The number of erythrocytes and leucocytes per mm^3, as well as the percentage ratio of leucocytes in smears stained by Pappenheims' method, were established. In serological investigations, the presence of hemagglutinins in the serum of parabiotic animals was detected by the agglutination test, and incomplete antibodies by Coombs' method.

In the previous experiments, KONIECZNA-MARCZYŃSKA and SKOWRON-CENDRZAK[7] demonstrated that in 60% of cases a hemolytic anemia occurs in homoioparabiosis between unrelated white mice, causing the anemic partner to die within two weeks. In mouse-hamster heteroparabiosis, in 88% of cases severe hemolytic anemia was observed only in mice. The mean survival of mice in heteroparabiosis was 6 days. A few heteroparabiotic pairs whose mice were not affected by anemia lived for 26 days. In the majority of cases with strong hemolytic anemia in mice, hemagglutinins and incomplete antibodies were detected in the serum of hamsters. The detected antibodies had species specificity and produced agglutinations with the erythrocytes of parabiotic and non-parabiotic mice coming from different strains. In parabiotic hamsters, there were no changes in the quantities of erythrocytes in successively examined samples.

SKOWRON-CENDRZAK and KONIECZNA-MARCZYŃSKA[8] stated leucopenia in homoioparabiosis of unrelated mice in both partners. In heteroparabiosis, a fall in the leucocyte count was observed only in hamsters on 4th day of parabiosis. This fall was statistically important and the value t according to the Students' test was 2.306 with the probability of error $p = 0{\cdot}05$. Leucopenia during heteroparabiosis may be explained on a serological basis. Probably hamsters have no great capacity for producing leucoagglutinins against the leucocytes of the mice. Percentage changes of leucocytes were noted only in mice during heteroparabiosis. There was a quantitative increase in neutrophil granulocytes equal to that in homoioparabiosis.

In 32 heteroparabiotic pairs of the hamster-mouse type, full thickness hamster skin grafts[9] measuring 3×3 cm were placed on the backs of the mice at different periods before parabiosis. It was shown that a preliminary immunisation of mice by hamster skin grafts in many cases protects them against hemolytic anemia. Only 18% of mice in heteroparabiosis developed a hemolytic anemia after preimmunisation. The mean survival period for immunised mice in heteroparabiosis was 7 days. A correlation was observed between the length of the period of preliminary immunisation before operation and the appearence of hemolytic anemia conditioning the survival time of mice in heteroparabiosis. The joining of mice in heteroparabiosis 2 or 4 days after transplantation of hamster skin led, in many cases, to hemolytic anemia or the death of the mice within 4 days of parabiosis. These data are in accordance with the results obtained in experiments on heteroparabiosis without preliminary immunisation. In heteroparabiosis carried out 7 days after skin grafting, the mice in many cases died within 3 days after operation. This fact may have been due to the coincidence of the strongest reaction in mice to hamster skin grafts and the parabiotic intoxication. In mice joined in heteroparabiosis 10 and 12 days after grafting the hamster skin, no symptoms of hemolytic anemia were observed; on the contrary, they survived longer in heteroparabiosis, from 10 to 15 days. Acquired transplantation immunity to hamster skin grafts in mice apparently induces a weaker immunological reaction to parabiotic intoxication on the part of the hamster partner.

Serum hemagglutinins in the hamster partner were observed only in one case with strong concurrent hemolytic anemia in the mouse partner.

In conclusion, it would appear that parabiotic intoxication and death of the mouse partners occur in spite of preliminary immunisation which frequently protects mice from hemolytic anemia. However, the protection thus achieved is only transient and the survival of the mouse partner is not much longer than that observed in heteroparabiosis without preliminary immunisation.

