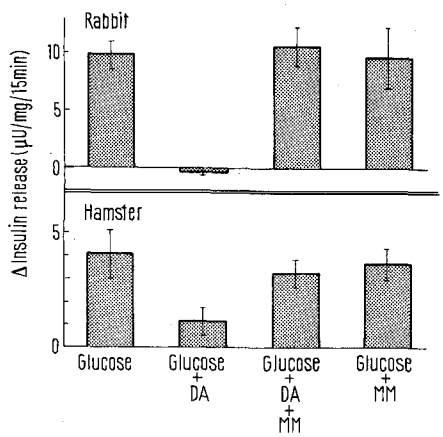
Results. The Figure demonstrates that dopamine inhibits glucose stimulated insulin release from both rabbit and hamster pancreas. This inhibition was blocked by methysergide. In these studies, methysergide alone did not alter glucose stimulated insulin release from either rabbit or hamster pancreas.

The Table shows that methysergide alone did not alter glucose stimulated insulin secretion from mouse pancreas in either $1 \times 10^{-3} M$ (experiment A) or $1 \times 10^{-4} M$ (experiment B) concentration. Experiments B, C and D show that dopamine significantly inhibited insulin secretion when present in concentrations of $1 \times 10^{-4} M$ to $1 \times 10^{-5} M$. With decreasing concentrations of dopamine the constant concentration of methysergide ($1 \times 10^{-4} M$) had a progressively greater ability to antagonize the inhibitory effect of dopamine (experiment B 93% to 82% inhibition, experiment C 87% to 47% inhibition, and experiment D 76% to 36% inhibition). In further studies $1 \times 10^{-5} M$ dopamine was the lowest dopamine concentration that would inhibit insulin secretion from mouse pancreas.



Effect of methysergide (MM) on the inhibition of glucose stimulated insulin secretion from rabbit and hamster pancreas by dopamine (DA). In the upper panel dopamine ($1 \times 10^{-4} M$) inhibited glucose stimulated insulin secretion from rabbit pancreas ($p < 0.01$) and this inhibition was blocked by methysergide. In the lower panel, dopamine ($2 \times 10^{-5} M$) inhibited glucose stimulated insulin secretion from hamster pancreas ($p < 0.05$) and this inhibition was also blocked by methysergide. In these studies the concentration of methysergide used ($1 \times 10^{-4} M$) did not alter glucose stimulated insulin secretion. The glucose concentration was 3 mg/ml. The bars represent the means and the brackets the SE of 6 observations in experiment one and 8 observations in experiment two.

Discussion. The present studies demonstrate that methysergide antagonizes the inhibition of insulin secretion by dopamine. Further studies indicate that methysergide also antagonizes the inhibitory effect of other catecholamines such as L-epinephrine, L-norepinephrine and L-isoproterenol upon in vitro insulin secretion from rabbit pancreas (unpublished observations). Thus, in at least one system (the pancreatic β-cell) methysergide antagonizes the actions of catecholamines as well as serotonin. These data indicate that methysergide cannot be considered as exerting its pharmacologic effects only through serotonin antagonism. The extent to which methysergide antagonizes catecholamine actions in other tissues needs to be reexamined.

Zusammenfassung. Isoliertes Maus-, Hamster- und Kaninchenpankreas wurde in einer physiologischen Pufferlösung mit 3,0 mg/ml Glukose inkubiert. Dopamin ruft eine erhebliche Verringerung der radioimmunologisch reagierenden Insulinsekretion hervor. Die durch Dopamin ausgelöste Hemmung lässt sich teilweise oder vollständig durch den Serotoninantagonisten 1-Methyl-D-lysergsäure butanolamid (Deseril) aufheben.

J. M. FELDMAN and H. E. LEBOVITZ

Division of Endocrinology, Department of Medicine, Duke University Medical Center, Box 2963, Durham (North Carolina 27710, USA), and Durhams Veterans Administration Hospital, Durham (North Carolina 27710, USA),
12 October 1971.

The Distribution of Lead in Human Deciduous Teeth

Lead absorbed into the body by various routes is stored in teeth and bone. ALTSHULER et al.[1] have demonstrated substantial increases in the lead content of deciduous teeth of children dying of lead poisoning. Asymptomatic children from areas where lead poisoning is frequent have significantly higher lead levels in shed deciduous teeth than controls from areas in which lead poisoning is unknown[2]. This suggests that the deciduous tooth may provide a means of identifying lead ingestion long after the ingestion has stopped.

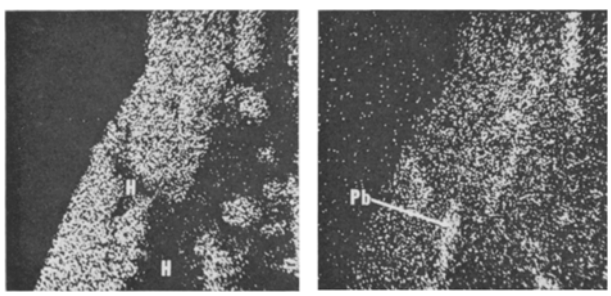
It would be of interest to locate the site of lead deposition in teeth as a means of more precisely fixing the time and duration of exposure. This preliminary report describes the use of the electron probe in the study of the distribution of lead in human dental tissues.

Deciduous teeth were cut longitudinally with a diamond saw, shadowed lightly with evaporated carbon, and examined directly in an electron probe microanalyzer (CAMECA). The electron beam voltage was arbitrarily chosen at 30 kV, with specimen currents adjusted to 100–200 nA. The characteristic L-alpha emission line of lead was detected using a quartz crystal focussing spectrometer and side window gas flow proportional counter. Scanning X-ray images were photographed to show localization of lead, phosphorus and calcium.

