Outbreak of Giardiasis

SIR,—In April 1971 a group of Swedish students visited Leningrad and subsequently 90% were found to be suffering from *Giardia lamblia* infestation with associated symptoms in the majority. This outbreak was reported by Andersson *et al.*,¹ who referred to previous outbreaks in similar circumstances.

Recently, in November and December 1973, 227 people went on two four-day trips from the Brighton area to Leningrad. A considerable number have suffered from protracted diarrhoea, abdominal pain, nausea, or vomiting since their return. Investigations are proceeding. To date *G. lamblia* cysts, often in large numbers, have been found in specimens from 27 out of 47 people examined, all of whom have had symptoms sufficient to take them to their family practitioner.

We are making this preliminary report in view of the fact that *G. lamblia* infestation is often regarded as being innocuous in adults and because we are beginning to learn of cases in persons who were not involved in either of these trips, though a visit to Leningrad has remained a common factor.

We should like to acknowledge the interest shown by Dr. W. S. Parker, Medical Officer of Health, Brighton, in these investigations.

—We are, etc.,

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¹ Andersson, T., Forssell, J., and Sterner, G., *British Medical Journal*, 1972, 2, 449.

Jaundice after Halothane

SIR,—Dr. W. H. W. Inman and Professor W. W. Mushin analyse 130 cases of jaundice following anaesthesia and surgery (in which halothane was used as part of the anaesthetic technique) reported to the Committee on Safety of Medicines over a period of nine years (5 January, p. 5). They report that "the interval between the last of a series of halothane anaesthetics and the onset of jaundice is significantly shorter than the corresponding interval following a single exposure." They suggest that this provides evidence of "some form of sensitivity" to halothane, and provides "strong evidence of a cause-effect relationship between the use of halothane and jaundice." Many debatable issues are raised by these authors. We shall confine ourselves, however, to commenting on the main theme of their paper as outlined above.

The anaesthetics unit at the London Hospital has been engaged in a nation-wide survey of postoperative jaundice and has collected more than 200 cases in three years, of which 175 included the use of halothane as part of the anaesthetic technique (33 following a single exposure). We have therefore analysed our data in a manner comparable to that used by Dr. Inman and Professor Mushin (see table). It can be seen that we are unable to confirm the finding on which their hypothesis rests—that is, that the time interval before the onset of jaundice following single exposure to halothane is longer than that following multiple exposures. A possible reason for the difference

Mean Intervals between Final Exposure to Halothane and Onset of Jaundice (Days)

No. of Exposures	Inman and Mushin	London Hospital Survey
1	11.7	6.7
2	6.7	7.5
3	4.6	6.7
4 or more	5.3	5.1

between the two sets of data may be that Dr. Inman and Professor Mushin have collected a highly selected and biased population sample. In support of this contention is the fact that they have collected only 130 cases of postoperative jaundice in nine years, whereas we have collected some 200 cases in three years. It is also surprising to find that Dr. Inman and Professor Mushin state that halothane has been involved in all cases reported to them. It is generally accepted that postoperative jaundice may occur following the use of any anaesthetic agent or technique, and in our series we have details of 26 cases in which halothane was not used. Furthermore, Dr. Inman and Professor Mushin quote a 51% death rate from hepatic failure in their series, compared with our series in which death from hepatic failure occurred in some 10% of cases.

The American National Halothane Study reported 82 cases of massive hepatic necrosis. The panel of experts decided that adequate reason, other than the anaesthetic agent, could be found to explain the liver damage in all but nine of these cases. The implication of this finding is that when liver damage occurs after anaesthesia and surgery, in a significant number of cases the anaesthetic agents are not directly involved. In other words, jaundice following anaesthesia and surgery may be unexplained or may have a clear cause, such as stones in the common bile duct, massive haemolysis, or viral hepatitis. When postoperative jaundice is unexplained the anaesthetic agent used must be considered as a possible aetiological factor. In many of the cases reported to Dr. Inman and Professor Mushin the biological data would not appear to be adequate for them to make this distinction. If this view is accepted, they have included cases where a clear cause other than halothane could have been established, and in these circumstances the possibility of hypersensitivity does not arise—a further reason why the figures on which their statistical analysis is based may be invalid. For this reason statistical analysis of the London Hospital figures has not been provided.

We would reiterate yet again that, in our view, the possibility of a cause-and-effect relationship between the use of halothane and postoperative liver damage cannot be denied^{1,2} but, as with previous "evidence," the data presented by Dr. Inman and Professor Mushin do not withstand careful scrutiny. It is disquieting to reflect that, on the basis of such dubious information, the Committee on Safety of Medicines has seen fit to take the step of circulating a letter to all doctors, dentists, and pharmacists drawing attention to this paper.—We are, etc.,

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- ¹ Simpson, B. R., Strunin, L., and Walton, B., *Proceedings of the Royal Society of Medicine*, 1973, 66, 56.
- ² Simpson, B. R., Strunin, L., and Walton, B., in *Controversy in Internal Medicine II*, ed. F. J. Ingelfinger, R. V. Ebert, M. Finland, and A. S. Reiman. Philadelphia, Saunders, 1974.

SIR,—The paper by Dr. W. H. W. Inman and Professor W. W. Mushin (5 January, p. 5) is a provocative contribution to the continuing debate about the existence and incidence of so-called "halothane hepatitis." It is a statistical analysis of the anaesthetic records of postoperative hepatitis cases reported to the Committee on Safety of Medicines. In spite of the difficulty of interpreting such data (such as allowing for the increased age of the patients) and the many cautionary points raised by Dr. Inman and Professor Mushin the committee also issued a general letter warning of the dangers of repeated halothane exposure.

The critical issue which is unanswered in the paper is how many of their cases can be attributed, with reason, to halothane. The expert panel of the much-quoted National Halothane Study¹ accepted only 10% of their postoperative hepatitis cases as being of unknown origin—that is, potentially due to halothane. If their figure of 10% were applied to the present paper one would be led to the conclusion that the incidence of hepatitis following multiple exposures is no greater than the overall incidence of hepatitis in the general population. It is unfortunate, in view of the small number of cases involved (at most 20 per year), that the authors did not follow up many of the reports or critically analyse the data available.

The interesting finding of the paper was that the latency of onset in the postoperative hepatitis cases following multiple operations is shorter than that following a single operation. Decreased latency of onset with repeated exposures is consistent with a number of both immunological and enzyme induction mechanisms but it cannot yet be regarded as pathognomonic of "halothane hepatitis."

We happen to be of the persuasion that halothane hepatitis is a real but rare phenomenon. However, to establish its true incidence it will be necessary to investigate the clinical, biochemical, immunological and histological aspects^{2,3} of each individual case that is subsequently reported. Such an approach may still not satisfy all critics but it will at least put the phenomenon on a sounder scientific basis than a necessarily ambiguous statistical analysis of case reports.

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- ¹ National Research Council, Sub-Committee on the National Halothane Study, ed. J. P. Bunker, Bethesda, National Institute of General Medical Sciences, 1969.
- ² Klatzkin, G., in *Toxicity of Anaesthetics*, B. R. Fink, p. 159. Baltimore, Williams and Wilkins, 1968.
- ³ Sherlock, S., *Gut*, 1971, 12, 324.

Pyrimethamine Toxicity

SIR,—With reference to the letter from Drs. Michael and Maxine Briggs (5 January, p. 40), how do the authors justify giving to "five healthy adult women who had been