mg/24 hours, total glucocorticoids 15.0 mg/24 hrs. Urinary volume 3,000 ml. Fasting blood sugar 69 mg%.

14.11.60 Chest X-ray N.A.D.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
1.11.60	1	550	0.4	15	Nil.	Neg.	35	
2.11.60	2	260	0.4	13	Nil.	Neg.	87	
3.11.60	3	124	0.4	11	++	Neg.	88	
4.11.60	4	70	0.4	10	+++	Neg.		Done
5.11.60	5		0.6	9	+++	Neg.		
6.11.60	6	96	0.2		trace	Neg.		
7.11.60	7	90	0.4		Nil.	Neg.		
8.11.60	8	66			Nil.	Neg.		
9.11.60	9	60						
10.11.60	10	50			Nil.	Neg.		
11.11.60	11	40						

Liver biopsy: This was performed on 4.11.60. Section of liver showed 2 foci of cellular degeneration and necrosis with acute inflammatory cell infiltration. Alcoholic hyalin was not observed. There was severe fatty vacuolation at the periportal zones and a fine intercellular fatty change throughout the lobules (gr.4) The portal triads showed numbers of chronic and occasional acute inflammatory cells. There was a slight increase in fibrous tissue at the triads (grp.II). Haemosiderin was marked throughout the lobules and clumps were noted in the parenchyma and at the portal tracts (gr.5). Glycogen was present (gr.4). There were no bile thrombi and bile duct hyperplasia was not observed.

[STAINS used: H. & E., silver impregnation, W.H.V.G., Sudan III, Prussian-blue reaction, Best carmine].

Course and management:

The patient was unable to answer questions on the first two days of admission. He then suffered from slurred speech for a further

three days. His speech defect and his mental state were normal six days after admission.

Assessment of Alcohol habits: Chronic alcoholic.

Assessment of Nutrition: Poor nutrition (pellagra).

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Pellagra.

CASE 20/60

A. N. AFRICAN MALE, 58 years.

Admitted 7. 11. 60 at 7. 20 a. m. Discharged 21. 11. 60

OUT-PATIENT DEPARTMENT

Admitted in Coma ? cause.

WARD

According to his relatives the patient had begun drinking a half bottle of cane spirits at 8 p. m. on the night before admission. He began groaning and became unconscious at 1 a. m. He had no fits. He evidently did not normally drink a lot. He had eaten a full lunch at midday but no supper before imbibing.

Examination: Semicomatose. Poor nutrition. No cyanosis, jaundice, anaemia or lymphadenopathy, Clubbing marked. Stridor.

C. V. S. Pulse regular and good volume. B. P. 140/90. Heart sounds closed.

R/S Stridor. Coarse crepitations all over chest. Bronchial breathing and ? cavity right apex.

Abd. Soft non-tender. No hepatomegaly or splenomegaly.

G. U. S. N. A. D.

C. N. S. Semicomatose - looks round the ward but not in contact with his surroundings. No neck stiffness. Kernigs negative. Cranial nerves appear intact. Responds to pin prick and deep pain. Slight hypotonia.
Deep tendon reflexes present and equal.

Abdominal reflexes 

Plantars 

DIAGNOSIS: ? Post alcoholic hypoglycaemia.

TREATMENT

Bloodwas taken for special investigations, a liver biopsy was performed and then 15 ml 50% I. V. dextrose solution was administered. The patient recovered consciousness immediately.

IMMEDIATE SPECIAL INVESTIGATIONS

Blood sugar 23 mg %, V.R.S. (blood alcohol) 20 mg%, Serum electrolytes, Na, 130 meq/l, K, 4.2 meq/l, P.I. 92%, blood urea 24 mg/100 ml. Hb 20.3g (141%), W.B.C. 20,000/cmm, Urine, trace acetone.
Liver biopsy - see later.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

He had drunk half a bottle of cane spirits on the evening before admission. He had awakened in hospital. He had eaten lunch but no supper on the day he imbibed.

Alcohol habits: He had commenced social drinking in 1942 and had always imbibed European liquor with his friends. He had drunk heavily in the weekends. He had stopped drinking in 1953, except for an occasional drink. He always imbibed European liquor. On the evening before admission a friend arrived with half a bottle of cane spirit and he drank it. (According to his relatives he had hardly imbibed since 1953). He did not add substances to his alcohol.

Dietary habits: Breakfast: Oat meal or Maltabella porridge, bread and tea.
Lunch: Bread.
Supper: Samp, Vegetables and meat occasionally.

Social history: Married with three children (boys of 17 and 9 years and a girl of 13 years). Family relationship is good. He received an invalidity grant of £2. 7. 6 every month. His wife also received a seven shilling food parcel every

two weeks. He paid rent of £1. 10. 0 per month.

Special interrogation: He had never had a similar attack previously. He did not suffer from fits. He had not taken herbal or other medicines. He suffered from asthma and had had tuberculosis, though he was now considered cured.

SPECIAL INVESTIGATIONS

7. 11. 60 Immediate special investigations see above.

10. 11. 60 17-Ketosteroids 2. 2 mg/24 hr, total glucocorticoids 5. 8 mg/24 hrs, Urine volume 870 ml.

14. 11. 60 Chest X-ray :-

"There is evidence of old fibrotic tuberculous scarring throughout both lung fields most marked in the lung apices. Numerous healed calcified foci evident. Although activity cannot be excluded on a single radiographic examination the lesions appear to be of very long standing".

21. 11. 60 Glucose tolerance test :

Fasting 63 mg/100 ml; ½ hour 70 mg/100 ml;
1 hr 90 mg/100 ml, 1½ hrs 90 mg/100 ml;
2 hrs 74 mg/100 ml; 2½ hrs 55 mg/100 ml;
3 hrs 45 mg/100 ml; 3½ hrs 49 mg/100 ml;
4 hrs 63 mg/100 ml.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver Biopsy
7. 11. 60	1	28	0. 2	12	++	Neg.	92	Done
8. 11. 60	2	24	0. 4		Nil.	Neg.		
9. 11. 60	3	40	0. 4		trace	Neg.		
10. 11. 60	4	50	0. 2		Nil.	Neg.		
11. 11. 60	5	48	0. 4		trace	Neg.		
12. 11. 60	6	30			Nil.	Neg.		
13. 11. 60	7	50			Nil.	Neg.		
14. 11. 60	8	52						
16. 11. 60	10	30						
18. 11. 60	12	22						

Liver Biopsy: This was performed on admission prior to therapy. Section of liver showed complete absence of glycogen (gr. O). No fatty vacuolation was observed but there was a severe fine intercellular fatty change (gr. 3). A slight increase in fibrosis was noted at the portal triads but there was also marked fibrosis in one area suggestive of post-necrotic cirrhosis (?grp. V). Haemosiderin was present in both the parenchyma and at the portal triads (gr. 4). No foci of necrosis or alcoholic hyalin were observed. Bile thrombi and bile duct hyperplasia were not noted.

[STAINS used: H. & E, silver impregnation, W. H. V. G., Perl's prussian-blue reaction, Best carmine, P. A. S., and Sudan III].

Course and management: On 10. 11. 60, three days after admission the liver was found to be 4 fd. and tender. Otherwise his course was uneventful. His nutrition, which was extremely poor showed marked improvement on discharge. He was given anti-tuberculous therapy in case his chest condition was still active.

Assessment of alcoholic habits: Non-alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS (1) Post-alcoholic hypoglycaemia.

(2) ?? Alcoholic hepatitis.

CASE 21/60

B.N. AFRICAN MALE, 5 years

Admitted 25.11.60 at 6.40 p.m. Died 26.11.60 at 2.30 p.m.

OUT-PATIENT DEPARTMENT

Admitted with convulsions ? cause.

WARD

History obtained from the mother was that she had left home at 7 a.m. in the morning, when both her children were well. On returning home at 8.30 a.m. when she intended to feed them, she found both her children asleep, and when the patient failed to awaken, she took him to a clinic arriving there at 9.15 a.m. He vomited there and a stomach washout after this revealed mucus and fluid, which had a strong smell of alcohol resembling Zulu beer. (There was Zulu beer in the house). At 3 o'clock in the afternoon the child began to fit and he was sent to hospital.

Diet: Given milk daily; also meat and vegetables.

Examination: The patient was a comatose well-nourished, slightly dehydrated child.
Mild cervical lymphadenopathy. No anaemia.
Afebrile.

C.V.S. Pulse 120/minute, regular.
Heart sounds closed.

R/S Respiratory rate normal.
Numerous scattered rhonchi throughout the chest.

Abd. Liver and spleen not palpable.

C.N.S. Deep tendon reflexes not obtained.
Plantars equivocal.

Ears N.A.D.

Throat N.A.D.

Past History: No previous fits or loss of consciousness.

Diagnosis: ? Alcoholic Poisoning.

COURSE AND MANAGEMENT

Blood was taken for blood sugar, electrolytes, CO_2 CP and F.B.C. estimation and a lumbar puncture was performed. No treatment was given. At 2.30 a.m. the blood sugar and the C.S.F. sugar were found to be 24 mgms%. The patient was immediately given 40 ccs 50% I.V. dextrose solution with mild improvement in his mental state but he remained semicomatose. A subsequent blood sugar taken at 3.30 a.m. was 146 mgms%. After this a continuous drip containing glucose was administered. The patient died at 2.30 p.m. on the 26th November 1960, having had an occasional convulsion on that day.

SPECIAL INVESTIGATIONS

25.11.60 Blood sugar 24 mg %.
C.S.F. Clear colourless fluid, globulin no increase, cells nil, Chlorides 760 mg/100 ml, Protein 10 mg%, Sugar 24 mg %.
Serum electrolytes; Na, 126 meq/l, K, 4.1 meq/l, Cl, 116 meq/l. CO_2 C.P. 7.6 meq/l.
Hb 11.5g% (81%), W.B.C. 8,000/cmm.

26.11.60 Bld sugar 146 mg%.

NECROPSY

This was done on 29.11.60. Macroscopical examination revealed no abnormality.

Histology: (1) Liver Sections showed glycogen (gr.3). There was no obvious fatty change.
(2) Sections from lung, kidney, heart, spleen pancreas, adrenal and pituitary showed no abnormality.

FINAL DIAGNOSIS:

Post- alcoholic hypoglycaemia.

CASE 22/60

M. M. AFRICAN MALE, 50 years

Admitted 17. 12. 60 at 9.40 a. m. Discharged 23. 12. 60.

OUT-PATIENT DEPARTMENT

According to the doctor's note, the patient had collapsed suddenly that morning, sweating profusely. Thereafter he was unable to move, or speak coherently. ? Cerebrovascular accident. He was admitted as an undiagnosed coma.

WARD

No history other than the above.

Examination:	Semi-comatose, restless, fair nutrition.
C. V. S.	Pulse 84 per minute, regular. B. P. 120/80. Heart sounds closed.
R/S	Chest clear.
Abd.	No hepatomegaly or splenomegaly.
G. U. S.	N. A. D.
C. N. S.	Semicomatose. Generalised rigidity. No localising signs.
Diagnosis:	Coma ? cause.

TREATMENT

Blood was taken for special investigations and then 50% I. V. dextrose was administered in case the patient was in hypoglycaemic coma. Immediate recovery of consciousness occurred.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 20 mg%, bld urea 20 mg%, serum electrolytes: Na, 139 meq/l, K, 3.3 meq/l, Cl, 97 meq/l, prothrombin index 78%.

Diagnosis: Hypoglycaemia ? cause.

HISTORY FROM PATIENT

The patient had been drinking Zulu beer and shimeyane with many others on the day before admission. He had retired to bed at about 7 p.m. and he had reawakened on the following morning at about 7 a.m. He had dressed and gone to the toilet. He had returned back to his bed 15 minutes later and had reawakened in hospital. He had not eaten on the day that he had been drinking. His last meal had been at 12.30 p.m. on the previous day.

Alcohol habits: He drank every weekend - Friday night, Saturday and Sunday - but never during the week. He did not add toxic additives to his liquor.

Dietary habits:
Breakfast: Mielie meal porridge.
Lunch: Bread.
Supper: Samp, mielies and porridge.

Social history: He worked during the week (5-day) and earned £2.10.0 per week at a factory. He was married with eight children. His wife was dead.

Special interrogation: He had never had a similar episode previously. He had never had a fit. He had not taken herbal medicines, had injections, or medicines.

Subsequent history: As far as he could find out, none of the other people with whom he drank suffered a similar attack.

SPECIAL INVESTIGATIONS

17.12.60 See above.

18.12.60 Bld sugar 130 mg%.

19.12.60 Routine urine - N.A.D. 17-ketosteroids 2.2mg/24 hrs, total glucocorticoids 2.2 mg/24 hrs.

21.12.60 Total protein 7.2g%, S. albumin 3.7g%, S. globulin 3.5g%, A:G Ratio 1.1:1.
Chest X-ray - "Opacities are seen in both upper lobes with contraction of the left upper lobe. The appearances are those of P.T.B." The cardiac outline is within normal limits. There is a small plaque of calcification in the aortic arch.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
17.12.60	1	186					78	
18.12.60	2	62			+	Neg.		
19.12.60	3	60			Nil.	Neg.		Done
20.12.60	4	44	0.7	5	Nil.	Neg.		
21.12.60	5	40	0.4	6	Nil.	Neg.		
22.12.60	6	50						
23.12.60	7	20						

Liver biopsy This was performed on 20.12.60. Section of liver showed small foci of necrosis accompanied by neutrophils and round cells. One focus showed a large multinucleated cell indicating regeneration. Alcoholic hyalin was not observed. A very rare fat vacuole was noted and there was no evidence of fine intercellular fatty change (gr 0-1). The portal triads were infiltrated by an occasional chronic inflammatory cell but haemosiderin was so severe that it was difficult to assess. There was no increase in portal fibrous tissue (grp I). Haemosiderin was marked both in the lobules and at the portal tracts (gr. 5). Glycogen was present (gr. 2). There was no bile duct hyperplasia and bile thrombi were not seen.

[STAINS used: H. & E. silver impregnation, Sudan III, Best carmine, and Perl's Prussian-blue reaction].

Course and Management:

The patient was transferred on 23. 12. 60, pulmonary tuberculosis having been diagnosed.

Assessment of alcohol habits:

Weekend drinker.

Assessment of nutrition:

Fair nutrition.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Pulmonary Tuberculosis.

CASE 23/60

A.M. AFRICAN MALE, 41 years

Admitted 17.12.60 at 2.30 p.m. Discharged 23.12.60.

OUT-PATIENT DEPARTMENT

No history available. Admitted as an undiagnosed coma.

WARD

No history available.

Examination:	The patient was in semicoma, restless. A strong smell of alcohol on his breath. Poor nutrition - hyperpigmentation.
C.V.S.	Pulse 92 per min. B.P. 70/50. Heart sounds closed.
Abd.	2 fd. hepatomegaly, firm with sharp edge. No splenomegaly.
C.N.S.	No neck stiffness. Pupils small equal and react to light. Hypotonia. Reflexes difficult to elicit. Plantars equivocal.
Diagnosis:	Coma ? hypoglycaemia.

TREATMENT

Blood was taken for special investigations but no treatment was administered.

3.30 p.m. B.P. 60/40. Pulse feeble. Respiratory rate 10 per minute. No response to stimuli - deep coma. Twenty millilitres 50% intravenous dextrose solution was given and the patient recovered consciousness. He was inebriated on recovery. A liver biopsy was performed.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 47 mg%, bld urea 29 mg%, prothrombin index

index 91%, serum electrolytes, Na, 113 meq/l, K, 3.6 meq/l, Cl, 107 meq/l, Hb 15.8g% (108%), W.B.C. 28,000/cmm (N. 72, L. 28).

Diagnosis: Hypoglycaemia ? Post-alcoholic.

History from patient: He had been drinking Zulu beer at the beer hall on the afternoon before admission. He had not eaten that day and his last meal had been at 5.30 p.m. on the day before. On the day of admission he had taken a half bottle of gin at 10 a.m. He had reawakened in hospital.

Alcohol habits: He drank Zulu beer every evening, becoming happy, and heavily in the weekends. At lunch time he had a pint of Zulu beer at the beer hall. He infrequently drank European liquor. He did not add toxic additives to his liquor.

Dietary habits: Samp, beans, porridge and maas was his usual diet. At lunch he had Zulu beer.

Social history: Unmarried. He had worked for a Construction Company for the past seven years. He received £11 per month. (His work permit confirmed it).

Special interrogation: He had never had a similar episode. He had never had a fit. He had not taken herbal medicines, injections or medicines prior to his admission.

SPECIAL INVESTIGATIONS

17.12.60	See above.
18.12.60	Routine urine N.A.D.
21.12.60	17-ketosteroids 12.9 mg/24 hrs, total glucocorticoids 3.5 mg/24 hrs. Total protein 7.2g%, S. albumin 3.7g%, S. globulin 3.5g%. A:G ratio 1.1/1.
22.12.60	Glucose tolerance test: Fasting 55 mg%, ½ hour 80 mg%, 1 hour 135 mg%, 1½ hours 110 mg%, 2 hours 80 mg%, 2½ hours 65 mg%, 3 hours 65 mg%, 3½ hours 55 mg%.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
17. 12. 60	1	336					91	Done
18. 12. 60	2	180			Nil.	Neg.		
19. 12. 60	3	108			Nil.	Neg.		
20. 12. 60	4	60	0. 6	7	Nil.	Neg.		
21. 12. 60	5	58	0. 6	6	trace	Neg.		
22. 12. 60	6	56						
23. 12. 60	7	30						

Liver Biopsy: This was performed on admission a few minutes after intravenous dextrose had been administered. Section of liver showed complete absence of glycogen (gr. O). Severe fine intercellular fatty change with an occasional fatty vacuole (gr. 4) noted. There were no foci of necrosis and alcoholic hyalin was not observed. The portal triads showed a few acute and chronic inflammatory cells and there was moderate portal fibrosis with peripheral linkage of triads - 'periportal fibrosis' (grp. III). Haemosiderin was present throughout the lobules and in the portal triads (gr. 5). No bile duct hyperplasi a or bile thrombi were observed.

[STAINS used: H. & E. silver impregnation, W. H. V. G., prussian-blue reaction, Sudan III, Best carmine, PAS].

Course and Management: The patient recovered consciousness after intravenous dextrose therapy but remained drowsy and was inebriated. His further course in hospital was uneventful.

Assessment of alcohol habits: ? Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hepatitis.

(2) Alcoholic hepatitis.

CASE 1/61

M. J. AFRICAN MALE, 30 years

Admitted 16.4.61 at 7.10 p.m. Discharged 22.4.61.

OUT-PATIENT DEPARTMENT

Admitted as an emergency. Moribund ? cause.

WARD

A relative stated that at 4 p.m. the patient had begun to sweat and had then collapsed and frothed at the mouth and he had thought the patient was having a fit. The patient was a heavy drinker and he had wondered whether he had been taking alcohol. No other history was obtainable.

Examination:	Moribund. Stertorous breathing. Pulse not palpable. Heart rate ⟨30 per minute. B.P. unrecordable. Frothing at the mouth. Not jaundiced. No evidence of head injury. Temperature 96°F.
R/S	Bilateral coarse rhonchi.
C.V.S.	Heart sounds distant and difficult to hear.
Abd.	Liver and spleen not palpable.

