The Activity of Certain Enzymes in Cadmium-Poisoned Chicks

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Cadmium poisoning of men and animals gives rise to a serum albumin of low molecular weight (minialbumin), immunologically indistinguishable from normal albumin but lacking in tryptophan and with a deficit of lysine (Kench, Gain & Sutherland, 1965; Kench & Sutherland, 1966, 1967).

Activities of a number of enzymes in the liver and other tissues of newly hatched cadmium-poisoned chicks have now been compared with those of normal controls before and after incubation with Cd^{2+} at a concentration similar to that present *in vivo*. The purified enzyme, when available, was incubated with a range of concentrations of Cd^{2+} . For the experiment *in vivo* the usual treatment was a single injection of 12–15 μg of Cd^{2+} (as $\text{CdCl}_2 \cdot 2\frac{1}{2}\text{H}_2\text{O}$, approx. 0.11–0.13 μmol) into a superficial blood vessel of the chick embryo 7 days before hatching. The liver of newly hatched chicks was rapidly homogenized and fractionated by differential centrifugation in mannitol–sucrose–EDTA medium (Johnson & Lardy, 1965). Concentrations of Cd^{2+} in the various cellular fractions were determined, after wet oxidation, by atomic absorption spectrophotometry (P. J. D. Gubb & J. E. Kench, unpublished work).

On the basis of their reactivity with Cd^{2+} the ten enzymes examined could be grouped as follows: (1) inhibited both *in vitro* and *in vivo*, lipamide dehydrogenase, δ -aminolaevulate synthetase and xanthine dehydrogenase; (2) inhibited *in vitro* but not *in vivo*, cytochrome oxidase and succinate dehydrogenase; (3) resistant *in vitro* but biosynthesis impaired *in vivo*, catalase; (4) stimulated *in vitro* and *in vivo*, tryptophan oxygenase in liver cytosol of chicks, which was stimulated *in vitro* ($<0.2\text{ mM}$ - Cd^{2+}) and *in vivo* (70 μM - Cd^{2+}), though inhibited by Cd^{2+} in concentrations exceeding 0.5 mM; rat liver tryptophan oxygenase behaves in a similar manner (Sutherland & Kench, 1969); δ -aminolaevulate dehydratase, erythrocytic adenosine triphosphatase and the malate dehydrogenase isoenzyme in liver cytosol were other enzymes whose activity was enhanced by Cd^{2+} at certain concentrations; (5) was relatively insensitive to Cd^{2+} both *in vitro* and *in vivo*, mitochondrial malate dehydrogenase; inhibition by Cd^{2+} of the purified enzyme from pig heart was additive to inactivation by iodine, the two inhibitors not competing for sites on the enzyme.

Our findings are in accord with selective reactivity of thiol groups in different proteins (Wallenfels & Eisele, 1970; Varrone, Consiglio & Covelli, 1970). Interaction of Cd^{2+} with enzymes may provide information on the localization of enzymes within mitochondria and other cellular structures.

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Anticonvulsant Drugs and Xylose Uptake by Cerebral-Cortex Slices

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Xylose and glucose may be transported into brain by a common mechanism (Gilbert, 1965; Joanny, Corriol & Hillman, 1969), and for permeability studies xylose has the advantage of not being metabolized by brain.

Studies of the effects of anticonvulsants on sugar uptake may throw light on the mechanism of action of these drugs, because glucose is the principal oxidizable substrate utilized by brain, and it may also influence the activity of cerebral enzymes and the stability of cerebral membranes.

In the present studies the uptakes of xylose by guinea-pig cerebral-cortex slices incubated at 37°C in oxygenated bicarbonate media, containing pyruvate as nutrient and raffinose as extracellular space marker, were measured under a variety of conditions. The slices were always preincubated for 30 min at 37°C in the absence of xylose before transfer to a similar medium containing xylose. Any drugs and inhibitors tested were dissolved in both preincubation and incubation media.

The uptake of xylose (50 mM) by the non-raffinose compartment of the slices over a 9 min period was significantly stimulated by acetazolamide (20 mM) and by ethosuximide (500 μM), whereas, as reported by Gilbert, Ortiz & Millichap (1966), diphenylhydantoin was without significant effect. Initial-velocity studies indicated that the apparent K_m and V_{max} for xylose were both increased by