

THE COMPLICATIONS OF ALCOHOLISM

An Epidemiological, Statistical and Nutritional Study
On Alcoholics Admitted to a General Hospital Psychiatric Unit.

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"Eau-de-vie; eau-de-mort, si elle fait vivre ceux qui la vendant, elle tue ceux qui la boivent".

(Water of life; water of death, if she gives life to those who sell her, she gives death to those who drink".)

17th Century.

".... The patient already knows, as well as the priest and moralist, that the indulgence is pernicious, and ultimately fatal: he is also aware, without the reasonings of medicine, that the constant repetition will destroy health;...."

".... When ebriety has become so far habitual that some disease appears in consequence, the physician is for the first time called in, and a task the most ungrateful devolves upon him...."

Thomas Trotter. 1804

An essay, medical, philosophical, and chemical, on drunkenness, and its effects on the human body. London, Longman & Rees.

"....A drunkards mind and stomach are alike, neither can retain what they receive; deep drinkers have shallow memories....."

Richard Younge.

The Drunkards Character.

London, 1638.

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SUMMARY

- 1) A study of alcoholics admitted to a general hospital psychiatric unit over a period of 4 years (527 males and 148 females) is presented. The various demographic, social and drinking characteristics are given and the male and female alcoholics are compared. The complications and associated physical conditions were studied epidemiologically and with special reference to blood vitamin levels in an attempt to elucidate their aetiology. A follow-up study was carried out to find the causes of death in these patients and at the same time the prognosis studied to ascertain its relationship to these complications.
- 2) There were more alcoholics in social classes I, II and V and in the widowed and divorced. The age pattern of alcoholics was similar to other studies with an almost normal distribution curve around the mean of 43.7 years in males and 45.4 years in females. The religion of the patients was similar to that of the surrounding area.
- 3) Over half of the alcoholics were admitted as emergencies; a quarter did not finish the course of in-patient treatment and one-fifth of the total were re-admitted during the four year period.
- 4) Whisky was the preferred drink among male alcoholics and "fortified wine" among females. The former had been drinking for considerably longer than the latter (a mean of 16.2 years compared to 9.9 years) and they drank, on average, much more,
(the/

(the equivalent of a bottle of whisky a day compared to the equivalent of a bottle of sherry per day).

5) A quarter of all the patients were given an associated psychiatric diagnosis of which most were in the personality disorder group.

6) There was a large incidence of behavioural disturbance, so that only one-third of men, but two-thirds of women, had no previous convictions. However more women (33%) than men (18%) had previous suicide attempts and more abused drugs than men (25% compared to 11%).

7) Male and female alcoholics were shown to have a number of differences especially in drinking habits noted above.

Female alcoholics were older, and they were admitted via other hospital wards or by Alcoholics Anonymous. They stayed longer in hospital and were admitted more frequently. They had more spouses who were alcoholic than males. They showed more evidence of malnutrition in the form of weight loss and clinical signs of nutritional disease and they had a higher incidence of alcoholic dementia and of the "rare" neuro-psychiatric disorders. They had a lower incidence of alcoholic epilepsy, delirium tremens, alcoholic hallucinosis and E.E.G. abnormalities, as well as hepatitis and previous gastric operations, but similar incidences of cirrhosis, neuropathy and anaemia.

8) Only 18% of patients had no associated physical condition. Almost one-fifth of the patients had each of the following, anaemia, peripheral neuropathy, gastritis, hepatitis, severe withdrawal signs and E.C.G. abnormalities and one-tenth had cirrhosis. These results are very similar to other studies despite differences/

differences in drinking habits and social class. There were only 8 patients who had had previous venereal disease and 4 who had previous pancreatic disease.

9) There was no objective evidence of withdrawal in 40% of the patients, on the other hand 20% had severe effects including delirium tremens. Alcoholics with delirium tremens tended to have associated cirrhosis, anaemia, peripheral neuropathy and epilepsy, as well as abnormal levels of whole blood thiamine and serum folate.

More female patients had alcoholic dementia which was related to increased age, increased length of excess drinking and peripheral neuropathy as well as subnormal whole blood thiamine and nicotinic acid levels.

Alcoholic epilepsy was associated with delirium tremens and with drug abuse, abnormal levels of S.G.O.T., S.G.P.T., serum proteins, whole blood thiamine and serum folate levels.

Alcoholic hallucinosis was associated only with paranoid psychosis though there were more patients in this group with raised S.G.O.T. levels and low whole blood thiamine levels.

Thus the alcoholic psychoses as a whole appear to have a relationship to nutritional factors.

10) Peripheral neuropathy was associated with delirium tremens, cirrhosis and dementia. Food intake was poorer in these patients and on admission they had more evidence of weight loss. Whole blood thiamine levels were low in 70% of the patients and there was an increase of abnormal protein levels. These findings confirm that nutritional factors are of importance in the condition, but there was also a relationship with the increased daily amount of alcohol./

alcohol, especially of fortified wine, and with the length of time of excess alcohol intake .

11) Whereas cirrhosis was related to delirium tremens, peripheral neuropathy, alcoholic cardiomyopathy and E.C.G. abnormalities, acute liver disease was related to another physical condition. Similarly an increased number of cirrhotics had abnormal whole blood thiamine levels which were not found in patients with acute liver disease. Patients with cirrhosis were older and had been drinking for longer than other alcoholic patients.

12) Gastritis, diagnosed on clinical grounds, was found in 17% of these alcoholics, was only related in male patients to various behavioural abnormalities. Most patients with gastric operations, found in 11% of male alcoholics and 4.5% of female alcoholics had their operations years after the start of heavy drinking. There was evidence of an increased incidence of peptic ulceration in these alcoholics.

13) Alcoholic cardiomyopathy was present in only nine male alcoholics, all of whom had been drinking to excess for over 20 years and had a heavy daily intake of alcohol. However 113 patients were shown to have E.C.G. abnormalities usually of a minor degree.

14) Anaemia was found in one-fifth of the patients, but was varied in nature, though in two-thirds of female alcoholics and a half of male alcoholics it was iron deficient in type.

It was associated with increased alcohol intake, especially "crude spirits". Nutritional factors were important and there was an association with cirrhosis and delirium tremens.

15) Female alcoholics were shown to have more evidence of nutritional deficiencies on most of the parameters utilised than/

than male alcoholics. It would seem that nutritional deficiency is important in delirium tremens, alcoholic dementia, alcoholic epilepsy, cirrhosis and peripheral neuropathy.

16) The average length of follow-up was four years, 10% of patients were untraced. Twenty-five per cent of patients were found to be improved, 20% worsened and 10% had died. The indicators of good prognosis were those in social classes I and II compared to social class V, decreased length of drinking and absence of behavioural abnormalities. Female patients did no better than male patients.

17) Male patients died mainly from cirrhosis, cardiovascular or respiratory disorders, including carcinoma of the bronchus, whereas females were much more likely to commit suicide.

18) There were many associated physical and behavioural abnormalities in this group of alcoholic in-patients. No clear pattern as to exact aetiology of the different conditions emerged though nutritional factors appear to play a part in the conditions which are classically considered to be the "complications" of alcoholism.

INTRODUCTION

Alcoholism is a world wide medical problem as judged from statistics issued by the World Health Organisation, by attendances at International Conferences on the subject and by papers which originate from most of the countries of the world. Scotland would appear to be in the middle range of the thirty countries ranked by the World Health Organisation in order of incidence. This figure is estimated using Jellinek's formula which uses the number of deaths from cirrhosis of the liver as a means of calculating the incidence of alcoholism, but this formula was rejected by the Scottish Home and Health Department's Report (1965) "Alcoholics - Health Services for their Treatment and Rehabilitation", which suggested that it had produced a false incidence in Scotland. However there are suggestions from hospital admission rates that Scotland has a higher incidence of alcoholism than England and Morrison (1964) concluded that these rates did indicate a true higher prevalence. First admission rates are seven times as high for men in Scotland compared to England and Wales and the Scottish death rate from alcoholism in 1969 was four times the rate for England and Wales. Thus it is not surprising that there have been significant contributions to the literature from every region of Scotland during the last decade, notably Kessel and Walton's book on the subject, but also Smith and Sclare (1964), Morrison (1964), Vallance (1965), Walton et al (1966), Pemberton (1967), Freeman and Hopwood (1968), Ritson (1968), McCance and McCance (1969)/

(1969) and Whittet (1970).

Purely from a logistic point of view the problem in Glasgow and the West of Scotland would appear to be a greater one than Scotland as a whole. However, with few notable exceptions, there have been few studies on the subject from the area, perhaps the sheer size of the problem has made it seem too overwhelming to make scientific study possible. The exceptions are those by Sclare, who has written two articles on the subject, firstly with Smith (1964) in the study of the characteristics of 100 male alcoholics admitted to the Eastern District Hospital Psychiatric Unit and then in 1970 he compared 50 female alcoholics admitted to the same unit with 50 male alcoholics. Vallance (1965) published a follow-up study on 68 male alcoholics admitted during the year 1960 to the Southern General Hospital Psychiatric Unit. Apart from these the only other contributions from the West of Scotland have been from the Crichton Royal Hospital which admits patients from a very wide area, including England.

The present study which is a detailed one of the complications of alcoholism has not previously been attempted in Scotland. It is important in view of the numbers of patients involved and their use of psychiatric, medical, surgical and other services, but there are implications for not only the individual complication but also from the more general one of where the alcoholic should be treated when considering the present trend towards more social and less medical use of treatment facilities for alcoholics, such as hostels and self-aid centres.

To obtain an overall picture of the complications of alcoholism the study was made on a large consecutive series of patients with alcoholism/

alcoholism admitted to a general hospital psychiatric unit in Glasgow, so that the series could be compared on basic epidemiological data with those of the other studies from Scotland and also some from England, as well as comparing the studies on the complications which have come from other parts of the world.

A further aim was to inter-relate the various complications and to relate them to blood levels of B complex vitamins in an attempt to elucidate more clearly the aetiology of some of the complications.

Finally a follow-up was carried out to assess both the cause of death and the prognosis in relation to the various complications.

REVIEW OF THE LITERATURE

1. HISTORICAL

The complications of alcoholism have been known virtually since the vine was cultivated. In the Book of Genesis, Noah is shown in drunken stupor with later remorse culminating in dramatic historical repercussions. In the Greek literature "madness" and violence are well illustrated in the Dionysian Rites. The first clinical account of one of the complications is probably that of Hippocrates who described the features of what is now called delirium tremens when he noted " - - - acute fever, trembling of the head particularly of the lower lip, after a while convulsions, complete delirium ...". In one Laerian he also wrote "If the patient be in the prime of life and if from drinking he has trembling hands, it may be well to announce beforehand either delirium or convulsion". It was not until the end of the 18th century, and being of the 19th, that further descriptions of delirium tremens were forthcoming. In 1813 Thomas Sutton coined the name delirium tremens and gave a good clinical description, but Romano (1941) points out that Lettsom had in 1787 given an equally good one. "It is preceded by tremors of the hands, restlessness, irregularity of thought, deficiency of memory, anxiety to be in company, dreadful nocturnal dreams, when the quantity of liquor through the day has been insufficient; - - - ". Ware writing in 1841, emphasised that the syndrome usually lasted from 60 to 72 hours and terminated spontaneously/

spontaneously in either death or recovery (cited by Cutshall, 1965).

Since Vesalius in the 16th century described "atrophy of the liver" in excessive imbibers of alcohol, other writers through the centuries have confirmed this connection, for example, Hart (1633), Johnston (1820) all quoted by Ratnoff and Patek (1942). Baillie in 1795 from the U.S.A. wrote "... we cannot see any necessary connection between that mode of life (inebriety) and this particular disease of the liver". Yeld (1898) reported on 195 cirrhotics and found that 31% were related to alcohol.

Peripheral neuropathy as a result of alcohol was described by Lettsom (1785) in his paper "Some Remarks on the Effects of Lignum Quassiae Amarae" and by Jackson (1822) in "A peculiar disease resulting from the use of ardent spirits". Their descriptions were of the severe late effects of the condition, none the less they were so graphic as still to be informative.

A century ago it was suggested that excess alcohol intake can have a deleterious effect on the heart. The term "cirrhosis of the heart" was coined by Walshe in 1873 to describe these effects and Bollinger (1888) called it "Muncheu Bierherz". McKenzie (1902) however first used the term "alcoholic heart disease", the term which has only recently been replaced by alcoholic cardiomyopathy.

The more specific neurological syndromes recognised as related to alcoholism were described in the latter part of the 19th century in the greatest detail. Wernicke in 1881 and Korsakoff in 1887 wrote accounts of the conditions which still use their eponymous names to describe them. Other writers had made earlier much less complete accounts of these two conditions. It was noted in/

in 1868 by Wilks that heavy brandy and absinth drinkers could develop locomotor ataxia. In 1903 Marchiafava and Bignami described the rare and apparently fatal condition in Italian peasants who drank excess quantities of red wine which to this day bears their name.

The acute effect of alcohol on the stomach producing "acute gastritis" was clearly noted by Beaumont in his famous study of 1833 when he found "erythema and abscess patches" in the stomach of Alexis St. Martin following an alcoholic debauch. In 1855 Bamberger attributed chronic gastritis to alcoholism. Friedreich in 1878 was the first to notice the relationship between pancreatitis and excess alcohol intake, "a general chronic interstitial pancreatitis may result from excessive alcoholism (drunkards pancreas)".

Even the higher incidence of suicide in alcoholics had been noted by Sullivan in 1900, and the connection with crime has been well documented mainly from a moralistic point of view throughout the centuries. One judge a hundred years ago is reputed to have said "Every crime is directly or indirectly connected with whisky".

Recently even further complications have been described. Hed et al in 1955 showed that excess alcohol intake can have a serious effect on peripheral muscles and called the condition alcoholic myopathy and in 1969 Mullin et al showed that some alcoholics develop choreiform movements mainly of a transitory nature which are apparently related to chronic alcoholism. It is also becoming increasingly clear that there are many biochemical abnormalities precipitated by abuse of alcohol. Hypoglycaemia following acute alcoholic excess in the chronic alcoholic was first/

first described by Brown and Harvey in 1941. In 1958 Zieve described the syndrome of transient hyperlipaemia, jaundice and haemolytic anaemia which now bears his name.

Although the complications of alcoholism are still being delineated, it is unlikely that the social and more obvious medical ones will ever be more accurately depicted than the illustration by Hogarth of "Gin Lane" published as a moralistic tract almost two hundred years ago.

2.2. Delirium Tremens and the Alcohol Withdrawal Symptoms

Since the early descriptions of delirium tremens by Lettson, Sutton and others over one hundred and fifty years ago, there has been little published on the condition in the United Kingdom until recently; and although there has been interest and many published papers from the United States of America and from the Continent, Cutshall was able to write in 1965 "the general approach to delirium tremens has gone through a dark age of more than a hundred years". While he was referring specifically to treatment, there has been some clarification of the condition. At the turn of the century Kraepelin, Wernicke and Bonhoeffer described alcoholic hallucinosis and distinguished this condition from delirium tremens. Recently (Victor and Adams, 1953 and Isbell et al, 1955) there have been clinical and experimental studies attempting to clarify the condition. In the past thirty years there have been excellent reviews on the subjects Bowman and Jellinek, 1941, Victor and Adams, 1953, Cutshall, 1965 from the U.S.A. and Lundquist, 1961 and Nielson, 1965 from Scandinavia. Bowman and Jellinek described the clinical features and course of the condition from all the papers published to the late 1930's.

Victor/

Victor and Adams laid stress on the genesis of the symptoms in their paper which presented extremely careful data on 153 patients during the period of alcohol withdrawal. They conclude that there is "a continuum of symptoms which tend to occur in a sequence of tremulousness, fits, hallucinosis and delirium following alcohol withdrawal". Both Cutshall and Nielson tended to be as interested in the effects of treatment as well as producing their own clinical data, so that they give many references to the comparison of various methods of treatment.

The rather complaisant attitude to delirium tremens in the United Kingdom which has prevailed until recently, in effect has reflected the attitude to alcoholism and which in turn reflects the general decline in alcoholism from the turn of the century in England and Wales until its recent emergence again. This is well illustrated in an annotation in The Lancet in 1958 which stated that "little is known of the pathogenesis of delirium tremens", and which suggested that previous mental illness suppressed by alcohol is released when the alcohol is withdrawn. This ignored the two most important papers on the aetiology of the condition which had by then been published. Victor and Adams excellent clinical study already quoted and the most important paper by Isbell and his colleagues from the N.I.M.H. Addiction Research Centre at Lexington; "An Experimental Study of the Aetiology of "Rum Fits" and Delirium Tremens". They give large amounts of alcohol to 10 volunteers, all former morphine addicts, for up to 87 days following which the alcohol was abruptly withdrawn. The results of the experiment are given in detail both when the subjects were drinking and during withdrawal.

All/

All the volunteers were given a good diet during the period on alcohol and before received oral and intramuscular injections of vitamins, the oral vitamins being continued while they received alcohol. Three of the subjects stopped drinking in less than a month. They had tremor, weakness and perspiration for one day after withdrawal. One who discontinued drinking after 34 days had mild symptoms for three days. The other six, who continued to drink for up to 87 days, showed marked symptoms; convulsions occurred in two; hallucinations with insight and clear sensorium were observed in two; and frank delirium occurred in two. These experiments demonstrated most of the clinical symptoms attributed by Victor and Adams to alcohol withdrawal.

These classic papers, clearly show that alcohol withdrawal is of prime importance in inducing a definite abstinence syndrome, including convulsions and delirium. Both had contradicted previous ideas on the subject prevalent in the United States of America at that time. It is well known that some patients apparently develop delirium tremens while still drinking and Piker on questioning 275 patients who had experienced delirium tremens found this to be the case in 75% (1937). Victor considers that even the relative reduction in alcohol intake that occurs overnight is sufficient to induce withdrawal symptoms in an alcoholic whose brain has become accustomed to large amounts of alcohol. He then slightly reduced their intakes further and gradually they developed more and more withdrawal signs.

Armstrong and Gould (1955) in one of the few papers from this country followed up Gould's hypothesis based on work from the United States concerning treatment of various psychiatric disorders with/

with vitamins (Spies and De Wolf, 1933, Rosenbaum and Merritt, 1938, Jolliffe, Wortis and Stein, 1941, and Sydenstricker and Cleckley, 1941,) that delirium tremens was due to vitamin deficiency and had given massive doses of Vitamin B and C in the condition. Gould summarised his ideas on delirium tremens and "other toxic infective deliria" in 1959 considering that all of these were due to abnormality of the carbohydrate metabolism of the brain brought about by vitamin deficiency which could become acute at times of increased metabolism, such as infection or rise in temperature. His papers induced a vogue for giving large dose parenteral vitamins in most delirious states which still continues despite no control trial to show its efficacy. Kershaw (1967) demonstrated that with increased signs of alcohol withdrawal there was increased evidence of thiamine deficiency as measured by whole blood thiamine using a microbiological assay technique. Morgan (1968) in a comparative study of alcoholic patients with and without hallucinosis concluded that typical delirium tremens may occur in the absence of dietary and biochemical evidence of thiamine deficiency and thus is likely to be due to sudden alcohol withdrawal in the habituated individual.

Most neuropathological studies show no specific changes in the brain of patients who die during an attack of delirium tremens, though Courville and Myers (1954) considered they had satisfactorily demonstrated the specific changes in all varieties of alcoholic neurological disease as well as in delirium tremens. This work has not been confirmed.

Leevy et al, 1953, performed liver biopsy on 66 patients with delirium/

delirium tremens and found that changes varied from a normal liver structure in 19 (29%), focal inflammation in 4 (6%), fatty infiltration in 20 (31%) and portal cirrhosis in 23 (35%). In 1958, Davidson and Solomon pointed out how difficult it could be to differentiate delirium tremens from impending hepatic coma, but how important this was in practice. They noted differences in the tremor, which is fine in delirium tremens but flapping in pre-hepatic coma; the speech is rapid in the former and slow in the latter; sleep and appetite are normal in hepatic encephalopathy, all of which can be used in diagnosis.

Lundquist (1961) has given a very complete survey of 74 patients with delirium tremens comparing them with a similar group of alcoholics without delirium. He found that there was a longer drinking history, fewer personality abnormalities, more raised levels of S.G.O.T. in the blood and there were many more deaths in the following three years, in those patients who had delirium tremens. He found no difference in either occupation or social background of these patients however. Whereas Faris and Dunham in their famous book "Mental Disorders in Urban Areas", comment on the social class distribution of patients with "alcoholic psychosis", finding that those with these disorders tend to be found in the lower social classes. Other workers in the United States of America have continued to produce figures relating to social class and environment to these complications of alcoholism. One of the more recent being from Rosenblatt et al, 1971, from Brooklyn who showed that the most severe withdrawal syndromes came from the area of the city with the least residential stability, highest unemployment, poorest education, low income and over-crowding, though in fact these/

these patients tended to have a slightly higher educational level than the rest of the populace. Thus Rosenblatt's work tends to confirm the "drift hypothesis" in alcoholism.

Most of the other reports concern the treatment of delirium, mainly by comparing one form of drug treatment with another. It is very difficult to compare these reports because of the number of drugs used, some use different phenothiazines, others compare minor tranquillisers with a placebo and others use a variety of drugs such as Chloral Hydrate, Paraldehyde or protein supplementation. In summary, it seems that it is necessary to treat individual symptoms with different drugs, but as it is dangerous to over-sedate in delirium and many of the sedatives have little extra value over a placebo, it is better to use careful nursing, rehydration and good nutrition without the use of sedative drugs as in fact was advocated by Magnon over a century ago, as cited by Cutshall. Gross (1967) considers the safest sedative drug in delirium tremens is Paraldehyde.

Animal studies have not proved very satisfactory as a means of studying delirium tremens, but recently Essig and Lam have reported on feeding ethanol to beagles by means of a gastric cannula, 1968. Of the 12 dogs in the initial interview, 4 died between the 10th and 39th days of chronic intoxication. In the other 8 the alcohol was withdrawn after 54 days of intoxication, 5 dogs developed convulsions within 11 and 48 hours, other abstinence signs were noted and one dog was apparently hallucinated. They suggested that this canine model could be useful to assay the effectiveness of drugs in treatment of delirium tremens. Gross and his many co-workers have/

have written recently on the hallucinosis found in alcoholic psychoses, (Gross et al, 1963, 1967, 1971 a and b). These workers seem to find that most patients fit into neither a classical picture of alcoholic hallucinosis, nor delirium tremens, so that they place 54.4% of their patients with alcoholic psychoses in a group labelled "mixed state". They have suggested a dual continuum of clouding of the sensorium and intensity of the hallucinatory experience so that patients may be placed in both these categories. They consider that in severe cases both disturbances are present, whereas in the mildest there is neither. They have described the clinical rating scale for symptoms in "acute" alcoholic psychoses, for example, hallucinations, nausea and vomiting, muscle pain, tinnitus, depression etc., to a total of 19 items each with a seven point score. They consider that this is an improvement on the previously quoted two, three or four grades of severity for the alcoholic withdrawal states.

2.3. Alcoholic Epilepsy

Although Hippocrates mentioned convulsions as a complication of alcohol excess, similar statements being made in the writings of the last century, there have been few precise studies until relatively recently. Lennox (1941) studied the effect of alcohol on 1, 254 patients with epilepsy over the age of 15 years. He found that 26% of these used alcohol moderately and 6% to excess - figures no greater than a control group. However alcohol was a factor in producing actual seizures, in only 6% of all patients but in 21% of those who used alcohol. It is interesting to note that Gunn has recently shown that alcohol does not play a significant part in the epilepsy that is found in an English prison population, Gunn (1972).

In 1942 Kalinowsky described two non-epileptic patients who developed seizures between 15 and 48 hours after cessation of alcohol. One of the patients developed delirium tremens following his last seizure. He points out that this epileptic phenomenon only occurred after prolonged consumption of alcohol and did not occur after acute intoxication and he compared these seizures to those in a series of barbiturate addicts following withdrawal of the drug. Walsh (1962) described two patients who developed Korsakoff's Psychosis after having alcohol withdrawal seizures. He suggested that the fits had resulted in utilisation of excess energy and caused a sudden B vitamin deficiency which had thus precipitated this psychosis.

Two of the volunteers, who were given continuous excess alcohol by Isbell in his experiments mentioned previously, developed grand mal convulsions. One of the volunteers had one seizure after 48 days drinking and 41 hours abstinence. The other developed seven seizures after 12 hours withdrawal and 78 days drinking.

Victor has reviewed the literature and given the results of a careful study on 241 alcoholic patients who either presented with seizures, or with other complications and then developed seizures, (Victor, 1968). All patients had grand mal type epilepsy except 12 who had focal epilepsy. Alcoholic epilepsy appeared to be rare before the age of 25 years. Only 8 patients had this condition before this age and these were all patients with idiopathic or post-traumatic epilepsy who had well documented fits before they began to drink. 41.5% of patients had only a single seizure, 55.2% had multiple seizures and 8 patients developed status epilepticus of whom 4 had focal seizures. Electro-encephalograms were normal
in/

in 103 of the 130 patients undertaken. Delirium tremens followed in 75 patients (31%). He considered this degree of abnormal E.E.G. was comparable with a similar large series of alcoholic patients without epilepsy and also with a normal adult male population, whereas he quotes that E.E.G. abnormalities occur in 50% to 75% of patients with idiopathic epilepsy. Some of his patients developed fits after receiving large doses of B vitamins, and as already commented Isbells's volunteers were receiving supplementary vitamins as well as a good diet. He thus refutes the previous suggestion that either pellagra or pyridoxine deficiency could be of aetiological significance in alcoholic epilepsy. Lerner et al, (1958), had demonstrated evidence of Vitamin B6 deficiency in 3 of 5 patients with alcoholic epilepsy by studying tests of tryptophan loading and xanthurenic acid excretion. Victor performed tests of photic stimulation on 44 alcoholic patients with spontaneous seizures, 40 alcoholic patients without epilepsy but with various withdrawal symptoms and 50 non-alcoholic patients with idiopathic epilepsy. In the alcoholics 35 of the 84 showed an abnormal response, and a close relationship was shown to exist between spontaneous seizures and an abnormal photic response. Only 1 of the 50 non-alcoholic patients with idiopathic epilepsy showed an abnormal response. He gave intravenous magnesium to some patients and abolished the abnormal photic responses immediately, though this did not stop the development of delirium tremens. He suggested that it was possible that two factors are involved in the alcohol withdrawal syndrome. One in the earlier phase characterised by occurrence of seizures and an abnormal photic stimulation response perhaps related to a low serum magnesium. Secondly a later phase accompanied by delirium tremens and independent/

independent of hypomagnesaemia. He discusses the various possibilities relating alcoholism and epilepsy; from the suggestion that alcohol only acts as a precipitant in people who have a lowered seizure threshold to secondary causes such as trauma, pellagra, pyridoxine deficiency, shifts in plasma volume, cerebral oedema, hepatic disease, diffuse cerebral atrophy and magnesium deficiency. He concludes that the most important factor in the genesis of alcoholic epilepsy is the withdrawal of alcohol after a period of chronic abuse.

2.4. Alcoholic Hallucinosiis

Although withdrawal of alcohol after a long period of abuse has been implicated especially in delirium tremens and by recent workers in alcoholic epilepsy, there is still debate as to its role in alcoholic hallucinosiis. Bleuler, who coined the name, considered that besides the alcoholism a longstanding schizophrenia was present; whereas Kraepelin believed that the auditory hallucinosiis of alcoholism was related to delirium tremens. Since then many continental workers have written on the subject. Bonhoeffer (1901) and others follow the view that it is independent of schizophrenia. Benedetti (1952) also agrees with this hypothesis, but pointed out how difficult it was to differentiate patients with alcoholic hallucinosiis and delirium tremens, as have Bowman and Jellinek (1941) and Gross and his colleagues already mentioned. Others stress the underlying constitution, Schneider (1928) considered this was manic-depressive in type; Kretschmer believed it to be schizoid. The writers of textbooks have rather surprisingly tended to take the view held by Bleuler.

In/

In the last few years however further work has been published suggesting other setiological factors. Victor and Hope (1958) reported in great detail on 76 patients with alcoholic hallucinations in a clear sensorium. They had already noted a frequency of 6% of alcoholic hallucinosis and almost 5% hallucinations with delirium in 266 alcoholics. When they studied the 76 patients with the alcoholic hallucinosis they discovered that 68 were benign and transient, 8 persisted for weeks or months and of these 4 were latterly indistinguishable from schizophrenia. In only 15 of the episodes was the alcoholic continuing to drink and they concluded that abstinence played a major part in many patients who suffer from alcoholic hallucinosis. In the few patients in whom the condition became chronic they were unable to isolate any factors involved, though they did not consider that this condition was due to latent schizophrenia.

Scott (1967) investigated 32 cases of alcoholic hallucinosis treated at the Maudsley Hospital in a 12-year period and compared them with matched groups of chronic alcoholics without psychosis and of those with delirium tremens. He found no evidence of an excess of schizophrenia in the close relatives of any of the groups who corresponded roughly with that in the general population. One finding was that while patients with alcoholic hallucinosis preferred beer and those with delirium tremens preferred spirits, the actual consumption of beer was still greater in the latter group. Pollock (1940) in an epidemiological study noted the high proportion of beer drinkers in the alcoholic hallucinosis group. Kraepelin had also suggested that those with alcoholic hallucinosis drink less and tend to drink lower proof alcoholic beverages than those with delirium tremens.

Morgan (1968)/

Morgan (1968) studied 17 chronic alcoholics during the week after withdrawal of alcohol using clinical and metabolic methods. Of the 9 patients who had been drinking continuously for 6 months or more before admission, 8 developed hallucinations and 3 delirium, truncal ataxia was present in 7 of the 9 and limb tremor occurred on average for 4 days after admission. Whereas of the 8 patients who had been drinking for less than 6 months, none had hallucinations, delirium or truncal ataxia and the average length of limb tremor was only 2 days. Using this evidence and by performing the pyruvate tolerance as a measure of thiamine deficiency, he concluded that alcoholic hallucinosis might be related to deficiency of thiamine in patients who continued to drink, whereas abstinence alone could precipitate delirium tremens. There was thus no single explanation for the aetiology of the hallucinatory states complicating alcoholism. Blackstock et al, 1972, have reported on a series of alcoholic patients with and without hallucinosis. They used both the red cell transketolase activity and the pyruvate tolerance tests as measures of thiamine deficiency in these groups, finding no significant difference between the two and thus not supporting Morgan's contention concerning this vitamin in alcoholic hallucinosis.

Bowman and Jellinek stated in 1941 "in view of the somewhat obscure status of the present knowledge of acute alcoholic hallucinosis, it would seem that further research is indicated". Thirty years later, the position seems even more clouded.

2.5. Alcoholic Paranoia

This condition has attracted little recent attention. The textbooks/

textbooks of psychiatry are especially vague. Henderson and Gillespie state "— probably a misnomer - alcoholism being in these cases a symptom, not the cause, of an underlying schizophrenic or paranoid predisposition". Myre Sim says "this is rarely an extension of the acute hallucinosis and is mainly evidence of an underlying paranoid state. With subsequent organic mental deterioration the picture becomes adulterated".

Shepherd (1961) described the part that alcohol plays in the development of the "morbid jealousy syndrome", where there is excessive suspicion directed against the spouse. It is easy to see how this can develop as a progression of certain personality traits in association with increasing impotence in the alcoholic and simultaneous decreasing affection of the alcoholic's wife as a result of his habits.

There is also the paranoid state which can develop in relation to alcoholic hallucinosis. Benedetti (1952) analysed 113 cases of alcoholic hallucinosis of whom 90 recovered within 6 months. The other 23 he termed "chronic", 13 became schizophrenic and 10 developed organic dementia. In Victor and Hope's series already mentioned, the 8 patients with persistent hallucinosis could not be differentiated from schizophrenics and not all of their persecutory delusions were dictated by the auditory hallucinatory experiences. They considered that repeat attacks of hallucinosis rendered the patient vulnerable to the chronic form of the condition. They could find no evidence to suggest that these patients were however in any way predisposed to schizophrenia which was in keeping with other workers such as Benedetti and apparently with Harder (1947), but not with earlier writers who considered that the excessive use of alcohol had released a latent schizophrenia.

2.6. Wernicke-Korsakoff Syndrome

Since Wernicke described a clinical and pathological study of 3 patients with mental symptoms, ophthalmoplegia and ataxia in 1881, there have been many papers on this syndrome which now bears his name, and it has become evident that the aetiology is due to thiamine deficiency. Apart from a few cases due to excessive vomiting, the patients seen with this syndrome are alcoholics who have obviously neglected their diet. Only 6 years following Wernicke's description, Korsakoff published the first of a number of papers on the "Amnesic Syndrome in Association with Neuropathy" which is now called by his name. He described it in alcoholism as well as other medical conditions such as typhoid and hyperemesis gravidarum, pointing out that the mental and somatic aspects were caused by the same mechanism though the neuropathy could be minimal. Neither Wernicke nor Korsakoff realised the connection between the two conditions, it required Bonhoeffer to do that in 1901 and for later writers to find similar pathological changes in them. While Pershing wrote "both the neuritis and cerebral symptoms are due to the action of some toxic substance, arising secondarily from perverted nutrition", in 1892, it was not until nearly 50 years later that the nutritional aetiology of the syndrome was again suggested (Bender and Schilder, 1933) and later confirmed (Bowman, Goodhart and Jolliffe, 1939), (Jolliffe, Wortis and Stein, 1941), (de Wardener and Lennox, 1947).

Recently Victor, Adams and Collins (1971) have written a monograph "The Wernicke-Korsakoff Syndrome" in which they review the literature, clinically describe 245 patients and include a pathological study of 82 of the patients. They show that Wernicke's Syndrome/

Syndrome in urban American society is a disease of alcoholics. While it is initially diagnosed by ocular palsy, nystagmus and ataxia, 90% of patients also have mental symptoms and 80% show neuropathy. The mental symptoms initially are those of either mild delirium or confusion, dullness and apathy, changing to a stage of amnesic-confabulatory (Korsakoff's) psychosis and can end as a permanent amnesic defect without confabulation. The pathological changes in patients during in the acute stages of Wernicke's disease or with chronic Korsakoff's psychosis, are essentially the same differing only in the age of the glial and vascular reactions. They thus suggest that the symptom complex should be called Wernicke's disease with or without Korsakoff's psychosis, or the Wernicke-Korsakoff syndrome in patients with both components of the disease. They described the detailed pathology in association with certain of the clinical features and suggest these components are caused by thiamine deficiency which could prevent the entire syndrome if given early enough. It should be noted however that there are differences in response to thiamine in patients with ocular palsy. Cole et al, (1969) showed that in three patients without liver disease there was a response to thiamine of only 4 hours, whereas in 2 patients with concomitant liver disease the eye signs took 24 - 48 hours to disappear and other vitamins, including Vitamin B12 and folate, may be required for full recovery. Even in 1939, Rosenbaum and Merritt, had shown that intravenous Vitamin B assisted improvement and prevented death in Korsakoff's syndrome, even when compared with a group of patients given a high calorie diet and vitamins and a group of patients with these plus liver supplemented.

2.7 Alcoholic Dementia

2.7 Alcoholic Dementia

While this term is in general use, the exact nature of the condition remains somewhat obscure. It also can be used very loosely, some people refer to patients with Korsakoff's psychosis as suffering from alcoholic dementia. Usually however what is meant is an alcoholic patient who has had a gradual deterioration in the various aspects which make up their personality, especially of intellect, but also of learning new material, of judgement and of memory. The patient would have no evidence of cerebro-vascular disease, trauma, syphilis or any other condition which might cause a dementing process.

The only recent extensive clinical survey is from Australia (Horvath et al, 1969). They found 72 patients with alcoholic dementia in 800 alcoholics who attended an alcoholic clinic in Melbourne. There was thus an incidence of 9% of patients who were all investigated by means of electro-encephalograms, air encephalograms and psychometric tests. Ten of the patients were found to have Korsakoff's psychosis. The condition increased with age and while there was three times the incidence in females as compared to males there was no relationship to social class. There was an association with other neurological complications of alcoholism, for example, peripheral neuropathy, epilepsy, Wernicke's encephalopathy, ataxia with cerebellar atrophy and delirium tremens, but not with the non-neurological complications. This work is only available in summary form and there is thus no detail of the tests performed and the results obtained.

Wechsler (1941) was one of the first to study alcoholics by psychometric tests. He chose two age groups, 36 - 42 years and 45 - 55 years, of alcoholics from "the chronic drinker who does not reach the State hospital". He found that the greatest "memory deficit"/

deficit" was noted on the digit-symbol sub-test and he felt that the "differences among our alcoholics are greater than the loss to be expected from the age factor alone", but these differences were not calculated in any statistical way. From Sweden Cleason and Carlsson (1970) studied 20 alcoholics who had been dried out for almost a month in hospital. There was evidence of dysfunction on a battery of psychometric tests in 17 of these of whom 10 were classed by the authors as "severe". Boeke (1967) summarised his findings on 26 alcoholics who had received treatment for 3 months and found that on 4 psychological tests and also on "psychiatric judgements", there was no difference to the results obtained when the patients were admitted. Allen et al, (1971) studied 8 alcoholic patients for 3 weeks after admission to hospital, initially giving them large doses of ethanol for 3 or 4 days before abruptly stopping this. They did serial learning procedures indicating that there was no improvement in this during two weeks of withdrawal.

Ryback (1971) has reviewed the literature and suggested that alcohol most clearly disrupts short-term memory, but also effects immediate and remote memory. He considered that there might be a continuum between the memory deficits in ordinary drinking, alcohol amnesia and the Wernicke-Korsakoff Syndrome. Goodwin et al (1969) have suggested that there are two forms of memory loss which have previously been labelled "blackouts". One type of amnesia had a sharp onset and was seldom followed by recovery of memory, the other type was less definite in onset and the subject was later able to recall events during this period.

Electro-encephalographic changes in alcoholism have been reported/

reported by Funkhauser et al (1953), and Arentsen and Sindrup (1963) who demonstrated abnormalities in 21% of 189 alcoholics and 31% of 317 alcoholics respectively. The former studies demonstrated that psychotic symptoms did not appear to increase the frequency of abnormality. In the latter study it was found that these abnormal features were mainly of "diffuse theta type abnormality" and were independent of head injury, which has been suggested as important in the aetiology of alcoholic dementia.

Neuberger (1957) performed a neuropathological survey of 42 alcoholics who died between 1953 and 1955. He found that there had been a reduction of the changes associated with Wernicke's encephalopathy as compared to previous surveys carried out between 1934 and 1943, and 1944 and 1953 from the same department. In the first ten year period there were 42 patients with Wernicke's lesions necropsy reducing to 13 in the next period and only 2 from 1953 to 1955. He did however find two patients with possible changes associated with Marchiafava-Bignami disease, but the commonest findings were of more or less severe, non-specific degeneration of the cerebellar granula layer. Mancall (1961) described "cerebral cortical atrophy" in alcoholics in which there is more degeneration of cortical cells mainly in the third layer and especially in the frontal lobe, than would be expected for the patient's age. He considered that intellectual deterioration in alcoholics might be due to this.

2.8 "Rare" Neuro-psychiatric Disorders Associated with Alcoholism.

Marchiafava-Bignami Disease

This rare condition was for many years after its first recognition in 1903 considered to be a disease of red wine drinkers in Italian peasants. It has become obvious that this is not/

not the case and it has been shown to occur in many countries of the world and to be a complication not only of alcoholism, but also of diseases in which there is malnutrition, (Merritt and Weisman, 1945). Two cases have now been described in Great Britain (McLardy, 1951, Ironside, Bosanquet and McMenemey, 1961). Characteristic changes of dementia, convulsions, hemiparesis and dysphasia are due to a slow degeneration of the corpus callosum and have also been observed in Wernicke's disease, but Victor, Adams and Collins did not find this association. It does seem likely however that some nutritional factor or factors are involved in the aetiology.

Central Pontine Myelinolysis

In 1959 Adams, Victor and Mancall described a new disorder in alcoholic patients suffering from malnutrition, in which there is a large symmetrical area of demyelination in the midline of the basal part of the upper and mid pons, producing an acute spastic bulbar paralysis with quadriplegia which is fairly rapidly fatal. In the 82 post-mortem cases of Wernicke-Korsakoff Syndrome, described by Victor, Adams and Collins, there were 6 cases of central pontine myelinolysis. Others have noted a similar association, but not every case has been related to obvious poor nutrition (Mathieson and Olszewski, 1960). It is thus not proven that the condition is due to a nutritional deficiency. Victor et al (1971) point out that the lesions are identically pathological to those in Marchiafava-Bignami Disease though in a different site.

Cortical Cerebellar Degeneration

It was noted in 1868 by Wilks that heavy brandy and absinthe drinkers could develop locomotor ataxia. It was again commented on/

on by Marie, Foix and Alajoumine in 1922. However in 1940 Romano, Michael and Merritt redescribed the condition in five alcoholic patients suggesting that it could be caused by a nutritional disturbance. Chodoff et al (1956) described 18 patients who were all alcoholic males in the age range 35 - 62 years. Victor, Adams and Mancall (1959) agreed with the nutritional aetiology when they described the condition in 50 alcoholics with necropsy findings in 11. These patients showed a remarkably uniform clinical picture, consisting of ataxia of the lower limbs, with relatively little involvement of the arms, or speech disturbance and nystagmus was uncommon. The anterior and superior aspects of the vermis of the cerebellum showed degeneration of all elements. Seventy five percent of Victor et al's cases were suffering from malnutrition, five of them having polyneuropathy and four Wernicke's syndrome. They consider that the cerebellar ataxia of Wernicke's disease and that of alcoholic cerebellar degeneration are the same disease, the latter term being used only when the cerebellar signs are clinically manifest.

Deficiency Amblyopia

In the 232 patients with Wernicke-Korsakoff syndrome described by Victor et al (1971) in whom visual fields could be tested, 6 showed evidence of impaired central vision and the presence of central scotomata indicating a nutritional retrobulbar neuropathy/

neuropathy. With a balanced diet and vitamins, 3 recovered and 3 improved despite continued smoking and drinking. In some of the accounts of Marchiafava-Bignami disease lesions indistinguishable from deficiency amblyopia were found. Once more showing how closely related are all these neurological conditions.

Laminar Cortical Sclerosis

Norel in 1939 reported on three severe alcoholics who at post-mortem had a spongy degeneration and gliosis of the cerebral cortex mostly in the third layer. Cases have since been seen at necropsy in association with Marchiafava-Bignami disease and also with Wernicke-Korsakoff syndrome though Victor et al (1971) have not observed it.

Portal-systemic Encephalopathy

This syndrome caused by the toxic effect of metabolites which have been incompletely broken down by the damaged liver, can therefore be found in alcoholics. Davidson and Solomon (1958) demonstrated the importance of differentiating this condition from delirium tremens in both of which there is confusion especially worse at night and tremor (which tends to be "flapping", in contrast to the fine tremor of delirium tremens). However sleepiness tends to increase in hepatic encephalopathy whereas anxiety and over-activity is usual in delirium tremens. It is essential in hepatic encephalopathy to/

to institute the correct dietary treatment, hence the importance of diagnosis.

Portal-systemic myelopathy may be diagnosed if the spinal cord appears to be exclusively affected (Liversedge and Rawson, 1966).

Chronic Hepatic Encephalopathy

This condition was described by Victor, Adams and Cole in 1965 in patients who develop an irreversible neurological disorder in association with liver disease, usually following repeated attacks of portal-systemic encephalopathy. Of their 27 patients 10 were alcoholic. Symptoms present include dementia, dysarthria, ataxia, choreoathetosis and pyramidal signs.

Transient Choreoathetotic Movement Disorder in Alcoholics

In 1970 Mullin, Kershaw and Bolt, described a relatively transient disorder in 12 alcoholics evident in the withdrawal phase but which could occasionally persist. There was no evidence of severe liver disease but two of the patients suffered from Wernicke's encephalopathy and there was a poor dietary intake in five others. None of the patients had taken phenothiazine drugs, but it was suggested that the mechanism of production of the movements was the same as those induced by phenothiazines.

2.9 Peripheral Neuropathy

The original and classic descriptions of this most well known complication of alcoholism were by Lettson (1887) and Jackson (1822) who related it rightly to a high intake of alcohol. A century later when it was realised that beriberi was a vitamin deficiency disease, Shattuck (1928) postulated that alcoholic polyneuropathy might have a similar aetiology. Shortly after this Minot,/

Minot, Strauss and Cobb (1933) studied 57 patients with alcoholic neuropathy and found that, though the dietary histories were unreliable, all could be considered to have had an inadequate diet for a long period. Jolliffe and Colbert (1936) went further by finding that alcoholics with a poor intake of Vitamin B had neuropathy but those with an adequate intake had no neuropathy. They then treated patients with neuropathy with varying amounts of Vitamin B. The patients who only received a borderline amount of Vitamin B showed no improvement, thereafter there was increasing improvement with increasing amounts of the vitamin. However Romano (1937) in a study of 131 alcoholics who had an incidence of 58% of neuropathy, found that 6.4% failed to respond to Vitamin B. In 1963 Zieve and Hill demonstrated that patients with neuropathy and associated liver disease were relatively unresponsive to vitamin therapy. Victor and Adams (1953) were so convinced by their clinical data that polyneuropathy in alcoholics was nutritional, that they considered the condition should be labelled "nutritional polyneuropathy". Fennelly et al (1964) to a large extent confirmed these clinical findings by measuring circulating blood levels of B-complex vitamins in 32 alcoholics with neuropathy and 17 without neuropathy. Eighty six per cent of alcoholics with neuropathy had a decrease in blood thiamine, but there were also diminished levels of folic acid, riboflavin, nicotinic acid, pantothenic acid, biotin, vitamin B6 complex and vitamin B12, so that only 10% of patients with neuropathy had no biochemical evidence of a vitamin B-complex deficiency. Forty four per cent of alcoholics without neuropathy had evidence of low circulating blood/

blood levels of B-complex vitamins. They also found signs of refractiveness to treatment in 7 of their patients and of these 6 had severe liver disease. Recently Knill-Jones et al (1972) in a study of 70 unselected patients with chronic liver disease found clinical evidence of peripheral neuropathy in 13, of whom only 6 were suffering from alcoholic cirrhosis. The occurrence of neuropathy could not be related to liver function, nor was it related to clinical diabetes or minor impairment of carbohydrate intolerance.

Mawdsley and Mayer (1965) performed conduction studies on patients with alcoholic polyneuropathy and compared them with a group of normal people. They found a reduction of conduction in motor and sensory fibres in both arms and legs in those with neuropathy and also some reduction in conduction distally in alcoholics without clinical signs of neuropathy. These changes became more marked and extended more proximally as the clinical signs increased in severity. They suggested that segmental demyelination was the significant pathological process. On the other hand Blackstock et al (1972) have, by using a range of electrophysiological techniques, found little evidence of disturbance in the large motor fibres in alcoholic neuropathy and suggested that the main pathology is in the nature of axonal degeneration. This would agree with the observations of Denny-Brown (1958) who noted the differences between beriberi and alcoholic neuropathy, the former tending to be mainly an abnormality of motor function and the latter a chronic sensory neuropathy. Walsh and McLeod (1970) investigated peripheral nerves by electrophysiological and histological means in alcoholics some/

some of whom continued to drink. They found that if the patient had an acute heavy drinking session, associated with a poor diet, there was active axonal degeneration. However, if the patient had a chronic heavy intake of alcohol, but a good diet, there was some evidence of regenerating fibres and this regeneration persisted even though the patients continued to take alcohol. Casey and Le Quesne (1970) studied 16 alcoholics who had minimal or no evidence of clinical peripheral neuropathy and found that there was evidence of a distal lesion to the nerves in 7 of the 16 patients studied.

Gardner (1972) has described 3 alcoholics who unexpectedly developed peripheral neuropathy after alcohol withdrawal and during treatment with large doses of parenteral vitamins, except vitamin B12 and folic acid. The only biochemical abnormality was a low serum folate level in each patient.

