Halothane hepatitis in children

SIR,—Dr J Gerald Kenna and colleagues (9 May, p 1209) present data confirming other reports that severe liver injury associated with halothane may occur in children. They speculate on the incidence of such injury and offer advice to paediatric anaesthetists on the use of halothane. Neither should go unchallenged.

Dr Kenna and coworkers suggest that severe liver injury induced by halothane may be as common in children as in adults. They quote studies with numerators of only 1 and 2 (and denominators of 200 000 and 165 000). An implausible sequence of events is invoked to generate the "missing" cases. Where is their evidence?

One of the authors, Dr Roger Williams, recently stated "its [halothane hepatitis in children] frequency may be very much lower than in the adult, one just can't say . . .,"[1] and other data published by these authors seem not to support the present hypothesis.[2]

Anaesthetists must be concerned with the total risk to the patient.[3] Thirteen professors of anaesthesia have recently presented the case for not abandoning halothane.[4] Its properties are especially desirable for inhalational induction of anaesthesia in children. The use of less desirable drugs for this purpose might create more rather than less morbidity and mortality in children.

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SIR,—While we agree with Dr J Gerald Kenna and colleagues (9 May, 1209) that halothane hepatitis may occur in children and may (extremely rarely) be fatal, we disagree with their concluding sentence: "repeated halothane exposure in children should be avoided if other means of anaesthesia are available."

To support this statement it would be necessary to prove, or at least have considerable evidence, that the mortality and morbidity from all causes with any suggested alternative would be less than those associated with halothane. To the best of our knowledge only one child has died from halothane hepatitis in Britain. Tragic though that is, it represents a remarkable record of safety in view of the extent of use of halothane in the past 30 years. The safety of any successor would have to be exceptional to better it.

This is especially relevant to gaseous induction of anaesthesia, the most common method of induction in preschool children. Halothane is particularly suitable for this technique as it irritates the upper airway less than any other inhalational agent. It is also associated with less laryngospasm and coughing than other agents, both on induction and on emergence from anaesthesia. Isoflurane is the only commonly used volatile inhalational agent that has not, as yet, been associated with hepatitis, but it also has the highest incidence of airway problems.

Whether the mortality and morbidity from airway (and possibly other as yet unknown) problems with isoflurane will be greater than those from hepatitis with halothane is a matter for conjecture as isoflurane has been in use for less than five years. Our opinion, however, is that this is likely, and we would therefore suggest that halothane should be used for the inhalational induction of anaesthesia in children, even if it has been administered previously.

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SIR,—The article by Dr J Gerald Kenna and colleagues (9 May, p 1209) seems to provide clear evidence that halothane hepatitis may occur in children. The finding of antibodies to halothane altered liver cell membrane antigens in children with fulminant liver failure may well offer the most specific pointer to this diagnosis yet. It is, therefore, unfortunate that no children were included in the control groups used in the validation of the techniques and that Dr Kenna and coworkers fail to give quantitative results with statistical significance for the six children in whom they detected halothane antibodies. Evaluation of the results is confounded further by the wide age range (11 months to 15 years) as older children may well behave like adults in response to halothane.

It is, however, the recommendation to clinical anaesthetists that "repeated halothane exposure in children should be avoided if other means of anaesthesia are available" that must be challenged most strongly. There certainly are alternative agents to halothane, but, although they may be less hepatotoxic, they are in other respects potentially more hazardous. There is at present no suitable agent for total intravenous anaesthesia in children, and abnormalities in liver function may occur after the administration of ketamine[1] or thiopentone.[2] Volatile agents will thus form the basis of most anaesthetics given to young children and are particularly useful for induction when venous access is difficult. Halothane is widely preferred as it is the least irritant to the airway and produces fairly smooth and rapid induction of anaesthesia. This is especially important in the management of children with airway obstruction such as acute epiglottitis, in whom halothane should remain the agent of choice. Isoflurane has many advantages, but unfortunately its pungency may cause irritation of the airway, with troublesome coughing, increased secretions, and laryngeal spasm, particularly in children undergoing day surgery without premedication. There is then a danger that in the infant or young child control of the airway might be lost before venous access is secured. Laryngospasm occurred in as many as 23% of children in one series.[3] Enflurane has also been found to cause more airway problems than halothane,[4,5] and the high inspired concentration required to produce adequate anaesthesia may cause pronounced cardiovascular and respiratory depression.[6]

A report of halothane hepatitis allegedly occurring in seven children is a cause for concern. These cases have, however, come to light over seven years during which time Dr Kenna and coworkers have tested serum from nine children and 86 adults who developed hepatitis after halothane anaesthesia. The impression that this rare complication occurs even less often in children is supported by the 84 cases reported to the Committee on Safety of Medicines during the same period,[7] in 62 of which the patients had adequate anaesthetic histories, with 24 patients dying (39%).

Curtailing the use of halothane for paediatric anaesthesia in line with the recommendations of Dr Kenna and colleagues might have serious consequences for patient safety. The very occasional case of halothane hepatitis might then be replaced by a much higher incidence of the complications associated with the introduction of less appropriate agents.

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SIR,—Dr J Gerald Kenna and colleagues (9 May, p 1209) present seven cases (one fatal) of halothane hepatitis in children from 1978 to 1985. They recommend that "repeated halothane exposure in children should be avoided if other means of anaesthesia are available." This recommendation conflicts with their own data and with previous published works.

Two studies in children surveyed roughly 400 000 anaesthetics, most of which included halothane, and found three patients who developed unexplained hepatitis after receiving halothane.[1,2] All three patients made a full recovery. In a study of anaesthetic mortality in England and Wales Lunn and Mushin surveyed five health regions.[3] Around 1 150 000 anaesthetics were reviewed, of which 12% (180 000) were in children aged under 15 years. Most of these children would have been exposed to halothane. No child in the study died of halothane hepatitis.

As far as I am aware, the King's College unit is the only centre in Britain and Ireland that measures serum concentrations of halothane antibodies. This unit may well serve as a diagnostic reference laboratory for a population in excess of 30 million. If 5% of these 30 million people are anaesthetised annually and 12% of those anaesthetised are under 15 years of age then 180 000 children are anaesthetised yearly in the King's College referral network. Most of these children would have been exposed to halothane as it is the premier volatile anaesthetic agent in children. This quick calculation gives a mortality from halothane hepatitis in children of 1 in 1 440 000—an enviable safety record.

Dr Kenna and coworkers present as fact what is still very much theory: that halothane hepatitis is an antibody mediated disease. Many workers are sceptical of this autoimmune hypothesis.[4] Dr Kenna and colleagues state that the diagnosis of halothane hepatitis may be confirmed by showing in vitro serum antibodies reacting with halothane altered guinea pig liver cell membrane determinants. The validity of this test remains very much in doubt, and its value has never been confirmed by an independent research centre.