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Zusammenfassung

In der Heteroparabiose Maus-Hamster kommt eine parabiotische Intoxikation und hämolytische Anämie bei der Maus in 88% der Fälle zustande. Eine Immunisation der Maus mit Hamsterhauttransplantaten, die 10–12 Tage vor der Parabiose unternommen wird, kann die Erscheinung der Anämie bis auf 18% der Fälle herabsetzen. In Heteroparabiosen, die mit starker hämolytischer Anämie bei der Maus verliefen, wurde stets die Anwesenheit der Hämagglutinine und unvollständiger Antikörper im Serum des parabiotischen Hamsters festgestellt.

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The Influence of Thenalidine[1] on Reserpine- and Serotonin-Induced Gastric Ulcers in Rats

It was shown earlier that large doses of reserpine, administered parenterally, produce gastric hemorrhagic erosions and ulcers in rats[2–4]. The exact mechanism of this effect is not yet clear, although some authors have suggested a certain role of serotonin and/or histamine in it[5,6]. The administration of serotonin(5-hydroxytryptamine) in large doses produces a similar effect on the rat's gastric mucosa[7,8].

It was reported elsewhere that the antihistamine thenalidine(1-methyl-4-amino-N'-phenyl-N'-(2'-thenyl)-piperidine, 'Sandosten') exhibits an antiserotonin action on the isolated rat's uterus[9], the tidal air of spinal cats[10], and on the rat's paws[11].

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The aim of this work was to find out if thenalidine can influence the gastric ulcer formation, induced by reserpine and serotonin.

Methods. Fifty albino rats, 180–220 g of body weight, were divided in 4 groups (Table). The group I was treated as a control with reserpine (Serpasil) 2 mg/kg daily i. p. throughout 3 days. The group II was also treated with reserpine in the same doses and at the same way, but 5 min before the administration of reserpine, the animals were injected with thenalidine 2 mg/kg i. p. On the fourth day, the animals of both groups were killed, their stomachs excised and examined.

30 mg/kg of serotonin(5-hydroxytryptamine creatinine sulfate) were given twice per day to the group III. The group IV was treated with the same doses of serotonin and in the same way, with a pretreatment with thenalidine 2 mg/kg s. c. 5 min before the administration of serotonin. After 24 h, the animals were killed, their stomachs excised and examined.

Results. Results are presented in the table with the following data: percentage, severity, and number of ulcers per rat, expressed in terms of Ulcer Index (U.I.)[12] in the glandular portion of stomach, and percentage of animals with hemorrhages. In the forestomach: percentage of animals with erosions.

In the first series of animals, thenalidine has produced a slight reduction of erosions and hemorrhages in the glandular portion, and an enhancement in the forestomach. However, in the second series, the animals treated with serotonin and thenalidine showed considerably less ulcers in the glandular portion (Fig. 2) than the animals treated only with serotonin (Fig. 1). The percentage of animals with hemorrhages was noticeably diminished.

Discussion. The administration of reserpine leads to a depletion of serotonin depots of the animal[13,14], so that reserpine-induced gastric erosions may be explained by means of such a mechanism[4,5]. This view is supported by the findings that 5-hydroxytryptophane[4] and serotonin[7,8] can produce gastric ulcers. However, reserpine is known also as a histamine-releaser[15]. It is of interest to note that serotonin *per se* has histamine-releasing properties[16]. Since the application of histamine (mixed with beeswax and mineral oil) also produces gastric ulcerations[17], it is possible to suppose a definite participation of this amine in the genesis of reserpine-induced ulcers.

The results presented in this paper supported the abovementioned view. Thenalidine feebly inhibits the ulcerogenic action of reserpine, because in this case its action is related to an effect of the liberated amines on the gastric mucosa. The serotonin-induced ulcers, after pretreatment with thenalidine, have been reduced to an extent which is less than half (Table), because of the direct antiserotonin action of thenalidine. However, the occurrence of these ulcers was not completely prevented, perhaps by reason of a histamine release after the administration of serotonin, or due to an incomplete blocking effect of thenalidine.