Thus while peripheral neuropathy in the alcoholic is often caused by deficiency of one or more of the B-complex vitamins, there are some patients in whom this is not the case. In these other nutritional deficiencies might be involved, or other abnormal metabolic factors might be the direct cause, or might indirectly affect utilisation of vitamins. None the less it is always recommended to give large doses of vitamin B-complex parenterally in patients with alcoholic neuropathy.

2.10 Alcoholic Myopathy

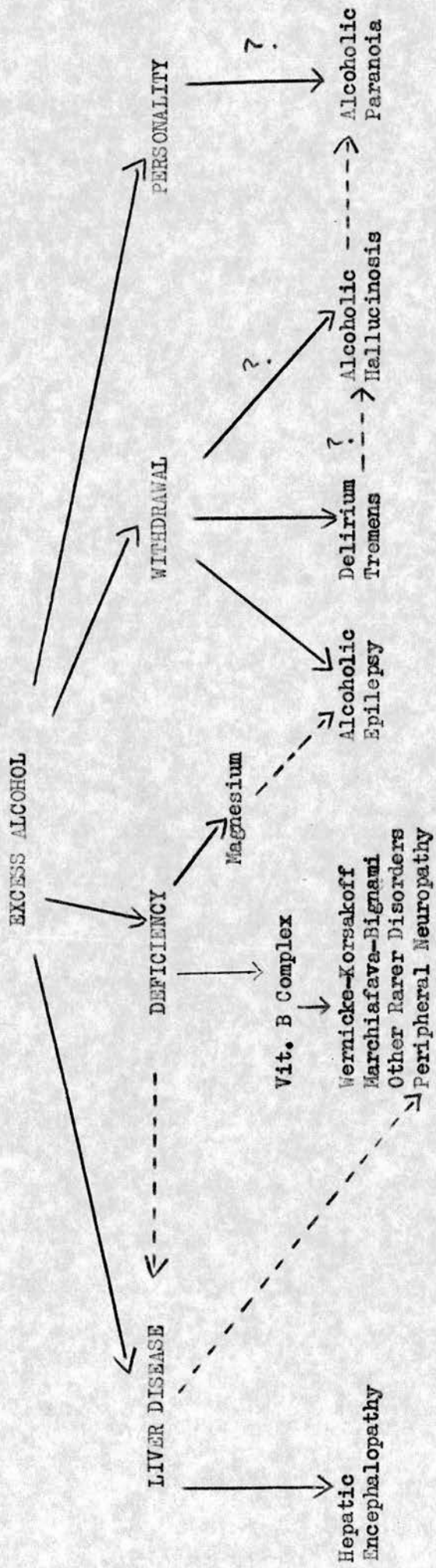
In 1955 Hed et al described a reversible acute myopathy associated with a chronic intake of alcohol. This myopathy was characterised by proximal muscle weakness, cramps, tenderness, swelling and occasionally by myoglobinuria, often after/

after a higher than normal intake of alcohol. If the patient stops drinking this usually recovers completely. However, in 1964 Ekblom et al demonstrated a chronic syndrome of weakness and wasting of proximal muscles especially of the pelvic girdles and thighs in chronic alcoholics which was shown by electromyographic and histopathological techniques to be a myopathy, similar in type to the acute myopathy but with less striking changes. Since then there have been reports of similar patients in the literature, (Perkoff et al (1967), Faris et al (1967), O'Brien and Goldstraw (1969)). Then in 1969 Carlsson et al pointed out that the muscle weakness they demonstrated in three groups of alcoholics of differing severity could be equally due to neuropathy or myopathy. The position remains even more confused since Faris and Reyes (1971) investigated 11 chronic alcoholics with the conclusion that alcoholic myopathy was the result of alcoholic neuropathy.

2.11 Relationship between the various Neurological Syndromes Associated with Alcoholism.

The only study attempting to correlate the various neurological complications of alcoholism comes from Chile by Ferrer et al (1970). They studied 23 (3 females and 20 males) chronic alcoholics with permanent neurological damage. They excluded all patients over 60, patients with other possible cerebral lesions not caused by alcohol, patients in whom acute neurological disease had not been chronic, that is, thus excluding the withdrawal symptoms. Patients were studied clinically and most had psychological testing, electroencephalograms, pneumo-encephalograms and C.S.F. examination.

They/



? Alcoholic Dementia

? Alcoholic Myopathy

DIAGRAM I

INTERRELATIONSHIP OF ALCOHOLIC NEUROLOGICAL DISEASE

They grouped patients neurologically in the usual classified anatomical clinical syndromes, but could find no correlation between these syndromes and other variables such as drinking habits, amount of alcohol intake and type of alcoholic beverage. Age of onset only related to the cerebellar type of alcoholic neurological disease and started after age 45 years. Only a quarter of the patients had a balanced diet. Six of the 23 patients had tuberculosis, these were distributed randomly among the neurological syndromes. There appeared to be no relationship to liver disease. The most important finding however being that in every patient examined practically all levels of the central nervous system were involved and that all patients exhibited psychological impairment of different degrees.

From the summary of the work to date it is very difficult to interrelate the various alcoholic neurological disorders. It is clear that deficiency of thiamine is aetiological in the Wernicke-Korsakoff Syndrome and that thiamine plus other vitamin B deficiencies may be involved in the Marchiafava-Bignami Syndrome, some of the rarer neurological disorders and also in peripheral neuropathy, it is by no means clear that other factors are not also involved. Similarly withdrawal of alcohol in habituated persons may well induce delirium tremens and alcoholic epilepsy, as well as possible alcoholic hallucinosis. Yet again other factors may be involved. The whole effect may be best summarised in Diagram I, but there are still many questions to be answered.

2.12 Alcoholic Liver Disease

2.12 Alcoholic Liver Disease

The connection between excessive intake of alcohol and liver disease has been well noted through the centuries. As stated Baillie wrote the first definitive description in 1795 " - - - we cannot see any necessary connection between that mode of life (inebriety) and this particular disease of the liver". Despite many papers on the subject since then Jolliffe and Jellinek were able to write in 1941 "we are little further forward than that", and today there is still much controversy as to the exact aetiology. Thus a study of the literature does as much to illustrate the social history of alcohol intake and the changing fashions of medical research as to clarify the relationship between alcohol and liver disease.

There have been exhaustive reviews of the subject. Jolliffe and Jellinek surveyed the whole of the literature to 1940 and others have approached the condition from different aspects. Ratnoff and Patek (1942) reviewed Laennec's cirrhosis, Isselbacher and Greenberger (1964) and Scheig (1970) have surveyed the metabolic effects of alcohol on the liver. Melmed (1967) and Ugarte and Valenzuela (1971) have used a more general approach.

Yeld (1898) reported on 195 cirrhotics and found that 60 (31%) were related to alcohol, but that there was no relation to the type of alcohol preferred. Jolliffe and Jellinek showed that the number of alcoholic cirrhotics occurring in all the reported cases of cirrhosis varied between 86% and 17.5%. The reverse figures of the incidence of cirrhosis in alcoholics varied from 19.8% to 2.4% with a mean of 9%, when diagnosed from autopsy figures out of a total of 1,961 autopsies. Wilkinson et al (1969) found an incidence of 9.8% in alcoholics attending/

attending their alcoholic clinic in Melbourne from 1964 to 1968; there being an increased incidence in female alcoholics, 16.8% as opposed to 8.1% for men. Ratnoff and Patek (1942) found a 54% incidence of alcoholic cirrhosis in 384 cases in the United States of America.

In the 1930's the idea that nutritional factors might be important in the aetiology of cirrhosis gained ground, and most of the controversy since then has been proponents of this hypothesis against the importance of the direct toxic effect of the alcohol. Recently Leevy (1967) has tried to suggest that both these opposing schools of thought might be correct - vide infra.

Ratnoff and Patek demonstrated how the incidence of cirrhosis in various countries was very similar despite a widely varying percentage of alcoholics, but there was a reduction in mortality from both alcoholism and cirrhosis in the U.S.A. during the prohibition era. They also demonstrated a male to female sex ratio of 2:1 in adult cirrhosis which was not present in 58 children with the disease. It is of interest to note that they quote a 19th century paper (Howard, 1887) reporting on 10 cases of alcoholic cirrhosis in children!

Scheig (1970) has summarised the pathological aspects of liver disease in alcoholics, dividing these into a) fatty infiltration, b) acute alcoholic hepatitis, c) Laennec's cirrhosis, d) haemochromatosis.

a) Fatty Infiltration (Hepatic Steatosis)

Addison (1836) observed that patients who died of liver failure after over-indulgence of alcohol showed at post-mortem evidence of a fatty liver, and in a recent survey from Chile, Ugarte and Valenzuela/

Valenzuela have reported that two thirds of two hundred liver biopsies on alcoholics were found to have this abnormality (1971). While it has been shown that deficiency of nutritional factors can be important e.g. pyridoxine (French, 1966), protein and choline (Best et al, 1949) in producing these changes of fatty infiltration, Lieber in many papers recently summarised in 1970 has demonstrated that alcohol can precipitate them when given to alcoholic volunteers even when they are on a good diet. He has also shown that the fat in the liver comes from dietary sources and can be reduced by giving a low fat diet.

The actual effects of this steatosis are not clear. There is little evidence that it is in fact "pre-cirrhotic" (Sherlock, 1968), and in a recent study of alcoholics with and without an enlarged liver, de Lint and Schmidt (1970) conclude that fatty infiltration does not precede the appearance of cirrhosis and that the two conditions are not aetiologically linked. Fat embolism can be a cause of sudden death in patients with a fatty liver (Cammermayer and Gjessing, 1951) though most patients with this condition apparently have no complications if they stop consuming alcohol.

b) Acute Alcoholic Hepatitis

Jaundice can occur in alcoholics before cirrhosis is established, accompanied by anorexia, nausea, fever, vomiting and upper abdominal pain with a tender hepatomegaly (Becket, Livingstone and Hill, 1961). While this condition can be misdiagnosed there is even more likelihood of misdiagnosis in patients with alcoholic hepatitis later defined by these authors./

authors, who have no jaundice (1962). Pathologically there is evidence of focal degeneration, marked fatty change, bile duct hyperplasia with an acute inflammatory reaction, and Mallory's hyaline reticulum is sometimes found (Mallory had first described this change in 1911). These findings have been confirmed by other workers (Green et al, 1963, Porta et al, 1963). There is a marked difference in prognosis between the groups with and without jaundice. Hardison and Lee (1966) found a 33% mortality when jaundice was present to the extent of a bilirubin level above 5 mgm.%. This condition was rarely fatal when the serum bilirubin level was much below this. Steroid therapy may be helpful in some patients especially in an intermediate group of patients who are not severely ill and yet only have a small rise in serum bilirubin (Davidson, 1971). Obviously these changes, which are precipitated by a relatively sudden excess of alcohol, can occur in either normal liver, fatty liver, fibrotic or cirrhotic liver, and this must be of importance in prognosis. Boivin, Oudea and Faubert (1970) performed electron microscopy on liver biopsy samples from 60 alcoholics without cirrhosis. They found that there was a series of changes detectable which could be classified in increasing severity from "cytoplasmic focal degeneration", through "giant mitochondria" leading to "amorphous globules and fibrillar degeneration". They consider that some patients can progress to cirrhosis from these changes.

c) Laennec's Cirrhosis

It has been mentioned that the actual incidence of cirrhosis of the liver varies considerably in different parts of the world.
It/

It is especially low in England though this has possibly not always been the case (Budd, 1845), and here alcohol is only apparently related aetiologically to a third of cirrhotics. This picture is similarly found in Scandinavia and Australia, but not in the rest of Europe and in America where alcoholism predominates as the cause and where even the clinical picture is different (Summerskill et al, 1960).

It is suggested that in Ireland where there is a low incidence, there is an apparently immunity to liver damage from alcohol.

It is essential to use post-mortem results when studying figures however, as these are always higher than non-autopsied death reports. It appears that cirrhosis is increasing in the richer countries, and it has been suggested that this may be due to an increased alcohol intake.

The controversy concerning whether alcoholic cirrhosis is due to nutritional deficiency or a direct toxic effect of the alcohol continues unabated. Leevy (1967) has attempted to marry the two hypotheses by showing that in the absence of an adequate diet (of protein, certain vitamins, and nucleic acid precursors), there is an insufficient amount of oxidative enzymes in the liver to metabolise alcohol sufficiently. At some stage there is thus a critical point at which both nutrients and alcohol can play a part in damaging the liver. This hypothesis/

hypothesis would account for many of the conflicting results obtained experimentally to date. However in their recent review, Ugarte and Valenzuela (1970) conclude " - - - hepatic damage in alcoholics results from the association of alcohol - dependent metabolic derangements and protein malnutrition plus a suggestive constitutional or genetic factor", thus adding a further factor.

The prognosis of a patient with alcoholic cirrhosis has been shown to depend on his future drinking habits by Rankin et al (1970) from Melbourne. Thus they followed up 56 alcoholic patients with histologically proven cirrhosis from between 10 months to 5 years. Of the 42 patients who continued to drink, 8 died and 23 had episodes of jaundice, hepatic encephalopathy, ascites or haemorrhage from oesophageal varices. Whereas all but one of 14 patients who stopped drinking were alive and free from symptoms at the end of the follow-up period - the other patient died of other causes.

d) Haemochromatosis

MacDonald (1965) has stressed that haemosiderosis and haemochromatosis may be caused by the interaction of chronic alcoholic ingestion with large amounts of dietary iron e.g. in wine, and that this can be expedited by folic acid deficiency. Apparently the necropsy incidence of haemochromatosis is highest in the Bantu, but is also high in France, Spain, U.S.A.,/

U.S.A. and Scotland whereas it is low in England, India and New Zealand for example.

2.13 Other biochemical changes associated with alcoholism and liver disease.

There are various biochemical abnormalities which can occur in alcoholism usually in association with liver disease.

i) Acquired Porphyria Cutanea Tarda

In association with hepatic damage some alcoholics can develop a disorder of hepatic porphyrin metabolism which results in cutaneous photo-sensitivity. While excessive excretion of uroporphyrin and some amounts of coproporphyrin in the urine and stool, there is no abdominal pain and neurological complications as would be found in the genetic variety. It has been suggested that increased hepatic storage of iron may be important in this condition as phlebotomy has a dramatic effect (Saunders, 1963).

ii) Zieve's Syndrome and Alcoholic Hyperlipaemia

In 1958 Zieve first described 20 alcoholic patients who developed jaundice, haemolytic anaemia and hyperlipaemia in association with a fatty or cirrhotic liver. Since that time there have been other reports from all parts of the world (Kessel, 1962, Hayash and Stemmermann, 1967, Gitlin, 1969). Losowsky et al (1963) studied 8 patients with lactescent serum of whom all but one had an increased concentration of all the lipid fractions in the plasma. In three of these the levels returned to normal with only alcohol withdrawal, and when alcohol was given to one the lipids rose again. Alcoholic hyperlipaemia may occur without any haemolytic anaemia or jaundice, and the pathogenesis of the haemolytic anaemia remains uncertain.

Gitlin/

Gitlin suggested that the abdominal pain often found in Zieve's syndrome is due to porphyria.

iii) Alcoholic Hypoglycaemia

Voegtlin et al (1943) performed glucose tolerance tests on 303 alcoholics, finding that 41% had a decreased glucose tolerance, 6% an increased glucose tolerance and a further 8% were "abnormal". He considered that these abnormalities were related to liver disease in the alcoholic. Tennent (1942) had previously investigated the effect of alcohol on the blood sugar in an attempt to delineate many prior conflicting reports in both man and experimental animals. He suggested that the effect was related to the previous nutritional state of the animal. Lieber (1966) demonstrated then that hypoglycaemia is liable to occur from alcohol when the liver stores have been depleted by starvation. Alcohol both stimulates carbohydrate metabolism thus decreasing the blood sugar and promotes glycogenolysis thus increasing the blood sugar. Hence if there is depletion of glycogen from whatever cause, alcohol will cause a hypoglycaemia. This can occur in the normal individual if he takes alcohol after a period of starvation. Brown and Harvey (1941) who first described alcoholic hypoglycaemia, noted the bizarre neurological manifestations in 6 drinkers of denatured alcohol. Neame and Joubert (1961) described 25 cases of post-alcoholic hypoglycaemia, all of whom had a concomitant mild alcoholic hepatitis. Apparently only one of Brown and Harvey's patients had evidence of liver damage.

Excess alcohol intake has also been shown to induce a diabetic type/

type of glucose intolerance. Lundquist (1965) performed intravenous glucose tolerance tests on 102 alcoholic patients within 7 to 21 days after hospital admission and found that 42 of these had mild diabetic type of glucose tolerance curves, of whom 27 had signs of liver dysfunction. No patient out of 27 alcoholics, who were not in the relatively recent withdrawal phase, showed these abnormalities. Recently Phillips and Safrit have confirmed this finding in two patients who were apparently showing evidence of diabetes when drinking alcohol which disappeared when they were abstinent for some time, (1971).

iv) Hyperuricaemia

On account of the increased lactate production in the liver of the alcoholic, there is a reduced renal clearance of uric acid by the kidneys, so that hyperuricaemia can be found in a state of alcoholic excess (Lieber et al, 1962).

2.14 Anaemia in Alcoholism

For almost a hundred years it has been noted that macrocytic anaemia can occur in liver disease (Krasnow et al, 1957). Thus the anaemia found in alcoholism can be due to many factors. Gastro-intestinal blood loss from oesophageal varices, folic acid and iron deficiency, haemolysis and reduced erythropoiesis (Jarrold and Vilter (1949), Movitt (1950), Jandl (1955), Krasnow et al (1957), Zieve (1958), Herbert et al (1963), Kimber et al (1965), Klipstein and Lindenbaum (1965, Leevy et al (1965)), may all be associated with liver disease. Anaemia may also occur from deficiency of vitamins caused by poor nutrition or may occur from blood loss from peptic ulcer (vide infra)./

(vide infra). In the United States of America iron deficiency in Skid Row alcoholics has also been noted to be caused by multiple blood donations. Finally, it is apparent that alcohol itself may have a direct effect on haemopoiesis, (McCurdy et al (1962), Waters et al (1966), Jarrold et al (1967), Lindenbaum and Lieber (1968)).

Bianco and Jolliffe (1938) were the first to make a study of anaemia in the alcoholic by investigating 184 patients with alcoholic addiction of whom 159 were "complicated", i.e. had additional polyneuritis, pellagra, stomatitis, encephalopathy or cirrhosis. In the 25 "uncomplicated" cases there was no evidence of anaemia compared to 61% of the "complicated" group. They did find however that macrocytosis was present in 50% of both groups. Jarrold and Vilter (1949) studied 30 patients with portal cirrhosis and showed that 65% of these had a macrocytic anaemia which failed to respond to liver and folic acid. Three patients with megaloblastic changes also had signs of multiple vitamin B-complex deficiency and had a poor diet. It is noteworthy that in a comparative study of cirrhosis in Boston and London, when the former were mainly alcoholic and the latter not, there was a higher incidence of macrocytic anaemia in Boston, (Summerskill et al, 1960).

There are somewhat conflicting reports on the presence or absence of folic acid deficiency in alcoholics and possibly these are related to the number of patients who have the various complications of alcoholism. Herbert et al (1963) found/

found a 93% incidence of folic acid deficiency in the United States and Fennelly et al (1964) found a 69% incidence of those patients with neuropathy and 61% of those without. However both of these groups studied were what is in effect a very biased sample. Carney (1967) in England discovered the surprising finding of a higher than normal mean serum folate level in alcoholics taken from an unselected consecutive series of psychiatric admissions to two psychiatric units, one in a general hospital and the other in a mental hospital. Gardner (1971) studied 51 alcoholic in-patients in London discovering a 47.5% incidence of subnormal serum folic acid levels. Williams and Girdwood (1970) showed no evidence of folate deficiency in 50 alcoholics admitted to the Alcoholism Unit of the Royal Edinburgh Hospital, but they do not indicate the number of alcoholics with low levels, only basing their results on means values. They also questioned the present parameters of folate deficiency. Klipstein and Lindenbaum (1965) studied 57 patients with Laennec's cirrhosis, demonstrating low serum folate levels and a rapid folic acid clearance in the 19 chronic alcoholics with cirrhosis who were still drinking and had megaloblastic anaemias. In all patients the serum B12 levels were normal or elevated. They considered that the increased requirements for folate were due to hyperactivity of the marrow secondary to gastro-intestinal bleeding, hypersplenism and haemorrhage. They could not detect any relationship between the anaemia and the type of alcoholic beverage consumed. Halstead et al (1967) investigated the absorption of labelled (H^3 FGA) folic acid in alcoholics and normal controls when given/

given alcohol showing that the uptake of folic acid was reduced in the chronic alcoholic, but not in the normal under the same circumstances. In the alcoholic who was not drinking the absorption was normal. Liver disease did not appear to be important in this abnormality.

It has also been shown that alcohol has a direct toxic effect on haemopoiesis. McCurdy et al (1962) discovered vacuoles in white and red cell precursors from the bone marrow of alcoholics within 24 hours of acute alcoholic intoxication. Waters et al (1966) performed radioactive iron studies on 16 alcoholics without evidence of liver disease, showing depressed iron utilisation in these patients. They confirmed McCurdy's findings of vacuoles in erythroid precursors even in the absence of anaemia. These vacuoles regressed when the alcohol was withdrawn. Although none of the patients had evidence of vitamin B12 deficiency, 50% were deficient in folic acid and 30% in iron. Similarly Jarrold et al (1967) showed that the vacuoles in the white and red cell precursors were not related to diet, serum folate, type of alcohol consumed, liver histopathology or type and degree of anaemia. Hourihane and Weir (1970) found a profound fall of the serum iron three days after withdrawal of alcohol in alcoholics, associated with a reversion of an abnormal accumulation of erythroblastic haemosiderin to normal. All these workers suggested that these effects were a direct result of the toxic effect of alcohol. Various workers have shown that excessive alcohol given to alcoholics will cause a fall in the platelet count which rises again when the alcohol is stopped. All have demonstrated that this is also a direct toxic effect of the alcohol (Ryback and Desforges/

Desforges (1970), Cowan and Hines (1971) and Heck and Gehrman (1972)).

The association of megaloblastic anaemia with haemochromatosis have been noted for many years. Koszewski (1952) discovered 9 examples of megaloblastic anaemia from 35 patients with haemochromatosis, all of these being chronic alcoholics.

Ten per cent of alcoholics with neuropathy in Fennelly et al's study (1964) were found to have vitamin B12 deficiency.

However levels of this vitamin in alcoholism are confused by the fact that in liver disease a higher than normal level often occurs due to the defective storage power of the liver. Roggin et al (1969) showed that 8 of 17 alcoholic patients without cirrhosis had evidence of vitamin B12 malabsorption.

It is thus seen that chronic alcoholism and its complications can have a very complex effect on the various factors necessary for normal blood formation. Mostly this would lead however to the development of anaemia, which if severe may require energetic treatment, but which will in the main respond to simple cessation of alcohol with the usual resultant improvement in diet.

2.15 Nutritional Deficiency and Alcoholism

The effects of malnutrition as a result of alcoholism have been well recognised for many years. In the 1930's, following the discoveries of individual vitamins, the various hypotheses concerning the exact nature of the complications of alcoholism were postulated. As it was then observed that the specific vitamin deficiency syndromes were clearly seen in some alcoholics. It appeared reasonable to suggest that the minor deficiency/

deficiency states could thus occur and might account for some of the other features of the condition. It was even suggested that the cause of alcoholism was in fact a vitamin deficiency state (Williams, 1952). Most of the papers at that time came from the United States of America, but there were very few scientific studies with biochemical results. While it is obvious that there are alcoholics who still develop the classical vitamin deficiency diseases such as pellagra, beriberi and possibly conditions like "the burning feet syndrome", there are a greater number of alcoholics who never show any symptoms of vitamin deficiency. Figueras et al (1953) screened 16,000 patients from the House of Correction in Chicago for clinical signs of specific vitamin deficiencies and found only 7 men with polyneuropathy and 7 with other signs of vitamin deficiency. They considered that the addition of B-vitamins to flour might account for this surprisingly low number. Neville et al (1968) in Pittsburgh admitted 34 alcoholics to an alcoholic research ward to investigate them for dietary intake, physical assessment and vitamin excretion tests. They discovered no significant differences between the mean excretion of vitamin metabolites by alcoholics and by normal controls except for thiamine excretion after an oral dose in female alcoholics. They concluded that the nutritional status of alcoholics was not markedly inferior to that of non-alcoholics of similar economic and health status.

It is clear that there are marked differences in the nutritional state of alcoholics in different centres which may depend on regional differences or on the type of patient admitted and studied, so that some results must have considerable bias./

bias. The work of Fennelly et al (1964) has already been mentioned. They demonstrated that 44% of alcoholics without neuropathy had low circulating levels of B-complex vitamins. All their patients however were admitted to hospital with some complication of alcoholism. It is obvious that they were severely ill, 5 had Wernicke's encephalopathy, 5 had pellagra and all were stated to have deficient diets.

Most other studies described alcoholic patients with various signs and symptoms and note the response to specific or multiple vitamin therapy. Blankenhorn and Spies (1936) described 200 patients with chronic alcoholism and pellagra of whom 60% had specific lesions of the mouth and tongue which appeared to precede the pellagra and which disappeared on treatment with yeast. Spies et al (1938) showed how the "neurasthenia" associated with pellagra responded to nicotinic acid. In 1933 Bender and Schilder described on clinical grounds five groups of "alcoholic encephalopathies". Then in 1939, Cleckley et al reported on 19 patients in stupor, two of whom were alcoholics, who had a dramatic response to nicotinic acid therapy. It was then shown by Jolliffe et al (1940) that a syndrome of clouding of consciousness, cog-wheel rigidity of the extremities and uncontrollable sucking and grasping reflexes occurring in chronic alcoholics responded dramatically to nicotinic acid, whereas those given thiamine died. They called the condition acute nicotinic acid encephalopathy, but agreed that other vitamins should be given at the same time.

Lester et al (1960) by using a saturation test showed that a series of alcoholics required 500 mgms. of ascorbic acid daily/

daily for a week before the urine became fully saturated, whereas the urine of controls was saturated in four hours after only one 500 mgm. dose. O'Keane et al (1972) measured the leucocyte ascorbic acids levels of 50 chronic alcoholics and assessed the intake of vitamin C from dietary histories. The mean leucocyte ascorbic acid level of the group was significantly lower than that of a matched group of controls, though no alcoholic had any features of scurvy. It was also shown that there was insufficient dietary intake of vitamin C.

Apart from the findings of Fennelly et al there has been little scientific study of the other B-complex vitamins in alcoholics. They demonstrated low levels of circulating biotin in 31% of alcoholics with neuropathy and of circulating vitamin B6, pantothenic acid and riboflavin in 24%, 18% and 10% respectively.

Vitamin D deficiency has been noted, en passant, in one patient with alcoholic cirrhosis in a series of patients with gastro-intestinal disease (Whittle et al, 1969). No extended series on alcoholics alone has been reported in this or in any of the other fat soluble vitamins.

While it is clear that many alcoholics have a deficient diet and that alcohol itself can have some effect on absorption of various food materials, it is difficult to be clear of any overall picture of the incidence of vitamin deficiencies in alcoholics as these vary considerably from region to region and reported series often become immediately biased.

2.16 Alcoholism and Gastro-intestinal Disturbances

Stomatitis and gingivitis as well as other symptoms referable to/

to the gastro-intestinal tract are found as part of the syndromes of vitamin B-complex deficiency, probably of a multiple aetiology. There are however other pathological entities which appear to be associated with alcoholism which are not so obviously caused by nutritional factors. Thus, parotid gland swelling is stated to be common in alcoholism and is especially reported in association with alcoholic cirrhosis, but even then Wolfe et al (1957) considered it to be similar to that previously reported in malnutrition.

a) Alcoholic Gastritis

One of the most common conditions found in alcoholics is gastritis. The acute effects of excess alcohol on the stomach were clearly noted by Beaumont as long ago as 1833 and in 1855 Bamberger noted that alcoholism could cause chronic gastritis. The literature was completely reviewed by Gray and Schindler in 1941. They pointed out that some groups of observers stress that alcohol is an important factor in the aetiology of chronic gastritis, whereas other groups do not believe this. They examined the stomachs of 100 male alcoholics gastroscopically in an attempt to solve the problem. Despite these patients having drunk on average 2.8 pints of alcohol daily for 20 years, 55% of the stomachs appeared normal. The only obvious correlation was between actual symptoms and the gastroscopic appearance. Only 7% of patients with a normal appearance had gastro-intestinal symptoms compared to 60% of those who were found to have moderately severe and severe gastritis. There was no correlation between the incidence and severity of the gastritis and the duration of alcoholism, the amount of alcohol drunk, the/



the abuse of nicotine, dental infection or vitamin deficiency. They concluded that the reason why some alcoholics develop gastritis and others do not remains obscure.

There has been little recent work to clarify this issue, despite the introduction of more refined investigative procedures. Palmer (1954) has shown how the acute changes after isolated episodes of drinking resolve completely. Edwards and Coghill (1966) in a study of 221 patients with non-ulcer dyspepsia noted a clear relationship between chronic atrophic gastritis and either regular beer drinking or heavy intermittent bouts of drinking. They found other factors of importance, for example, heavy cigarette smoking and drinking hot tea, but all these factors appeared to act independently of one another. Wolff (1970) studied 1,006 patients by means of gastric biopsy and found that 207 with a normal mucosa drank more alcohol than the 435 patients with chronic gastritis, so that the problem of the role of alcohol in the aetiology of this condition as a whole is no nearer solved than 30 years ago.

b) Peptic Ulcer and Partial Gastrectomy

There is a reported higher incidence of peptic ulcer in association with alcoholism. Navratil and Wenger (1955) found an incidence of 24.5% in 200 male alcoholics, and Hagnell and Wretmark (1955) found 18.5% in their series of 130 male alcoholics over half of whom had the ulcer before the alcoholism. In a controlled series the incidence was 8.1%. The duodenal ulcer to gastric ulcer ratio was 7:1 among the alcoholics compared with 2.3:1 in the non-alcoholics. Wilkinson et al (1971) demonstrated an incidence of 7.2% in their 1,000 alcoholics using stringent diagnostic criteria. The condition was diagnosed a long time before either the patient or his physician considered that/

that there was a drinking problem, and a quarter were diagnosed within five years of the start of heavy drinking.

Whitlock (1961) described 27 patients (17 men and 8 women) who developed psychiatric illness after gastrectomy, of whom 9 men were alcoholics. Five of these 9 were moderate and 4 heavy drinkers before the operation. He points out that the speed of absorption of alcohol is increased after gastrectomy so that repeated intoxicating doses might possibly increase the craving for alcohol. Many patients however continue to drink in moderation after gastrectomy without becoming alcoholics. He also considered that the pain of peptic ulcer may restrict their alcohol intake before the operation. When the ulcer is removed this brake is also removed and at the same time early post-operative symptoms such as "dumping" give an added excuse for an increase in alcohol intake which thereby becomes an addiction. He summarises the literature finding that there had been little comment from either British or American writers. Dick et al (1959) found that in other published work the incidence of post-operative alcoholism varied from 5.4% to 70%. Lereboullet et al (1955) noted that the incidence of partial gastrectomy was four times more frequent among alcoholics as among non-alcoholics. In half of their patients the alcoholism started from 3 months to 5 years after the operation. A third of Hagnell and Wretmark's series of alcoholics with peptic ulcer have had partial gastrectomies. Poloni (1953) from Italy is quoted by Whitlock as observing that a tenth of a series of patients with partial gastrectomy became severe alcoholics. There is also an increase in psychoneurotic features after partial/

partial gastrectomy so that some authors consider alcoholism after operation is in the nature of a "syndrome shift".

c) Pancreatitis

While it has been realised for many years that there is a relationship between alcohol ingestion and pancreatitis, what the exact incidence and mechanism of this relationship is, is difficult to elucidate. A summary of the findings to the 1950's was made by Drieling et al (1952) who quotes Friedereich in 1878 as being the first to note the relationship.

The incidence of acute pancreatitis caused by a high alcohol intake has been reported in various papers from between 10 to 66%, and it is accepted that repeated attacks of acute pancreatitis lead to the chronic form (Drieling et al, 1952). Clark (1942) reported on 36 patients with definite alcohol related pancreatitis, who came to autopsy in a 5 year period. There were 10 females and 26 males in the series with pathological changes in the pancreas varying from massive haemorrhagic pancreatitis to only microscopic abnormalities. In all patients the gall bladder and biliary tracts were normal, but cirrhosis or fatty liver were constant accompaniments. The cause of death was from acute pancreatitis in 15, cirrhosis in 11, acute or chronic alcoholism in 8 and trauma in 2. Clerk also states that in 150 cases of acute and chronic alcoholism at necropsy there were 27 patients with pancreatitis. He could detect no difference in various parameters including drinking habits between these 27 and the other 123. Howard and Jordan (1960) showed that of 1,350 patients with pancreatitis from the literature, 357 were alcoholic though they had personally observed/

observed an incidence of 26.6%. They considered that all cases of patients with chronic calcific pancreatitis were alcoholic. They suggested that pancreatitis is liable to develop on average nine years after the commencement of heavy drinking and 6 years after this the pancreas may become calcified or diabetes may develop. In 8 years of the development of pancreatitis steatorrhoea may ensue and on average 11 years following this death is likely.

The possible mechanism of the development of pancreatitis has been studied extensively. It is known that alcohol is a strong stimulator of pancreatic secretion from its action on the stomach (Woodward et al, 1951). Different concentrations of alcohol in direct contact with the duodenum will also cause a rapid rise in pressure in the biliary and pancreatic ducts in the experimental animal, but these concentrations will not be reached in the human after taking alcohol orally even in high concentration. Israel et al (1969) found that concentrations of 2.5% - 3% maximum were reached in human volunteers, after taking up to 20% solutions of ethanol. Shapiro, Wrubley and Britt (1966) have suggested that increased pressure in the pancreatic duct associated with increased secretion in the gland could cause acute pancreatitis, and give reason why alcohol could cause this. Some workers have found that the volume of pancreatic secretion is increased in cirrhosis of the liver (Van Goldsenhoven et al (1963), Sun et al (1967)), but there was a deficient secretion of pancreatic enzymes in cirrhosis. This may be a function of dietary protein deficiency as many workers have tended to stress the importance of this in the aetiology of chronic pancreatitis.

d) Malabsorption in Alcoholism

While/

While it has been known for some time that alcoholics can suffer from diarrhoea which may be more common in beer drinkers where there is a high fluid intake, it has recently been discovered that malabsorption of various substances may occur in alcoholism. Fast et al (1959) found faulty absorption of I 131-labelled glycerol-trioleate in 12 of 19 alcoholic cirrhotics, none of whom had ascites. Baraona et al (1962) followed up this work and found evidence of malabsorption of fat, d-xylose and abnormalities on x-ray of the small intestine in patients with cirrhosis, but found no difference between those with alcoholic cirrhosis and those without, suggesting that the aetiology was related to the cirrhotic state and not to the alcoholism. Then, in 1969, Roggin et al demonstrated 29 male alcoholics (who were said to be without liver disease, but who appeared on study of their clinical details to have at least evidence of acute hepatic damage) that there was evidence of malabsorption of various indices in 93% of these patients. Thus, the faecal fat was abnormal in 60%, the faecal nitrogen in 52% and the d-xylose absorption test in 76%. They suggested that this could be related to either malnutrition, pancreatic insufficiency, deficiency of bile salts, or alteration in the mucosa of the small intestine. It has also been demonstrated that the absorption of L-Methionine is reduced if alcohol is taken (Israel et al, 1969). Halsted, Griggs and Harris (1972) have shown that malabsorption of folic acid may occur in the presence of a prolonged high alcohol intake in association with folate deficiency (vide supra). Thus the diarrhoea in alcoholism may be due to the various factors suggested above; by Roggin et al.

e) Summary/

e) Summary

Once more while it is evident that there are many well recognised effects of alcohol and alcoholism on the gastrointestinal tract, the exact aetiology would appear to be still obscure and there may be a multiplicity of factors involved in the production of these effects.

2.16 Alcoholic Cardiomyopathy

Myerson (1971) in a review of the topic has shown how the excessive intake of alcohol can have a deleterious effect on the heart. As with other complications, in the 1930's and 1940's it was considered that nutritional factors were of prime importance in the aetiology of "alcoholic heart disease". It has become evident more recently however that there are various causes and presentations of the condition which has become known as alcoholic cardiomyopathy. Although earlier papers on the subject were written from Great Britain, Brigden re-aroused interest in it in this country in 1957, when he described 13 severe alcoholics with heart disease out of 50 cases he had seen with uncommon myocardial disease. None of these had evidence of beriberi heart disease with typically raised cardiac failure. Then in 1959, Evans described what he thought were typical E.C.G. changes in 20 alcoholics. He especially noted a "cloven" type of abnormality of the T wave, but also other changes in 17 of the patients confined to the T waves. These changes were confirmed by a study from Edinburgh by Priest et al (1964), but others have suggested that the changes are non-specific, while admitting they can occur in alcoholic heart disease.

Brigden and Robinson (1964) gave a clinical account of

50 alcoholic patients with heart disease, excluding the usual degenerative causes. They demonstrated three clinical syndromes. Firstly, cardiac beriberi which occurred in 5 heavy beer drinkers, two of whom had had a previous gastrectomy, possibly providing even more susceptibility to thiamine deficiency. The second group presented with arrhythmia especially atrial fibrillation, with and without heart failure. The third group had hypokinetic heart failure, cardiomegaly and E.C.G. evidence of severe myocardial disease. Others have confirmed these findings which have been summarised by Sanders (1970) and Myerson (1971). Alexander (1967) reported on electron microscopic studies in alcoholic cardiomyopathy which revealed typical swollen mitochondria with other changes which he maintained are if occurring together diagnostic. Despite a great deal of research it is still not clear whether the cardiomyopathy is caused by a direct toxic effect, vitamin deficiency (it has been suggested that repeated subliminal thiamine deficiency may be important) or protein deficiency.

Speculation and interest was increased in 1965-1967 when an "epidemic" of acute heart disease with a 50% mortality occurred in heavy beer drinkers in Quebec. This was eventually related to excess cobalt used to increase the "head" of the beer and similar outbreaks have occurred in other parts of North America and also in Louvain, Belgium, from similar causes. There had been an epidemic of a similar type due to arsenic in Manchester in 1900. However this condition appears to be quite different to the types of alcoholic cardiomyopathy mentioned above and/

and has not progressed our understanding of the exact aetiology of this (Sanders, 1970).

2.17 Alcoholism and Chest Disease

It has been accepted that alcoholics are susceptible to acute chest infections and attacks of delirium tremens can be associated with pneumonia. Schmidt and de Lint (1972) have shown that pneumonia accounted for 27 deaths out of 639 men and 99 women who had died from a large cohort of alcoholics in Ontario. This figure was 3.5 times the expected frequency. Other investigators (Sundby, 1967, Lipscomb, 1959) have made similar findings. They have attributed this to delay on the patients part in seeking help, personal neglect and low resistance. It has been suggested that part of this low resistance might be due to liver disease (Chomet and Gach, 1967) which was not confirmed by Schmidt and de Lint, who only found liver pathology in 6 out of the 27 patients. They point out that there is also a high mortality from pneumonia in smokers, who are common among alcoholics.

For reasons similar to that mentioned for pneumonia, tuberculosis is often especially noted in alcoholics. Hudson and Rhodes (1969) and (1971) concentrated on the difficulties in follow up of 28 Skid Row tuberculous alcoholics, 13 of whom were initially lost to follow up. This latter group tended to be younger, stayed less in hospital, had a higher incidence of psychiatric illness and many were later found to have been re-hospitalised and not necessarily on account of tuberculosis. However the patients who were followed up showed generally poorer/

poorer functioning and there was little improvement in their general physical health or little decrease in the number of arrests for drink related offences than before hospitalisation. Olin and Grzybowski (1966) compared chronic alcoholic prisoners in Toronto and found that the incidence of tuberculosis was 17% in the alcoholics but only 1% in the other offenders on x-ray diagnosis. These differences were confirmed by Mantoux testing when positive results were obtained in 80% of the alcoholics and 33% of the others. They stated that the overall population has an incidence of 20%. In South Wales a retrospective study of the x-rays of 243 alcoholics admitted over a long period to a psychiatric hospital showed an incidence of previous tuberculosis much higher than reported for the rest of the population i.e. 83 per 1,000 compared to 10 per 1,000 (Foreman and Chalke, 1972).

2.19 The effect of Alcoholism on the Endocrine System

There have been some relatively recent, if sporadic, attempts to study endocrine function in alcoholics. Goldberg (1962) carried out thyroid function studies on 100 chronic alcoholics (74 males and 18 females). He discovered that 45 showed evidence of hypothyroidism, but unfortunately does not comment on the sex of the 8 subjects on whom he obtained borderline results. He considers that the hypothyroidism was secondary to the alcoholism.

Adreno-cortical function has recently been studied in 4 alcoholics by Mendelson et al (1971). They gave alcohol for 11 to 29 days to these alcoholics finding a close relationship between serum cortisol and blood alcohol levels and with the urinary/

urinary excretion of various catecholamines and blood alcohol level. The maximal excretion of epinephrine occurred during the withdrawal phase. Thus alcohol ingestion apparently stimulated both the adrenal cortex and adrenergic activity.

The diuresis induced by alcohol is accepted as due to the depressant action of alcohol on the hypothalamic centres which control the output of anti-diuretic hormone from the post-pituitary gland. Roberts (1963) however discovered the paradoxical finding that after alcohol ingestion, diuresis continues despite the resultant increase in plasma osmotic concentration. This did not occur if salt was given with the alcohol, even though this was not sufficient to raise the osmotic concentration as high as the usual post-alcoholic diuretic phase. The subjects receiving salt with alcohol did not feel thirsty, nor did alcoholics on admission to hospital with a high osmotic concentration of the plasma, while the blood alcohol was raised. Both these findings suggest that alcohol inhibits the "thirst centre".

Shaw et al (1970) examined the brains from the cadavers of 25 alcoholics showing lower potassium and chloride and higher sodium values than in controls. They could only make tentative suggestions as to the cause of these findings, but felt that there was probably expansion of the cellular compartment.

2.20 Kidney Complications in Alcoholics

Apart from the central hyperthalamic effect on the urine, Benatre et al (1972) have recently been reported as finding that the alcoholic was liable to suffer from renal medullary necrosis./

necrosis. They found three instances in 165 patients at autopsy in association with alcoholic cirrhosis. They considered that infection as well as anaemia might be partly responsible.

2.21 Skin Disease in Alcoholics

As well as the effects of nutritional deficiency, such as pellagra, hepatic disorders, such as spider naevi, haemosiderosis and haemochromatosis and the disturbances associated with porphyrin metabolism, there have been reports of other skin diseases in alcoholics (Texon (1950), Olin (1966), and Rosset and Oki (1971)). Texon found an incidence of 6.5% of skin disorders in males and 6.7% in females admitted to a general hospital. Of these almost half were suffering from psoriasis. Olin examined 227 Skid Row alcoholics in Toronto jails and found 10.1% with "chronic dermatitis" and 0.9% with acne. Rosset and Oki reported on 307 men and 48 women alcoholics admitted to a public hospital who were examined by dermatologists within 2-3 days of admission, and from whom a careful history of previous skin diseases was taken. They showed that 44% of men and 33% of women had one or more skin conditions, 5.6% had acne rosacea, 10.1% seborrhoea capitis, 7.8% seborrhoeic dermatitis, but there was in fact a total of 33 different conditions.

2.22 Dupuytren's Contracture

The association between alcoholism and Dupuytren's contracture was confirmed by Wolfe, Summerskill and Davidson (1956). This condition appeared to be more common in male alcoholics with cirrhosis. Thus they found 66% in alcoholic cirrhotics, 27% in/

in alcoholics without cirrhosis, and only 12% in male controls. Similarly the comparative study of cirrhosis in Boston and London (Summerskill et al, 1960) showed that Dupuytren's contracture was not found in non-alcoholic cirrhotic patients. However, Su and Patek (1970) have found no relationship between Dupuytren's contracture and cirrhosis of the liver though they do confirm the relationship between alcoholism. They studied 405 male patients with Dupuytren's contracture showing it to be rare in patients less than 40 years. There was no correlation between alcoholism and the condition in the 41-50 year age group, but there was a clear association in the 51-60 year age group.

2.23 Venereal Infection in Alcoholism

Olin in 1966 found in his survey of the "Skid Row Syndrome" (in which he used the chronic drunkenness offender in prison) that 30% had been known to have had gonorrhoea and 7% to have had syphilis. Sundby found that the mortality rates for alcoholics, diagnosed before 1940, was three times greater for syphilis than the rates for Norway as a whole, and that 10% of these were diagnosed as having syphilis before discharge from hospital (1967).

2.24 Violence and Alcoholism

a) Traffic Accidents

The effect of alcohol on traffic accidents has been well documented in Britain, the effect of alcoholism has tended to be submerged/

submerged in studies of the effect on alcohol on driving skills. Many studies have shown that even small amounts of alcohol can cause deterioration of driving skills and that performance and judgement progressively deteriorate as the blood alcohol level increases (Drew et al, (1958), Cohen et al (1958)). These studies are obviously relevant to alcoholics whose blood alcohol level is often raised. Thus Santamaria (1967) showed in a study of the drinking traffic offender that when the blood alcohol level was above 100 mgms. per 100 ml. in a person involved in a traffic offence, then the person was probably an alcoholic. This level was rarely found in moderate social drinkers. He also quotes a Swedish study which found that two thirds of drivers contributing to traffic accidents where alcohol was involved were "alcohol misusers". Brenner (1967) in a study of the deaths of 1,343 alcoholics showed that motor vehicle accidents were four and a half times more common in alcoholics than in non-alcoholics. It has also been suggested by Haddon and Bradess (1959) that a high proportion of one-vehicle accidents out of all traffic accidents occurring in a population implies that many of those involved heavy drinking.

Selzer and Weiss (1966) have been one of the few psychiatrists to investigate alcoholism in traffic deaths. Unfortunately they do not define their terms well, and as many of the persons they studied were dead, they relied heavily on relatives' accounts. They found "serious chronic drinking problems" in 32 of the 72 drivers responsible for the fatal accidents. In the age group 22-41 years drivers responsible for accidents were predominantly alcoholic, /

alcoholic, whereas they were not in the 16-21 year old group. Two of the three drivers older than 61 had been chronic alcoholics for many years. Thirteen of the 32 drivers with drinking problems had previously been arrested for drunk driving or drunk and disorderly conduct. Glatt (1964) has written concerning alcoholism and "impaired or drunken driving". He found that nearly a quarter of about 200 male alcoholics, and an eighth of 75 female alcoholics had been in trouble because of drunken driving. Every third male and every second female alcoholic driver admitted having got into trouble for drunken driving, which had first happened at the age of 32. He noted that alcoholic amnesias first occurred on average at the age of 30 years and the patients themselves only admitted that they were "alcoholics" at the age of 41 years. He later extended his survey and found that only 4 of 25 male and 3 of 18 female alcoholics denied ever having driven "under the influence". He described how some patients admitted driving during an alcoholic "blackout", for example, waking up wondering where they had left the car only to find it in the garage! Glatt also pointed out that the risk of driving can be heightened by the fact that alcoholics may also abuse sedative or stimulating drugs. Wilkinson et al (1971) showed that 12.2% of male alcoholics attending their clinic had suffered a serious traumatic accident (most of these were traffic accidents). These accidents tended to occur within 13.9 years of heavy drinking making it an early sign of impending alcoholism.

b) Other Accidents

In women alcoholics Wilkinson et al found that the 8.6% of traumatic injuries were mainly sustained in the home as opposed/

opposed to the accidents sustained to men which occurred mainly as a result of traffic accidents. Olin in his study of the chronic drunkenness offender found an incidence of 55% with limb fractures or amputations and 14% skull fractures. Presumably many of these were as a result of traffic accidents, but not all. In Brenner's study of accidental death in alcoholics 14 of the 217 deaths were from falls. Eighteen of the 738 deaths in alcoholics reported by Schmidt and de Lint (1972) were from falls. It has been suggested that the large number of fires in Glasgow is related to the apparent high consumption of alcohol, and 13 of the deaths reported by Schmidt and de Lint were as a result of fire.

