L'isoniazide interfère avec le fonctionnement de différentes enzymes. Elle inhibe la diphosphopyridine nucléotidase chez l'oursin[5]. Elle déprime l'activité des enzymes fonctionnant avec le phosphate de pyridoxal comme coenzyme. Certaines de ces enzymes jouent un rôle important dans le métabolisme des protéines. Nous n'avons toutefois pas observé d'effets végétalisants chez les œufs traités par différents inhibiteurs de la diphosphopyridine nucléotidase et des enzymes à phosphate de pyridoxal. HULTIN[6] a montré récemment que le chloramphénicol, à concentration élevée, inhibe l'incorporation de la valine dans les protéines de l'œuf d'oursin et empêche l'activation des ribosomes et la formation des polyribosomes nécessaires aux synthèses protéiques. Le chloramphénicol partage d'ailleurs ces propriétés avec le dinitrophénol et le cyanure, deux agents qui se sont montrés, dans certaines conditions, capables d'exercer une influence végétalisante sur l'œuf d'oursin[7,8]. Selon des recherches effectuées sur différents organismes, le chloramphénicol interférerait avec la fixation de l'acide ribonucléique messager sur les ribosomes[9]. Les effets comparables exercés sur la segmentation et la détermination embryonnaire par le chloramphénicol et l'isoniazide suggèrent que cette dernière substance interfère probablement avec la synthèse des protéines par un mécanisme analogue à celui du chloramphénicol. Nous signalerons pour terminer, les très intéressantes recherches de LUBIN[10]. Cet auteur a montré que les ions potassium sont nécessaires à l'établissement des synthèses protéiques. Les ions lithium sont capables d'entrer en compétition avec les ions potassium et d'empêcher son action initiatrice sur les synthèses protéiques. Or, chez l'oursin, les ions potassium protègent les œufs contre les effets des ions lithium[11,12]. Ces études ouvrent une voie d'approche intéressante pour l'étude du mode d'action des ions lithium chez l'oursin. L'ensemble de ces données indique que les synthèses protéiques dont l'œuf est le siège pendant la période de détermination embryonnaire, c'est à dire jusqu'au stade blastula-mésenchyme, jouent un rôle essentiel dans le processus de la détermination embryonnaire. Les synthèses protéiques liées à la détermination des structures ectodermiques seraient plus sensibles aux effets des agents végétalisants que les synthèses protéiques responsables de la détermination des structures entomésodermiques.

Summary. Isonicotinic acid hydrazide (isoniazid) causes vegetalization of whole larvae of the sea urchin *Paracentrotus lividus*. The effects of isoniazid are compared with those of chloramphenicol and lithium ions. The protein synthesis during the phase of reversible determination, i.e. to the late blastula stage, appears to be of paramount importance in the differentiation of larvae. It is suggested that the protein synthesis connected with the determination of ectodermal structures is more sensitive to the action of vegetalizing agents than the protein synthesis connected with the determination of entomesodermal structures.

R. LALLIER

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The Effect of Various Diuretic Agents on Renal Electrolyte and Urea Concentration Gradients in Rats

In 1951 it was established by WIRZ, HARGITAY, and KUHN[1] that a tissue fluid osmolarity gradient exists from the renal cortex towards the tip of the papilla. Very little is known concerning how this osmolarity gradient is changed by various diuretic agents. In this preliminary report small samples of tissue from the tip of the papilla, inner medulla, outer medulla, and renal cortex after administration of various diuretic agents in therapeutic doses at the moment of maximal urine flow were analysed for sodium, potassium, and urea and the concentrations per 1 l of tissue water compared with the values in urine samples obtained just before sacrificing the animals.

The urine flow 1–2 h after intravenous injection of Aminophylline (12 mg/kg) was 2 times, and natriuresis 5 times higher than in the control group; nevertheless, the concentration of sodium, potassium and urea in all renal tissue samples did not differ significantly from control values (Figure A). If, however, the rats were sacrificed only 10–15 min after Aminophylline injection, a decrease in papillary sodium concentration was observed. After Meralluride or Salyrgan administration (2–4 mg Hg/kg) there were no changes in the concentration of sodium and urea in any tissue sample. On the contrary, a decrease in potassium concentration in the cortex and papilla was always found (Figure B). Figure C shows the changes in sodium gradient after acetazolamide (2 mg/kg), chlorothiazide (2–6 mg/kg), and hydrochlorothiazide (3 mg/kg) administration. Their effect on the urea concentration gradient was very similar. The concentration of potassium in the cortex was decreased by all three sulphonamides. Furosemid (Lasix, 20 mg/kg i.v.), however, caused a total disappearance of sodium and urea concentration gradients without any effect on the potassium concentration.