TREATMENT

Because of his moribund state, no further examination was carried out and he was given 50 ml 50% I.V. dextrose solution in case he was in post-alcoholic hypoglycaemia, after blood had been taken for special investigations. An immediate recovery of consciousness, rise in pulse and B.P. occurred, but he remained confused for a few hours.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 47 mg%, serum electrolytes K 3.6 meq/l, Cl, 102 meq/l.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

This was taken on 17.4.61 as he had been confused after dextrose therapy. He had had a gavine party on Friday night, two days before

admission, and he had been drinking again on the morning of admission. He could not remember how he had come to hospital or when he had last eaten prior to drinking.

Alcohol habits: He drank heavily in the weekends including Friday night. He did not add toxic substances to his liquor.

Dietary habits: Samp, mielie rice, mielie meal porridge, beans (3 times per week). Occasionally meat.

Social history: Married with two children. He worked at a chemical factory and received £16 per month.

Special Interrogation: He had never had a similar attack previously. He did not suffer from fits. He had not taken herbal medicines, injections or medicines prior to admission.

SPECIAL INVESTIGATIONS

16.4.61 See above.

17.4.61 Routine urine N.A.D.

Total serum protein 8.0g%, serum albumin 4.0g%, serum globulin 4.0g%
A.G ratio 1:1.
Bld urea 20 mg%.

18.4.61 Hb 13.0g% (87%).
P.C.V. 38(mm) W.B.C. 8,000/cmm.
M.C.H.C. 34%,
E.S.R. 38 mm/hr.

19.4.61 17 ketosteroids 9.1 mg/24 hrs,
total glucocorticoids 1.8 mg/24 hrs,
urine volume 870 ml.

Date	Days	T	B	A. P.	U.	U. B.	P. I.	Liver biopsy
16.4.61	1							Not done
17.4.61	2	40	0.5	3	Nil.	Neg.	100	
18.4.61	3		0.7	7	Nil.	Neg.	100	
19.4.61	4	80	0.7	11				
20.4.61	5	54						

Course and management:

Following his initial dextrose therapy the patient remained confused but was rational on the following day (±12 hours). His subsequent course was uneventful.

Assessment of alcohol habits:

Heavy weekend drinker.

Assessment of nutrition:

Fair nutrition.

FINAL DIAGNOSIS:

(1) Post alcoholic hypoglycaemia.

[In September 1961, the patient was admitted with a blood dyscrasia. He had not had a similar attack since his discharge on 22.4.61].

CASE 2/61

B. V. INDIAN FEMALE, 35 years.

Admitted 24. 4. 61 at 10. 20 a. m. Discharged 14. 5. 61.

OUT-PATIENT DEPARTMENT

Relatives stated that the patient had been drinking cane spirit on the night before admission. She had been found unconscious on the following morning. She was admitted as ? alcoholic coma.

WARD

History as above.

Examination:	Semicomatose. Pupils dilated and react to light. Odour of alcohol on her breath. Temperature 99°F.
C. V. S.	Pulse 100 per minute. B. P. 130/80. Heart sounds closed.
R/S	Bilateral rhonchi.
Abd.	Liver and spleen not palpable.
C. N. S.	No paralysis.

Deep tendon reflexes equal and normal.

Plantar reflexes ↓↓

Diagnosis: ? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations followed by the intravenous administration of 50 ml 50% I. V. dextrose solution. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 27 mg%, P. I. 78%, blood urea 24 mg%, serum electrolytes; Na, 154 meq/l, K, 4. 6 meq/l, Cl, 102 meq/l, bld urea 24 mg%, Hb 9. 8g%, W. B. C. 34, 000/cmm. (N 93, L3, M4).

Diagnosis: Hypoglycaemia ? Post-alcoholic

HISTORY FROM PATIENT

The patient had been drinking a small bottle of cane spirit on the night before admission. She had been intoxicated when she had finished it and had retired to bed at 8.30 p.m. She had reawakened in hospital. She had eaten curry and rice at midday on the day before admission.

Alcohol habits: She drank cane spirit one day a week. (This was later confirmed by her relatives who said she did not drink much and they did not regard her as a heavy drinker.

Dietary habits: No breakfast.
Lunch and Supper: Mielie rice, rice and bread.

Social history: She was married with three children (16 and 8 year old girls and a five year old boy). She worked in a flat for £3 per month. Her husband received £8 per month.

Special Interrogation: She had never had a similar attack previously. She did not have fits. She had not taken herbal medicines, had injections or taken tablets prior to her admission.

SPECIAL INVESTIGATIONS

24.4.61	See above.
25.4.61	Total protein 7.0g%, serum albumin 3.8g%, S. globulin 3.2g%. A:G ratio 1.2:1. Hb 8.1g%, W.B.C. 10,000/cmm. P.C.V. 32%(mms)
26.4.61	17-ketosteroids 5.0 mg/24 hrs, total glucocorticoids 0.6 mg/24 hrs., urine volume 690 ml.
4.5.61	Glucose tolerance test: Fasting 74 mg%, ½ hour 104 mg%, 1 hr 124 mg%, 1½ hr 118 mg%, 2 hrs 98 mg%, 2½ hour 74 mg%.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver Biopsy
24.4.61	1	110	0.9	5	Nil.	Neg.	78	Not done
25.4.61	2	118	1.0	5	Nil.	Neg.	68	
26.4.61	3	86	0.8	6	Nil.	Neg.	90	
27.4.61	4	52	0.9	6	Nil.	Neg.		
28.4.61	5	60	0.8	6	Nil.	Neg.		
29.4.61	6	54						
30.4.61	7							
1.5.61	8	56						
2.5.61	9	58						
3.5.61	10	44						
4.5.61	11	58						
6.5.61	13	40						

Course and management:

The patient had an uneventful recovery. She was given iron on discharge.

Assessment of alcohol habits: Non-alcoholic.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Post alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 3/61

E.K. AFRICAN FEMALE, 50 years

Admitted 1.5.61 at 10.20 a.m. Discharged 1.6.61.

OUT-PATIENT DEPARTMENT

The relatives stated that she had been drinking gavine on the day before admission and that she had come home intoxicated and had retired to bed, without eating. She had been found in coma that morning. She was admitted as ? post-alcoholic hypoglycaemia ? cerebro-vascular accident.

WARD

History as above.

Examination:	Comatose. Poor nutrition, slight oedema of lower limbs. Alcoholic odour on her breath.
C.V.S.	Pulse 120 per minute. B.P. 130/80. Heart sounds closed.
R/S	Scattered rhonchi. Crepitations in left axilla.
Abd.	Liver and spleen not palpable.
C.N.S.	Comatose. Pupils constricted. All deep tendon reflexes brisk. Abdominal reflexes absent. Plantar reflexes equivocal.
Diagnosis: ?	Post alcoholic hypoglycaemia.

TREATMENT

Blood was initially taken for special investigations and after that 65 ml 50% I.V. dextrose solution was administered. The patient regained consciousness but remained confused.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 28 mg%, bld urea 47 mg%, serum electrolytes Na, 130 meq/l, K, 5.0 meq/l, Cl, 110 meq/l, Hb 11.6g% (78%), P.C.V. 36 mms, M.C.H.C. 32%, W.B.C., 18000/cmm.

Diagnosis: Hypoglycaemic ? post-alcoholic.

HISTORY FROM PATIENT

She had been drinking gavine and Zulu beer on the day before admission from midday till 5 p.m. She had eaten samp and beans before her drinking bout but she had eaten nothing after that. She could not remember what had happened to her till she had reawakened in hospital.

Alcohol habits: According to her relatives she was a heavy drinker but she stated she only drank gavine and zulu beer in the weekends (her history appeared to be unreliable).

Dietary habits:
Breakfast: Porridge and condensed milk.
Lunch: Mielie meal porridge samp and occasionally beans.
Supper: Mielie meal porridge.

Social history: She was unemployed. She received £ 1 per month pension. She lived with her daughter and a family of eight.

Special interrogation: She had never had a similar attack or fits. She had not taken herbal medicines, injections or tablets before her admission.

SPECIAL INVESTIGATIONS

1.5.61 See above.
4.5.61 Serum proteins: Total protein 7.5g%, S. albumin 3.6g%, and serum globulin 3.9g%, A:G ratio 0.9:1.
5.5.61 17-ketosteroids 7.7 mg/24 hours, total glucocorticoids 2.7 mg/24 hours. Urine volume 940 ml/24 hrs.
10.5.61 Chest X-ray ? pulmonary tuberculosis left apex.
12.5.61 17-ketosteroids 5.4 mg/24 hours, total glucocorticoids 6.0 mg/24 hours. Urine volume 1300 ml.
17.5.61 Hb 9.8g% (66%), P.C.V. 32(mm) M.C.H.C. 31%, W.B.C. 12,000/cmm.
18.5.61 Chest X-ray reviewed by tuberculosis hospital. Patient accepted as a case of pulmonary tuberculosis.

Date	Days	T	B	A.P.	U.	U.B.	P.I.	Liver biopsy
4.5.61	4	88	0.7	15			100	Not done
5.5.61	5	68	1.0	15	Nil.	Neg.		
6.5.61	6	84	0.7	12	Nil.	Neg.		
8.5.61	8	44	0.5	3	trace	Neg.		
9.5.61	9	22	0.4	10	Nil.	Neg.		

Course and management:

On 3.5.61 the patient's B.P. was found to be 220/120 and her liver 2 fd. On 8.5.61 bronchial breathing was noted at the left apex and the chest X-ray on the 10.5.61 suggested pulmonary tuberculosis. Crystalline penicillin was initially administered, but on 13.5.61 Streptomycin, I.N.H. and pyridoxine were commenced. On 18.5.61, the patient was transferred to a tuberculosis hospital.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

(3) Pulmonary tuberculosis.

CASE 4/61

N. T. AFRICAN FEMALE, 40 years

Admitted 20. 5. 61 at 10. 20 a. m. Discharged 2. 6. 61.

OUT-PATIENT DEPARTMENT

Her relatives stated that she had taken a lot of alcohol on the day before admission and that she had not eaten. She had been found unconscious that morning. She was admitted in coma ? hypoglycaemic.

WARD

History as above.

Examination:	Semicomatose. Alcoholic odour on her breath. No anaemia, jaundice, oedema or generalised lymphadenopathy.
C. V. S.	Feeble pulse ? 120 per minute. B. P. 100/70. Heart sounds closed.
R/S	Scattered rhonchi but nil else of note.
Abd.	Liver and spleen not palpable.
C. N. S.	Semicomatose. Pupils constricted. Hypertonia and generalised rigidity.
Diagnosis:	? Post alcoholic hypoglycaemia ? Alcoholic coma.

TREATMENT

After blood had been taken for special investigations, 50 ml 50% intravenous dextrose solution was administered. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 34 mg%, blood alcohol (V. R. S.) 75 mg%, P. I. 100%, serum electrolytes: Na, 152 meq/l, K, 4.4 meq/l, Cl, 90 meq/l, Hb 14. 2g% (97%), W. B. C. 7, 000/cmm. Routine urine: P_H 6. 0, Acetone ++++. Nil else abnormal.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

The patient had been drinking Zulu beer on the day before admission. She had retired to bed intoxicated at 8 p.m. She had not remembered anything till she had awakened in hospital. She had eaten a few beans for breakfast on the day she had imbibed but had no lunch or supper.

Alcohol habits: She usually drank Zulu beer in the weekends but did not always become intoxicated. She did not drink during the week. She did not add toxic substances to her liquor.

Dietary habits: Mielie meal porridge, samp and beans.

Social history: She had 4 children, 2 adults and 2 youths. She did not work but looked after her children at home.

Special interrogation: She had never had a similar episode previously and she did not have fits. She had not taken herbal medicines, injections or tablets before admission.

SPECIAL INVESTIGATIONS

20.5.61	See above.
22.5.61	Bld urea 12 mg%. Chest X-ray N.A.D. 17-ketosteroids 10.7 mg/24 hrs, total glucocorticoids 18.6 mg/24 hrs, urine volume 2120 ml.
23.5.61	Total serum proteins 7.5g%, S. Albumin 3.9g%, S. Globulins 3.2g%, A:G ratio 1.1:1.

Date	Days	T	B	A. P.	U.	U. B.	P. I.	Liver biopsy
20. 5. 61	1	164	0. 3	9	Nil.	Neg.	100	Not done.
21. 5. 61	2	108	1. 0	10				
22. 5. 61	3	86	1. 0	10	Nil.	Neg.		
23. 5. 61	4	88	0. 8	10	+	Neg.		
25. 5. 61	6	98	1. 0	8	Nil.	Neg.		
26. 5. 61	7		0. 2					
29. 5. 61	10		0. 3	8				

Course and Management:

Uneventful course.

Assessment of alcohol habits: Heavy weekend drinker.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 5/61

Z.R. AFRICAN FEMALE, 4 years

Admitted 22.5.61. Discharged 7.6.61

OUT-PATIENT DEPARTMENT

Admitted in coma ? cause.

WARD

The child had been found comatose on the morning of admission. She had been quite well on the previous day. She had never had a fit or been in coma before.

Dietary habits: Samp, mielie meal porridge and vegetables.

Past history: Nil of note.
She was the 7th child of a family of 8 - all well.

Examination: Semi-comatose. Alcoholic odour on her breath. No signs of injury. Temperature 98°F.

C.V.S. Bradycardia. Heart sounds normal.

R/S Numerous scattered rhonchi.

Abd. N.A.D.

C.N.S. No neck rigidity.
Ears N.A.D.
Semi comatose.
Pupils react to light and accommodation.
Corneal reflex present.
No deep tendon reflexes obtained.
Plantar reflexes ↓↓

Diagnosis: ? Alcoholic intoxication ? post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigation followed by intravenous administration of 25 ml 50% dextrose solution. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 19 mg%, bld alcohol (V.R.S.) 14 mg%, bld urea 41 mg%, serum electrolytes: Na 143 meq/l, K 4.4 meq/l, Cl, 99 meq/l, Hb 13.0g% (87%), P.C.V. 38 (mms) M.C.H.C. 34%, W.B.C. 29,000/cmm (N 79, L15, M 4).

Diagnosis:

Hypoglycaemia ? Post-alcoholic.

HISTORY FROM MOTHER

The father was a heavy gavine drinker and she felt it was likely that the child had taken some on the morning of admission, as she had not eaten anything that day. She had not been taking herbal medicines, injections or tablets.

SPECIAL INVESTIGATIONS

22.5.61 See above.

Serum proteins: Total protein 7.0g%.

S. albumin 3.3g%, S. globulin 3.7g%

A:G ratio 0.9:1.

5.6.61 Glucose tolerance test, with 25 gm glucose by mouth produced a flat curve, but technical difficulties were encountered - ? accurate.

Date	Days	T	B	A.P.	U.	U.B.	P.I.	Liver Biopsy
22.5.61	1	92	0.8	30				Not done
23.5.61	2	162	0.8	25			92	
24.5.61	3	220			Nil.	Neg.		
25.5.61	4	136	0.7		+	Neg.		
26.5.61	5	130	0.2	14	Nil.	Neg.		
27.5.61	6				Nil.	Neg.		
29,5.61	8		0.3	14	Nil.	Neg.		
30.5.61	9	58						
1.6.61	11	40	0.2					
5.6.61	15	40						

Course and management:

Uneventful course in hospital.

Assessment of alcohol habits: Non-alcoholic.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hepatitis.

(2) Alcoholic hepatitis.

CASE 6/61

G.N. AFRICAN FEMALE, 40 years

Admitted 2/9/61 at 3.30 p.m. Discharged 9.9.61.

OUT-PATIENT DEPARTMENT

No history available ? cerebrovascular accident
? Post-epileptic state.

WARD

No history available.

Examination:	A comatose adult female, with a stale odour (? alcohol) on her breath. Pellagrinous dermatitis. Temperature 97°F.
C.V.S.	B.P. 150/100. Heart sounds closed.
R/S	Chest clear.
Abd.	Liver and spleen not palpable.
C.N.S.	Comatose. Pupils react to light. Hypertonia. Increased deep tendon reflexes in lower limbs (knee and ankle jerks).
Diagnosis:	? hypoglycaemic coma.

TREATMENT

Blood was taken for special investigations followed by the administration of intravenous 50% dextrose solution. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 25 mg%, Hb 16.0g% (110%), W.B.C. 7,000/cmm
Routine urine Acetone ++, nil else of note.

Diagnosis: Hypoglycaemia ? cause.

HISTORY FROM PATIENT

She had been drinking a large amount of Zulu beer on the afternoon prior to admission. She had not eaten on the day she had imbibed and she had only had breakfast of porridge on the day prior to that, though she had not taken alcohol on that day. She could not remember anything till awakening in hospital.

Alcohol habits: She was a heavy weekend drinker, drinking Zulu beer and shimeyane, but never gavine. She occasionally obtained brandy or gin. She also drank two to three times during the week.

Dietary habits: Breakfast: Mielie meal porridge, maas.
Lunch: No lunch.
Supper: Samp, occasionally beans.

Social history: She was married, but had no children. Her husband did not drink much alcohol. She did not work.

Special interrogation: She had never had a similar episode previously and she did not suffer from fits. She had not taken herbal medicine, tablets or an injection before admission.

SPECIAL INVESTIGATIONS

2.9.61 See above.

3.9.61 17-ketosteroids $<$1 mg/24 hours, total glucocorticoids $<$1 mg/24 hours, Urine volume 2,570 ml.

4.9.61 Bld urea 18 mg%.

6.9.61 Total serum proteins 5.0 g%, S. albumin 2.0g%, S. globulin 3.0g%.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
2.9.61	1	112			Nil.	Neg.		Not done
3.9.61	2							
4.9.61	3	60	0.8	9	trace	Neg.	80	
6.9.61	5	42	0.6	7	trace	Neg.	94	
7.9.61	6	74	0.3	6	+	Neg.		
8.9.61	7		0.7	6	Nil.	Neg.		
9,9.61	8	66	0.7		Nil.	Neg.		

Course and Management

The patient had an uneventful recovery, her pellagrinous dermatitis having improved prior to discharge.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition (Pellagra).

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

(3) Pellagra

(4) Chronic alcoholic.

CASE 7/61

F. S. AFRICAN FEMALE, 26 years.

Admitted 29.9.61 at 2.40 p.m. Discharged 7.10.61.

OUT-PATIENT DEPARTMENT

The patient arrived in coma. A strong smell of alcohol was noted on her breath. Relatives stated that she had been drinking alcohol. She had later had a fit and had become comatose.

Examination:	Subnormal temperature. A strong odour of alcohol was noted on her breath. Stertorous breathing.
C.V.S.	N.A.D.
C.N.S.	Comatose. Generalised rigidity. No localising signs.

Post-alcoholic hypoglycaemia was suspected and the patient was given 20 ml 50% intravenous dextrose solution intravenously, after taking blood for special investigations.

WARD

History as above.