The number of minor injuries in patients who attend casualty departments which are related to alcohol is enormous and these injuries are repeated in alcoholics and tend to be more serious. Moore and Gray (1941) commented on the 16,054 alcoholics treated at a relief station from 1923 - 1938 of whom 14,678 had traumatic complications, most commonly to the head, but next to the arms and legs. Abrasions, contusions and lacerations were commonest followed by strains, sprains and fractures.

c) Suicide and Attempted Suicide in the Alcoholic

It has been well known for many years that alcoholism is associated with suicide. Stenback, Achte and Rimon (1965) quote that Seelan, in 1864, noted the close relationship between alcoholism and suicide in the Finnish population. Sullivan, in 1900, demonstrated high suicide rates in occupations where alcoholism was rife and made a careful statistical survey/

survey of suicide and its relation to alcoholism. Kessel and Grossman (1961) in their paper "Suicide in Alcoholics" reviewed the surprisingly sparse literature quoting incidences of between 20% and 11% of alcoholics who die actually commit suicide. Of 220 male alcoholics discharged and followed up for 5 years by Norvig and Nielson (1956), 7% have committed suicide. Kessel and Grossman themselves found similar incidences of suicide (8% and 7%) in male alcoholics followed up for 5½ years from two separate units in London. Most writers comment on how the suicidal act is often performed within a relatively short time of discharge from hospital, so that in Kessel and Grossman's series most occurred within 3½ years of discharge.

Glatt (1961) found that about a quarter of his middle class alcoholics had attempted suicide at some time prior to admission to hospital. In Moss and Beresford Davies' series they found 10.2% of alcoholics in Cambridgeshire had attempted suicide during a three year period and this figure was higher (24%) in females. In London's Skid Row, Edwards et al (1966) found 10 of 51 men had attempted suicide, 7 of whom were surgical spirit drinkers.

Other workers have studied the problem from the reverse aspect. Batchelor (1954) studied 200 consecutive patients who had attempted suicide and who were admitted to a general hospital finding that 21.5% gave a personal history of excessive drinking and a further 8% were under the influence of alcohol at the time of their suicidal attempt, but were not pathological drinkers. Among his various conclusions was the one that the "chronic alcoholic" does not typically commit suicide, but that sufferers from psychopathic and depressive states who repeatedly abuse alcohol frequently do. Robins et al (1959) managed to obtain/

obtain histories in 119 of 134 consecutive successful suicides and discovered that 26% had been chronic alcoholics.

Mayfield and Montgomery (1972) studied 34 patients admitted to a Veterans' Administration Hospital with self-inflicted wounds and found that 29 could be classed as alcoholics, 26 being intoxicated at the time of the suicidal attempt. Patel et al (1972) in a study of self-poisoning from Glasgow, covering the years 1956 - 1971, showed that among the male patients heavy drinking preceded the overdose of drugs in 70% of cases and among the female patients 40% had taken alcohol before the overdose.

2.25 Drug Abuse

Edwards et al (1966) in their study of Skid Row alcoholics in London, demonstrated that while several of the men expressed "fiercely moralistic" views about drug taking and though true dependence was rare, yet experimentation with a variety of drugs was very common. Rathod and Thomson (1971) have shown that of 95 male alcoholics admitted to their special unit, six had at some time been dependent on drugs such as barbiturates or amphetamines, while of the 32 females 8 had been dependent. This difference was not statistically significant. Devenyi and Wilson (1971) investigated 893 alcoholics and found that 10% were abusing barbiturates of whom one-third could be classed as true addicts. In a study of drug abuse from Dundee, Ballinger (1972) has shown that 18% of alcoholic inpatients are liable to have abused drugs, mainly sedatives and minor tranquillisers. These findings have/

have confirmed the idea that the use of psychotropic drugs in alcoholism should be avoided.

2.26 Criminality in Alcoholism

While a great deal of attention has always been focused on the effect of alcohol on crime, which is hardly surprising when one considers that, for example, there were 79,070 proven offences for drunkenness in England and Wales in 1968, there has only recently been much interest in the alcoholic and crime, which has produced papers from all over the world, including Britain. The concern in this country led to a Home Office Report on the "Habitual Drunken Offender", which points out that many chronic drunkenness offenders are alcoholics. As a result imprisonment is not therefore the most appropriate means of management for such an offender who really needs a means of support and rehabilitation. The Home Office hope this will stem from increasing understanding of the problem mainly by careful research. The report derived much of its data from work carried out by The Addiction Research Unit at the Institute of Psychiatry by Edwards and his colleagues. Most of these offenders were of working-class origin, had minimal schooling, were on the whole unmarried and were also at the lower end of the normal range of intelligence. Despite being in London, over half the total were of Scots and Irish birth. It is interesting to note that although it has been assessed that there are only 200 women in England and Wales who can be classed as "habitual drunken offenders", a very few have a disproportionate effect on statistics, for example, 16 women accounted for 10% of the annual/

annual receptions into Holloway Prison. Gibbens and Silberman (1970) from a sample of 404 prisoners from three contrasted prisons in London found that 40% were excessive drinkers, despite excluding drunken offenders.

Even in serious offences there is a large amount of evidence implicating alcohol. In 1944, East observed that alcohol was a dominant or contributory cause of homicide in 19 of 100 murderers. He quotes Hopwood and Milner's study of 1,000 male admissions to Broadmoor Criminal Lunatic Asylum covering 20 years (1934). Excessive alcoholism was found in only 131 cases and even then in only 58 was alcohol thought to be the main factor in the crime. At the same time as this study in the United States the position was quite different, Gray and Moore found that 66% of 1,637 males in the Massachusetts State Prison were "alcoholists", a similar figure being found among 928 women prisoners in the Massachusetts Reformatory for Women. Gillies (1965) has shown that of 66 murderers he examined in the West of Scotland from 1953 - 1964, 36 were affected by alcohol at the time of the offence. He relates this to the low social class of the offenders and the cultural patterns of the locality. He also found that 17 of the 70 victims were affected by alcohol at the time they were assaulted, and that this contributed materially to the outcome. Cuthbert (1970) in his study of murder in the North East of England found that alcohol was a major factor in half the 70 murderers he had examined. He pointed out that 70% of those in whom alcohol was a factor were acquitted of murder and convicted of manslaughter instead, suggesting that Northern juries are not unmindful/

unmindful of regional mores. Gillies had previously stated "It was intriguing to note how those involved --- prosecution, defence, police, prisoner, relatives and witnesses --- laid small stress on the influence of drink", in the different culture of the West of Scotland.

2.27 Alcoholism as a Cause of Death

From the preceding account of the many complications of alcoholism it is obvious that many of them will lead to death and that therefore there could well be a higher death rate in alcoholics than in non-alcoholics. Pearl (1926) studied life tables and divided a population into 8 groups ranging from abstinent to heavy, steady drinkers. He showed that heavy drinking had a marked effect on the expectation of life, even over that of moderate drinkers, so that the former were liable to die on average 8 years earlier than the latter. The problem has been studied in more detail by various writers, (Jellinek, 1942, Lipscomb, 1959, Sundby, 1967, and Schmidt and de Lint, 1969, 1972.).

Jellinek, (1942) studied causes of death in alcoholics in the United States in one whole year, 1940, whereas Lipscomb (1959) followed up 676 treated alcoholic patients after 3 years and wrote concerning the 34 who had died. In 1967, Sundby, wrote a monograph on the alcoholics who had died to the end of 1962 of a cohort of 1,722 male alcoholics who were treated in the Oslo University Department of Psychiatry between 1925 and 1940. He excluded the 22 who died on their first day in hospital and unable to trace only 29 of the patients. As part of his paper he made a special study of "vagrant alcoholics" who he defined/

defined as those who had greater than three penal sentences, as opposed to the non-vagrant alcoholic. Schmidt and de Lint (1972) studied the patients who had died out of 5,359 men and 1,119 women who had sought treatment at their alcoholic clinic in Toronto between 1951 and 1963. All these workers arrive at very similar conclusions. They all find an increased mortality among alcoholics and Schmidt and de Lint found this to be higher for female alcoholics, more due to the fact that women in the general population have a lower death rate than men. All workers found a higher mortality among the younger age groups, which in Sundby's series was even higher in younger vagrant alcoholics. As far as specific causes of deaths are concerned, violent death, such as suicide, accident, homicide are all increased over that which would be expected. Similarly there was an increased number of deaths from carcinoma of the larynx, pharynx, lung and upper digestive tracts. Schmidt and de Lint comment that this could be related partly to heavy cigarette smoking in alcoholics, but point out that the development of cancer of the larynx, pharynx and oesophagus is affected by heavy drinking. Schmidt and de Lint found that gastric and intestinal mortality did not differ from that which would be expected, though Sundby did find a certain increase which he did not think was particularly related to dietary factors as it was not increased in his "vagrant" group. Sundby also found an increased expected death rate from syphilis, tuberculosis, other respiratory disease and coronary heart disease. The increased expected mortality rate/

rate from cirrhosis of the liver was not different between his vagrant alcoholics and his non-vagrant alcoholics, which again he uses to suggest that nutritional factors may not be of importance in the aetiology of cirrhosis. Schmidt and de Lint found no deaths ascribed to cancer of the liver which had previously been reported to be as high as 30% in alcoholics with cirrhosis, (Lee, 1966).

In Olin's study of "Skid Row" alcoholics already quoted he studied the causes of parental death of these alcoholics taken during routine history taking and found it to be in close agreement with the generally accepted statistical causes of death.

2.28 Studies giving an account of all the Physical Complications of Alcoholism

There have been few studies giving comprehensive accounts of all the physical complications of alcoholism and none attempting to relate these to elucidate the exact aetiology of the complications. Most of the other studies already commented on have been of individual complications and this invariably leads to bias if one is relating this to alcoholism and alcoholics as a whole.

There have been surveys of the part that alcoholism plays in medical wards (Nolan, 1965, Green, 1965). Nolan (1965) made a prospective study of 900 admissions, including 154 private patients, to the medical wards of a teaching hospital in Connecticut and found that 124 were alcoholics i.e. about 13%. In 90 of the illnesses which precipitated these admissions/

admissions there was a direct cause and effect relationship with the alcoholism. The commonest presenting problem, was acute bacterial pneumonia which occurred in 17% of the alcoholics and only 6.5% of the non-alcoholics. Cirrhosis, acute gastritis, pancreatitis, seizures and pulmonary tuberculosis were also more common as presenting complaints in alcoholics, but arteriosclerotic heart disease, cerebro-vascular accidents and malignant disease were less common in alcoholics. The mortality rate was higher in the alcoholic males. He considered that in 60% of the alcoholics the alcoholism had interfered with treatment. He felt that his figures minimised the true incidence of alcoholism but comments "the variety of diseases associated with alcoholism is impressive".

In the same year Green surveyed 1,000 consecutive patients admitted to the adult medical wards of a general hospital in Melbourne in an attempt to find the incidence of alcoholism among these. 841 were able to answer his questionnaire. He found that about 12% were alcoholic (1 in 5 males and 1 in 27 females). He considered that one third of these alcoholics admitted to hospital for medical complications were directly related to the drinking, especially those with gastrointestinal complications, neurological ones and a few with cardio-vascular complications. One patient was admitted with malnutrition. A further 21.6% of these patients were admitted to hospital with illnesses known to be more common in alcoholics, or to be possibly related to excessive drinking, for example, haematemesis from a duodenal ulcer, two patients with Klebsiella pneumonia and two with hypothermia. Six patients, or 5.9% of the alcoholics were admitted to hospital for/

for suicidal overdose of drugs. He considered that 39.2% of the alcoholics were admitted to hospital with illnesses which were unrelated to their excessive drinking, and that he had minimised the incidence of alcoholism, MacKay (1959) found that 12% of admissions to the professorial medical unit in Melbourne could be directly related to alcoholism and a further 5% in whom alcohol might be considered contributory. Smithurst (1965) from a hospital in Brisbane, which served a more affluent population, found a similar incidence of alcoholism among medical patients.

The only survey of the complications of alcoholism studied in an alcoholic population prior to the author commencing his study was that of Texon, who in 1950, published a survey of the medical aspects of 500 alcoholics admitted to the alcoholic ward of a general hospital in New York, (382 were males and 118 were females). He mainly concerned himself with liver disease which he diagnosed on purely clinical grounds finding that only 16% of patients had "a normal liver", 73% had "a fatty liver" and 8% had cirrhosis. He tabulated associated physical conditions in 202 of the patients which included 34 with vitamin deficiencies and 22 with peptic ulcer, or gastric operation. Eight patients were mentioned as being addicted to barbiturates.

Since then Wilkinson et al (1971) have reported on a survey of the physical complications of 1,000 consecutive alcoholics who attended the out-patient department of their alcoholic unit in Melbourne over the period from 1964-1968. They found that two-thirds of these had some physical disability, 55% of which were/

were symptomatic and 15% asymptomatic. These complications were generally found to increase with age and also with the length of drinking history, both of which are obviously related. The incidence of acute alcoholic liver disease was 25%, peripheral neuropathy 19%, hypertension 16.9%, alcoholic gastritis 13.3%, chronic bronchitis 17.3%, cirrhosis 9.8% (the diagnosis being confirmed by liver biopsy), "chronic brain syndrome" 8.8%, epilepsy 7.8%, peptic ulcer 7.2% and major traffic accidents 11.6%. They considered that the last two complications were early ones and could, if recognised as such, be used for preventative measures.

2.29 Prognosis

There have been many papers on this aspect of alcoholism especially from Scotland (Glatt, 1961, Vallance, 1965, Walton et al, 1966, Pemberton, 1967, Freeman and Hopwood, 1968, Ritson, 1968, and McCance and McCance, 1969). The results from Scotland have been summarised admirably by McCance and McCance, 1969, and by Warder and Ross, 1971. In summary, whereas apparently good results can be obtained by careful choice of patients who are then treated in special "alcoholism units", McCance and McCance show that in fact these facilities appear to be rather less important than certain characteristics of the alcoholic himself: such as living alone, being of low social class, drinking cheap wine, belonging to a heavy drinking sub-culture, having unstable marital relations and previous convictions, all mitigate against a good prognosis.

2.30 Summary

2.30 Summary

It was partly because of the superficiality of the paper by Texon, which is frequently quoted in the literature, and partly that other papers only related the complications of alcoholism to findings at death or to findings in medical wards that the present study was undertaken. Since then the work by Wilkinson et al has appeared which presents data very similar to that collected by the author. However, as will be seen laying stress on different aspects. This review of the literature has had to be incomplete, as the world literature on individual complications of alcoholism is vast, for example, 50 references alone can be found relating tuberculosis and alcoholism. The survey has therefore been selective attempting to illustrate the diverse approaches as far as possible from a clinical point of view, while at the same time showing how many of the studies, especially from the United States of America, do not appear to be related to the practise of psychiatry and even to medicine in the West of Scotland. It has been shown there is no paper illustrating the complications of alcoholism from Great Britain.

It has been evident in this survey that the exact aetiology of many of the complications of alcoholism remains in doubt. From a period when it was considered that nutritional factors were the cause of almost all the complications of alcoholism, we have entered a period when this is being questioned and more workers are tending to lay more stress on the direct toxic effect of the alcohol.

METHOD

The study was carried out on all patients who were admitted between May 1st, 1964 and April 30th, 1968, on account of excess alcohol intake to the Southern General Hospital Psychiatric Unit, Glasgow. This is a 90-bedded unit (32 male and 58 female), which also houses the University of Glasgow Department of Psychological Medicine and which accepts patients from a wide area of the West of Scotland, though obviously the greatest number come from Glasgow itself. No patient is admitted to the Unit recommended under the Mental Health (Scotland) Act, 1960. This four year period was chosen as the author was currently working in the Department, and shortly after it a consultant was appointed whose main interest was alcoholism and who immediately changed the admission and treatment policy concerning alcoholics.

Patients were included in the study if they had been incapacitated by prolonged excessive drinking which interfered with their physical or mental health, or had led to social disturbance, or economic difficulty. It was expected using this definition that some patients would be included who might have become "alcoholics" on account of their personality or some other psychiatric illness such as depression.

The survey was partly prospective and partly retrospective. The author's patients were studied prospectively and it was originally intended to study this group only, but it was found/

found to be a very biased group and it did not in any way mirror the typical alcoholic admitted to the Unit. As a result all the alcoholics admitted to the Unit were studied, accepting that the resulting reduction in information on making part of the study retrospective was justifiable to obtain a better overall picture which might be more applicable to alcoholics as a whole, again accepting that alcoholics admitted to hospital do not necessarily reflect alcoholics in the community.

Male patients other than the author's were easily identified, as a special admission list was kept on the male ward. However, until 1966 when a diagnostic classification was introduced throughout the Department, the case records of all female admissions had to be perused to obtain the required information concerning diagnosis. Three possible alcoholic patients were excluded, all female, two were admitted in an intoxicated state and discharged within hours without imparting any information. One other patient was suspected of being an alcoholic or drug abuser, but her notes disappeared from the ward shortly before the patient herself. Thus little information was available for assessment. There was little doubt that she herself had in some way stolen her own notes.

The various parameters listed below were initially punched onto punch cards, the information being taken directly from the case records. Specific figures such as biochemical results were punched as normal or abnormal and then the exact figure written on the cards. The results from these cards were later transferred to forms (Appendix I) which were designed to make the information easily transferable to computer punch cards for analysis.

1. Patient's name, date of birth, age and last known address were written on the punch cards, which were then filed alphabetically and when the total number had been collected were number alphabetically.
2. Dates of admission and discharge were listed in full.
3. The patient's general practitioner and his address was noted if known.
4. Any other psychiatric diagnosis which was mentioned as part of the final formulation was copied on to the card in full. For purposes of analysis these diagnoses were divided into nine sub-groups:- non-specific, aggressive or hysterical personality disorders, depression, schizophrenia, subnormal intelligence, sexual deviation, neurosis, and epilepsy.
5. Previous admission to psychiatric unit was punched as either to the Southern General Hospital Psychiatric Unit, or to another psychiatric unit so that reference could be made to patients who had been admitted to both of these.
6. Length of stay in hospital was punched into five divisions, less than one week (up to 6 full days), one to three weeks (7 - 20 days), three to six weeks (21 -41 days), six to twelve weeks (42 - 84 days), and greater than twelve weeks.
7. Whether the patient was admitted as an emergency or not was indicated, as was the means of referral, whether by general practitioner, Alcoholics Anonymous, Telephone Samaritans, self-referred, from another hospital, (for this purpose other wards, e.g. medical or surgical in the Southern General Hospital were classed as "other hospital"). Finally it was noted whether the/

the patient was referred from legal sources (though for the reasons mentioned earlier this was infrequent).

8. Religion was punched as Protestant, Roman Catholic, other (Episcopalian or Jewish) and none, where this was clearly stated.

9. Occupational level was taken from the "Classification of Occupations" published by Her Majesty's Stationery Office in 1966, and punched in the usual five social classes.

10. Civil state was divided into married, single, widowed, divorced and separated. Patients were considered "separated" if they had been separated from their spouses for longer than a week, as suggested by Vallance (1965), as many wives separate from their husbands in an attempt to manipulate his admission to hospital and obtain treatment before some reconciliation.

11. Main alcoholic beverage was divided into whisky, "other spirits", "wine" (in Glasgow this refers to "fortified wine", which is usually a cheap type of sherry or port), beer, "crude spirits" (if the patient admitted to ever having taken any type of Methylated Spirits or surgical spirits or hair lacquer he was included in this group). It was often difficult to ascertain the main alcoholic drink. Many patients had progressed from "mainly whisky" to "mainly wine" and in these cases the chosen drink over the previous year was taken. Some patients drink whisky when they can afford it slipping to wine when money becomes more scarce, which is sometimes towards the middle of a week. These patients would be punched in both categories and finally placed for the computer analysis in the/

the "mixture" group. Some patients had no specific alcoholic drink mentioned in their notes and these were classed as "not known".

12. A note was taken of patients who drank in "bouts". In Glasgow it is common for patients to drink to excess over the weekend period with virtually no alcohol in the middle of the week. As a result patients were considered for inclusion as bout drinkers, if there was a period of at least two weeks between each drinking episode.

13. An assessment of the daily intake of alcohol was taken direct from the notes and later converted by means of the nomogram devised by Mellor (1970) to grams of alcohol expressed as absolute alcohol per day.

14. Length of time drinking to excess was taken as being the patient's own assessment of the time he had drunk excessively, or the interviewing psychiatrist's interpretation of this. It was not felt that the length of time the patient began to experience symptoms was applicable to this study, though it is accepted that some workers might consider this the more accurate figure. The groups were divided into six, less than one year, one to two years, two to five years, five to ten years, ten to twenty years and greater than 20 years.

15. Food intake was classed as "poor", or "satisfactory" as a result of the history. Unfortunately there were many patients from the retrospective study in whom this was not recorded.

16. Weight loss was assessed either from the history or from evidence of rapid weight gain following admission to the/

the ward. While it was routine to weigh all patients on admission, unfortunately many patients did not have their height recorded so that this information alone was not very useful, unless as indicated it was repeated provided they stayed in the ward long enough.

17. Previous offences against the law were categorised into "severe" which involved a term of prison in excess of six months and included serious assault, manslaughter, child neglect or robbery with violence; "minor drinking offences", either "drunk and disorderly conduct" or "breach of the peace", for which sentences are rarely in excess of three months; "other minor offences" not directly related to alcohol, e.g. theft; "driving offences"; or "none". The number of offences in each group to which the patient admitted was also noted so that for purposes of analysis groups in which "multiple crimes" and "multiple minor drinking offences" could be also analysed.

18. Reference was made to patients who had attempted suicide at any time before admission.

19. A section was used for the patients "mode of discharge", either against medical advice, whether after taking alcohol in the ward or returning to the ward drunk, or whether discharged after completing the course of treatment. It was the policy in the Unit to discharge patients if they consumed alcohol on the premises or returned to the ward in a drunken state. In practice, patients were usually allowed to "sleep it off" and occasionally were reprimanded, but were rarely kept in the ward after this had happened more than once.

20. Family history of alcoholism was broken down into six/

six groups, father, mother, husband/wife, sibling, "other", or none. Thus for transfer to the computerised data, groups of "multiple" and "not recorded" could be added.

While this category depends to a large extent on the patient's own assessment, occasionally various members of the family had been admitted to the Southern General Hospital and in some cases husband and wife were included in the present survey as was one mother and son.

21. Respiratory disease was punched as present if either the patient admitted to this, or if x-ray revealed evidence of it. It was routine procedure in the Unit for patients to have a chest x-ray on admission.

22. Anaemia was diagnosed if the haemoglobin level was less than 13.0 grams per 100 ml. in male patients and less than 12.0 grams per 100 mls. in female patients, though in 4 female patients levels above these were accepted as abnormal as clear abnormalities were noted from the examination of the blood film. It was routine for all admissions to have a haemoglobin level, packed cell volume and mean corpuscular haemoglobin concentration as well as blood films performed, though occasionally patients were in for too short periods especially over a weekend to have them done.

23. Nutritional disease. If there was positive clinical evidence of nutritional deficiency, a punch was made in this section of the card. Evidence of vitamin deficiency, such as sore tongue, signs of scurvy, the skin rash of pellagra, or severe weight loss, was included.

24. Gastritis. The patient was considered to have this condition/

condition mainly on clinical grounds. History of repeated attacks of nausea and vomiting associated with abdominal pain which was not especially localised, which was exacerbated by alcohol and which usually settled when the patient abstained, was taken as diagnostic. In only 3 patients was there radiological evidence of "chronic gastritis" on barium meal examination, other patients had no obvious abnormality on x-ray.

25. Peptic ulcer. This diagnosis was only made if the patient had previous or present radiological evidence of peptic ulceration.

26. Gastric operation. When there was a history of any gastric operation, details were obtained from the hospital concerned so that accurate information regarding the operation and the operative findings could be ascertained.

27. Pancreatitis. Pancreatic function tests were rarely performed on patients admitted to the Psychiatric Unit and when it was done on patients with abdominal pain, they were always negative except in two patients who had a previous history. Two patients diagnosis was made at autopsy.

28. Cirrhosis of the liver. This diagnosis was based on the presence of an enlarged, firm liver or abnormal liver function tests (variety were used, serum bilirubin, zinc sulphate and thymol turbidity, serum protein and protein electrophoresis, S.G.O.T. and S.G.P.T.) which remained after a period of abstinence of at least 3 weeks, or of radiological evidence of oesophageal varices. It was very rarely confirmed by liver biopsy.

29./

29. Hepatitis. If there was an enlarged or tender liver on admission which rapidly settled, or if there were abnormal liver function tests which also became normal within 3 weeks, the diagnosis of alcoholic hepatitis was made.

30. Neuropathy. This diagnosis was also made on clinical grounds. Usually symptoms of paraesthesia or pain in the limb peripheries were associated with signs of loss of touch, pain or limb reflexes, but occasionally the diagnosis was made if the symptoms were convincing even in the absence of signs.

31. "Rare" neurological diseases. This label was used on the punch card to indicate such conditions as Wernicke-Korsakoff Syndrome, or transient choreoathetosis which were considered to be associated with alcoholism.

32. Electro-encephalographic abnormalities. One number was punched on the card if the patient had a normal electro-encephalogram and a different one was punched if the patient had an abnormal electro-encephalogram.

33. Withdrawal symptoms. These were classed into five groups. Those with none, "mild" (slight tremor only), "moderate" (tremor, anxiety and insomnia), "severe" (marked tremor, restlessness, and nightmares) and frank delirium tremens.

34. Psychiatric complications. Alcoholic hallucinosis. This was considered to be present when the patient suffered from auditory hallucinations usually of a derogatory type in the presence of clear consciousness. It had usually been present for only a short time before admission and almost always disappeared/

disappeared during the patient's stay in the ward.

Alcoholic paranoid psychosis was considered present when there were marked paranoid symptoms which seemed to be worsened by heavy consumption of alcohol. These paranoid ideas were usually directed against the spouse and the patient usually said they had settled before his discharge from hospital.

Alcoholic dementia - this was only diagnosed when severe memory impairment persisted for longer than 2 weeks and in the absence of obvious arteriosclerosis or other cause of organic brain damage.

35. Cardiovascular disease. Electrocardiographic abnormality.

Patients with a normal electrocardiogram were indicated on the punch cards as well as patients with an abnormal one.

Alcoholic cardiomyopathy. Patients had the typical changes of this condition in the absence of any other precipitating cause and with typical E.C.G. changes. These were included in this diagnosis.

36. "Other complications". If there was specific mention in the notes of any other physical abnormality which might have some relation to alcoholism it was included in this section e.g. Dupytren's contracture, previous rib or other fractures, diabetes or chronic renal infection. Diagnosis was actually written on the punch card.

37. Drug abuse. If the patients admitted to recent drug abuse this was punched in four categories - barbiturate, amphetamines, narcotic or minor tranquillisers (the actual type abused was noted).
It/

It was thus possible to ascertain the patients who were abusing more than one substance.

38. Biochemical abnormalities. Any abnormality of the Wasserman Reaction or Gonococcal Compliment Fixation Test (G.C.F.T.) was punched on the card. Liver function tests - when results were available the appropriate section on the punch card was punched and the actual result was then written on the card so that these could be transferred to the computer form as normal or abnormal. Normal levels for the Southern General Hospital Laboratory were as follows:-

Serum Glutamo Oxalo Transaminase (S.G.O.T.) 8-40 units per ml.

Serum Glutamo Pyruvate Transaminase (S.G.P.T.) 5-30 units per ml.

Serum Proteins Albumin 3.8 - 5.4 grams %.

Globulin 1.8 - 3.0 grams%.

Total 6.8 - 8.0 grams %.

Abnormal patterns on protein electrophoresis were also noted.

Serum Cholesterol abnormality was also noted - the normal level for the Laboratory was 120 - 270 mgms. %.

39. Vitamin estimations. Whole blood thiamine and nicotinic acid levels were measured by microbiological methods under the supervision of the author. Patients who had received vitamin therapy, either orally or parenterally, within one month of admission were excluded from these assays, as were any who had been on antibiotics within the previous two weeks. Blood was withdrawn on admission and one hour after breakfast/

breakfast on the morning after admission and placed in heparinised containers. It was then stored at a temperature of minus 20° centigrade. Whole blood thiamine was measured microbiologically using *Lactobacillus fermenti* (N.C.I.B. 6991). After treating the blood enzymatically with diastase to release thiamine pyrophosphate from the red blood cells (Baker and Sobotka, 1962), the methods described by Edwards was then followed (Edwards et al, 1957). Whole blood nicotinic acid was assayed by the method described by Sarett et al (1945) using *Lactobacillus plantarum* (N.C.I.B. 8864) with slight modifications (Kershaw, 1967).

Serum vitamin B12 estimations were performed by Dr. J. Adams using the *Euglena gracilis* method described by Hutner et al (1956).

Serum folic acid was estimated using *Lactobacillus casei* in the method described by Waters and Mollin (1961).

40. Psychological testing. Again these were divided into those that were found to have no abnormality and those with some degree of abnormality.

41. Follow-up study. This part of the study was initially an attempt to estimate the number of patients who had died, by May 1970, i.e. 2 years after the end of the in-patient period. However this was extended to include a crude estimate of prognosis as it was found that the patients' general practitioners had to be contacted to trace most of them.

Initially the Southern General Hospital notes were all perused to discover how well the patients were doing at that/

that time. If patients had been abstinent for over a year they were classed as "cured"; if they appeared to have been in stable work and had considerably diminished their drinking they were said to be "improved"; if there was little change in their drinking, social or physical state they were classed as "I.S.Q."; if patients had deteriorated either physically, mentally or socially, for example, they had separated, they were said to have "worsened". Note of date and cause of death were taken in the patients who had died. Early in 1970 the general practitioners of the patients who had been unable to be traced through the Southern General Hospital notes were circulated with a letter (Appendix 2) which was aimed at assessing the patient's physical state, but which also included information about prognosis. There was an extremely good response to this letter though many general practitioners had not seen the patient for some considerable time.

During the period 1964-1969 a large area of Glasgow which was served by the Southern General Hospital was demolished and many patients were thus rehoused and had been lost sight of by their general practitioners. By the end of 1970 it was possible to circulate the mental hospitals, general hospital psychiatric units and prisons in the West of Scotland to reduce the number of patients who were still not traced. Following this the Executive Councils in the area were circulated and thus it was possible to find further patients and their general practitioners. A letter was sent to some patients whose general practitioners had not replied to two letters addressed to/

to them, but this had a very poor response, most of the patients had in fact moved. Early in 1972 the total number of patients traced was low enough to be able to approach the Register Office in Edinburgh who allowed the author to examine the records of all their list of deaths from 1964 to the end of 1971.

Thus the follow-up period varied considerably from a few patients who were traced within 2 years to some who were followed up after 6 years. As most of the patients were in fact followed up by early 1970 the average follow-up period was 4 years. It is clear that most of the patients who had died to the end of 1971 were probably traced, though there must have been some who were followed up and then died after this who would be missed.

Statistical Analysis.

Various statistical aids were used to test for significance, correlation and discrimination.

Students 't' test, and Chi^2 tests were employed at various parts of the study. Discriminant function analysis comparing most of the data obtained with various groups of complications was performed with the aid of Miss E. Sinclair and Dr. Hewitson, Department of Mathematics, Strathclyde University using an ICL 1905E and an IBM 370/155 for computing facilities. They also performed correlation coefficients for the various groups of complications. An analysis of variance was utilised to test the results of thiamine levels in different withdrawal symptoms.

4. RESULTS

In all Tables percentages have been assessed to the nearest 0.5% so that the totals in these columns do not necessarily add up to 100%.

Only statistically significant results have been marked on the Tables.

4.1 Patient Data (Tables 1 and 2)

It is seen from Table 1 that during the four year period, 527 male and 148 female (3.5:1) patients were admitted who fulfilled the criterion of having at some time been physically, mentally or socially incapacitated by prolonged excessive drinking or had themselves sought help for their drinking habits. When re-admissions are included in the total alcoholics accounted for 40% of the total male admissions of 1,633 patients and 8.7% of the 2,472 female admissions (Table 2). Just over three quarters of these patients were admitted once only during the period and rather more females were admitted over three times.

TABLE 1. Alcoholic patients admitted to Southern General Hospital Psychiatric Unit during period of investigation, 1st May, 1964 to 30th April, 1968.

	No.	%	Ratio
MALE	527	78	3.5
FEMALE	148	22	1
TOTAL	675	100	-

TABLE 2.

NUMBER OF ADMISSIONS OF PATIENTS

<u>MALE</u>				<u>FEMALE</u>			
Patients	%	Admiss. Readmiss.	%	Admissions	Patients	%	Admiss. Readmiss.
426	81	426	66	Once	107	72	107
85	16	170	26	Twice	25	17	50
13	2.5	39	6	x3	9	6	27
1	0.5	4	2.3	x4	5	5	20
1		5		x5	1		5
1		6		x6	0		0
0				x7	1		7
Total	527	650			148		216

Total Male Admissions to Unit = 1,633
 % Alcoholic Admissions = 40%

Total Female Admissions to Unit = 2,472
 % Alcoholic Admissions = 8.7%

4.2 Age (Tables 3 and 4)

The mean age of the male patients was 43.70 years and of the female patients was 45.42 years. This difference was not statistically significant. The age range and distribution was very similar for both sexes, though there was a slight excess of female patients admitted over the age of 55 years (this figure only just reached statistical significance). (Figure 1)

TABLE 3. Age.

	Mean	Median	St. Dev.
MALE	43.70 years	44	±10.65
FEMALE	45.42 years	44	±11.08

4.3 Civil State (Table 5)

Just over half the patients admitted were married. The only sex difference was that whereas 13% of female patients admitted were widows, only 6% of male patients were widowers. This result was statistically significant $P < 0.025$.

4.4 Social Class (Table 6)

There was no sex difference as to the distribution among the social class.

TABLE 6./

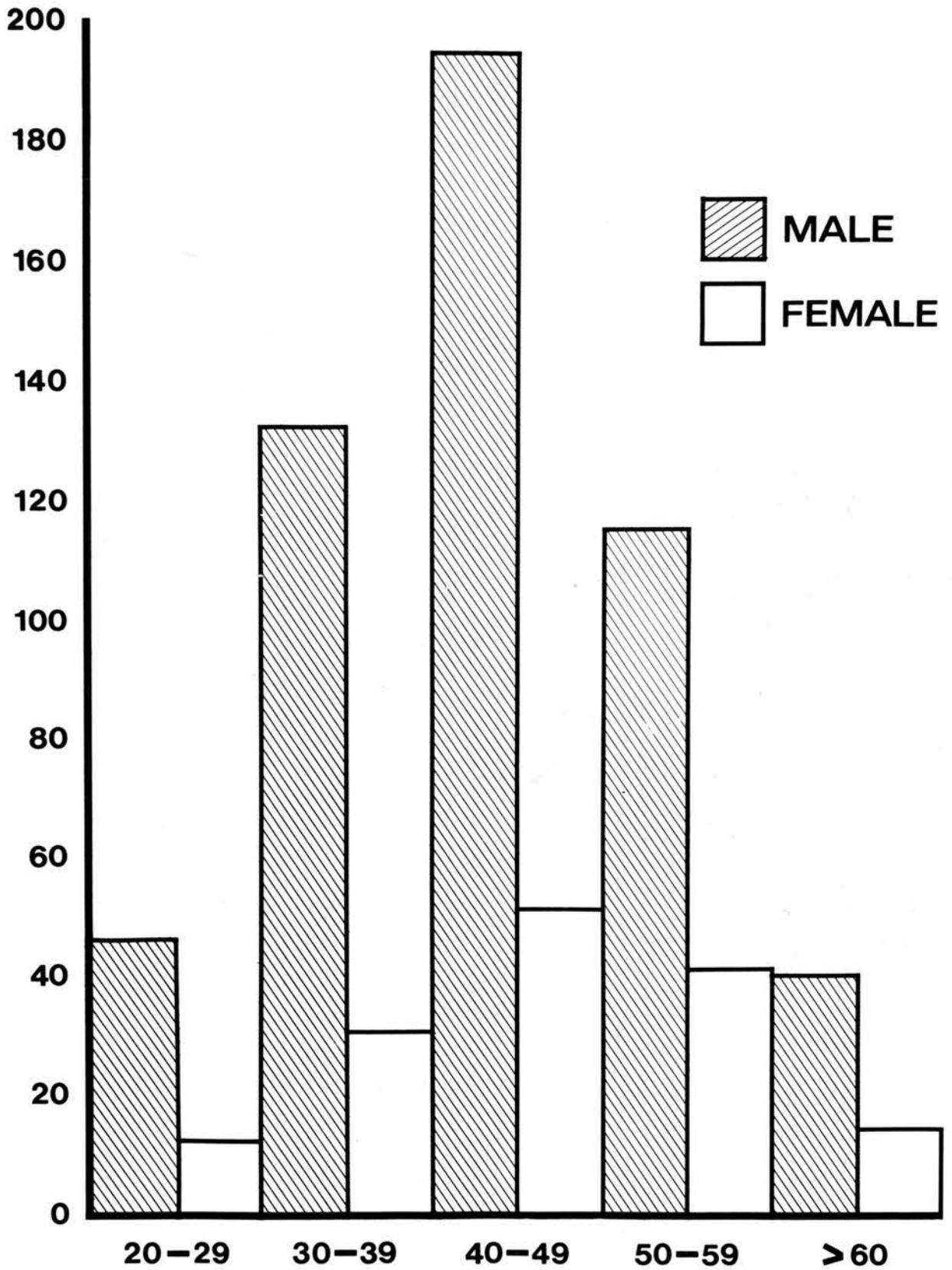


FIGURE 1. AGE IN 10 YEAR INTERVALS

TABLE 4. Age in 5 year intervals.

	Age in years		20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	> 65
MALE	No.		15	31	62	70	109	85	80	35	29	11
	%		3	6	12	13	21	16	15	7*	5*	3*
FEMALE	No.		5	7	14	16	25	26	22	19	8	6
	%		3	4.5	9	11	17	18	15	13*	5.5*	4*
TOTAL	No.		20	38	76	86	134	111	102	54	36	17
	%		3	5.5	11.5	12.5	20	16.5	15	8	5	2.5

$$* \chi^2 = 3.90$$

Sig at 5%

P < 0.05

TABLE 5. Civil State.

	Married		Single	Widowed	Divorced	Separated
	No.	%				
MALE	286		74	33 ^o	59	75
	54		14	6	11	14
FEMALE	84		15	19 ^o	14	16
	57		10	13	10	10
TOTAL	370		89	52	73	91
	55		12	7.5	11	13.5

$$\chi^2 = 5.82$$

$$P < 0.025$$

TABLE 6. Social Class

		I	II	III	IV	V	NK
MALE	No.	30	82	156	129	130	-
	%	6	15	30	24	24	-
FEMALE	No.	13	20	35	42	36	2
	%	9	14	24	28	24	1
TOTAL	No.	43	102	191	171	166	2
	%	6.5	15	29	25	24.5	-

4.5 Religion (Table 7)

Two-thirds of the patients were Protestant, one-third Roman Catholic, and only one male patient was Jewish. Ten male patients said they were either atheists, agnostics or had no religion.

TABLE 7. Religious Affiliations

		Prot.	R.C.	Other	None	NK
MALE	No.	352	162	3	10	0
	%	67	31	0.5	21	-
FEMALE	No.	99	48	0	0	1
	%	66	33	-	-	-
TOTAL	No.	451	210	3	10	1
	%	67	31	0.5	1.5	-

4.6. Nonconcomial Data (Tables 8 - 12)

About half the patients came from the surrounding areas of Glasgow which could be said to be the hospital's "catchment area". A further 20% came from other parts of Glasgow and the remainder from the surrounding counties including a few patients from the Scottish Islands, as the hospital is near to Glasgow Airport. Very few patients actually stated they were of "no fixed abode", though many more male patients were living in common lodging houses.

While for 83% of the patients it was the first admission to the Southern General Hospital Psychiatric Unit, it was the first psychiatric admission for only 55% so that many patients had previously been in other Units. The proportion of male to female patients was similar except that rather more male patients proportionately had been previously in the Southern General Hospital and in other hospitals but this figure only just reached statistical significance. (Table 8)

Over half the patients were admitted as emergencies, and while these were usually without appointment through the duty registrar, a few were referred to the out-patient clinic and then admitted immediately. (Table 9)

TABLE 9./

TABLE 8 Previous Psychiatric Admissions

	First Psychiatric Admission	PREVIOUS ADMISSIONS				First admiss. to S.G.H.	Not Known
		To other Psychiatric Unit or Hospital	To Both S.G.H. and Other Hospital	To S.G.H. Only			
MALE	No.	138	50*	47	430	-	
	%	26	9.5	9	82	-	
FEMALE	No.	51	6*	11	130	1	
	%	34	4	7	87	1	
TOTAL	No.	189	56	58	560	1	
	%	28	8.5	8.5	83	-	

$$*\chi^2 = 3.90$$

$$P < 0.05$$

TABLE 9. Mode of Admission

		Emergency	"Waiting List"
MALE	No.	282	245
	%	53.5	46.5
FEMALE	No.	91	57
	%	61.5	38.5
TOTAL	No.	373	302
	%	55.5	44.5

By far the most patients were referred from their general practitioner, but 9% came from other hospitals or other wards in the Southern General Hospital, and almost the same number referred themselves (significantly more men than women). Only a small number (3.6%) were referred by Alcoholics Anonymous and then admitted, but significantly more females were admitted in this manner. (Table 10)

More male patients stayed less than one week, many discharging themselves within a day or two, but this figure did not reach statistical significance. However, more female patients stayed greater than 6 weeks and this figure did reach statistical significance. (Table 11)

12.5% of the patients discharged themselves from the Unit some of these obviously after taking alcohol either in or out of the ward. However a further 14.5% of male patients and 4.5% of female patients were discharged by the medical staff after taking alcohol (this figure reached significance $P < 0.005$).

It/

TABLE 10. Means of Referral.

	G.P.		Other Hosp. or Unit		Self	A.A.	Council of Alcoholism	Samaritans	Prob. Order	Not Known
MALE	No.	360	45°	53	14°	27	6	1	21	
	%	68.5	8.5	10	2.5	5	1.5	-	4	
FEMALE	No.	109	16°	5	10°	5	-	-	3	
	%	73	11	3.5	7	3.5	-	-	2	
TOTAL	No.	469	61	58	24	32	6	1	24	
	%	70	9	8.5	3.5	4.5	1	-	3.5	

$${}^{\circ}\chi^2 = 5.72$$

$$P < 0.025$$

$${}^{\circ}\chi^2 = 5.16$$

$$P < 0.025$$

TABLE 11. Length of Time in Hospital

		< 7 days	7-20 days	21-41 days	42-84 days	> 84 days (3 mths.)
MALE	No.	76	230	182	36 ⁰	3
	%	14.5	43.5	34.5	7	1
FEMALE	No.	13	55	54	20 ⁰	6
	%	9	37	37	13.5	4
TOTAL	No.	89	285	236	56	9
	%	13	42	35	8.5	1.5

$$\chi^2 = 5.55$$

$$P < 0.025$$

TABLE 12. Discharge.

		Self Discharge	Medical Discharge After Alcohol	Self Discharge After Alcohol	Medical Discharge After Treatment
MALE	No.	50	77 ⁺	17	383
	%	9.5	14.5	3	73
FEMALE	No.	14	7 ⁺	2	125
	%	9	4.5	1.5	84
TOTAL	No.	64	84	19	508
	%	9.5	12.5	3	75.5

$$+\chi^2 = 8.49$$

$$P > 0.005$$

It is seen that only three quarters of the patients thus finished their course of treatment.

4.7 Drinking History (Tables 13 to 17)

It is seen from Table 13.1 that whisky is by far the most preferred type of alcohol of male patients and from Table 13.2 that this is often drunk in association with beer and that many male patients will also drink wine at other times. Female patients have a preference for wine and also for spirits other than whisky, though a great many will also drink whisky. None the less very few admit to drinking beer. An equal proportion of male and female patients admitted to drinking the cruder forms of alcohol. This is also illustrated in Figure 2.

It is clearly seen from Table 14 and the diagrammatic representation of this (Figure 3) that there is considerable difference in the quantities of alcohol admitted to have been taken by male and female patients. Only one tenth of male patients admitted to taking less than 150 grams of alcohol per day, whereas over one third of women said they took this quantity. (On the nomogram devised by Mellor, 1970, one bottle of fortified wine would be equivalent to 120 grams and a bottle of whisky or other spirit would be double this). One third of men admitted drinking greater than 350 grams of alcohol per day whereas only 5% of women admitted to this quantity. Both these figures for lower and higher consumption of alcohol were highly significant, so it is clear that men drink or admit to drinking far more alcohol than women.

Similarly/

Similarly it is clear from Table 15 and Figure 4 that female alcoholics have apparently drunk for considerably shorter periods than male alcoholics. A half of female alcoholics admitted to having drunk to excess for less than 5 years, whereas 20% of male alcoholics gave this as the period they had drunk to excess. At the other end of the scale a third of male alcoholics had drunk for longer than 20 years compared to only one tenth of female alcoholics.

Less than 10% of both male and female patients could be considered to be bout drinkers, that is with periods of at least between each episode of drinking.

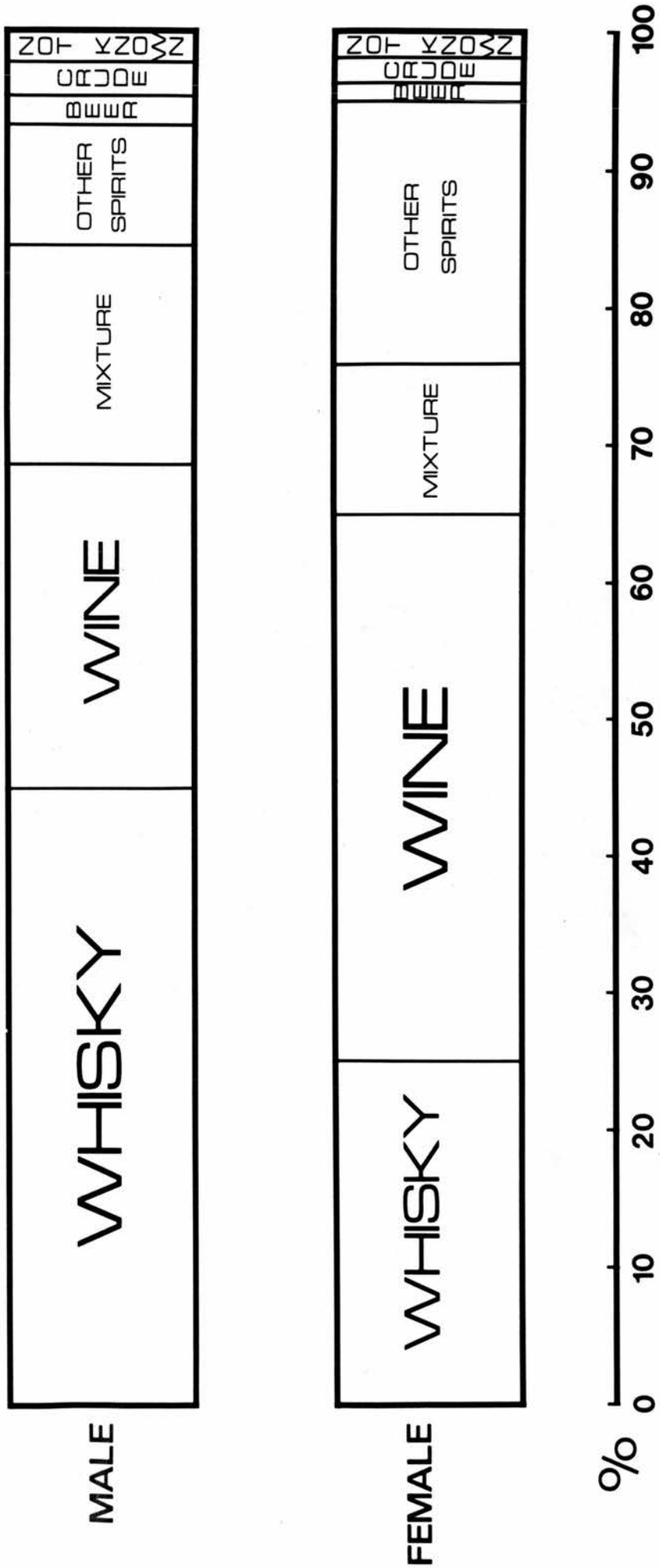
There was a family history of excess alcohol intake in just over a quarter of both male and female patients. The largest number of individual relatives drank excessively were fathers and it is interesting to note that the ratio of fathers to mothers, who drank to excess, is 3.5 : 1 which is very similar to the ratio of male to female alcoholics in this series. Considerably more male alcoholics gave a history of excessive drinking in the father than female alcoholics and this is significant at the less than 0.001 level. Conversely female alcoholics give a higher incidence of excessive drinking in their spouses than did male alcoholics. This also is significant at the less than 0.001 level. It should be noted from Tables 17.1 and 17.2 that female alcoholics with husbands, who are also alcoholics, have no other relatives with this complaint.