The paradoxical effect of thenalidine on the forestomach is quite opposite to the effect of Cortisol[12]. This nonglandular portion, covered with squamous epithelium, reacts otherwise than does the stomach corpus (glandular portion). It is thus obviously that the mechanisms of the ulcer production in the two parts of rat's stomach are different.

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Groups	Treatment	No. of animals	Ulcer index[a]	Hemorrhages in %	Ulcers in the Forestomach in %
I	Reserpine 2 mg/kg i. p.	15	18,3	30	20
II	Reserpine and Thenalidine 2 mg/kg i. p.	15	14,2	26,6	40
III	Serotonin 30 mg/kg s. c.	10	18,9	87	—
IV	Serotonin and Thenalidine 2 mg/kg s. c.	10	8	60	—

[a] Ulcer Index (U. I.) is calculated by adding incidence divided by 10, severity (in pluses), and number of ulcers per rat[12].

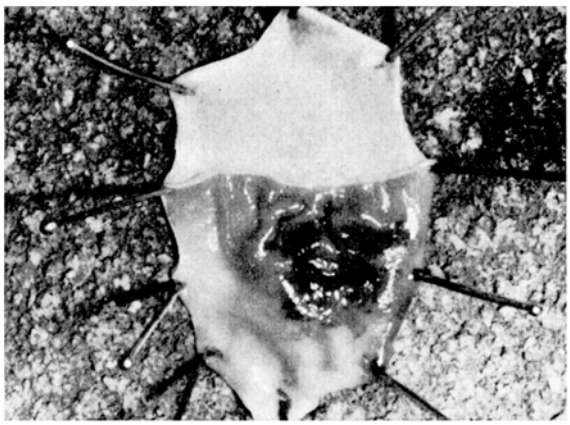

Fig. 1

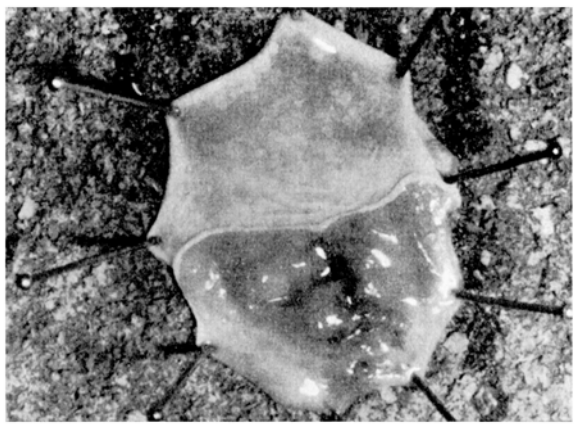

Fig. 2

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Zusammenfassung

Die Vorbehandlung mit Thenalidin (Sandosten) führt zur Verminderung der mit Serotonin hervorgerufenen hämorrhagischen Erosionen im Magen der Ratten. Thenalidin zeigt einen Effekt auf das mit Reserpin bewirkte Magengeschwür und verstärkt die Vormagengeschwürbildung bei den Ratten.

Effect of the Non-Protein Fraction of Rabbit Hypothalamic Extract on the Function of Adenohypophysial Autografts in the Anterior Chamber of the Eye of Hypophysectomized Rats

It was found in previous experiments[1] that the non-protein fraction of aqueous extract of rabbit hypothalami increased acid phosphatase activity in rat pituitary homogenates. Evidence was also submitted indicating the existence of a relationship between pituitary acid phosphatase activity and the formation of thyrotrophic hormone (TSH), and suggesting that the hypothetical hypothalamic factor activating pituitary acid phosphatases may be a hypothalamic TSH-hypophysiotrophic factor[2].

Experiments were carried out *in vivo* to verify this assumption. Since the systemic (intravenous) administration of even relatively high doses of extract does not significantly influence thyroid function in intact rats[3], evidently because this method does not give a sufficiently high concentration of the factor in the hypophysial portal vessel blood, the problem was approached by the local administration of the non-protein fraction of hypothalamic extract to adenohypophysial autografts in the anterior chamber of the eye of hypophysectomized rats.