Examination:	On admission to the ward the patient was fully conscious and she had lunch immediately on arrival.
C.V.S.	N.A.D.
Abd.	Liver and spleen not palpable.
C.N.S.	N.A.D.
Diagnosis:	? Post-alcoholic hypoglycaemia.

Diagnosis: ? Post-alcoholic hypoglycaemia.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 25 mg%.

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

She had been drinking a large amount of Zulu beer with a number of others on the day before admission. They had commenced drinking at midday and had finished at 5 p.m. She had retired to bed intoxicated and had reawakened in hospital. On the day of imbibing she had eaten breakfast - thick putu - but she had not eaten anything else. On the night before the party she had eaten samp and a little meat.

Alcohol habits: She drank Zulu beer in large quantities over the weekend and also three times during the week in lesser amounts. She did not add toxic substances to her alcohol.

Dietary habits:

Breakfast:	Rarely anything.
Lunch:	Soup, porridge and samp.
Supper:	Rice occasionally.
	Meat occasionally.

Social history: She did not work and was not married. She was supported by her boy friend with whom she lived.

Special interrogation: She had never had a similar episode or a fit previously. She had not taken herbal medicines, had injections or taken tablets before her admission.

SPECIAL INVESTIGATIONS

29.9.61 See above.

30.9.61 Serum proteins: Total protein 6.0g%, S. albumin 2.6g%, S. globulin 3.4g%, A:G ratio 0.8:1.
Bld urea 25 mg%.
Routine urine: Occasional leucocytes noted.
Otherwise N.A.D.

2. 10. 61 Hb 12. 5g% (86%), P. C. V. - 39 (mm³) M. C. H. C. 33%. (N58, L22, M13, E7). Neutrophils show toxic granulation.

3. 10. 61 17-ketosteroids ⟨1 mg/24 hrs.
Glucocorticoids ⟨1 mg/24 hrs.
Urine volume 2500 ml.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
30. 9. 61	2		0. 5	17	Nil	Neg	82	Not done.
2. 10. 61	4	320	0. 9		Nil	Neg	92	
3. 10. 61	5				Nil	Neg.		
4. 10. 61	6	104	0. 5		+	Neg		
6. 10. 61	8	40	0. 7	13				

Course and management:

Uneventful course in hospital.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 8/61

N. B. AFRICAN FEMALE, 4 years

Admitted 2. 10. 61 at 2. 50 p. m. Died 3. 10. 61.

OUT-PATIENT DEPARTMENT

The patient arrived in a stuporose state, with a history of having imbibed gavine. She was admitted as ? gavine intoxication.

WARD

The mother stated that her daughter had been found in coma at 8 a. m. on the day of admission. She had been away from home since early that morning and when she had returned at 8 a. m. to feed the child, she had found that she would not awaken and that she had smelt of gavine which she had known to be in the house. The child had previously been quite well and had never had a fit or been in coma. She had not been taking medicines.

Dietary history: The patient was initially breast fed. At the time of admission she was receiving mielie meal porridge, rice, cabbage, fresh cow's milk (2 cups per day) and meat frequently.

Social history: She was their only child. The father was alive and well and he adequately supported the family.

Past history: She had always been well except for one attack of diarrhoea and vomiting.

Examination: Semicomatose. Breathing heavily.
Strong odour of alcohol on her breath.
Well nourished and well hydrated.
No anaemia, oedema, or cyanosis.
Ears and throat normal.

C. V. S. Pulse 120 per minute, regular.
Heart sounds normal.

R/S Percussion normal.
Rhonchi at both bases. No crepitations.

Abd. Soft abdomen.

No hepatomegaly or splenomegaly.

C.N.S. Semicomatose.
No neck stiffness.
Generalised flaccidity.
Deep tendon reflexes absent.
Plantar reflexes not obtained.

Diagnosis: ? Acute hepatic damage following gavine
?? hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 25 ml 50% intravenous dextrose solution was given. There was no recovery of consciousness. A 5% dextrose drip (with 25 ml 50% dextrose solution added) was commenced.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 17 mg%.

Diagnosis: Post-alcoholic hypoglycaemia.

Course and Management:

The patient died 15 hours after admission. Crystalline penicillin, 500,000 units on admission and 250,000 units six-hourly was commenced but was discontinued because the chest was considered normal.

NECROPSY:

(1) The lungs showed bronchopneumonia.

(2) The liver showed moderate fatty change.

(3) The adrenals, kidneys, pancreas and spleen were natural.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) Bronchopneumonia.

CASE 9/61

J.K. AFRICAN MALE, 40 years

Admitted 15.10.61 at 10.05 a.m. Discharged 17.11.61.

OUT-PATIENT DEPARTMENT.

Admitted as ? epileptiform seizures.

WARD

The son stated that his father had been imbibing in the weekends but he did not know whether he had done so before the present illness. He had found him unconscious at about 7.30 a.m. No other history was available.

Examination:	Cold clammy, sweating, semicomatose patient. Temperature 97°F. No anaemia, cyanosis or lymphadenopathy. Stale odour of alcohol on his breath.
C.V.S.	Pulse 84 regular, thready. B.P. 100/60. Heart sounds closed.
R/S	Chest clear.
Abd.	Liver and spleen not palpable.
C.N.S.	Semicoma. No neck stiffness. Deep tendon reflexes diminished. Responds to painful stimuli. Plantars equivocal.
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 20 ml 50% intravenous dextrose solution was administered. The patient recovered consciousness immediately.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 43 mg%, serum electrolytes: Na, 124 meq/l, K, 4.8 meq/l.

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

The patient had been drinking a large amount of Zulu beer in the afternoon on the day prior to admission. He had been dead drunk after drinking it but had recovered later and had drunk a little more the same evening at about 6 p.m. On the following day he had awakened at about 6 a.m. but had later lost consciousness. He had reawakened in hospital. He had not eaten on the day that he had imbibed.

Alcohol habits: He always drank heavily on Saturdays but often on Friday night and Sundays as well. He did not add toxic additives to his alcohol.

Dietary habits:

Breakfast:	Porridge. Mielie rice, bread and tea.
Lunch:	Samp, meat and vegetables.
Supper:	Bread and thick porridge (putu).

He ate breakfast and lunch at the hospital compound.

Social history: He was employed at King Edward VIII hospital workshops, where he emptied rubbish bins. He was paid £14 per month. He was married and had two children (8 and 10 years). His wife did not imbibe and was well.

Special interrogation: He had never had a similar episode previously. He had no history of fits. He had not been taking herbal medicines, injections or tablets before his admission.

SPECIAL INVESTIGATIONS

15.10.61	See above.
16.10.61	Bld urea 17 mg%. Total serum proteins 6.4g%, S. albumin 2.8g%, S. globulin 3.6g%. A:G Ratio 0.8:1. Routine Urine - N.A.D. 17-ketosteroids 1.6 mg/24 hours, total glucocorticoids 4.8 mg/24 hours. Urine volume 2050 ml/24 hours.

24. 10. 61 Chest X-ray - N. A. D.

26. 10. 61 17-ketosteroids 7. 7 mg/24 hours, total glucocorticoids 3. 1 mg/24 hours. Urine volume 2795 ml/24 hours.

3. 11. 61 Glucose tolerance test: Fasting 69 mg%, ½ hour 120 mg%, 1 hour 84 mg%, 1½ hours 76 mg%, 2 hours 76 mg%, 3 hours 52 mg%, 3½ hours 55 mg%, 4 hours 62 mg%.

7. 11. 61 Hb 14. 2g% (97%), P. C. V. 43 (mms), M. C. H. C. 33%, E. S. R. 21 mms/hr, W. B. C. 14, 000/cmm.

8. 11. 61 17-ketosteroids 11. 8 mg/24 hours, total glucocorticoids 5. 9 mg/24 hours, urine volume 1770 ml/24 hours.

Date	Day	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
16. 10. 61	2	60	0. 6	7	++	Neg.	96	
17. 10. 61	3	42	0. 5	7	++	Neg.		
18. 10. 61	4	60	0. 6	8	+	Neg.		
19. 10. 61	5	70	0. 8	7	+	Neg.		
20. 10. 61	6	70	0. 5	9	++	Neg.		
23. 10. 61	9				trace	Neg.		
25. 10. 61	11	50			Nil.	Neg.		
26. 10. 61	12				Nil.	Neg.		
27. 10. 61	13				Nil.	Neg.		
3. 11. 61	17	50			Nil.	Neg.		
9. 11. 61	23	20			Nil.	Neg.		Done

Liver biopsy: Inadequate tissue was obtained. A small portion of liver stained with Sudan III showed no fatty change.

Course and management: The patient's blood pressure was usually about 200/110 (see B. P. on admission). His course in hospital was uneventful.

Assessment of alcohol habits: Heavy weekend drinker ?? early chronic alcoholic.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS (1) Post-alcoholic hypoglycaemia.
(2) ? Alcoholic hepatitis.

Subsequent history: The patient had no further attacks of hypoglycaemia in the next year. He had continued to imbibe in the weekends.

CASE 10/61

M. J. AFRICAN MALE, 70 years

Admitted 28. 10. 61 at 11. 40 a. m. Discharged 3. 11. 61.

OUT-PATIENT DEPARTMENT

No history available. The patient was admitted in coma ? cerebrovascular accident with hypertension (B. P. 180/100).

WARD

No history available.

Examination:	Comatose old man, lying flaccid and unable to respond to supraorbital pressure, though his eyes roved around. An alcoholic odour was noted on his breath. No sweating. Temperature 97. 5°F. No jaundice, cyanosis, oedema or lymphadenopathy.
C. V. S.	Pulse 88 per minute, regular, good volume B. P. 190/110. Heart sounds closed.
R/S	Rhonchi ++ Nil else of note.
Abd.	The liver and spleen were not palpable.
C. N. S.	Comatose. Pupils small and react to light. No obvious cranial nerve lesion. Hypotonia. Deep tendon reflexes absent in the arms and diminished at the knees and ankles. Plantar reflexes equivocal. No response deep pressure. Fundi - N. A. D.
Diagnosis:	? Post-alcoholic hypoglycaemia (suspected from alcoholic odour on his breath).

TREATMENT

Blood was taken for special investigations and then 30 ml 50% intravenous dextrose solution was administered. He immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 18 mg%, bld urea 32 mg%, serum electrolytes, Na, 135 meq/l, K, 5.0 meq/l, Cl, 93 meq/l.
P.I. 70%.
Hb 14.4g% (97%), W.B.C. 6,000/cmm.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

The patient stated that he had taken gavine, approximately half a large brandy bottle, on the day before admission, commencing in the morning and finishing at 3 p.m. He had been very drunk at the end of it and he had retired to bed. He had awakened at 8.30 a.m. on the day of admission, and he had washed and had eaten a slice of brown bread with a nip of gavine. After about thirty minutes he had begun to sweat and he had later awakened in hospital. He had eaten lunch - porridge and some meat - on the day he had imbibed.

Alcohol habits: He usually drank Zulu beer, once a week, in the weekends, but he occasionally took gavine. He claimed he was not a heavy drinker.

Dietary habits: Breakfast: Mielie meal porridge.
Lunch: Bread.
Supper: Occasionally rice.
Ate meat twice per week.

Social history: He had retired from his job three years previously. He lived with a friend and his wife.

Special interrogation: He had never had a similar episode previously. He had not taken herbal medicines, tablets or injections before admission. He had never had a fit.

SPECIAL INVESTIGATIONS

28. 10. 61 See above.

29. 10. 61 Serum proteins. Total serum protein 6.4g%, S. albumin 3.2g%, S. globulin 3.2g% A:G ration 1:1

1. 11. 61 17-ketosteroids 0.6 mg/24 hours, total glucocorticoids $<$1 mg/24 hours, urine volume 990 ml/24 hours.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
28. 10. 61	= 1	58	0.6	5	Nil.	Neg.	70	Not done.
29. 10. 61	2	42	0.5	4	Nil.	Neg.		
30. 10. 61	3	80	0.8	9	+	Neg.		
31. 10. 61	4	116	0.4	3	++	Neg.		
1. 11. 61	5	92	0.4	3	trace	Neg.		
2. 11. 61	6				+	Neg.		

Course and management:

Examination after dextrose therapy showed normal systems. The blood pressure returned to 130/80. On 3. 11. 61 he demanded that he was discharged.

Assessment of alcohol habits : ? Heavy weekend drinker.

Assessment of nutrition : Fair nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 11/61

F.N. AFRICAN MALE, 32 years

Admitted 6.11.61 at 5.55 p.m. Discharged 14.12.61.

OUT-PATIENT DEPARTMENT

No history available. Admitted as ? intracerebral haemorrhage.

WARD

No history available.

Examination:	Comatose. Eyes roving. No anaemia, jaundice, cyanosis or clubbing. Temperature 97°F.
C.V.S.	Pulse 108 per minute. B.P. 170/110. Heart sounds closed.
R/S	Stertorous breathing. Rate 28 per minute. Rhonchi throughout both lung fields.
Abd.	Soft abdomen. Liver 1 fd. Spleen not palpable. Bowel sounds not heard.
C.N.S.	Comatose. Pupils react to light. Subconjunctival haemorrhage. Deep tendon reflexes not obtainable. Plantar reflexes ↑↑
Diagnosis:	Coma ? cause.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 17 mg%, blood alcohol (V.R.S.) 3 mg%, Skull X-ray - N.A.D. Hb 17.2g% (118%), W.B.C. 8,000/cmm, bld urea 30 mg%, C.S.F. sugar 10 mg%, otherwise N.A.D.

TREATMENT

Prior to the administration of intravenous dextrose solution, at 11.00 p.m., a rapid examination of the patient was undertaken.

Examination: Pulse 128/min. B.P. 130/70,
Comatose.
No deep tendon reflexes obtained.

Blood was taken for repeat blood sugar and then 40 ml 50% intravenous dextrose solution was administered. There was immediate improvement in his level of consciousness. He mumbled words but remained stuporose and disorientated.

Diagnosis: Hypoglycaemia ? cause.

HISTORY FROM PATIENT

The patient remained confused and disorientated for two days and was mentally normal on 9.11.61, though his speech was slurred. He stated that he had had a Zulu beer party on the day before admission with a number of friends, but he could remember nothing till he found himself in hospital.

Alcohol habits: He said he was a heavy drinker, particularly in the weekends.

Special Interrogation: He had not had a similar episode previously.

SPECIAL INVESTIGATIONS

6.11.61	See above. Repeat bld sugar (11.00 p.m.) 32 mg%.
7.11.61	Fasting bld sugar 98 mg%. Total serum protein 6.2g%, S. albumin 2.2g%, S. globulin 4.0g%. A:G ratio 0.6:1.
9.11.61	Hb 14.2g% (97%). Routine urine - N.A.D.
10.11.61	17-ketosteroids 1.0 mg/24 hrs, total glucocorticoids $<$1.0 mg/24 hrs., urine volume 1330 ml.

14.11.61. A.C.T.H. Response Test.

Day of hospitalisation on which A.C.T.H. commenced.	Type of Steroid	Unstimulated steroid excretion mg/24 hrs.	A.C.T.H. Stimulation and aftermath. Days: 1*	2*	3	4	5
8	17 - oxo.	1.0	3.8*	8.1*	4.9	5.0	
	Total gluco.	<1.0	9.6*	46.3*	58.9	<1.0	1.4

*Days on which A.C.T.H. given 100 units A.C.T.H. I.M. gel bd.

6.12.61 Glucose tolerance test: Fasting 75 mg%, ½ hour 138 mg%, 1 hour 122 mg%, 1½ hours 97 mg%, 2 hours 69 mg%, 2½ hours 64 mg%, 3 hours 67 mg%, 3½ hours 69 mg%, 4 hours 72 mg%.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
6.11.61	1	150	0.5	7			100	
7.11.61	2	46	0.5	6				
8.11.61	3		0.8	9				
9.11.61	4	24	0.7	4	trace	Neg.		No tissue obtained
10.11.61	5	36	0.5	7	trace	Neg.		
11.11.61	6		0.4	9	++	Neg.		
12.11.61	7				+	Neg.		
13.11.61	8				+	Neg.		
14.11.61	9				Nil.	Neg.		
15.11.61	10				Nil.	Neg.		
16.11.61	11				Nil.	Neg.		
17.11.61	12				Nil.	Neg.		

Course and management: The patient remained incoherent on 7.11.61 but was improving on 8.11.61, though his speech was slurred and he was confused. On 9.11.61 his speech remained slurred but he was orientated. On 11.11.61 he was fully orientated and his speech was normal. The remainder of his admission was uneventful.

Assessment of alcohol habits: Heavy drinker mainly in the weekends.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS: (1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 1/62

M. E. AFRICAN MALE, 50 years

Admitted 11.3.62 at 2.55 p.m. Discharged 2.4.62.

OUT-PATIENT DEPARTMENT

Admitted in coma ? cause ? broncho-pneumonia.

WARD

A friend stated that the patient had been very drunk on going to bed on the night before admission. He had drunk two gallons of shimeyane. The house physician suspected that the patient was in post-alcoholic hypoglycaemic coma and administered intravenous dextrose, after blood had been taken for special investigations, without further examination.

TREATMENT

50 ml 50% intravenous dextrose solution was administered. The patient immediately recovered consciousness but remained confused during the rest of that day.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 29 mg%, Hb 14.4g% (99%), W.B.C. 20,000/cmm (N84, L7, M5, band forms 4).

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

The patient had eaten lunch and supper of samp and putu. After supper, at about 6 p.m. he and a few friends had commenced to drink. He drank two gallons of shimeyane and also had 3 cups of gavine. He could not remember going to bed. He had reawakened in hospital on the following afternoon.

Alcohol habits: He took a nip of gavine three times per week, but drank a lot on Friday night, Saturday and Sunday - usually 3 cups of gavine and shimeyane. He did not add toxic substances to his alcohol.

Dietary habits: He mainly ate putu, samp and meat.

Social history: He worked a five day week at a factory.

Special interrogation: He had never had a similar episode previously and he did not suffer from fits. He had not taken herbal medicines, tablets or injections prior to his admission.

Subsequent history: He did not know whether his friends had remained well.

Examination after treatment (13.3.62) An adult male of fair nutrition, fully conscious and co-operative. No anaemia, jaundice, clubbing or lymphadenopathy.

C.V.S. Pulse 80 per minute. B.P. 170/130. J.V.P. = 0 Heart sounds closed.

R/S Dullness over left base. Crepitations at left base.

Abd. Slight epigastric tenderness. Liver and spleen not palpable. No free fluid.

C.N.S. Cranial nerves intact. No neck stiffness. Power and tone normal. Sensation normal. Plantar reflexes ↓↓

Diagnosis: Left basal pneumonia ? aspiration pneumonia

SPECIAL INVESTIGATIONS

11.3.62 See above.
Bld urea 39 mg%, Total serum proteins 5.5g%, S. albumin 2.3g%, S. globulin 3.2g%, A:G ratio 0.7:1.
W.B.C. 8,000/cmm.
17-ketosteroids 3.9 mg/24 hours, total glucocorticoids 6.9 mg/24 hours, urine volume 3,560 ml.
Routine urine - N.A.D.

