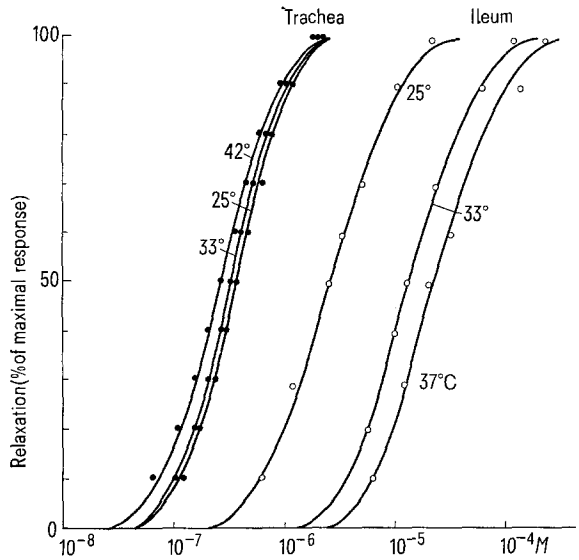
Result. On ileum the elevation of the temperature from 25° to 33 °C resulted in a pronounced shift of the dose-response curve of orciprenaline to the right, whereas a further increase of the temperature to 37 °C did not cause a further shift (Figure). This diminution of the affinity of orciprenaline is indicated by the pD_2-values (Table). The pD_2-value 5.0 at 33 °C is significantly lower than that of 5.71 at 25 °C. The relatively small difference of temperature from 33 °C to 37 °C did not alter the affinity. At 42 °C the loss of affinity was so high that it was impossible to get the required amounts of orciprenaline dissolved. – The elevation of temperature from 25° to 37 °C decreased the affinity of the resorcin Th 1165a from 6.46 ± 0.06 ($n = 6$) to 5.87 ± 0.06 ($n = 8$).

On the tracheal chain the temperature was without any influence on the dose-response curve of orciprenaline as well as on its pD_2-values (Figure and Table). Likewise the affinity of Th 1165a was not changed, as is indicated by the pD_2-value of 8.13 ± 0.09 ($n = 7$) at 25 °C and 8.05 ± 0.07 ($n = 5$) at 42 °C.

Discussion. The present results show that on ileum the effect of orciprenaline is also dependent on the temperature, as are the effects of isoprenaline and of Th 1165a. On the tracheal chain, on the contrary, the affinity of orciprenaline is not influenced by increasing the temperature. The resorcin derivatives Th 1165a and orciprenaline show the same effects on both organs, ileum and tracheal chain, under the influence of temperature alteration. This observation implies that the resorcin configuration determines the behaviour of both agents and that the prolongation of the side chain in the case of Th 1165a is exclusively responsible for the 20 to 40 times higher affinity obtained for Th 1165a compared with orciprenaline on ileum and trachea.

The different responsiveness of the trachea on the one hand and ileum on the other to the adrenergic drugs under the conditions of temperature changes might be explained by results from our laboratory using the metabolic inhibitor iodoacetic acid (IAA). IAA was able to re-shift the dose-response curves of all three amines mentioned to the left on ileum but not on trachea, indicating a relatively low metabolic activity of the trachea and a higher one of the ileum[6]. Temperature increase would, therefore, be expected to stimulate the metabolism to a much higher degree in the ileum than in the trachea. Consequently, the observed loss of affinity for amines in the ileum might be due to changes of the intracellular pH. If our assumption is correct lowering of the extracellular pH in the trachea should lead to lowering of the intracellular pH and concomitantly to a diminished affinity of the amines. Such a diminished affinity could indeed be obtained after lowering of the extracellular pH[6], thus indicating the importance of the metabolic activity of the organs for the sensitivity of the β-receptors.



Influence of temperature changes on the dose-response curves of orciprenaline on trachea and ileum. On tracheal chain (●—●) the increase of temperature from 25° up to 42 °C did not alter the dose-response curve of orciprenaline. Note the strong shift to the right in the case of ileum (○—○) by increasing temperature. (Numbers of experiments are identical with those given in the Table).

Zusammenfassung. Versuche am Ileum des Kaninchens und der Trachea des Meerschweinchens mit dem Resorcinderivat Orciprenalin[7] bei 25 bis 42 °C führten zu folgenden Ergebnissen: Temperaturerhöhung verminderte am Ileum die Affinität des Orciprenalins, an der Trachea dagegen war sie ohne Einfluss[8].

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Long Term Retention of Colloidal Thorium Dioxide in the Liver and Spleen of *Xenopus laevis* Daudin

Colloidal thorium dioxide (ThO_2) can be used as a contrast medium in radiography and has been especially effective in demonstrating lymphatic movements and drainage in amphibians[1]. Colloidal thorium dioxide is also useful as a tracer substance in ultrastructural studies owing to its easily identifiable electron-dense appearance[2–4]. It is well established in anurans[1] and in mammals including man that injected colloidal ThO_2 is rapidly removed from the circulating fluids and taken up by the reticulo-endothelial system (RES), in particular by phagocytic cells of the liver and spleen[2,5]. With radioactive tracers such as ThO_2 that have a slow biological half-life, prolonged deposition in cells of the RES can result eventually in a carcinogenic response[6]. An experiment was therefore performed to determine the long term retention capacities of liver and spleen in young *Xenopus* frogs receiving a single injection of colloidal ThO_2 in view of the fact that these animals possess a relatively simple RES even in comparison with other common anuran genera[7].

