ACUTE HEPATIC FAILURE IN CHILDHOOD

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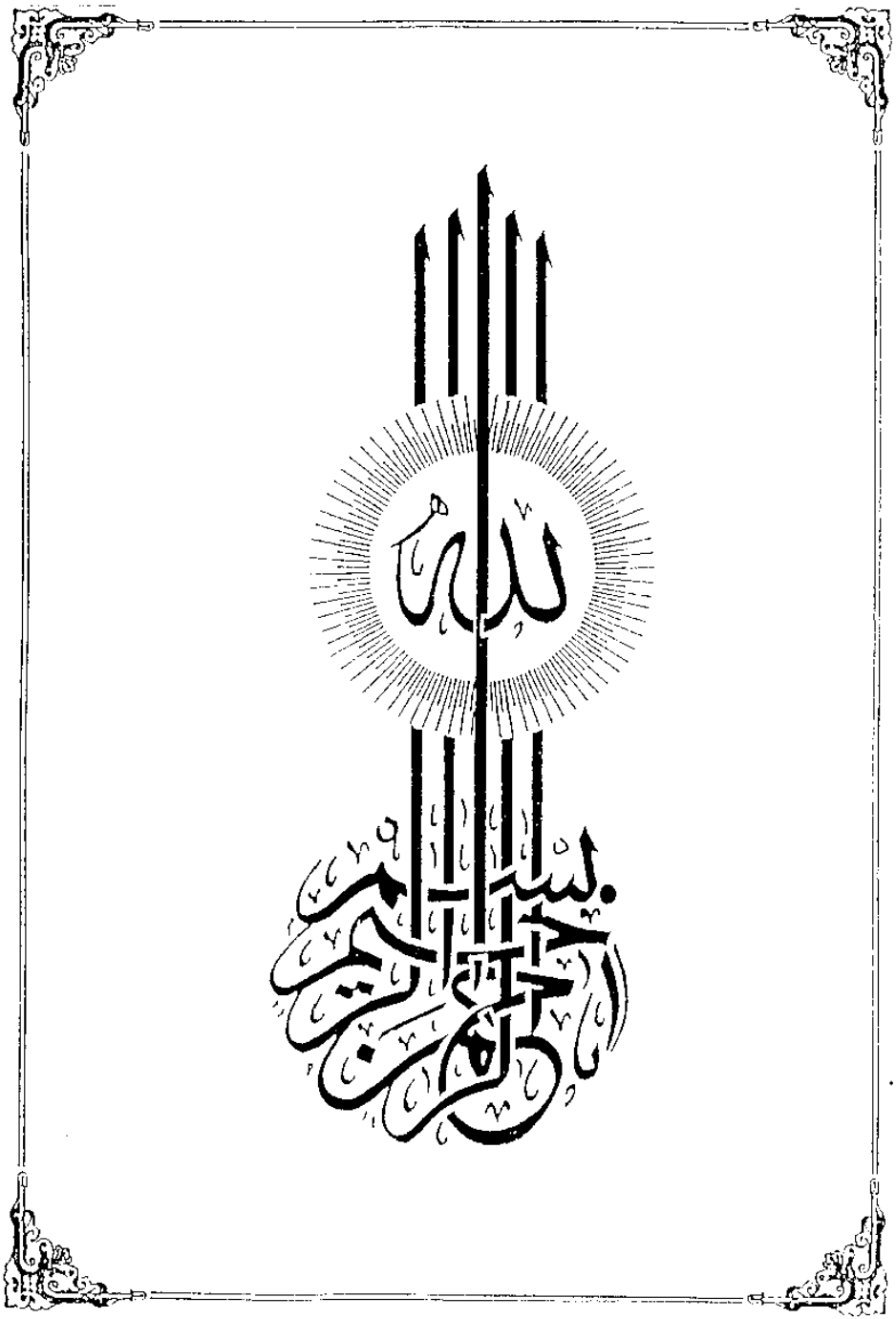

A C K N O W L E D G M E N T

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C O N T E N T S

INTRODUCTION

I N T R O D U C T I O N

Since the liver is vital to the maintenance of metabolic homeostasis within the body, any derangement of its normal functions is quickly reflected as malfunction of other organ systems. Severe derangement in function leads to striking change in intermediate metabolism and the accumulation of toxic substances normally cleared from the circulation. As a result , other vital organs i.e. brain, kidney, cardiovascular system, etc, are profoundly affected, leading to the clinical manifestations of hepatic coma, renal failure and cardiovascular collapse.

A great deal of research effort has been directed towards a clearer understanding of pathophysiology of hepatic failure , however, the exact mechanisms of failure and the underlying factors involved have not been completely identified.

Although the occurrence of fulminant hepatic failure is not common in pediatric age group , it must represent a differential diagnostic possibility in any unconscious infant or child presenting at an emergency ward.

Despite the comprehensive literature on the pathogenesis of liver failure, no consistent approach to the

management of hepatic failure has emerged. Although little can be done for patients with end-stage chronic liver failure, patients presenting with acute fulminant hepatic failure can ultimately survive if coma can be prevented or its effect minimized.

The aim of this essay is to overview and discuss the aetiology , pathophysiology and diagnosis of acute hepatic failure in children with special reference to the recent advances in its management.

PART (I)

AETIOLOGY OF ACUTE HEPATIC FAILURE IN CHILDHOOD

* DEFINITION .
* VIRAL HEPATITIS.
* DRUG INDUCED FHF.
* REYE'S SYNDROME.
* HEPATOCEREBRAL DEGENERATION (WILSON'S DISEASE).
* BUDD-CHIARI SYNDROME.

