

tion) and the developing pattern of enzyme activities and endocrine functions are all responsible for the pronounced difference between adult and infant rats.

Finally, it is worth pointing out that cortisone administration to infant rats appears always to speed up development (e.g. pancreatic and intestinal functions, Rokos et al.⁶) while adrenalectomy slows down development (e.g. β -galactosidase activity in the gut, Koldovský et al.⁷), maintaining high enzyme activity if such is the usual state in the suckling period, or low enzyme activity if that is the normal condition in infancy. A similar phenomenon has been shown in this paper.

Zusammenfassung. Hoher Acetoacetatanteil in Leber junger Ratten wird durch Kortikosteronverabreichung *in vivo* am 10. Tag nach Geburt erniedrigt. Bei erwachsenen

Ratten kein Hormoneinfluss. Adrenalektomie (14. Tag nach Geburt) führt zu hoher Produktion (19. Tag). Nur bei erwachsenen, nicht hungernden Ratten ist dies weniger ausgeprägt.

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⁶ J. ROKOS, P. HAHN, O. KOLDOVSKÝ, and P. PROCHÁZKA, *Physiol. Bohemoslov.* 12, 213 (1963).

Effect of Sulphates on the Intestinal Absorption of Sr-85 in Rats

In our previous experiments, barium sulphate was shown to be an effective means for diminishing the absorption of radioactive strontium from the intestine shortly after exposure in rats and man¹⁻³. In further work, the effect of various sulphates and their combinations on the metabolism of orally administered Sr-85 in rats was compared. Several factors which might influence the effectiveness of the treatment were also studied. The details of this work will be published elsewhere.

When different sulphates were given orally in equimolar amounts 10 min after Sr-85 administration, 40 to 60% less of Sr-85 was retained in the femurs of rats receiving sodium, magnesium, calcium and barium sulphates, whereas strontium sulphate reduced the skeletal retention of Sr-85 only by 30% compared with controls.

The effect of individual sulphates and their combinations was compared under the same experimental conditions (Table). There was a significant difference in the retention of Sr-85 between the groups receiving calcium and barium sulphates only, or calcium sulphate with sodium and magnesium sulphates, and those receiving barium and sodium or magnesium sulphates. The addition of excess SO_4^{2-} ions markedly increased the effectiveness

of barium sulphate, so that nearly 80% less of Sr-85 was retained in the bones of treated animals in comparison with controls.

Several barium sulphate preparations showed different affinity to Sr-85 *in vitro* as well as *in vivo*. However, when excess SO_4^{2-} ions were added, the proportion of adsorbed Sr-85 increased substantially and all preparations exerted similar effect.

When up to 100 μMoles of carrier strontium were added either to Sr-85 solution or to the suspension of sulphates, only slight differences in the effectiveness of sodium and barium sulphates were observed. The sulphates seem to be equally effective in younger and in older animals.

Barium sulphate alone, given to starved or fed animals, decreased the retention of Sr-85 only in starved rats, while in the fed group it was ineffective. However, following the administration of barium sulphate combined with sodium sulphate, the skeletal retention of Sr-85 was reduced by 90 and 50% in the starved and fed animals respectively.

In other experiments, the effectiveness of various amounts of sulphates given orally in a single dose 10 min after Sr-85 contamination was investigated. The Figure presents such data on a semi-logarithmic plot. The relative decrease of skeletal Sr-85 with the increasing dose of barium sulphate follows a straight line through the whole dose range investigated. Similar dose dependence can be demonstrated in the case of sodium sulphate or its combinations with barium sulphate, but only when increasing the doses up to a certain level. Best results were obtained when 1.6 mMoles of barium and sodium sulphates were given, i.e. 93 and 94% reduction in the skeletal content of Sr-85 in treated rats as compared with controls.

When treatment was delayed, its effect decreased with time. Even the best acting agents, given 80 min after Sr-85 administration to starved rats, lost their effectiveness. However, one single dose given early after contamination was found to be sufficient to decrease substan-

Retention of Sr-85 2 days after oral administration in rats treated with various sulphates and their combinations

No. of rats	Agents ^a	% of dose in femur ^b
12	Controls	1.12 \pm 0.34
6	CaSO ₄	0.79 \pm 0.32
6	BaSO ₄	0.53 \pm 0.16
6	CaSO ₄ + Na ₂ SO ₄	0.47 \pm 0.17
6	CaSO ₄ + MgSO ₄	0.53 \pm 0.18
6	BaSO ₄ + Na ₂ SO ₄	0.25 \pm 0.13
6	BaSO ₄ + MgSO ₄	0.27 \pm 0.18

^a 0.8 mMol of each sulphate was given orally 10 min after Sr-85 administration to fasted animals. ^b Mean \pm standard error of the mean multiplied by t - value for 95% confidence level.

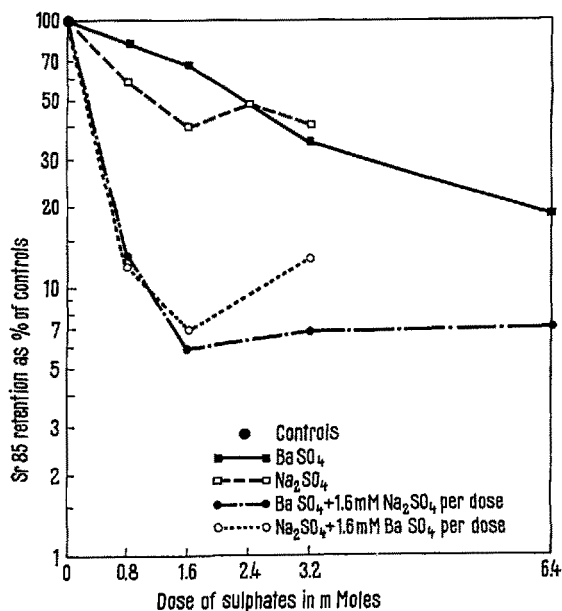
¹ V. VOLFF, *Nature* 184, 1401 (1959).

