ANAEMIA IN CHRONIC LIVER DISEASE

THESIS

SUBMITTED FOR THE

DEGREE OF DOCTOR OF MEDICINE

IN THE

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA

BY

CARLIEN LORRAINE KIMBER

CONTENTS

Cirrhosis of the liver is a common disease especially in those areas where the consumption of alcohol is high. However, the true frequency of cirrhosis in the population is difficult to assess because in many instances patients do not manifest clinical disability of the disease during life and the cirrhosis is detected only at autopsy.

In the United States both alcoholism and cirrhosis of the liver are important social problems. In 1955 the certified death rate due to alcoholism was 1.3 per 100,000 population and that due to cirrhosis of the liver was 10.2 per 100,000 population (W.H.O. Epidemiological and Vital Statistics Report, 1958). In Europe generally, the death rates due to alcohol and cirrhosis have shown a steady rise over recent years and in 1955 the death rate in France from cirrhosis of the liver was 30.3 per 100,000. In the same year the Australian death rate was 2.4 per 100,000 from alcoholism and 4.8 per 100,000 from cirrhosis (W.H.O. Epidemiological and Vital Statistics Report, 1958). However, the death rate from portal cirrhosis remains high even in Eastern countries with a predominantly Moslem or Buddist population where alcoholism is rare (Fernando, Medonza and Rajasuriya, 1958; Kinare and Purandare, 1958). In these underdeveloped countries profound nutritional deficiency is generally held responsible for the development of cirrhosis, although tropical infections such as malaria have also been incriminated (Davidson, 1960).

The frequency with which alcoholism leads to cirrhosis of the liver remains uncertain. However, Seely (1960) showed that in Canada

the rising incidence of cirrhosis of the liver correlated well with the increasing consumption of beverage alcohol. Furthermore, in most Western countries alcohol is considered to be the most important aetiological factor in the development of cirrhosis (Ratnoff and Patek, 1942; Wood, 1958; Caroli and Pequignot, 1959; Mackay, 1959). However, in the United Kingdom alcoholism is less commonly incriminated, due perhaps to the prohibitive excise duty on wines and spirits and the lower alcoholic content of the nation's beer. Sherlock (1955) found that only 18 per cent. of cases with cirrhosis were associated with alcoholism, whereas 33 per cent. followed viral hepatitis and 49 per cent. were of unknown aetiology. In one Australian series comprising 100 unselected patients with chronic liver disease, there were 51 cases of alcoholic cirrhosis; 24 cases of active chronic hepatitis (L.E. cell test negative); and 4 cases of lupoid hepatitis (Wood, 1958; Mackay and Wood, 1962).

There are a number of clinical syndromes associated with cirrhosis. Some patients have non-specific symptoms such as anorexia, nausea and general malaise and the stigmata of liver disease may be detected only by careful clinical examination. Other patients have oedema and ascites with intermittent episodes of stupor and sometimes coma, the result of hepatocellular failure; while others present initially with gastro-intestinal bleeding due to the development of portal hypertension. Even where alcohol is incriminated as an aetiological factor, the drinking habit may have ceased months or years previously. On the

other hand, patients may present during an acute alcoholic debauch with malaise, fever, anorexia, vomiting and jaundice. Usually in these cases the liver is greatly enlarged due to fatty infiltration; the changes of cirrhosis are not marked; and the disorder may be reversed by abstinence (Davidson and Phillips, 1954). In 2,377 patients reviewed by Blaisdell and Cohn (1961) the chief presenting symptom was ascites in 46 per cent; gastro-intestinal bleeding in 23 per cent; hepatic coma in 18 per cent; jaundice in 9 per cent; and both jaundice and ascites in 4 per cent.

The natural history of cirrhosis of the liver is variable but it is generally agreed that episodes of bleeding and hepatic coma herald a poor prognosis, and that death is usual within two or three years. Ratnoff and Patek (1942) reported that death was due to hepatic failure in 32 per cent. of cases; to bleeding in 22 per cent. of cases; and to infections in 17 per cent. of cases. However, after the introduction of antibiotics, deaths from infection have occurred less frequently (Chase, Martel and Olivetti, 1957; Wallach, Hyman and Angrist, 1957; Blaisdell and Cohn, 1961).

In view of the high incidence of protein, mineral and vitamin deficiency, it is not surprising that anaemia occurs frequently in these patients. Furthermore, anaemia may develop because the liver is the site of storage of many haematinic principles; the site of protein synthesis; and the source of many enzymes necessary for haemoglobin production.