Material and methods. 50 small *Xenopus laevis* frogs, 30–40 mm snout/vent length, weighing on average 2.65 g,

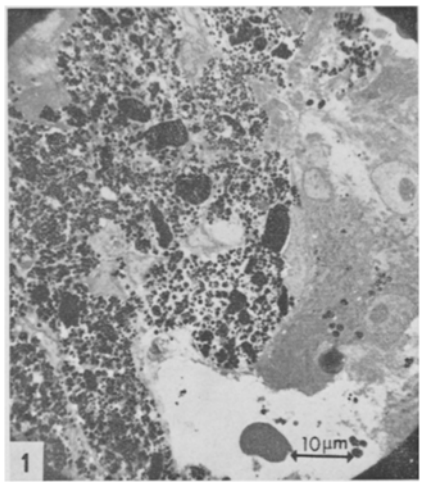

Fig. 1. Particles of thorium dioxide packing Kupffer cells of liver of frog 3 years after injection.

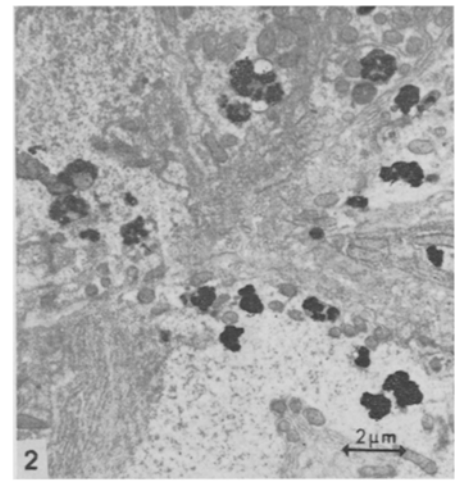

Fig. 2. Thorium dioxide particles localized in lysosome-like bodies in liver parenchymal cells of frog 3 years after injection.

6 months after the completion of metamorphosis, were used in the experiment. The frogs were maintained in a 20 °C room in constant light and fed tubifex or chopped earthworms. 5–15 nm particle size thorium dioxide[8] was dispersed in distilled water and injected into the dorsal lymph sac of the frogs so that each received a single injection of 10 mg ThO_2 in 0.1 ml distilled water. This colloidal sol is quite acidic, though the animals did not appear to be unduly affected. Control frogs were injected with equal volumes of distilled water. Animals were sacrificed under 1:1,000 MS 222 anaesthesia after 5 days, 47 days, 5 months and 3 years. The liver and spleen were removed and cut where necessary into small cubes in ice cold 3% glutaraldehyde in 0.1 *M* sodium cacodylate buffer followed by post-fixation in veronal acetate buffered 1% osmium tetroxide. The specimens were subsequently dehydrated in graded ethanols, treated with propylene oxide and embedded in Epon 812. Ultrathin sections were mounted on uncoated copper grids and briefly stained in lead citrate prior to examination in an AEI EM6B or AEI Corinth 275 electron microscope.

Results and discussion. Apart from a small number of deaths, which may possibly have resulted from the treatment, the experimental animals survived well until the termination of the experiment showing no obvious deleterious effects compared with the controls. By the time of the first examination at 5 days the ThO_2 particles were found in large amounts in Kupffer cells of the liver and also to a lesser degree in the parenchymal cells, where they were localized in lysosome-like bodies. ThO_2 particles were also found, though in much smaller accumulations, in the cytoplasm of a number of macrophage-like splenic cells. The particulate nature and appearance of the ThO_2 is quite characteristic and cannot really be confused with anything else in these preparations; this is also made clear by its absence from control preparations.

There was no appreciable change in the apparent amount or distribution of the ThO_2 in the liver (Figures 1 and 2) or spleen even at the end of the experiment, 3 years after the single injection. It would thus appear that colloidal material is rapidly taken up by these organs and retained in specific cells for considerable periods, possibly indefinitely. Moreover, it would appear that the liver, possibly by virtue of its large size, is the main site of clearance of the lymph-borne colloidal particles in particular by Kupffer cells.

These observations confirm a light microscopic study on similar *Xenopus* frogs after injection of other colloidal material[7] and are in line with similar results found in other frogs[1] and in mammals[2,4,9]. Thus, even in anurans with relatively simple reticulo-endothelial systems weakly radioactive materials once taken into the body are not eliminated even over prolonged periods and it is likely that they may ultimately, by virtue of their radioactive nature, give rise to pathological effects. *Xenopus* frogs may prove to be most effective experimental animals in which to study ways of clearing the RES of such colloidal radioactive materials[10,11].

Résumé. Des observations ultrastructurales ont montré que le thorium bioxyde colloïdal (ThO_2) s'accumule dans le foie et la rate des grenouilles, *Xenopus laevis*, jusqu'à 3 ans après une seule injection de 10 mg pratiquée sur le jeune animal, 6 mois après sa métamorphose.

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