Cycloheximide, an inhibitor of protein synthesis, if used in a dose of 20 μg/ml, lowered by 30% the level of labeling of the blood polymorphs but did not affect that of the wound polymorphs.

During activation of the polymorph on leaving the blood to enter the wound, opposite changes were thus found in two of its functionally connected processes, namely RNA synthesis and protein synthesis: the first was intensified, the second weakened. This observation contradicts the view that RNA is an intermediary in protein synthesis, and that maximal production of it is observed in cells forming a large quantity of protein. To verify this conclusion again on an object closest to polymorphs, we compared levels of RNA and protein synthesis in precursor cells of polymorphs, which were present in large numbers in blood samples taken from our patients. The tests showed that a high level of RNA synthesis in the precursor cells corresponded to intensive protein synthesis (Fig. 3a, b). The absence of this relationship in the wound polymorphs suggests that RNA synthesis in the activated polymorph may serve some other process unconnected with protein synthesis.

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TERMINATION OF THE OVARIAN CYCLE IN A YOUNG MOUSE JOINED TO AN OLD MOUSE IN PARABIOSIS

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Weakening of the function of the reproductive system during aging is an established fact. Meanwhile it is possible by certain procedures to restore, albeit partially, the function of the sex organs in aging animals. For example, transplantation of the mediobasal region of the hypothalamus of newborn rats into the third ventricle of old females caused an increase in weight of the ovaries and uterus of the latter, with the appearance of ovarian follicles at different stages of development [8]. Transplantation of the ovaries of young mice into animals with age-dependent depression of reproductive function led to resumption of cyclic changes in the vaginal epithelium, restored the luteinizing hormone level [6], and increased the frequency of pregnancy [10]. These and other investigations have shown that changes in the reproductive system during aging are due both to changes in the central control mechanisms and to disturbances of ovarian function. To study the role of the central and peripheral control mechanisms during aging of the reproductive system, and also the possibility of restoring this function through the influence of a young animal on an old one, through the ex-

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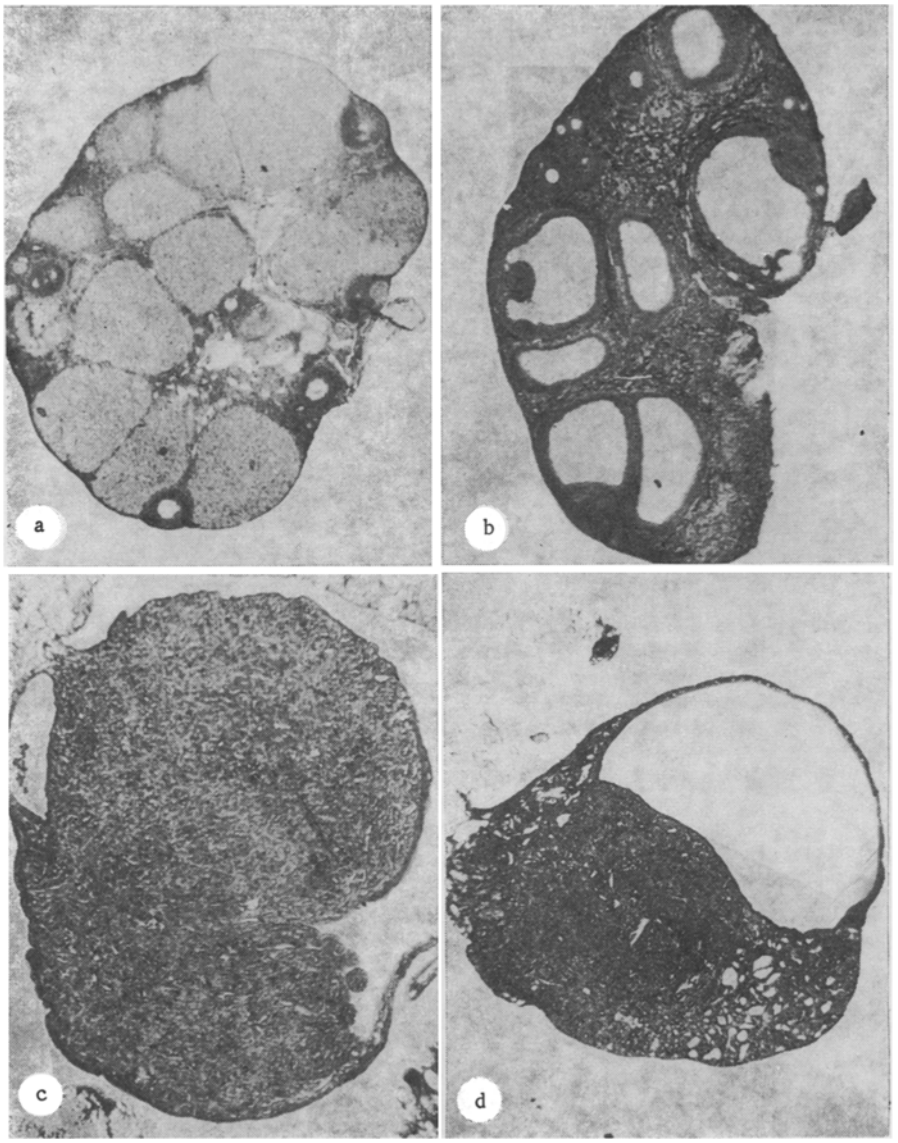

Fig. 1. Ovaries of parabiotic partners: a) young mouse joined to a young mouse; b) young mouse connected to an old mouse; c) old mouse joined to a young mouse; d) old intact mouse. Hematoxylin and eosin, 120×.

change of humoral factors and circulating cells between the two animals, the investigation described below was undertaken using a model of heterochronous parabiosis.