21.3.64 Glucose tolerance test: Fasting 98 mg%, ½ hour 148 mg%, 1 hour 120 mg%, 1½ hours 98 mg%, 2 hours 92 mg%, 2½ hours 92 mg%, 3 hours 82 mg%, 3½ hours 72 mg%.

21.3.62 17-ketosteroids 5.5 mg/24 hours, total glucocorticoids 9.6 mg/24 hours, urine volume 2,350 ml.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
11.3.62	1	86	0.6	9	Nil.	Neg.		
12.3.62	2	60	0.5	10	Nil.	Neg.	73	
13.3.62	3				Nil.	Neg.		
14.3.62	4	112	1.0	8	+	Neg.		
15.3.62	5	38	0.9	7	+++	Neg.		
16.3.62	6	50	0.9	8	trace	Neg.		
17.3.62	7	34	1.2	8	trace	Neg.		
19.3.62	9	36	0.6	11	Nil.	Neg.		
20.3.62	10	30	0.8		Nil.	Neg.		
21.3.62	11				Nil.	Neg.		
22.3.62	12							Done

Liver biopsy: This was performed on 22.3.62. Section of liver showed no fatty vacuoles but mild fine intercellular fatty change was noted (gr. 1). No foci of necrosis or alcohol hyalin were observed. A few acute and chronic inflammatory cells were noted at the portal triads. A moderate portal fibrosis ("periportal fibrosis") was present (grp III). Haemosiderin was noted throughout the lobules and clumps of haemosiderin were present in the parenchyma and at the portal tracts. (gr. 4). Glycogen was present (gr. 3). No bile thrombi or bile duct hyperplasia were observed.

[Stains used: H. & E. silver impregnation, W.H.V.G., Prussian-blue reaction, Sudan III, Best carmine].

Course and management: The pneumonia soon responded to penicillin and sulphadimidine therapy. The remaining course in hospital was uneventful.

Assessment of alcohol habits: Heavy drinker, mainly in the weekend.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.
(2) Alcoholic hepatitis.
(3) Pneumonia ? aspiration.

CASE 2/62

G.M. INDIAN MALE, 44 years

Admitted 25.2.62 at 10.20 p.m. Discharged 15.3.62.

OUT-PATIENT DEPARTMENT

No history was available but the patient smelt strongly of alcohol. It was thought that he was either in alcoholic coma or in post-alcoholic hypoglycaemia. He was given 10 ml 50% intravenous dextrose solution, after blood had been taken for special investigations. The patient responded immediately but remained confused and boisterous.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 46 mg%.

Diagnosis: Post-alcoholic hypoglycaemia.

WARD

No adequate history could be taken. The patient said he had been drinking heavily.

Examination (after treatment)

Strong odour of alcohol. Poor nutrition.
Congested conjunctiva.

C.V.S. Pulse 100 per minute. B.P. 140/95.
Heart sounds closed.

R/S N.A.D.

Abd. Liver and spleen not palpable.

C.N.S. Very happy, confused and inebriated.
Pupils equal, dilated and react to light.
No neck stiffness.
Plantar reflexes ↓↓

HISTORY FROM PATIENT

It was impossible to obtain an accurate account of the preceding few days from the patient.

Alcohol habits: He was drinking daily and heavily, and he considered himself to be a drunkard.

Dietary habits: Did not eat much. He took more alcohol than food.

SPECIAL INVESTIGATIONS

25.2.62 See above.
26.2.62 Bld urea 43 mg%, Hb 15.1g% (103%), W.B.C. 20,000/per cmm. P.C.V. 49 %, M.C.H.C. 31%.
27.2.62 Bld urea 20 mg%.
Total serum protein 6.5g %, S. Albumin 2.7g%, S. globulin 3.8g%, A:G ratio 0.7:1.

Date	days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
25.2.62	1		0.2	9				
26.2.62	2		0.8	5	Nil	Neg.	100	
27.2.62	3	50	0.8	7	+	Neg.	100	Done
28.2.62	4				Nil	Neg.		
1.3.62	5	50	1.7	9	Nil	Neg.		
2.3.62	6	84	1.3	7	Nil.	Neg.		
3.3.62	7	152	1.0	8	Nil.	Neg.		
5.3.62	9	148	0.4	7	Nil.	Neg.		
6.3.62	10	36						
8.3.62	12	34						
9.3.62	13	40						

Liver biopsy: This was performed on 27.2.62. A focus of necrosis was observed and was infiltrated by numbers of round cells. Alcoholic hyalin was not present. The portal triads showed numbers of chronic inflammatory cells and there was an increase in fibrous tissue with stellate extension suggestive of "periportal fibrosis". (grp. III). Extreme fatty vacuolation and fine intercellular fatty change were noted (gr. 4). Haemosiderin was absent (gr. O). Glycogen was observed (gr. 3). Bile thrombi were not noted and there was no bile duct proliferation.

[STAINS used: H. & E, silver impregnation, Sudan III, W.H.V.G., prussian blue reaction, Best carmine].

Course and management: During the first week of hospitalisation the patient was confused and from the second day of admission he was considered to be suffering from delirium tremens. He was discharged on 15.3.62 well and mentally normal.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Chronic alcoholic.

SECOND ADMISSION Admitted 2. 4. 62 at 3.05 p.m.
Died 3. 4. 62.

OUT-PATIENT DEPARTMENT

Admitted in coma. A relative stated that he was a chronic alcoholic and that he had been found in a coma on that morning. Coma ? cause.

WARD

History as above.

Examination: Comatose and looks very ill.
Poor nutrition.
Pulse 86 per minute, B.P. 70/50.
Pupils dilated.
Strong odour of alcohol.

Diagnosis: Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 100 ml 50% intravenous dextrose solution and 2 ml coramine were administered. The patient remained in coma.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 31 mg%.

A liver biopsy was performed within a few minutes of administering 50% intravenous dextrose solution.

Diagnosis: Post-alcoholic hypoglycaemia.

SPECIAL INVESTIGATIONS

Liver biopsy: This was performed on 2.4.62 within a few minutes of administering 100 ml 50% intravenous dextrose solution. Section of liver showed no glycogen (gr. 0). A large focus of necrosis with numerous acute and chronic inflammatory cells was present. Alcoholic hyalin was not observed Extreme fatty vacuolation and some fine intercellular fatty change was present. The portal triads showed infiltration by acute and chronic inflammatory cells and there was an increase in fibrous tissue with stellate extension. There was a suggestion of lobular distortion (? grp. IV). Haemosiderin pigment was not noted (gr. 0). Bile duct proliferation and bile thrombi were not observed.

[STAINS used: H. & E., silver impregnation, Best carmine, and P.A.S.]

Course and management: Despite dextrose therapy the patient remained in coma, though his level of consciousness had improved. Examination at 4 p.m. on the same afternoon revealed coma, but no other obvious abnormality of the central nervous or other systems. 50% intravenous dextrose solution was administered at midnight with slight improvement in the level of consciousness, but the patient died $2\frac{1}{2}$ hours later. A post mortem was refused on religious grounds.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

(3) Chronic alcoholic.

CASE 3/62

M. M. AFRICAN MALE, 46 years

Admitted 15.3.62 at 4.10 p.m. Discharged 3.4.62.

OUT-PATIENT DEPARTMENT

No history available. He was admitted as a case of coma ? cause.

WARD

No history available. The house physician suspected post-alcoholic hypoglycaemia and he administered 50% intravenous dextrose solution (? alcoholic odour on his breath).

TREATMENT

Blood was taken for special investigations and then 150 ml 50% intravenous dextrose solution was administered. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 35 mg%, Hb 15.7g% (106%), W.B.C. 7,000/cmm, serum electrolytes, Na, 169 meq/l, K 3.4 meq/l and Cl, 106 meq/l.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

Examination of patient (after therapy): Well-orientated, fair nutrition.

C.V.S. B.P. 150/90.
Heart sounds closed.

R/S Numerous rhonchi at both bases.

Abd. Liver and spleen not palpable.

C.N.S. Cranial nerves, motor and sensation normal.

HISTORY FROM PATIENT

The patient had been drinking shimeyane on the day before admission. He had imbibed in the afternoon after eating a full lunch of vegetables and meat. He had retired to bed at 8 p.m. and he had not been drunk. He had awakened at 8 a.m. on the following morning

and he had commenced to eat bread and porridge. He could not remember anything after that till he awakened in hospital.

Alcohol habits: He drank heavily in the weekends. He only drank Zulu beer and shimeyane.

Dietary Habits: Breakfast: Tea, milk, sugar, bread and butter.
Lunch: Tea, and meat 5 times per week.
Supper: Bread, tea and vegetables, and meat.

Social history: He was married with two wives and nine children. He had his own plot of land on which he farmed vegetables. He also had tenants, who had to pay rent.

SPECIAL INVESTIGATIONS

15.3.62 See above.

17.3.62 Chest X-ray - N.A.D.
Routine Urine - N.A.D.

19.3.62 Total serum proteins 6.2g%, S. albumin 2.6g%, S. globulin 3.6g%, A:G ratio 0.7:1
17-ketosteroids 3.2 mg/24 hrs, total glucocorticoids 10.8 mg/24 hrs, urine volume 2060 ml.

23.3.62 Glucose tolerance test: Fasting 95 mg%, ½ hour 140 mg%, 1 hour 120 mg%, 1½ hour 106 mg%, 2 hour 85 mg%, 2½ hour 85 mg%, 3 hour 80 mg%, 3½ hour 74 mg%.

2.4.62 17-ketosteroids 5.5 mg/24 hrs, total glucocorticoids 4.5 mg/24 hours, Urine volume 1560 ml.

3.4.62 17-ketosteroids 7.2 mg/24 hours, total glucocorticoids 4.0 mg/24 hours, Urine volume 2550 ml.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
17.3.62	3	40	1.0	6	+	Neg.	80	
18.3.62	4				Nil.	Neg.		
19.3.62	5	44	0.6	6	Nil.	Neg.	100	
20.3.62	6	96	0.6	7	Nil.	Neg.		
21.3.62	7	52	0.7	6	Nil.	Neg.		
22.3.62	8				Nil.	Neg.		
23.3.62	9				Nil.	Neg.		
24.3.62	10				Nil.	Neg.		Done on 27.3.62

Liver biopsy: This was performed on 27.3.62. Section of liver showed a number of small foci of acute inflammatory cell infiltration containing neutrophils and eosinophils but necrosis of the parenchyma was not apparent. No alcoholic hyalin was observed. The portal triads showed numbers of acute and chronic inflammatory cells. There was no increase in portal fibrosis (grp. I). A mild fatty vacuolation and fine intercellular fatty change was noted. Haemosiderin was noted in the liver lobules and clumps of haemosiderin were present in the parenchyma and at the portal triads (gr. 5). Glycogen was noted (gr. 3). No bile thrombi or bile duct hyperplasia were seen.

[STAINS used: H. & E., P.T.A.H., silver impregnation, W.H.V.G., Perl's prussian blue reaction, Best carmine].

Course and management: Uneventful course in hospital.

Assessment of alcohol habits: Weekend drinker.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS:

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 4/62

J. Z. AFRICAN MALE, 30 years.

Admitted 26. 3. 62 at 8. 55 p. m. Discharged 5. 4. 62.

OUT-PATIENT DEPARTMENT

The patient had been picked up in a ditch. He smelt of stale alcohol. He was admitted as a case of alcoholic coma.

WARD

No further history available. In case he was suffering from post-alcoholic hypoglycaemia, (? alcoholic odour) the house physician administered 50 ml 50% intravenous dextrose solution after blood had been taken for special investigations. The patient recovered consciousness immediately.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 19 mg%.

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

The patient could not remember the two days prior to admission. He said he might have been drinking.

Alcohol habits: He drank heavily in the weekends and usually imbibed Zulu beer or shimeyane but never gavine. He did not add toxic additives to his liquor.

Dietary habits: Breakfast: Putu (thick porridge).
Lunch: Putu.
Supper: Putu.
He occasionally ate samp and beans and chicken legs once per week.

Social history: He worked in a factory (£14 per month). He was married with three children. His wife and children were well. His wife rarely drank alcohol.

Special interrogation: He had not had a similar episode previously. He had never had a fit. He had not been taking herbal medicines or tablets or had injections.

SPECIAL INVESTIGATIONS

26.3.62 See above.
27.3.62 Routine urine - N.A.D.
Bld urea 38 mg%.
Hb 16.9g% (115%), P.C.V. 50% (mm) M.C.H.C. 34%,
W.B.C. 10,000/cmm, platelets 388,000/cmm.
Total serum proteins 6.2g%.
S. albumin 3.1g%, S. globulin 3.1g%, A:G ratio 1:1.
17-ketosteroids 11.0 mg/24 hours, total glucocorticoids 11.0 mg/24 hours, urine volume 880 ml.
30.3.62 Glucose tolerance test: Fasting 81 mg%, ½ hour 103 mg%, 1 hour 120 mg%, 1½ hours 114 mg%, 2 hours 114 mg%, 2½ hours 103 mg%, 3 hours 91 mg%, 3½ hours 74 mg%.
2.4.62 17-ketosteroids 10.9 mg/24 hrs, total glucocorticoids 7.8 mg/24 hrs, Urine volume 1330 ml.

Date	Days	T	B	A.P.	U.	U.B.	P.I.	Liver biopsy
26.3.62	1	180	0.9	10	Nil.	Neg.	100	
27.3.62	2	92	0.8	8	Nil.	Neg.		
28.3.62	3	36	1.0		Nil.	Neg.		
30.3.62	5				Nil.	Neg.		
31.3.62	6				Nil.	Neg.		Done 3.4.62

Liver biopsy: This was performed on 3.4.62. Section of liver showed a focus of necrosis infiltrated by neutrophils and round cells. No alcoholic hyalin was observed. The portal triads showed a round cell infiltration and there was no increase in fibrous tissue (grp. I). Fat vacuolation was not noted and fine intercellular fatty change was mild. Haemosiderin was present throughout the lobules and an occasional clump was seen in the parenchyma and at the portal triads (gr. 4). Glycogen was present (gr. 4). Bile thrombi and bile duct hyperplasia were not observed.

[STAINS used: H. & E., P.T.A.H., silver impregnation, W.H.V.G., prussian blue reaction. Best carmine].

Course and management:

The patient had an uneventful course in hospital. Amnesia remained for the two days prior to admission.

Assessment of alcohol habits:

Heavy weekend drinker.

Assessment of nutrition:

Poor nutrition.

FINAL DIAGNOSIS

(1) Post - alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 5/62

M. P. INDIAN FEMALE, 60 years.

Admitted 23. 5. 62. at 1. 30 p. m. Discharged 1. 6. 62.

OUT-PATIENT DEPARTMENT

No history available. Admitted as a cerebrovascular accident with hypertension.

WARD

No history available.

Examination:	Comatose. Slow and shallow breathing. Temperature 97°F. Smell of stale alcohol on her breath.
C. V. S.	Pulse 144 per minute. B. P. 180/100. Heart sounds closed.
R/S	Respiratory rate 10 per minute. Chest clear.
Abd.	Liver and spleen not palpable.
C. N. S.	Comatose. Pupils dilated. Deep tendon reflexes present and equal. Plantar reflexes ↓↓
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT

The patient was given 40 ml 50% intravenous dextrose solution after blood had been taken for special investigations. The patient recovered consciousness within a few minutes. She said she had taken a half bottle of cane spirit on the evening prior to admission.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 14 mg%, serum electrolytes, Na, 152 meq/l, K, 4. 8 meq/l, Cl 115 meq/l. PI, 97%, Routine urine N. A. D. Hb 11. 2g% (76%), P. C. V. 38(mms), M. C. H. C. 29%, W. B. C. 12, 000/cmm. (P. 90, L7, M3), E. S. R. 33 mms/hr.

HISTORY FROM PATIENT

She had been drinking a half bottle of cane spirit on the evening before admission. She had commenced at 5 p.m. on her own. She did not remember going to bed but had awakened at 5 a.m. the next morning, when she had arisen andhad washed her face. She became giddy and had fallen down, but she had been able to return to bed. She had reawakened in hospital. She could not remember whether she had eaten on the day she had imbibed.

Alcohol habits: She stated she drank on Fridays and Wednesdays when she obtained money, but her son said she drank much more than this and he considered her to be a chronic alcoholic. She drank cane spirit and did not add any substances to it.

Dietary habits: Breakfast: Bread and milk.
Lunch: Mutton and potatoes.
Supper: Milk.
(This seemed unlikely as she was of poor nutrition).

Social history: She stayed with a neighbour, her husband having died 5 years previously. Her son gave her food and money. Her son was a factory worker and he earned £4 per week. She did not work.

Special interrogation: She had never had a similar episode previously and she did not have fits. She had not taken herbs, tablets or injections before her admission.

SPECIAL INVESTIGATIONS

23.5.62 See above.

24.5.62 Total serum proteins 6.7g%, S. albumin 2.3g%, s. globulin 4.4g%. A:G ratio 0.5:1.
Chest X-ray: "There is a right sided pneumothorax with ill-defined shadowing in the left upper zone suggestive of tuberculosis".

25.5.62 17-ketosteroids 3.8 mg/24 hrs, total glucocorticoids <1 mg/24 hrs. Urine volume 1320 ml.

31.5.62 17-ketosteroids 3.2 mg/24 hrs, total glucocorticoids 6.0 mg/24 hrs, urine volume 1200 ml.

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
23.5.62	1	72	1.0	11	Nil.	Neg.	97	Done.
24.5.62	2	100	1.0	11	+++	Neg.		
25.5.62	3	64	1.0	12	+++	Neg.		
26.5.62	4	104	1.0	10	Nil.	Neg.		
27.5.62	5				Nil.	Neg.		
28.5.62	6	68	1.0	14	Nil.	Neg.		
29.5.62	7	32	1.0	13	Nil.	Neg.		
1.6.62	10	14	0.9	10				

Liver biopsy: This was performed 45 minutes after 40 ml 50% intravenous dextrose solution had been administered. Section of liver showed moderate glycogen deposition (gr. 1-2). Foci of necrosis with acute inflammatory cell infiltration were noted. Evidence of cellular regeneration was noted in some foci. On haematoxylin and eosin section alcoholic hyalin was possibly present but Mallory's P.T.A.H. stain did not confirm it. Severe fatty vacuolation and severe fine intercellular fatty change were present (gr. 4). The portal triads showed a number of chronic and a few acute inflammatory cells and there was a slight increase in fibrous tissue (grp. II). Haemosiderin was not noted (gr. 0). There was no bile duct hyperplasia and bile thrombi were not seen.

[STAINS used: H. & E., P.T.A.H., silver impregnation, W.H.V.G., prussian-blue reaction, Best carmine, Sudan III].

Course and management: The patient suffered from anorexia on the first few days of her admission but her subsequent course was uneventful. Her usual blood pressure was 130/90 (C.F. admission). She was discharged on anti-tuberculous therapy.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Chronic alcoholic.

(4) Pulmonary Tuberculosis.

CASE 6/62

C.M. INDIAN FEMALE, 65 years

Admitted 25. 8. 62 at 10.15 a.m. Discharged 18.9.62.

OUT-PATIENT DEPARTMENT

Admitted in coma ? cerebro-vascular accident.