Twelve specimens from urban children, 2 with known histories of lead poisoning, were examined. Lead was detected in variable amounts in all the teeth. The Figure shows the X-ray images of an area of tooth encompassing enamel, the dentoenamel juction and dentine. In these areas, zones of regular mineralisation (indicated by

[1] L. F. ALTSHULER, D. B. HALAH and B. LANDING, J. Pediat. *60*, 224 (1962).
[2] H. NEEDLEMAN, O. TUNCAY and I. SHAPIRO, Nature, Lond., in press.
[3] F. BRUDEVOLD and L. T. STEADMAN, J. dent. Res. *35*, 430 (1956).

uniform calcium and phosphorus emissions) and 'hypomineralization' (a deficiency of calcium and phosphorus emissions) were noted. In almost all cases, the lead was deposited either in or at the periphery of the 'hypomineralized' zones. The same pattern of deposition was also noted in the root dentine, especially in areas adjacent to the pulp. This localization effect was found in teeth of asymptomatic children and in those diagnosed as having suffered from lead poisoning. No lead was detected in surface enamel. This was a surprising finding in view of the report of BRUDEVOLD et al.[3] that a very high percentage of lead occured in the most superficial layers of this tissue.



X-ray scanning images for phosphorus (left) and lead (right). The region shown in this figure (200 μm × 200 μm) is close to the cemento-enamel junction. Areas of dense lead localization (Pb) can be seen to approximate to 'hypomineralised' zones (H) of the phosphorus scan. The calicum S-ray scan (not shown here) was identical to the phosphorus image.

The presence of a considerable quantity of lead in the body of the dentine and in the enamel suggests that lead is incorporated into the tooth structure during matrix formation and mineralization. Furthermore, the appearance of lead in root dentine indicates that it is also taken up by the tooth during root formation and the deposition of secondary dentine. Thus, chemical analysis of the tissues formed before and after tooth eruption could be used to provide a history of lead ingestion during different phases of the life cycle of the tooth[4].

Résumé. Douze dents de lait d'enfants citadins, dont deux ayant une intoxication saturnine reconnue, ont été examinées par un microanalyseur à sonde électronique. On a retrouvé du plomb dans toutes les dents, avant tout à la périférie des zones hypominéralisées; mais pas à la surface de l'émail. Les résultats suggèrent que le plomb est incorporé dans la dent pendant la formation de la matrice et sa minéralisation, ainsi que durant la formation de la racine et du dépot de dentine secondaire.

K.G. CARROLL, H. NEEDLEMAN[5], O.C. TUNCAY and I.M. SHAPIRO

School of Dental Medicine, University of Pennsylvania, Harvard Medical School, The Children's Hospital Medical Center, 300 Longwood Avenue, Boston (Massachusetts 02115, USA),
24 September 1971.

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[5] For reprints: H. NEEDLEMAN, 300 Longwood Avenue, Boston.

Relationship Between Hypothermia and some Chlorpromazine Induced Metabolic Changes in Mouse Brain

The effects of chlorpromazine (CPZ) on the rapid conversion of glucose into amino acids and its relationship to chlorpromazine induced hypothermia have been investigated.

Methods. Female SAS/ICI albino mice, 25–40 g, were given 0.9% saline, 5 ml/kg or CPZ 20 mg/kg i.p. 30 min after this they were given 5 μCi (U-^{14}C)-D-Glucose i.p. The animals were killed 30 min afterwards and the cerebral hemispheres rapidly frozen in liquid nitrogen, homogenized in 3 ml of ice-cold 10% trichloracetic acid (TCA) and then chemically fractionated and the radioactivity of the fractions determined by liquid scintillation counting[1].

For the estimation of individual amino acids brain samples were extracted with a total of 9 ml 80% ethanol and 5 ml distilled water. This extract was passed through a Zeo-Karb 225 resin column in the H^+ form to separate the amino acid containing fraction. The eluate was analyzed by quantitative paper chromatography[2]. The percentage recovery of radioactivity was 68.5 ± 13.3% ($N = 13$) and amino acid levels were individually corrected to 100%. Glutamine concentration and the combined concentrations of glutamic acid, γ-aminobutyric acid and glutathione (GGG) were estimated colorimetrically[3].

The body temperature was measured by a rectal thermistor probe. Overall, the mean rectal temperatures in which body temperature was maintained (by placing the mice in a 38–40 °C incubator) were: control 37.65 °C ($N = 20$); CPZ 37.80 °C ($N = 19$). For animals with uncontrolled body temperatures these were: control 37.40 °C ($N = 26$); CPZ 29.20 °C ($N = 24$).

The results were examined by *t*-test or an analysis of variance using the multiple comparison technique[4].

Results. The effect of CPZ on the uptake of radioactivity is shown in Table I. There is no significant change in total uptake of radioactivity but the percentage incorporation of radioactivity into the TCA fraction is markedly increased by CPZ during hypothermia and is reduced but not abolished when body temperature is maintained. The relationship between radioactivity in the TCA fraction and temperature of animals treated with CPZ is shown in the Figure. When the body temperature was allowed to fall, no significant change in individual amino acids was produced (Table II).

The percentage radioactivity of the amino acids of the total TCA fraction was: control 70.9% (S.D. = 16.1; $N = 7$); CPZ 67.9% (S.D. = 11.1; $N = 6$); significance of difference: $P > 0.05$; $t = 0.4$.

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