Rupture has, however, been recorded in patients with rheumatoid arthritis, systemic lupus erythematosus and renal disease. In some of these patients the tear occurred within the substance of the tendon, and in others the tendon attachment had been avulsed, and in several patients the lesion was bilateral. Infiltration of the tendon fibres by injection of steroids after a spasm has led to rupture of the substance of the tendon. A tear in the absence of appreciable trauma should alert the clinician to the possibility of associated disease.

The obvious diagnostic feature is loss of active extension of the knee joint. The patella may lie higher than normal and a defect may be felt below it. A small fragment of bone may be displaced with the tendon from the lower pole of the patella, and unless the doctor appreciates the significance of this the injury may be missed as a minor fracture of little consequence. The treatment of choice is operative repair at the time of injury. The ligament is sutured back to the inferior pole of the patella with stainless steel wire; and the lateral expansions, which are frequently torn as well, are also repaired. The knee is immobilised for six weeks before flexion is allowed.

Difficulty arises when the diagnosis is not made immediately after injury. In this event, or when the initial repair is unsatisfactory, the knee may require a reconstructive operation, of which several kinds have been described. Kelikian and Filipe used the semitendinosus tendon as a substitute for the torn patellar tendon, and Levin carried out reconstruction using a Dacron graft. Rao reinforced the damaged tendon with fascia lata, and both he and Kelikian emphasised the importance of a preliminary period of traction. Recently Ecker has reported four cases in which the reconstruction used the gracilis and semitendinosus tendons supplemented by heavy-gauge stainless steel wire. The wire was left in position for the first six weeks while healing occurred, and was then removed to prevent fragmentation before the patients started active movements. They did not need preliminary traction as the patella could be mobilised during the operation and brought down to its normal position. All four patients returned to their former level of activity, but none had been engaged in competitive sport.

Disruption of the patellar tendon is an uncommon injury, but in most patients the diagnosis should not be difficult. Immediate operative repair is the treatment of choice. When the diagnosis is delayed the patient may need a reconstructive procedure if he is to regain full active extension of the knee joint. Disruption of the tendon in the absence of appreciable trauma should alert the clinician to the possibility of associated disease.

The principle of Occam's razor—that wherever possible phenomena should be assumed to have a single cause—has been one of the cornerstones of clinical science; but such an approach does not help in understanding multifactorial syndromes such as liver failure or jaundice. Certainly the principle is a part explanation of the continuing controversy about the "cause" of liver damage after halothane.

In the face of apparently irreconcilable pieces of evidence exponents of any hypothesis have had to ignore or discount inconvenient observations, and publications on the topic are notable for selective quotation. At last, however, some commentators are prepared to acknowledge the possibility that a combination of mechanisms may sometimes operate. The next step is examination of the proposition that there must be at least two mechanisms to encompass the experimental evidence and clinical experience.

Fortunately, the practical problem facing the clinical anaesthetist is a diminishing one. Though its design has been strongly criticised, a recent trial of repeated anaesthesia has shown that enflurane delivered from a calibrated vapouriser is very unlikely to give rise to hepatic damage, probably because of its lesser amount of hepatic metabolism. Enflurane has physical properties that make it an acceptable clinical alternative to halothane, so making it suitable for repeat anaesthetics. Since, however, many years and many repeat anaesthetics were needed before an association was recognised between halothane and liver damage anaesthetists would be advised to keep an open mind about enflurane. And, apart from the use of enflurane, there are other acceptable techniques based on halogenated vapours, even though to employ them for a minor procedure may look like taking a sledgehammer to crack a nut.

Use of any routine alternative regimen, however, requires that the overall mortality and morbidity from all causes associated with it should be lower than with a repeat of halothane. Anaesthetists who remain impressed with the overall safety of halothane will therefore want to consider whether there is any way to lessen the risk of hepatic damage after halothane or any marker to identify the patient who is particularly at risk. The clinical need for such advice is the justification for a further review of the current evidence on possible aetiological mechanisms. Animal models have been
developed which respond to halothane both qualitatively and quantitatively like the human liver\(^1^{10}\); in both the model and in man a reductive metabolic pathway has been identified that is considerably stimulated by moderate hypoxia and by certain enzyme-inducing agents. The metabolites that are found suggest that reactive intermediates are formed, and studies with radiocarbon-labelled halothane have shown that when this pathway is stimulated an increase occurs in covalent binding to lipids of metabolites derived from the halothane. An associated increase is also found in the model in serum concentrations of alaninaminotransferase, and also centrilobular hepatic necrosis, features accepted as part of the normal picture of liver damage related to halothane in man. Appropriate controls have none of these findings. A reasonable sequence of causation seems to be: halothane with special factors (hypoxia and enzyme induction) \(\rightarrow\) enhanced metabolism \(\rightarrow\) reactive metabolites \(\rightarrow\) binding to intracellular elements \(\rightarrow\) cell damage \(\rightarrow\) release of transaminases and hepatic cellular necrosis.

