	Without lead	16 mm Pb	Without lead
No. 1	—	1 living, 6 dead sterile	8 living
No. 2	4 living	5 dead	8 living
No. 3	sterile	sterile	7 living
		9 dead	(removed from lead for delivery)
No. 4	—	4 dead	5 living
No. 5	5 living	6 dead (under Pb only for the delivery)	

the existence of a lethal effect, resulting most probably from the influence of cosmic ray showers upon the embryos. However, even these unambiguous results obtained in every single case investigated are not yet convincing. It seemed, therefore, necessary to investigate this lethal effect upon a greater number of animals, thus enabling a statistical check.

Experiments on white mice. The experiments were performed in the wooden tower laboratory of the institute. The animals were kept in a glass box of 60×130 cm basis and 40 cm height. Electric heating maintained a temperature of 25–30 °C within this box. The fresh air entered near the bottom of the box and could escape under the glass cover. The animals were installed immediately below the glass cover in 14 seperate cages with aluminium walls, asbestos base, and covered with a wire net. Lead of 16 mm thickness was placed externally upon the glass box at a height of 10 cm above the animals.

First set: Here our aim was only to prove anew the effect of the showers. All the animals were kept under lead. 23 animals delivered in the course of three months 139 living, and 14 dead young; from these 139 animals 99 perished within a week after their birth. The mean loss was 82 ± 7 p.c.

The computation of the error was performed by reckoning for every animal seperately the ratio of the still-births plus dead young to the sum of all the animals within the litter. The standard deviation from the mean value of the 23 cases were then computed for each individual case, and with the method of the least squares we thus determined the mean error of the mean value.

Second set: The lead was now removed from one half of the box, thus only about half of the animals were kept under lead, the other half, in quite similar conditions and upon identical diet, were kept without lead, but they were covered with a slate layer instead of lead in order to secure identical illumination. Within three months 21 animals kept under lead delivered 98 living and 4 dead offspring, besides two cases in which we were not able to count the number of the dead young. Out of the 98 living young 64 perished within a week after their birth, the mean loss being

$$71 \pm 6 \text{ p.c.}$$

This figure is in good agreement with that of the first set.

Conversely, out of the animals kept without lead, 16 delivered 93 living and 1 dead young in the course of the same three months. 23 of the 93 died within a week after their birth, the mean loss was:

$$22 \pm 9 \text{ p.c.}$$

The loss difference:

$$49 \pm 11 \text{ p.c.}$$

represents the lethal effect due to the lead layer. The effect can be considered as real, since it is greater than four times its mean error. It is worthy of mention that, whereas all the rabbits begot under lead dead offspring, mice delivered mostly living progeny, which, however, perished within a short time after their birth. The birth rate was slightly higher without lead than with lead.

Since the intensity of cosmic ray corpuscules is practically the same with or without lead, the results, seem to indicate that the biologic effect must be attributed to the showers. (16 mm of lead is the most efficient thickness for generating cascade showers.) The difference in the biologic effect of the shower radiation compared to that of radioactive sources might be due to the following causes:

(1) From radio-active sources the heavily ionizing α- and β-rays are not able to penetrate into deeper layers of the body, and γ-rays or X-rays produce only about 100 ions per cm path in the body, hence, even when strong sources are used, ionization within a cell will not be very important. Conversely, a cosmic ray particle can penetrate through the whole body and produces there about 100,000 ions per cm of its path.

(2) The effect of radio-active radiation consists merely in ionization, a process which is reversible in consequence of recombination, whereas on account of their tremendous energies the cosmic ray particles can initiate irreversible nuclear transformations within a cell.

(3) In the core of a shower the particle density may be so great that a single cell is hit simultaneously by more than one ray.