4.8 Associated Psychiatric Diagnosis (Table 18)

It is seen from Table 18 that just over a quarter of the patients/

MAIN ALCOHOLIC PREFERENCE

FIGURE 2.



% 0 10 20 30 40 50 60 70 80 90 100

TABLE 13.1 Main Type of Alcohol Preferred.

		Whisky	Wine	Mixture	Other Spirits	Beer	"Crude"	Not Known
MALE	No.	237 ⁺	127 ⁺	82	45 ⁺	11	13	12
	%	45	24	15	8.5	2	2.5	2
FEMALE	No.	37 ⁺	59 ⁺	17	28 ⁺	1	3	3
	%	25	40	12	19	1	2	2
TOTAL	No.	274	186	99	73	12	16	15
	%	40.5	27.5	14.5	11	1.5	2.5	2.0

$$^{\dagger} \chi^2 = 9.88$$

$$^{\dagger} \chi^2 = 8.81 \quad \chi^2 = 7.66$$

P < 0.005 P < 0.005

P < 0.005

TABLE 13.2 Type of Alcohol Consumed

		Whisky	Wine	Other Spirits	Beer	"Crude"	Not Known
MALE	No.	370 *	233	+ 59	+ 185	22	12
	%	70	42	11	20	4	2
FEMALE	No.	75 *	86	+ 41	+ 10	6	3
	%	50	57	27	7	4	2
TOTAL	No.	445	319	100	195	28	15
	%	66	47	15	29	4	2

$$* \chi^2 = 4.35$$

P < 0.05

$$+ \chi^2 = 17.18$$

P < 0.001

$$+ \chi^2 = 28.72$$

P < 0.001

TABLE 14. Amount of Alcohol in Grams per Day.

		0-49	50-149	150-249	250-349	350-449	450-549	550-549	650-649	<750	Not Known
MALE	No.	0	59 +	132	52	59	56	26	17	20	106
	%	0	11	25.5	10	11	10.5	5	3	4	20
FEMALE	No.	1	51 +	36	21	6	0	2	0	0	31
	%	1	34	24	14	4	-	1	-	-	21
TOTAL	No.	1	110	168	73	65	56	28	17	20	137
	%		16.5	25	11	9.5	8.5	4	25	3	20

$$+\chi^2 = 29.8$$

P < 0.001

$$\chi^2 = 30.50$$

P < 0.001

AMOUNT OF ALCOHOL IN GRAMS PER DAY

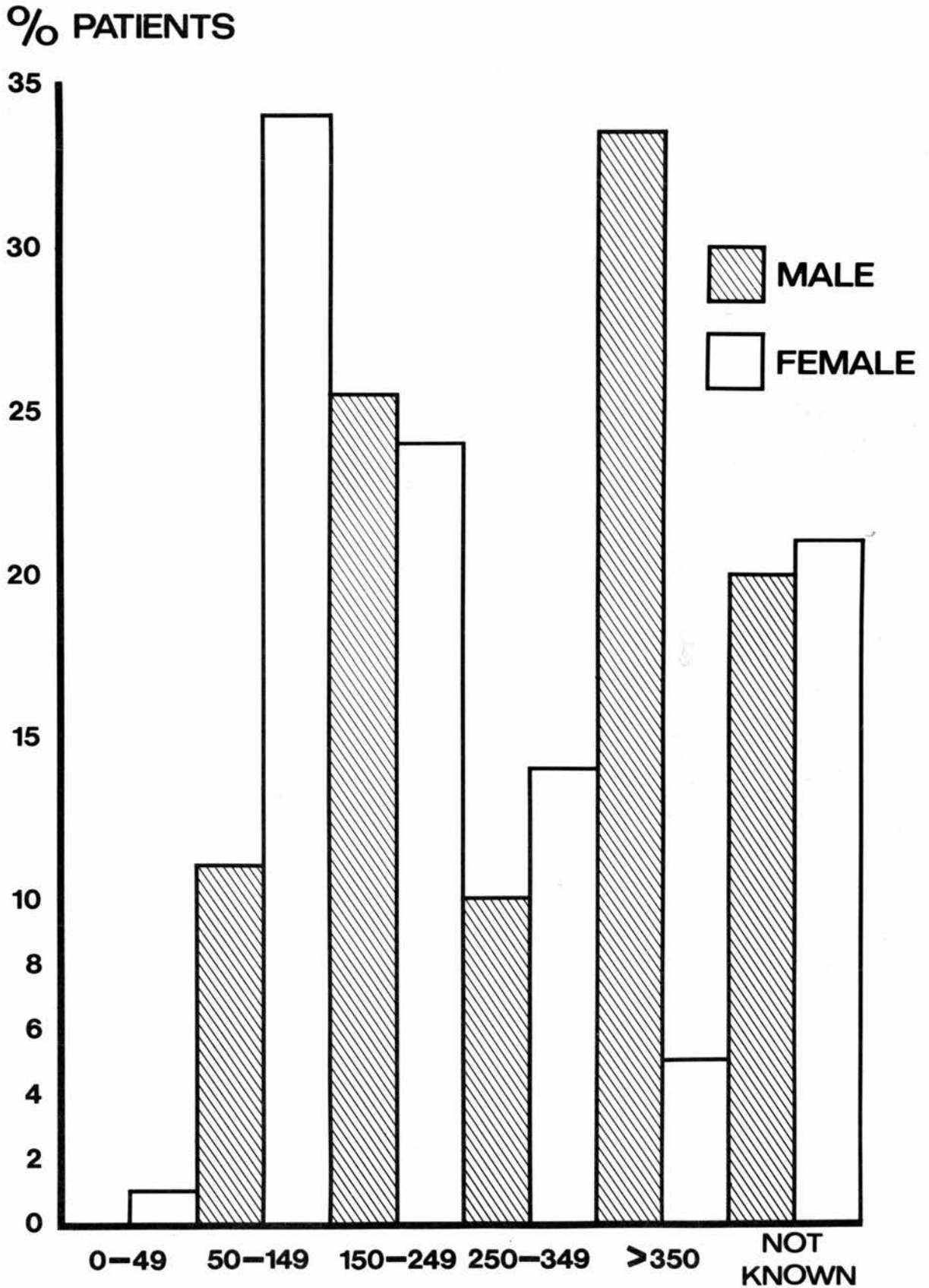


FIGURE 3.

TABLE 15. Length of Time Drinking to Excess.

		0-1	1-2	2-5	5-10	10-20	> 20	Not Known
MALE	No.	9	16	69	97	153	180	3
	%	2	3	14	18	28	34	1
FEMALE	No.	11	19	41	35	27	13	2
	%	7	14	28	24	18	9	1
TOTAL	No.	16	35	110	132	178	193	5
	%	2.5	5	16.5	20	26.5	28.5	1

$$\chi^2 = 12.04 \quad P < 0.001$$

$$\chi^2 = 19.37 \quad P < 0.001$$

$$\chi^2 = 12.19 \quad P < 0.001$$

$$\chi^2 = 16.5 \quad P < 0.001$$

$$\chi^2 = 4.19 \quad P < 0.05$$

$$\chi^2 = 22.92 \quad P < 0.001$$

FIGURE 4.

LENGTH OF TIME DRINKING TO EXCESS

% PATIENTS

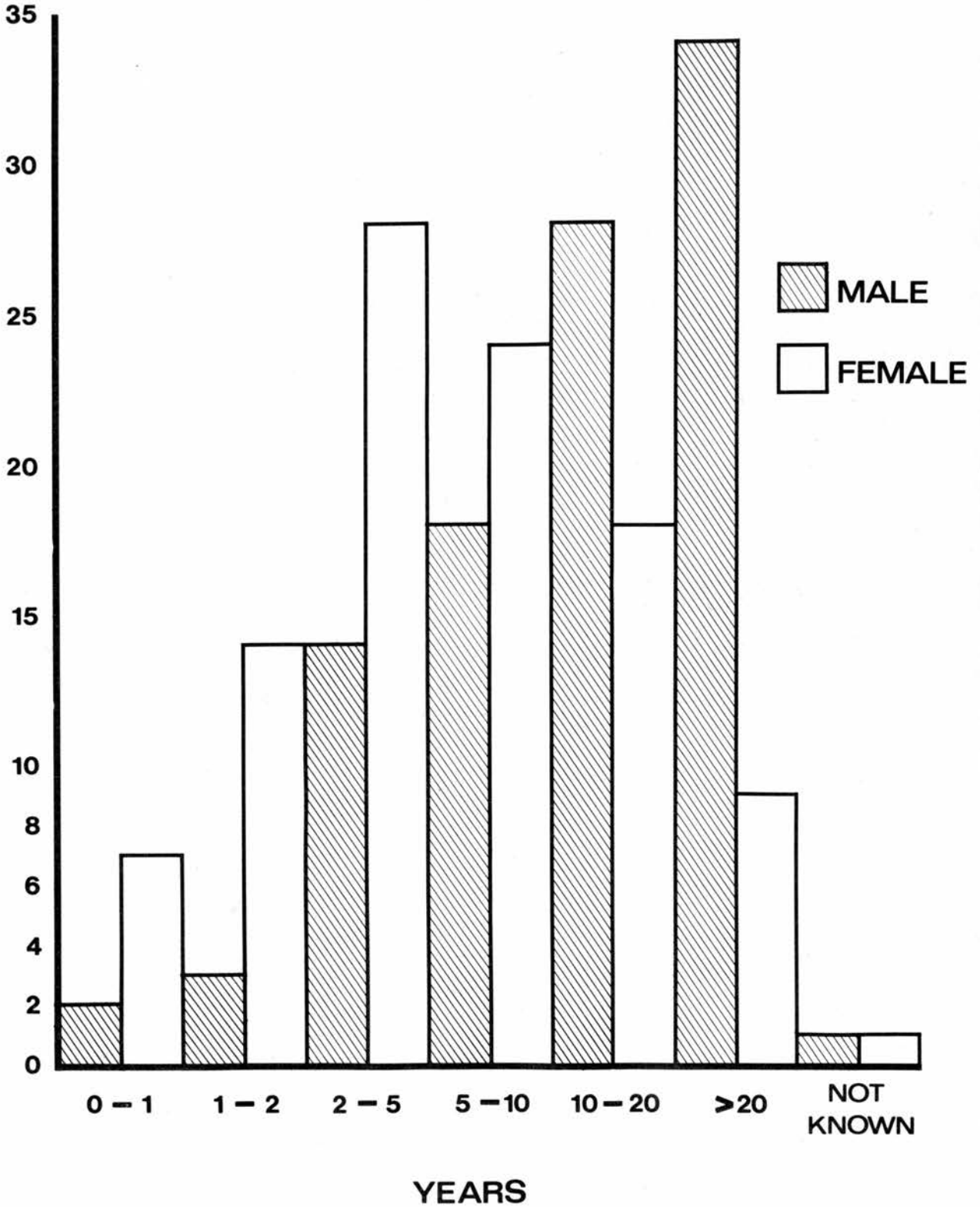


TABLE 16. Bout Drinking.

	Bouts		Steady		Not Known	
	No.	%	No.	%	No.	%
MALE	46		478		3	
		9		90		1
FEMALE	10		138		0	
		7		93		0
TOTAL	56		616		3	
		8.5		91		0.5

TABLE 17.1 Family History of Excess Alcohol Intake

		Father	Mother	Husband/ Wife	Sibling	Other	Nil
MALE	No.	88 *	24	13 *	42	26	381
	%	17	4.5	2.5	8.5	5	72
FEMALE	No.	8 *	4	14 *	5	5	114
	%	5.5	3	9	3.5	3.5	77
TOTAL	No.	96	28	27	47	48	495
	%	14	4	4	7	7	73

* $\chi^2 = 11.16$

P < 0.001

* $\chi^2 = 16.6$

P < 0.001

TABLE 17.2. Family History of Excess Alcohol Intake.

	Only Father		Only Mother		Only Husband/ Wife		Only Sibling		Only one Other Relative		Multiple	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
MALE	60	°	10		9	*	14		11		42	
	12		2		2		2.5		2		8.5	
FEMALE	6	°	2		14	*	2		4		6	
	4		1.5		9		1.5		3		4	
TOTAL	66		12		23		16		5		48	
	10		2		3.5		2.5		1		7	

° 2 =6.01

P 0.025

° 2 =18.93

P 0.001

TABLE 18. Associated Psychiatric Diagnosis

	Personality Disorder		Depression	Neurosis	Schizophrenia	Low I.Q.	Sexual Deviation	Epilepsy	No Psychiatric Diagnosis	
	Non Specific	Aggressive								Hysterical
MALE	No.	7	4	17	13	7	2	5	1	395
	%	14	1.5	3	2.5	1.5	0.5	1		75
FEMALE	No.	1	12	8	4	1	1	1	2	102
	%	11	8	5.5	3	1	1	1	1.5	70
TOTAL	No.	8	16	25	17	8	3	6	3	497
	%	1	2.5	3.5	2.5	1	0.5	1	0.5	74

patients were considered to have an associated psychiatric diagnosis, the vast majority of these being classed as personality disorders. There were no differences in male and female alcoholics in the range and number of these psychiatric diagnoses.

4.9 "Behavioural Disturbances" (Tables 19 to 21)

A half of the male patients and only a quarter of the female patients had had previous offences and this difference is reflected also in the numbers with multiple offences, and a quarter of the male patients had been convicted of these and only 6% of female patients. Both these differences are significant at the less than 0.001 level.

When different behavioural abnormalities are considered however there is a reverse state of affairs. Whereas a third of female patients had attempted suicide at some time during their lives, only a fifth of male patients had done so and this was significant at the less than 0.005 level.

Again a quarter of female patients had abused drugs at some time or other, whereas only one tenth of male patients had done so. Most of the patients were in fact abusing drugs on admission. The differences in drug abuse are evident in relation to barbiturates and minor tranquillisers, but not to amphetamines which were abused by male and female patients in almost equal proportions.

4.10 Alcoholic Withdrawal Signs (Table 22)

TABLE 19. Previous Suicidal Attempts

	No.	%
MALE	95	18
FEMALE	49	33
TOTAL	144	21

$$\chi^2 = 9.51$$

$$P < 0.005$$

TABLE 20. Previous Offences

		Severe	Minor Drinking	Minor Drinking < 2	Driving	Multiple Offences	Nil	Not Known
MALE	No.	21	63	21	19	*132	+180	91
	%	4	12	4	3.5	25.5	34	17
FEMALE	No.	2	17	7	1	*9	+95	17
	%	1	12	5	1	6	64	12
TOTAL	No.	23	80	26	10	141	275	108
	%	3.5	12	4	1.5	21	40.5	16

$$*\chi^2 = 18.13 \quad +\chi^2 = 16.35$$

$$P < 0.001 \quad P < 0.001$$

TABLE 21.1 History of Drug Abuse.

	Barbiturates		Amphetamine		Narcotics		Minor Tranquillizers		Barb.+ Amphet.		Barb.+ Tranquil.		Barb.+ Amphet.+ Tranquil.		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
MALE	21	4	7	1.5	2	0.5	2	0.5	10	2	8	1.5	1	7	58	+ 11
FEMALE	16	10	3	2.5	0		5	3.5	4	3	5	3.5	1	3	37	+ 25
TOTAL	37	5	10	1.5	2	0.5	7	1	14	2	13	2	2	10	95	14

$$\chi^2 = 8.99$$

$$P < 0.005$$

$$+\chi^2 = 13.2$$

$$P < 0.001$$

TABLE 21.2 History of Drug Abuse.

		Total Barbiturate Abuse	Total Amphetamine Abuse	Total Minor Tranquilliser Abuse
MALE	No.	°46	25	+18
	%	9	5	3
FEMALE	No.	°28	11	+14
	%	19	7	9
TOTAL	No.	74	36	32
	%	11	5.5	5

$\chi^2 = 9.39$
P < 0.005

$\chi^2 = 8.24$
P < 0.010

4.10 Alcoholic Withdrawal Signs (Table 22)

It is seen that 40% of patients have no evidence of alcohol withdrawal. This figure rose to nearly 50% of female patients but there was no significant difference compared to males. While more male than female patients suffered from delirium tremens again there was no significant difference. It should be noted that about one third of both male and female patients had clear evidence of alcohol withdrawal.

4.11 Nutritional State (Tables 23 to 25)

There was clinical evidence of nutritional deficiency in 10% of female patients, but only 4% of male patients and this reached statistical significance (Table 23). This difference is reflected in patients with obvious weight loss when one third of female patients gave a history of this as opposed to only 19% of male patients (Table 25). Whereas there was a similar sex difference in those patients who gave a history of poor food intake, this did not reach statistical significance (Table 24). It should be noted that there was a considerably larger number of male patients than female patients in whom these latter two factors were not elicited.

4.12 Complications and Physical Accompaniments of Alcoholism

Neuro-psychiatric complications (Tables 26 to 28)

There was a relatively small number of patients who suffered from the recognised psychiatric complications of alcoholism and so that for comparing differences it should be noted that the number of female patients is very small. There was a tendency for more male than female patients to suffer/

TABLE 22. Withdrawal Signs.

		0	Mild	Moderate	Severe	Delirium Tremens
MALE	No.	202	144	74	26	81
	%	38	27	14	5	15
FEMALE	No.	70	29	23	10	16
	%	47	20	15.5	7	11
TOTAL	No.	272	173	97	36	97
	%	40.5	25.5	14.5	5	14.5

TABLE 23. Clinical Nutritional Abnormalities.

	No.	%
MALE	19	4
FEMALE	15	10
TOTAL	34	5

$$\chi^2 = 9.0$$

$$P < 0.005$$

TABLE 24. Food Intake.

		Poor	Satisfactory	Not Known
MALE	No.	170	197	160
	%	32	37	31
FEMALE	No.	59	70	19
	%	40	47	13
TOTAL	No.	229	267	179
	%	34	39.5	26.5

TABLE 25. Weight.

		Loss	Static	Not Known
MALE	No.	*99	223	205
	%	19	42	39
FEMALE	No.	*45	79	24
	%	30	53	17
TOTAL	No.	144	302	229
	%	21	45	34

$$*\chi^2 = 5.73$$

$$P < 0.025$$

TABLE 26. Psychiatric Complications

		Hallucinosiis	Paranoid	Dementia
MALE	No.	39	22	* 24
	%	7.5	4	4.5
FEMALE	No.	5	3	* 18
	%	3.5	2	12
TOTAL	No.	44	25	42
	%	6.5	4	6

$$*\chi^2 = 9.74$$

$$P < 0.005$$

TABLE 27. Psychological Testing

	Abnormal	Normal	Abnormal as % of Alcoholic	Abnormal as % of Tested Alcoholic
MALE	* 27	* 41	5	40
FEMALE	* 19	* 12	13	61

$$*\chi^2 = 5.8$$

$$P < 0.025$$

TABLE 28. Neurological Complications.

	Male		Female		Total	
	No.	%	No.	%	No.	%
Peripheral Neuropathy	98	18	23	16	121 -	18
Epilepsy	37	7	7	4.5	44 -	6.5
"Rare" Neuro-Psychiatric Disorders	8	2	9	6	17 -	2.5
E.E.G.	6	1.5	5	3.5	11 (of 127)	

TABLE 29. Liver Disease.

	Male		Female		Total	
	No.	%	No.	%	No.	%
Cirrhosis	64	12.5	15	10	79 -	12
"Hepatitis"	88	17	18	12	106 -	17

suffer from alcoholic hallucinosis and alcoholic paranoid psychosis, but this difference did not reach significance. On the other hand there was a larger number of female patients suffering from alcoholic dementia, a difference which did reach statistical significance ($P < 0.005$). This difference is also illustrated in the patients who had an abnormality on formal psychometric assessment. These latter results should be considered in the light of the differences between the numbers of older male and female patients previously noted. When the rarer neuro-psychiatric disorders are considered of the seventeen 10 suffered from Wernicke-Korsakoff syndrome, 5 suffered from choreoathetotic movement disorder and two from hepatic encephalopathy. Five of the 10 patients with Wernicke-Korsakoff syndrome were female. Rather more male patients than female patients had alcoholic epilepsy, whereas more female than males had abnormal electro-encephalograms. It is seen that only 10% of the E.E.G's. performed were in fact abnormal.

Almost 20% of patients had evidence of peripheral neuropathy but there was no significant sex difference despite the previous nutritional differences noted.

Liver disease (Table 29)

The incidence of alcoholic cirrhosis found on clinical and biochemical grounds was 12% with little male-female difference. Rather more, 17%, patients were considered to have acute liver disease but this increase was due to male patients only.

Gastro-intestinal disease (Table 30)

There was a tendency for male patients to suffer more from gastro-intestinal disease, but although 11% of male patients had/

had had gastric operations, and only 4.5% of female patients this difference did not reach statistical significance. Certainly more female than male patients had proven peptic ulcers and this difference did reach statistical significance $P < 0.025$. It is seen how rare pancreatic disease is in alcoholic patients admitted to this Psychiatric Unit.

Anaemia (Table 31)

Twenty per cent of patients were found to be suffering from anaemia and while there were slightly more female patients in proportion to male patients this difference did not reach statistical significance. When the variety of anaemia is considered, almost two-thirds of female patients suffered from iron deficiency anaemia compared to under a half of male patients, but again this difference did not reach statistical significance. Conversely rather more male patients than female patients were considered to have a normo- chromic anaemia. About 10% of both male and female patients clearly suffered from macrocytic anaemias to which some were obviously related to folic acid deficiency, a smaller number than these had obviously haemolytic anaemias. (4 female and 6 male patients).

Respiratory diseases (Table 31)

It is seen from this Table that 11% of patients had respiratory diseases mainly chronic bronchitis, though a few had bronchopneumonia on admission and a further 3.5% had a history of tuberculosis.

Cardiovascular disease (Table 31)

Only 9 male patients had evidence of alcoholic cardiomyopathy. Considerably more patients had an abnormality on electrocardiographic examination, though these abnormalities varied considerably from reports/

TABLE 30. Gastro-Intestinal Disorders.

	Male		Female		Total	
	No.	%	No.	%	No.	%
Gastritis	90	17	20	14	110	17
Gastric Operations	54	11	7	4.5	61	9
Peptic Ulcer	17*	3	13*	9	30	4.5
Pancreatic Disease	3	1	1		4	0.5

* $\chi^2 = 7.47$
 $P = < 0.025$

TABLE 31.

	Male		Female		Total	
	No.	%	No.	%	No.	%
Anaemia	99	19	36	24	135	20
Resp. Diseases (excluding T.B.)	60	11.5	13	9	73	11
T.B.	19	3.5	3	2	22	3.5
Cardiomyopathy	9	1.5	0		9	1
E.C.G. Abn.	90	17	23	15.5	113 (of 272)	

reports of "sinus tachycardia", to "evidence of left ventricular hypertrophy" and "ischaemic changes".

Other Complications

It is seen from Table 32.1 there are a small number of patients who suffered from other conditions which might be considered related to alcoholism. Thus 18 male patients and 1 female patient had evidence on x-ray of previous fractures, usually of rib fractures, some had previous fractured skulls. Two percent of patients had obvious skin diseases of various kinds the commonest being psoriasis. Eleven patients were found to be suffering from diabetes and there were smaller numbers with a variety of conditions. Five male patients had had nephrectomies, three bilateral Dupytren's Contracture and two bilateral parotid swellings. There is no mention of female patients having either Dupytren's Contracture or parotid swelling. Previous venereal infection was only found in 1.5% of patients, 2 patients gave histories of previous syphilis and 1 of previous gonorrhoea. Two other patients had a positive gonococcal complement fixation test, 1 a strongly positive and 1 a weak positive Wasserman reaction.

Number of Complications

Only 12% of patients were found to have no complications whatsoever though previous offences were excluded from this calculation. A further 4% of both male and female patients had only previous suicide as their "complication", and a further 16 patients in all had abused drugs and attempted suicide. There is thus left 36% of patients (Table 32.2) who have either one or two complications/

TABLE 32.1 "Complications"

	Male		Female		
	No.	%	No.	%	
Offences	256	49	36	24	
Previous Suicide	95	18	49	33	$\chi^2 = 9.51$ $P < 0.005$
Anaemia	99	19	36	24	
Peripheral Neuropathy	98	18	23	16	
E.C.G. Abnormality	90	17	23	16	
Gastritis	90	17	20	14	
Hepatitis	88	17	18	12	
Delirium Tremens	81	15	16	11	
Drug Abuse	58	11	37	25	$\chi^2 = 13.22$ $P < 0.001$
Respiratory Disorders (inc.T.B)	79	14.5	16	10	
Cirrhosis	64	12.5	15	10	
Gastric Operations	54	11	7	4.5	
Hallucinosiis	39	7.4	5	3.5	
Dementia	24	4.5	18	12	$\chi^2 = 9.74$ $P < 0.005$
Epilepsy	37	7	7	4.5	
Nutritional Abnormality	19	4	15	10	$\chi^2 = 9.00$ $P < 0.005$
Peptic Ulcer	17	3	13	9	$\chi^2 = 7.47$ $P < 0.025$
Paranoid Psychosis	22	4	3	2	
"Rare" Neuro-Psychiatric	8	2	9	6	
Previous Fractures	18	3	1	1	
Skin Diseases	11	2	4	3	
Diabetes	8	1.5	3	2.5	
Cardiomyopathy	9	1.5	0	0	
Prev. Venereal Disease	7	1.5	1	1	
Pancreatitis	3	1	1	1	

TABLE 32.2 Number of "Complications"

	None	One	Two	Three	Four	Five	Six	Seven	Eight	Nine	Ten
MALE	No.	115	109	94	61	42	22	6	6	1	1
	%	13	21	17	12	8	4	2.5	2.5		
FEMALE	No.	17	29	27	20	12	3	2	4	0	2
	%	12	19	18.5	14	8	2	6	6		
TOTAL	No.	87	147	121	81	54	25	8	10	1	3
	%	12	20.5	18	12.5	8	3.5	3.5	3.5		

complications and nearly half the patients had three or more complications. The four patients who had most complications all suffered from serious nutritional abnormality with associated liver disease, neuro-psychiatric disorder, delirium tremens and cardiovascular abnormality.

4.13 Biochemical Abnormalities (Table 33)

Although it was considered routine for alcoholic patients to have a battery of liver function tests performed, in only two-thirds were serum enzymes estimated. This is partly due to the fact that early in the study these tests were not routinely included and some patients were not in hospital long enough to have blood withdrawn. Over two-fifths of S.G.O.T. levels in male patients who had these estimations performed were found to be abnormal, though only just over a quarter of the levels were abnormal in females. This difference is more marked when S.G.P.T. levels are considered and the difference between 31.5% in male patients and 17.5% in female patients reaches the statistically significant level of $P < 0.025$. This disparity perhaps more clearly shows the differences noted in clinical liver disease between male and female patients which did not reach statistical significance. Ten per cent of all alcoholics were found to have serum protein abnormalities and there was little difference in the two sexes. Relatively few patients had cholesterol abnormalities and these will not be considered again. However it should be noted that two male patients were found to be suffering from Zieve's syndrome with grossly/

TABLE 32. Biochemical Results

	MALE				FEMALE			
	Abnormal	Normal	Abnormal as % of Alcoholics	Abnormal as % of Estimations	Abnormal	Normal	Abnormal as % of Alcoholics	Abnormal as % of Estimations
S.G.O.T.	180	198	28.5	43	29	73	20	28
S.G.P.T.	109	237	21	31.5 °	18	84	12	17.5 °
Protein Abnormality	53	250	10	17.5	18	90	12	17
Cholesterol	18	179	3	9	5	66	3	7

$$^{\circ}\chi^2 = 5.22$$

$$P < 0.025$$

grossly abnormal cholesterol and other serum lipid estimations as well as the other features. These levels in these two patients fell to normal during their period of abstinence in hospital.

4.14 Blood Vitamin Levels (Table 34)

The most obvious finding from these results is that over 10% of all the alcoholics were found to have abnormal whole blood thiamine levels and this was a half of those estimated. Only a very small number of patients had abnormal nicotinic acid levels (1.5% of male patients and 2% of female patients). Of the 16 patients with abnormal Serum B12 levels 8 were considerably raised and 8 were in the borderline range. The differences between the 11% of male patients who had low serum folic acid levels of those estimated compared to the third of female patients was highly significant. ($P < 0.001$) It should be noted that the number of abnormal to normal levels was higher in female than in male patients though this was only significantly so, when serum folic acid was considered.

4.15 Comparison of Ages of Alcoholics with Various Complications (Table 35)

It is noted that for all groups of patients, except for those with peptic ulcer and anaemia, female patients tend to be older than male patients on average. The mean age of alcoholic males is increased in patients with anaemia, delirium tremens, cirrhosis, cardiomyopathy and alcoholic dementia over that for the alcoholics as a whole. These findings are reproduced in female alcoholics who have especially high mean ages in those with delirium tremens, cirrhosis and dementia. All of these differences only just reach statistical significance at the 0.05 level in view/

TABLE 34. Blood Vitamin Levels.

	MALE				FEMALE			
	Abnormal	Normal	Abnormal as % of Alcoholics	Abnormal as % of Estimations	Abnormal	Normal	Abnormal as % of Alcoholics	Abnormal as % of Estimations
Whole blood Thiamine	53	50	10	51	20	18	13.5	52.5
Whole blood Nicotinic acid	8	105	1.5	7	3	30	2	10
Serum B12	10	68	2	13	6	30	4	20
Serum folic Acid	6	48	1	11 *	9	18	6	32 *

* $\chi^2 = 22.13$

P < 0.001

TABLE 35. Ages of Alcoholics with Complications

GROUP	MALE			FEMALE		
	No.	Mean Age	Standard Deviation	No.	Mean Age	Standard Deviation
General	527	43.7	10.65	148	45.42	11.08
Prev. Suicide	95	40.44	11.06	49	42.14	10.47
Anaemia	99	47.29	10.24	37	46.59	10.86
Peripheral Neuropathy	98	45.15	11.07	23	49.87	11.78
E.C.G. Abnormality	90	44.9	10.19	23	47.5	12.61
Gastritis	90	42.47	11.26	20	43.6	13.06
Hepatitis	88	42.72	8.79	18	45.38	11.01
Delirium Tremens	81	45.88	10.18	16	57.75	8.54
Drug Abuse	58	44.62	8.72	36	45.14	11.77
Cirrhosis	64	47.03	10.18	15	55.60	8.97
Gastric Operations	54	45.91	10.32	7	45.57	9.91
Peptic Ulcer	30	45.80	10.18	10	41.9	5.19
"Psychiatric"	74	45.49	11.41	24	51.46	9.81
Hallucinosiis	39	41.88	8.9	5	46.20	9.35
Dementia	24	52.54	9.97	18	53.83	10.09
Paranoid	22	42.65	11.4	3	50.33	6.8
Cardiomyopathy	9	49.0	8.21	0	-	-
Death	49	52.26	8.56	17	54.65	10.08

view of the large standard deviations.

4.16 Comparison of Alcoholics as a whole (general group) with Alcoholics with Various Complications and Male and Female groups compared. (Tables 36 to 40)

When χ^2 tests are performed using various degrees of freedom depending on the number of sub-groups present, some differences become more evident and can thus be easier analysed. These differences are given in the Tables 36 to 39 and the crude figures from which these are derived are shown in Appendix 4.

In Table 36.1 when comparing male and female alcoholics by social class, statistical significance is reached at the $P < 0.01$ level which is produced by a slight increase in classes I and IV females which combine with a certain decrease in class III female patients. A much clearer difference is discovered when male and female cirrhotic patients are compared by social class. Female alcoholics with cirrhosis are seen to derive from classes I and II much more than male patients with the same condition ($P < 0.01$). When male patients are compared for social class between various groups and alcoholics as a whole, it is seen that the only differences which reach statistical significance are found in male patients with anaemia who tend to come from classes I and II and those with gastritis who tend to come from class V.

Concerning civil status male patients with anaemia are seen to come from the widowed and the single compared to a general group and those with gastritis to come from the divorced group. Male and female differences are evident especially in delirium/

TABLE 36. Comparison of Patient Data with Complications.

[Significance of χ^2 Distribution with "n" degrees of Freedom (P values)]

36.1 Male v. Female

	General	Neuropathy	Delirium Tremens	"Psychiatric"	Anaemia	Cirrhosis
Civil Status		0.01	0.005	0.005	0.01	
Social Status	0.01					0.001

36.2 Male, General v. Groups

	Anaemia	Gastritis
Civil Status	0.001	0.005
Social State	0.001	0.001
Religion	0.005	0.001

delirium tremens and "psychiatric" complications when there is found to be an increase in the female widowed alcoholics and a decrease in female single alcoholics with these conditions. Similar differences are seen though at a less significant statistical level in female patients with neuropathy and anaemia compared to male patients with the same condition.

It is noted that for religious affiliation significantly more male patients with gastritis than in the general group stated that they had no religion.

When the various data concerning hospital admission and discharge are considered, it is seen that there are some clear differences in the various complications. Thus male alcoholics with delirium tremens are more likely to be admitted as emergencies than other male alcoholics and arrive from more sources than female patients with delirium tremens who are only referred from either their general practitioner, or from other hospitals or wards in the Southern General Hospital. This latter point also differentiates female patients with delirium tremens from other female alcoholics. The difference noted in Table 10 concerning the means of referral between the two sexes becomes highly statistically significant ($P < 0.001$) when it is cumulatively assessed. The difference is marked when patients with a history of previous suicide are considered, female patients are then more likely to be admitted via their general practitioners than male patients who appear more likely to refer themselves. Female patients with anaemia are referred from other hospitals in comparison with male patients. In general, as is shown in Table 11, female patients tend to stay longer in/

TABLE 37 Comparison of Nosocomial Data with Complications
 [Significance of χ^2 distribution with "n" Degrees of Freedom (P values)]

37.1 Male v. Female

	General	Suicide	Neuropathy	Delirium Tremens	"Psychiatric"	Anaemia	Gastritis	Cirrhosis
Means of Referral	0.001	0.005		0.001		0.01		
Length of Admission	0.001		0.01				0.005	0.005
No. of Admissions	0.001	0.005	0.005		0.01	0.001		
Discharge	0.05							

37.2 General v. Complications

	Suicide	Neuropathy	Delirium Tremens	Anaemia	Gastritis	Cirrhosis
Mode of Admission			0.001			
Means of Referral	0.01		FO.005		0.001	0.010
Length of Admission		0.005		0.001	0.005	
No. of Admissions		0.001		FO.025	0.010	
Discharge				FO.025	0.001	

(The only significant difference in female patients are marked F, the others refer to male patients)

in hospital than male patients with alcoholism. This tendency is especially marked in female patients with gastritis, cirrhosis, and neuropathy when compared with similar male groups. Male patients with neuropathy and anaemia are also more likely to stay in hospital longer than the male alcoholics as a whole, whereas those with gastritis stay a shorter time. While it is clear that female alcoholics were admitted more often during the four year period than male alcoholics, this is also true of female patients with anaemia and previous suicide attempts as well as neuropathy and less clearly so than those with "psychiatric " complications.

Male patients with neuropathy tend to be admitted more than other alcoholics and those with alcoholic gastritis tend only to be admitted once. Female patients with anaemia are more likely to be re-admitted than the general group of female alcoholics.

It has already been shown (Table 12) that male patients tend to discharge themselves or to drink in the ward more often than female patients and this would appear to be especially true in patients with alcoholic gastritis as compared to other male alcoholics. On the other hand female patients with anaemia tend to stay in hospital for the full course of treatment recommended by the medical staff.

The various factors considered under drinking history are compared with the complications in Table 38. There are marked differences between male and female alcoholic patients which have already been seen in Tables 13 to 17, male alcoholics tend to drink more whisky and less "wine" which includes/

includes sherry and less of other spirits, for example, gin, vodka or brandy, they have drunk for longer and take in more alcohol daily than female alcoholics. When the various groups are considered female alcoholic patients drink more "wine" and "other spirits than whisky"; who have previously attempted suicide, who suffer from anaemia; who have alcoholic gastritis, than the similar male alcoholic groups. The amount of alcohol consumed daily is so much less in female patients than male patients that most of the various groups of complications have a similar difference. Those with a history of previous suicide, "psychiatric complications" and anaemia reach the $P < 0.001$ level. Those with neuropathy reach the 0.005 level, those with delirium tremens and cirrhosis the 0.01 level and those with gastritis the 0.025 level. There is no difference in the male and female patients who have had previous gastric operations in the amount of alcohol they drink. When male alcoholics are compared to the various groups, those with neuropathy and gastritis drink more ($P < 0.001$) as do those with anaemia ($P < 0.005$) and cirrhosis ($P = 0.025$). The differences are not so marked in female patients, those with anaemia tend to drink more ($P < 0.01$) and those with previous suicide similarly ($P = 0.025$). Very similar findings are obtained when the length of excess drinking is considered between male and female patients except that there is no difference in the length of drinking in the groups with delirium tremens, but the female patients with gastric operations tend to have drunk for a lesser time than male patients with the same condition. Male patients with neuropathy/

TABLE 38. Comparison of Drinking History with Complications

Significance of χ^2 distribution with "n" Degrees of Freedom (P values)

38.1 Male v. Female

	General	Suicide	Neuropathy	Delirium Tremens	"Psychiatric"	Anaemia	Gastritis	Gastric Operations	Cirrhosis
Type of Alcohol	0.001	0.001				0.001	0.005		
Amount of Alcohol	0.001	0.001	0.005	0.01	0.001	0.001	0.025		0.01
Length of Excess Drinking	0.001	0.001	0.005		0.001	0.001	0.025	0.01	0.005

38.2 General v. Groups (F = female)

	Suicide	Neuropathy	Anaemia	Gastritis	Cirrhosis
Type of Alcohol	F0.01	0.025	F0.01 0.01	0.025	0.005
Amount of Alcohol	F0.025	0.001	F0.01 0.005	0.001	0.025
Length of Excess Drinking		0.001	F0.025	0.005	0.005
Bout Drinking		0.025	0.005	0.001	

neuropathy, gastritis and cirrhosis all tend to have drunk for longer than the male alcoholic patients as a whole. Similarly female patients with anaemia have drunk for longer than female alcoholics as a whole. Bout drinking is shown to be significantly increased in male patients with gastritis and decreased in those with anaemia and neuropathy compared to male alcoholics as a whole.

The female patients in this series are more likely to have poor food intake and evidence of weight loss than male alcoholic patients. This difference is especially evident in female patients with previous suicide attempts and in those with anaemia compared to the corresponding male groups. When male patients alone are considered food intake tends to be poorer in those with anaemia, neuropathy, cirrhosis and gastritis and weight loss more evident in those with neuropathy, gastritis and cirrhosis compared to the male alcoholics as a whole. Whereas in female patients the only comparison reaching statistical significance is that for weight loss which is more evident in female patients with anaemia.

It is seen from Table 39 that whereas individually there appeared to be no difference when the possible aetiological psychiatric diagnosis was considered in male and female alcoholics (Table 18) when the multiple differences are considered this does reach statistical significance. These differences are also seen in female alcoholics who have previously attempted suicide and in those with gastritis and previous gastric operations all of whom are more likely to have had some associated psychiatric diagnosis, especially of personality disorder. Male patients who have/

TABLE 29 Comparison of Factors with Complications
 [Significance of χ^2 distribution with "n" Degrees of Freedom (P values)]

29.1 Male v. Female

	General	Suicide	Neuropathy	Delirium Tremens	Anaemia	Gastritis	Gastric Operations	Cirrhosis
"Food" Intake	0.001							
"Weight"	0.001	0.001			0.025			
Aetiological Psych. Diagnosis	0.001	0.001				0.001	0.010	
"Offences"	0.001	0.001	0.001	0.005	0.01			0.010

29.2 General v. Groups (F = female)

	Suicide	Neuropathy	Anaemia	Gastritis	Cirrhosis
"Food" Intake		0.005	0.001	0.025	0.025
"Weight"		0.005	0.025	0.005	0.010
Aetiological Psych. Diagnosis	0.005	0.001	0.025	0.001	0.001
"Offences"		0.010	0.025	0.001	

have attempted suicide and those with gastritis are more likely to have had a diagnosis of personality disorder or other psychiatric condition than the male alcoholic group as a whole. Conversely those with neuropathy and cirrhosis are less likely to have had a psychiatric diagnosis. In female patients, those with a previous suicide are more likely, and those with anaemia less likely to have had a psychiatric diagnosis given to them.

Male alcoholics are much more likely to have had previous offences than female alcoholics, except for those with gastritis and gastric operations. And when male alcoholics are considered separately those with gastritis are more likely to have had previous offences than alcoholics as a whole and those with neuropathy and anaemia are less likely to have had offences.

4.17 Multiple Discriminate Analysis to determine the differences between Male and Female Alcoholics. (Table 40)

The multiple discriminate analysis determines the various factors which may be used to differentiate male and female alcoholics in the order of importance. The analysis showed that the only two variables not necessary in this differentiation were religion and gastritis. However many of the other factors did not reach a high degree of differentiation, which can be considered to be an "F value" above two. Twenty one of the 41 variables reached this level as shown in Table 40. It is seen that the length of time of excess drinking is by far the most important discriminating factor (females drinking for considerably less time than males).

Age/

TABLE 40.Summary of Results of Multivariate AnalysisDifferentiating Male and Female Alcoholic Patients.

Group	"F Value"
1. Length of Excess Drinking.	89.22
2. Age.	24.20
3. Weight.	18.56
4. Previous Suicidal attempt.	18.21
5. Main Alcoholic Beverage.	11.47
6. Amount of Alcohol.	12.58
7. "Rare" Neuro-psychiatric Disorders.	12.66
8. Number of Admissions.	9.21
9. Gastric Operations.	9.45
10. Length of Stay.	7.95
11. Previous Admissions.	5.68
12. Epilepsy.	5.22
13. Nutritional Abnormality.	4.77
14. Drug Abuse.	3.98
15. Respiratory Disorders.	3.16
16. E.E.G. Abnormality.	2.78
17. Hepatitis.	2.27
18. Mode of Admission.	2.55
19. Hallucinosiis.	2.62
20. Dementia.	1.85
21. Withdrawal.	2.06

Age is seen to be another factor, females tending to be older. Similarly more females have lost weight on admission than male alcoholics, and more have previously attempted suicide. The type and amount of alcohol intake are important in this differentiation (females tending to drink more "wine" and drinking considerably less than males). The incidence of "rare" psychiatric disorder is higher in female patients, as are the incidence of nutritional abnormalities, drug abuse and alcoholic dementia. Females are also differentiated from the male patients by having a greater number of admissions during the four year period, being admitted for a longer time and having fewer previous admissions. They also had fewer gastric operations, alcoholic epilepsy, respiratory disorders, hepatitis, alcoholic hallucinosis and a tendency to have less severe withdrawal signs.

4.18 Inter-Correlations of the Complications of Alcoholism. (Tables 41 and 42)

Correlation coefficients for various factors with values more than 0.2 are shown in Table 41 and for nine of the complications with correlation coefficients of more than 0.15 in Table 42. Some of these results would not appear to require much explanation, such as age and length of excess drinking, food intake and weight loss, weight loss and nutritional abnormality and E.C.G. abnormality and cardiomyopathy. In particular the correlations between anaemia and cirrhosis, anaemia and delirium tremens, cirrhosis and neuropathy, cirrhosis and delirium tremens, cirrhosis and cardiomyopathy, cirrhosis and E.C.G. abnormality, neuropathy and delirium tremens, neuropathy and dementia, and epilepsy and delirium tremens.

TABLE 41. Characteristics and Complications of Alcoholic Patients within Groups Correlation. $> \pm 0.2$

Age

Time of excess drinking	0.321
Mode of discharge	0.223
Dementia	0.217

Length of Admission

Dementia	- 0.212
----------	---------

Mode of Admission

Means of Referral	- 0.360
Delirium Tremens	- 0.233

Length of Excess Drinking

Previous Admission	- 0.220
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Food Intake

Weight	0.611
--------	-------

Weight

Nutrition Abnormality	0.263
-----------------------	-------

Anaemia

Delirium Tremens	- 0.202
Cirrhosis	0.241

Nutritional Abnormality

"Rare" Neuro-psychiatric Disorder	0.211
-----------------------------------	-------

Cirrhosis

Neuropathy	0.241
Delirium Tremens	- 0.360
E.C.G. Abnormality	0.210
Cardiomyopathy	0.280

Neuropathy/

TABLE 41 continued/Neuropathy

Delirium Tremens	0.225
Dementia	0.243
Cirrhosis	0.241

Delirium Tremens

Mode of Admission	0.233
Anaemia	0.202
Cirrhosis	0.260
Neuropathy	0.225
Epilepsy	0.266

Epilepsy

Delirium Tremens	0.267
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"Rare" Nutritional Disorders

Dementia	0.346
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Hallucinosiis

Paranoid	0.232
----------	-------

E.C.G. Abnormality

Cardiomyopathy	0.224
----------------	-------

TABLE 42. Within Group Correlation of Complications. $> \pm 0.15$

* $> \pm 0.2$

Suicide

Age	0.170
Means of Referral	- 0.162
No. of Admissions	- 0.178
Social Class	- 0.173
Hallucinosiis	0.181

Anaemia

Age	- 0.151
Nutrition	0.168
* Cirrhosis	0.241
Neuropathy	0.151
* Delirium Tremens	- 0.202

Neuropathy

Anaemia	0.151
* Cirrhosis	0.241
"Rare" Neuro-psych. Disorder	0.177
* Delirium Tremens	0.225
* Dementia	0.243

Cirrhosis

Age	- 0.157
Length of Excess Drinking	- 0.163
* Anaemia	0.241
* Neuropathy	0.241
* Delirium Tremens	- 0.260
Dementia	0.185
* E.C.G. Abnormality	0.210
* Cardiomyopathy	0.280
"Rare" Neuro-psych. Disorder	0.154

Delirium Tremens/

TABLE 42. continued/

Delirium Tremens

Age	0.159
* Mode of Admission	- 0.233
Offences	0.168
* Anaemia	- 0.202
Nutrition	- 0.150
* Cirrhosis	- 0.260
Hepatitis	- 0.193
* Neuropathy	- 0.225
* Epilepsy	- 0.266
E.C.G. Abnormality	- 0.167

Hallucinosiis

* Paranoid	0.232
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Dementia

* Age	- 0.217
* Length of Excess Drinking	- 0.212
Nutritional Abnormality	0.156
Cirrhosis	0.186
* Neuropathy	0.243
* "Rare" neuro-psych. Disorder	0.346

Cardiomyopathy

* Cirrhosis	0.280
* E.C.G. Abnormality	0.224

E.C.G. Abnormality

* Cirrhosis	0.210
Delirium Tremens	- 0.167
* Cardiomyopathy	0.224

4.19 Biochemical Results. (Table 43)

It is seen that high values of the serum enzymes S.G.P.T. and S.G.O.T. are, as to be expected, found in cirrhosis and hepatitis, but are also observed in delirium tremens when compared to the patients with no withdrawal signs, and in alcoholic epilepsy and gastritis. S.G.O.T. levels are also raised in alcoholic hallucinosis when compared to other alcoholics. When serum protein abnormalities are considered, these are especially found in cirrhosis, delirium tremens, neuropathy, anaemia and the "rare" neuro-psychiatric disorders. Abnormal results are also found in alcoholic epilepsy, E.C.G. abnormality, associated with poor food intake and with clinical malnutrition ($P < 0.01$) and in alcoholic dementia and E.E.G. abnormality ($P < 0.05$).

