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To: All Members of the LIA Health and Safety Committee

Re: Lead Absorption in Children

I believe you will be interested in the attached copy of an article on the above subject which appeared in the May, 1967 issue of the British Medical Journal.

You will note that the results of the study reported in the paper showed no evidence of a relationship between mentally defective children and high blood lead levels in children as claimed by Moorcrieff et al in a paper published in 1964.

It is a pleasure to be able to send you some favorable information on this subject.

Very truly yours,

J. C. Thomas

James C. Thomas
Assistant Director
Health and Safety

JCR/jv
Attachment

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Lead Absorption with Lead

For study of the animals, without necessity for immunosuppressive therapy. Halothane anaesthesia was effective; the animals were kept fairly light throughout the procedure and were usually on their feet within a few hours of the operation. In those animals surviving more than a week classical liver failure did not appear to be the cause of death. However, the gastrointestinal haemorrhage may well have been due to inadequate liver function, though the exact mechanism has not been determined. It will certainly be of interest to study the gastric secretion, metabolism of histamine, the haemodynamics of portal venous flow, and the composition and distribution of bile in these animals. Peptic ulceration is a common complication of orthotopic liver transplantation in dogs. The British workers have also observed gastrointestinal haemorrhage in pigs with orthotopic liver transplants and have demonstrated superficial mucosal erosions in the cardiac portion of the stomach. A perforated duodenum after was the cause of death of one of the pigs in the French experiment.

In our pig herd ship grafts are rejected aggressively when the donor and recipient are unrelated (Baines, 1967), and even in littermate rejection is the rule, though ship grafts may persist up to three weeks. The mechanism of acceptance of an orthotopic liver transplant in our long-term surviving animal at seven months and a similar animal of the control group at nine months (French, personal communication) has not been determined. Though splenectomy has little effect on the survival time of transplanted livers in most species that have been studied, it is possible that splenectomy in pigs with liver transplants may influence the outcome of the transplant.

This early experience encourages us to pursue further studies with liver transplantation in the pig.

Summary

Our preliminary experience with orthotopic liver transplantation in the pig is reported. Of the 19 operations performed 13 animals survived the procedure and six lived for a week or more. One pig with an orthotopic liver transplant from a littermate lived for seven months after operation without any immunosuppressive therapy and died from intestinal obstruction, with minimal macroscopical evidence of liver damage.

We wish to thank Dr. Mark Zablowitz for the help he has given with the anaesthetics of the pigs and we acknowledge the excellent technical assistance that we have received from the staff of the Department of Surgery, University of Cambridge, and the Agricultural Research Council at Babraham. We are most grateful to Dr. R. D. Kiers for providing facilities at the A.R.C. Babraham.

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Lead Absorption in Children

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The possibility of a causal relationship between lead absorption and mental retardation has been suggested by Moller et al. (1964). They claimed that lead was a greater factor in producing mental retardation than previously thought and that the ingestion of lead in the blood was the only certain way of demonstrating excessive exposure to lead. It was believed that a blood lead level of over 10 $\mu\text{g}/100\text{ ml}$ was an indication of intoxication, because 10 percent of children were examined and all but two had levels below this. This problem has been studied in Manchester and Belfast, a detailed paper will also appear going to extensive measurements programme.

Clinical Material

It is necessary to know the possible role of lead poisoning in the causation of mental retardation. The children and young people who were examined were selected from the list of children in the Manchester and Belfast areas who had been referred for examination to the Manchester and Belfast hospitals for mental retardation and the parents of these children were contacted by letter. A detailed description of the children's history was taken from these letters and a detailed clinical examination was conducted that determined the presence of lead poisoning. There are obvious

contraindications of examining such children suffering from a variety of medical and surgical diseases, but there was no possibility of conducting a sufficiently large number in normal health. The children were drawn from the same population as the mentally handicapped children but were not matched for race or social class. The children with Down's syndrome were analysed separately from the other mentally handicapped children to see if the blood lead level of a group with a known syndrome differed significantly from the rest. The blood lead level of 10 $\mu\text{g}/100\text{ ml}$ was chosen as the possible dividing line between normal and abnormal on the previous experience of the Manchester and Belfast groups. The blood lead measurements were taken on fasting blood samples of about 10 $\mu\text{g}/100\text{ ml}$.

All the children were examined and a total of 100 children were examined. The blood lead levels were 10 $\mu\text{g}/100\text{ ml}$ and 24 were below 10 $\mu\text{g}/100\text{ ml}$. The children were 10 and 1 respectively. The children were divided into three groups with blood lead levels below 10 $\mu\text{g}/100\text{ ml}$, 10 $\mu\text{g}/100\text{ ml}$ and 24 $\mu\text{g}/100\text{ ml}$. The 11 children whose blood lead levels were 10 $\mu\text{g}/100\text{ ml}$ included 10 of the group of mentally handicapped children (seven, two of whom were girls, and five of the controls). In 10 of them the blood lead level had returned to a value below 10 $\mu\text{g}/100\text{ ml}$ at the end of each of the first two groups and 10 of the controls had a level of above 10 $\mu\text{g}/100\text{ ml}$ on the second examination.

* The first two are Manchester Child Development Centre, and the third is the Department of Paediatrics, Manchester General Hospital.

Statistical analyses of the results in the three groups of mentally handicapped children of uncertain aetiology, mongol children, and controls gave the results shown in the Table. The data indicate that the three groups do not differ significantly as regards blood lead levels.