It would be of interest to investigate whether the effect remains the same for showers created in iron instead of in lead; in which case it would be possible through magnetization of the iron to spread out the particles in the core of the shower over a wider area and consequently to examine the influence mentioned in point 3 separately. We should like to emphasize the importance of investigating with a sufficiently large number of individuals whether a permanent morbid change does occur in the females or not, and further whether the offspring born under lead are not more resistent against cosmic ray showes, i.e. whether a certain adaptation does not take place. Experiments with this purpose are now in progress.

Acknowledgements should be expressed to the head and owner of the Angora rabbit farm, Mrs. E. Fabinyi, for much advice and extreme thoughtfulness, which were a great help in our Angora rabbit experiments.

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Institute for Experimental Physics, University of Budapest, July 2, 1947.

Zusammenfassung

Angorakaninchen und weiße Mäuse wurden unter einer Bleischicht gezüchtet, deren Dicke (16 mm) die günstigste für die Auslösung von kosmischen Kaskadenschauern ist. Die Versuche ergaben einen Überschuß der Totgeburten und der Verluste innerhalb der ersten Woche von 49 ± 11 % gegenüber den unter gleichen Bedingungen gehaltenen Kontrolltieren. Eine dauernde Beschädigung der Muttertiere sowie eine sterilisierende Wirkung scheint nicht vorzuliegen.

Urinary Excretion of Water-soluble Vitamins and Phosphorylation

Against the value of test doses applied for the estimation of vitamin deficiencies, the following objection can

be made: after several thiamin or riboflavin test doses have been administered to the organism, the urinary excretion after the test injections does not increase, but changes irregularly. After the vitamin has been given for a long time, the excretion gradually diminishes.

In order to explain this behavior, we had to examine on what the excretion of water-soluble vitamins depends in the healthy, well-supplied organism.

For the present we observed the excretion of riboflavin in normal rats[1]. Riboflavin, as a component of the yellow ferment, is used in the tissues in phosphorized form. In one series of experiments we poisoned the rats with monojodacetic acid in order to paralyze phosphorylation, in another series we gave adenosin triphosphate (Atriphos) in order to increase the phosphorylation rate.

The excretion of riboflavin decreased in the first group of rats and increased in the second group. Thus phosphorylation influences the excretion of administered riboflavin in that it raises the excretion when increased and decreases it when depressed.

Decreased excretion after several injections of riboflavin in the normal organism is probably caused by the decrease and perhaps by the exhaustion of phosphorylation. As regards the exhaustion of the phosphorylation process in case of sugar in the kidney, RUSZNYÁK *et al.*[2] already have given data.

Administration of dextrose to rats decreased the urinary excretion of riboflavin. We observed the same after thiamin. Both materials are phosphorylated when used in the tissues. We suppose that after administration of dextrose or thiamin, the mechanism of phosphorylation was sooner exhausted.

The urinary excretion of riboflavin and thiamin depends first of all on the state of saturation of the organism, while in a normally supplied organism it rather depends on the phosphorylation. The more vitamin undergoes phosphorylation in the body, the more appears in the urine, and the lower is the level of phosphorylation, the smaller is the urinary excretion.

The fate of the not excreted and, according to our experiments, unphosphorylated riboflavin in the organism is quite unexplained. Experiments in which we determine the riboflavin content of several organs and of the whole body of rats after administration of this vitamin are going on.

I. MAGYAR

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Zusammenfassung

In einem genügend mit Vitaminen versorgten Organismus hängt die Ausscheidung der wasserlöslichen Vitamine von der Phosphorylierung ab. Bei Versuchen an Ratten zeigte sich folgendes: Wird die Phosphorylierung durch Monojodessigsäure gehemmt, so wird weniger Riboflavin ausgeschieden. Nach Darreichung von Adenosintriphosphat erscheint dagegen mehr Riboflavin im Harn. Die Verminderung der Ausscheidung nach Dextrose oder Thiamin ist wahrscheinlich darauf zurückzuführen, daß diese Substanzen den Mechanismus der Phosphorylierung in größerem Ausmaß in Anspruch nehmen.

