THE USE OF CORTICOSTEROIDS IN REFRACTORY ASCITES

Thesis

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The M.S. Degree in Tropical Medicine

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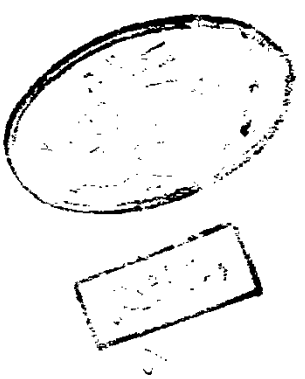

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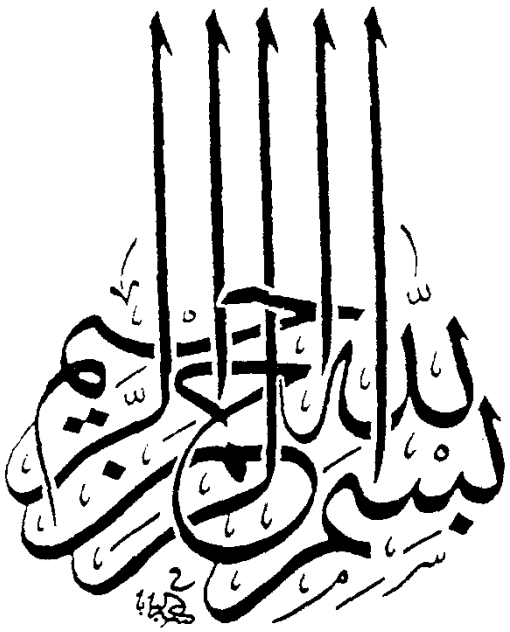

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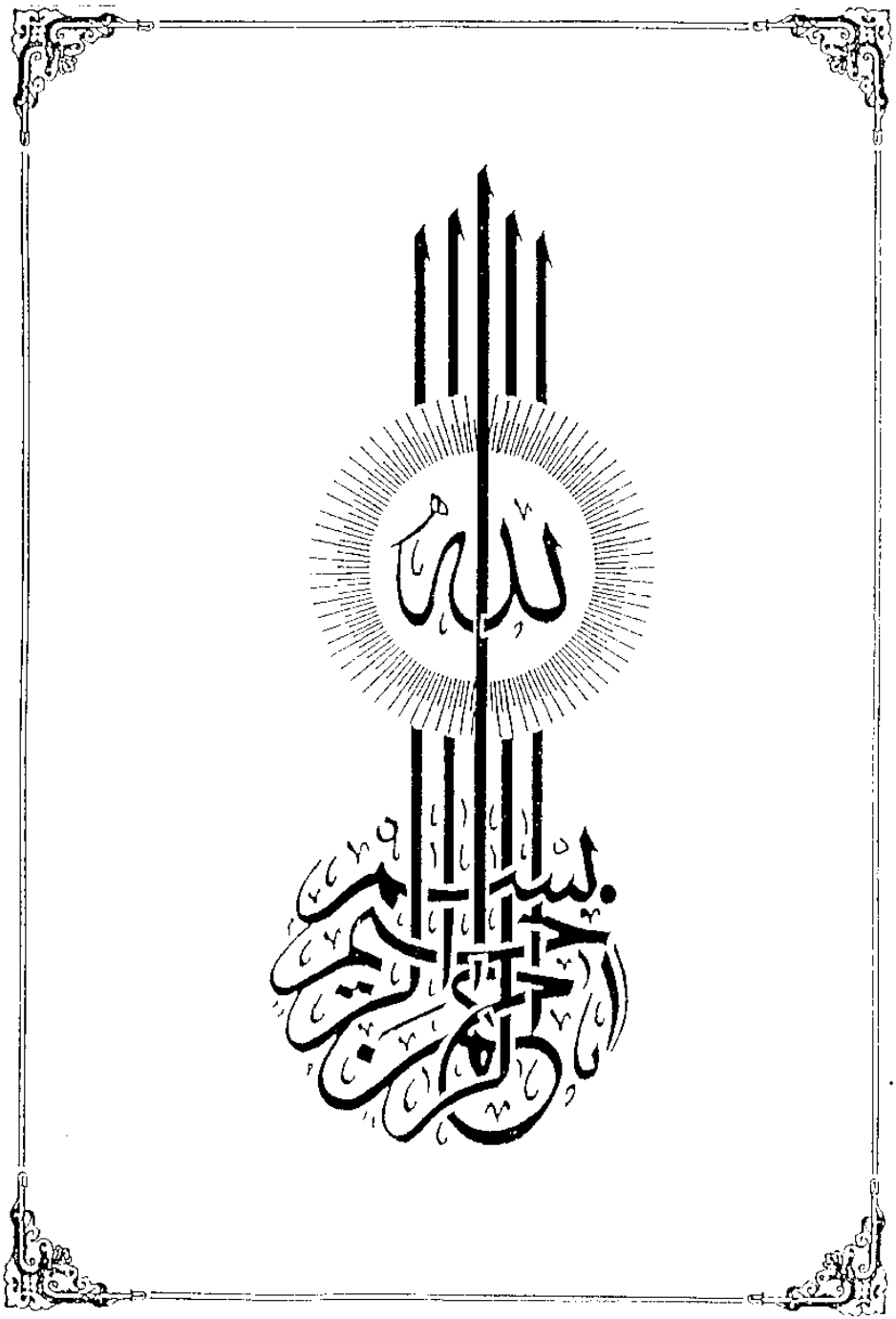