4.20 Blood Vitamin Results (Tables 44 and 45)

Whole blood thiamine levels are found to be more abnormal in alcoholics who drink wine as opposed to other alcoholic beverages ($P < 0.001$) and in delirium tremens ($P < 0.01$), neuropathy, alcoholic dementia, cirrhosis, anaemia and associated with weight loss, ($P < 0.05$). Only one normal whole blood thiamine level was discovered from 8 patients over the age of 65 and only 3 were normal out of 11 over the age of 60. There was a close relationship with the "rare" neuro-psychiatric disorders, alcoholic epilepsy and E.E.G. abnormalities though these numbers were very small. When mean levels are considered, those patients with delirium tremens are lowest, but alcoholic dementia and alcoholic hallucinosis were also low. Diagram 5 shows the clear relationship that occurs with whole blood thiamine levels and withdrawal signs. As the signs of alcohol withdrawal increase the mean whole blood thiamine level falls. An analysis of variance/

TABLE 43. Biochemical Correlations (comparing abnormal and normal results)TABLE 43.1. S.G.P.T.Cirrhosis and Hepatitis $P < 0.001$

	Abn.	Normal	
Withdrawal	26	142	$\chi^2 = 41.10$
D.T's.	38	29	$P < 0.001$

	Abn.	Normal	
Epilepsy	22	10	$\chi^2 = 28.02$
No Epilepsy	104	311	$P < 0.001$

	Abn.	Normal	
Gastritis	32	49	$\chi^2 = 6.26$
No Gastritis	94	272	$P < 0.010$

TABLE 43.2 S.G.O.T.

Cirrhosis and Hepatitis $P < 0.001$

	Abn.	Normal	
Withdrawal	38	181	$\chi^2 = 32.9$
D.T's.	47	21	$P < 0.001$

	Abn.	Normal	
Epilepsy	24	154	$\chi^2 = 18.00$
No Epilepsy	8	263	$P < 0.001$

	Abn.	Normal	
Gastritis	45	38	$\chi^2 = 9.03$
No Gastritis	133	233	$P < 0.005$

	Abn.	Normal	
Hallucinations	7	171	$\chi^2 = 6.12$
No. Halluc.	28	243	$P < 0.010$

TABLE 43.3 Serum Protein Abnormalities

Correlations. Abn. v. Normal Results.

	χ^2	P <
Cirrhosis	88.46	0.001
Delirium Tremens	24.63	0.001
Neuropathy	13.86	0.001
Anaemia	13.02	0.001
"Rare"	8.58	0.005
Epilepsy	6.39	0.010
E.C.G.	5.59	0.010
Poor Food Intake	5.17	0.010
Nutritional	5.15	0.010
Dementia	4.62	0.050
E.E.G.	4.35	0.050

TABLE 44. Whole Blood ThiamineTABLE 44.1 Whole Blood Thiamine CorrelationsAbnormal v. Normal Levels

	χ^2	P <
"Wine" with other Alcohol	11.27	0.001
Delirium Tremens with nil With.	6.83	0.010
Neuropathy	4.78	0.050
Dementia	4.78	0.050
Cirrhosis	4.75	0.050
Weight Loss	4.75	0.050
Anaemia	4.6	0.050

TABLE 44.2 Whole Blood Thiamine: Mean Levels

Group	Number	Mean Level μ G/ml.
<u>Control</u>	36	20.4
<u>Alcoholics</u>		
No Complications	23	22.6
No Withdrawal Signs	48	21.8
Mild Withdrawal Signs	29	19.5
Moderate Withdrawal Signs	23	17.8
Severe Withdrawal Signs	9	17.9
Delirium Tremens	29	14.7
Peripheral Neuropathy	31	17.7
Cirrhosis	23	19.0
"Hepatitis"	23	18.0
Alcoholic Paranoia	7	18.4
Alcoholic Dementia	15	16.4
Alcoholic Hallucinosi	9	16.3

FIGURE 5.

**RELATIONSHIP OF WHOLE BLOOD THIAMINE LEVEL
TO ALCOHOL WITHDRAWAL SIGNS**

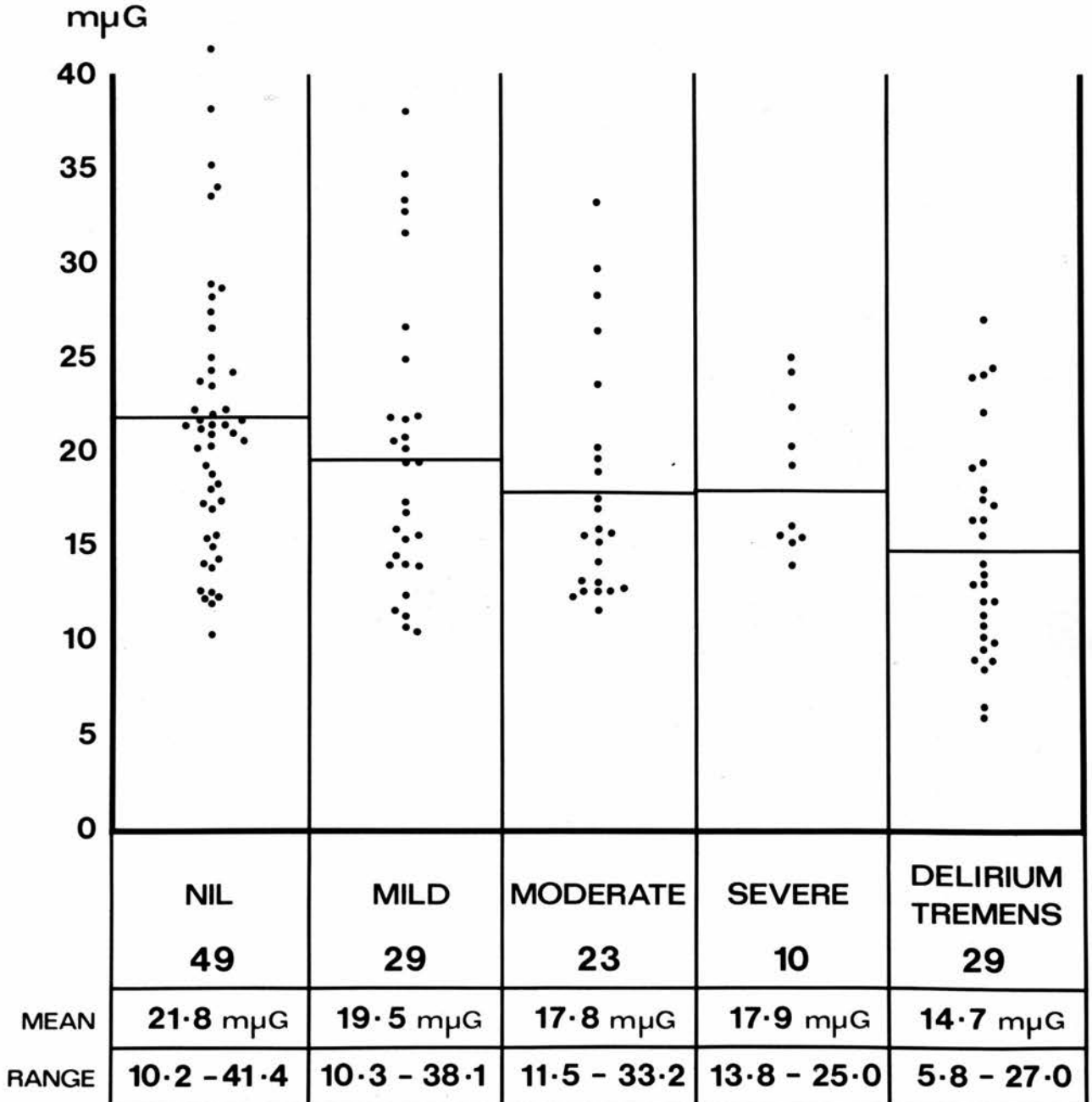


TABLE 45

Serum Folic Acid and Whole Blood Nicotinic Acid Correlations
(Abnormal and Normal Levels)

<u>Serum Folic Acid</u>	χ^2	P <
"Wine" v. Other alcohol	5.99	0.025
Delirium Tremens	3.98	0.050
<u>Whole Blood Nicotinic Acid</u>		
Anaemia	11.4	0.001
Dementia	4.94	0.05

TABLE 46. Prognosis

TABLE 47.

Correlations with Prognosis

		Poor Prognosis		Better Prognosis	
		χ^2	P <	χ^2	P <
Social Class I & II v. V		4.04	0.050	4.12	0.050
Amount of Alcohol: <149G v. >250G/day				11.25	0.001
Length of Excess Drinking <1 yr. v. >20 yrs.		7.76	0.010	4.13	0.050
<u>Offences</u>	Multiple v. No Offences	12.69	0.001	8.9	0.010
	Offences v. No Offences	12.45	0.001	6.29	0.025
Discharge: Medical v. Non-Medical		5.94	0.025	10.36	0.005
Personality Disorder: Absent v. Present				4.59	0.007

variance performed on these results shows a high degree of correlation ($P < 0.001$).

Serum folic acid levels are especially abnormal in wine drinkers and in those patients with delirium tremens, epilepsy and the "rare" neuro-psychiatric disorders. Whole blood nicotinic acid levels are low in anaemia and in dementia. There were so few low levels of serum vitamin B12 that it was not possible to show any obvious relationships.

4.21 Prognosis (Tables 46 and 47)

These results show that almost 10% of the patients were dead within 7½ years, almost 10% were not able to be traced, 20% were classed as worse, 30% had no change, almost 30% could be considered improved. There was very little difference when male and female patients were compared. While rather more female patients were considered to be "cured" than male patients, fewer were "improved", so that the numbers of male and female patients who were "better" were very similar. More female patients were "not traced" than male patients and this rather surprisingly was especially so for a few elderly women who were originally admitted in delirium tremens and who had certainly not died in Scotland during the follow-up period.

When the various factors studied were correlated with prognosis (Table 47) there was found to be few which reached significance. A better prognosis was discovered in those patients in social classes I and II compared to social class V; who drank less than 149G of alcohol daily, as opposed to those who drank more than 250 G. of alcohol daily; who had been drinking for less than one year when compared to those drinking for longer than 20 years; with no offences as opposed to those with offences and especially with multiple offences; who managed to stay in the ward to receive the treatment course compared/

TABLE 46. Prognosis.

	Dead	Worse	I.S.Q.	Imp.	Cure	Still I.P.	N.T.
MALE	49 9.5	109 21	172 32	99 19	45 9	3 0.5	50 9.5
FEMALE	17 11	29 20	41 27	20 13.5	20 13.5	2 1.5	19 13
TOTAL	66 9.5	138 21	213 31.5	119 17.5	65 9.5	5 1.0	69 10
				27			

compared to those who did not, and to patients without personality disorder. Conversely a poor prognosis was associated with a longer drinking history, previous offences, especially multiple ones, and those who discharged themselves from the ward or who drank in the ward and were thus discharged.

4.22 Causes of Death in Alcoholics. (Table 48)

Table 48 lists the main causes of death in the 66 patients who were found to have died in the follow-up period. As already pointed out it is possible that a few patients who had died during the last year of the study, but who had previously been traced, may have been missed.

It is seen that while 6 of the 49 male deaths occurred during an admission period in the four years of the study, no female patient died as an in-patient in this time. Other differences were also found, whereas only 2 of the 49 male deaths were apparently from suicide, 6 of the 17 female deaths were clearly from this cause. Conversely there were more of the male deaths attributable to liver disease. When the various complications are correlated with the patients who died, the only ones that reach statistical significance are cirrhosis and anaemia ($P < 0.025$). However this significance disappears when those patients who died during an admission period in the study are excluded. Those patients who were addicted to barbiturate drugs have a greater chance of dying in the follow-up period ($P < 0.05$). When male and female patients are compared for previous suicide attempts, female patients who have attempted suicide have a much higher risk of dying in the $7\frac{1}{2}$ year period ($P < 0.001$). More of the females died within 18 months of discharge from hospital and similarly more of the female deaths could be directly or indirectly attributable to the effects of alcohol. However, these differences are eliminated/

TABLE 48 Main Cause of Death in Order of FrequencyMale Alcoholics (49)

Cirrhosis	11
Coronary Thrombosis	10
Respiratory Diseases (Including T.B.)	8
Carcinoma of Bronchus	4
Cerebral Thrombosis	3
Delirium Tremens	2
Hypertension	2
Alcohol Poisoning	1
Malnutrition	1
Suicide by Drowning	1
Drug Overdose	1
Fracture of Skull (Accid.)	1
Carcinoma of Epiglottis	1
Diabetes Mellitus	1
Subarachnoid Haemorrhage	1
Bilateral Pyelonephritis and Hypertension	1
	<hr/>
	49

6 died as in-patients in series.

14 of 43 died within 18 months of discharge.

Female Alcoholics (17)

Drug Overdose	6
Hepatic	2
"Found Dead" - Alcohol Poisoning	1
Malnutrition	1
?Cardiac Failure	1
Burnt in Fire	1
Coronary Thrombosis	1
Bronchitis + Pneumonia	1
Cerebral Thrombosis	1
Carcinoma of Colon	1
Pulmonary Embolism in Childbirth	1
	<hr/>
	17

11 of 17 died within 18 months of discharge.

eliminated when deaths from drug overdose are excluded.

5. DISCUSSION

5.1 Demographic Features

It is clear that to enable a complete, final assessment of the complications and associated physical illnesses of a group of alcoholics studied, comparison with other studies of alcoholic patients from a demographic point of view is necessary. Only in this way is it possible to assess whether data from this study could be applicable to alcoholic in-patients either in Scotland or elsewhere or even to alcoholics as a whole. Thus, on studying the paper of Fennelly et al (1964) one would imagine that there is a very large incidence of nutritional abnormality in alcoholics in the United States of America, this is dispelled when taken in conjunction with the paper by Figueroa et al (1953) where in a very large series of alcoholic in-patients to a mental hospital, there was found to be a very low incidence of nutritional disorder.

The main comparisons are illustrated in Tables 49 to 53, where previous applicable Scottish studies are compared as well as the relevant figures obtained by Moss and Beresford-Davies (1967) for their assessment of the alcoholic population of the county of Cambridge and those of Wilkinson et al (1971) from Melbourne, which is the only other large study on the physical complications of alcoholism.

Table 49 shows the social data from various reports, and figures for the 1966 sample census have been included by calculating the appropriate figures from the results for Glasgow and Lanarkshire. It is seen that there is, as with other studies, an excess of social classes I, II and V in the male alcoholic in-patients and

a/

TABLE 42. Social Class of Alcoholics from various Sources expressed as %.

	MALE						FEMALE				
	PMK	Vallance 1965	Sclare 1970	McCance Kingsseat 1969	Clas. & Lenark. Census 1966	Moss and Beresford Davies. England	Wilkinson et al 1971 Australia	PMK	Sclare 1970	Moss + B. Dav. England	Wilk. et al Australia
I	6	5.9	2	11	3	8.3	8.9	9	2	21.8	10.3
II	15	29.4	6		7	18.1	8.9	14	6	37.9	3.4
III	30	38.2	58	30	57	28.2	14.0	24	42	12.6	25.7
IV	24	4.4	8	38	17	26.2	15.6	28	14	19.5	4.0
V	24	22.1	18		13	19.1	51.6	24	20	8.0	55.4

TABLE 50. Religion of Glasgow Alcoholics (%)

	MALE		FEMALE	
	PMK	Sclare 1970	PMK	Sclare 1970
Prot.	67	58	66	56
R.C.	31	42	33	44

a consequent reduction in class III over the general population. This is exaggerated possibly in the present series as the population for Glasgow and Lanarkshire will contain a lower percentage of social classes I and II than some of the surrounding areas from which part of the population of the Southern general Hospital Psychiatric Unit accepts patients. It is also obvious that more classes I and II patients would attempt to obtain admission to the University Department of Psychological Medicine than their local mental hospital. This disparity has been commented on by McCance (1969) and he illustrates it by showing social class difference in two Aberdeen mental hospitals, one of which accepts patients from the county of Aberdeen and the other from Aberdeen City. His figures for Kingseat Hospital, accepting the patients from Aberdeen City, are included as these are more relevant to the present study. There is some degree of disparity between the figures from the present study and those of Vallance (1965) from the same Unit, but obtained in 1960. During this period there was a further consultant appointed to the Unit and a total change of junior staff. It is possible that there is a trend for general practitioners to ask for admission of a different group of patients. Rather surprisingly the present data for male patients is nearest in pattern to that of Moss and Beresford Davies whose population from the mainly rural county of Cambridge could hardly be more different than that for Glasgow. The most important comparison is the most widely disparate, in that there were many more social class V patients in the Melbourne study.

As/

As far as females are concerned there is a much less extensive literature. Moss and Beresford Davies found a higher social class in female alcoholics from Cambridgeshire than either Sclare, or the present study from Glasgow and there is an increased incidence of class V female patients in Melbourne.

When religious affiliation is considered, only Sclare's figures are applicable (Table 50). The differences obtained are probably due to local factors, as the area near to the Eastern District General Hospital, to which Sclare admits patients, contains a higher Roman Catholic population than the area surrounding the Southern General Hospital. While it is difficult to obtain figures for religious population by age, those for the Roman Catholic population of Glasgow and Dunbartonshire derived from the Catholic Directory for Scotland, would suggest that the figures obtained by Sclare and myself are similar to the general distribution.

Comparison of civil status is seen in Table 51. There is a higher incidence of divorced male alcoholics in the present series compared to the 1960 series of Vallance and to the figures of Moss and Beresford Davies. Both Sclare and Moss and Beresford Davies found a larger number of single men among their alcoholics. As far as female alcoholic patients are concerned there were more widowed and divorced patients than either Sclare or Moss and Beresford Davies found. They considered that bereavement was not a precipitating factor in female alcoholics whereas these figures would suggest the reverse.

When the ages of the patients are studied (Tables 52 and 53) it is seen that the mean age of Sclare's patients are younger than any of the other compared studies. This is brought out when the groups are broken down more fully, so that it is obvious that/

that Sclare admitted a younger age group of patient, which may account for his increased incidence of single males.

The age distribution in the present series is very similar to most of the other studies of other alcoholic in-patients in so far as it shows a near normal distribution around a mean age in the middle forties which is slightly higher in females than in males. This has been employed by Moss and Beresford Davies as illustrating that alcoholism is multifactorial in aetiology. Smith and Sclare (1964) showed a remarkable drop in the number of male alcoholics over the age of 50 and suggested that this might be due to either 1) alcoholics may drink themselves to death before the age of 50, 2) after the age of 50 they may be more likely to be admitted to medical and surgical wards, 3) the social pressures to seek help for their drinking habits may decrease after the age of 50 and 4) there may be an increase in the number of patients who remit after the age of 50.

There was not this great decrease in patients from the age of 50 onwards in the present series. However, nor was there any great increase in death rate under the age of 50, or any evidence that patients remit more over the age of 50, perhaps all the factors indicated by Smith and Sclare may play a part.

Thus the demographic data on the alcoholic patients in the present series has similarities to many of the other studies on alcoholic in-patients. There is an increase in social classes I, II and V and in the widowed and divorced compared to the population at risk. There is a tendency for more female alcoholics to be married when compared to male alcoholics. The age range is also very similar to that found in other surveys. The differences in social class which reflect local admission/

TABLE 51. Civil State in Various Studies (as %)

	MALE				FEMALE		
	PWK	Vallance	Sclare	Moss and Beresford Davies..	PWK	Sclare	Moss and Beresford Davies..
Married	54	54.3	54	61.7	57	64	71.1
Single	14	16.2	24	28.7	10	16	12.5
Widowed	6	7.4	6	3.6	13	6	10.6
Divorced	11	5.9		5.9	10		5.8
Separated	14	16.2	16	-	10	14	-

TABLE 52. Mean Ages in Different Studies

	PWK	Vallance	Sclare	Moss and Beresford Davies.	Wilkinson et al
MALE	43.7 yr. ±10.65	44.0 ±9.6	40.5	44.3 ±13.8	44.7 ±9.9
FEMALE	45.42 ±11.08	-	41.2	47.0 ± 15.7	48.3 ±9.9

TABLE 53. Ages of Glasgow Alcoholics Compared (%)

MALE	-29	-39	-49	-59	≥60
PMK	9	25	37	22	8
Sclare	20	18	42	16	4
FEMALE					
PMK	4.5	+ 20	35	* 28	9.5
Sclare	12	+ 38	35	* 6	10

$\chi^2=4.88$ $\chi^2=7.87$ $\chi^2=17.15$
 $P<0.05$ $P<0.001$ $P<0.001$

TABLE 54. Duration of Alcoholism in Scottish Studies (%)

MALE	0-1	-2	-5	-10	-20	20	NK
PMK	2	3	14	18	29	34	1
Vallance	1.5	16.2	20.6	38.2	23.5	-	-
Sclare		24	18	22	22	14	
McCance Kingsseat	9	22	69	-	-	-	-
FEMALE							
PMK	7	14	28	24	18	9	1
Sclare		66	12	16	2	4	

admission and treatment policies are much more obvious when patients in Australia and U.S.A. are considered, there many of the published papers include more of class V or the "Skid Row" type of alcoholic than in most of the series from Great Britain.

5.2. Nosocomial Data

Over half the patients were admitted as emergencies thus indicating that it would be relatively difficult to have a very rigid admission policy. While over half the patients stayed less than 3 weeks and over 10% stayed less than one week, most of these patients discharged themselves or drank while in the ward. Thus a quarter of all the patients did not even persist with the course of treatment. Yet a fifth of all the patients had to be re-admitted during the four year period, these findings confirming Sclare's suggestion that the patients tend to use the hospital unit in Glasgow as a "port of call during a storm" and not necessarily apparently have any serious therapeutic aims. This is confirmed by the fact that for only just over half of the patients was it their first psychiatric admission, many having been in other psychiatric units before. However, over 80% were admitted to the Southern General Hospital Psychiatric Unit for the first time. Thus in Glasgow at least there appears to be a certain amount of shuttling around from one hospital unit to another obviously using a different "port of call" with each emergency.

5.3. Drinking History

It is hardly surprising that whisky is the preferred type/

type of beverage for Scottish alcoholics. From Edinburgh Ritson (1968) found that 71% of his male patients preferred whisky and from Glasgow, Sclare (1970) showed that 60% of his drank whisky, similarly 70% of the present series of male patients consumed whisky. In both these Glasgow surveys however, wine was consumed by about 40% of patients, the main difference being that of those admitted to the Eastern District Hospital, 40% also drank beer compared to only 20% of those admitted to the Southern General Hospital. The figures for female patients in Glasgow are similar though more of the present series took "wine" compared to the survey quoted by Sclare. However, in Melbourne both male and female alcoholics studied by Wilkinson et al (1971) preferred beer. So that whereas in the present study 9% of men and 7% of women admitted to taking beer, the corresponding figures for Melbourne were 90% and 70%.

The mean daily intake for alcoholic men in the present survey was approximately 293 G. of alcohol (this is about 1 bottle of whisky or other spirits) and for women approximately 150 G. of alcohol (which is the equivalent of just over a bottle of fortified wine). The equivalent figures from Melbourne were 265 ± 110 G. and 170 ± 65 G. respectively. In view of the difficulties in obtaining accurate alcoholic intakes from patients these differences would hardly be significant, though it is possible that as beer was by far the greatest type of alcohol consumed in Melbourne the total alcohol would be likely to be less. When length of alcoholism is considered, the mean for men is 16.2 years and for women 9.9 years, though/

though again it must be stressed how difficult these figures are to obtain accurately. It is seen from Table 54 that there is a tendency for the present series to have a longer drinking history than other Scottish studies. However Wilkinson's survey in Melbourne found that males there drank for 18.8 ± 8.1 years on average, and this is remarkably similar to Olin's series of "Skid Row" alcoholics in Toronto which was 18.7 years. The Melbourne female alcoholics drank for 12.6 ± 11.2 years on average. Thus similar large series abroad appear to drink for longer, before seeking help.

The percentage of "bout" drinkers at 8.5% is identical to that in Melbourne by Wilkinson et al. There would appear to be less evidence of family history of excess drinking in the present series than in other Scottish studies (Table 55). However, as Sclare has shown, and Rathod and Thomson (1971) to a lesser extent, alcoholic women tend to be married to husbands who are also alcoholic, and alcoholic men have more alcoholic fathers. The results shown in Table 17 illustrate that those women married to alcoholic husbands have no other family history whatsoever and while the numbers are obviously small, it does suggest that their husbands' drinking is probably the most important factor in their own excessive intake.

5.4 Behavioural disturbances.

Various studies in the past already referred to have indicated that alcoholics have a relatively high incidence of behavioural abnormalities and from these studies it has been difficult to decide whether cause, effect, association with a common aetiology or even coincidence are of importance. It seems likely that there/

TABLE 55 Family History of Alcoholism in Scottish Studies (%)

	PWK	Sclare	Vallance	Ritson
MALE	28.5	34	35+	48
FEMALE	23	40	-	-

TABLE 56 Previous Suicide Attempts in Various Studies (%)

	PWK	Sclare	Moss + Beresford Davies	Glatt (1961)	Pemberton (1967)
MALE	18	16	7	24	12
FEMALE	53	34	24		22

there are probably different mechanisms at work in different patients. Thus, at a simple level, an alcoholic may well only break the law when he is apprehended for being drunk and incapable. On the other hand his drinking may result in such social isolation and degradation that he may indulge in more serious crime to obtain more drink, or he may consider suicide as the only solution, on the other hand an abnormal personality may at one time abuse drugs at another alcohol and at the same time may involve himself in various crimes, either petty or of a more serious nature.

In the present series while the incidence of associated psychiatric diagnosis was about 25%, a diagnosis of personality disorder predominating, the incidence of criminal behaviour was about 50%. It should be pointed out that one third of these were for single or repeated minor drinking offences, but a great many involved multiple offences including ones that were not necessarily directly related to an excess alcohol intake. Only one third of male patients had actually not been convicted of any crime whatsoever, whereas two thirds of females had never been convicted. Therefore if criminal behaviour is considered a complication of alcoholism it is by far the most common one in male alcoholics in the present series.

When previous suicide attempts are considered, females are considerably in excess of male alcoholic patients. A finding confirmed by Solare (1970), Rathod and Thomson (1971) and by Moss and Beresford Davies (1967) who studied the incidence over three years (Table 56). While the detailed data on this group of patients will be discussed later, it is worth while commenting/

commenting on the inter-relationship of the various "behavioural disturbances" at this stage. About a half of both male and female patients who had attempted suicide were given an associated psychiatric diagnosis, but whereas 20 of the 49 females also abused drugs, only 17 of the 95 males did so. This difference is statistically significant at the $P < 0.025$ level. These differences in drug abuse only reflect, though with smaller incidences, the large differences in males and females in the alcoholics as a whole. These differences were not found by Sclare (1970) or by Rathod and Thomson (1971). The relatively high incidences however are confirmed with the recent work by (Ballinger, 1972 and Devenyi and Wilson, 1971,). Just under half of male and female patients who abused drugs were considered to have an associated psychiatric disorder mainly of the personality disorder group. A half of this group of female patients (20 out of the 37) had attempted suicide, whereas only one third of the male patients had (18 out of the 58).

The incidence of associated psychiatric disorder in the present study is less than some of the previously quoted series. Thus, Ritson considered that 25% of his patients suffered from severe personality disorder, a further 41% had a moderate disorder and 13% a mild disorder. This compares with 17% of the present patients. He also found that 17% of his patients suffered from psychoneurosis corresponding to 2.5% of the present series. Similarly Sclare found that 20% of his female alcoholics were considered to be depressed, whereas only 5.5% of this series were so diagnosed.

When the associated "behavioural disturbances" are considered/

considered two thirds of the female alcoholics with personality disorder had attempted suicide and a third had abused drugs. Whereas in male patients with a similar diagnosis, a half had attempted suicide and about a fifth abused drugs.

There were marked differences in psychiatric diagnoses at different age groups. Thus if patients over 60 were considered about one seventh of both male and female patients were considered to be depressed, this being the main associated diagnosis. Conversely below the age of 30 three quarters of female alcoholics (9 out of the 12 patients) and over half of the male alcoholics (28 out of the 46 patients) were considered to have some psychiatric diagnosis mainly of a personality disorder group. The percentage of patients with personality disorder approximately halves with each decade to the age of 50 so that over this age both male and female patients have less than 5%. There was a corresponding trend when previous suicides were broken down in age groups though the difference was not so marked. However, when drug abuse is considered these differences do not occur. Similarly in male alcoholics there were large differences in proportion who had any previous offences at different age groups, so that below 30 over half the patients had had convictions, whereas over 60 years the corresponding figure was one-fifth. This difference was not so clear in female alcoholics though the numbers were very small. It should be noted that though the proportional difference is very large in these 10 year age groups, the number of patients in each group is not very different below the age of 50.

All these figures confirm the findings of Rosenberg (1969) who/

who studied young alcoholics (45 males and 5 females) in Sydney, that the age at which addiction to alcohol occurs depends, at least in part, on the severity of the personality disorder. These patients had high incidences of police convictions, suicidal attempts and previous admissions to hospital. He also showed that compared with older alcoholics they were more likely to have had a parent who drank excessively and have come from a broken home.

The other finding with regard to the presence of personality disorder is in relation to the complications where in males there was a higher incidence of gastritis, but a lesser incidence of neuropathy and cirrhosis. Female patients with anaemia are less likely to have an associated psychiatric diagnosis. Thus some of the severer complications appear to be negatively related to a diagnosis of personality disorder. Presumably this is in part due to the younger age group of these patients.

These behavioural disorders are also important in so far as prognosis is concerned. Thus a worse prognosis was found in the presence of multiple offences and self-discharge from the ward and a better prognosis was found in patients who had no personality disorder.

5.5. Differences between Male and Female Alcoholics

It is in agreement that there are more male alcoholics than female alcoholics. Surveys in the community (Helgason, 1964, and Moss and Beresford Davies, 1967) and on in-patients (Texon, 1950, Pemberton, 1967, Winokur and Clayton, 1968, Sclare, 1970, Wilkinson et al, 1971 and Rathod and Thomson, 1971), have estimated the number of women alcoholics
at/

at from one-sixth of the total to about one-third and the present 22% is within this usual range. There has been the suggestion that the condition is different in women. Winokur and Clayton considered that more women suffered from an affective illness and this was also found by Sclare. Pemberton found that the prognosis was poorer in females and that disturbed marital relationships was especially related to a poor outcome in these females.

The figures from the present study confirm that there are important differences between the male and female alcoholic. The greatest difference separating the sexes is in the length of excess drinking, which is illustrated in Figure 4 and Tables 15 and 40. Despite this finding, which is reported by all workers, the incidence of most of the associated physical complications in this series does not show any statistical difference between the sexes. The important differences in this respect are however in nutritional abnormality and in dementia, both of which might be a pointer in elucidating reasons for this paradox, suggesting that increased age and nutritional factors are of importance as well as the total amount of alcohol in the aetiology of these physical complications. Sclare, in his series found less hepatic and less cerebral damage in his females who however tended to be younger. Wilkinson et al found more cirrhosis and chronic brain syndrome in their patients whom it should be remembered nearly all drank beer. She explained these findings on possible hormonal grounds as she found an increased prevalence in the fifth and sixth decades in these female patients. Other workers have found an increased incidence of malnutrition in women alcoholics and have implicated this as aetiological in the complications, a finding which is confirmed here. Thus as well as/

as overt nutritional abnormality, weight loss was found more in female patients and there was an increase in the "rare" neuro-psychiatric disorders which includes patients with Wernicke's encephalopathy. While there was also more female patients with a lowered serum folate level this was not the case when whole blood thiamine or nicotinic acid levels were considered. It is thus clear that this series of patients shows there is an increased incidence of malnutrition in female alcoholics.

Another important finding is in the difference in age distribution between male and female alcoholics. There were considerably more men than women over the age of 55 years in this group. As there were more widows than widowers in this group it is suggested that the increased alcoholic intake could be a response to their bereavement and loneliness.

As well as the finding that female alcoholics have a decreased length of time of excess drinking, so that on average this commenced at 35.5 years compared to 27.7 years in males, they were shown to drink different alcoholic beverages such as fortified wine (mainly sherry) and spirits other than whisky (mainly gin, but also vodka and even less commonly brandy). They also stated that they had drunk less alcohol per day than male alcoholics i.e. they drank about 150 G. of alcohol per day or the equivalent of a bottle of sherry per day, or half a bottle of most spirits. Thus female alcoholics take in considerably less alcohol than males.

However apart from the complications already mentioned the other differences are not very significant. While female alcoholics/

alcoholics have had a history of fewer gastric operations, they had more evidence of peptic ulcer so that when these were added together there were no significant differences between the sexes. There were differences found on the multiple discriminant analysis so that women had less incidence of epilepsy, respiratory disorders, E.E.G. abnormality, hepatitis, delirium tremens, and hallucinosis. Other differences in behaviour patterns have already been discussed.

There were differences concerning the admission of female alcoholics to hospital, so that they tended to be admitted via other wards and also by Alcoholics Anonymous rather than directly by their general practitioners. These findings would confirm previous suggestions that they are reticent about their habits and certainly would be ashamed to go to their own doctors. They stayed longer in hospital and were admitted more often in the four year period. Despite these findings there is very little difference in the prognosis between male and female alcoholics in this series.

5.6 "Complications" of Alcoholism

Table 57 shows the results of the various comparable studies of the physical associations and complications of alcoholism. The paper of Wilkinson et al even studied alcoholics in Melbourne over a very similar period to the present survey. The most important differences are in the increased incidence of peripheral neuropathy and of cirrhosis in female alcoholics. Although Wilkinson did not tabulate them there was apparently a lower incidence of delirium tremens in the Australian series, but the incidences of Wernicke's encephalopathy and of alcoholic dementia were only slightly higher. There was a greater number of Australian patients with peptic ulcer, but Wilkinson did not quote/

TABLE 57 Physical Complications in Various Studies Compared (expressed as %)

Total Numbers	PMK		Wilkinson et al (1971)		Texon (1950)		Olin (1966)
	Male	Female	Male	Female	Male	Female	Skid Row
	527	148	825	175	382	118	227
Acute Liver Disease	17	12	26	23	86	63	20
Peripheral Neuropathy	18	16	18	25	-	-	13
Gastritis	17	14	15	10	-	-	14
Respiratory	14.5	10	26	16	12	9.5	43
Cirrhosis	12.5	10	8	17	8	7	12
Epilepsy	7	5	8	5	-	-	8
Dementia	5	12	8	14	-	-	16
Peptic Ulcer + Partial Gastrectomy	14	13.5	8	4	6	0	9
Pancreatitis	1	1	2	1	-	-	0
Cardiomyopathy	1.5	0	2	1	-	-	-
Prev. Fractures	3	1	12	9	4	6	55
			"Traumatic Injuries"		"Fractures & Abrasions"		
Barb. Addiction	9	19	-	-	1.3	2.5	
Veneral Diseases	1.5	1					37

quote figures for gastric operations. What is remarkable is perhaps the degree of similarity when it is remembered that there are considerable differences in social class and alcoholic beverages in the two series. Similarly there are not dramatic differences in Olin's series of Skid Row alcoholics except in respiratory disease, alcoholic dementia and especially previous fractures and venereal disease. Texon's figures for physical complications from a new alcoholic admission ward in New York tend to be lower than either the Australian series or the present one, except for acute liver disease which is found to be five times higher than my series, though he used purely clinical and somewhat vague terms of reference.

Only 18% of patients in the present series had no evidence of physical illness, whereas in Wilkinson's series there were about a third. She did not mention anaemia or E.C.G. abnormality however, on the other hand I did not include hypertension in my study. Sclare stated that about a half of his patients had evidence of physical disease other than cerebral involvement.

Sclare found significantly high levels of serum glutamic oxaloacetic transaminase in his male patients and of iron deficiency in his female patients. These trends were found in the present survey, but did not reach statistical significance. However, there was a significant difference in serum glutamic pyruvate transaminase levels.

The alcoholic has thus a high chance of having physical abnormality by the time he is admitted to a psychiatric hospital for treatment. These diseases are not necessarily very obvious to the patient and many are reversible if he stops drinking.

It/

It is thus important to assess the exact aetiology.

Wilkinson showed that whereas the prevalence of physical disability was not affected by social class, it occurred more frequently with increasing age and with a longer history of excess drinking. She showed that peptic ulcer disease and traumatic injuries from road accidents were early complications, frequently occurring within 5 years of the commencement of their excess drinking, delirium tremens occurred after 5 years and cirrhosis and dementia after 15 years of alcoholic excess.

It is not possible in the present study to exactly replicate Wilkinson's findings. However, it is seen that alcoholic dementia, cirrhosis, delirium tremens and anaemia are associated with increasing age of the alcoholics. This is especially so in females with delirium tremens when no patient was under the age of 45, and with cirrhosis when no patient was under the age of 40. It is these groups of female patients in fact which counts for the statistical significance in the total number of alcoholics. In female patients psychiatric complications such as paranoid psychosis and alcoholic hallucinosis also tend to be present with increasing age, but the numbers are too small to influence the total figures. Length of excess drinking is also related clearly to cirrhosis, alcoholic dementia and peripheral neuropathy. Thus one could consider that the findings of Wilkinson have tended to be confirmed.

However only previous suicide is of significance in younger alcoholics and the shorter time of drinking is only related to gastritis. It is not shown that peptic ulceration is present in alcoholics who have been drinking for a shorter time, though this/

this does not disprove Wilkinson's findings.

Delirium Tremens

While the clinical survey of Victor and Adams (1953) and the experimental work of Isbell et al (1955) have demonstrated that alcohol withdrawal in the dependent person is of prime importance in the aetiology of delirium tremens, other workers have shown how the condition is associated with both liver disease and nutritional factors (Leevy et al, 1953, Lundquist, 1961 and Kershaw, 1967). The present study clearly confirms the importance of these other factors. Tables 42 and 43 show that there is an association with cirrhosis, anaemia and alcoholic neuropathy and Figure 5 shows the clear relationship previously demonstrated with whole blood thiamine levels. The relationship with abnormal levels of S.G.O.T., S.G.P.T. and serum proteins also confirm the association with liver disease and that with serum folate confirms the association with nutritional aspects. These associations do not necessarily imply aetiological significance, but could be interpreted as suggesting that delirium tremens, cirrhosis and nutritional deficiency all occur in the severe alcoholic. It is also possible that they play a part if not in the aetiology but in influencing the course of the condition.

The factor of age has also been shown to be of importance in the present series of patients with delirium tremens, especially in females when no patient under the age of 45 was considered to have delirium tremens. This may be related to the length of excess drinking as when male and female patients with/

with delirium tremens were compared, which did not reach statistical significance whereas it was highly significant when male and female alcoholics as a whole were compared. In female patients there was found to be an increase in the number of widows so that a third of the 19 widows in the series suffered from delirium tremens, whereas none of the 15 single female patients were considered to have the condition. Presumably this is partly again a reflection on the patient's age. Female patients with delirium tremens tended to drink less alcohol per day than males with delirium tremens, though this difference only reached significance at the $P < 0.01$ level.

Most of the findings which were brought out by Lundquist (1961) in his series of patients with delirium tremens was confirmed. He found there were fewer personality abnormalities in this group compared to a similar group of alcoholics without delirium and in the present series patients with previous criminal offences are on the whole less likely to suffer from delirium tremens. This is especially so in female patients where only 1 of the 16 had had any previous criminal offence. It has been suggested that if alcohol is withdrawn for periods then delirium tremens may be less likely. It is possible that admission to prison may have played a part in these findings, though there was no difference found in bout drinkers in the series.

Alcoholic Epilepsy

This condition is clearly related to delirium tremens.

Thus/

Thus of the 44 patients 21 had delirium tremens and only one-fifth mild or no withdrawal signs, compared to three-fifths of the alcoholics as a whole. This would tend to confirm the findings that epilepsy is a withdrawal phenomenon. The other association is with drug abuse so that 17 patients of the 44 also abused drugs and this obviously is again related to withdrawal, drug abuse playing about the same part in alcoholic epilepsy as alcohol.

There is a relationship with abnormal levels of S.G.O.T., S.G.P.T., and serum proteins so thus liver damage may well be of some significance. There would also appear to be a relationship with thiamine deficiency so that of the 10 patients with alcoholic epilepsy tested, 8 were found to be low and of the 9 patients with serum folate, 4 were also found to be low.

While these findings would be in agreement with those of Victor (1968) that withdrawal of alcohol is the prime factor in the genesis of alcoholic epilepsy, as only 6.5% of alcoholic patients develop epilepsy it would suggest that other factors could be of importance and the present findings would suggest that liver damage, drug abuse and nutritional factors could all play a part, findings which would tend to be against those of Victor.

Alcoholic Hallucinosiis

The percentage of alcoholics with this condition was found to be 6.5% which is almost a half of that in the series described by Victor and Hope in 1958. Again whereas they found that almost half of their patients had associated delirium tremens, only one-fifth of the present series were the two conditions combined. The main associated condition is with alcoholic paranoid/

paranoid psychosis, so that 6 of the 44 patients appeared to have both alcoholic hallucinosis and alcoholic paranoid psychosis. There was also an association with low serum S.G.O.T. levels. While 6 of the 9 patients with alcoholic hallucinosis who had whole blood thiamines tested, 6 were found to be low, but only 1 of the 10 serum folate levels was low. When the 9 patients with the whole blood thiamine levels performed were compared to 9 patients as closely matched as possible, but without alcoholic hallucinosis, only 2 of the levels were low. Thus there is a tendency to agree with Morgan (1968) who considered that thiamine deficiency might be important in some patients with alcoholic hallucinosis who continued to drink.

Alcoholic Paranoid Psychosis

There were only 25 patients out of the 675 who were diagnosed as having this condition. The only clear association is with alcoholic hallucinosis. However it is worth noting that the 7 patients who had whole blood thiamine levels performed, 4 were found to be low and of these 3 had associated alcoholic hallucinosis.

Eleven of the 25 patients were in social class V and no patient was from social class I. Nearly quarter of the patients were seaprated, including the two patients in social class II so that this is a condition which is in part related to isolation, but this is possibly secondary rather than of primary aetiological importance. Only a quarter of the patients gave whisky as their preferred drink. It is thus difficult to make any generalisations from these patients in the present analysis.

Alcoholic Dementia

Considerably more female patients by proportion than male patients/

patients were found to be suffering from this condition which was associated with increasing age and increasing length of excess drinking. There was a correlation with peripheral neuropathy and with the "rare" neuro-psychiatric disorders as most of the patients suffering from Korsakoff's psychosis were also included in the patients with dementia. When this group were excluded however there were still half the patients with dementia who had evidence of peripheral neuropathy. Subnormal levels of whole blood thiamine and of nicotinic acid were found in alcoholic dementia as were abnormal serum protein levels. If three patients with Korsakoff's psychosis were excluded 8 out of the 11 patients who had whole blood thiamine estimated were found to be abnormal. These findings would suggest that there is a relationship between alcoholic dementia and nutritional factors, though increasing age is of importance and it should be pointed out how difficult it is in alcoholic patients to exclude earlier forms of arteriosclerosis.

The findings of this survey are very much in keeping with those of Horvath et al (1969) who found however an overall incidence of 9% of patients with alcoholic dementia, 7 of whom had Korsakoff's psychosis. The incidence in the present series was 6% with a rather higher percentage of those patients with Korsakoff's psychosis. However, they found three times more evidence of dementia in female patients compared to male patients, almost exactly the same as in the present series. They also found an association with the neurological complications of alcoholism, but not with the non-neurological complications.

"Rare" Neuro-Psychiatric Disorders

In/

In this mixed group of 17 patients, 10 suffered from Wernicke-Korsakoff syndrome of whom only 3 could be considered to have classical Wernicke's psychosis on admission. Only 2 patients were considered to have hepatic encephalopathy and the other 5 were included in the choreoathetotic movement disorder group as described by Mullin, Kershaw and Bolt (1970). While the numbers are very small the patients with both movement disorder and Wernicke-Korsakoff syndrome have a considerably higher incidence in female patients.

The author did not consider that any of the patients in the series suffered from Marchiafava-Bignami disease, central pontine Myelinolysis or deficiency amblyopia.

Alcoholic Psychoses

Delirium tremens, alcoholic hallucinosis, alcoholic paranoid psychosis, Wernicke-Korsakoff syndrome and the even rarer neurological complications could be included by some psychiatrists in the group of alcoholic psychoses. There is no clear pattern however in the conditions except that nutritional factors appear to be the most important part though it should be noted that there is considerable overlap when these patients are classified and analysed. It would seem that this part of the study would need to be enlarged in a prospective way to be more profitable.

Peripheral Neuropathy

This classical condition associated with alcoholism was found in about a fifth of the patients admitted, a very similar percentage to that found by Wilkinson et al (1971) despite marked differences in social class and drinking habits.

Patients with this condition were obviously considered more readily/

readily for admission as both male and female patients with neuropathy tend to be admitted more often to hospital and to stay in hospital longer than alcoholics as a whole.

The male patients with neuropathy tended to be single and divorced and female patients to be widowed, thus the condition is associated with isolation. However, there is also a relationship to the total amount of alcohol consumed as both increased amount and increasing length of time of excess drinking were related to this condition. There was also a relation to a continuous drinking pattern and to the drinking of fortified wine.

The patients with neuropathy tended to have fewer previous offences and to have fewer associated psychiatric diagnoses than other alcoholics.

Peripheral neuropathy was associated with delirium tremens, cirrhosis and to alcoholic dementia. There was a statistical relationship to abnormal serum protein levels and to whole blood thiamine levels. In male patients it was clearly found that food intake was poorer and there was more weight loss than in other alcoholic patients. Thus nutritional factors are of great importance in the aetiology of peripheral neuropathy. Not such a high percentage of patients with neuropathy had low thiamine levels (70% of the 31 estimated) than those of Fennelly et al (1964) who found 86.2% had low levels. When alcoholics without neuropathy were considered, 40% of the present series and 44% of Fennelly's series were found to have blood thiamine levels significantly lower than normal. Fennelly did not find any relationship to alcoholic intake whereas the present shows a clear relationship from this point of view.

The/

The association with cirrhosis is important both from a treatment point of view and as a possible aetiological factor. Fennelly et al, and others, have noted unresponsiveness to vitamin therapy in patients with alcoholic cirrhosis and Knill-Jones et al (1972) found evidence of peripheral neuropathy in cirrhotic patients even though this was not related to excess alcohol intake. The author has never convinced himself that he has seen any patient with myopathy in the absence of neuropathy.

Alcoholic Liver Disease

Cirrhosis

Cirrhosis was found to be present in 12% of the present series of patients. The percentage of female patients being only slightly less than male patients, which is at variance with that of Wilkinson et al. However, she found an overall incidence of almost 10%. Jolliffe and Jellinek (1940) surveyed the world literature finding that 9% of alcoholics had evidence of cirrhosis at autopsy.

Cirrhosis was found to be associated with delirium tremens, peripheral neuropathy, cardiomyopathy and E.C.G. abnormalities. There was a relationship to an increase of subnormal whole blood thiamine levels. There was a tendency for cirrhosis to be found with increasing age of the patient and with an increased length of drinking.

When male cirrhotics were considered, it was found that they drank more wine than other alcoholic beverages, on the other hand they drank less of mixtures of alcoholic beverages which in fact included many patients who drank wine. Similarly they appeared to be less likely to consume spirits other than whisky. They drank more than male alcoholics/

alcoholics as a whole and were drinking excessively for a longer period. They were more likely to have had a poor diet and have lost weight.

Most of the above findings are not in agreement with those of Wilkinson, Santemaria and Rankin (1969) who did not find that wine drinking and dietary neglect were significant in alcoholic patients with cirrhosis in Melbourne. They did however find a relationship with duration of alcohol abuse, and as noted because of the higher incidence in female patients in the 5th and 6th decades, considered that hormonal imbalance may predispose the liver to the toxic effects of alcohol.