The acceleration of tubular urine flow in Henle's loops after infusion of hypertonic mannitol solution diminishes or abolishes the sodium concentration gradients, so-called 'washout effect', as shown by MALVIN and WILDE[2]. Diuretics which inhibit the reabsorption of electrolytes in the proximal tubule, could work via this 'washout'

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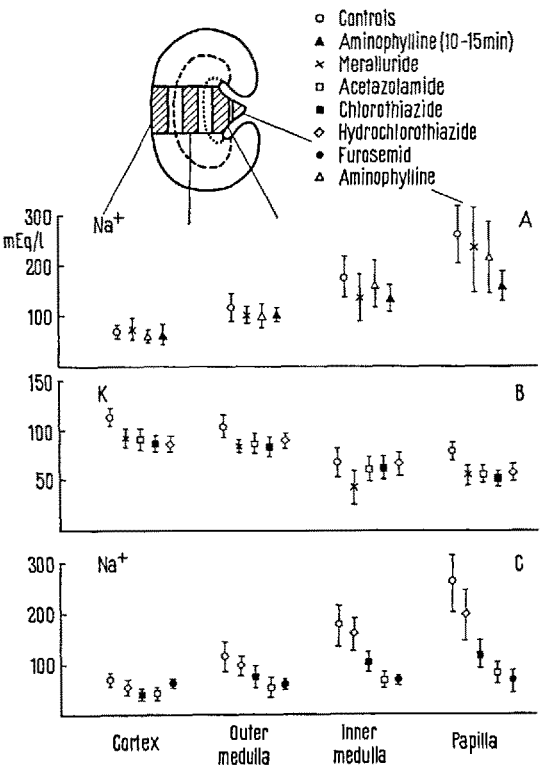
mechanism. The fact that there was no effect on concentration gradients after Aminophylline (1–2 h after administration) and after organic mercury injection need not be interpreted as a distal effect of these diuretic agents; it is more probable that the increase in flow through the loops of Henle was not sufficiently high to cause this 'washout effect', as the increase in urine flow in anaesthetized rats was only twice as high as in the control group. On the contrary, the decrease of sodium concentration gradient in rats sacrificed soon (10–15 min) after Aminophylline injection could be mediated via the increased blood flow through the vasa recta in the renal medulla, because purine diuretics shortly after injection cause a renal hyperaemia (SMITH[3]).



Sodium and potassium concentration gradients in rat kidneys. A, sodium gradients in control rats and 1–2 h or 10–15 min after administration of Aminophylline and Meralluride. B, potassium gradients in control rats and after Meralluride, acetazolamide, chlorothiazide and hydrochlorothiazide administration. C, sodium gradients in control rats and after acetazolamide, chlorothiazide, hydrochlorothiazide, and Furosemid (Lasix). The values are expressed in milliequivalents per 1 l of tissue water. Each point represents the mean value of 10 rats together with the standard deviation.

The efficacy of sulfonamides on the sodium concentration gradient decreases in the following order: acetazolamide, chlorothiazide, hydrochlorothiazide; nevertheless, their diuretic effect was in all experiments nearly the same and high diuretic potency of hydrochlorothiazide unaccompanied by any change in the sodium gradient is in good agreement with the results of BAER et al.[4]. These substances have the same order of efficacy on carboanhydrase inhibition in vitro; any correlation between this fact and our results could be difficult to evaluate. It is possible that each of these three substances influences different parts of the nephron: acetazolamide could work in proximal parts of the nephron while the thiazides could act in more distal parts. The complete disappearance of concentration gradients after Furosemid administration is not surprising, as its proximal effect is unquestioned (DEETJEN[5], VORBURGER[6]) and its explanation by the 'washout effect' seems therefore very probable.

In these experiments neither the osmolarity of tissue fluid nor of urine was directly measured. However, calculation of the 'osmolarity' according to the formula $C_{osm} = 2(C_{Na} + C_K) + C_{urea}$, where C denotes molarity, showed very good agreement between the urine 'osmolarity' and 'osmolarity' of tissue fluid on the tip of the papilla in all experiments.

Zusammenfassung. Die Konzentrationsgradienten von Na^+ und Harnstoff im Rattennierengewebe werden durch intravenöse Applikation von Merallurid, Salyrgan und Hydrochlorothiazid nicht beeinflusst. Die Änderung des Na-Gradienten nach Aminophyllin hängt von der Injektionszeit ab. Acetazolamid-, Chlorothiazid- und Furosemid-Injektion führt jedoch zur Senkung oder zum Verschwinden eines Na-Gradienten. Die Kaliumkonzentration in der Rinde und Papilla wird durch Hg- und Sulfonamid-Diuretica erniedrigt.

J. HELLER, V. ŠKRHOVÁ, and J. VOSTÁL

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Renal Lesions Induced by the Simultaneous Administration of Angiotensin and Hexadimethrine Bromide

During studies on the pathogenesis of the lesions caused by the antiheparin agent hexadimethrine bromide[1,2], we observed renal infarction in some rats which had been given angiotensin followed by hexadimethrine bromide. Further investigations of this subject are described in the present paper.

Methods. A total of 76 female rats of the Wistar strain were used. Fourteen of the animals were given an intraperitoneal injection of 0.5 mg angiotensin (Hypertensin

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