INTRODUCTION

Cholelithiasis is a major cause of morbidity in the western world and in the United States about 500,000 cholecystectomies are performed annually. Although cholecystectomy provides a safe and effective treatment a non-surgical treatment has been sought for several reasons. The medical expenses and loss of time from the work force have an important impact on the national economy. Many patients fear general anaesthesia and major abdominal surgery, and may find postoperative disability for several weeks an inconvenient and expensive detraction from their vocation.

Most gallstones are composed mostly of cholesterol, a lipid which can be easily dissolved by many organic solvents. The rapid dissolution of cholesterol gallstones in the gallbladder would therefore seem potentially feasible, if a biologically tolerable solvent could be delivered safely and effectively to the gallbladder. Diethyl ether and chloroform were evaluated in vivo several decades ago but discarded because they proved to be unpleasant or toxic\(^1\). Mono-octanoin was the first direct contact cholesterol gallstone solvent shown to be practicable\(^4\). Its major shortcoming is that it solubilises cholesterol very slowly so that the stones must be in contact with the solvent for several days to weeks to dissolve substantially.

We were therefore stimulated to search for a rapidly acting and safe solvent for direct cholesterol gallstone dissolution. An ether which retained the cholesterol solubilising characteristics of diethyl ether but remained liquid at body temperature, methyl tert-butyl ether (MTBE), was identified. MTBE is a laboratory solvent and an octane enhancer for gasoline so that, acute toxicity studies were already available and suggested a very low level
METHYL TERT-BUTYL ETHER

Methyl tert-butyl ether is an aliphatic hydrocarbon with a boiling point of 55°C. It is a potentially explosive and flammable agent with a lower limit of explosivity of 1.5 to 2 volumes per cent, but appears to be more stable than diethyl ether partly because it is less likely to form peroxides. Toxicity studies in animals suggest that MTBE and diethyl ether have similar but low toxicity. Intravenous infusion of MTBE in rats can cause intravascular haemolysis. MTBE dissolved 200–300 mg cholesterol gallstones in vitro completely within 1 hour. We therefore started studies of its efficacy in animals.

Percutaneous Transhepatic Gallbladder Catheter Placement

A simple, safe, and inexpensive method of introducing the solvent into the gallbladder was the first requirement. By placing a fine catheter through the hepatic parenchyma into the gallbladder via the gallbladder–hepatic attachment, we hoped to be able to safely remove the catheter after one or two days without a major risk of bile leakage. We therefore first tried out in animals a 5 F.G. (1.7 mm diameter) pigtail catheter which we had designed for percutaneous transhepatic gallbladder placement in patients.

Animal Studies

Dogs were prepared by surgically implanting human gallstones and the pigtail catheter into the gallbladder. After healing, MTBE was infused and aspirated for 4–16 hours. Histological examination of the gallbladder mucosa by light microscopy and scanning electron microscopy demonstrated only slight changes. Clinical, laboratory, and histological evaluation revealed no evidence of significant systemic toxicity.

Human Studies

Studies in humans have confirmed the efficacy and safety suggested by the in vitro and animal studies. Percutaneous transhepatic catheter placement has been accomplished in more than 70 patients without failure. We have found fluoroscopic guidance after oral contrast ingestion most convenient for catheter placement, but we have occasionally used ultrasonography in the absence of adequate opacification of the gallbladder.

The pigtail catheter is placed with at least one full loop of catheter in the gallbladder and the pigtail in the fundus, and as many stones as possible are manipulated into the centre of the pigtail (Figure 1). The volume of radio-