When male and female patients with alcoholic cirrhosis were compared, it was found that there were considerable differences in social class. Although there were 64 male cirrhotics and 15 female, 2 males were from class I compared to 5 females, but on the other hand 15 males were from class III but no females, 14 males were from class IV but only 1 female. No female cirrhotic was under aged 40. These class I female alcoholics tended to drink whisky which does not agree with the findings in male cirrhotic alcoholics who were shown to drink more fortified wine. It is difficult to account for these marked sex differences though Leevy's suggestion of nutritional factors as well as excess alcohol both being of importance in the aetiology of cirrhosis and Wilkinson's suggestion of hormonal factors in females are both possible partial explanations. Nonetheless as most workers point out there are far more alcoholics who do not develop cirrhosis than do, many who drink equally large amounts for equally long periods. It is possible that further more sophisticated analysis of/

of the present series will be of value in this puzzle.

Alcoholic Hepatitis

Although 17% of male alcoholics and 12% of female alcoholics were considered to suffer from acute liver disease, this did not reach statistical significance on the simple chi squared test, but it did so when the results were subjected to multivariate analysis. Wilkinson et al (1971) did not find any obvious sex difference though Sclare noted that his male patients tended to have more abnormal S.G.O.T. levels. In the present series more males had abnormalities of S.G.P.T. levels ($P < 0.025$).

There was no relationship with other associated physical abnormalities, nor was there evidence that nutritional factors were in any way related to hepatitis than other alcoholics. There are thus no pointers at the moment as to which patients develop hepatitis or not.

Gastro-Intestinal Disease

Gastritis

Less than one fifth of the alcoholics gave any history suggestive of gastritis. The condition was not related to other physical conditions in these patients. However, there was a relationship to abnormal levels of S.G.O.T. and S.G.P.T. in the serum, which would suggest that in the absence of a pathological diagnosis some of the patients were in fact suffering from early liver disease which is producing the clinical features of vomiting and nausea.

Male patients who were considered to have gastritis however differed from the rest of the alcoholics in many ways.

It/

It could be stated that they tended to be more behaviourally abnormal. Thus they were more likely to be divorced; to clearly state they had no religion; they stayed in hospital for a shorter period, only being admitted once; they discharged themselves against medical advice; and they had a non-specific personality disorder with an increased number of offences. They tended to drink in bouts which could mean that they had to drink in this manner because of vomiting or the stomach was unable to accept insult by alcohol when it only came periodically. There was a tendency for drinkers of spirits other than whisky and also of "crude spirits" to suffer from the condition, though they drank these in larger amounts than other alcoholics, they were more often in the two to five year excess drinking period than in the longer periods. This group of patients included more who said they had a poor food intake and associated weight loss which might be a consequence of their vomiting rather than an aetiological factor.

The female patients with gastritis showed no special characteristics as opposed to other female alcoholics.

In so far as nausea and vomiting associated with alcoholism appears to occur at a relatively early stage of the excess drinking in male alcoholics, it can be said to be one of the earlier signs of the alcoholism. Despite this there was no very obvious improved prognosis in these patients as will be seen later.

Gastric Operations

The incidence of 11% in male alcoholics and 4.5% in female alcoholic patients for gastric operations would appear to be high/

high and would be in keeping with the findings of Lereboullet et al (1955). A half of their patients appeared to become alcoholics after the operation. This was not confirmed in the present series where only 10 of the patients appeared to start their period of heavy drinking following the gastric operation, on the other hand 34 had the operation years after the period of excess drinking had commenced (in 7 of the patients the information was not adequate to assess). There was no difference in the number of offences or in the prognosis in patients who had peptic ulcer, or those who had had gastric operations, so that there is little evidence that patients with gastric operations in general absorb alcohol to the point of drunkenness any more than others, as was suggested by Whitlock in his patients with partial gastrectomies. Nor was there any evidence that this group of patients showed any association with other associated physical abnormalities, suggesting that these operations do not necessarily increase the tendency to either nutritional abnormality nor to liver disease as might be expected. It should be pointed out however that not all the patients had had partial gastrectomy, though most had, and it is possible that more detailed analysis of the patients with partial gastrectomy, including length of time following the operation, might show more significant results. Simple analysis comparing patients with partial gastrectomy and gastro-enterostomy did not show any great difference between the two groups of patients.

The only statistical significant finding in patients with gastric operation was that three of the seven female patients were considered to be suffering from a personality disorder and comparatively fewer male patients had this diagnosis ($P < 0.01$).

It/

It would seem that this high incidence of gastric operation in alcoholics is mainly a result of the excess alcohol intake which predisposes to pathology thereby leading to operation.

Peptic Ulceration

Only a comparatively small percentage of male patients compared to female patients were found to be suffering from this condition. However the incidence of gastric operation and peptic ulcer combined shows that there is a very similar total incidence. This is of the order of 14% and is higher than that in the general population which reaches a maximum of 10% in the age group 45 to 54 years in men and to 6% until the age of 55 in women.

There was no very obvious difference between alcoholic patients with peptic ulcers and alcoholics as a whole. They did not appear to have drunk for shorter periods than the other alcoholics, though the material was not presented in such a way as to see whether the peptic ulcers developed at an earlier part of their drinking, as suggested by Wilkinson et al (1971).

Cardiovascular Abnormalities

Only 9 of the male patients were found to suffer from alcoholic cardiomyopathy and none of the female patients. In view of the small numbers it is difficult to compare these patients. However, all of them had been drinking for over 20 years and had high daily intake of alcohol. As could be expected there was a relationship in abnormal E.C.G.'s., but there was also a clear relationship with cirrhosis, over half the patients were found to have this condition.

113 of the patients had E.C.G. abnormalities, though these varied/

varied considerably most were only minor ones. As yet no analysis of the different types of abnormalities in these patients has been made. There was also a relationship between E.C.G. abnormalities and patients with cirrhosis and with abnormal levels of serum protein. This latter finding is of special significance as various workers postulated that deficiency of protein may be of importance in alcoholic heart disease.

Anaemia

A large number of both male and female alcoholic patients were found to be anaemic, though there was a slightly higher percentage of female patients this did not reach statistical significance. Sclare found that female patients suffered more commonly from iron deficiency anaemia but while two-thirds of my female patients with anaemia were iron deficient and only a half of the male patients, these figures also did not reach statistical significance.

The associated physical conditions with anaemia were found to be cirrhosis and delirium tremens, less significantly peripheral neuropathy and nutritional disorders were possibly related. There was also a statistically significant increased number of abnormal results of serum protein estimations and of low levels of whole blood thiamine and nicotinic acid. These findings would suggest that anaemia is related either to liver disease, or to nutritional factors, or to both. It is very difficult to isolate the exact aetiology in each case however. Thus in the 21 patients with macrocytic anaemia some were clearly related to liver/

liver disease, some were obviously purely nutritional, but others were an association of both and as has already been shown the anaemia of liver disease is a complicated condition in any case.

There was a tendency for the alcoholics with anaemia to be older and to drink more alcohol per day than alcoholics as a whole. Male alcoholics with anaemia were especially found to be among the widowed, to have a poor food intake and they tended to drink "crude" spirits so that 6 of the 13 "crude" spirit drinkers had anaemia, although none of the 3 female "crude" spirit drinkers had anaemia. There were fewer bout drinkers in anaemic patients. There was less evidence of behavioural abnormality in anaemic alcoholics, so that they tended to stay for the full course of treatment in hospital and had fewer offences. Female alcoholics with anaemia were much less likely to have an associated psychiatric diagnosis.

It is of importance to note the relationship between anaemia and alcoholism in these patients and their likelihood of dying during the follow-up period ($P < 0.025$), even though this relationship disappears when patients who died during the admission are excluded. Nonetheless it is obviously of importance to do routine haematological investigations on all alcoholics both as a simple indicator of possible nutritional abnormality and even as a prognostic indicator.

Other Physical Conditions

A wide variety of associated physical conditions was found in over 12% of patients as is seen from Table 32. In this series only a small number of patients were shown to have previous fractures/

fractures, skin disease, or previous venereal diseases, all of which have been found in much higher percentages in other series (Wilkinson et al (1971), Texan (1950) and Olin (1966)).

It is possible that these differences were related to the retrospective nature of the study for bilateral parotid swelling was only noted in two male patients but this was not especially looked for, and bilateral Dupuytren's contracture was rarely noted.

It is difficult to comment on the incidence of respiratory disorders when Olin in his Skid Row alcoholics found 43% who suffered from respiratory disease, whereas only 14% were found in the present series. The incidence of previous tuberculosis, about 3.5%, only included two male patients who were discovered to have the condition on admission and were transferred to a chest hospital.

Biochemical Abnormalities

While the results of this series are not exactly comparable to those described by Kay, Murfitt and Glatt (1959) it would appear that there are considerably fewer abnormalities of liver function than in the earlier study. They discovered 73% of patients with some abnormality and over half with abnormality of serum proteins. Only 17% of the estimations were abnormal in the present series. They demonstrated that female alcoholics tended to have more evidence of abnormality whereas the reverse is shown in the present series.

Less than 10% of serum cholesterols were found to be abnormal. Some were low and a few were raised e.g. 1 female patient was found to have hypothyroidism. Only 2 patients were considered to have the classical biochemical findings of Zieve's syndrome.

Although/

Blood sugar levels were not estimated routinely though they were performed in some patients who were considered to be relatively unrousable on admission, no level was abnormally low.

5.7 Nutritional Factors in Alcoholism

It is seen from Table 58 where the various estimates of nutritional deficiency are compared with those conditions giving a statistical relationship, it would appear that delirium tremens, anaemia and alcoholic dementia have a closer association than alcoholic hallucinosis, epilepsy, cirrhosis or peripheral neuropathy.

These findings are in general in accord with some of the previous work. However, it is perhaps surprising that peripheral neuropathy, apparently a relatively straightforward condition, was not more positively related to the various estimates of nutritional deficiency, whereas alcoholic dementia which appears to be a mixture of pathological entities was. This may be due to inclusion of most of the patients with Wernicke-Korsakoff's syndrome in the category of alcoholic dementia which would alter the results in favour of a nutritional association. However, it is seen that the "rare" neuro-psychiatric conditions do not have such a close statistical relation to the various nutritional parameters. It is obviously of extreme importance that all the alcoholics over 65 had low whole blood thiamine levels, whereas in a control group of elderly hospitalised patients, including patients with senile and arteriosclerotic dementia, there were none with low levels. This would certainly suggest that at this age alcoholics either greatly reduce their food intake or that their metabolism is altered in some way so that thiamine is utilised more rapidly./

TABLE 58 Relationship of Nutritional "Factors" and Various Complications of Alcoholism

	Whole Blood Thiamine	Whole Blood Nicotinic Acid	Serum Folic Acid	Clinical Nutritional Disorder	Serum Protein Abnormality
Delirium Tremens	+	-	+	+	+
Anaemia	±	+	-	+	+
Dementia	±	±	-	+	±
Alc. Hallucinosiis	+	-	-	-	-
Alc. Epilepsy	+	-	-	-	±
Cirrhosis	±	-	-	-	+
Peripheral Neuropathy	±	-	-	-	+

rapidly.

These low levels have obvious implications in the aetiology of alcoholic dementia. As there is evidence of deficiency of nicotinic acid and protein and obvious clinical signs of nutritional deficiency were also found in alcoholic dementia, the evidence is that there is a generalised nutritional disturbance due to poor food intake. It might be that deficiency of multiple nutritional factors produces a generalised dementia compared to the more localised lesion resulting in Wernicke-Korsakoff's syndrome that ensues from thiamine deficiency.

It is of interest that the group of patients with most clear evidence of nutritional disturbance in the present series is that with delirium tremens. These alcoholics are by implication the most severe, it is possibly only to be expected that they will have a poorer food intake than the others. However the other groups, albeit small, with evidence of thiamine deficiency are those with alcoholic hallucinosis and alcoholic epilepsy. Both conditions of which are considered by Victor and Adams not to be related aetiologically to vitamin deficiency. If this is true it suggests that both conditions are found as late and severe complications, directly or indirectly of excess alcohol intake.

The relationship between anaemia and nutritional deficiency is hardly to be surprised, though paradoxically there was not a clear relationship with serum folate levels, one nutritional factor that might especially seem to be of importance.

Cirrhosis does not have the clear association that other studies might suggest, there is a relationship to whole blood thiamine levels/

levels, and as expected to abnormal blood protein levels.

Wine drinkers are especially liable to have microbiological evidence of folate and thiamine deficiency.

There are important therapeutic implications from the above findings. It is essential to treat the serious conditions discussed above with vitamins and while ideally one should be able to give individual vitamins when there are clear indications, at the present state of knowledge this is not possible and one has to use multiple vitamin preparations. Oral treatment should be all that is required in, for example, elderly alcoholics with no obvious clinical abnormalities; or in delirium tremens or alcoholic epilepsy where again there is no clear indication of clinical nutritional abnormality.

5.8 The Inter-relationship of the various "Complications".

These inter-relationships are shown in a very diagrammatic form in Figure 6.

These are by no means simple, nor is it possible to come to any aetiological conclusions from them. It is still not totally clear whether some of the conditions described are even caused by excess alcohol, though the only conclusion one can arrive at, is that alcohol to excess does play a part directly or indirectly in these conditions. The still unexplained question is why do only about a fifth of alcoholics develop some of the conditions, and not all of them. Individual and multiple factors would appear to be of importance. It would be plausible to suggest that alcohol and nutritional factors are both important in various "complications" perhaps involved in some critical way in enzyme function, as has been suggested by Leevy in the in the aetiology of alcoholic cirrhosis, and it may be that specific enzyme differences are important/

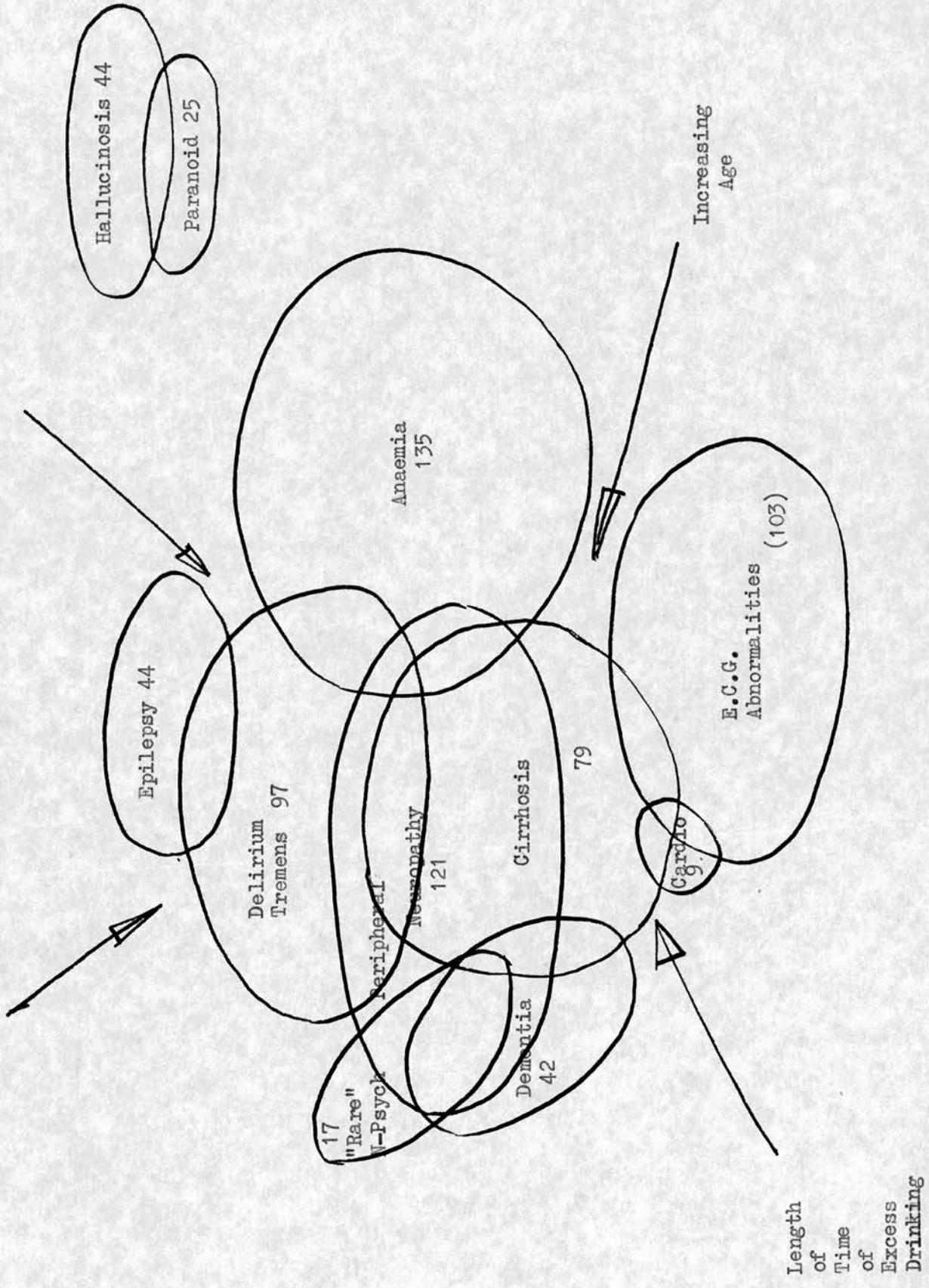


Fig. 6. Inter-relationships of "Complications" of Alcoholism

important in actually making the individual susceptible to the alcohol, thus initiating the pathology of the individual complication.

5.9 Previous Suicide.

This is dealt with separately in view of the importance of this in alcoholics, and as will be seen the inter-relations are different to the physical conditions already dealt with. There was an association with younger alcoholics, and with a lower social class. There were more patients with an associated psychiatric diagnosis, so that almost half of this group were given one as opposed to a quarter of alcoholics as a whole, though there was surprisingly no excess of patients with the associated diagnosis of depression. (Only 2 of 25 patients with a diagnosis of depression on admission attempted suicide). More patients with alcoholic hallucinosis than other groups attempted suicide, though none actually succeeded in the follow-up period. Female alcoholics tended to have the associated diagnosis of hysterical personality disorder, than females who had not attempted suicide. These findings could be interpreted as agreeing with Batchelor's (1954) observation that it is not chronic alcoholics who attempt suicide, but patients with personality disorders who behave in this way as part of their life pattern. On the other hand however, there were 74 alcoholics who had attempted suicide and not been given another psychiatric diagnosis.

More female suicidal alcoholics drank "spirits" than other female alcoholics. The group of patients as a whole were admitted more often in the period under review, and alcoholics who had attempted suicide tended to refer themselves.

When male/female differences are studied, they reflect male/female differences found in the alcoholics as a whole, females drank less alcohol, for a shorter time, and to prefer fortified wine and spirits/

spirits other than whisky. They are more likely to have lost weight, but less likely to have had previous offences.

Although 5 of the 49 females who had attempted suicide actually succeeded in the follow-up period, this did not differ statistically from deaths in the other alcoholics. Only three of the males who had attempted suicide died in the follow-up period, none actually committing suicide. Only one patient with alcoholic hallucinosis had died at follow-up, and he died from tuberculosis. In view of the numbers of suicidal alcoholics this is encouraging, though there are no indications from these figures how many attempted suicide again.

5.10 Prognosis

The results of the assessment at follow-up, which is longer than other published work of prognosis in alcoholics, is as a result somewhat less complete. It is disappointing not to be able to trace over 10% of the female patients, especially when this included some older women who were admitted in delirium tremens and yet have not died, at least in Scotland.

The figures from the studies in Scotland are shown in Table 59, as is seen they are very similar to those reported by Vallance from the same unit earlier, though he was able to trace almost all of his 68 patients. It is important to stress that the patients were not selected for any special treatment programme. If they remained in hospital for the full course, they all received very typical and fairly standard treatment including, various measures for withdrawal, individual support, social help, introduction to Alcoholics Anonymous, and most were offered follow-up at the out-patient clinic. There were obvious differences in individual treatment apart/

TABLE 59. Comparison of Prognosis in Scottish Studies (%)

	PMK	Vallance 1965	McCance (Kingsseat 1969)	McCance (Cormhill 1969)	Ritson 1966	Freeman + Hopwood 1968	Pemberton 1967 Male Female
Length	±4yrs.	2 yrs.	1 yr.	1 yr.	6/12	4/12-18/12	1 1/4 yrs.
Abstinent	9.5		4	16.5	47	14	
Improved	17.5	25	16.5	29.5	22	9	36
I.S.Q.	31.5	44	72.0	46.5	30	73	20
Worse	21	31					50
Dead	9.5	3	2.0	5.5		4	

apart from this, depending not only on the individual needs, but also on the interests of the consultants, junior and other staff, so that some patients received individual psychotherapy, group therapy, a few were in a group especially for alcoholism and for a period of about 6 months, all alcoholics admitted under one consultant received aversion therapy by mild electric shock, as part of a special study into this, though it was not found to be especially useful in the population studied. As McCance (1969) has clearly shown the best results are obtained with a selected group of alcoholics admitted to a specialised unit when it can be expected that almost half of the patients will improve. While the present results on first glance appear to be rather poor, with at worst 60% who may not have improved, on the other hand a quarter of the patients improved after four years, which is not too discouraging considering the population included a half who were from social classes IV and V.

Since July 1968, the policy of alcoholic admissions has changed, as a result of which more alcoholics are admitted for frequent periods of drying out, and at the same time an intensive form of therapy involving frequent group meetings has been introduced. It would thus be of interest to study the prognosis since then to assess the value of this form of therapy in a group of patients who while undergoing intensive therapy do not come from the carefully selected, upper social classes of most of the other intensive units.

The present study has produced some different results, on statistical analysis, from most of the other studies. Despite the fact that 30% of married and single patients improved compared to only/

only 18% of those who were separated, this did not reach statistical significance. Similarly nor was there any difference between male and female patients despite the fact that 9% of males were abstinent compared to 13.5% of females. The social class differences, though superficially similar to other studies in so far as over one-third of patients in social classes I and II improved compared to one-fifth of social class V, these differences only just reached statistical significance at the P 0.05 level. The two important areas which indicated a better prognosis are those with decreased alcohol intake and the absence of psychopathic behaviour. Conversely a worse prognosis is related to an increased length of drinking and to the presence of behavioural disorder as indicated by criminality, self-discharge from the unit and the presence of a personality disorder.

There was no statistical relationship between any of the complications or physical associations and the outcome, except to the patients who died, who will be discussed separately. This finding tends to negate previous explanations for the decreasing incidence of alcoholism with age as being to the development of complications and thus stopping drinking.

5.11 Causes of Death in Alcoholism

There have been no surveys of the causes of death in alcoholics in this country since the turn of the century, apart from incidental comments of those studying either prognosis or suicide in alcoholism. Most of the published work from other countries have confirmed the adverse effects of alcoholism on mortality (Jellinek(1940)from the U.S.A., Sundby (1967) from Norway/

Norway and the work of Schmidt and de Lint (1972) from Toronto) shown this in extensive surveys. The findings of the present study are similar to these others, though the different patterns of mortality in male and females was not found by Schmidt and de Lint, who in fact found the reverse of these figures. It is possible that the number of male alcoholics who were found dead, and considered for example to have coronary thrombosis, could have taken their own lives. However a similar argument is used by Schmidt and de Lint to explain their opposite findings of a slight excess of male suicides.

Probably less than half of the male deaths, that is by excluding cardiac and respiratory causes, could be directly related to their excess drinking. Whereas over two-thirds of the female deaths would appear to be related. It should be noted that a larger proportion of females died within 18 months of discharge from the ward than the male patients. It is noteworthy to comment on two of the other deaths in the female patients. Thus the female who died from carcinoma of the colon was almost certainly suffering from the condition while a patient in the ward as she was investigated with this in mind, but with negative results, and she died with the condition just over a year after discharge. The patient who died in childbirth, while drinking heavily for a long period before admission did in fact do extremely well and remained abstinent for almost two years before dying so tragically.

The only important physical antecedent which reached statistical significance was apparently related to death in the alcoholics were those of cirrhosis and anaemia, but these failed to do/

do so when the six males who died during their hospital admission period were excluded.

6. GENERAL CONCLUSIONS

It is seen that the range of associated physical conditions encountered in this group of alcoholic in-patients to a general hospital psychiatric unit is considerable, and encompasses the whole of medicine. The actual incidences of the conditions must be considered to be the minimum, in view of the fact that much of the study was retrospective. On the other hand those conditions which were directly considered related to the excess alcohol intake were found to be similar to other studies suggesting that at least these results are not too far underestimated.

Wilkinson et al (1971) showed that 15% of their patients had asymptomatic physical disability. This fact in conjunction with the high proportion of disorders which might present at other than psychiatric units has important implications both in diagnosis of alcoholism, which can obviously masquerade in many guises, in management policy for alcoholics and also in consideration of the actual morbidity involved. Thus the present trend in some areas is to consider that alcoholics do not necessarily need psychiatric or medical care, and social workers or other alcoholics may be deployed in "drying-out centres". It is plain that while the medical approach to treatment may have its critics, and may not have been dramatically successful in the past, on the other hand many patients will require some form of medical supervision at some time and at the very least medical assessment would appear to be essential if an alcoholic is to be completely "cared for". As far as morbidity is concerned, if it is accepted that almost 2% of the total population of Scotland is an alcoholic, then the amount/

amount of physical disorder, much of it requiring attention in hospital, is of the order of 1% of the population. The studies of Nolan (1965) who found that 13.8% of 900 consecutive admissions to general medical wards in Newhaven, U.S.A., could be related to alcoholism, and of Green (1965) who found that one in eight patients admitted to adult medical wards in Australia were alcoholics, would tend to confirm these findings. Thus it is possible that one in ten of medical admissions in Scotland could be related to alcoholism though this is often disregarded by physicians or surgeons unless the patient actually develops delirium tremens.

While there are many interesting findings which have emerged from this study, which by attempting to be comprehensive has tended to be rather complicated, it is perhaps disappointing that there are few new or conclusive results, especially in regard to elucidating the exact aetiology of some of the apparent complications of the condition. Perhaps there are still too many variables involved, though it was hoped that an analysis of a large unbiased sample of alcoholics, if that is possible in in-patients, would result in the isolation of some of these variables. While this has not occurred, it would appear that nutritional factors are of importance in the aetiology of some of the complications of alcoholism than some other recent studies would suggest.

There is still scope for analysing other present results by even more sophisticated methods, such as a further discriminate analysis between the various groups of complications, or a cluster analysis inter-relating the various physical associations. Most studies usually discover more problems than solutions, and/

and this has been the case here. The author has realised during the study how little we know of the alcoholic psychoses, and it is intended to perform an intensive study of patients with this diagnosis in the future. It is also hoped to continue the survey prospectively with possible continuous computer analysis of the results.

Although the title of the study was considered justified, some workers would not agree that many of the conditions apparently found in association with alcoholism are in any way necessarily related aetiologically. On the other hand other workers would consider that the effect the alcoholic has on his family, both immediately and in the future, on his work and on the rest of society could equally be called "complications". All of these features are now receiving the attention that they should have many years ago. It was not the intention of the author to bring these out in the present study, nor can a survey of this type indicate the intense personal, and family misery inflicted by the alcoholic, a misery which is not able to be measured but which is immeasurable.

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REFERENCES

- ADAMS, R.D., VICTOR, M. and MANCALL, E.L., (1959), "Central Pontine Myelinolysis". *Arch. Neurol. and Psychiat.* 81: 154-172.
- ADDISON, T., (1836), "Observations on fatty degeneration of the liver". *Guys Hosp. Rep.* 1: 476.
- ALEXANDER, C.S., (1967), "Electron Microscopic observations in alcoholic heart disease". *Brit. Heart J.* 29: 200-206.
- ALLEN, R.P., FAILLACE, L.A. and REYNOLDS, D.M., (1971), "Recovery of memory functioning in alcoholics following prolonged alcohol intoxication". *J. Nerv. Ment. Dis.* 153: 417-423.
- ALLGEN, L-G., (1966), "Some clinical biochemical methods used for the diagnosis of liver disease, especially in psychiatric cases (delirium tremens) and after treatment with potentially hepatotoxic drugs". *Scand. J. Clin. Lab. Invest.* 18, Suppl. 92: 158-172.
- ARENTSEN, K. and SINDRUP, E., (1963), "Electro-encephalographic investigation of alcoholics". *Acta psychiatr. Scand.* 39: 371-383.
- ARMSTRONG, P. (1971) "Statistical Methods in Medical Research". Blackwell Scientific. Oxford and Edinburgh.
- ARMSTRONG R.W. and GOULD, J., (1955), "The nature and treatment of delirium tremens and allied conditions". *J. Ment. Sci.* 101: 70-84.
- BAILLIE, M.S., (1795), "The morbid anatomy of some of the most important parts of the human body". London, quoted by Sherlock, 1968.
- BAKER, H. and FRANK, O., (1968), "Clinical Vitaminology. Methods and interpretation". Wiley Interscience, New York and London.
- BAKER, H., FRANK, O., FENNELLY, J.J. and LEEVY, C.M., (1964), "Method for assaying thiamine status in man and animals". *Amer. J. clin. Nutr.*, 14: 197-201.
- BAKER, H. and SOBOTKA, H., (1962), "Microbiological assay methods for vitamins". *Advanc. clin. Chem.*, 5: 173-235.
- BALLINGER, B., (1972), "Drug addiction in Dundee". *Brit. J. Addict.* 67: 215-220.
- BAMBERGER, H., (1855), "Chronischer magencattarah", in Virchow, R Handbuch der speziellen Pathologie und Therapie, Erlangen, Vol. 3, p.302.

- BATCHELOR, I.R.C., (1954), "Alcoholism and attempted suicide".
J. Ment. Sci. 100 451-461.
- BEAUMONT, W., (1833), "Experiments and Observations on the
Gastric Juice and Physiology of Digestion". p.237
J.P. Allen, Plattsburg.
- BECKETT, A.G., LIVINGSTONE, A.V. and HILL, K.R., (1961),
"Acute alcoholic hepatitis". Brit. Med. J. II:
1113-1119.
- BECKETT, A.G., LIVINGSTONE, A.V. and HILL, K.B., (1962),
"Acute alcoholic hepatitis without jaundice". Brit.
Med. J. II: 580-582.
- BENDER, L. and SCHILDER, P., (1933), "Encephalopathia
alcoholica". Arch. Neurol. and Psychiat., 29: 990-1053.
- BENEDETTI, G., (1952), "Die Alkoholhalluzinosen". Georg Thieme,
Stuttgart.
- BEST, C.H., HARTCROFT, W.S., LUCAS, C.C. and RIDOUT, J.H.,
(1949), "Liver damage produced by feeding alcohol or
sugar, and its prevention by choline". Brit. Med. J.,
II: 1001-1006.
- BIANCO, A. and JOLLIFFE, N., (1938), "The anaemia of alcohol
addicts". Amer. J. Med. Sci. 196: 414-420.
- BISCHOFF, A., (1971), "Die alkoholische polyneuropathie".
Dtsch. med. Wsch. 96:317-322.
- BLACKSTOCK, E.E., GATH, D.H., GRAY, B.C. and HIGGINS, G., (1972),
"The role of thiamine deficiency in the aetiology of
the hallucinatory states complicating alcoholism".
Brit. J. Psychiat. 121: 357-364.
- BLACKSTOCK, E., RUSHWORTH, G. and GATH, D., (1972),
"Electrophysiological studies in alcoholism". J. Neurol.
Neurosurg. Psychiat. 35: 326-334.
- BLAKE, A., (1840), "A practical essay on delirium tremens".
London.
- BLANKENHORN, M.A. and SPIES, T.D., (1936), "Oral complications of
chronic alcoholism". J.A.M.A. 107:641-642.
- BLEULER, E., "Textbook of Psychiatry". (Trans. A.A. Brill),
Macmillan, New York, 1930.
- BOEKE, P.E., (1967), "Some remarks about the alcohol-dementia
in clinically treated alcoholics". Report of International
Conference, "Recent findings in research and treatment of
alcoholism and other dependencies". Groningen.

- BOIVIN, O., OUDEA, P. and FAUBERT, R., (1970), "Acute alcoholic liver damage". Alcohol and Alcoholism. Edit. Popham. p. 252-263
- BOLLINGER, O., (1884), "Ueber die Haufigkert und Ursachen der idiopathischen Herzhypertrophie in Munchen". Deut. Med. Wehnschr., 10: 180.
- BONHOEFFER, K., (1901), "Die akuten Geisteskrankheiten der Gewohnheits trinker". G. Fischer, Jena.
- BOWMAN, K.M., GOODHART, R. and JOLLIFFE, N., (1939), "Observations on the role of vitamin BI in the aetiology and treatment of Korsakoff's psychosis". J. Nerv. Ment. Dis. 90: 569-575.
- BOWMAN, K.M. and JELLINEK, E.M., (1941), "Alcoholic mental disorders". Quart. J. Stud. Alcohol. 2: 312-390.
- BRENNER, B., (1967), "Alcoholism and fatal accidents". Quart. J. Stud. Alc. 28: 517-528.
- BRIGDEN, W., (1957), "Uncommon myocardial diseases: The non-coronary cardiomyopathies". Lancet. 2: 1179-1184, 1243-1249.
- BRIGDEN, W.W. and ROBINSON, J.F., (1964), "Alcoholic heart disease". Brit. Med. J. II: 1283-1289.
- BRIGHT, R., (1827), quoted by Ratnoff and Patek (1942).
- BROWN, T., McP. and HARVEY, A.M., (1941), "Spontaneous hypoglycaemia in "smoke" drinkers". J. Amer. med. Ass. 117: 12-15.
- BUDD, G., (1845), "Diseases of the Liver". Churchill, London.
- CAMMERMEYER, J. and GJESSING, R., (1951), "Fatal myocardial fat embolism in periodic catatonia with fatty liver". Acta Med. Scand. 139: 358-367.
- CARLSSON, C., DENCKER, S.J., GRIMBY, G. and TICHY, J., (1969), "Muscle weakness and neurological disorders in alcoholics". Quart. J. Stud. Alcohol. 30: 585-591.
- CARNEY, M.W.P., (1967), "Serum folate values in 423 psychiatric patients". Brit. Med. J. 4: 512-516.
- CHARLTON, R.W., JACOBS, P., SEFTEL, H. and BOTHWELL, T.H., (1964), "Effect of alcohol on iron absorption". Brit. Med. J. II: 1427-1429.
- CHODOFF, P., ARITH, T. and TOUPIN, H., (1956), "Parenchymatous cortical cerebellar atrophy". J. nerv. ment. Dis. 123: 376-382.

- CHOMET, B. and GACH, B.M., (1967), "Lobar pneumonia and alcoholism: An analysis of 37 cases". Amer. J. Med. Sci. 253: 300-304.
- CLAESON, I-K. and CARLSSON, C., (1970), "Cerebral dysfunction in alcoholics: A psychometric investigation". Quart. J. Stud. Alcohol. 31: 317-323.
- CLARK, E., (1942), "Pancreatitis in acute and chronic alcoholism". Amer. J. Dig. Dis. 9: 428-431.
- CLECKLEY, H.M., SYDENSTRICKER, V.P. and GEESLIN, L.E., (1939), "Nicotinic acid in the treatment of atypical psychotic states associated with malnutrition". J.A.M.A. 112: 2107-2110.
- COHEN, J., DEARNLEY, E.J. and HANSEZ, C.E.M., (1958), "The risk taken in driving under the influence of alcohol". Brit. Med. J. I: 1438-1442.
- COLE, M., TURNER, A., FRANK, O., BAKER, H. and LEEVY, C.M., (1969), "Extra ocular palsy and thiamine therapy in Wernicke's encephalopathy". Amer. J. clin. Nutr. 22: 44-51.
- COURVILLE, C.B. and MYERS, R.O., (1954), "Effects of extraneous poison on the nervous system". Bull. Los Angeles neurol. Soc. 19: 22-28, 66-95.
- COWAN, D.H. and HINES, J.D., (1971), "Thrombocytopenia of severe alcoholism". Ann. Intern. Med. 74: 37-43.
- CUTHBERT, T.M., (1970), "A portfolio of murders". Bri. J. Psychiat. 116: 1-10.
- CUTSHALL, B.J., (1965), "The Saunders Sutton Syndrome: An analysis of delirium tremens". Quart. J. Stud. Alcohol. 26: 423-448.
- DAVIDSON, C.S., (1971), "Alcoholic hepatitis". New Eng. J. Med. 284: 1378.
- DAVIDSON, E.A. and SOLOMON, P., (1958), "The differentiation of delirium tremens from impending hepatic coma". J. ment. Sci. 104: 326-333.
- DE LINT, J. and SCHMIDT, W., (1970), "Mortality from liver cirrhosis and other causes in alcoholics". Quart. J. Stud. Alcohol. 31: 705-709.
- DE LINT, J. and SCHMIDT, W., (1971), "The epidemiology of alcoholism". pp. 423-442 "Biological Basis of Alcoholism," edit Israel, Y. and Mardones, R. Wiley Interscience, New York.
- DENNY-BROWN, D., (1958), "Special problems concerning beriberi: The neurological aspects of thiamine deficiency", in beriberi. Fed. Proc. 17: Suppl. No. 2.

- DE WARDENER, H.E. and LENNOX, B. (1947), "Cerebral beriberi-Wernicke's encephalopathy". *Lancet* I 319-320.
- DEVENYI, P. and WILSON, M., (1971), "Abuse of barbiturates in an alcoholic population". *Canad. med. Ass. J.* 104: 219-221.
- DICK, W., FISCHER, R. and SAUTTER, G., (1959), "Magenresektion und alkoholismus". *Dtsch. med. Wschr.* 84: 311-316.
- DREILING, L.A., RICHMAN, A. and FRADKIN, N.F., (1952), "The role of alcohol in the aetiology of pancreatitis: Study of the effects of intravenous ethyl alcohol on the external secretion of the pancreas". *Gastroent.* 20: 636-646.
- DREW, G.C., COLQUHOUN, W.P. and LONG, H.A., (1958), "Effect of small doses of alcohol on a skill resembling driving". *Brit. Med. J.* II: 993-998.
- EAST, W.N., (1944), "Delinquency and crime", in *Recent Progress in Psychiatry*, Vol. 3: Edit. Fleming, pp 382-398. London.
- EAST, W.N., (1913), "On attempted suicide, with an analysis of 1,000 consecutive cases". *J. Ment. Sci.* 59: 428-478.
- EDWARDS, F.C. and COGHILL, N.F., (1966), "Aetiological factors in chronic atrophic gastritis". *Brit. Med. J.* II: 1409-1415.
- EDWARDS, G., HAWKER, A., WILLIAMSON, V. and HENSMAN, C., (1966), "London's Skid Row". *Lancet.* I: 249-252.
- EDWARDS, M.A., KAUFMAN, M.L. and STORVICH, A., (1957), "Microbiological assay for thiamine content of various species of animals and man". *Amer. J. Clin. Nutr.* 5: 51-55.
- EKBOM, K., HED, R., KIRSTEIN, L. and ASTROM, K.E., (1964), "Muscular affection in chronic alcoholism". *Arch. Neurol.* 10: 449-458.
- ESSIG, C.F. and LAM, R.C., (1968), "Convulsions and hallucinatory behaviour following alcohol withdrawal in the dog". *Arch. Neurol.* 18: 626-632.
- EVANS, W., (1959), "The electrocardiogram of alcoholic cardiomyopathy". *Brit. Heart J.* 21: 445-456.
- FAHLGREN, H., HED, A., and LUNDMARK, C., (1957), "Myonecrosis and myoglobinuria in alcohol intoxication". *Acta med. scand.* 158: 405-412.

- FARIS, A.A. and REYES, M.G., (1971), "Reappraisal of alcoholic myopathy". *J. Neurol. Neurosurg Psychiat.*, 34: 86-92.
- FARIS, A.A., REYES, M.G. and ABRAMS, B.M., (1967), "Sub-clinical alcoholic myopathy: Electromyographic and biopsy study". *Trans. Amer. neurol. Assoc.* 92: 102-106.
- FARIS, R.E.L. and DUNHAM, H.W. (1939), "Mental Disorders in Urban Areas". New York.
- FENNELLY, J.J., FRANK, O., BAKER, H. and LEEVY, C.M., (1964), "Peripheral neuropathy of the alcoholic. I. Aetiological role of aneurin and other B-complex vitamins". *Brit. Med. J.* II 1290-1293.
- FERRER, S., SANTIBANEZ, I., CASTRO, M., KRAUSKOPF, D. and SAINT-JEAN, H., (1970), "Permanent neurological complications of alcoholism", in *Alcohol and Alcoholism*. Edit. Popham, University of Toronto Press, Toronto, 1970.
- FIGUEROA, W.G., SARGENT, F., IMPERIALE, L., MOREY, G.R., PAYNTER, C.R., VORHAUS, L.J. and KARK, R.M. (1953), "Lack of avitaminosis among alcoholics". *Amer. J. Clin. Nutr.* 1: 179-199.
- FINCH, E.S., DALE B.G., JOSKE, R.A. and SAINT, E.G., (1952), "Studies in chronic alcoholism: III. Laboratory Studies". *Med. J. Aust.* I: 738-742.
- FREEMAN, T. and HOPWOOD, S.E., (1968), "Characteristics and response to treatment for an unselected group of alcoholics". *Scot. med. J.* 13: 237-241.
- FRENCH, S.W., (1964), "Effect of chronic alcohol ingestion on liver enzyme changes induced by thiamine, riboflavine, pyridoxine or choline deficiency". *J. Nutr.* 88: 291-302.
- FRIEDERICH, N., (1878), "Diseases of the Pancreas" in von Zienversn, H. "Cyclopedia of the Practice of Medicine" pp 549-630, William Woods, New York. Quoted by Dreiling et al, 1952.
- FOREMAN, H.M. and CHAIKE, H.D., (1972), "Tuberculosis and alcoholism: A pilot study". *J. Alc.* 7: 12-14.
- FUNKHAUSER, J.B., NAGLER, B. and WALKE, N.D., (1953), "The electroencephalogram of chronic alcoholism". *Sth. Med. J. (Bgham. Ala.)* 46: 423-428.
- GARDNER, A.J., (1971), "Folate status of alcoholic in-patients". *Brit. J. Addict.* 66: 183-184.
- GARDNER, A.J., (1972), "Neuropathy after alcohol withdrawal". *J. Neurol. Neurosurg. Psychiat.* 35: 323-325.
- GENERAL REGISTER OFFICE (1966), "Classification of Occupations". H.M.S.O., London.

- GIBBENS, T.C.N. and SILBERMAN, M. (1970), "Alcoholism among prisoners". *Psychol. Med.* 1: 73-78.
- GILLIES, H., (1965), "Murder in the West of Scotland". *Brit. J. Psychiat.* 111: 1087-1094.
- GITLIN, N., (1969), "Zieve's syndrome and porphyrinuria in an alcoholic". *Brit. Med. J.* I: 96-98.
- GLATT, M.M., (1961), "Drinking habits of English (middle class) alcoholics". *Acta Psych. Scand.* 37: 88-113.
- GLATT, M.M., (1961), "Treatment results in an English mental hospital alcoholic unit". 37: 143-168.
- GLATT, M.M., (1964), "Alcoholism in "impaired" and drunken driving". *Lancet* I: 161-163.
- GOLDBERG, M., (1962), "Thyroid function in chronic alcoholism". *Brit. Med. J.* II: 746-749.
- GOODWIN, D.W., CRANE, J.B. and GUZE, S.B., (1969), "Phenomenological aspects of the alcoholic 'blackout'". *Brit. J. Psychiat.* 115: 1033-8.
- GORWITZ, K., BAHN, A., WARTHEN, F.J. and COOPER, M., (1970), "Some epidemiological data on alcoholism in Maryland: Based on admissions to psychiatric facilities". *Quart. J. Stud. Alcohol.* 31: 423-443.
- GOULD, J., (1959), "The enzymatic basis of certain psychoses", in *Recent Progress in Psychiatry*, Vol. 3 pp 213-252. London. 1959.
- GRAY, S. and SCHINDLER, R., (1941), "The gastric mucosa of chronic alcohol addicts". *J.A.M.A.* 117: 1005-1011.
- GREEN, J.R., (1965), "The incidence of alcoholism in patients admitted to medical wards of a public hospital". *Med. J. Aust.* I: 465-466.
- GREEN, J.S., MISTILIS, S. and SCHIFF, L., (1963), "Acute alcoholic hepatitis: A clinical study of 50 cases". *Arch. Int. Med.* 112: 67-78.
- GROSS, M.M., HALPERT, E. and SABOT, L., (1963), "Some comments on Bleuler's concept of acute alcoholic psychoses". *Quart. J. Stud. Alcohol.* 24: 54-60.
- GROSS, M.M., HALPERT, E. and SABOT, L., (1968), "Toward a revised classification of the acute alcoholic psychoses". *J. nerv. ment. Dis.* 145: 500-508.
- GROSS, M., (1967), "Management of acute alcohol withdrawal states". *Quart. J. Stud. Alcohol.* 28: 655-666.

- GROSS, M.M., ROSENBLATT, S.M., CHARTOFF, S., HERMANN, A., SCHACHTER, M., SHEINKIN, D. and BROMAN, M., (1971a), "Evaluation of acute alcoholic psychoses and related states". *Quart. J. Stud. Alcohol.* 32: 611-619.
- GROSS, M.M., ROSENBLATT, S.M., LEWIS, E., MALENOWSKI, B. and BROMAN, M., (1971b), "Hallucinations and clouding of sensorium in alcohol withdrawal". *Quart. J. Stud. Alcohol.* 32: 1061-1069.
- GUNN, J., (1972), "Epileptic prisoners and their drinking problems". *Epilepsia (amst.)*, 13: 489-497.
- HADDEN, W. and BRADESS, V.A., (1959), "Alcohol in the single vehicle fatal accident". *J. Amer. med. Ass.* 169: 1583-1593.
- HAGNELL, O. and WRETMARK, G., (1957), "Peptic ulcer and alcoholism; a statistical study in frequency, behaviour, personality traits and family occurrence". *J. Psychosom. Res.* 2: 35-44.
- HALSTED, C.H., GRIGGS, R.C. and HARRIS, J.W., (1967), "The effect of alcoholism on the absorption of folic acid (H³-PGA) evaluated by plasma levels and urine excretion". *J. Lab. & Clin. Med.* 69: 116-131.
- HAREDER, A., (1947), "Das wesen der alkohol-halluzinose". *Schweitz Arch. Neur.* 58: 102., quoted by Victor and Hope (1958).
- HARDISON, W.G. and LEE, F.I., (1966), "Prognosis in acute liver disease of the alcoholic patient". *New Eng. J. Med.* 275: 61-66.
- HART, J., (1633), quoted by Ratnoff, O.D. and Patek, A.J., (1942). "The Natural History of Laennec's Cirrhosis of the Liver". *Medicine.* 21: 207-268.
- HAYASHI, T. and STEMMERMANN, G.N., (1967), "Chronic alcoholism with pancreatitis, cirrhosis and hyperlipaemia, (Zieve's syndrome, report of a case studied at necropsy)". *Arch. Int. Med.* 120: 465-471.
- HECK, J. and GEHRMANN, G., (1972), "Alkoholische thrombozytendepression". (Platelet depression in chronic alcoholics). *Dtsch. med. Wschr.* 97: 1088-1092.
- HED, R., LARSSON, H. and WAHLGREN, F. (1955), "Acute myoglobinuria: Report of a case with a fatal outcome". *Acta Med. Scand.* 152: 459-463.
- HELGASON, T., (1964), "Epidemiology of Mental Disorders in Iceland". *Acta. Psych. Scand. Suppl.* 173.
- HENDERSON and GILLESPIE, "Textbook of Psychiatry". 10th Edition, Edit. Batchelor, 1969. Oxford University Press. London.