The blood lead was estimated by the method used by the Department of Industrial Medicine (Medical Research Council) modified to use 3 ml. of blood (King and Thompson, 1961; Moncrieff et al., 1966).

Statistical Analysis of Results

Group	No. in Group	Mean	S.D.	r (Correlation between Blood Lead Level and Age in Years)
Mentally handicapped	121	31.6 $\mu\text{g}/100 \text{ ml.}$	17.7	0.224
Mongols	15	35.1 $\mu\text{g}/100 \text{ ml.}$	19.3	0.146
Controls	75	30.9 $\mu\text{g}/100 \text{ ml.}$	20.9	0.144

Discussion

The three groups do not differ significantly as regards blood lead levels, which strongly suggests that within the limits of this study there is no evidence that lead intoxication is playing a significant part in the aetiology of the mental retardation. The findings among the children with Down's syndrome do not indicate that, even if lead intoxication is not of aetiological significance, these particular children are more at risk from the ingestion of lead than the controls. Spence (1959) reported values of 60 $\mu\text{g}/100 \text{ ml.}$ or over as pathological, though drawing attention to the fact that a single determination of lead in the blood in normal individuals may be temporarily above levels generally regarded as toxic. In this study the range of blood lead levels is marked among the controls at the mentally retarded (Figs 1, 2, and 3) and from the mongol

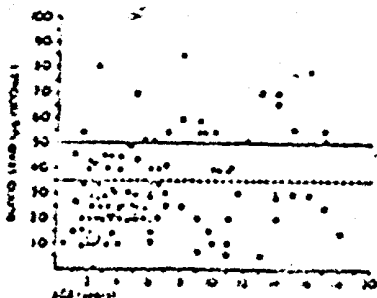


Fig. 1—Levels of lead in blood of mentally handicapped children of uncertain aetiology.

of these figures that a normal blood lead level of which can be diagnosed is possible. There is a possibility of a wide variation of the blood lead level in groups of mentally handicapped children, but this does not seem likely enough to bias the duration of exposure as a definite factor.

It may be possible whether a finding of a blood lead value above an accepted level of 40 $\mu\text{g}/100 \text{ ml.}$ and above the present perception of the normal range of blood lead level, which the best clinical evidence suggests is 40 $\mu\text{g}/100 \text{ ml.}$ is found among these children suggests that they may not be as severely retarded as they are perceived to be. It is likely that the blood lead level is a poor indicator of the degree of a child's mental retardation. The test value is reported to show the following: a concentration may be a finding of differentiating value, but it is not sufficient to lead poisoning from the use which has been exposed to a temporary concentration of the lead. The plumbism calcium disodium sulphate will can differentiate

between normal individuals and those with increased exposure to lead. Whitaker et al. (1962) showed that the average excretion of lead in the urine in the 24 hours after administration of the drug was 165 $\mu\text{g}/\text{L.}$ in normal children, 993 $\mu\text{g}/\text{L.}$ in those with suspected lead poisoning, and 1,546 $\mu\text{g}/\text{L.}$ in those with classic lead poisoning.

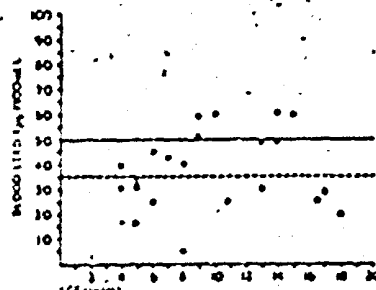


Fig. 2—Levels of lead in blood of mongol children.

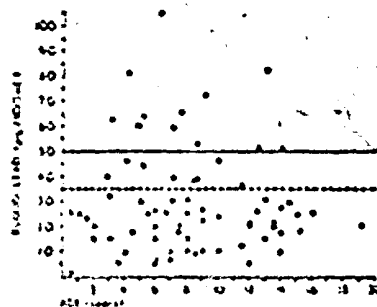


Fig. 3—Levels of lead in blood of control group of children.

"Normal" values of blood lead are known to vary from rural to urban surroundings, owing to opportunities for absorbing lead. Chalmers (1958) has stressed that blood lead measurements require careful interpretation and that several movements are necessary to ascertain trends. He lists the following factors which may be of significance: the haemoglobin, intercurrent infections, concurrent liver disease, current or recent administration of chelating agents, current or recent excessive absorption of lead, and the time interval since excessive absorption ceased. Similarly the treatment with chelating agents of a child, possibly resulting from a known cause, who may have been previously poisoned by lead, has to be considered. The child is not a normal child again with a blood lead level of 40 $\mu\text{g}/100 \text{ ml.}$ who improves on treatment, but this is a situation in which a clinician should be aware of the type of child and the situation that clinical criteria would not seem sufficient on their own.

Increased exposure, hypercalcaemia, and a number of other factors may be a cause of a behaviour of a mentally handicapped child. Therefore, before the diagnosis of lead intoxication can be made, it is necessary to consider a child, by finding a concentration of lead in the urine of more than 150 $\mu\text{g}/\text{L.}$ in the 24 hours after a test dose of ethylenediamine calcium disulphate. The test dose of a large number of children with plumbism should be given and E.D.T.A. or plumbism should be given. In view of the possible nephrotoxic effects of E.D.T.A. and plumbism and the children, the rules of treatment for the individual patient must be weighed against the possible advantages.