WARD

The relatives stated that the patient was a heavy drinker and that she had been drinking steadily on the previous day. She had been found in coma that morning.

Examination:	Elderly thin Indian female. Poor nutrition. Comatose. Breath smelling of stale alcohol. Temperature 96°F. No anaemia, jaundice or lymphadenopathy.
C.V.S.	Pulse 100 per minute, regular. B.P. 110/70. Heart sounds closed.
R/S	Breathing - increased rate and depth. Trachea central. Good air entry. Bilateral rhonchi. No crepitations.
Abd.	Soft abdomen. Liver and spleen not palpable. No ascites. Bowel sounds present.
C.N.S.	Comatose. Pupils dilated. Hypertonia in R. arm and leg. Deep tendon reflexes increased on right. Plantar reflexes equivocal.

Diagnosis: ? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 40 ml 50% intravenous dextrose solution was administered. The patient immediately recovered consciousness and a liver biopsy was then performed.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 21 mg%, bld urea 40 mg%, serum electrolytes, Na, 152 meq/l, K, 3.1 meq/l, Cl, 95 meq/l, P.I. 100%, Hb 16.6 g% (114%), W.B.C. 13,000/cmm.

Diagnosis: Post-alcoholic hypoglycaemia.

HISTORY FROM PATIENT

She had been drinking on the day before admission and she had drunk cane spirit between 5.30 and 6.30 p.m. She could not remember what had happened but she had reawakened in hospital. She had eaten a full lunch of curry and rice at midday on the day she had imbibed.

Alcohol habits: She drank cane spirit daily and gavine on one occasion a week. She had been drinking heavily for 5 to 6 years and her relatives said she was a chronic alcoholic. She did not add substances to her liquor.

Dietary habits: Mielie rice, potatoes and rice curry. She ate meat 1-3 times per week.

Social history: She obtained money by doing laundry. She used the money to buy alcohol. She lived with her son.

Special interrogation: She had never had a similar episode previously. She had never had a fit. She had not taken herbs, tablets or injections prior to her admission.

SPECIAL INVESTIGATIONS

25.8.62 See above.
Serum electrophoresis: S. albumin 2.6g%, S. globulins α_1 0.4g%, α_2 0.8g%, β 1.0g%, γ 1.2g%, Total protein 6.0g%.

27. 8. 62 17-ketosteroids 1.4 mg/24 hrs, total glucocorticoids 2.0 mg/24 hrs, urine volume 1560 ml.
Routine urine - N. A. D.

28, 8, 62 Total serum proteins 6.2g%, S. albumin 2.7g%, S. globulin 3.5g%, A:G ratio 0.8:1.

31. 8. 62 Glucose tolerance test: Fasting 100 mg%, ½ hour 124 mg%, 1 hour 124 mg%, 1½ hour 126 mg%, 2 hours 110 mg%, 2½ hours 110 mg%, 3 hours 110 mg%, 3½ hours 84 mg%, 4 hours 84 mg%.

A. C. T. H. Response Test

Day of hospitalisation on which A. C. T. H. commenced.	Type of Steroid	Unstimulated steroid excretion mg/24 hrs.	A. C. T. H. Stimulation and aftermath. Days: 1*	2*	3	4	5	6
12	17-oxo	<1.0	2.0	1.3	1.1	<1.0	<1.0	<1.0
	Total gluco	<1.0	2.2	6.3	10.2	<1.0	1.7	<1.0
	Urine volume (ml)	1600	1200	1300	1210	1600	1800	1750

*Days on which A. C. T. H. given, 100 units I. M. A. C. T. H. gel b. d.

Date	Day	T.	B	A. P.	U.	U. B.	P. I.	Liver biopsy
25. 8. 62	1	30	1.1	12	trace	Neg.	100	Done
26. 8. 62	2	90	1.3	10	trace	Neg.		
27. 8. 62	3		1.2	6	trace	Neg.		
28. 8. 62	4	80	1.7	8	trace	Neg.		
29. 8. 62	5		1.4	9	+	Neg.		
30. 8. 62	6	46	1.3	11	+	Neg.		
31. 8. 62	7	30	1.1	10	Nil.	Neg.		
4. 9. 62	11	14	0.9	8				
7. 9. 62	14	30						

Liver biopsy: This was performed on 25. 8. 62 within a few minutes of dextrose therapy. Section of liver showed absence of glycogen (gr. 0). Fatty vacuolation was mild but extreme fine intercellular fatty change was present (gr. 4). The portal triads showed no inflammatory cells but there was a moderate increase in fibrous tissue ("periportal fibrosis") (grp. III). Haemosiderin was absent (gr. 0). No foci of necrosis were observed. There was doubtful alcoholic hyalin. Bile thrombi and bile duct hyperplasia were not seen.

[STAINS used: H. & E., silver impregnation, Sudan III, Best carmine and PAS].

Course and management: The patient had an undiagnosed fever (100°F) during the first few days of admission. Terramycin (250 mg 6 hourly, x 7 days) was administered. The remaining course was uneventful.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis,

(3) Chronic alcoholic.

CASE 7/62

M. M. AFRICAN MALE, 48 years

Admitted 12. 8. 62 at 1. 25 p. m. Discharged 15. 8. 62.
(returned for test 17. 8. 62).

OUT-PATIENT DEPARTMENT

No history available. Admitted in coma ? cause.

WARD

No history available. A rapid examination by the house physician revealed a cold, middle-aged man with hypertonia. Hypoglycaemia was suspected and intravenous dextrose solution was given after blood had been taken for special investigations.

TREATMENT

50 ml 50% intravenous dextrose solution was given. The patient recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 30 mg%, bld urea 34 mg%.

Diagnosis: Hypoglycaemia ? cause.

Examination (after therapy):

Middle-aged African adult.
Warm periphery.
No pallor, cyanosis, jaundice, clubbing or oedema. Temperature 99°F.

C. V. S. B. P. 180/110. Pulse 92 per minute, regular.

R/S Trachea central.
Resp. rate 20 per min.
Percussion normal.
Breath sounds vesicular.
Rhonchi in both fields.

Abd. Soft and non-tender.
Liver 3 fd - firm with smooth surface, slightly tender. No splenomegaly.

C.N.S. Fully conscious.
Reflexes intact and equal.
Sensation intact.
Cranial nerves intact.
Fundi - cataract left eye.

HISTORY FROM PATIENT

He had imbibed two gallons of Zulu beer on the afternoon before admission and he had gone to bed at 8 p.m. He had awakened at 3 a.m. and had gone to work without eating. At 11 a.m. he became drowsy and he had awakened in hospital. He had eaten dumplings at 8 p.m. on the night before imbibing, but he had eaten very little during the day.

Alcohol habits: He drank 1/-d worth of K.B. every day, but in the weekends he drank heavily. He did not add toxic additives to his liquor.

Dietary habits: Breakfast: Mielie meal porridge.
Lunch: Samp.
Supper: Rice.
Meat once per day.

Social history: He was married and had four children. He had worked at the same factory for 17 years and was paid £3 per week.

Special Interrogation: He had never had a similar episode before. There was no history of fits. He had not taken herbal medicines, tablets or injections before his admission.

SPECIAL INVESTIGATIONS

12.8.62 See above.
14.8.62 Serum total protein 7.5g%, S. Albumin 3.1g%, S. globulin 4.4g%, A:G ratio 0.7:1.
15.8.62 17-ketosteroids 2.2 mg/24 hrs, total glucocorticoids <1.0 mg/24 hrs, urine volume 1750 ml.
17.8.62 Routine Urine - N.A.D.

Date	Day	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
12. 8. 62	1							Not done
13. 8. 62	2	20	1. 3	8			94	
14. 8. 62	3	52	0. 4	10	Nil.	Neg.		
15. 8. 62	4	60			++	Neg.		
17. 8. 62	6	30			Nil.	Neg.		

Course and management: Uneventful course. The patient had wanted to return to work four days after admission. He had returned for special investigations two days later as requested.

Assessment of alcohol habits: Weekend drinker.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

CASE 8/62

G. M. AFRICAN MALE, 21 years

Admitted 19.9.62 at 6.40 p.m. Discharged at 1.10.62.

OUT-PATIENT DEPARTMENT

Comatose. No history available ? hypoglycaemic.

WARD

No history available. The house physician administered intravenous dextrose solution to exclude hypoglycaemic coma.

TREATMENT

50 ml 50% intravenous dextrose solution was administered after blood had been taken for special investigations. The patient recovered consciousness.

Examination (after treatment):

	Young adult. Fair nutrition. No pallor, cyanosis, clubbing or jaundice. No lymphadenopathy. Temperature 100°F.
C.V.S.	Pulse 92 per minute regular. B.P. 130/95. J.V.P. = 0. Heart sounds closed.
R/S	Trachea central. Resp. rate 22 per min. Chest clear.
Abd.	Liver and spleen not palpable.
C.N.S.	Pupils equal and react to light. Cranial nerves intact. No neck stiffness. Tone and power - normal. Deep tendon reflexes equal. Sensation normal. Fundi normal.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 21 mg%, bld urea 37 mg%, Hb 13.9g% (91%), W.B.C. 18,000/cmm.

Diagnosis: Hypoglycaemia ? cause.

HISTORY FROM PATIENT

He said he had gone to work on the morning of admission without eating and at 12 noon he had taken a cup of gavine and had gone to sleep. He had reawakened in hospital that evening. Evidently he had been found fast asleep at 3 p.m. and he could not be awakened. He had never had a similar episode before.

Alcohol habits and dietary habits not taken.

SPECIAL INVESTIGATIONS

19.9.62 See above.

20.9.62 Total serum protein 7.1g%.
S. albumin 3.4g%.
S. globulin 3.7g%.
A:G ratio 0.9:1
Hb 13.1g% (89%), P.C.V. 39 (mms) M.C.H.C. 34%,
W.B.C. 17,000/cmm. E.S.R. 29 mms/hr.

21.9.62 A.C.T.H. Response Test.

Day of hospitalisation on which A.C.T.H. commenced.	Type of Steroid	Unstimulated steroid excretion mg/24 hrs.	A.C.T.H. Stimulation and aftermath. Days: 1*	2*	3	4	5	6
4	17-oxo	-	17.0	2.8	17.3	4.1	3.4	2.8
	Total gluco-	<1.0	19.4	9.7	32.1	10.7	5.0	1.0
	Urine volume(ml)	2535	1400	2250	1500	2500	2500	2200

* days on which A.C.T.H. given, 100 units I.M.
A.C.T.H. gel b.d.
(Batch No. 4169 Frederiksberg Copenhagen, Denmark).

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
20.9.62	2		0.7	14			92	Not done
21.9.62	3		0.9	8				
22.9.62	4				Nil.	Neg.		
23.9.62	5				Nil.	Neg.		
24.9.62	6		0.4	10	Nil.	Neg.		
25.9.62	7				Nil.	Neg.		
26.9.62	8		0.3	11	Nil.	Neg.		
27.9.62	9				Nil.	Neg.		

Course and management:

Uneventful course in hospital.

FINAL DIAGNOSIS

Post-alcoholic hypoglycaemia.

CASE 9/62

S. Z. AFRICAN MALE, 23 years.

Admitted 20.9.62 at 11.35 p.m. Discharged 22.9.62.

OUT-PATIENT DEPARTMENT

No history available. Comatose ? post-epileptic state ? post-alcoholic hypoglycaemia.

WARD

No history available. Comatose. The house physician suspected hypoglycaemic coma and administered intravenous dextrose.

TREATMENT

20 ml 50% intravenous dextrose solution was administered after the blood had been taken for special investigations. The patient immediately recovered.

Examination (after therapy).

	Fully conscious. No anaemia, jaundice, oedema, or lymphadenopathy. Fair nutrition.
C.V.S.	Pulse 56 per minute, regular. B.P. 170/100. J.V.P. = 0. Heart sounds closed.
R/S	Trachea central. Vocal fremitus and resonance equal R. & L. Breath sounds vesicular. No adventitious sounds.
Abd.	Soft and non-tender abdomen. No mass. Liver and spleen not palpable. No ascites.
C.N.S.	Pupils equal and react to light. Motor and sensation - normal. Deep tendon reflexes present and equal. Plantar reflexes ↓↓

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 25 mg%.

Diagnosis: Hypoglycaemia ? cause.

HISTORY FROM PATIENT

The patient had eaten supper on the day before admission at 7 p.m. and had then commenced to drink gavine. He had imbibed late into the night. At 6 a.m. the following morning he had commenced to drink gavine again and he had continued till 11 a.m., when he had fallen asleep. He had reawakened in hospital during the night. (Evidently he had been found in coma at 6 p.m.). He had not eaten anything on the morning of admission. He had never had a similar attack before.

Alcohol habits: Heavy drinker (a detailed history was not taken).

Dietary habits: Samp, mielie-meal porridge, mielie rice and potatoes were his average daily diet.

Social history: He had been employed by the Durban Corporation till 3 months before admission - unemployed after that.

SPECIAL INVESTIGATIONS

20.9.62 See above.

21.9.62 Routine urine - N.A.D.

22.9.62 Total urinary glucocorticoids 1.1 mg/24 hrs.
Urine volume 1065 ml/24 hrs.

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
21.9.62	2	60	0.9	10	Nil.	Neg.		Not done
22.9.62	3		1.2	10				

Course and management:

The patient demanded to be discharged on 22.9.62.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ?? Alcoholic hepatitis.

CASE 10/62

P.S. AFRICAN FEMALE, 30 years

Admitted 7.10.62 at 2.00 p.m. Discharged 8.11.62.

OUT-PATIENT DEPARTMENT

The patient was brought to hospital by the police, who had arrested her on the previous day for drunkeness. They had found her in coma, in her cell, that morning.

Coma ? Post-alcoholic hypoglycaemia.

WARD

The patient was immediately given intravenous dextrose solution prior to examination.

TREATMENT

After taking blood for special investigations 75 ml 50% intravenous dextrose solution was administered. The patient immediately recovered consciousness but was slightly confused.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 20 mg%, bld urea 31 mg%.

Diagnosis: Post-alcoholic hypoglycaemia.

Examination (after treatment).

A little confused.
Hydration good.
No pallor or clubbing.
No lymphadenopathy.
Temperature 98°F.

C.V.S. Pulse 100 per minute, regular.
B.P. 130/80.
Heart sounds closed.

R/S N.A.D.

Abd. Liver 1 fd., non-tender.
No splenomegaly.

C.NS. Cranial nerves intact.
Deep tendon reflexes present and equal.
Plantar reflexes ↓↓

HISTORY FROM PATIENT

The patient had eaten breakfast of porridge and a little meat at 6.30 a.m. on the day before admission. She did not eat lunch but instead had commenced to drink shimeyane (obtained by her husband) with four other people. She had drunk a large quantity (estimated by her as 1½ Winchester bottles) and had been arrested by the police later in the afternoon. She could remember nothing after that till she had reawakened in hospital.

Alcohol habits: She drank in the weekends but she had drunk more heavily on this occasion.

Dietary habits: Breakfast: Porridge, mielie rice.
Lunch: Mielie rice and porridge.
Meat twice a week.
Supper: Same as lunch or nothing.

Social history: She had worked as a floor polisher till two months before admission. Her husband worked as a gardener (£14 per month). He drank in the weekends and occasionally during the week.

Special interrogation: She had never had a similar episode previously and she did not suffer from fits. She had not taken herbal medicines, injections or tablets before admission.

SPECIAL INVESTIGATIONS

7.10.62 See above.

8.10.62 Routine urine - N.A.D.
Hb 8.6g% (58%), P.C.V. 32(%) M.C.H.C. 27%.
W.B.C. 8000/cmm. Hypochromic anaemia.
Serum electrophoresis. S. albumin 1.3g%,
S. globulins α_1 0.6g%, α_2 0.7g%, β 0.9g%, γ 1.8g%,
Total protein 5.3g%.

Chest X-ray - "There is an extensive mottled shadowing throughout the whole of the lung fields, but particularly marked in the upper and lower zones. There is ? cavity formation in the left apical zone. A tuberculosis process is favoured".

10. 10. 62 Total serum protein 4. 9g%, serum albumin 1. 7g%, S. globulin 3. 2g%, A:G ratio 0. 5:1.

12. 10. 62 17-ketosteroids <1. 0 mg/24 hrs, total glucocorticoids <1. 0 mg/24 hrs, Urine volume 1550 ml/24 hrs.

15. 10. 62 Routine urine - N. A. D.

18. 10. 62 A. C. T. H. Response test :

Day of hospitalisation on which A. C. T. H. commenced.	Type of Steroid	Unstimulated steroid excretion mg/24 hrs.	A. C. T. H. Stimulation and aftermath. Days : 1*	2*	3	4
12	17-oxo	<1. 0	<1. 0	4. 5	5. 5	2. 2
	Total gluco	<1. 0	9. 3	11. 2	6. 9	<1. 0
	Urine volume	1550	1350	1800	2500	2580

*Days on which A. C. T. H. given, A. C. T. H. gel 100 units I. M. b. d. [Batch No. 4169, Fredericksberg, Copenhagen, Denmark].

23. 10. 62 Hb 9. 8g% (67%), P. C. V. 29% (mm) M. C. H. C. 34%, reticulocytes 3. 2%, W. B. C. 13, 000/cmm.

27. 10. 62 Lumbar puncture: globulin increased, protein 222 mg%, Chlorides 760 mg%, sugar 67 mg%, microscopy, Rbc's ++.
No organisms noted.

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
8.10.62	2	70	0.6	7	+	Neg.	72	
9.10.62	3	80	0.7	7	Nil.	Neg.		
10.10.62	4	90	0.5	5	Nil.	Neg.		
11.10.62	5	60	0.6	6	Nil.	Neg.		
12.10.62	6	70	0.3	6	Nil.	Neg.	93	
13.10.62	7	60	0.4		Nil.	Neg.		
14.10.62	8				Nil.	Neg.		
15.10.62	9	60	0.4		Nil.	Neg.		
16.10.62	10	50	0.3		Nil.	Neg.		Done 17.10.62

Liver biopsy: This was performed on 17.10.62. Section of liver showed numbers of foci of necrosis with neutrophils, round cells and plasma cells. It could be miliary tuberculosis as cells, resembling epithelioid cells, were present in one focus but no Langhan's giant cells were observed. Alcoholic hyalin was not noted. Extreme fatty vacuolation and fine intercellular fatty change was seen. The portal triads showed acute and chronic inflammatory cells and there was a slight increase in fibrous tissue (grp. II). Haemosiderin was present throughout the lobules (gr. 3). Glycogen was present (gr. 1). There was no bile duct hyperplasia or bile thrombi.

[STAINS used: H & E, silver impregnation, W.H.V.G. and Best carmine).

Course and management: The patient was initially given tetracycline for her chest condition. After a weeks treatment no improvement had occurred and streptomycin (1 g daily) and I.N.H. (200 mg tds) were commenced on 13.10.62. On the 25th October the patient was found to be drowsy and two days later had neck stiffness and a severe headache. A lumbar puncture was performed and a diagnosis of miliary tuberculosis was considered. The patient subsequently improved and was transferred to a tuberculosis hospital.