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By careful and patient manipulation of the diet and diuretics, it is possible to obtain a satisfactory diuresis in the majority of patients with ascites secondary to chronic liver disorder (the patient loses an average of 0.5 kg/day unless peripheral oedema is present, when a loss of up to 1 kg/day is desirable). Patients who do not respond to the standard therapeutic regimen are designated as having refractory ascites. Before considering a patient truly refractory, it is important to ensure that the difficulty in controlling the ascites is not due to: patient non compliance particularly in relation to dietary salt restriction, inadvertent sodium administration in the form of medication or intravenous fluids, inadequate diurectic therapy, or electrolyte imbalance particularly hypokalaemia and alkalosis which may impair renal tubular sodium excretion.

A number of factors may precipitate the development of refractory ascites in a patient with liver disease including: deterioration of liver function as a result of active liver cell damage or the development of a complicating primary hepatocellular carcinoma or other internal

malignancy, spontaneous bacterial peritonitis, chylous ascites and hepatic venous thrombosis (Budd Chiari Syndrome).

In these resistant cases alternative therapy must be considered.

Repeated small paracentesis each day 4-6 litres are removed over a period of 3-4 hours by fine catheter, while 40 gram salt free albumin are infused intravenously over the same period. This line of treatment is helpful, but there is a danger of inducing hypovolaemia, hyponatraemia, hypokalaemia, hepatic coma and renal failure.

Mannitol infusions have been recommended, but these are seldom efficacious. The Rhone-pulenc reinfusion apparatus has been introduced to reinforce a protien-rich ultrafilterate of ascitic fluid, but high protein content of ascites may clog the membrane and infection of fluid is a contra-indication. Transient pyrexia, pulmonary oedema and intra-peritoneal haemorrhage are complications of this line of treatment.

Le Veen and Co-workers have described a -peritoneovenous shunt which gives very satisfactory long term results. The peritoneum is drained by a plastic tube which contains a pressure-sensitive valve situated extra-peritoneally,

and which passes subcutaneously to enter the external jugular vein or the superior Vena cava. Following the shunt there is an increase in Cardiac output and renal blood flow, and a marked diuresis. Most patients can be maintained on long-term minimal dietary salt restriction with or without low doses of diuretics. Operative mortality is 13% in patients with Le Veen Shunt and many complications may occur including: bleeding from oesphageal varices, pulmonary oedema, shunt dysfunction with occlusion and thrombosis, disseminated intravascular coagulation and infection of all types including peritonitis and bacterial endocarditis.