EXPERIMENTAL METHOD

Female CBA mice obtained from the "Stolbovaya" Nursery, Academy of Medical Sciences of the USSR, were used. Operations to form parabiotic pairs were carried out in accordance with the method described previously [5]. The estrous cycle was studied by microscopy of vaginal smears. Serum levels of progesterone and estradiol were determined by radioimmunoassay [3] and the prolactin concentration in the adenohypophysis was determined by electrophoresis in a micromodification [2]. The histological structure of the ovaries was studied in serial sections 6-7 μ thick, stained with hematoxylin and eosin. The results were analyzed by nonparametric statistical methods.

EXPERIMENTAL RESULTS

Investigation of vaginal smears showed the absence of cyclic changes in the vaginal epithelium of all mice aged 17 weeks, joined for 6 weeks in parabiosis with mice aged 24-26 months

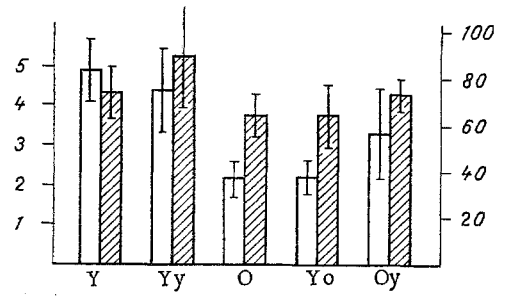

Fig. 2. Serum progesterone (unshaded columns) and estradiol (shaded columns) levels of parabiotic partners. Abscissa, experimental groups of animals: Y) single young; Yy) young, joined to young; O) single old; Yo) young joined to old; Oy) old joined to young. Age of young animals was 5 months, of old animals 24-26 months. Ordinate, on left — progesterone concentration (in nmoles/liter); on right — estradiol concentration (in pmoles/liter).

TABLE 1. Prolactin Concentration in Adenohypophysis (M ± m)

Parameters	Experimental groups of animals				
	Y	Yy	O	Yo	Oy
Prolactin concentration, % of total protein	13,6±0,4	12,0±0,3	10,7± ±0,6	14,0± ±0,8	11,6± ±0,5
Number of animals in group	10	10	11	9	9

Legend. Abbreviations of experimental groups the same as in Fig. 2.

Many keratinizing scales were observed daily in the smears, sometimes mixed with leukocytes, corresponding to the state of permanent estrus. Anestrus was preserved in the old parabiotic partners and also in single animals of the same age. In young single mice cyclic changes were present in the vaginal epithelium with a period of 4.1 ± 0.2 days. The duration of the estrous cycle in young animals joined to young animals was lengthened to 8.2 ± 1.8 days ($P < 0.01$). Synchronization was absent between the partners in this case.

The ovaries of young mice joined in parabiosis to other young mice preserved the morphological characteristics typical of that age. They contained follicles at various stages of development and corpora lutea of different generations (Fig. 1a). Considerable changes could be observed in the ovaries of young mice joined to old mice, reflecting disappearance of the ovarian cycle (Fig. 1b). Large follicles with thin walls and the almost total absence of corpora lutea were observed. These glands, according to several features, resembled the ovaries of old intact mice and of old mice joined in parabiosis with young mice (Fig. 1c, d), where signs of atrophy were found, with predominance of stromal cells, single cysts, and absence of lutein tissue.

The effect of age was expressed differently at the level of sex hormones and blood. Whereas in old animals the progesterone concentration was lower than in young ($P < 0.02$), these experimental groups did not differ in their estradiol levels (Fig. 2). Keeping young animals for 8-9 weeks in parabiosis with old led to a significant fall in the progesterone level in the former ($P < 0.03$) with no change in the latter. The formation of homochronous pairs of young animals did not affect this parameter. The estradiol level showed no significant change after the various experimental procedures. No correlation could be found between levels of these hormones in the two partners in parabiosis.

The results of investigations of the prolactin concentration in the adenohypophysis are given in Table 1. In old single mice this parameter was lower than in young single mice ($P < 0.001$). It was lowered also when young animals were joined to others of the same age ($P < 0.01$). The prolactin level was unchanged in old animals if young were joined to them. The prolactin level in the adenohypophysis of the latter was the same as in single young animals, but higher than in young mice joined to other young mice ($P < 0.03$).

When a young animal was joined in parabiosis to an old animal, ovarian function was thus depressed in the former without any appreciable change in its level in the latter. The structural changes discovered in the young partner resembled the initial period of aging of these glands [12]. The mechanism of this phenomenon is not clear. Absence of synchronization of the estrous cycles of the parabiotic partners as well as the absolute absence of correlation between sex hormone levels of the partners are evidence that equalization of their blood concentrations with the existing rate of exchange of blood between the partners (about 1%/min) [1] did not take place. Otherwise the establishment of a progesterone level in young mice, joined to old, at an intermediate level between the young and old control animals would have been expected. In fact, this parameter fell to the level in old mice. This phenomenon likewise cannot be explained by the participation of trophic hormones, for the blood level of follicle-stimulating hormone in mice does not fall with aging [9], and the prolactin concentration in the young partners in heterochronous parabiosis was unchanged. Meanwhile equalization of the concentrations of luteinizing hormone in the two partners was doubtful, for the time required for this to take place is 3-4 h, and its half-life in the body is only 20-30 min [11]. It can be postulated on the basis of the facts described above that there exist other, possibly yet unknown factors, which accumulate in the body during aging and are able to accelerate aging of the reproductive system of the young parabiotic partner. Considering the results of previous investigations [1, 4, 7, 13], it can be tentatively suggested that the action of these factors also extends to other systems.

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