haben sich mit der Strahlenschutzwirkung des Oxytryptamins und Reserpins beschäftigt.

Wir wollen nicht behaupten, dass in der protektiven Wirkung der auf die Hämopoese – oder isoliert auf die Thrombozytopoese – entfaltete Effekt der UV-Bestrahlung der entscheidende Faktor ist, höchstwahrscheinlich handelt es sich um eine Komplexwirkung. Da aber im Zustandekommen des Bestrahlungssyndroms bzw. des Strahlentodes der geschädigten Hämopoese eine wesentliche Rolle zukommt, ist anzunehmen, dass an der günstigeren Gestaltung der Überlebensverhältnisse bei den UV-behandelten Tieren möglicherweise auch die thrombopoetische Wirkung der UV-Strahlung mitbeteiligt ist.

Um einen näheren Einblick in den Wirkungsmechanismus der UV-Strahlung zu gewinnen, soll einerseits die Wirkung der zu verschiedenen Zeitpunkten angewandten kombinierten Behandlung und andrerseits der Effekt des vor der Röntgenbestrahlung gegebenen – den UV-thrombopoetischen Serumfaktor enthaltenden – Serums auf die Mortalität röntgenbestrahlter Mäuse untersucht werden.

Summary. 300 r whole body X-ray irradiation of mice did not decrease the circulating platelet count, if this dose was preceeded by 24 h of ultraviolet-irradiation. More animals survived the X-ray (500, 550, 600 r) injury, if the irradiation occurred after ultraviolet treatment given 24 and 48 h before. The number of days survived is also increased. The ultraviolet light seems to have some protective effect against injury caused by X-ray.

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Changes of Ultrafiltrable Hydroxyproline in Blood Serum during Development of Carrageenin Granuloma and during Aging of Rats and Guinea-Pigs

Free hydroxyproline (HYPRO) is a constant component of animal tissues as well as of biological liquids[1–6]. Equally peptides containing HYPRO were proved by us to exist in different tissues[7–9]. In this study we present proofs of their presence and changes in serum of rats and guinea-pigs during aging and the development of carrageenin granuloma in the subcutis of guinea-pigs.

Kivirikko and Liesmaa[10] did not find changes of the content of free HYPRO in serum in two age groups of rats, although the growth hormon increased its level in the serum. Houck and Jacob[11] proved that, parallel with the decrease of collagen content in the necrotic area of the skin after croton oil, an increase of serum HYPRO takes place. It would seem, therefore, that HYPRO has its origin in the degraded collagen of skin. This is the reason why we were interested in how free and peptide-HYPRO change in the course of formation and also in the following resorption of collagen in carrageenin granuloma. That is why the substances mentioned were examined simultaneously with the analysis of the serum also in the granulation tissue.

Method. The serum of the animals was deproteinated by high pressure ultrafiltration with Nojax Cellulose Casings Visking Corp. membrane at a temperature of 1–2°C and pressure of 7 atm. for a total time of approximately 17 h. In deproteinated serum, the content of HYPRO was determined before and after the hydrolysis (6 N-HCl, 140°, 3 h). In this way, the content of free and total ultrafiltrable HYPRO[12] was determined. From the difference, we determined the peptidic HYPRO.

The blood serum for the particular determinations mentioned was pooled from blood of 2–3 guinea-pigs or rats.

The granulation tissue of the subcutis of adult guinea-pigs (350–550 g) was analysed on certain days after the subcutaneous injection of carrageenin for the concentration of deoxyribonucleic acid, free HYPRO, HYPRO bound in peptides and collagen proteins[7,9].

Results. The content of ultrafiltrable HYPRO in the serum of rats and guinea-pigs decreases during aging (Table). There occurs a decrease of free HYPRO, as well as of peptides with HYPRO which we did not find in the serum of adult animals at all or only in traces. The average concentration of ultrafiltrable HYPRO in adult animals is 4 μg/ml serum, in old animals 1–2 μg/ml serum.

The changes of serum ultrafiltrable HYPRO during development of granuloma in adult guinea-pigs are shown in the Figure where, for the sake of comparison with changes in the same biochemical indices, the changes in the granuloma are indicated at the upper part of the graph. It is evident that the pronounced increase of ultrafiltrable HYPRO is caused mainly by the presence of peptides with HYPRO in the serum. The changes in the serum go chronologically parallel with the changes of the substances studied in the granulation tissue, e.g. the maximal changes occur between the 6th and 10th day after the application of carrageenin. The value of the compounds studied in the serum are statistically significantly increased on the 6th to 10th day ($P < 0.01$) compared with the values from the 2nd to 3rd and the 16th to

Changes in serum ultrafiltrable hydroxyproline – free and conjugated – in rats and guinea-pigs of different age

Age	Hydroxyproline μg/ml free	combined	total
Rats			
1 month	10.2	2.4	12.6
2 months	7.5	1.5	9.0
12 months	4.2	0	4.2
18 months	2.0	0	2.0
Guinea-pigs			
200–300 g	4.6	0.8	5.4 ± 0.7
350–500 g[a]	4.0	0	4.0
700–900 g	1.5	0	1.5

[a] Used as controls for carrageenin granuloma – see Figure.