Assessment of alcohol habits: Weekend drinker.
Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.
(2) ? Alcoholic hepatitis.
(3) Miliary tuberculosis.

CASE 11/62

Excluded from series

CASE 12/62

A. N. AFRICAN MALE, 36 years

Admitted 21. 10. 62 at 3. 20 p. m. Died 25. 10. 62 at 4. 30 a. m.

OUT-PATIENT DEPARTMENT

Admitted in coma. A stale smell of alcohol was noted on his breath. ? Post-alcoholic hypoglycaemia.

After taking blood for special investigations 20 ml 50% intravenous dextrose solution was administered. The patient recovered consciousness.

WARD

Examination after treatment

Fully conscious.
Breath smelling of stale alcohol.
No pallor and no clubbing.

C. V. S. Pulse 90 per minute, regular.
B. P. 130/90. J. V. P. = 0.
Heart sounds closed.

R/S Chest clear.

Abd. Abdomen soft and non-tender.
Liver 2 fd., non-tender.
No splenomegaly.
Bowel sounds normal.

C. N. S. N. A. D.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 25 mg%.

Diagnosis: Post-alcoholic hypoglycaemia.

HISTORY FROM PATIENT

The patient had drunk about a half pint of gavine and half a gallon of Zulu beer between 8 a. m. and 3 p. m. on the day before

admission. On the previous day between 2 and 5 p.m. he had imbibed one gallon of Zulu beer and a quarter pint of gavine. He was extremely drunk after the second bout of drinking and he had fallen by the road side. He had no recollection of what had happened. He had awakened in hospital. He had not eaten on the day before admission.

Alcohol habits: He had been drinking heavily and daily for one year. He usually drank Zulu beer and gavine. He did not add toxic substances to his liquor.

Dietary habits: He ate putu and samp at 3 meals a day.

Social history: He did not work. He was married. His wife was well. She occasionally drank Zulu beer. He had no children.

Special Interrogation: He had never had a similar episode previously and he did not suffer from fits. He had not taken herbal medicines, tablets or injections before admission.

SPECIAL INVESTIGATIONS

21.10.62 See above.
22.10.62 17-oxosteroids 3.8 mg/24 hours, total glucocorticoids 3.0 mg/24 hours, urinary volume, 1900 ml/24 hours.
23.10.62 Chest X-ray - Rt. upper lobar consolidation was noted.

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
21.10.62	1	110	2.5	13				
22.10.62	2	220	1.6	12			100	Done
23.10.62	3	270	2.8	9	++	Neg.		
24.10.62	4	60	1.5	6	Nil.	Neg.		

Liver biopsy: This was performed on 22.10.62. Section of liver showed a focus of necrosis. The cells had acidophilic cytoplasm and it was possibly ischaemic in origin. There was no cellular infiltration and alcoholic hyalin was not observed. Fat vacuolation was absent and fine intercellular fatty change was severe. The portal triads were oedematous and showed numerous acute and chronic inflammatory cells. There was a severe diffuse septal fibrosis (early cirrhosis) with distortion of lobular .....

pattern (grp IV). Proliferation of small bile ducts was noted but no bile thrombi were observed. Haemosiderin was prominent throughout the lobules and clumps were seen in the parenchyma and at the portal triads (gr. 5). Glycogen was present (gr. 2).

[STAINS used: H & E, P. T. A. H., silver impregnation, W. H. V. G., prussian-blue reaction, Best carmine].

Course and management: On 23. 10. 62 the patient had a fever of 101°F and signs of pneumonia. Chest X-ray confirmed a right upper lobar pneumonia. Penicillin and sulphatriad were administered but his condition deteriorated and he died on 25. 10. 62.

Assessment of Alcohol habits: ? Chronic alcoholic.

Assessment of Nutrition: Fair nutrition.

NECROPSY

Macroscopical examination revealed a right upper lobar pneumonia.

HISTOLOGY

(1) Lung - section showed a lobar pneumonia.

(2) Liver- Multiple centrilobular foci of necrosis were noted. There was no cellular reaction or alcoholic hyalin. An early portal cirrhosis (grp IV) was confirmed and numerous lymphocytes were present at the portal triads and in the fibrous tissue. Bile duct proliferation was noted, but bile thrombi were not observed. Siderosis was marked (gr. 5). Fine intercellular fatty change was present.

(3) Kidneys - The proximal and distal tubules showed cloudy swelling.

(4) Sections from adrenal and pituitary were natural.

FINAL DIAGNOSIS
(1) Post-alcoholic hypoglycaemia.
(2) Alcoholic hepatitis.
(3) ? Chronic alcoholic.
(4) Lobar pneumonia.

CASE 13/62

L. M. AFRICAN FEMALE, 60 years.

Admitted 2. 12. 62 at 7. 30 a. m. Discharged 24. 12. 62.

OUT-PATIENT DEPARTMENT

Brought in comatose. The relatives stated that the patient was a chronic alcoholic and that she had been drinking shimeyane and gavine all day on the day before admission. She had commenced drinking at about 11 a. m. in the morning, with numerous other people, and stopped at about midnight. She was very drunk on retiring to bed. She had not awakened that morning and had been brought to hospital. She had not eaten for two days and had last eaten porridge.

Examination:	Deep coma. Cold + Pellagrinous dermatitis. Temperature 98°F. Strong smell of stale alcohol on her breath.
C. V. S.	Pulse 80 per minute, regular and good volume. B. P. 150/80. Heart sounds closed.
R/S	Respiration slow and shallow. Rhonchi bilaterally.
Abd.	Liver 3fd. No splenomegaly.
C. N. S.	Deep coma. Small constricted pupils. Deep tendon reflexes not obtainable. Plantar reflexes: no reaction.
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 100 ml 10% sodium pyruvate was administered. No response occurred and after 30 minutes a repeat blood sugar was taken and 20 ml 50% intravenous dextrose solution was given. The patient regained consciousness within three minutes. She was inebriated on awakening.

WARD:

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar (before pyruvate) 47 mg%. Bld sugar (after pyruvate) 50 mg%, serum electrolytes, Na, 139 meq/l, K 3.6 meq/l, Cl, 85 meq/l., bld urea 27 mg%, Routine urine Acetone ++++. Nil else of note.

Diagnosis: Post-alcoholic hypoglycaemia.

HISTORY FROM PATIENT

History as above.

Alcohol habits: She admitted that she was a chronic alcoholic. She had been drinking heavily and whenever possible, for years.

Dietary habits: Mainly alcohol - Zulu beer, shimeyane and gavine, otherwise sour porridge.

Special interrogation: She had not had a similar episode before, She did not suffer from fits.

Examination (after therapy).

Malnourished. Puffiness of face. Pellagrinous rash on neck and face. Slighe oedema of legs. Mucosa ? pale. No jaundice and no lymphadenopathy.

C.V.S. Pulse 110 per minute, regular, good volume.
B.P. 140/70. J.V.P. = 0.
Heart sounds closed.

R/S Movement and air entry R = L.
Rate 18 per minute.
VR = VR. VF = VF.
?? bronchial breathing lung apices.
Bilateral rhonchi.

Abd. Liver 3 fd., firm and tender.
No splenomegaly.

C.N.S. Pupils equal and react to light.
Cranial nerves normal.
Motor and sensation normal.
Deep tendon reflexes brisk and equal.
Plantar reflexes equivocal.

SPECIAL INVESTIGATIONS

3.12.62 Hb 12.4% (84%), P.C.V. 41%, M.C.H.C. 30%, W.B.C. 11,000/cmm.
17-ketosteroids 1.0 mg/24 hrs, total glucocorticoids 1.3 mg/24 hrs, urine volume 1010 ml/24 hours.

5.12.62 Serum electrolytes: Na, 143 meq/l, K 3.2 meq/l, Cl, 107 meq/l.
Total serum protein 6.6g%, S. albumin 3.0g%, S. globulin 3.6g%, A:G ratio 0.8:1.
17-ketosteroids 4.4 mg/24 hrs, total glucocorticoids 2.5 mg/24 hrs, urine volume 1850 ml/24 hrs.

7.12.62 Chest X-ray : No heart or lung lesion noted.

10.12.62 17-ketosteroids 6.6 mg/24 hours, total glucocorticoids 2.3 mg/24 hrs, urine volume 3098 ml/24 hrs.

14.12.62 Glucose tolerance test: Fasting 89 mg%, ½ hour 150 mg%, 1 hr. 139 mg%, 1½ hrs. 106 mg%, 2 hrs. 97 mg%, 2½ hours 103 mg%, 3 hrs. 103 mg%, 3½ hrs. 97 mg%, 4 hrs 64 mg%.

19.12.62 Water loading test:
7-11 p.m. starved, no fluids.
11-8.30 a.m. Passed 890 ml urine.
Given 1000 ml water at 9.00 a.m.
By 12.45 p.m. had passed 930 ml urine.

Conclusion: Normal response to water loading.

20.12.62 A.C.T.H. Response Test:

Day of hospitalisation on which A.C.T.H. given.	Type of Steroid	Unstimulated Steroid excretion	A.C.T.H. Stimulation and aftermath (mg/24 hrs. Days: 1*	2*	3*	4	5
18	17-oxo	0.8	9.1		11.5	9.8	
	Total gluco	2.0	9.1		10.5	5.6	
	Urine volume (ml/24 hrs).		3200			4200	

*A.C.T.H. I.M. 100 units b.d. on day 1. (batch No.4169 Fredericksberg, Copenhagen, Denmark). A.C.T.H. 25 units. I.V. over 8 hrs on days 2 & 3. (Batch No.4030, F. C. D.).

Date	Day	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
2.12.62	1	120	0.8	6	trace	Neg.	52	
3.12.62	2	80	0.6	5	"	Neg.	100	
4.12.62	3		0.2	9	"	Neg.		Done
5.12.62	4	80	0.9	7	Nil.	Neg.		
6.12.62	5	80	0.8	5	Nil.	Neg.		
7.12.62	6	120	0.6	8				
10.12.62	9	40		6	Nil.	Neg.		
12.12.62	11	20	0.5	4				

Liver biopsy: This was performed on 4.12.62. Section of liver showed severe fatty vacuolation and fine intercellular fatty change (gr.4). No foci of necrosis or alcoholic hyalin were observed. The portal triads showed an infiltration by round cells and there was a moderate increase in fibrous tissue ('periportal fibrosis') (grp.III). Haemosiderin was present throughout the lobules (gr.3). Glycogen was noted (gr.4). No bile duct hyperplasia or bile thrombi were observed.

[STAINS used: H. & E. silver impregnation, W.H.V.G., prussian blue reaction, Sudan III, Best carmine].

Course and management:

The patient became disorientated four days after admission, but had improved two days later. Her condition was diagnosed as a mild alcoholic psychosis. She demanded her discharge for Christmas on 24. 12. 62.

Assessment of alcohol habits: Chronic Alcoholic.

Assessment of nutrition: Poor nutrition (Pellagra).

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

(3) Chronic alcoholic.

(4) Pellagra.

CASE 14/62

L. Z. AFRICAN FEMALE, 57 years

Admitted 13. 11. 62 at 7. 10 a. m. Discharged 28. 11. 62

OUT-PATIENT DEPARTMENT

A relative stated that he had tried to awaken her that morning at 4. 00 a. m., but she had not responded. She had been drinking on the previous evening.

Admitted in coma ? post-alcoholic hypoglycaemia.

WARD

History as above.

Examination:	Comatose, middle aged African female. No pallor, cyanosis, jaundice, clubbing or oedema. Subnormal temperature, 94°F.
C. V. S.	Pulse 88 per minute, regular, good volume. B. P. 140/90. J. V. P. = 0. Heart sounds closed.
R/S	Resp. rate 22 per minute. Chest clear.
Abd.	Liver 4 fd., firm and non-tender, no splenomegaly.
C. N. S.	Comatose. Cranial nerves apparently intact. No response to pen prick or deep pressure pain. Deep tendon reflexes diminished. Plantar reflexes no response.
Diagnosis:	? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 75 ml 50% intravenous dextrose solution was administered. She immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

13.11.62 Bld sugar 39 mg%, bld urea 40 mg%,
Routine urine: Acetone ++++. Nil else of note.

Diagnosis: Hypoglycaemia ? post-alcoholic.

HISTORY FROM PATIENT

She had been drinking on the day before admission with three friends, commencing at 7 p.m. They had drunk a large golden syrup tin full of shimeyane. She had been mildly intoxicated at the end and had retired to bed at 9 p.m. She had reawakened in hospital. She had eaten mielie meal porridge and vegetables at noon on the day she had imbibed, but nothing else.

Alcohol habits: She drank shimeyane about four times per week including Saturdays. She never drank gavine or European liquor.

Dietary habits: Breakfast: Porridge, Bread, tea.
Lunch: Samp or beans.
Supper: Samp or beans.
Meat once per week.

Social history: Her husband was dead. She stayed on her own and a male friend supplied her with money. She did not work.

Special interrogation: She had never had a similar episode before. There was no history of fits. She had not taken herbal medicines, injections or tablets before her admission. She did not add toxic substances to her liquor.

SPECIAL INVESTIGATIONS

13.11.62 See above.
Total serum protein 7.0g%. Serum albumin 2.8g%. Serum globulin 4.2g%.

14.11.62 Routine urine N.A.D.
Hb. 11.3g% (77%), P.C.V. 26 (mms), M.C.H.C. 31%, W.B.C. 4,000/cmm. Serum electrophoresis: S. albumin 2.2g%, S. globulin α_1 0.9g%, α_2 1.0g%, β 1.1g%, γ 1.6g%, Total protein 6.8g%.
17-ketosteroids 2.0 mg/24 hours, total glucocorticoids 5.8 mg/24 hours, urine volume 780 ml/24 hours.

16.11.62 Chest X-ray: No lung or heart lesion noted.
17-ketosteroids 2.6 mg/24 hours, total glucocorticoids 7.8 mg/24 hrs, urine volume 940 ml/24 hrs.

20.11.62 A.C.T.H. Response Test.

Day of hospitalisation on which A.C.T.H. commenced.	Type of Steroid	Unstimulated steroid excretion (mg/24 hrs).	A.C.T.H. Stimulation and aftermath (mg/24 hrs) Days: 1*	2*	3	4	5
	17-oxo	5.5	5.6	10.6	24.7	12.5	4.3
	Total gluco	8.7	42.6	29.5	39.4	9.6	3.0
	Urine volume (ml/24 hrs)	1900	1700	2000	1520	1300	1830

* Days on which A.C.T.H. given 100 units I.M. gel b.d. (Batch No. 4169, Fredericksberg, Copenhagen, Denmark).

27.11.62 Glucose tolerance test: Fasting 54 mg%, ½ hour 84 mg%, 1 hour 96 mg%, 1½ hour 84 mg%, 2 hour 60 mg%, 2½ hour 58 mg%, 3 hour 56 mg%, 3½ hour 60 mg%, 4 hour 64 mg%.

Date	Days	T	B	A.P.	U	U.B.	P.I.	Liver biopsy
13.11.62	1	20	0.8	9				
14.11.62	2	60	1.3	8	trace	Neg.	86	
15.11.62	3	30	1.3	8	trace	Neg.		Done
16.11.62	4				++	Neg.		
17.11.62	5				trace	Neg.		
18.11.62	6				Nil.	Neg.		
19.11.62	7	32	0.7	5	Nil.	Neg.		
20.11.62	8		0.7	13				

Liver biopsy: This was performed on the 15.11.62. Section of liver showed a small focus of necrosis with neutrophilic infiltration. Alcoholic hyalin was not noted. Fatty vacuolation was moderate but severe fine intercellular fatty change was observed. (gr.4). The portal triads showed chronic and occasional acute inflammatory cells and there was a slight increase in fibrous tissue (grp.II). Haemosiderin was present throughout the lobules (gr.3). Glycogen was noted (gr.3). There were no bile thrombi or bile duct hyperplasia.

[STAINS used: H. & E., silver impregnation, W.H.V.G., prussian-blue reaction, Sudan III, Best carmine and P.T.A.H.]

Course and management: The patient had an uneventful course in hospital.

Assessment of Alcohol habits: ? Chronic Alcoholic.

Assessment of Nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis

(3) ? Chronic Alcoholic.

CASE 15/62

I. M. AFRICAN MALE, 58 years

Admitted 29. 10. 62 at 11. 40 a. m. Discharged 15. 12. 62.

OUT-PATIENT DEPARTMENT

No history available. Admitted in coma ? cause.

WARD

No history available. Temperature 96. 6°F. Shallow breathing, pulse 76 per minute. B. P. 115/70.

The house physician administered intravenous dextrose solution, after taking blood for special investigations, in case the patient was in hypoglycaemic coma.

TREATMENT

50 ml 50% intravenous dextrose solution was given. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 30 mg%, bld urea 24 mg%, serum electrolytes: Na, 128 meq/l, K, 4. 3 meq/l, Cl, 87 meq/l.
Hb. 14. 7 g% (99%), W. B. C. 10,000/cmm.

Diagnosis: Hypoglycaemia ? cause.

Examination (after therapy). A thin African adult male of fair nutrition. Extremely black in colour. No pallor, clubbing or jaundice.

C. V. S. Pulse 76 per minute, B. P. 115/70. Heart sounds closed.

R/S ? bronchial breathing left apex.

Abd. Liver 1½ fd, firm and non-tender. No splenomegaly.

C.N.S. Fully conscious.
Fundi N.A.D.
Reflexes not obtainable.

HISTORY FROM PATIENT

He had imbibed 2 pints of Zulu beer and a half glass of gavine on the day prior to admission and had arrived home intoxicated at 5.30 p.m. He had gone to bed at 6 p.m. without eating and had awakened at 8 a.m. An hour later he had begun to speak slowly and had started to sweat profusely. He had reawakened in hospital. According to his wife he had had a convulsion prior to coming to hospital. He had eaten putu only, on the day he had been drinking, at breakfast at 7 a.m.

Alcohol habits: He usually drank on Saturday and Sunday and became intoxicated, but he was not a heavy drinker.

Assessment of alcohol habits: Weekend drinker.

Dietary habits: Breakfast: Putu.
Lunch: Putu or vegetables.
Supper: Putu, bread, tea.

Social history: He did not work any more. He was happily married.

Special interrogation: He had never had a similar episode nor had a fit previously. He had not taken herbal medicines, tablets, or injections. He did not add toxic substances to his liquor.

Past history: He had tuberculosis in 1957 and 1958, and had been treated at a tuberculosis hospital. In 1956 he had noticed increased pigmentation of the face and body and this had persisted. In 1959 he was admitted to a mental home in a confused state. He had clear periods between attacks, during which he used to dream about enemies. He was discharged in 1960 and had been well till his admission.

SPECIAL INVESTIGATIONS

29. 10. 62 See above.
Chest X-ray "Gross fibrotic change is noted in the left upper lobe and apical zone. A small patch is also noted in the right lobe".

5. 11. 62 17-ketosteroids 3.3 mg/24 hrs, total glucocorticoids <1.0 mg/24 hrs, urine volume 2670 ml/24 hours.

6. 11. 62 Total serum protein 6.8g%, S. albumin 2.9g%, S. globulin 3.9g%, A:G ratio 0.7:1.