Male rats (descendants of the Wistar strain, Velaz, Prague) acclimatized at 25 ± 2°C and fed on a standard Larsen diet with water *ad libitum*, were hypophysectomized by the parapharyngeal route. About one third of the pituitary (adenohypophysis) was aspirated into a No. 24 intramuscular needle with blunted point. An incision of about 2 mm was made with a fine scalpel in the cornea of the upper half of the left eye. The aspirated adenohypophysial tissue was then introduced into the anterior chamber of the eye (only partial disintegration of the aspirated one-third of the adenohypophysis took place during the procedure). Only completely hypophysectomized animals were taken into account, and in animals with autografts the eye was subjected to histological examination. The results of this examination will be given in a separate report.

There were four groups of animals: I–15 controls, II–12 hypophysectomized animals, III–10 hypophysectomized animals with autografts, to which (in the anterior chamber of the eye) 0·02 ml physiological saline was administered daily from the first to the seventh day after transplantation, IV–15 animals with autografts, to which (in the anterior chamber of the eye) 0·02 ml aqueous solution of the non-protein fraction of rabbit hypothalamus, prepared by the method described in a previous communication[1], was administered daily. 1 ml solution contained the equivalent of two rabbit hypothalami. One day after the seventh injection, all the animals were killed by exsanguination and the thyroids, adrenals, testes, and seminal vesicles were weighed.

The results are shown in the Table. Hypophysectomy was followed by plainly evident involution of all the organs in question, while autotransplantation of the adenohypophysis partially inhibited this involution. Administration of hypothalamic fraction to the autografts discernibly limitted the involution of the thyroid (thyroids of the group IV were significantly–$p < 0{\cdot}01$–heavier than those of group III). Involution of the other organs (adrenals, testes, seminal vesicles) was the same or greater in group IV than in group III, however. The 'weight of the adrenals: weight of the thyroid' quotient was 2·34 ± 0·16 in group III and 1·65 ± 0·14 in group IV; $p < 0{\cdot}01$.

It appears that the local application of the hypothalamic fraction stimulated TSH-secretion by the adenohypophysial autografts and did not change, or possibly inhibited, secretion of ACTH and gonadotrophins. This is in agreement with findings mentioned on relationships between the hypothalamic factor, activating pituitary acid phosphatases *in vitro* (which is present in the non-protein fraction of the hypothalamic extract) and secretion of TSH by the adenohypophysis. The possibility that its action is non-specific cannot yet be excluded.

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Group	I Controls	II Hypophysectomized	III Hypophysectomized + autograft	IV Hypophysectomized + autograft + hypothalamic fraction
No. of animals	15	12	10	15
Initial weight g	235	248	232	244
Final weight g ± σ	247 ± 5	207 ± 8	204 ± 5	205 ± 7
Thyroids mg% ± σ_M	7·00 ± 0·37	4·50 ± 0·37	4·92 ± 0·38	6·42 ± 0·39[a]
Adrenals mg% ± σ_M	14·90 ± 0·64	9·50 ± 0·36	11·1 ± 0·68	9·60 ± 0·42[b]
Testes g% ± σ_M	1·05 ± 0·04	0·88 ± 0·03	1·04 ± 0·05	0·95 ± 0·04[c]
Seminal vesicles mg% ± σ	195 ± 15	107 ± 5	118 ± 14	96 ± 7 [d]
Quotient 'weight of adrenals: of thyroids' weight	2·19 ± 0·12	2·26 ± 0·22·	2·33 ± 0·16	1·56 ± 0·14[e]

Comparison of group III and IV by Fisher's *t*-test: $p =$ [a] <0·01; [b] 0·05; [c] 0·2; [d] 0·1; [e] <0·01.

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