- HERBERT, V., ZALUSKY, R. and DAVIDSON, C.S., (1963),
"Correlation of folate deficiency with alcoholism
and associated macrocytosis, anaemia and liver disease".
Ann. Int. med. 58: 977-988.
- HIPPOCRATES. Epidemics, III, 5.
- HOME OFFICE REPORT. "Habitual Drunken Offenders".
H.M.S.O. London, 1971.
- HOPWOOD, J.S. and MILNER, K.O., (1940), Brit. J. Inebr.
38: 51, quoted by East, W.N. in Recent Progress in
Psychiatry, I: p 391. publ. J. Ment. Sci. 1944.
- HORVATH, T., WILKINSON, P., SANTAMARIA, J.N., and RANKIN,
J.G., (1969), "Dementia in alcoholics". (Abstr.)
Austral. Ann. Med. 18: 165.
- HOURIHANE, D.O'B. and WEIR, D.G., (1970), "Suppression of
erythropoiesis by alcohol". Brit. Med. J.
1: 86-89.
- HOWARD, J.M. and JORDAN, G.L., (1960), "Surgical Disease of the
Pancreas". Lipincott. Philadelphia; Pitman Medical London.
- HOWARD, R.P., (1887), "On hepatic cirrhosis in children".
Trans. Assoc. Amer. Phys. 2: 1-36.
- HUDSON, R.M. and RHODES, R.J., (1971), "A follow-up study
of tuberculous Skid Row alcoholics. II. Hospital and
post-hospital attitudes and care". Quart. J.
Stud. Alcohol. 32: 116-122.
- IRONSIDE R., BOSANQUET, F.D. and McMENEMEY, W.H., (1961),
"Central demyelination of the corpus callosum
(Marchiafava-Bignami Disease)". Brain. 84: 212-230.
- ISELL, H., FRASER, H.F., WIKLER, A., BELLEVILLE, R.E. and
EISENMAN, A.J., (1955), "An experimental study of the
aetiology of 'rum fits' and delirium tremens".
Quart. J. Stud. Alc. 16: 1-33.
- ISRAEL, Y. and MARDONES, Edit. (1971). "Biological Basis of
Alcoholism". New York.
- ISRAEL, Y., VALENZUELA, J.E., SALAZAR, I. and UGARTE, G.,
(1969), "Alcohol and amino-acid transport in the human
small bowel". J. Nutr. 98: 222-224.
- ISSELBACHER, K.J. and GREENBERGER, N.J., (1964), "Metabolic
effects of alcohol on the liver". New Eng. J. Med.
270: 351-356, 402-410.
- JACKSON, J., (1822), "A peculiar disease resulting from the
use of ardent spirits". New Eng. J. Med. 11: 351.

- JANDL, J.H., (1955), "The anaemia of liver disease; Observations on its mechanism". *J. Clin. Invest.* 34: 390-404.
- JARROLD, T. and VILTER, R.W., (1949), "Haematological observations in patients with chronic hepatic insufficiency: Sternal bone marrow morphology and bone marrow plasmocytosis". *J. Clin. Invest.* 28: 286-292.
- JARROLD, T., WILL, J., DAVIES, A.R., DUFFEY, P.H. and BRAMSCHRIEBER, J.L., (1967), "Bone marrow erythroid morphology in alcoholic patients". *Amer. J. Clin. Nutr.* 20: 716-722.
- JELLINEK, E.M., (1942), "'Death from alcoholism' in the United States in 1940; a statistical analysis". *Quart. J. Stud. Alc.* 3: 495-500.
- JELLINEK, E.M., (1959), "The withdrawal syndrome in alcoholism". *Canad. med. Ass. J.* 81: 536-541.
- JOHNSON, J., (1820) quoted by RATNOFF, O.D. and PATEK, A.J., (1942) "The natural history of Laennec's Cirrhosis of the liver". *Medicine* 21: 207-268.
- JOLLIFFE, N., BOWMAN, K.M., ROSENBAUM, L.A. and FEIN, H.D., (1940), "Nicotinic acid deficiency encephalopathy". *J.A.M.A.* 114: 307-312.
- JOLLIFFE, N. and COLBERT, C.N., (1936), "Aetiology of polyneuritis in alcohol addiction". *J.A.M.A.* 107: 642-647.
- JOLLIFFE, N. and JELLINEK, E.M., (1941), "Vitamin deficiencies and liver cirrhosis in alcoholism. Part VII, Cirrhosis of the liver". *Quart. J. Stud. Alcohol.* 2: 544-583.
- JOLLIFFE, N., WORTIS, H. and STEIN, M.H., (1941), "Vitamin deficiencies and liver cirrhosis in alcoholism". Part IV. The Wernicke Syndrome. Part V. Nicotinic Acid Deficiency Encephalopathy. Part VI. Encephalopathies with possible Nutritional involvements. *Quart. J. Stud. Alcohol.* 2: 73-97.
- JOSKE, R.A. and TURNER, C.N., (1952), "Studies in chronic alcoholism: I. The clinical findings in 78 cases of chronic alcoholism". *Med. J. Aust.* 1: 729-734.
- KALINOWSKY, L.B., (1942), "Convulsions in non-epileptic patients on withdrawal of barbiturates, alcohol and other drugs". *Arch. Neurol. Psychiat.* 48: 946-956.
- KAY, W.W., MURFITT, K.C. and GLATT, M.M., (1959), "Liver damage in addictive alcoholics". *J. Ment. Sci.* 105: 748-754.
- KERSHAW, P.W., (1967), "Blood thiamine and nicotinic acid levels in alcoholism and confusional states". *Brit. J. Psychiat.* 113: 387-393.

- KESSEL, L., (1962), "Acute transient hyperlipaemia due to hepatopancreatic damage in chronic alcoholics".
Amer. J. Med. 32: 747-757.
- KESSEL, N. and GROSSMAN, G., (1961), "Suicide in alcoholics".
Brit. Med. J. II: 1671-1672.
- KESSEL, N. and WALTON, H., (1965), "Alcoholism". Penguin Book,
London.
- KIMBER, C. DELLER, D.J., IBBOTSON, R.N. and LANDER, H., (1965),
"The mechanism of anaemia in chronic liver disease".
Quart. J. Med. 34: 33-64.
- KLIPSTEIN, F.A. and LINDENBAUM, J., (1965), "Folate deficiency in
chronic liver disease". Blood. 25: 443-456.
- KNILL-JONES, R.P., GOODWILL, C.J., DAYAN, A.D. and WILLIAMS, R.,
(1972), "Peripheral neuropathy in chronic liver disease:
Clinical, electrodiagnostic and nerve biopsy findings".
J. Neurol. Neurosurg. Psychiat. 35: 22-30.
- KOSZEWSKI, B.J., (1952), "The occurrence of megaloblastic
erythropoiesis in patients with haemochromatosis".
Blood. 7: 1182-1195.
- KRASNOW, S.E., WALSH, J.R. ZIMMERMAN, H.J. and HELLER, P.,
(1957), "Megaloblastic anaemia in 'alcoholic cirrhosis'".
Arch. Int. Med. 100: 870-880.
- KORSAKOFF, S.S., (1887), "Disturbance of psychic function in
alcoholic paralysis and its relation to the disturbance
of the psychic sphere in multiple neurotosis of non-
alcoholic origin". Vestnik. Psichiatrii, Vol. IV,
fascicle 2.
- KRAEPELIN, E., (1946), "Lectures on Clinical Psychiatry".
(Trans. Johnstone) William Wood and Co., New York.
- KRETCHMER, E., quoted by NOYES, A.P., "Modern Clinical
Psychiatry". Saunders, Philadelphia and London. 1940.
- LANCET Annotation (1958), "Delirium tremens". II: 892-893.
- LEDERMANN, S., *Alcool-Alcoolisme-Alcoolisation; Mortalité,
Morbidity Accidents due Travail, Institut National d'Etudes
Démographiques, Travaux et Documents, Cahier No. 41,
Presses Universitaires de France, 1964. p 417ff,*
quoted by de Lint, J. and Schmidt, W. (1971) in Biological
Basis of Alcoholism. edit. Israel, Y. and Mardones, R.,
New York.
- LEE, F.I., (1966), "Cirrhosis and hepatoma in alcoholics".
Gut. 7: 77-85.
- LEEVEY, C.M., (1967), "Clinical diagnosis, evaluation and treatment
of liver disease in alcoholics". Fed. Proc. 26:
1474-1481.

- LEEVEY, C.M., BAKER, H., TENHOVE, W., FRANK, O. and CHERRICK, G.R., (1965), "B-complex vitamins in liver disease of the alcoholic". *Amer. J. Clin. Nutr.* 16: 339-346.
- LEEVEY, C.M., PATRYLO, I. and DOODY, W., (1953), "Hepatic abnormalities in alcoholics with delirium tremens". *Quart. J. Stud. Alcohol.* 14: 568-575.
- LENNOX, W.G., (1941), "Alcohol and epilepsy". *Quart. J. Stud. Alcohol.* 2: 1-11.
- LEREBOULET, J., PLUVINAGE, R., (1956), "L'atrophie cerebrale des alcooliques, ces consequences, medico-sociales". *Bull Acad. Nat. Med.* 140: 398-401.
- LENER, A.M., DeCARLL, L.M. and DAVIDSON, C.S., (1958), "Association of pyridoxine deficiency and convulsions in alcoholics". *Proc. Soc. Exper. Biol. & Med.* 98: 841-843.
- LESTER, D., BUCCINO, R. and BIZOCCO, D., (1960), "The vitamin C status of alcoholics". *J. Nutr.* 70: 278-282.
- LETTSON, J.C. (1787), "Some remarks on the effects of *Lignum Quassiae Amarae*". *Mem. med. Soc. Lond.* 1: 128-165.
- LIEBER, C.S., (1970), "Pathogenesis of fatty liver and cirrhosis: Biochemical approach", in *Alcohol and Alcoholism*, Edit. Popham. R.E. Toronto, pp 197-211.
- LIEBER, C.S., JONES, D.P., LOSOWSKY, M.S. and DAVIDSON, C.S., (1962), "Inter-relation of uric acid and ethanol metabolism in man". *J. Clin. Invest.* 41: 1863-1870.
- LINDENBAUM, J. and LIEBER, C.S., (1968), "Effects of ethanol on blood and bone marrow". *Amer. J. Clin. Nutr.* 21: 533-534.
- LIPSCOMB, W.R., (1959), "Mortality among treated alcoholics". *Quart. J. Stud. Alcohol.* 20: 596-603.
- LIVERSEDGE, L.A. and RAWSON, M.D., (1966), "Myelopathy in hepatic disease and porto-systemic venous anastomosis". *Lancet*, I: 277-279.
- LOSOWSKY, M.S., JONES, D.P., DAVIDSON, C.S. and LIEBER, C.S., (1963), "Studies of alcoholic lipaemia and its mechanism". *Amer. J. Med.* 35: 794-803.
- LUNDQUIST, G., (1961), "Delirium tremens". *Acta psychiat. Scand.* 36: 443-466.
- LUNDQUIST, G.A.R., (1965), "Glucose tolerance in alcoholism". *Brit. J. Addict.* 61: 51-55.
- McCANCE, C. and McCANCE, P.F., (1969), "Alcoholism in North-East Scotland: Its treatment and outcome". *Brit. J. Psychiat.* 115: 189-198.

- McCURDY, P.R., PIERCE, L.E. and RATH, C.E., (1962), "Abnormal bone marrow morphology in acute alcoholism". *New Eng. J. Med.* 266: 505-507.
- MACDONALD, R.A., (1965), "Haemochromatosis and cirrhosis in different geographic areas". *Amer. J. Med. Sci.* 249: 36-46.
- MACKAY, I.R., (1959), "A survey of alcoholics". *Med. J. Aust.* 2: 176-180.
- MACKAY, I.R., (1966), "The effects of alcohol on the gastrointestinal tract". *Med. J. Aust.* II: 372-376.
- MACKENZIE, J., (1902), "The Study of the Pulse". Edinburgh and London.
- McLARDY, T., (1951), "A case of Marchiafava's disease". *Proc. Roy. Soc. Med.* 44: 685-686.
- MACRAE, A.K.M., RATCLIFF, R.A.W. and LIDDLE, S.M., (1972), "Alcoholism in Scotland in the 1960's". *Health Bulletin.* Edin. 30: 16-22.
- MAGNON, V., (1871), *Etude Experimentale et Clinique sur l'Alcoolisme, Alcool et Absinthe; Epilepsie Absinthique*. Renou & Maulde, Paris. quoted by CUTSHALL, 1965.
- MALLORY, F.B., (1911), "Cirrhosis of the liver; Five different types of lesion from which it may arise". *Bull. Johns Hopkins Hosp.* 22: 69-75.
- MANCALL, E.L., (1961), "Some unusual neurological diseases complicating chronic alcoholism". *Amer. J. Clin. Nutr.* 9: 404-413.
- MARCHIAFAVA, E. and BIGNAMI, A., (1903), "Sopra un'alterazione del corpo calloso osservata in soggetti alcooliste". *Riv. Patol. Nerv. Ment.* 8: 544-549.
- MARIE, P., FOIX, C. and ALAJOUANINE, T., (1922), "De l'Atrophie Cerebelleuses Tardive a predominance Corticale". *Rev. Neurol.* 38: 849-885 & 1082 - 1111.
- MATHIASON, G. and OLSZEWSKI, J., (1960), "Central pontine myelinolysis with other cerebral changes". *Neurology.* 10: 345-354.
- MAWDSLEY, C. and MAYER, R.F., (1965), "Nerve conduction in alcoholic polyneuropathy". *Brain.* 88: 335-356.
- MAYFIELD, D.G. and MONTGOMERY, D., (1972), "Alcoholism, alcohol intoxication and suicide attempts". *Arch. Gen. Psychiat.* 27: 349-353.
- MELLOR, C.S., (1970), "Nomogram for calculating mass of alcohol in different beverages". *Brit. Med. J.* II: 703.

- MELMED, R.N., (1967), "Alcohol and the liver". Hospital Medicine. 2: 297-299.
- MENDELSON, J.H., OGATA, M. and MELLO, N.J., (1971), "Adrenal function and alcoholism. I. Serum cortisol". Psychosom. Med. 33: 145-157.
- MERRITT, H.H. and WEISMAN, A.D., (1945), "Primary degeneration of the corpus callosum, (Marchiafava-Bignami Disease)". J. Neuropath. Exptl. Neurol. 4: 155-163.
- MINOT, G.R., STRAUSS, M.B. and COBB, S., (1933), "Alcoholic polyneuritis; Dietary deficiency as a factor in its production". New Eng. J. Med. 20: 1244
- MOREL, F., (1939), "Une forme anatomo-clinique particuliere de l'alcoolisme chronique: Sclerose corticale laminaire alcoolique". Rev. Neurol. 71: 280-288.
- MOONEY, H.B., (1965), "Pathologic jealousy and psychochemotherapy". Brit. J. Psychiat. 111: 1023-1042.
- MOORE, M. and GRAY, M.G., (1941), "Alcoholism at the Boston City Hospital". Quart. J. Stud. Alc. 2: 18-34.
- MORGAN, H.G., (1968), "Acute neuropsychiatric complications of chronic alcoholism". Brit. J. Psychiat. 114: 85-92.
- MORRISON, S.L., (1964), "Alcoholism in Scotland". Health Bulletin (Edin.) 22: 12-19.
- MOSS, M.C. and BERESFORD DAVIES, E., (1967), "A Survey of Alcoholism in an English County". St. Ann's Press, Altrincham.
- MOTTO, J.A., (1968), "Acute alcohol-withdrawal syndromes; A controlled study of phenothiazine effectiveness". Quart. J. Stud. Alcohol. 29: 917-930.
- MOVITT, E.R., (1949), "Megaloblastic bone marrow in liver disease". Amer. J. Med. 7: 145-149.
- MULLIN, P.J., KERSHAW, P.W. and BOLT, J.M.W., (1970), "Choreoathetotic movement disorder in alcoholism". Brit. Med. J. 4: 278-281.
- MYERSON, R.M., (1971), "Effects of alcohol on cardiac and muscular function", in "Biological Basis of Alcoholism". Edit. Israel and Mardones, p 183-208. Wiley Interscience, New York.
- NAVRATIL, L. and WENGER, R., (1955), "Alkoholismus und magengeschwiis". Munch. med. Wschr. 97: 1457-1459.
- NEAME, P.B. and JOUBERT, S.M., (1961), "Postalcoholic hypoglycaemia&toxic hepatitis". Lancet. II 893 - 897.

- NEVILLE, J., EAGLES, J., SAMSON, G. and OLSEN, R.E., (1968), "Nutritional status of alcoholics". *Amer. J. Clin. Nutr.* 21: 1329-1340.
- NEUBERGER, K.I., (1957), "The changing neuropathologic picture of chronic alcoholism". *A.M.A. Arch. Path.* 63: 1-6.
- NIELSON, J., (1965), "Delirium tremens in Copenhagen". *Acta psychiat. scand. Suppl.* 187. pp1-92.
- NOLAN, J.P., (1965), "Alcohol as a factor in illness of university service patients". *Amer. J. med. Sci.* 249: 135-142.
- O'BRIEN, E.T. and GOLDSTRAW, P., (1969), "Alcoholic myopathy". *Brit. Med. J. II*: 785-786.
- OGATA, M., MENDELSON, J.H., MELLO, N.K. and MAJCHROWICZ, E., (1971), "Adrenal function. II. Catecholamines". *Psychosom. Med.* 33: 159-180.
- O'KEANE, M., RUSSELL, R.I. and GOLDBERG, A., (1972), "Ascorbic acid status of alcoholics". *J. Alcoholism.* 7: 6-11.
- OLIN, J.S., (1966), "Skid Row Syndrome; a Medical Profile of the Chronic Drunkenness Offender". *Canad. med. Ass. J.* 95: 205-214.
- OLIN, J.S. and GRZYBOWSKI, S., (1966), "Tuberculosis and alcoholism". *Canad. med. Ass. J.* 94: 999-1001.
- PALMER, E.D., (1954), "Gastritis: A revaluation". *Medicine.* 33: 199-290.
- PATEL, A.R., ROY, M. and WILSON, G.M., (1972), "Self-poisoning and alcohol". *Lancet.* II 1099-1103.
- PEARL, R., (1926), "Alcohol and Longevity". Knopf, New York.
- PEARSON, S.B., (1813), "Observations on brain fever". *Edin. med. surg. J.* 9: 326-332.
- PEMBERTON, D.A., (1967), "A comparison of the outcome of treatment in female and male alcoholics". *Brit. J. Psychiat.* 113: 367-374.
- PERKOFF, G.T., DIOSO, M.M., BLEISCH, V. and KLINKERFUSS, G., (1967), "A spectrum of myopathy associated with alcoholism: I. Clinical and laboratory features. II. Light and electron microscopical observations". *Ann. Int. Med.* 62: I, 481-492. II, 493-510.
- PERSHING, H.T., (1892), "Alcoholic multiple neuritis with characteristic mental derangement". *Int. Med. Mag.* 1: 803-809.
- PHILLIPS, G.B. and SAFRIT, H.F., (1971), "Alcoholic diabetes, induction of glucose intolerance with alcohol". *J.A.M.A.* 217: 1513-1519.

- PIKER, P., (1937), "On the relationship of sudden withdrawal of alcohol to delirium tremens". Amer. J. Psychiat. 93: 1387-1390.
- POLLOCK, H.M., (1940), "Use and effect of alcohol in relation to alcoholic mental disease before, during and after prohibition". Ment. Hyg. 24: 112.
- POPHAM, R.E., Edit. (1970), "Alcohol and alcoholism". (International Symposium on Alcoholism, Santiago, 1966), University of Toronto Press, Toronto.
- PORTA, E.A., BERGMAN, B.J. and STENI, A.A., (1965), "Acute alcoholic hepatitis". Amer. J. Path. 46: 657-689.
- PRIEST, R.G., BINNS, J.K. and KITCHEN, A.H., (1966), "Electrocardiogram in alcoholism and accompanying physical disease". Brit. Med. J. I: 1453-1455.
- RANKIN, J.G., WILKINSON, P. and SANTAMARIA, J.N., (1970), "Factors influencing the prognosis of the alcoholic patient with cirrhosis". Aust. Ann. Med. 19: 232-239.
- RATHOD, N.H. and THOMSON, I.G., (1971), "Women alcoholics: A clinical study". Quart. J. Stud. Alcohol. 32: 45-52.
- RATNOFF, O.D. and PATEK, A.J., (1942), "Natural history of Laennec's cirrhosis of the liver: An analysis of 386 cases". Medicine. 21: 207-268.
- RHODES, R.J. and HUDSON, R.M., (1969), "A follow-up study of tuberculous Skid Row alcoholics. I. Social adjustment and drinking behaviour". Quart. J. Stud. Alcohol. 30: 119-128.
- RIGGS, H.E. and BOLES, R.S., (1944), "Wernicke's disease: A clinical and pathological study of 42 cases". Quart. J. Stud. Alcohol. 5: 361-370.
- RITSON, B., (1968), "The prognosis of alcohol addicts treated by a specialized unit". Brit. J. Psychiat. 114: 1011-1029.
- ROBERTS, K.E., (1963), "Mechanisms of dehydration following alcohol ingestion". Arch. Intern. Med. 112: 154-157.
- ROGGIN, G.M., IBER, F.L., KATER, R.M.H. and TABON, F., (1969), "Malabsorption in the chronic alcoholic". Johns Hopkins. med. J. 125: 321-330.
- ROMANO, J. (1937), "Deficiency syndromes associated with chronic alcoholism". Amer. J. Med. Sci. 194: 645-651.
- ROMANO, J., (1941), "Early contributions to the study of delirium tremens". Ann. Med. Hist. 3: 128-139.

- ROMANO, J., MICHAEL, M. and MERRITT, H.H., (1960), "Alcoholic cerebellar degeneration". Arch. neurol. psychiat. 44: 1230-1236.
- ROSENBAUM, M. and MERRITT, H.H., (1938), "Korsakoff's syndrome. A clinical study of the alcoholic form with special regard to prognosis". A.M.A. Arch. Neurol. and Psychiat. 41: 978-983.
- ROSENBERG, C.M., (1969), "Young alcoholics". Brit. J. Psychiat. 115: 181-188.
- ROSENBLATT, S.M., GROSS, M.B., BROMAN, M., LEWIS, E. and MALENOWSKI, B., (1971), "Patients admitted for treatment of alcohol withdrawal syndromes: An epidemiological study". Quart. J. Stud. Alcohol. 32: 104-115.
- ROSSET, M. and OKI, G., (1971), "Skin diseases in alcoholics". Quart. J. Stud. Alcohol. 32: 1017-1024.
- RYBACK, R.S., (1971), "The continuum and specificity of the effects of alcohol on memory". Quart. J. Stud. Alcohol. 32: 995-1016.
- RYBACK, R. and DESFORGES, J., (1970), "Alcoholic thrombocytopenia in three in-patient drinking alcoholics". Arch. Intern. Med. 125: 475-477.
- SANDERS, M.G., (1970), "Alcoholic cardiomyopathy: A critical review". Quart. J. Stud. Alcohol. 31: 324-368
- SANTAMARIA, J.N., (1967), "Treatment of the drinking traffic offender". Med. J. Aust. 2: 724-727.
- SARETT, H.P., PEDERSON, R., and CHELDELIN, V.H., (1945), "Microbiological assay methods for nicotinic acid". Arch. Biochem. 7: 77-85.
- SAUNDERS, S.J., (1963), "Iron metabolism in symptomatic porphyria - a preliminary communication". S. Afr. J. Lab. Clin. Med. 9: 277-282.
- SCHEIG, R., (1970), "Effects of ethanol on the liver". Amer. J. Clin. Nutr. 23: 467-473
- SCHMIDT, W. and de LINT, J., (1969), "Mortality experiences of male and female alcoholic patients". Quart. J. Stud. Alcohol. 30: 112-118.
- SCHMIDT, W. and de LINT, J., (1972), "Causes of death of alcoholics". Quart. J. Stud. Alc. 33: 171-185.
- SCHNEIDER, K., quoted in Henderson and Gillespie, "Textbook of Psychiatry". O.U. Press, London 1969.
- SCHNEIDER, K., (1928), "Handbuch der Geisteskrankheiten". J. Springer, Berlin.

- SCLARE, A.B., "The female alcoholic". Brit. J. Addict. 1970. 65: 99-107.
- SCOTT, D.J., (1967), "Alcoholic hallucinosis". Brit. J. Addict. 62: 113-125.
- SCOTTISH HOME AND HEALTH DEPARTMENT (1965), "Alcoholism - Report on Health Services for treatment and rehabilitation". H.M.S.O.
- SCOTTISH HOME AND HEALTH DEPARTMENT. HOSPITAL IN-PATIENT STATISTICS. 1964-1970. Edinburgh.
- SHATTUCK, G.C., (1928), "Relation of beriberi to polyneuritis from other causes". Amer. J. Trop. Med. 8: 539-543.
- SHEPHERD, M., (1961), "Morbid jealousy; Some clinical and social aspects of a psychiatric symptom". J. ment. Sci. 107: 687-753.
- SHERLOCK, S., (1968), "Diseases of the Liver and Biliary System". Fourth Edition. Blackwell; Oxford and London.
- SIM, M., (1968), "Guide to Psychiatry". 2nd. Edit. Livingstone, Edinburgh.
- SMALL, M., LONGARINI, A. and ZAMCHEK, N., (1959) "Disturbances of digestive physiology following acute drinking episodes in "Skid Row" alcoholics". Amer. J. Med. 27: 575-585.
- SMITH, M.A.E. and SCLARE, A.B., (1964), "Alcoholism in Glasgow". Scot. med. J. 9: 514-520.
- SMITHURST, B.A., (1965), "The incidence of alcoholism in patients admitted to the medical wards of a public hospital". Med. J. Aust. 1: p738.
- SPIES, T.D., RING, C.D., GELPERIN, J. and BEAN, W.B., (1938), "The mental symptoms of pellagra: Their relief with nicotinic acid". Amer. J. med. Sci. 196: 461-475.
- SPIES, T.D. and DeWOLF, H.F., (1933), "Observations on the aetiological relationship of severe alcoholism to pellagra". Amer. J. med. Sci. 186: 521-525.
- STENBACK, A., ACHE, K.A. and RIMON, R.H., (1965), "Physical disease, hypochondria, and alcohol addiction in suicides committed by mental hospital patients". Brit. J. Psychiat. 111: 933-937.
- SU, C-K. and PATEK, A.J., (1970), "Dupytren's contracture, its association with alcoholism and cirrhosis". Arch. Intern. Med. 126: 278-281.
- SULLIVAN, W.C., (1900), "The relation of alcoholism to suicide in England, with special reference to recent statistics". J. Ment. Sci. 46: 260-281.

- SUMMERSKILL, W.H.J., DAVIDSON, C.S., DIBLE, J.H., MALLORY, G.K., SHERLOCK, S., TURNER, M.D. and WOLFE, S.J., (1960), "Cirrhosis of the liver: A study of alcoholics and non-alcoholic patients in Boston and London". *New Eng. J. Med.* 262: 1-9.
- SUNDBY, P., (1967), "Alcoholism and Mortality". National Institute for Alcohol Research. Publ. No. 6. Universitetsforsaget; Oslo.
- SUTTON, T., (1813), "Tracts on Delirium Tremens, on Peritonitis, and on Some Other Internal Inflammatory Affections, and on the Gout". London.
- SYDENSTRICKER, V.P. and CLECKLEY, H.M., (1941), "The effect of nicotinic acid in stupor, lethargy and various other psychiatric disorders". *Amer. J. Psychiat.* 98: 83-92.
- SYDENSTRICKER, V., (1943), "Psychic manifestations of nicotinic acid deficiency". *Proc. Roy. Soc. Med.* 36: 169-171.
- TASHIRO, W. and LIPSCOMB, W.R., (1963), "Mortality experiences of alcoholics". *Quart. J. Stud. Alcohol.* 24: 203-210.
- TEXON, M., (1950), "Medical aspects of an alcoholic service in a general hospital". *Quart. J. Stud. Alcohol.* 11: 205-211.
- UGARTE, G. and VALENZUELA, J., (1971), "Mechanisms of liver and pancreas damage in man". pp133-161 in *Biological Basis of Alcoholism*, Edit. Israel, Y. and Mardones, New York.
- VALLANCE, M., (1965), "Alcoholism: A two-year follow-up study". *Brit. J. Psychiat.* 111: 348-356.
- VICTOR, M., (1968), "The pathophysiology of alcoholic epilepsy". *Res. Publ. Ass. nerv. ment. Dis.* 44: "The Addictive States". 431-454.
- VICTOR, M. and ADAMS, R.D., (1953), "The effect of alcohol on the nervous system". *Res. Publ. Ass. nerv. ment. Dis.* 32: "Metabolic and Toxic Diseases of the Nervous System". 526-573.
- VICTOR, M., ADAMS, R.D. and COLE, M., (1965), "The acquired (non-Wilsonian) type of chronic hepatocerebral degeneration". *Medicine.* 44: 345-396.
- VICTOR, M., ADAMS, R.D. and COLLINS, G.H., (1971), "The Wernicke-Korsakoff Syndrome". Oxford.

- VICTOR, M., ADAMS, R.D. and MANCALL, E.L., (1959),
A restricted form of cerebellar cortical degeneration
occurring in alcoholic patients". A.M.A. Arch. neurol.
1: 579-688.
- VICTOR, M. and HOPE, J.M., (1958), "The phenomenon of auditory
hallucinations in chronic alcoholism; A critical
evaluation of the status of alcoholic hallucinosis".
J. nerv. ment. Dis. 126: 451-481.
- VOEGTLEN, W.L., O'HOLLAREN, P. and O'HOLLAREN, N., (1943),
The glucose tolerance of alcoholic addicts; A study of
303 cases". Quart. J. Stud. Alcohol. 4: 163-182.
- WALLGREN, H. and BARRY, III, H., (1970), "Actions of Alcohol".
Elsevier Publishing Company. Amsterdam, London, New York.
- WALSH, J.C. and MCLEOD, J.G., (1970), "Alcoholic neuropathy; An
electrophysiological and histological study". J.
Neurol. Sci. 10: 457-467.
- WALSH, P.J.F., (1962), "Korsakow's psychosis precipitated by
convulsive seizures in chronic alcoholics". J. Ment.
Sci. 108: 560-563.
- WALSH, W.H., (1873), "A Practical Treatise on the Disease of the
Heart and Great Blood Vessels". p359., Smith, Elder London,
quoted by Myerson, R.M. (1971) in "Biological Basis of
Alcoholism". edit. by Israel Y. and Mardones, T.
- WALTON, H.J., RITSON, F.B. and KENNEDY, R. (1966), "Response of
alcoholics to clinic treatment". Brit. Med. J. ii:
1171-1174.
- WARDER, J. and ROSS, C. (1971), "Alcoholism and its treatment in
Scotland: A critical review". Brit. J. Addict. 66: 110-122.
- WARE, J., (1841), "On the treatment of delirium tremens".
Med. Commun. Mass. med. Soc. 6: 175-182.
- WATERS, A.H. and MOLLIN, D.L., (1961), "Studies on the folic acid
activity of human serum". J. Clin. Path. 14: 335-344.
- WATERS, A.H., MORLEY, A.A. and RANKIN, J.G., (1966), "Effect of
alcohol on haemopoiesis". Brit. Med. J. II: 1565-1568.
- WAYBURN, E. and GUERARDI, C.R., (1940), "Relation between multiple
peripheral neuropathy and cirrhosis of the liver".
Arch. Int. Med. 66: 161-173.
- WECHSLER, D.A., (1941), "The effect of alcohol on mental
activity". Quart. J. Stud. Alcohol. 2: 479-485.
- WERNICKE, C., (1881), "Lehrbuch der Gehirnkrankheiten für
Aerzte und Studierende". Vol. 2 Kassel. pp229-242.

- WHITTET, M.M., (1970), "Epidemiology of alcoholism in the Highlands and Islands: Interim observations".
Hlth. Bull. (Edin.), 28: 8-13.
- WHITTLE, H., BLAIR, A., NEALE, G., THALASSINOS, N.,
McLAUGHLIN, M., MARSH, M.N., PETERS, T.J., WEDZICHA, B.
and THOMPSON, G.R., (1969), "Intravenous vitamin D in the
detection of vitamin D deficiency". Lancet. I 747-750.
- WILKINSON, P., SANTAMARIA, J.N. and RANKIN, J.G., (1969),
"Epidemiology of alcoholic cirrhosis". Aust. Ann.
Med. 18: 222-226.
- WILKINSON, P., JORNACZEWSKI, A., RANKIN, J.G. and
SANTAMARIA, J.N., (1971), "Physical disease in
alcoholism. Initial survey of 1,000 patients".
Med. J. Aust. Vol. I : 1217-1223.
- WILKS, S., (1868), "Lectures on diseases of the nervous system.
General paralysis of the insane". Med. Times Gaz.
2: 470.
- WILLIAMS, I.R. and GIRDWOOD, R.H., (1970), "The folate status
of alcoholics". Scot. med. J. 15: 285-288.
- WILLIAMS, R.J., (1952), "Alcoholism as a nutritional problem".
J. Clin. Nutr. 1: 32-35.
- WINOKUR, G. and CLAYTON, P.J., (1968), "Family history studies IV:
Comparison of male and female alcoholics". Quart. J.
Stud. Alcohol. 29: 885-891.
- WOLFE, S.J., SUMMERSKILL, W.H.J. and DAVIDSON, C.S., (1957),
"Parotid swelling, alcoholism and cirrhosis". New Eng.
J. Med. 256: 491-495.
- WOLFF, G., (1970), "Does alcohol cause chronic gastritis".
Scand. J. Gastroent. 5: 289-291.
- WOODWARD, E.R., ROBERTSON, C., RUTTENBERG, B.S. and SHAPIRO, H.,
(1957), "Alcohol as a gastric secretory stimulant".
Gastroent. 32: 727-737.
- WORTIS, H., (1940), "Delirium tremens". Quart. J. Stud.
Alcohol. 41: 251-267.
- WORTIS, H., (1941), "Introductory remarks on Dr. Thomas Sutton's
description of delirium tremens". Quart. J. Stud. Alcohol.
2: 177-178.
- YELD, R.A., (1898), "Alcoholic cirrhosis". St. Barts. Hosp. Rep.
34: 215-229.
- ZIEVE, L., (1958), "Jaundice, hyperlipaemia and haemolytic anaemia:
A heretofore unrecognised syndrome associated with
alcoholic fatty liver and cirrhosis". Ann. Intern. Med.
48: 471-496.

ZIEVE, L. and HILL, E., (1963), "Vitamin unresponsiveness, progression of classical signs of neuropathy and pellagra during therapy". Amer. J. Clin. Nutr. 13: 312-317.

APPENDIX 1

ALCOHOLISM SURVEY

2-5 SEX NUMBER

--	--	--

1 = male
2 = female

SURNAME

FORENAME

ADDRESS

S.G.H. NO.

6-7 AGE

--	--

D.O.B. / /

8 LENGTH OF STAY
in Weeks

1	1-3	3-5	6-12	12+
1	2	3	4	5

9 MODE OF ADMISSION

EMERGENCY	WAITING LIST
1	2

10 MEANS OF REFERRAL

GP	AA	C of A	SAM	SELF	OTHER HOSP or WARD	JUD	NK
1	2	3	4	5	6	7	8

11 NO. OF ADMISSIONS

x1	x2	x3	x4	x5	x6	x7
1	2	3	4	5	6	7

12 RELIGION

PROT	R.C.	OTHER	0	NK
1	2	3	4	0

13 SOCIAL CLASS

I	II	III	IV	V	NK
1	2	3	4	5	0

14 CIVIL STATE

M	S	W	D	SEP	NK
1	2	3	4	5	0

15	MAIN ALCOHOLIC BEVERAGE	W	F	Mixt	Sp	B	C	NK
		1	2	3	4	5	6	0

16	BOUPTS	YES	NO
		1	2

17	AMOUNT IN GMS/ ALC per day	0-	50-	150-	250-	350-	450-	550-	650-	750	NK
		1/49	2/149	3/249	4/349	5/449	6/549	7/649	8/749	9	0

18	LENGTH OF TIME EXCESS DRINKING YRS.	0-1	1-2	2-5	5-10	10-20	>20	NK
		1	2	3	4	5	6	0

19	FOOD	POOR	SATIS	NK
		1	2	3

20	WEIGHT	LOSS	STAT	NK
		1	2	3

21	OFFENCES	SEVERE	D+D B of P	DRIVING	<1 MINOR	MULT	0	NK
		1	2	3	4	5	6	7

22	PREVIOUS SUICIDE ATTEMPT	YES	NO
		1	2

23	DISCH.	SELF	AFT ALC	BOTH	NEITHER
		1	2	3	4

24	AETIOL.	PERSONALITY DISORD			DEP	SCHIZ	LOW I.Q.	SEX DEV	NEUROTIC	EPIL	0
		NON SPEC	AGG	HYS							
		1	2	3	4	5	6	7	8	9	0

COMPLICATIONS

		YES	NO
	25 RESP. DIS.	1	2
	26 *ANAEMIA	1	2
	27 NUTRITIONAL ARN.	1	2
GI	(28 *GASTRITIS	1	2
	(29 *GASTRIC OPN.	1	2
	(30 PEPTIC ULCER	1	2
HEP	(31 *CIRRHOSIS	1	2
	(32 HEPATITIS	1	2
NEURO	(33 *NEUROPATHY	1	2
	(34 EPILEPSY	1	2
	(35 RARE	1	2
	(36 E.E.G.	1	2

37	WITHDRAWAL	0	MILD	MOD	SEV	DT's
		1	2	3	4	5

		YES	NO
* PSYCH	(38 HALLUCINOSIS	1	2
	(39 PARANOID	1	2
	(40 DEMENTIA	1	2
	(41 E.C.G.	1	2
	(42 CARDIOMYOPATHY	1	2
	(43 "OTHER" COMPLI.	1	2

APPENDIX 3

GARTNAVEL ROYAL HOSPITAL PSYCHIATRIC SERVICES

1055 Great Western Road,
Glasgow.
G12 0XH

CONFIDENTIAL.

(Date)

Dear

I am at present doing a survey on some of the patients who were admitted to the Southern General Hospital when I worked there. I have been unable to trace your general practitioner and I wondered if you would either let me have his name so that I may ask him how you have been keeping, or whether you would return this letter to me answering the following questions.

- 1) Did you find your stay in hospital useful? Yes/No
- 2) When you left hospital did you feel Improved/Just the same/Worse?
- 3) Do you now feel Improved/Just the same/Worse?
- 4) In the interim period have you had
 - a) any other illnesses?
 - b) any further nervous trouble?

Name and address of general practitioner.

Yours sincerely,

P.W. Kershaw,
Consultant Psychiatrist.

Appendix 5

The program BMD07M performs a multiple discriminant analysis in a stepwise manner. At each step a variable is entered or deleted using the following criteria:

- 1) The variable with the largest F value is entered.
- 2) The variable with an F value too low is deleted.

The output consists of:

- 1) Group means and standard deviations.
- 2) Within groups covariance matrix.
- 3) Within groups correlation matrix.
- 4) At each step:
 - (a) Variables included and F to remove.
 - (b) Variables not included and F to enter.
 - (c) U statistic and approx. F statistic to test equality of group means.
 - (d) Matrix of F statistics to test the equality of means between each pair of groups.
- 5) After the last step:
 - (a) Classification functions.
 - (b) Classification matrix.
- 6) For each case:
 - (a) Posterior probability of coming from each group.
 - (b) Square of the Mahalanobis distance from each group.
- 7) Summary table.

There are four main steps in the computational procedure using the following notation:

- p = number of variables.
g = number of groups used for analysis.
t = total number of groups.
 n_m = number of cases in group m.

n = total number of cases.

x_{mki} = value of variable i for case k of group m .

1. The following are calculated:

$$\text{Means } \bar{x}_i = \frac{1}{n} \sum_{m=1}^g \sum_{k=1}^{n_m} x_{mki} \quad i = 1, 2, \dots, p$$

$$\text{Group means } \bar{x}_{mi} = \frac{1}{n_m} \sum_{k=1}^{n_m} x_{mki} \quad \begin{matrix} i = 1, 2, \dots, p \\ m = 1, 2, \dots, t \end{matrix}$$

Group standard deviations

$$s_{mi} = \sqrt{\frac{1}{n_m - 1} \sum_{k=1}^{n_m} (x_{mki} - \bar{x}_{mi})^2} \quad \begin{matrix} i = 1, 2, \dots, p \\ m = 1, 2, \dots, t \end{matrix}$$

$$W = \{w_{ij}\} ; w_{ij} = \sum_{m=1}^g \sum_{k=1}^{n_m} (x_{mki} - \bar{x}_{mi}) (x_{mkj} - \bar{x}_{mj})$$

$$T = \{t_{ij}\} ; t_{ij} = \sum_{m=1}^g \sum_{k=1}^{n_m} (x_{mki} - \bar{x}_i) (x_{skj} - \bar{x}_j) \quad \begin{matrix} i = 1, 2, \dots, p \\ j = 1, 2, \dots, p \end{matrix}$$

Within groups covariance matrix

$$V = \{v_{ij}\} ; v_{ij} = \frac{1}{n-g} w_{ij} \quad \begin{matrix} i = 1, 2, \dots, p \\ j = 1, 2, \dots, p \end{matrix}$$

Within groups correlation matrix

$$R = \{r_{ij}\} ; r_{ij} = \frac{w_{ij}}{\sqrt{w_{ii} w_{jj}}} \quad \begin{matrix} i = 1, 2, \dots, p \\ j = 1, 2, \dots, p \end{matrix}$$

with r and $n-g-r+1$ degrees of freedom

(d) F values for each variable.

(1) If variable j has been entered

$$F_j = \frac{a_{jj} - b_{jj}}{b_{jj}} \frac{n-r-g+1}{g-1}$$

with $g-1$ and $n-r-g+1$ degrees of freedom.

(2) If variable j has not been entered

$$F_j = \frac{b_{jj} - a_{jj}}{a_{jj}} \frac{n-r-g}{g-1}$$

with $g-1$ and $n-g-r$ degrees of freedom.

(e) U statistic to test equality of group means

$$U = \text{Det}(W_{11}) / \text{Det}(T_{11})$$

with $(r, g-1, n-g)$ degrees of freedom.

(f) Approximate F statistic to test equality of group means

$$F = \frac{1 - U^{1/s}}{U^{1/s}} \frac{ms + 1 - rq/2}{rq}$$

$$\text{where } S = \sqrt{\frac{r^2 q^2 - 4}{r^2 + q^2 - 5}} \quad \text{if } r^2 + q^2 \neq 5$$

$$S = 1 \quad \text{if } r^2 + q^2 = 5$$

$$m = \frac{n - r + q + 3}{2}$$

$$q = g - 1$$

and $(rq, ms + 1 - rq/2)$ degrees of freedom

(g) Tolerance values:

$$W_i = a_{ii}/t_{ii} \quad i = r + 1 \dots p$$

3. To move from one step to the next the following rules hold:

(a) If one or more variables entered have a control value of 1 and an F value less than "F to remove" the one with the smallest F will be deleted.

(b) If no variable satisfies (a) then from the variables which passed the tolerance level and have greatest control value the one with greatest "F to enter" is selected.

4. After the last step the following are calculated:

(a) Value of mth classification function evaluated at case k of group l

$$S_{lmk} = C_{m0} + \sum_{j=1}^r C_{mj} x_{ljk}$$

(b) Posterior probability of case k in group l having come from group m

$$P_{lmk} = \frac{\text{Exp}(S_{lmk})}{\sum_{i=1}^g \text{Exp}(S_{lil})}$$

(c) The square of the Mahalanobis distance of case k in group m from group l

$$D_{lmk}^2 = (n-g) \sum_{i=1}^r \sum_{j=1}^r (x_{mki} - \bar{x}_{li}) a_{ij} (x_{mkj} - \bar{x}_{lj})$$

44	PREV. ADM.	S.G.H.	OTHER HOSP	BOTH	0
		1	2	3	4

45	DRUGS	BARB	AMPH	"OPIATE"	TRANQUI.	B+Amp	B+0	Amp+0	ALL	9	0
		1	2	3	4	5	6	7	8	9	0

46	F.H.	F	M	H/W	SIB	OTHER	MULT	0
		1	2	3	4	5	6	7

BIOCHEM.

	ABN	NORMAL	NOT PERF.
47 B12	1	2	3
48 FOLATE	1	2	3
49 THIAMINE	1	2	3
50 NIC. ACID	1	2	3
51 CHOLESTEROL	1	2	3
52 PROTEINS	1	2	3
53 SGOT	1	2	3
54 SGPT	1	2	3

55	PSYCHOLOGICAL TESTING	1	2	3
----	-----------------------	---	---	---

PROGNOSIS

56	DEAD	WORSE	I.S.Q.	IMP.	CURE	N.T.
	1	2	3	4	5	6

GARTNAVEL ROYAL HOSPITAL

GLASGOW.

Dear Doctor,

I am attempting a study of alcoholics admitted to the Southern General Hospital, Psychiatric Unit, from 1964 to 1968. While this is mainly concerned with the physical complications of alcoholism I am interested in the prognosis in connection with these complications. I would therefore be grateful, should you have any further information on the following patient who was under your care at that time, if you would fill in the enclosed form and return it to me in the stamped addressed envelope enclosed.

Yours sincerely,

PETER W. KERSHAW
Consultant Psychiatrist.

A. If DEAD give cause of death _____
Approx date of death _____

B. Physical Illness which could be connected with alcoholism _____
Peripheral Neuropathy _____
Cirrhosis _____
Other _____

C. Assessment of Alcoholism: "Cured" _____
(Abstinent for more than one year)
Improved _____
I.S.Q. _____
Worse _____

Patient's Name _____ Age: _____
Address _____ D.o.B. _____

Date seen at S.G.H. _____

Choreoathetotic Movement Disorder in Alcoholism

P. J. MULLIN,* M.B., B.S., D.P.M.

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Summary: A syndrome of choreoathetosis in association with alcoholism has been found in 12 patients. It appeared to occur more often in women, was transient, and may have been associated with alcohol withdrawal. It was not associated with gross liver disease, phenothiazine administration, or familial chorea, and no consistent abnormalities in whole blood thiamine or nicotinic acid, in serum magnesium, or in serum vitamin B₁₂ levels were present.

Introduction

While neurological complications of alcoholism have been described for over a hundred years, choreoathetosis has only been indirectly mentioned in association with alcoholism, in so far as it occurs as a complication of advanced hepatic cirrhosis, usually with a portosystemic shunt (Victor *et al.*, 1965) or as a manifestation of hypomagnesaemia (MacIntyre, 1963).

Patients and Methods

Twelve patients (six women and six men) were admitted to hospital on account of alcoholism or its complications between December 1967 and July 1969. Though their age range was from 29 to 67 years, the mean age of 48 was about five years greater than that of alcoholics admitted to one of

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the units. Half the patients drank mainly whisky, four mainly wine, one beer, and one sherry and cider. This is typical of Glasgow alcoholics, where beer is usually taken as an adjuvant to more potent drinks.

Family histories were taken by one of us (J. B.) who has had considerable experience in obtaining these in connexion with work on Huntington's chorea (Bolt, 1970). All investigations were done as soon as possible after admission. Whole-blood thiamine and nicotinic acid were measured microbiologically, using modifications of the original methods of Edwards *et al.* (1957) and Sarett *et al.* (1946), respectively. Serum folate was measured by the method of Waters and Mollin (1961) and serum vitamin B₁₂ by that of Hutner *et al.* (1956). The serum copper oxidase was measured by the method of Ravin (1961) and the serum magnesium by an atomic absorption method.

Results

The abnormal movements were commonly present in the upper half of the body and were essentially transient in character. There was a wide variety of facial movements, some patients showing eyebrow raising or blinking, others tongue protrusion. Almost all had grimacing of the perioral muscles. The facial movements when present were characteristically rapid, and laterality was shown by four cases. The oral movements had a typically twisting, pursing character; the hand and forearm movements had a sinuous, writhing character while the leg movements tended to be sudden and jerky. In 10 of the 12 patients abnormal movements were present on admission; in the other two they appeared on the fourth and fifth days after admission. Though the movements are described as "transient," their duration varied from a few hours in Case 8 to a year in Case 1. One patient (Case 9) still had reduced abnormal movements five months after they were first noted, though the possibility that he continued to drink cannot be entirely excluded. Nevertheless, there appears to be no recurrence of the movements if the patient remains abstinent. One patient (Case 4) had a return of abnormal movements when he resumed drinking as an inpatient. In two patients (Cases 3 and 10), who have been known over a period of years, the clinical picture has fluctuated, the movements being much more obvious during periods of drinking and gradually diminishing during periods of abstinence.