[1] Detailed data in Acta medica Hungarica, in print.

[2] ST. RUSZNYÁK, M. FÖLDI, and G. SZABÓ, Exper. *3*, 420 (1947).

Prévention de l'œdème aigu expérimental du poumon par un antihistaminique de synthèse dérivé de la thiodiphénylamine[1]

L'œdème aigu du poumon est dû à une transsudation brusque de sérosité dans les alvéoles et les tissus interstitiels du poumon à travers les capillaires pulmonaires. Cette sérosité mêlée à l'air remonte vers les voies respiratoires supérieures et, est expectorée sous forme de spume sanguinolente. L'œdème du poumon se distingue des autres œdèmes de l'économie par son apparition soudaine, son évolution rapide et éventuellement sa résolution complète.

Il est aisé de provoquer un œdème aigu du poumon chez le lapin en lui injectant une dose suffisante d'adrénaline par voie intraveineuse[2].

Aussitôt après l'injection d'adrénaline, la pression artérielle monte verticalement à 20–22 cm/Hg et s'y maintient 2 à 3 minutes. Le lapin présente une apnée de 20 à 30 secondes après quoi la respiration redevient régulière. Au bout de 5 à 6 minutes, la pression revient à son niveau initial tout en continuant sa courbe descendante; la respiration devient dyspnéique et cette dyspnée s'aggrave rapidement. L'animal s'affaisse, il est cyanosé, une crise convulsive annonce l'exitus; une écume rosée apparaît aux narines et à la bouche; la pression est voisine de 0 et l'animal meurt, 10 minutes environ après l'injection.

L'autopsie révèle un cœur très dilaté, des poumons énormes, très œdématiés, non collabescent à l'ouverture du thorax. Ils sont couverts sur de grandes surfaces de plages hémorragiques.

A la dose de 0,25 mg/kg d'adrénaline, 60% de nos lapins (17 sur 27) ont présenté ce tableau et ont succombé au plus tard 10 minutes après l'injection. Les autres ont survécu plusieurs heures. Tous ont présenté à l'autopsie des lésions nettes d'œdème pulmonaire.

Or nous avons constaté que l'injection préalable de 20 mg/kg de N-diméthylamino-2-propyl-1-thiodiphénylamine (3277 RP) empêche d'une manière saisissante l'apparition de ce syndrome extrêmement grave dans la totalité de nos essais (portant sur 15 animaux).

Les lapins ayant reçu une injection hypodermiqued e 20 mg/kg de 3277 RP présentent dans les trente minutes qui suivent quelques troubles banaux: légère ataxie ou atonie musculaire. Or, si nous injectons alors la même dose d'adrénaline, 0,25 mg/kg, nous constatons que son effet hypertensif est intégralement conservé. L'apnée habituelle est moins prononcée. Cependant la dyspnée ne se produit pas et les animaux ne manifestent pas de tirage respiratoire ni de cyanose. La pression descend progressivement vers la normale ou un peu au dessous de sa valeur initiale et s'y maintient. L'animal détaché présente quelques troubles ataxiques dus au 3277 RP et se rétablit complètement dans les heures qui suivent.

Les animaux traités par l'antihistaminique montraient une augmentation de volume du cœur comparable aux témoins. Par contre, leurs poumons collabaient normalement et ne présentaient que dans de rares exceptions une légère augmentation de poids. C'est ainsi que le poids moyen des poumons des témoins est de 32 g tandis que celui des poumons des lapins traités est de 13 g, le poids moyen des poumons d'un lapin normal étant de 10 à 12 g environ.

[1] B. N. HALPERN, Arch. int. Pharmacol. Thér. *74*, 314 (1947); J. Allergy *18*, 263, 272 (1947).

[2] HALLION et NEPPER, J. Physiol. Pathol. gén. *13*, 887 (1911).