schiedenartigen Kationenaustauschern hin, die unter anderem auch eine Erklärungsmöglichkeit für die Organspezifität gewisser Amine abgeben. Ein synthetischer Ionenaustauscher mit Sulfosäuregruppen als aktiven Zentren vermag in Gegenwart einer äquivalenten Menge Natriumionen Amine im allgemeinen sehr bevorzugt einzutauschen, wobei von den gewählten Aminen nur *d*-Glucosamin schwächer als Natrium festgehalten wird. Entsprechend diesen Modellversuchen ist anzunehmen, dass auch physiologische makromolekulare Polyelektrolyte, die – wie etwa Heparin – ähnlich aktive Zentren besitzen, im Organismus mit Aminen biogener oder exogener Natur in stärkere Wechselbeziehung treten können als mit anorganischen Kationen.

Ganz andere Verhältnisse finden sich jedoch am sauren Ionenaustauscher mit Carboxylgruppen als aktiven Zentren. Hier werden die Amine ganz unterschiedlich stark eingetauscht; die Natriumionen spielen eine sehr wichtige Rolle und werden zum Teil bedeutend stärker aufgenommen. Analog zu diesen Befunden können wohl Carboxylgruppen tragende Organstrukturen, wie sie etwa in neuraminsäurehaltigen Grenzflächen vorliegen, nur mit gewissen Aminen bevorzugt in Wechselbeziehung treten, währenddessen andere Amine infolge des Einflusses anorganischer Kationen weniger selektiv aufgenommen werden.

Ein Vergleich der Aktivitätsreihen der beiden Harze zeigt ausserdem, dass gewisse Amine in den beschriebenen Systemen sehr unterschiedlich stark eingetauscht werden können: So wird beispielsweise Mezcalin vom Sulfosäureharz mit 75,2% ausgesprochen bevorzugt festgehalten. Seine Aufnahme am Karboxylgruppenharz ist mit 37% geringer als die der Natriumionen mit 46,6%.

Angesichts der Häufigkeit von biogenen Makromolekülen mit Polyelektrolytcharakter dürften im Organismus Ionenaustauschvorgänge, sei es an Depot- oder an Rezeptorstrukturen, eine bedeutsame Rolle spielen, wobei die biogenen Ionenaustauschsysteme – in ähnlicher Weise wie die von uns verwendeten Harze – ihre spezifische Funktion vor allem der Art ihrer ladungstragenden Gruppen verdanken.

Summary. The influence of an inorganic cation (sodium) was studied upon the distribution of physiologically or pharmacologically important amines on two different acid ion exchangers. When cation and amine are added in equivalent amounts to an exchange system of corresponding capacity, the distribution pattern of the amine shows differences which are characteristic of the active groups (SO_3H, COOH) of the relevant exchanger. Such reactions are thought to be of importance in biological activities of polyelectrolytes.

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Calcification of the Parathyroids Induced by Calciphylaxis[1]

Calciphylaxis is a condition of hypersensitivity in which during a 'critical period' after sensitization by a systemic calcifying factor (e.g., vitamin-D compounds, parathyroid hormone), treatment with certain challengers (e.g. metallic salts), causes an acute local tissue calcification followed by inflammation and sclerosis. A topical calciphylaxis thus induced by subcutaneous injection of challengers results in a cutaneous calcinosis reminiscent of calcareous scleroderma. However, in suitably sensitized (e.g., dihydrotachysterol-treated) rats, calciphylactic reactions can also be elicited rather selectively at predetermined sites (e.g. in the pancreas, bile ducts, uterus, spleen, Kupffer cells, lungs, salivary glands, lacrimal glands) by the intravenous administration of challengers that have a particular affinity for one or the other organ[2-4].

Here we should like to report on the production of an almost selective parathyroid calcification by the use of chromium salts as calciphylactic challengers.

Materials and Techniques. Fifty female Holtzman rats with an initial body weight of 105 g (range 100–110 g) were subdivided into five equal groups treated as follows: Group 1: Dihydrotachysterol (DHT); Group 2: $CrCl_2$; Group 3: $CrCl_3$; Group 4: DHT + $CrCl_2$; Group 5: DHT + $CrCl_3$. DHT (Calcamin®, Wander) was given at the dose of 1 mg in 0.5 ml corn oil by stomach tube once on the first day. Chromous chloride ($CrCl_2$, 3.5 mg in 0.35 ml of water) and chromic chloride ($CrCl_3 6H_2O$, 10 mg in 1 ml water) were injected intravenously once on the second day. All animals were killed with chloroform on the sixth day. After inspection with a stereoscopic loupe, specimens of various organs were fixed in alcohol-formol for the subsequent histochemical demonstration of calcium by the v. Kóssa technique.