The only other neurological abnormalities found were muscle weakness in Cases 1, 2, 3, 4, and 6; sensory impair-

Clinical Features and Investigations

	1	2	3	4	5	6	7	8	9	10	11	12
Sex	F. 51	F. 43	F. 54	M. 34	F. 53	M. 67	F. 48	M. 44	M. 52	M. 29	F. 41	M. 55
Age at referral
Choreiform movements:
Time of appearance
Duration	1 yr.	1 wk.	1-8 wk.	3 wk.	24 hr.	5th day 12 hr.	4th day 24 hr.	3 hr.	5 mth.	1 mth.	56 hr.	12 hr.
Site	+	+	+	+	+	-	+	+	+	+	+	+
Face	+	+	+	+	+	+	-	+	+	+	+	+
Arms	+	+	+	+	+	+	-	+	+	+	+	+
Legs	+	+	+	+	+	+	-	+	+	+	+	+
Trunk	+	+	+	-	-	-	-	-	-	-	-	-
S.G.O.T. (Dade units)	..	62	50	240	18	100	43	48	14	142	26	232
S.G.P.T. (Dade units)	..	70	15	60	13	15	16	28	6	20	18	25
Whole-blood thiamine (ng./ml.)	..	10.8	10.2	29.1
Serum folate (ng./ml.)	1.2	..	6.8	3.6	4.0	2.7	..	10.0	4.8	..

A = Present on admission. + = Present. - = Absent.

ment in Cases 1, 3, and 4; and finger-nose dysmetria in Case 2, this being the only sign of cerebellar dysfunction in the series. Comparatively minor degrees of hepatomegaly were found in Cases 4, 9, and 3, the latter showing the only other clinical sign of hepatic impairment in the series—that is, prominent vascular spiders on the legs.

Routine tests of liver function showed only minor abnormalities—the serum transaminase levels are shown in the Table; the serum bilirubin and zinc sulphate turbidity levels were slightly raised in Cases 12 and 5, respectively, alpha₂-globulins were increased in Cases 1 and 6 and gamma-globulin in Case 3. The bromsulphthalein retention was increased in Cases 1 and 7 (17% and 14%, respectively), falling to normal one month after admission. Whole-blood thiamine and serum folate estimations are shown in the Table; serum B₁₂, nicotinic acid, and magnesium were normal in all patients in whom they were estimated. Serum copper oxidase, calcium, phosphate, and uric acid were normal in all cases. No patient had an abnormal E.E.G. One (Case 4) had a slight degree of pneumonic consolidation on admission and another (Case 6), who was aged 67, showed E.C.G. evidence of ischaemia, otherwise no other abnormalities were found. Liver biopsies are reported in the case histories.

Full psychological testing was carried out in eight patients: three (Cases 7, 8, and 10) showed no sign of intellectual impairment; four (Cases 3, 4, 9, and 11) showed slight changes, including memory impairment, general deterioration on performance tests, perseveration, and confabulation; and one (Case 1) showed a more pronounced impairment, and though her tests improved during her stay of 18 months in hospital she still had amnesia for a period of some months about the time of her index admission.

Illustrative Case Histories

Case 1.—A woman born in 1916 started to take excess alcohol in 1963 and was first admitted to hospital in August 1967. She gave a history of taking a "bottle of wine" daily for eight months. She settled well with minimal withdrawal symptoms but failed to attend for follow-up. In January 1968 she was readmitted to a medical ward with complaints of weakness, limb pain, and vomiting. She was emaciated and had typical choreiform movements. Severe peripheral neuropathy, ophthalmoplegia, and a variable confusional state were also present. A diagnosis of Wernicke's encephalopathy was made. Six hours after administration of intravenous Parentrovite she was more alert, replied more rapidly to questions, and was able to move her limbs on command. During the next few days she developed pronounced withdrawal symptoms and subsequently a Korsakoff psychosis, which persisted for

three months. Her choreiform movement disorder and peripheral neuropathy gradually improved so that she was walking with aid nine months after admission and walked unassisted on discharge at 18 months. Liver biopsy some months after admission showed no abnormality. She had no history of head injury, phenothiazine intake, or family history of Huntington's chorea; her mother and brother drink heavily.

Case 2.—A woman born in 1926 was admitted to hospital in 1969 with a complaint of leg weakness of three months' duration and anorexia for the preceding month. During the year before admission she had taken a "quarter to half" a bottle of whisky daily. On examination she had profound weakness of the muscles of the face and upper and lower limbs. Choreiform movements were present in the hands and forearms, being more pronounced on the right than the left side. Tendon reflexes were absent in the lower limbs, and the plantar responses were flexor. She was disorientated and confabulating. After a period of initial improvement her condition suddenly deteriorated and she died of bronchopneumonia a week after admission. She had never received phenothiazines. There was no family history of alcoholism or neurological disease. At necropsy the liver weighed 1,800 g., histological examination showing fatty change with bile duct proliferation and minimal fibrosis. The brain (examined by Dr. J. Hume Adams) weighed 1,300 g., no abnormalities being noted on macroscopic examination. Histological examination, however, revealed the typical changes of a rather subacute Wernicke's encephalopathy. In addition, some rarefaction and reactive gliosis in the wall of the third ventricle and a very light fibrillary gliosis here and there in the white matter were found. There was no evidence of degenerative changes in the anterior thalamic nuclei or basal ganglia.

Case 3.—A woman born in 1913 started to take excess alcohol in 1962, probably half a bottle of whisky daily. She was first referred in 1965 and since then has had many admissions both to psychiatric and to medical wards on account of alcoholism or its complications—for example, visual hallucinations, self-poisoning attempts, septicaemia, and occasional epileptic seizures. She developed choreoathetotic movements in 1967. The movements gradually ceased after admission, alcohol being then withdrawn and, as a rule, parenteral vitamins being given. On one well-documented occasion, however, parenteral vitamins were withheld and the abnormal movements persisted until these were given one month later. Liver biopsy in 1968 showed a slight degree of fatty change and some evidence of cirrhosis without necrosis. Her father died at the age of 52 years from "alcoholic" liver cirrhosis. Her brother had haemochromatosis and cerebellar signs. In the past she had received chlorpromazine but never in excessive dosage.

Discussion

The syndrome described here is thus a transient choreoathetosis more usually affecting the upper half of the

body. The picture is similar to that described by Hunter *et al.* (1964) secondary to prolonged administration of phenothiazine drugs. There was, however, no evidence that any of these patients had received phenothiazine drugs over prolonged periods or even in high doses over short periods. Chlorpromazine, in fact, had a beneficial effect on the movements of one patient (Case 10). Another (Case 9) was known to have taken excessive quantities of diazepam before admission, but there is no reason to suspect this drug as a possible aetiological factor.

Women appear more prone to develop choreiform movements with both phenothiazines and alcohol; the ratio of men to women is about 4:1 in the total admissions for alcoholism to one of our psychiatric units over a period of four years. The sex ratio of 1:1 in the cases described here thus shows a preponderance of females.

Possibly these represent early cases of Huntington's chorea, but detailed family histories have shown no evidence of any neurological disorder apart from that referred to in Case 3. While denial of the family history is not uncommon in Huntington's chorea for various reasons (Hans and Gilmore, 1968), no connexion between these families and any of the families with Huntington's chorea in the western region of Scotland previously collected by Bolt (1970) was established. In the latter study excessive drinking was alleged to have occurred in 24 men and four women from the total of 695 patients for whom records were available or who were reliably reported as suffering or having suffered from Huntington's chorea. The sex ratio of 6:1 in the patients with Huntington's chorea thus resembles that in uncomplicated alcoholism rather than that of the cases reported here. Other hereditary degenerations such as Wilson's disease are similarly excluded by the absence of a family history, gross liver disease, and the characteristic neurological, biochemical, and radiological findings.

Choreiform movements have been observed previously in the presence of severe liver disease and portosystemic shunts (Victor *et al.*, 1965; Hurwitz and Montgomery, 1965; Toghill *et al.*, 1967). Victor *et al.* (1965) studied 27 patients with severe liver disease (23 of whom had previous portal encephalopathy) who developed a chronic neurological disorder which they called hepatocerebral degeneration. Of these 27, 11 were alcoholics and some of these exhibited typical choreoathetotic movements: one was said to be indistinguishable from Huntington's chorea. They seem to have had more severe liver disease than the patients we have described. While liver function tests were completely normal in only two of our 12 patients the changes in the remaining ten were

minor and similar to those normally found in alcoholics admitted to the units. Thus none of our patients, including the two with histological evidence of liver damage, has ever had ascites or oedema though three (Cases 2, 3, and 9) gave a history of previous "hepatitis." Possibly Case 3 could be suffering from chronic hepatocerebral degeneration although she has never had any episode of portosystemic encephalopathy and in periods of abstinence, providing that she is well nourished, the choreiform movements disappear. Victor *et al.* (1965) did not describe complete remission of the movements in their paper. Thus possibly all our patients are suffering from a very early form of chronic hepatocerebral degeneration, especially as the movements we describe are so transient.

Nutritional factors must always be considered in any condition which is related to alcoholism. Owing to the frequency with which oral or parenteral vitamins are administered to alcoholics useful estimations of blood thiamine and nicotinic acid levels could be obtained in only a few cases; of these the blood thiamine was low in three (Cases 1, 2, and 3) whereas the nicotinic acid levels were within normal limits. The fact that on admission two of the patients (Cases 1 and 2) were suffering from Wernicke's encephalopathy, a very rare condition, in itself suggests a causal relationship. The diet of five other patients was poor but that of the remainder adequate. In general patients who had had a poor diet had more persistent movements, and, as noted earlier, on one occasion one patient had a rapid improvement in her movements following treatment with parenteral vitamins a month after admission. There is, however, no evidence from the literature that patients with Wernicke's encephalopathy exhibit choreoathetosis. Jolliffe *et al.* (1940) described a severe encephalopathy with cog-wheel rigidity responding to nicotinic acid but not to thiamine and occurring in patients on a poor diet, some of whom had classical pellagra.

Despite the lack of definitive support for a deficiency of thiamine or nicotinic acid in our findings, Woods and Pendleton (1925) reported choreoathetosis in association with dietary deficiency states, and the latter must remain one of the more likely causes. Interestingly Alexander (1942), in describing an alcoholic with severe cirrhosis who developed rhythmic tremors of the hands, arms, mouth, and eyes—in other words the condition which would now be called acquired hepatocerebral degeneration—postulated that the aetiology might be "lack of a metabolic catalyst or vitamin."

Hypomagnesaemia was not found in those patients in whom the serum magnesium was estimated. Though

choreiform movements are described in relation to hypomagnesaemia it is not clear whether they are related to magnesium depletion, coincidental liver disease (Fishman, 1965), or to some of the other deficiencies mentioned in many of these reports—for example Flink *et al.* (1954) and Hammarsten and Smith (1957). Since magnesium diuresis does occur in alcoholics (Kalbfleisch *et al.*, 1963) minor fluctuations in its level might possibly interfere with the functioning of enzyme systems within the hepatic cell.

The transient nature of the disorder suggests that it may be related to alcohol withdrawal; the relationship was quite definite in Cases 5, 6, 7, and 8, but Cases 3, 7, and 10 showed the movements while drinking heavily. There was no apparent correlation between the extent of distribution of the condition and the type of beverage consumed or the duration of alcoholism. It is not clear why the condition is more common in female alcoholics.

The neuropsychiatric syndromes associated with liver disease have generally been attributed to failure of the liver to detoxify protein breakdown products. Victor *et al.* (1965) suggested that a subtle abnormality of liver function may exist in those cases in which neurological disorder antedates detectable derangement of liver function or ammonium metabolism. Such an abnormality could presumably result from a disruption of intracellular systems secondary to a deficiency of a variety of factors, known or unknown.

The only constant aetiological factor in our cases is their high alcohol intake. It seems not unreasonable, however, to suppose that they represent an early transient form of the chronic hepatocellular degeneration of Victor *et al.* (1965). This, together with the existence of Wernicke's encephalopathy in two of our cases and the probability or possibility of vitamin deficiency in several more (poor diet, gastritis, motor, sensory, or memory impairment, the latter being noted in all but two cases), opens up an interesting field for speculation.

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REFERENCES

- Alexander, L. (1942). *Research Publications, Association for Research in Nervous and Mental Disease*, 21, 334.
- Bolt, J. M. W. (1970). *British Journal of Psychiatry*, 116, 259.
- Edwards, M. A., Kaufman, M. L., and Storvick, C. A. (1957). *American Journal of Clinical Nutrition*, 5, 51.
- Fishman, R. A. (1965). *Archives of Neurology*, 12, 562.
- Flink, E. B., Stutzman, F. L., Anderson, A. R., Konig, T., and Fraser, R. (1954). *Journal of Laboratory and Clinical Medicine*, 43, 169.
- Hammarsten, J. F., and Smith, W. O. (1957). *New England Journal of Medicine*, 256, 897.
- Hans, M. B., and Gilmore, T. H. (1968). *British Journal of Psychiatry*, 114, 93.
- Hunter, R. K., Earl, C. J., and Thornicroft, S. (1964). *Proceedings of the Royal Society of Medicine*, 57, 758.
- Hurwitz, L. J., and Montgomery, D. A. D. (1965). *Archives of Neurology*, 13, 421.
- Hutner, S. H., Bach, M. K., and Ross, G. I. M. (1956). *Journal of Protozoology*, 3, 101.
- Jolliffe, N., Bowman, K. M., Rosenblum, L. A., and Fein, H. D. (1940). *Journal of the American Medical Association*, 114, 307.
- Kalbfleisch, J. M., Lindeman, R. D., Ginn, H. E., and Smith, W. O. (1963). *Journal of Clinical Investigation*, 42, 1471.
- MacIntyre, I. (1963). *Scientific Basis of Medicine: Annual Reviews*, p. 216.
- Ravin, H. A. (1961). *Journal of Laboratory and Clinical Medicine*, 58, 161.
- Sarett, H. P., Pederson, R. L., and Cheldelin, V. H. (1946). *Archives of Biochemistry*, 7, 77.
- Toghill, P. J., Johnston, A. W., and Smith, J. F. (1967). *Journal of Neurology, Neurosurgery and Psychiatry*, 30, 358.
- Victor, M., Adams, R. D., and Cole, M. (1965). *Medicine*, 44, 345.
- Waters, A. H., and Mollin, D. L. (1961). *Journal of Clinical Pathology*, 14, 335.
- Woods, A. H., and Pendleton, L. (1955). *Archives of Neurology and Psychiatry*, 13, 549.

BLOOD THIAMINE AND NICOTINIC ACID
LEVELS IN ALCOHOLISM AND
CONFUSIONAL STATES

BY

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Blood Thiamine and Nicotinic Acid Levels in Alcoholism and Confusional States

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It has been routine psychiatric practice in recent years to prescribe vitamins in alcoholism and confusional states and sometimes in other organic psychoses. The doses given are massive, varying from about ten to twenty times those strictly necessary in deficiency states. This empirical therapy is supported neither by controlled trials nor by direct evidence of vitamin deficiency.

Vitamin therapy in psychiatric conditions has developed gradually. Even before vitamins were discovered, the mental changes associated with disease states such as beri-beri and pellagra were well known and were shown to be helped by giving various fresh foods. As the individual vitamins were discovered, the various deficiency states began to be separated. In 1940, Jolliffe demonstrated that a severe encephalopathy with cog-wheel rigidity, grasping and sucking reflexes associated with poor nutrition and often with classical pellagra could be cured by nicotinic acid but not by thiamine (Jolliffe *et al.*, 1940). Shortly after, Sydenstricker and Cleckley (1941) described how patients suffering from stuporose states improved when treated with nicotinic acid, even if there was no clinical evidence of pellagra. Some patients required large amounts of nicotinic acid for improvement, and the authors suggested that toxic psychoses or states of exhaustion might be relieved by nicotinic acid.

That Wernicke's encephalopathy is caused by thiamine deficiency was finally proved by de Wardener and Lennox (1947) in their report on 52 patients they had attempted to treat in Changi P.O.W. camp. Thiamine cured the ophthalmoplegia and anorexia and improved the mental state, but often other B vitamins were required to restore a complete mental normality. By the middle 1940's it was well established that severe mental changes and

psychiatric disturbance could be caused by vitamin deficiency. To cure these states, intravenous vitamin preparations were given in much larger dosage than the normal intake.

Between 1953 and 1959 Gould suggested that many organic psychiatric states (including delirium tremens, acute alcoholic psychosis, post-operative confusional states, delirium due to drugs and Korsakoff's state, as well as some cases of dementia) were due to a disturbance of brain metabolism. His theory suggested that "toxins" affected the enzyme systems of the neurones (Gould, 1959) and that to overcome these toxins and by-pass various metabolic pathways high blood levels of B vitamins were necessary. He held that in this way, on account of the large amounts present in the extracellular fluid, vitamins pass into the cell directly by osmosis instead of by the usual mechanisms which involve energy transfer against the osmotic gradient. Since then, parenteral doses of vitamins have become almost a routine treatment in organic psychoses.

The use of vitamins (in these large doses) rests on speculative theory unless there is a history of dietary deficiency, or clinical evidence of vitamin deficiency and/or malabsorption. To prove or disprove Gould's hypothesis is difficult, but two approaches are possible. One method is to use restriction experiments and assess the mental state during increasing deficiency and replacement. Such experiments have proved inconclusive. Another method is the clinical or biochemical assessment of vitamin deficiency in organic psychoses. An investigation using this approach is described in this paper.

METHOD

Whole blood thiamine and nicotinic acid were measured by microbiological methods in

patients admitted to a general hospital Psychiatric Unit, suffering from alcoholism, dementia and confusional states. Patients who had received vitamin therapy within one month of admission either orally or parenterally were excluded from the series, as were any who had been on antibiotics within the previous two weeks. As a result the group with confusional states was small. Occasionally insufficient blood was received for both assays to be done on the same patient, so that the numbers for each vitamin are not identical. A control group (consisting of patients in the Unit suffering from schizophrenia or anxiety states and of hospital staff) was studied to ascertain normal values. The mean age of the control group was 38.4 years, of the alcoholic group 46.5 years, and of a group suffering from dementia 70.7 years. The 50 alcoholics consumed all types of drink—apart from methylated or surgical spirit. Of the 14 patients with dementia, 12 had senile dementia, 2 were arteriosclerotic; none of these had an acute confusional state such as would be associated with an intercurrent infection or other cause.

All alcoholics were investigated for evidence of liver disease both clinically and by measurement of serum bilirubin, alkaline phosphatase, SGOT, SGPT and protein electrophoresis. Evidence of peripheral neuropathy, weight loss and signs of malnutrition or vitamin deficiency was noted. Their dietary histories were obtained and were considered poor if a meal containing protein was not taken regularly. These patients rarely ate fruit or wholemeal bread.

For vitamin estimation, blood was withdrawn on admission or one hour after breakfast on the morning after admission and stored at a temperature of -20°C . Whole blood thiamine was measured microbiologically using *Lactobacillus fermenti* (NCIB 6991). Heparinized blood was treated enzymatically with diastase to release thiamine pyrophosphate from the red blood cells (Baker and Sobotka, 1962) and the method described by Edwards was then followed (Edwards, *et al.*, 1957).

For nicotinic acid, the method of preparation of whole blood described by Baker and Sobotka (1962) and the assay method described by Sarett *et al.* (1945) were used, though the

growth response was measured turbidimetrically after 16 hours' growth of *Lactobacillus plantarum* (NCIB 8864) at 37°C . instead of acidimetrically after 72 hours at 30°C . Both assays were performed using Difco Assay Medium.

RESULTS

The results of blood levels for thiamine are illustrated in Figures 1 and 2.

In Figure 1 three groups of patients (with alcoholism, delirium tremens and dementia) are compared with the control group. The thiamine levels in the control series are seen to range from 19.8 m $\mu\text{G/ml}$. to 39.9 m $\mu\text{G/ml}$. with a mean of 24.8 m $\mu\text{G/ml}$., whereas in the alcoholic group of 31 patients the range is 13.8–38.4 m $\mu\text{G/ml}$. and the mean is 25.4 m $\mu\text{G/ml}$. The levels in seven out of nine patients with delirium tremens are subnormal and the mean is only 17.6 m $\mu\text{G/ml}$. All nine patients with dementia have thiamine levels within the control range.

In Figure 2 the alcoholics are divided into groups by their withdrawal symptoms.

Twelve patients had no symptoms, 9 had "mild" symptoms (slight tremor only), 5 had "moderate" symptoms (tremor, anxiety and insomnia), 5 had "severe" symptoms (marked tremor, restlessness, and nightmares) and 9 had frank delirium tremens. Although there is an overlap in whole blood thiamine levels, the

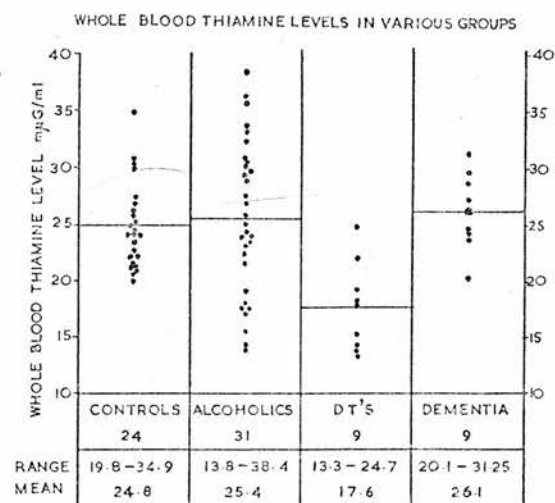


FIG. 1.

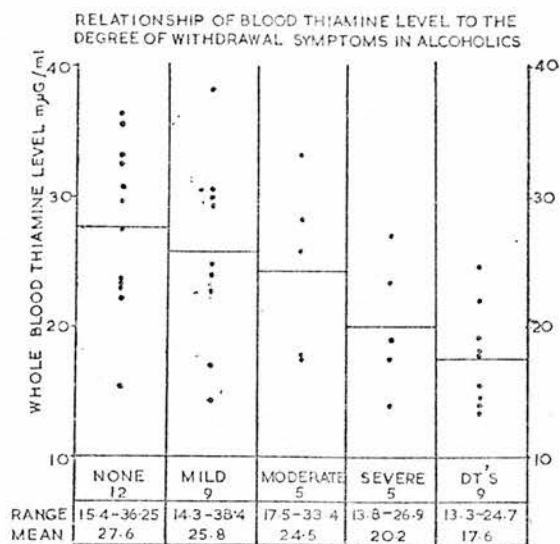


FIG. 2.

mean levels fall steadily as the severity of the withdrawal symptoms increases and the between groups variance is significant at the 1 per cent. level ($F=4.19$).

The results for nicotinic acid are illustrated in Figure 3.

In 26 controls the range is seen to be from 1.1 $\mu\text{G/ml.}$ to 2.93 $\mu\text{G/ml.}$ with a mean of 1.63 $\mu\text{G/ml.}$ In the group of 30 alcoholics the mean is 1.77 $\mu\text{G/ml.}$ but with three below the normal range. The 15 delirium tremens patients show a mean of 1.71 $\mu\text{G/ml.}$ with three below normal. The mean level in the 12 patients with dementia is 1.85 $\mu\text{G/ml.}$ with one very high level; as far as could be ascertained this last patient had received no vitamin therapy in the previous six months, nor was there any evidence of liver disease to account for the high level.

In 13 patients who had peripheral neuropathy in association with alcoholism, thiamine estimations were performed on 11 of whom four had abnormally low levels and of the 13 two were found to have low levels of nicotinic acid. None had low levels of both vitamins.

Four of 9 patients with alcoholic cirrhosis in whom thiamine was estimated had low levels, and in 12 in whom nicotinic acid was estimated one had a low level.

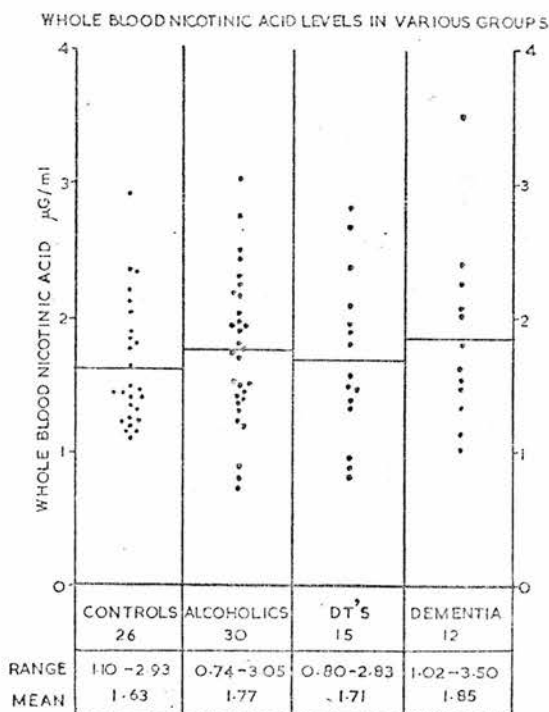


FIG. 3.

Nine out of 13 patients with a definite history of poor dietary intake associated with chronic alcoholism were found to have low levels of thiamine, but only two had low nicotinic acid levels.

Two alcoholics who had bright red tongues and one who had angular stomatitis were found to have normal thiamine levels. Three patients with low levels of thiamine (two also had low nicotinic acid levels) were underweight, but so also were three patients with normal levels. However, 8 alcoholics put on weight either during their stay in the ward or during follow-up, even though they had "normal" weights on admission. Of these patients 5 had normal blood thiamine levels and 3 low levels.

There was no evidence that the type of alcohol consumed or the intake (which ranged from one half-bottle of whisky daily for four years to six bottles of wine and one bottle of whisky daily) was related to the blood vitamin levels. However, there did tend to be a history of recent increase in alcohol consump-

tion in patients who showed the more severe withdrawal symptoms, and this possibly contributed to the lower levels of thiamine in these states.

DISCUSSION

Experiments with volunteers involving vitamin restriction have given inconclusive and inconsistent results. Human variation has played a considerable part in this, and conclusions are hard to draw from the small numbers which can be studied in this type of experiment. One of the earliest studies was that of Williams *et al.* (1942) who reported the effects of induced thiamine deficiency in man. Weakness, insomnia, muscle pain, vomiting and weight loss developed relatively rapidly on a diet severely deficient in thiamine and a few subjects complained of apathy, difficulty in thinking and poor memory. In a different experiment, (Williams *et al.*, 1943) a small amount of thiamine was supplied without any caloric restriction, in the hope of producing a more moderate and prolonged deficiency state. The subjects became moody, irritable and unco-operative, and a few became agitated and depressed. Similar symptoms were described by Elsom *et al.* (1940), who gave a diet deficient in many B vitamins to a human volunteer. Within five weeks she was depressed, "nervous" and irritable, with memory loss and difficulty in concentration. She did not become wholly symptom-free on thiamine alone, and required yeast in addition. Brozek (1957) reported on the psychological effects of experimental thiamine deficiency. His volunteers complained of apathy and anorexia within a few days, and when these symptoms became extreme or if inco-ordination occurred the experiment was stopped by giving thiamine. The Minnesota Multiphasic Personality Inventory was given when volunteers were in this state of deficiency, and demonstrated increased scores on hysteria, hypochondriasis and depression. Tests of manual speed, co-ordination time and reaction time showed impairment, but intelligence showed no change. One subject developed an abnormal gait, which did not improve until he had taken thiamine for some months.

The most recent experiment of this type was

performed by Ziponin (Ziponin *et al.*, 1965). He used a urinary excretion test to demonstrate thiamine deficiency; five out of his eight patients developed symptoms of malaise, headache, muscle pain and vomiting within 9 to 27 days of commencing the thiamine-deficient diet. The other three remained asymptomatic despite the apparent deficiency.

With recent developments in vitamin assay, more direct measurements of vitamin deficiency have become possible. However, the only published studies of blood levels of B vitamins concern chronic alcoholics (Baker *et al.*, 1964; Fennelly *et al.*, 1964; Leevy *et al.*, 1965). These patients were admitted to the metabolic ward of a general hospital because of their serious physical condition. 86 per cent. of 49 alcoholics with peripheral neuropathy and 44 per cent. without neuropathy had lowered blood thiamine or other B complex vitamins. The appropriate vitamin was given to patients shown to be lacking in that vitamin. This caused improvement in peripheral neuropathy in some, but others received large doses of all B vitamins with little effect. This latter group of patients tended to have concomitant liver disease. In the present series 6 out of 13 alcoholics (46 per cent.) with peripheral neuropathy had low thiamine or nicotinic acid levels, and 7 out of 25 (28 per cent.) of those without neuropathy. Only one patient with neuropathy had a low level of both vitamins. In Fennelly's series there was no correlation between severity of neuropathy and level of blood vitamins, and this was confirmed in the present study, though the numbers studied were small.

Zieve (1963) described nine patients with alcoholic polyneuropathy who did not respond to various B vitamins, and he postulated a deficiency of co-factors necessary for effective utilization of the B vitamins by the tissues.

In cirrhosis, 4 out of 9 patients in this series had low thiamine levels and 2 out of 10 low nicotinic acid levels; one patient had low levels of both. In the series reported by Leevy *et al.* (1965), 40 per cent. of 47 alcoholics with a fatty liver had hypovitaminaemia of two or more B-complex vitamins, their figures rising to 50 per cent. in 68 alcoholics with cirrhosis.

Fennelly also showed that the low blood

vitamin levels were related not to alcoholic intake but to poor diet as estimated from a dietary history. Of the patients in the present series who had a history of dietary deficiency, 9 out of 13 had low thiamine levels. Recently, Buckle (1965) has utilized blood pyruvate and keto-glutaric levels to study alcoholics on an inadequate diet. Abnormality of blood pyruvate level was found to the same degree in acute as in chronic dietary deficiency. The test, however, is far from specific for thiamine deficiency.

In alcoholic withdrawal states, the blood thiamine levels (Figure 2) diminish with increasing severity of the withdrawal symptoms, those with delirium tremens having the lowest mean levels. The experimental work of Ishbell *et al.* (1955), and the careful clinical observations of Victor and Adams (1953), confirm that delirium tremens is essentially a withdrawal phenomenon, although the exact aetiology remains obscure. Ishbell gave large amounts of alcohol to seven volunteers for up to 87 days while they were having an adequate diet with vitamin supplements. Before alcohol was withdrawn they were given I.M. vitamins in large quantities. None the less severe withdrawal states ensued in all, and four developed delirium tremens. There is little doubt that these subjects were not vitamin deficient. Victor and Adams demonstrated that more severe states of withdrawal occur with longer and higher daily alcohol consumption. It is probable, therefore, that the low thiamine levels found in the present series indicate the extent of the alcoholism which is the actual cause of delirium tremens, though it is possible that there is a multifactorial aetiology in which vitamin deficiency may be a factor. Two of the 7 patients with delirium tremens were known to eat at least one good meal a day, but these two patients had been precipitated into delirium tremens by infection, suggesting that their depleted vitamin stores may have been suddenly "exhausted" by the intercurrent illness.

The study confirms that vitamin B deficiency is a common accompaniment of severe alcoholism and that vitamin supplements are consequently of value in the treatment of alcoholic withdrawal states. It does not follow that either large doses or parenteral ad-

ministration are essential, since there is no evidence that alcoholics suffer from mal-absorption.

Because so many of the patients suffering from confusional states had already been given vitamins, only a few could be investigated. One patient with Wernicke's encephalopathy and a lung abscess, who had not received antibiotics, was shown to have a blood thiamine of 13 $\mu\text{G}/\text{ml}$. Similarly, one depressed patient with severe anorexia, who on admission demonstrated mild organic psychiatric changes, was shown to have a low blood thiamine level. His mental state improved dramatically on treatment with parenteral vitamins, and his depressive state was then successfully treated with imipramine. He has since remained perfectly well, and his blood thiamine level remains normal. Two other patients of interest were sisters. The first was admitted in an acute psychotic episode due to hypothyroidism. She was living in squalor, but though she had evidence of folic acid deficiency she had normal levels of thiamine, nicotinic acid and vitamin B_{12} . Her sister, admitted shortly after, showed evidence of organic impairment on psychological testing, and had low levels of blood thiamine and nicotinic acid and folic acid deficiency. For years both patients had lived on a diet consisting of tomatoes, tea and bread. It is possible that the slower rate of metabolism in the first sister protected her from becoming as vitamin deficient as her sister. Both were given vitamin supplements (with thyroid in the former) and all signs of organic psychosis disappeared.

In the present series, there was no evidence of thiamine or nicotinic acid deficiency in dementia. Krawiecki and co-workers (1957) demonstrated that 7 out of a group of 25 male senile psychiatric patients showed memory improvement following intramuscular injection of Parentrovite, whereas only 3 patients out of 25 controls receiving an inert preparation showed improvement. They state that three patients treated with Parentrovite were able to be discharged from hospital as "recovered", but the memory changes in these patients appear to have been slight. Post (1959) has summarized the work so far—"scientifically designed trials of biological treatment of established old age

dementia have failed to introduce effective therapies."

Recent work by Strachan and Henderson (1965) on patients with various psychiatric disorders has demonstrated unsuspected lowered vitamin B₁₂ levels and has re-emphasized the value of making this investigation in psychiatric cases. It is possible that the blood levels of other B vitamins may become an equally important investigation, although the actual level by itself may not provide adequate information. Other factors have to be considered: the effect of the blood-brain barrier, the existence of liver disease and the effect on enzyme formation, and possible inconsistencies between the intracellular content and the blood level. Tests of excretion, saturation or tolerance may in future be shown to give more useful evidence of total body depletion of vitamins.

SUMMARY

Whole blood thiamine and nicotinic acid levels have been measured in psychiatric patients. There was no difference in the levels of these vitamins in patients with dementia compared with a control group. In patients suffering from delirium tremens 7 out of 9 had low whole blood thiamine levels and 3 out of 15 had low nicotinic acid levels. There was a positive relationship between increasing symptoms of alcoholic withdrawal and a decreasing mean thiamine level. Some patients with alcoholic peripheral neuropathy were found to have low thiamine and nicotinic acid levels. A few patients with confusional states were found to have low vitamin levels, and all these had had poor dietary intake. The assay of B vitamins may become of increasing value in psychiatric diagnosis. Although the use of vitamins in delirium tremens is justified, there is no evidence to suggest that parenteral administration or massive doses are necessary.

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REFERENCES

- BAKER, H., FRANK, O., FENNELLY, J. J., and LEEVY, C. M. (1964). "Method for assaying thiamine status in man and animals." *Amer. J. clin. Nutr.*, **14**, 197-201.
- BAKER, H., and SOBOTKA, H. (1962). "Microbiological assay methods for vitamins." *Advanc. clin. Chem.*, **5**, 173-235.
- BROZEK, J. (1957). "Psychologic effects of thiamine restriction and deprivation in normal young men." *Amer. J. clin. Nutr.*, **5**, 109-120.
- BUCKLE, R. W. (1965). "Blood pyruvic and ketoglutaric acids in thiamine deficiency." *Metabolism*, **14**, 141-149.
- DE WARDENER, H. E., and LENNON, B. (1947). "Cerebral beri-beri (Wernicke's encephalography)." *Lancet*, **i**, 11-17.
- EDWARDS, M. A., KAUFMAN, M. L., and STORVICH, C. A. (1957). "Microbiological assay for thiamine content of various species of animals and man." *Amer. J. clin. Nutr.*, **5**, 51-55.
- ELSON, K. O., LEVY, F. H., and HEUBLIN, G. W. (1940). "Clinical studies of experimental human vitamin B complex deficiency." *Amer. J. med. Sci.*, **200**, 757-764.
- FENNELLY, J. J., FRANK, O., BAKER, H., and LEEVY, C. M. (1964). "Peripheral neuropathy of the alcoholic. I. aetiological role of aneurism and other B-complex vitamins." *Brit. med. J.*, **ii**, 1290-1293.
- GOULD, J. (1959). "The enzymatic basis of certain psychoses." In: *Recent Progress in Psychiatry*, **3**, 213, 213-252. London: H. K. Lewis.
- ISRBELL, H., FRASER, H. F., WIKLER, A., BELLEVILLE, R. E., and EISENMAN, A. J. (1955). "An experimental study of the aetiology of 'rum fits' and delirium tremens." *Quart. J. Stud. Alcohol*, **16**, 1-33.
- JOLLIFFE, N., BOWMAN, K. M., ROSENBAUM, L. A., and FEIN, H. D. (1940). "Nicotinic acid deficiency encephalography." *J. Amer. med. Ass.*, **114**, 307-312.
- KRAWIECKI, J. A., COUPER, L., and WALTON, D. (1957). "The efficiency of parentovite in the treatment of a group of senile psychotics." *J. ment. Sci.*, **103**, 601.
- LEEVY, C. M., BAKER, H., TENHOVE, W., FRANK, O., and CHERICK, G. (1965). "B-complex vitamins in liver disease of the alcoholic." *Amer. J. Clin. Nutr.*, **16**, 339-346.
- POST, F. (1959). "Early treatment of persistent senile confusion." *Geront. Clin.*, **1**, 114-121.
- SARETT, H. P., PEDERSON, R. L., and CHELDELIN, V. H. (1945). "Microbiological assay methods for nicotinic acid." *Arch. Biochem.*, **7**, 77-85.
- STRACHAN, R. W., and HENDERSON, J. G. (1965). "Psychiatric syndromes due to avitaminosis B₁₂ with normal blood and marrow." *Quart. J. Med.*, **34**, 303-317.
- SYDENSTRIKER, V. P., and CLECKLEY, H. M. (1941). "The effect of nicotinic acid in stupor, lethargy and various other psychiatric disorders." *Amer. J. Psychiat.*, **98**, 83-92.

- VICTOR, M., and ADAMS, R. D. (1953). "The effect of alcohol on the nervous system." *Res. Publ. Ass. nerv. ment. Dis.*, **32**, 526-573.
- WILLIAMS, R. D., MASON, H. I., SMITH, B. F., and WILDER, R. M. (1942). "Induced thiamine deficiency and the thiamine requirements of man." *Arch. intern. Med.*, **69**, 721-738.
- POWER, M. H., and WILDER, R. M. (1943). "Induced thiamine (Vitamin B₁) deficiency in man." *Arch. intern. Med.*, **71**, 38-53.
- ZIEVE, L., and HILL, E. (1963). "Vitamin unresponsiveness" progression of classical signs of neuropathy and pellagra during therapy." *Amer. J. clin. Nutr.*, **13**, 312-317.
- ZIPONIN, Z. Z., NUNES, W. T., POWELL, R. C., WARING, P. O., and SAUBERLICH, H. E. (1965). "Excretion of thiamine and its metabolites in the urine of young adult males receiving restricted intakes of the vitamin." *J. Nutr.*, **85**, 287-296.

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	MALE									FEMALE								
	General	Previous Suicide	Neuropathy	Delirium Tremens	"Psychiatric"	Anaemia	Gastritis	Gastric Opns.	Cirrhosis	General	Previous Suicide	Neuropathy	Delirium Tremens	"Psychiatric"	Anaemia	Gastritis	Gastric Opns.	Cirrhosis
Mode of Admission	527	95	98	81	74	99	90	54	64	148	49	23	16	24	36	20	7	15
Emergency	282	64	51	68	47	62	46	29	39	91	36	16	12	14	24	12	2	6
Waiting List	245	31	47	13	27	37	44	25	25	57	13	7	4	10	12	8	5	9
Means of Referral																		
G.P.	361	46	67	41	45	68	54	33	40	109	36	17	7	18	22	11	6	12
A.A.	14	5	3	3	1	-	1	-	3	10	1	1	-	-	3	3	-	-
C. of Alc.	27	6	6	5	4	6	10	2	4	5	1	-	-	1	2	3	-	-
Sam.	6	2	1	2	-	-	1	1	1	-	-	-	-	-	-	-	-	-
Self	53	14	7	10	14	11	11	12	3	5	2	-	-	-	2	1	-	-
Other Hosp.	45	18	9	16	8	10	8	4	10	16	7	5	9	5	6	1	1	3
Not Known	21	4	5	4	2	4	5	2	3	3	2	-	-	-	1	1	-	-
Length of Stay																		
1 week	76	13	10	15	12	10	14	6	10	13	5	-	1	1	2	1	-	-
1-3	230	37	41	28	24	35	35	23	19	55	17	6	5	6	13	6	1	4
3-5	182	33	32	31	25	44	34	20	29	54	16	9	5	7	13	9	3	4
5-12	36	11	13	7	11	8	7	4	6	20	9	6	3	7	5	1	3	5
12+	3	1	2	-	2	2	-	1	-	6	2	2	2	3	3	3	-	2
No. of Admissions																		
1	426	60	77	62	60	79	77	40	56	107	31	15	12	14	22	14	7	11
2	85	27	18	17	10	15	8	8	5	25	10	4	3	4	8	4	-	2
3	13	7	2	2	3	3	3	5	2	9	4	1	-	3	2	1	-	1
4	1	-	-	-	1	-	-	-	-	5	4	2	-	2	3	1	-	-
5	1	-	1	-	-	1	1	1	1	1	-	-	-	-	-	-	-	-
6	1	1	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-	1	-	1	1	1	1	-	-	1
Religion																		
Protestant	352	53	76	53	46	64	59	33	46	99	29	18	13	18	25	15	5	12
Roman Catholic	162	37	20	28	26	33	26	19	18	48	20	5	3	6	11	5	2	3
Other	3	1	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-
None	10	4	2	-	1	1	4	2	-	-	-	-	-	-	-	-	-	-
Social Class																		
I	30	3	6	5	3	7	4	4	2	13	3	5	1	3	4	-	2	5
II	82	7	21	15	11	22	16	6	17	20	4	3	3	5	6	1	-	4
III	156	24	19	15	12	20	25	17	15	35	9	5	3	3	7	3	3	-
IV	129	25	22	20	17	21	18	8	14	42	18	3	4	7	9	9	2	1
V	130	26	30	26	31	29	27	19	16	36	15	7	5	6	10	7	-	4

Married	286	42	53	43	35	46	46	25	34	84	24	12	7	9	18	6	6	7
Single	74	17	13	14	12	20	11	6	8	15	6	-	-	1	-	3	-	-
Widowed	33	8	11	5	5	13	6	6	6	19	6	8	6	8	7	3	1	6
Divorced	59	13	8	8	9	4	14	6	4	14	7	-	2	3	3	4	-	1
Separated	75	15	13	11	13	16	13	11	12	16	6	3	1	3	8	4	-	1
Not Known	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Means of Discharge

Self	50	14	10	7	7	7	13	7	4	14	6	3	2	2	3	3	-	1
After Alcohol	77	15	18	10	10	12	7	7	9	7	4	-	-	1	-	2	1	-
Both	17	4	2	-	2	3	6	2	1	2	2	-	-	-	1	-	-	-
Medical Discharge	383	62	68	64	55	77	54	38	50	125	37	20	14	21	32	15	6	14

Type of alcohol

Whisky	237	34	42	41	25	42	33	20	33	37	7	6	7	11	6	4	1	8
Wine	127	28	31	15	24	26	21	15	21	59	21	12	7	10	21	12	3	4
Mixture	82	14	12	12	13	11	19	8	5	17	4	1	-	2	4	-	2	-
Spirits	45	8	6	6	3	8	10	3	3	28	14	3	1	1	5	3	-	2
Beer	11	2	2	2	1	3	1	2	1	1	1	-	-	-	-	-	-	-
Brandy	13	4	3	3	4	6	5	4	1	3	2	1	1	-	-	1	1	1
Not Known	12	5	2	2	4	3	1	2	-	3	-	-	-	-	-	-	-	-

amt. of Alcohol (Gms per day)

0-49	0	0	0	0	0	0	0	0	0	1	1	-	-	-	-	-	-	-
50-149	59	7	10	8	7	9	10	3	6	51	14	5	5	9	6	6	2	4
150-249	132	15	20	23	11	25	19	13	20	36	7	4	2	4	8	5	2	5
250-349	52	10	10	8	6	10	15	5	8	21	8	7	4	2	9	3	1	1
350-449	59	12	15	7	13	10	14	10	9	6	1	2	1	3	2	2	-	1
450-549	56	15	12	9	7	13	11	5	6	-	-	-	-	-	-	-	-	-
550-649	26	4	5	1	3	4	4	-	2	2	2	-	-	-	2	1	-	-
650-749	17	3	7	5	4	6	3	4	5	-	-	-	-	-	-	-	-	-
750+	20	8	6	4	2	3	5	2	2	-	-	-	-	-	-	-	-	-
Not Known	106	21	13	16	21	19	9	12	6	31	16	5	4	6	9	3	2	4

Length of Time Excess Drinking

0-1 yrs.	9	1	-	2	-	2	-	-	-	11	1	-	1	-	1	-	-	-
1-2	16	4	-	2	1	1	1	1	-	19	6	-	-	-	1	2	1	-
2-5	69	15	11	7	4	6	15	6	4	41	18	9	4	8	9	5	4	3
5-10	97	23	20	12	14	21	16	12	7	35	12	6	2	5	11	6	-	6
10-20	153	28	29	26	21	26	27	13	21	27	7	6	5	7	8	5	1	4
20+	180	24	38	30	34	41	31	21	32	13	4	2	4	3	5	2	-	2
Not Known	3	-	-	2	-	2	-	1	-	2	1	-	-	1	1	-	1	-

es	46	6	6	6	4	6	10	3	4	10	2	1	2	-	2	1	-	1
o	478	89	91	74	69	93	79	51	59	138	47	22	14	24	34	19	7	14
ot Known	3	-	1	1	1	-	1	-	-	-	-	-	-	-	-	-	-	-
<u>Food Intake</u>																		
oor	170	32	45	38	37	46	32	22	31	59	20	17	12	12	20	11	3	11
atisfactory	197	33	29	17	19	24	35	20	12	70	21	4	2	9	12	7	3	3
ot Known	160	30	24	26	18	29	23	12	21	19	8	2	2	3	4	2	1	1
<u>Weight</u>																		
oss	99	13	30	25	21	31	21	11	19	45	16	13	10	12	16	6	3	8
ationary	223	37	30	24	28	27	42	22	20	79	24	6	3	9	14	9	3	4
ot Known	205	45	38	32	25	41	27	21	25	24	9	4	3	3	6	5	1	3
<u>Psychiatry</u>																		
on-specific personality dis.	76	33	9	7	10	10	14	10	5	16	10	1	-	1	4	2	1	-
aggressive	7	3	1	1	1	-	-	-	-	1	-	-	-	-	-	-	-	-
ysterical	4	3	-	-	1	-	1	-	-	12	10	-	-	1	1	4	2	-
epression	17	1	1	4	2	4	-	1	1	8	1	2	1	-	1	-	-	-
chizophrenia	7	3	-	1	4	2	-	1	1	1	-	-	-	-	-	-	-	-
ow I.Q.	2	-	-	-	1	-	-	-	-	1	-	-	-	-	-	-	-	-
ex Deviation	5	1	2	1	-	1	1	-	1	1	-	-	-	-	-	-	-	-
eurotic	13	3	3	-	1	3	3	3	-	4	-	-	-	-	1	-	-	-
pilepsy	1	-	-	-	-	-	-	-	-	2	1	-	-	1	2	1	-	1
None	395	46	82	67	54	71	59	56		102	26	20	15	21	27	13	4	14
<u>Offences</u>																		
evere	21	6	3	-	2	4	5	5	3	2	1	-	-	1	1	-	1	-
minor	63	15	9	8	13	8	18	6	6	17	9	-	-	3	5	5	-	-
Driving	19	1	1	1	-	2	4	6	2	1	1	-	-	-	-	-	-	-
Multiple Minor	21	7	3	-	1	4	3	2	1	7	2	2	1	1	1	2	1	1
Multiple	132	30	25	14	28	21	22	17	12	9	5	1	-	1	3	3	-	-
None	180	22	39	36	19	37	24	12	29	95	22	17	14	17	22	8	4	13
ot Known	91	14	18	22	11	23	14	6	11	17	9	3	1	1	4	2	1	1