6. 11. 61 A. C. T. H. Response Test.

Day of hospitalisation on which ACTH commenced	Type of Steroid	Unstimulated Steroid excretion mg/24 hours	A. C. T. H. Stimulation and aftermath (mg/24 hrs) Days : 1*	2*	3	4	5	6
8	17-oxo	3.3	3.6	3.1	2.2	2.0	2.7	2.7
	Total gluco	<1.0	<1.0	<1.0	<1.0	8.0	<1.0	3.3
	Urine vol (ml/24 hrs).	2670	2920	2520	2950	2750	2700	

* Day on which A. C. T. H. given, I. M. gel 100 units b. d. [Batch No. 4169 Fredericksberg, Copenhagen, Denmark].

16. 11. 62 Glucose tolerance test: Fasting 80 mg%, ½ hour 120 mg%, 1 hr. 128 mg%, 1½ hr 104 mg%, 2 hr 88 mg%, 3 hr 104 mg% 3½ hr 96 mg%, 4 hr 80 mg%.

Date	Day	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
29. 10. 62	1	90	0.7				100%	
30. 10. 62	2				Nil	Neg.		
31. 10. 62	3	20	0.2	10	trace	Neg.		Done
1. 11. 62	4	30	1.0	4	Nil.	Neg.		
2. 11. 62	5	20	0.5	6	Nil.	Neg.		
3. 11. 62	6	30						

Liver biopsy: This was performed on 31. 10. 62. Section of liver showed mild fatty vacuolation and mild fine intercellular fatty change (gr. 1). There were no foci of necrosis and alcoholic hyalin was not observed. The portal triads showed an occasional round cell and there was no increase in fibrous tissue (grp. I). Haemosiderin was present throughout the lobules (gr. 3). Glycogen was noted (gr. 4). Bile thrombi were not seen and there was no bile duct hyperplasia.

[STAINS used: H. & E., P. T. A. H., silver impregnation, W. H. V. G., Sudan III].

Course and management:

The patient developed diarrhoea and vomiting on 17. 11. 62, and vomiting continued on the following day. On 19. 11. 62 he complained of extreme weakness and on examination was collapsed, had an unrecordable blood pressure and an impalpable pulse. The possibility of an Addisonian crisis was considered. His extreme pigmentation had been noted on admission and later examination had shown pigmentation of his tongue and buccal mucosa. After taking blood for special investigations, hydrocortisone was administered, by the intravenous route, in dextrose saline (100 mg hydrocortisone/ litre). His blood pressure rose to 100/70 and his pulse was 96 per minute, regular. He felt better and "strong again". His total fluid intake during that day was 6 1/4 litres and his urine output was 5 litres. Special investigations, taken before treatment showed: bld urea 70 mg%, serum electrolytes, Na, 108 meq/l, Cl, 78 meq/l, and K, 5. 8 meq/l, bld sugar 88 mg%. A diagnosis of Addison's disease was made. X-ray of his abdomen did not show any calcification. On 20/11/62 therapy with cortisone (12½ mg bd.) and Nacl (1 gm Q. I. D.) was started. It was discontinued on the 29. 11. 62 and the patient remained well.

Water loading tests:

29. 11. 62 (while on cortisone)

6 p. m. - 8. 00 a. m. No food or water.
8. 00 a. m. given 1200 ml water.
8. 00 a. m. - 1. 00 p. m. - passed 1080 ml urine.

6. 12. 62 — 6 p.m. - 11 p.m. No food or water.
11 p.m. - 8.00 a.m. 1100 ml urine passed.
8.00 a.m. Given 1200 ml water.
8.00 a.m. -12.40 a.m. 180 ml urine passed.

The test was compatible with adrenal insufficiency.

RE-ADMISSION

The patient was discharged on 15. 12. 62 and readmitted on 4. 1. 63 to repeat his water loading test and to perform an intravenous ACTH stimulation test. He had been quite well during his discharge.

Type of urinary steroid.	Unstimulated steroid excretion mg/24 hrs.	ACTH Stimulation and after-math. mg/24 hours. Days:				
		1*	2*	3	4	5
17-oxo	1.2	5.6	2.5	4.6	1.4	1.8
Total gluco	1.5	5.0	3.1	8.4	11.2	3.1
Urine vol. ml/24 hrs.	1810	1525	1750	1750	1920	1870

*Days on which ACTH given, 25 units I.V. ACTH administered over 8 hours in 1 litre 5% dextrose water. (A.C.T.H. Batch No.4030 Fredericksberg, Copenhagen, Denmark).

Water Loading Tests:

7. 1. 63 — 6 p.m. - 11 p.m. No food or water.
11 p.m. - 8 a.m. Passed 810 ml urine.
8 a.m. given 1000 ml water.
9 a.m. 75 ml urine.
11 a.m. 90 ml urine.
12 noon 40 ml urine.

Total 205 ml in four hours.

Routine urine N.A.D.

23. 1. 63

6 p.m. - 11 p.m. No food or water.
11 p.m. - 8 a.m. 455 ml urine passed.
8 a.m. Given 1000 ml water.
9 a.m. 30 ml urine.
11 a.m. 90 ml urine.
12 noon 125 ml urine.

Total urine 245 ml in four hours.

Routine urine N.A.D.

28. 1. 63

After Cortisone 12½ mg bd for four days.
6 p.m. - 11 p.m. No food or water.
11 p.m. - 8 a.m. 225 ml urine.
8 a.m. Given 1000 ml water.
9 a.m. 90 ml urine.
10 a.m. 195 ml urine.
11 a.m. 255 ml urine.
12 noon 120 ml urine.

Total urine output over four hours 690 ml.
Routine urine N.A.D.

Water loading tests showed adrenal insufficiency. The urine output was improved by cortisone administration.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Addison's disease.

CASE 1/63

M. P. AFRICAN FEMALE, 40 years.

Admitted 1. 1. 63 at 4. 20 p. m. Discharged 10. 1. 63.

OUT-PATIENT DEPARTMENT

Relatives stated that the patient had been drinking heavily on the day before admission and that she had fallen on the stairs. She had not lost consciousness but the same day she had been found in coma at 2 p. m. She was noted to have a laceration over the right parietal region and was admitted in coma to a surgical ward with a diagnosis of head injury.

WARD

History as above.

Examination: Deep coma.
Slight pallor of gums.
No lymphadenopathy, cyanosis, jaundice or oedema.
Temperature 100°F.

A strong odour of alcohol was noted on her breath.

A laceration, 2 cms long, was noted over the right parietal area. An old scar was present on the left.

C. V. S. Pulse 100 per minute, regular.
B. P. 100/50. J. V. P. = 0.
Heart - soft systolic murmur at the apex.

R/S Trachea central.
Respiratory note, 20 per minute.
Breath sounds vesicular.
Rhonchi scattered over both lung fields.

Abd. Abdomen soft and non-tender.
No masses palpable.
Liver and spleen not palpable.
No ascites. Bowel sounds normal.

C. N. S. Deep coma.

No further examination was done, as the house surgeon, who had just been round the medical wards, suspected post-alcoholic hypoglycaemia.

TREATMENT

After taking blood for special investigations, 75 ml 50% intravenous dextrose solution was administered. The patient immediately recovered consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 22 mg%, serum electrolytes: Na, 126 meq/l, K, 4.0 meq/l, Cl 93 meq/l, Hb 10.3g% (70%). W.B.C. 21,000/cmm.

Diagnosis: Post-alcoholic hypoglycaemia.

HISTORY FROM PATIENT

She had taken a cup of gavine, at noon, after which she had felt slightly intoxicated. Later she had a party on "White" liquor and she had subsequently fallen down the stairs. She had not known when she had become unconscious. She had eaten a meal of bread and tea at 7 p.m. on the previous evening. She had eaten breakfast and lunch on that day.

Alcohol habits: She said she occasionally drank a lot and she had been drinking on this occasion as it was New Year. She denied chronic alcoholism.

Dietary habits:
Breakfast: Bread, porridge.
Lunch: Putu, bread, beans.
Supper: Meat twice a week; otherwise bread or porridge.

Social history: She was not married and she had no children. She worked as a polisher and also did the washing, earning £4.12.0 per month.

Special interrogation: She had not had a similar episode previously and had never had a fit. She had not taken herbal medicines, tablets or injections. She did not add toxic substances to her liquor.

SPECIAL INVESTIGATIONS

1. 1. 63 See above.
X-ray chest and skull - N. A. D.

2. 1. 63 Hb 8. 5g% (85%), P. C. V. 26 (mm³), M. C. H. C. 33%, W. B. C. 5, 000/cmm (N53, M6, L40, E1), platelets 198, 000/cmm, film: mild anisochromasia and polychromasia.
Total serum protein 5. 6g%, S. albumin 3. 3g%, S. globulin 2. 3g%, A:G ratio 1. 5:1.

3. 1. 63 17-ketosteroids 2. 1 mg/24 hours, total glucocorticoids 13. 7 mg/24 hours, urine volume 1440 ml/24 hrs.

4. 1. 63 Routine urine N. A. D.

9. 1. 63 17-ketosteroids 6. 9 mg/24 hrs, total glucocorticoids 19. 3 mg/24 hrs, urine volume 2570 ml/24 hrs.

10. 1. 63 Water loading test.

6 pm - 11 pm.	No food or water.
11 pm - 8 am.	Passed 540 ml urine.
8 am.	Given 1000 ml water.
9 am.	140 ml urine.
10 am.	330 ml urine.
11 am.	300 ml urine.
12 noon	180 ml urine.

Total urine passed in four hours 950 ml.

14. 1. 63 Glucose tolerance test: Fasting 80 mg%.
½ hour 140 mg%, 1 hour 133 mg%, 1½ hrs 94 mg%, 2 hrs 67 mg%, 2½ hrs 53 mg%, 3 hrs 67 mg%, 3½ hrs 80 mg%.

17. 1. 63 Given 25 units A. C. T. H. I. V. over 8 hours (Batch No. 4030, Fredericksberg, Copenhagen, Denmark).
17-ketosteroids 13. 1 mg/24 hrs, total glucocorticoids 26. 6 mg/24 hrs, urine volume 2580 ml/24 hrs.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
2. 1. 63	2	40	0. 2	6			100	Done.
3. 1. 63	3	30	0. 2	5	trace	Neg.		
4. 1. 63	4	30	1. 0	8	+	Neg.		
5. 1. 63	5	38	0. 9	6	Nil.	Neg.		
6. 1. 63	6				Nil.	Neg.		
7. 1. 63	7	30	0. 9	7	Nil.	Neg.		

Liver biopsy: This was performed on 2. 1. 63. Section of liver showed mild fatty vacuolation but fine intercellular fatty change was severe (gr. 4). There were no foci of necrosis and alcoholic hyalin was not observed. The portal triad showed occasional acute and chronic inflammatory cells. There was no increase in portal fibrosis (grp. I). Haemosiderin was not seen (gr. O). Glycogen was present (gr. 4). There was no bile duct proliferation and bile thrombi were not observed.

[STAINS used: H. & E., Sudan III, silver impregnation, W. H. V. G. and Best carmine].

Course and management:

On 2. 1. 63 the patient was given 2 pints of blood (Hb 8. 3g%). The blood film had suggested blood loss. Her course in hospital was otherwise uneventful. Her scalp wound healed satisfactorily.

Assessment of alcohol habits: Weekend drinker.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ?? Alcoholic hepatitis.

(3) Scalp laceration.

CASE 2/63

E. K. AFRICAN MALE, 35 years.

Admitted 7. 1. 63 at 1. 10 p. m. Discharged 4. 2. 63.

OUT-PATIENT DEPARTMENT

No history available.

Examination:	Comatose. Poor nutrition. Cold. Strong alcoholic odour on his breath. No anaemia, jaundice or cyanosis.
C. V. S.	Pulse 86 per minute. B. P. 140/90. Heart sounds closed.
R/S	N. A. D.
Abd.	Hepatomegaly.
C. N. S.	Hypertonia. Deep tendon reflexes increased. Plantars equivocal.
Diagnosis:	? Alcoholic coma. ? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 100 ml 10% sodium pyruvate was administered. The patient did not respond. A repeat blood sugar was obtained after thirty minutes and 15 ml 50% intravenous dextrose solution was given. The patient immediately responded but was confused, laughing and very noisy. He appeared to be inebriated.

WARD

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 15 mg% (before and after sodium pyruvate) hb 12. 6g% (86%), P. I. 78%, routine urine: Acetone +++, nil else of note. A liver biopsy was performed within minutes of the administration of the dextrose solution.

Diagnosis: (1) Post - alcoholic hypoglycaemia.
(2) ? Alcoholic intoxication.

Examination (after dextrose thereapy):

Temperature 97.6°F.

C.V.S. Pulse 70 per min, regular. B.P. 140/90.
Heart sounds closed.

R/S Resp. rate 18 per minute.
Chest clear.

Abd. 3 fd hepatomegaly - non-tender.
No splenomegaly.
No free fluid.
Bowel sounds present.

C.N.S. Disorientated. Apparently inebriated.
Cranial nerves intact.
Deep tendon reflexes brisk.
Plantars ⇓⇓
Sensation intact.

Course: At 3.15 p.m. (3 hours after admission) the patient was found in semicoma and having generalised convulsions. Blood was taken for blood sugar and blood alcohol, and 75 ml intravenous dextrose solution was administered. The patient immediately recovered consciousness but was still mildly inebriated. He vomited and the contents smelt strongly of alcohol.

Results of special investigations:

Bld sugar 15 mg%, bld alcohol 70 mg% (0.7%).

HISTORY FROM PATIENT

He had been drinking heavily on the night before admission and he had drunk till 7 a.m. in the morning. He had imbibed gavine, wine and cane spirit with a number of other people. He had been very drunk at 7 a.m. He did not know what had happened but he had reawakened in hospital. He had not eaten on the day prior to admission.

Alcohol habits: He drank frequently and almost every day. He had been drinking for twenty years and daily for two years.

Dietary habits: Breakfast: Mielie meal porridge.
Lunch: Samp.
Supper: Potatoes and cabbage.

Social history: He was not married. He had two children from the same woman with whom he no longer lived. He had stopped working three years previously.

Special interrogation: He had not taken herbal medicines, tablets or injections before his admission. He did not add toxic substances to his liquor. He had never had a similar attack previously. He did not suffer from fits.

SPECIAL INVESTIGATIONS

7. 1. 63 Immediate special investigations.

9. 1. 63 17-ketosteroids 1.5 mg/24 hours, total glucocorticoids 12 mg/24 hours, Urine volume 1050 ml/24 hours.

10. 1. 63 Total serum protein 4.8g%, serum albumin 1.4g%, serum globulin 3.4g%. A:G ratio 0.4:1.

15. 1. 63 Chest X-ray - N. A. D.

16. 1. 63 ACTH Response Test

Day of hospitalisation on which ACTH commenced	Type of urinary Steroid	Unstimulated steroid excretion (mg/hrs).	ACTH Stimulation and aftermath (mg/24 hrs) Days: 1*	2*	3*	4
10	17-oxo	1.5		9.2	4.7	6.7
	Total gluco	12.0		52.3	26.1	31.7
		1050			1060	2220

*Days on which ACTH was given, 25 units I. V. over 8 hours (Batch No. 4030, Fredericksberg, Copenhagen, Denmark).

24. 1. 63 Hb 10. 1g% (68%), P. C. V. 32%, M. C. H. C. 32%, E. S. R. 61 mms/hr, W. B. C. 4,000/cmm.
V. D. R. L. (slide) non-reactive.
Kolmer cardiolipin (W. R.) non-reactive.
Bld urea 20 mg%.
C. S. F. Protein 38 mg%, chloride 720 mg%, sugar 63 mg%, Microscopy - No organisms or cells noted.

25. 1. 63 Skull X-ray N. A. D.

Date	Day	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
7. 1. 63	1	160	1. 3	20	Nil.	Neg.	78	Done
8. 1. 63	2	110	1. 8	18	trace	Neg.		
9. 1. 63	3	90	1. 6	16	++	Neg.		
10. 1. 63	4	200	1. 3	17	++	Neg.		
11. 1. 63	5	200	1. 0	17	+++	Neg.		
12. 1. 63	6	110	1. 2	14	+++	Neg.		
14. 1. 63	8	138	0. 8	16				
15. 1. 63	9				++	Neg.		
16. 1. 63	10	110	1. 2	13				
17. 1. 63	11				+	Neg.		
22. 1. 63	16	50	0. 5	11	Nil.	Neg.		

Liver biopsy: This was done on 7. 1. 63 within minutes of the administration of 50% intravenous dextrose solution. Section of liver showed an absence of glycogen (gr. 0). A focus of necrosis, with parenchymal cells showing acidophilic cytoplasm and pyknotic nuclei, and with neutrophilic infiltration, was noted. Alcoholic hyalin was not observed. There was extreme fatty vacuolation and severe fine intercellular fatty change (gr. 4). Haemosiderin was found only in the Kuppfer cells (gr. 1). The portal triads showed acute and chronic inflammatory cells and there was a slight increase in fibrous tissue (grp. II). Bile thrombi were not seen and there was no bile duct hyperplasia.

[STAINS used: H. & E. Best carmine, P. A. S., silver impregnation, W. H. V. G., Sudan III].

Course and management:

On 22. 1. 63 the patient was found to be mentally confused and morose. He had an expressionless face and answered questions in monosyllables. Prior to 22. 1. 63 he had been quiet and mentally dull. Examination at the psychiatric clinic was undertaken and a diagnosis of alcoholic psychosis was made. He was given largactil (25 mg tds) phenergin (25 mg q. i. d) and plebex (2 ml I. M. x 5 days). He subsequently improved and was discharged on 4. 2. 63.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Alcoholic psychosis.

(4) Chronic alcoholic.

CASE 3/63

G. M. FEMALE AFRICAN, 40 years

Admitted 8. 1. 63 at 12 noon. Discharged 5. 2. 63.

OUT-PATIENT DEPARTMENT

Comatose. No history available. ? Cerebrovascular accident.

WARD

No history available.

Examination: Comatose.
Mild pellagrinous dermatitis on her face.
? stale smell on her breath.
No anaemia, jaundice, cyanosis or clubbing.
Skin cold. Temperature 98°F.
No dehydration, tongue moist.

C.V.S. Pulse 128 per minute. B.P. 165/120.
Heart sounds closed.

R/S Scattered rhonchi.
Respiratory rate 22 per minute.

Abd. Soft abdomen.
Liver just palpable.
No splenomegaly.
Bowel sounds present.

C.N.S. Comatose.
Pupils equal and react to light.

Deep Tendon Reflexes:	R	L
Biceps	+	-
Knee	+	++
Ankle	+	+
Plantar reflex	↑	↑
Abdominal reflex	+ / +	+ / +

Diagnosis: ? Post-alcoholic hypoglycaemia.