Results. At autopsy, the most striking finding was the intense calcification of the parathyroids. The rat possesses

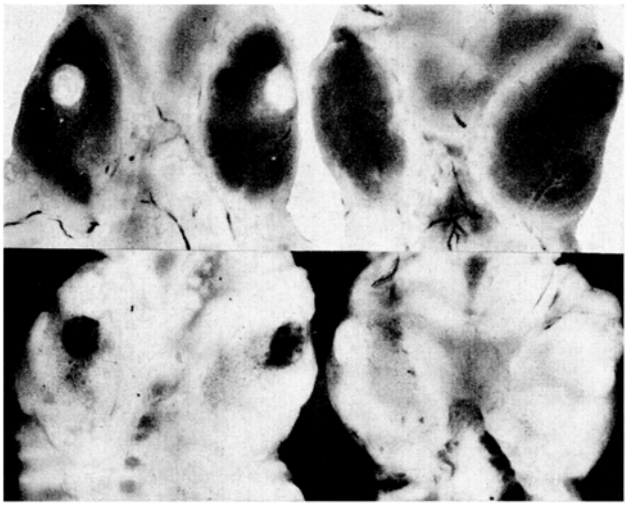

Fig. 1. Selective calcification of the parathyroids, in two rats sensitized with DHT. In addition, one (left) received $CrCl_3$. The calcified parathyroids are white in the fresh (top) and black in the $AgNO_3$-stained specimen (bottom).

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[2] H. SELYE, P. JEAN, and R. VEILLEUX, Proc. Soc. exp. Biol. Med. *104*, 409 (1960).

[3] H. SELYE and K. NIELSEN, Acta morphol., Acad. Sci. Hungar. *10*, 327 (1961).

[4] H. SELYE, Allergie und Asthma, in press.

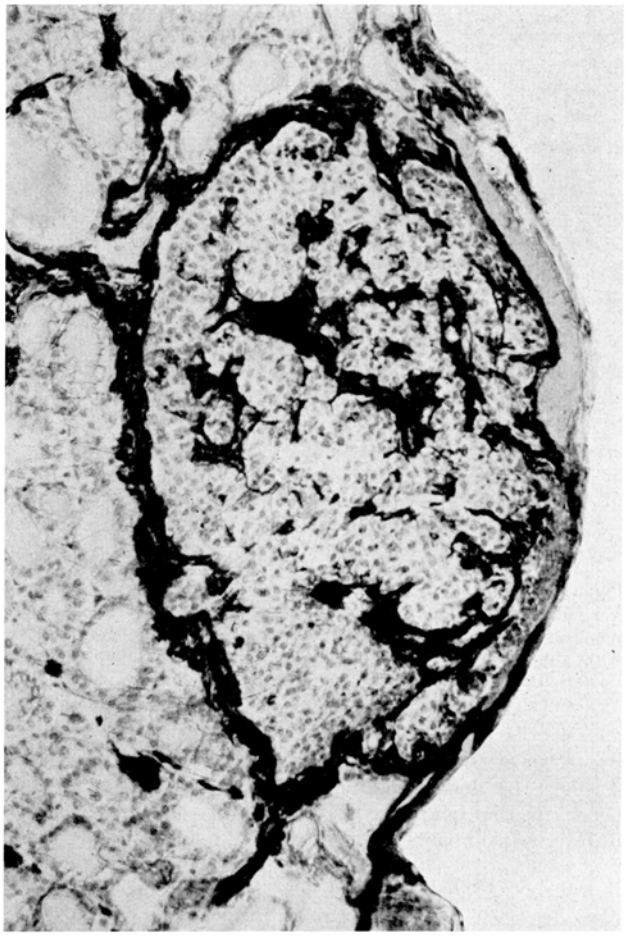

Fig. 2. Histologic aspect of the calcified parathyroid, showing selective deposition of calcium salts in the stroma of the parathyroid, with slight spreading into the adjacent thyroid stroma. The parenchymal cells are unaffected (von Kóssa × 150).