² V. VOLFF, *Phys. Med. Biol.* 6, 287 (1961).

³ V. VOLFF, in *Diagnosis and Treatment of Radioactive Poisoning* (International Atomic Energy Agency, Vienna 1963), p. 131.

tially the whole body burden as well as the skeletal content of Sr-85 in treated animals.

It is probable that sodium and magnesium sulphates reduce the absorption of stable strontium from the gastro-intestinal tract, presumably by the formation of



Effect of increasing doses of sodium and barium sulphates and their combinations on skeletal retention 2 days after oral Sr-85 administration in rats. Each point represents an average of values from 5-6 animals. Total skeletal content was calculated by multiplying the amount of Sr-85 in one femur by a factor of twenty.

insoluble strontium salts⁴. On the other hand, with carrier-free Sr-85 the observed result may be due to an effect of absorbed sulphate on urinary excretion of strontium, or due to impaired intestinal absorption of the strontium sulphate complex⁵.

In the case of barium sulphate, strontium is bound mainly by adsorption. *In vitro* this occurs to a larger extent when SO₄²⁻ ions are present in excess, *in vivo* one should remember the physiological action of soluble sulphates, too, which hasten the passage through the intestine and act as saline diuretics.

In the experiments described above, the effect of barium sulphate with sodium or magnesium sulphates on the intestinal absorption of Sr-85 was shown to be substantially better than that of the individual sulphates. In view of the fact that the agents tested are non-toxic and can be readily used in man, the experimental results reported may be of practical significance, especially when rendering first aid after accidental radiostrontium ingestion.

Zusammenfassung. Unter diversen Sulfaten zeigte die Kombination Barium-Natriumsulfat bei frühzeitiger Applikation stärkste Reduktion des Radiostrontiumgehalts im Skelett (über 90%).

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⁴ N. S. MACDONALD, R. E. NUSBAUM, F. EZMIRLIAN, R. C. BARBERA, G. V. ALEXANDER, P. SPAIN, and D. E. ROUNDS, *J. Pharmacol. exp. Therap.* 104, 348 (1952).

⁵ M. WALSER, J. W. PAYNE, and A. A. BROWDER, *J. clin. Invest.* 40, 234 (1961).

Paralysies révélatrices de la leucémie de Gross chez le rat

L'atteinte du système nerveux est relativement rare au cours des leucémies murines virales. Elle a cependant été signalée par divers auteurs, récemment en particulier par STANSLY^{1,2}. Nous avons observé un grand nombre de paralysies dans notre souche de rats Wistar CF inoculés à la naissance avec le virus de Gross.

Le virus provient initialement du laboratoire du Dr Gross³. Il a été entretenu régulièrement dans notre laboratoire par passage sur rat Wistar CF. Les rats sont inoculés, par voie intrapéritonéale, dans les 24 h suivant la naissance, avec 0,2 ml d'un extrait acellulaire préparé selon la méthode de Moloney, à partir du sang ou de la rate de rats leucémiques.

Parmi 120 rats, inoculés avec 8 extraits différents provenant de 4 générations successives de rats inoculés avec des passages acellulaires, et ayant survécu jusqu'au sevrage (30^e jour), 104 (86%) ont été atteints de leucémie. Dans 47 cas (45%), la maladie a comporté une atteinte du système nerveux central révélée par une paralysie flasque des pattes postérieures. Des paralysies ont été observées dans les lots d'animaux inoculés avec chacun des 8 extraits acellulaires utilisés. Le dernier extrait a été inoculé à 14 animaux, 13 ont été atteints de paralysies.

Les animaux témoins non inoculés, observés durant la même période, n'ont jamais présenté de paralysies.

A l'autopsie, l'examen macroscopique révèle dans la grande majorité des cas une leucémie généralisée atteignant le thymus, la rate et les ganglions. L'histologie confirme alors l'envahissement diffus de ces organes par des cellules indifférenciées ou par des lymphoblastes. En outre, les mêmes cellules infiltrent les poumons, les reins et la moelle osseuse. Les frottis de sang révèlent souvent une hyperleucocytose (en général supérieure à 30 000/mm³) avec passage dans le sang de nombreuses cellules leucémiques.

Par contre, dans 2 cas, l'examen macroscopique et histologique des organes hématopoïétiques n'a révélé aucun signe de leucémie, l'infiltration leucémique étant strictement limitée à la région lombo-vertébrale.

Quel que soit le degré d'envahissement leucémique, l'explication des paralysies est fournie aisément, dans

¹ P. G. STANSLY et H. D. SOULE, *J. Nat. Cancer Inst.* 29, 1083 (1962).

² P. G. STANSLY et H. D. SOULE, *Proc. Am. Assoc. Cancer Res.* 5, 60 (1964).

³ Nous remercions vivement le Dr GROSS de nous avoir confié le virus de Gross adapté au rat.