TREATMENT

Blood was taken for special investigations and then 20 ml 50% intravenous dextrose solution was administered. There was an immediate recovery of consciousness.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 38 mg%, bld alcohol 0 mg%, bld urea 48 mg%, Hb 14.9% (102%), W.B.C. 9,000/cmm, P.I. 95%, Routine urine acetone +. Nil else of note.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

At 2 p.m. on the day before admission the patient had been drinking large quantities of Zulu beer and half a pint of gavine. By 3 p.m. she had been intoxicated and could not remember any more till she had awakened in hospital. She had not eaten on the day she had imbibed, and had eaten only porridge on the previous day.

Alcohol habits: She drank daily, usually Zulu beer, but gavine when she was able to obtain it. She was intoxicated on most days. She preferred drinking alcohol to eating. She had been drinking heavily for ten years and had taken alcohol for twenty years.

Dietary habits:

Breakfast:	Porridge.
Lunch:	Putu and cabbage. Meat twice per week.
Supper:	Samp or putu.

Social history: She did not work. She was married and had three children (19, 18 and 16 years). Her husband did not drink. He earned £7 per month.

Special interrogation: She did not add toxic substances to her liquor. She had never had a similar episode previously. She did not suffer from fits. She had not taken herbal medicines, tablets or injections before her admission.

SPECIAL INVESTIGATIONS

8. 1. 63 See above.

10. 1. 63 17-ketosteroids 2. 5 mg/24 hrs, total glucocorticoids 2. 1 mg/24 hrs, urine volume 1280 ml/24 hrs.

11. 1. 63 Chest X-ray N. A. D.
Routine urine: Microscopy pus cells +, occasional rbc per H. P. F. Nil else of note.

15. 1. 63 ACTH Response Test.

Day of hospitalisation on which ACTH commenced	Type of urinary steroid	Unstimulated steroid excretion (mg/24 hours)	ACTH Stimulation and aftermath (mg/24 hours) Days: 1*	2*	3	4	5
8	17-oxo	0. 5	6. 8	11. 5	14. 6	15. 7	10. 5
	Total gluco.	4. 5	14. 1	28. 8	43. 5	32. 5	10. 5
	Urine volume ml/24 hrs	1770	1580	1300	830	3480	4130

*Days on which ACTH given, 25 units I. V. over 8 hours (Batch No. 4030, Fredericksberg, Copenhagen, Denmark).

25. 1. 63 ACTH Response Test.

Day of hospitalisation on which ACTH commenced	Type of urinary steroid	Unstimulated steroid (mg/24 hours)	ACTH STimulation and aftermath (mg/24 hours). Days 1*	2*	3	4	5	6
18	17-oxo	3. 1	7. 8	5. 8	5. 2	1. 8	2. 2	4. 6
	Total gluco	2. 6	28. 8	45. 9	4. 3	11. 1	2. 7	5. 8
	Urine volume ml/24 hrs	3290	2990	3000	2100	3100	3740	2650

*Days on which ACTH given, ACTH gel 100 units b. d. I. M. (Batch No. 85 Fredericksberg, Copenhagen, Denmark).

5.2.63 Glucose tolerance test: Fasting 76 mg%, ½ hour 118 mg%, 1 hr. 145 mg%, 1½ hrs 130 mg%, 2 hrs. 110 mg%, 2½ hrs. 88 mg%, 3 hrs. 75 mg%, 3½ hrs. 81 mg%, 4 hrs. 69mg%.

Date	Day	T	B	A.P.	U	U. B.	P.I.	Liver biopsy
8.1.63	1	70	0.4	6	trace	Neg.	95	
9.1.63	2	40	0.8	6				
10.1.63	3	40	0.5	9	trace	Neg.		
11.1.63	4	40	0.6	5	+	Neg.		Done.
12.1.63	5	20	0.6	5	+	Neg.		
14.1.63	7	36	0.6	8	trace	Neg.		
15.1.63	8				Nil.	Neg.		

Liver biopsy: This was performed on 11.1.63. Section of liver showed foci of necrosis infiltrated by neutrophils and round cells. In one focus round cells predominated. Alcoholic hyalin was not observed. Fat vacuolation was mild but moderate fine intercellular fatty change was present (gr. 2). The portal triad showed a few chronic inflammatory cells and there was no increase in fibrous tissue. Haemosiderin was present in the parenchyma at the periphery of the lobules (gr. 2). Glycogen was noted (gr. 4). There were no bile thrombi and bile duct proliferation was not observed.

[STAINS used: H. & E., silver impregnation, W.H.V.G. Sudan III, Best carmine, P.A.S.].

Course and management: The patient had an uneventful course in hospital. Her normal blood pressure was 130/80 (cf admission).

Assessment of alcohol habits: Chronic alcoholic.
Assessment of nutrition: Poor nutrition (pellagra).

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

(3) Chronic alcoholic.

CASE 4/63

V. K. AFRICAN FEMALE, 34 years.

Admitted 16. 1. 63 at 8.30 p.m. Discharged 1. 2. 63.

OUT-PATIENT DEPARTMENT

There was a history of possible intake of ethyl alcohol by the patient. She was comatose and was admitted as ? post-alcoholic hypoglycaemia.

WARD

No history available.

Owing to the possibility of post-alcoholic hypoglycaemia, intravenous dextrose solution was administered after taking blood for special investigations.

TREATMENT

The patient was given 40 ml 50% intravenous dextrose solution. She recovered consciousness after 20 ml of dextrose.

Examination (after therapy).

Young healthy looking African female.
No anaemia, cyanosis or jaundice. No oedema and no lymphadenopathy. Not pyrexial.

C.V.S. Pulse 70 per minute, regular.
B.P. 130/90. J.V.P. = 0.
Heart sounds closed.

R/S N.A.D.

Abd. Soft abdomen.
Liver 1 fd, non-tender.
No hepatomegaly.
No free fluid.

C.N.S. Pupils equal and react to light.
Cranial nerves normal.
Fundi N.A.D.
Tone, power and reflexes: normal.
Sensation: normal.

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 34 mg%, Serum electrolytes; Na 143 meq/l, K. 4.0 meq/l, Cl 108 meq/l, bld urea 37 mg%, Hb 13.3g% (90%), P.C.V. 41 mms, M.C.H.C. 32%, E.S.R. 23 mms/hr, W.B.C. 7,000/cmm, P.I. 85%.

Diagnosis: Hypoglycaemia ? Post-alcoholic.

HISTORY FROM PATIENT

She had commenced drinking gavine with a friend at 7 a.m. in the morning. She had imbibed about three quarters of a pint when she had fallen asleep. She had awakened at about noon but she had felt weak. She had remembered nothing after that till she had reawakened in hospital. She had not eaten breakfast that day or anything on the previous day.

Alcohol habits: She stated she only drank Zulu beer on Sundays (cf gavine on admission). (She was an extremely difficult patient and probably imbibed much more than that).

Dietary habits:
Breakfast: Porridge.
Lunch: Samp or putu.
Supper: Samp or putu. Meat twice a week.

Social history: She did not work and she was not married. She had five children ranging from 13 years to five months old. They were from separate fathers. Her brother helped her with money.

Special interrogation: She had never had a similar episode before. She had never had a fit. She had not been taking herbs, tablets or injections before admission. She did not add toxic substances to her liquor.

SPECIAL INVESTIGATIONS

16. 1. 63 See Above.
17. 1. 63 Total serum protein 7.0g%, serum albumin 4.0g%, serum globulin 3.0g%, A:G ratio 1.3:1.
19. 1. 63 17-ketosteroids 0.2 mg/24 hours, total glucocorticoids 1.7 mg/24 hours, urine volume 1070 ml/24 hours.

24. 1. 63 ACTH Response test

Day of hospitalisation on which ACTH commenced	Type of urinary steroid	Unstimulated steroid excretion(mg/24 hrs)	ACTH Stimulation and aftermath(mg/24 hrs) Days:				
			1*	2*	3	4	5
9	17-oxo	1.7	3.3	25.5	2.3	3.7	1.1
	Total gluco	3.4	16.6	23.2	13.9	3.4	1.2
	Urine volume (ml/24 hrs)	1100	1170	960	1020	2100	1650

*Days on which ACTH given, ACTH gel 100 units I. M. b. d. (ACTH Batch No. 85, Fredericksberg, Copenhagen, Denmark).

31. 1. 63 Glucose tolerance test:
Fasting 80 mg%, ½ hr 140 mg%, 1 hr 160 mg%, 1½ hr 167 mg%, 2 hr 150 mg%, 2½ hr 114 mg%, 3 hr 87 mg%, 3½ hr 73 mg%, 4 hr 54 mg%.

Date	Day	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
16. 1. 63	1						85	
17. 1. 63	2	150	1.8	7				
18. 1. 63	3	128	0.9	9				
19. 1. 63	4	86	0.7	7	trace	Neg.		
20. 1. 63	5				trace	Neg.		
21. 1. 63	6	120	0.4	9	trace	Neg.		
22. 1. 63	7	144			Nil.	Neg.	93	done
25. 1. 63	10	12	0.5	9	Nil.	Neg.		

Liver biopsy: This was performed on 22. 1. 63. Section of liver showed a small focus with round cell and neutrophil infiltration (? focus of necrosis). Alcoholic hyalin was not observed. Severe fatty vacuolation was present (gr. 4). The portal triads showed occasional acute and chronic inflammatory cells. There was no increase in portal fibrous tissue (grp. 1). Haemosiderin was noted only in the Kuppfer cells (gr. 1). Glycogen was observed (gr. 1). No bile thrombi were seen and bile duct hyperplasia was not noted.

[STAINS used: H. & E., P.T.A.H., silver impregnation, W.H.V.G., Sudan III, Best carmine and Perl's prussian blue reaction].

Course and management:

The patient had an uneventful course in hospital. She was unco-operative and desired to be discharged.

Assessment of alcohol habits: Chronic alcoholic.

Assessment of nutrition: Fair nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) Alcoholic hepatitis.

CASE 5/63

B. M. AFRICAN FEMALE, 35 years

Admitted 16. 1. 63 at 9 a. m. Discharged 1. 2. 63.

OUT-PATIENT DEPARTMENT

She was brought to hospital by her boy-friend who could not awaken her. No other history was available. She was comatose and smelling of alcohol. Post-alcoholic hypoglycaemia was suspected and intravenous dextrose solution was administered after taking blood for special investigations.

TREATMENT

50 ml 50% intravenous dextrose solution was given. The patient did not awaken immediately and was sent to the ward.

WARD

The patient was conscious on arrival.

Examination (after therapy).

An African female smelling of alcohol.
Temperature 98°F.
No cyanosis, jaundice, oedema or lymphadenopathy.
? anaemic, ? rash of scabies over body.

C.V.S. Pulse 80 per minute, regular.
B.P. 120/70. J.V.P. = 0.
Ejection systolic murmur at the apex.

R/S Bronchial breathing and whispering pectoriloquy at left apex.
Vocal resonance and fremitus ↑ on L.
Rhonchi scattered throughout both lung fields.

Abd. Liver 2-3 fd, firm and non-tender.
No splenomegaly.

C.N.S. Cranial nerves intact.
No neck stiffness.
Pupils regular, equal and react to light.
Tone, power and deep tendon reflexes, normal.
Plantar reflexes ↓↓

IMMEDIATE SPECIAL INVESTIGATIONS

Bld sugar 18 mg%, hb 12.6g% (82%), P.C.V. 38(%), M.C.H.C. 33%, E.S.R. 31 mm/hr, W.B.C. 8,000/cmm.

Diagnosis: 1. Post-alcoholic hypoglycaemia.
2. ? left apical pulmonary tuberculosis.

HISTORY FROM PATIENT

She said she had taken a glassful of gavine and some shimeyane, with a friend, on the day before admission, at 11 a.m. At 6 p.m. she had imbibed a further half glass of gavine and had gone to bed. She had awakened in the morning at about 5 a.m. but had not felt well and she had gone back to bed. She reawakened in hospital. Her diet on the preceding days was not known.

Alcohol habits: She said she drank heavily in the weekends and usually on one occasion during the week. She drank gavine and shimeyane (She was an unreliable witness).

Dietary habits: Breakfast: Porridge and tea.
Lunch: Bread.
Supper: Putu or rice. Meat twice a week.

Social history: She did not work. She was not married and she lived with her boy friend who supported her. She had no children.

Special interrogation: She thought she had had a similar episode a year previously but she had not come to hospital and had recovered consciousness at home. She had no history of fits. She had not taken herbal medicines, tablets or injections. She did not add toxic substances to her liquor.

SPECIAL INVESTIGATIONS

16. 1. 63 See above.
Routine urine - N. A. D.
Total serum proteins 6. 7g%, S. albumin 3. 5g%, S. globulin 3. 2g%, A:G ratio 1. 1:1.

Chest X-ray: "The heart, trachea and the mediastinal contents are displaced towards the left side. There is a well marked fibrosis and infiltration in the left upper lobe with marked contraction of volume. There is compensatory emphysema of the left lower lobe, with a well marked oligaemia of the left lung field. The right lung was clear.
Conclusion : The appearances are compatible with chronic inactibe fibroid tuberculosis of the left upper lobe."

23. 1. 63 A. C. T. H. Response Test.

Day of hospitalisation on which ACTH commenced.	Type of urinary steroid	Unstimulated steroid excretion (mg/24 hours)	ACTH stimulation and aftermath (mg/24 hrs) Days 1*	2*	3	4	5
9	17-oxo	3. 1	6. 7	7. 1	4. 6	1. 8	0. 8
	Total gluco	1. 1	1. 5	12. 2	24. 2	9. 1	18. 1
	Urine volume (ml/24 hrs)	1450	1870	1890	2000	1600	2250

*Days on which ACTH given; ACTH I. M. gel 100 units b. d.
(ACTH Batch No. 85, Fredericksberg, Copenhagen, Denmark.)

30. 1. 63 Glucose tolerance test:

Fasting 70 mg%, ½ hour 117 mg%, 1 hour 128 mg%,
1½ hour 111 mg%, 2 hour 83mg%, 2½ hour 117 mg%,
3 hour 100 mg%, 3½ hour 72 mg%, 4 hour 94 mg%.

Date	Days	T	B	A. P.	U	U. B.	P. I.	Liver biopsy
16. 1. 63	1	110	0. 9	5				
18. 1. 63	3	50	0. 3	7				
19. 1. 63	4	70	0. 4	6	Nil.	Neg.		
21. 1. 63	6	48	0. 4	5				
22. 1. 63	7	74	0. 3	5	Nil.	Neg.	100	Done
25. 1. 63	10	24	0. 5	9				

Liver biopsy: This was performed on 22. 1. 63. Section of liver showed small foci of necrosis with acute and chronic inflammatory cell infiltration. Alcoholic hyalin was not observed. Fatty vacuoles were not noted but fine intercellular fatty change was severe. The portal triads showed acute and chronic inflammatory cells and there was no increase in portal fibrous tissue. (gr. I). Haemosiderin was present throughout the liver lobules (gr. 3) and glycogen was observed (gr. 3). Bile thrombi were not seen and there was no bile duct hyperplasia.

[STAINS used: H. & E, silver impregnation, W. H. V. G. prussian blue reaction and Best carmine].

Course and management:

The patient had an uneventful course in hospital.

Assessment of alcohol habits:

? Chronic alcoholic.

Assessment of nutrition:

Poor nutrition.

FINAL DIAGNOSIS

(1) Post-alcoholic hypoglycaemia.

(2) ? Alcoholic hepatitis.

ADRENAL AND PITUITARY STATUS OF PATIENT

Personal care to exclude clinical pituitary or adrenal disease was undertaken from Case 6/61. In none of the previous cases had it been observed by me or the medical staff in charge of the patients. Subsequently in only one patient, Case 15/62, was any clinical endocrine disease diagnosed. This patient had Addison's disease.

LABORATORY METHODS

BIOCHEMICAL METHODS

The specimens were collected by myself. Clotted blood was centrifuged and separated immediately. If haemolysis was noted the specimen was recollected.

Blood sugar:

The specimen of blood for glucose estimation was collected into a sodium fluoride anticoagulant. Blood glucose ("true" blood sugar) was estimated by a colorimetric method. The proteins were precipitated by sodium tungstate and copper sulphate, and the cuprous oxide was estimated by the blue colour produced with a phosphomolybdi c acid solution. (Folin and Wu, 1920; King and Wooton, 1956). A blood sugar below 51 mg% (Folin and Wu) was considered compatible with hypoglycaemia.

Serum total bilirubin:

The blood for serum bilirubin estimation was centrifuged immediately to remove all blood cells. A standard laboratory method (King and Wooton, 1956) was used. The serum was treated with diazotised sulphanilic acid, with the addition of ammonium sulphate and ethyl alcohol to precipitate the protein and the colour produced compared colorimetrically

against methyl red. (Normal 0.2 - 0.8 mg%).

Alkaline phosphatase :

The alkaline phosphatase activity of cell-free serum was estimated by a standard laboratory method, (King and Wooton, 1956), by determination of the liberated phenol with Folin and Ciocalteu's phenol reagent. The phosphatase activity was expressed as King-Armstrong units per 100 ml. (Normal 3-12 K.A. units, Children 10-20 K.A. units).

Serum glutamic oxaloacetic-acid-transaminase (S.G.O.T.)

activity was estimated by Hergt and Langins' (1957) simplified modification of the original method of Karmen et al., (1955). All blood specimens were centrifuged immediately and retaken if there was any trace of haemolysis. The measurements were carried out in an air-conditioned room at 23°C (± 1°C). No temperature corrections were made. (Normal 7-40 Karmen units).

Urinary bilirubin :

This test was done by a standard laboratory procedure using Fouchet's reagent. The blue or green colour obtained on filter paper was reported as negative, trace, +, ++, or +++.

Urinary urobilin:

This was done by the zinc test with Schlesinger's reagent. A green fluorescence becomes apparent where urobilin or urobilinogen is present. It was reported as nil (not increased), trace, +, ++ or +++.

Blood alcohol:

Blood alcohol, measured as volatile reducing substances (V.R.S.), was determined by the method of Bowden and McCallum (1949) (Normal 0-20 mg%).

Serum proteins were estimated by a modified biuret reaction as described by Weichselbaum (1946). Serum electrophoresis was done by the method of Joubert et al., (1959).

Serum amylase:

This was done by Wohlgemuth's method (Harrison, 1957) (Normal 3-10 Wohlgemuth units per ml).

Serum electrolytes:

Serum sodium and potassium were estimated by standard flame photometry. Serum chloride was estimated by a mercurimetric method of Schales and Schales (Harrison, 1957).

Blood Urea :

This was performed by standard laboratory method (King and Wootton, 1956).

Urinary 17-oxosteroid excretion (17-ketosteroids) was performed by Joubert's (1960) modification of the method of Holtorff and Koch (1940) and total urinary glucocorticoid excretion by the method of Moxham and Nabarro (1956). Accurate 24-hour specimens were collected as soon as possible following admission.

The Prothrombin index was done by Quick's method (Dacie, 1956).

HAEMATOLOGICAL METHODS

Standard methods as described by Dacie (1956) were used.

HISTOLOGICAL METHODS

Standard staining techniques were used. (Pearse, 1953).

Phosphotungstic acid haematoxylin (P. T. A. H.) was stained by the method of Edwards and Mallory (1949).

[Staining was done at the histopathology departments of Natal University Medical School, Durban, and the Radcliffe Infirmary, Oxford, England.]

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