It has been observed by us that corticosteroids in small tapering doses when added to conventional diuretics increase diuresis and cause relief of refractory ascites secondary to chronic liver disorder.

The aim of this work is to assess the validity of this observation for the relief of refractory ascites secondary to chronic liver disorder.

REVIEWS OF LITERATURE

Chapter (I)

ANATOMY AND PHYSIOLOGY OF THE PERITONEUM

The peritoneum is the largest and most complexely arranged serous membrane in the body and consists, in the male, of a closed sac a part of which lines the abdominal wall whilst the remainder is reflected over the contained viscera. In the female, the free ends of the uterine tubes open into the peritoneal cavity. Histologically it consists of a single layer of flattened mesothelial cells which covers a layer of loose connective tissue. It has been claimed that the mesothelial cells possess a phagocytic capacity, and that they may leave the surface to form free macrophages. They may also transform into fibroblasts, and fusion between layers of fibroblasts of mesothelial origin may lead to macroscopic adhesions between the peritoneal surface of adjacent structures **[Warwick and Williams, 1973].**

Last [1972] described the parietal peritoneum as the part which lines the walls of the abdominal cavity. It clothes the anterior and posterior abdominal walls, the undersurface of the diaphragm and the cavity of the pelvis. It is attached to these

walls by extraperitoneal areolar tissue. The visceral peritoneum is the continuation of the parietal peritoneum which leaves the posterior wall of the abdominal cavity to invest certain viscera. The peritoneal cavity is divided into two main parts; the greater sac; which is the part of the cavity seen as we incise the parietal peritoneum of the anterior abdominal wall, and the lesser sac: which is a large peritoneal recess behind the stomach. The opening through which the two sacs communicate is called the epiploic foramen, which lies between the first part of the duodenum and the under surface of the liver **[Mahran et al., 1976].**

Woodburne (1978) defined the mesentry as the peritoneal reflection from body wall to the small intestine, and the mesocolon as a similar attachment of the large intestine. Many peritoneal folds or sheets are designated as ligaments of the peritoneum e.g. the falciform ligament which is a peritoneal fold connecting the anterior abdominal wall with the liver slightly to the right side of the median plane. From the under surface of the diaphragm, the peritoneum is relfected on the upper surface

of the liver. This reflection is known as the upper layer of the coronary ligament. The lower layer of coronary ligament is the peritoneal reflection from the undersurface of the liver to the front of the right kidney and right suprarenal gland **[Mahran et al., 1976].**

The Omentum :

A double layer connecting the stomach to another structure .The lesser omentum runs from the lesser curvature of the stomach and the first inch of the duodenum to the under surface of the liver. The greater omentum connects the greater curvature of the stomach with the anterior border of the pancreas **[Grant, 1958].**

Physiological aspects:

The primary function of the peritoneum is to provide a slippery surface over which the abdominal viscera can freely slide. A small amount of fluid is normally present in the peritoneal cavity. The total surface area of the peritoneum is approximately 1.7 mt^2 which is as large as the total surface of the skin. Much of the peritoneal membrane acts as a passive, semipermeable barrier to the bidirec-

tional diffusion of water and most solutes the peritoneum can be made to act as a capillary kidney, though somewhat ineffeciently. Solutions introduced into the peritoneal cavity gradually approach equilibrium with plasma. The peritoneal clearance of solutes is decreased in shock and can be significantly altered by vasoactive drugs, temperature, inflammation oxygen tension and other factors **(Nance, 1985).**

With regards to the question of the absorption of fluid effusions from the peritoneal cavity, substances in complete solution (solute) are probably absorbed directly into the blood capillaries, whereas particulate matter in suspension probably passes into the lymph vessels, with the aid of phagocytes (polymorph nuclears and monocytes). Normally small volumes of fluid are transferred across the peritoneal surfaces. Therapeutically, however, considerable volumes of fluid may be administered via the intraperitoneal route. Whilst conversely, certain blood-born substances such as urea can be dialysed from the blood stream into fluid artificially circulated through the peritoneal cavity **(Warwick and Williams, 1973).**