only two parathyroids which are embedded near the posterior margin of the thyroid. Normally, it is difficult to distinguish them from the surrounding thyroid tissue. Neither DHT alone (Group 1) nor the chromium salts alone (Group 2 and 3) altered the appearance of the glands but after treatment with $CrCl_2$ or $CrCl_3$ following DHT sensitization (Group 4 and 5), the parathyroids could easily be distinguished from the surrounding reddish-brown thyroid tissue as brilliant white nodules. On defatted specimens stained with the $AgNO_3$ technique, these parathyroids were selectively blackened, thereby suggesting that the calcium was presumably deposited in the form of silver reducing phosphates (Figure 1). Previous observations had shown that in various organs (e.g. pancreas, salivary glands), calcium deposition induced by calciphylaxis is almost invariably limited to the stroma[4]. This proved to be the case also in the present experiments. The parathyroid parenchyme remained free of calcium but the stroma was heavily impregnated with v. Kóssa positive material which tended to spread even into the stroma of the surrounding thyroid (Figure 2).

In groups 4 and 5, varying degrees of connective tissue calcification were also noted within the salivary and Brunner's glands, pancreas, renal cortex, diaphragma and pulmonary septa. The calcification was most intense and most selectively limited to the parathyroids in group 5. However, this fact is no proof of a fundamental difference in the action of the two chromium salts since $CrCl_3$ makes a perfect solution, while $CrCl_2$ forms a poorly tolerated suspension at the dose level used and hence could not be given at the same dose level as the $CrCl_3$.

Résumé. Une calcification des glandes parathyroïdes a été réalisée chez le rat par sensibilisation avec une dose orale unique de dihydrotachystérol suivie, le lendemain, d'une seule injection intraveineuse de $CrCl_2$ ou $CrCl_3$.

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Free Radicals in Animal Tissues

The recent work of Commoner, Lippincott, and Passoneau[1], on free radicals associated with enzyme systems, and Gordy, Ard, and Shields[2] on irradiation of compounds of biochemical significance, represents two approaches to the analysis of free radicals in biological materials using electron spin resonance techniques.

In order to correlate free radical concentrations with the metabolic activity of tissues under different conditions, we have examined the free radical concentration of various whole tissues. As lyophilization has been shown to cause the production of unpaired electrons[3], liquid nitrogen temperatures were used to trap and stabilize free radicals in tissue samples. The tissues were thus frozen but kept hydrated.

Fresh tissues were removed as quickly as possible from freshly killed Norway Rats, and packed into silica glass tubes with an internal diameter of 4 mm, and immediately cooled to 77 K. Absorption of microwave power was analysed at a carrier wave frequency of 9000 Mc/s and a magnetic field of 3000 Gs. The concentration of free radicals was determined by comparison with the absorption curves obtained from a standard carbon sample. Figure 1 shows the pattern of signals obtained from heart,

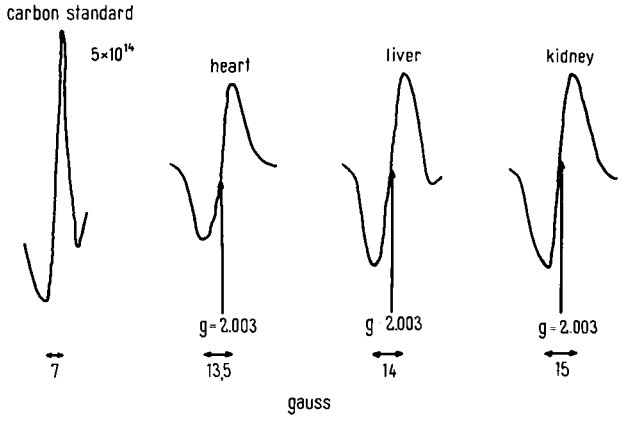

Fig. 1. The signals obtained from a carbon standard (5.1×10^{14}), rat heart muscle; rat liver, and rat kidney.

[1] B. Commoner, B. B. Lippincott, and J. V. Passoneau, Proc. Nat. Acad. Sci. *44*, 1099 (1958).

[2] W. Gordy, W. B. Ard, and H. Shields, Proc. Nat. Acad. Sci. *41*, 983 (1955).

[3] F. K. Truby and J. W. Goldzeiher, Nature *182*, 1371 (1958).