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BIVCEN

USES OF ANTIOXIDANT COMPOUNDS TO PREVENT REPERFUSION INJURY DURING ORTHOTOPIC LIVER TRANSPLANTATION

THESIS

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by

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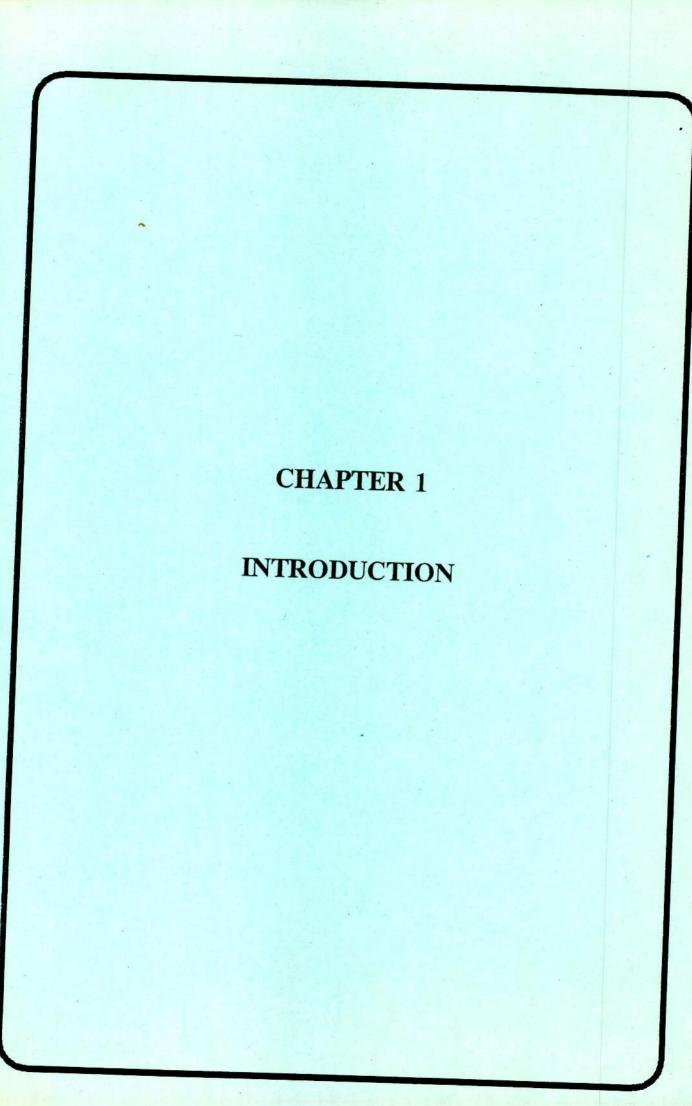
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CHAPTER 1: INTRODUCTION

The ability to transplant organs and tissue provides alternative surgical options for treatment of organ failure. Often major factors in the successful outcome of transplantation are the availability of donor organs and the viability of tissue once implanted. [1]. Management of the patient undergoing liver transplantation has improved since major advances have occurred in both surgical and anaesthetic techniques.

A team approach among the various care givers is important for successful outcome of this major procedure. [2]. This team approach starts with patient selection and preoperative preparation and includes intra-operative and post-operative care. A close interaction and understanding between all the staff involved optimizes patient outcome [2].

Today, liver transplantation is a well established and effective treatment for end stage liver disease.

1.1 HISTORY OF LIVER TRANSPLANTATION

The field of liver transplantation has expanded since the first successful animal experimental procedures reported by Welch and associates in 1955 who reported a good donor liver function. [3,4]. This was followed by Starzl and colleagues [5] initially in animals and then in humans. In the early years of liver transplantation, heterotopic liver transplantation seemed attractive where an extra liver is inserted at an ectopic site, as in the paravertebral gutter or in the pelvis. The first such procedure in a human was reported by Absolon et al in 1964. [6]. The initial results were discouraging and the number of auxiliary grafts performed to date is much lower than that of orthotopic liver transplants, where the new liver exactly replaces the native liver. The auxiliary liver graft frequently did not receive adequate portal venous blood flow and so it atrophied rapidly.

The first successful orthotopic transplantation of the liver was performed in 1963 by Starzl and colleagues in Pittsburg [7], followed by Moore et al in Boston [8] and Demirleau and associates in Paris [9].

The most problems in liver transplantation were difficulty in the surgical technique and the low patient survival and the high morbidity rates during the early years [12]. This was largely due to the poor physical condition of recipients and the massive bleeding caused by abnormal vascularization and defects in coagulation system. Other problems initially were the difficulty in preserving the donor organ.

1.2 PERIOPERATIVE CARE OF THE LIVER TRANSPLANT PATIENT

Perioperative care of the patient undergoing liver transplantation is one of the most challenging clinical situations that the surgeon, anaesthesiologist and critical care physician currently encounter [10].

1.2.1 PATIENT SELECTION PROCESS

The preoperative evaluation of patients prior to liver transplantation consists of a multidisciplinary approach designed to characterize the type and extent of the hepatic abnormality and to identify functional abnormalities in other organ systems. Potential liver transplant recipients undergo a three-step evaluation before they are accepted for transplantation. Step 1 consists of a review of blood chemistry, liver function tests, coagulation tests, renal function tests, pulmonary function tests and an electro cardiogram. Following step 1 of the evaluation, the patient's history is presented to the Liver Transplant Patient Selection Conference, which is a multidisciplinary group that considers the candidacy of the patient prior to proceeding with further investigations. Step 2 includes the evaluation of fungal, viral and parasitic serologies, an immunologic profile, an upper gastrointestinal endoscopy, an echo cardiograph and a mesenteric angiogram. After step 2 the patient's laboratory and test results are again reviewed at the Liver Transplant Selection Conference, at which time the patient is accepted as a transplant candidate and placed on the list with other activated patients. During step 3 the patient awaits transplantation and receives instructions on post surgical considerations including immunosuppressive medications and blood pressure management. In the event that the patient experiences a rapid decline in hepatic function or has acute hepatic failure, step 1 through to step 3 can be

condensed so that a search for a donor organ can be initiated at the earliest possible date [11].

Indications and Contraindications for liver transplantation:

The appropriate selection of candidates for liver transplantation continues to evolve but the major indications for OLT in adult patients can be grouped into four categories [12,13], detailed in Table 1.

The decision to perform liver transplantation in patients with chronic irreversible disease or fulminant hepatic failure due to certain conditions is not particularly difficult because it is well established in this patient that survival without transplantation is likely to be less than one year with medical treatment alone [12,13,14]. The first report of the European Liver Transplant Registry showed that the main indication of transplantation was cirrhosis with primary biliary cirrhosis predominating [15].