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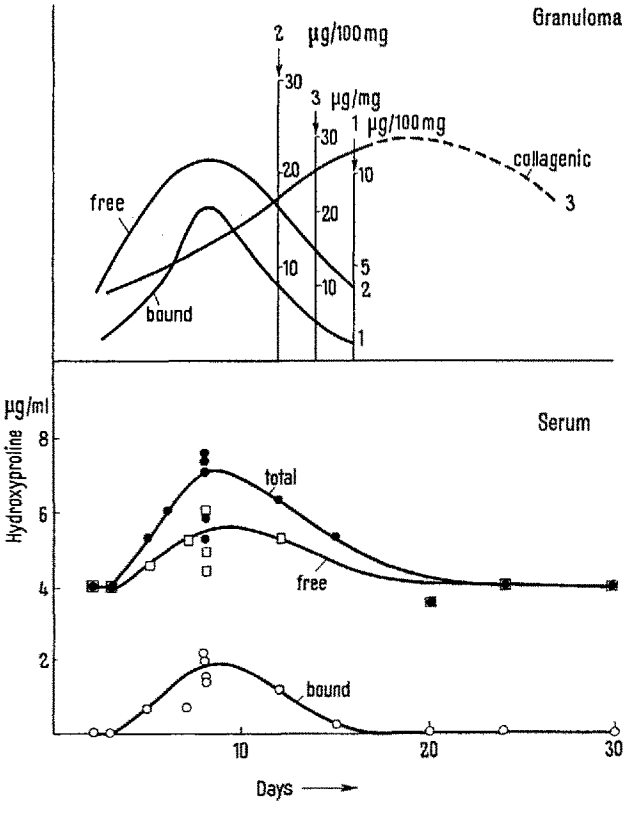
40th day. At the time of the resorption of collagen structure in granuloma, the level of the compounds studied in serum was within the bounds of the norm.

Discussion. The age changes in ultrafiltrable HYPRO in serum are, according to our experience, parallel with the decrease of the level of these substances in different organs (not yet published)[13].

The HYPRO containing peptides which we did not find in the serum of adult animals increased again during the development of carrageenin granuloma. The increase of serum HYPRO compounds could theoretically be expected in three periods of the development of fibrotic granuloma: (1) at the time of the infiltration of the subcutis of the polymorphonuclear leucocytes when an increased proteolytic activity occurs, (2) at the time of collagen formation or its precursors, (3) at the time of the degradation of collagen at the phase of the resorption of the granuloma. Our results favour the second possibility. Although the morphologically provable accumulation of polymorphonuclears precedes the increase of ultrafiltrable HYPRO in granuloma tissue, and also the serum and peptidic HYPRO correlate rather with the accumulation of fibroblasts, our results are not a direct proof that peptides are precursors of collagen. According to HOUCK and JACOB[14], who found an increase of serum HYPRO during inflammation of the skin induced by croton oil, we expected a second peak of ultrafiltrable serum HYPRO at the phase of the resorption of collagen. Our negative finding could perhaps be explained by the different mechanism of destruction of collagen during croton inflammation, perhaps in the carrageenin granuloma.

As the increase of the serum ultrafiltrable HYPRO occurs in the early stage of the fibroplastic inflammation, we suppose that the study of these substances could serve for an early diagnosis of fibrotic diseases (precirrhosis, presilicosis)[15].



Time correlation of serum and granuloma changes in ultrafiltrable—free and conjugated—and collagen hydroxyproline. The upper part describes schematically tissue changes, for details see [7–9].

Zusammenfassung. Die Konzentration des ultrafiltrierbaren Oxyprolins im Serum der Ratten und Meerschweinchen senkt sich während des Alterns. Bei erwachsenen Tieren ist peptidisch gebundenes ultrafiltrierbares Oxyprolin nicht mehr nachweisbar. Während des 6.–10. Tages der Entwicklung des Carrageeningranuloms bei Meerschweinchen steigt die Konzentration des freien und peptidisch gebundenen Oxyprolins im Serum gleichlaufend mit der Erhöhung dieser Stoffe im Bindegewebe des Granuloms.

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[13] The discrepancy of our results and of KIVIRIKKO and LIESMAA[10] could be explained by analysing younger and older rats in our experiments where the decreasing trend is evident (Table).

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Induced Increase of Meprobamate Metabolism in Rats Pretreated with Phenobarbital or Phenaglycodol in Relation to Age

In a previous work a remarkable increase of meprobamate metabolism in rats pretreated with phenobarbital or phenaglycodol was reported[1]. The mechanism which produces an increase of meprobamate metabolism is not yet clear but some sort of enzymatic adaptation of the liver of the pretreated animals was supposed[2–4]. In the work reported here, a possible difference in the induction capacity of increased metabolism of meprobamate between different ages of rats was examined.

Rats of Sprague-Dawley strain, weighing 300 g and 180 days old (adult rats), weighing 160 g and 60 days old (young rats), weighing 70 g and 32 days old (immature rats) were used. The determination of meprobamate concentrations in serum and brain was carried out according to the method of HOFFMAN and LUDWIG[5]. Phenobarbital and phenaglycodol were injected intraperitoneally in doses of 80–100 mg/kg, 48 h before the injection of meprobamate (150 mg/kg i.p.).

Figure and Table show that metabolism of meprobamate in phenobarbital or phenaglycodol pretreated rats markedly increased, and, on the other hand, younger rats can metabolize meprobamate more rapidly than older rats. For example: *in vivo* metabolisms of meprobamate by 100 g of body weight for 2 h after the injection were as follows: 3.5 mg for adult rats, 5.3 mg for young rats and

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