The important practical lesson from this work is that it draws attention to a group of patients in whom the use of halothane a second time would be theoretically more hazardous: patients who are fat, elderly, likely to have enzyme induction, being stressed with other reactive metabolites (from radiotherapy, for example), having an operation or anaesthetic technique with an appreciable effect on liver blood flow, having an incision or postoperative complication predisposing to hypoxia, and likely to be still metabolising a dose of halothane given within the previous two weeks. All these factors have been implicated in “halothane hepatitis” in one or more clinical reports. Care in avoiding repeat halothane anaesthetics in these circumstances would probably reduce the already low incidence of this complication even further.

Could this mechanism of toxicity account for all the clinical, experimental, and epidemiological evidence? That is what the followers of Occam would like, but it presents one serious logical difficulty. Though some studies of repeat anaesthesia have not particularly incriminated halothane in liver enzyme changes,\(^1^{11}^{15}\) three other studies\(^\text{13}^{14}\) found an unsuspectedly high incidence—between 20% and nearly 40%—of raised activities of liver enzymes after exposure to a second or subsequent dose. Yet the incidence of massive hepatic necrosis is generally agreed to be very low.\(^10\) If these cases are respectively the base and the apex of a pyramidal progression of quantitatively determined toxic injury, where is the middle? Why is moderate damage with some jaundice not seen relatively often after halothane anaesthesia? Since it is not, we must conclude either that there is an additional factor that is necessary to convert the mild into the near lethal or else that there is more than one aetiological mechanism.

Candidates for the second aetiology include the much postulated sensitisation and the now less popular suggestion of viral hepatitis. Certainly abnormalities in immune mechanisms may be identified in some cases;\(^14\) probably the covalently bound metabolites could induce the changes described—but these could be merely an associated finding rather than a causal factor. If the relation is causal it seems to apply only in an as yet undefined subgroup: there is no evidence that this subgroup is determined genetically, the only hypothesis so far advanced. The scientific basis for sensitisation as a general aetiological hypothesis is therefore shaky. The case reports of hepatic damage in two anaesthetists\(^17^{18}\) are, on one view, the only really compelling reason for believing at all in sensitisation as a “cause” of hepatic damage after halothane.\(^19^{20}\)

Though viral infection may be dismissed equally validly as a general explanation, the possibility is worth mention.

Anesthesia and surgery undertaken during the incubation phase of a viral infection probably exacerbate the effects on the liver;\(^21\) but calculations suggest that the annual number of cases of liver damage due to viral hepatitis ought to be far more than the total cases of unexplained liver damage after surgery that actually occur.\(^22\) Even if we allow for selective under-reporting, at least some cases of “halothane hepatitis” are probably viral, especially when there has been only one exposure, when the severity of the injury is out of all proportion to the dose, and when the interval between exposure and onset is particularly short or unduly long.

Not much can be done by the anaesthetist to guard against such a random hazard. What he can do is to try to limit the number of cases induced by other mechanisms. If he believes in sensitisation, then only scrupulous avoidance of a second exposure to halothane—ever—can at present assure him from the charge of taking an unnecessary risk. He could even argue that if halothane should not be used on any given occasion in case it is needed another. Belief in sensitisation also implies the use of a halothane-free anaesthetic machine—but how many halothane molecules are needed to induce the reaction? If the anaesthetist, however, rejects this notion in favour of a primary direct toxic effect he can readily identify the patients with high-risk factors. Most patients may then have halothane when it is the agent of choice.

\(^16\) Vergani D, Tsantoulas D, Eddleston ALWF, Davis M, Williams R. Sensitisation to halothane-altered liver components in severe hepatic necrosis after halothane anaesthesia. Lancet 1978;i:801-3.