* Definition:

Trey and Davidson (1970) defined fulminant hepatic failure (FHF) by the appearance of hepatic encephalopathy (HE) within 8 weeks of onset of acute deterioration of liver function with absence of a previous liver damage. Benhamou and Rueff (1973) suggested a shorter period of 3 weeks and accepted a superimposed acute hepatic failure on a chronic liver disease in the definition.Roggers (1980) suggested the term subacute hepatic failure in whom the first signs of encephalopathy have not appeared until after the patient has been ill for more than 8 weeks. These patients tend to be older and on admission they are less likely to have a history of fever and are more likely to be negative for HA and B viruses. It is possible that these patients represent part of the spectrum of acute non A non B hepatitis (Gimson and Williams , 1983).

Lloyd-still (1985) has recently reviewed mortality from liver disease to assess the implications of hepatic transplantation programs . Acute HF was present in 42 % of patients that died from hepatic failure where as 58% had preexisting chronic liver disease.

Acute hepatic failure may occur as a result of massive insult to the liver causing cell destruction and

total deramgement in organ function. The list of causes is long (Table 1) but the commonest causes are viral hepatitis and drug induced hepatitis. More recently with an increasing awareness of Reye's syndrome the distribution of incidence has changed somewhat.

Table (1) : Aetiological Factors in Acute Hepatic Failure in Childhood.

Infections:

- Viral hepatitis
- Adenovirus
- Infectious mononucleosis
- Disseminated herpes simplex v.
- Leptospirosis.
- Coxsackie virus.
- Q fever.
- Clostridum perfringes.

Metabolic:

- Reye's syndrome
- Congenital inborn error's of Kreb's Henselit cycle,
- Wilson's disease.

Drugs-Chemicals-Poisons:

- Acetaminophen (pracetamol)
- Breyllium
- Carbon tetrachloride
- Ethanol
- Halothane
- INH
- Imuran
- Methyl dopa
- Phosphorous
- Rifampicin.
- Salicylates.
- Sodium valpprate.
- Tetracycline.
- Vitamin A.
- Mushrooms(Amanita phallcides).

Ischemia and Necrosis:

- Acute circulatory failure.
- Acute Budd Chiari syndrome.
- Acute pulmonary failure.
- Ligation of hepatic artery.
- Heat stroke.

Data obtained from Trey (1972), Howard and Mowat (1983) Katz and Flores (1985) and Corall and Williams (1986).

. Viral Hepatitis:

Viral hepatitis represent the commonest group in most series of FHF. Trey (1972) reported that viral hepatitis was responsible for 50 % - 75 % of cases of acute hepatic failure 38 % of these cases were in the pediatric age group (0 - 14 y.). Gimson and Williams (1983) reported that 44 % of cases admitted to King's collage hospital (1973-1981) with FHF to be due to viral hepatitis. This relatively lower percentage was due to predominance of cases due to paracetamol overdose in the UK.

Type A and B and non A non B hepatitis have all been implicated in this syndrome. However the predominance of one type over the others is contraversal. Rakela et al. (1978) found only 10 % of cases to be caused by HAV while the rest were equally distributed between HBV and non A non B viruses. Gimson and Williams (1983) reported 32% for HAV and 24 % for HBV. Mathieson et al. (1980) did not observe a significant difference.

In Egypt, although no such statistical reports have been done to cases with acute liver failure, epidemiological studies points to the importance of HBV

as a disease of childhood and young adults especially those subjected to vaccination, injection, blood transfusion and dental manipulation (Osman et al., 1975 ; El-Kholy, 1979; Abdel-Wahab, 1985). Kamal (1982)upon studying HBsAg presence in 535 subjects with ages of 0-15 years found an incidence of about 10% among Egyptian infants and children. A higher percent, about one fourth, was reported by Abdel Ghaffar (1983) in children subjected to repeated blood transfusions 50% of these children were subjected to post transfusion hepatitis. In contrast WHO expert comitte on viral hepatitis (1976)has stated that more than 50% of cases of hepatitis in children under 15 years of age in developed countries were HAV infection.

Thomas and Morjardiono (1984) have suggested that in Africa and far East majority of people will be infected with HB virus at some time during their life,often at or near birth. Although infection is often asymptomatic with development of long life immunity; half of the people develop symptomatic acute hepatitis and 1% of these cases develop FHF with 80% fatality.

Smedile et al. (1982) have found that half of the patients with persumed fulminant B hepatitis were cases of delta infection occurring in chronic carriers of HBV.

Delta agent is an incomplete RNA virus that only replicate in HBV infected people to cause excerbation of hepatitis.

FHF due to other Viruses:

Uncommon viral causes of FHF are Epstein Barr virus (Davis et al., 1980), herpes simplex, echovirus(Hughes et al., 1972) and cytomegalovirus. Coxsackie virus B infection was reported to cause FHF in some newly borns (Benirschke et al., 1958) and adolescents (Read et al., 1985). The latter authors reported an associated cardiac failure and evidence of severe myocarditis at autopsy.

Ketz and Flores (1985) listed adenovirus, Coxsackie virus infectious mononucleosis, dissiminated herpes simplex, leptospirosis and Q fever and clostridium perfriges as other possible rare causes of FHF.

Mechanism of FHF in Viral Hepatitis:

It is now generally accepted that HBV is not directly cytopathic to liver cells and that liver necrosis is dependent upon the host's immune response directed at viral determinants at the hepatocyte membrane(Edgington and Chisari, 1975).

Woolf et al. (1976) suggested that while a controlled response with gradual lysis of infected hepatocytes