of infiltration by monocytes, and of marked edema observable at this stage of the reaction, i.e., it does not necessarily depend on the direct action of immunologic factors on the lysosomal membranes. In both cases, however, enzymes entering the cytoplasm from the lysosomes induce processes of autolysis, which may play a role in the pathogenesis of rejection of the grafted heart.

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AMYLOID TRANSFER FROM A SYNGENEIC GRAFT OF AMYLOID SPLEEN IN INTACT AND AMYLOID MICE

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UDC 616-003.821-02:617-089.843-092.9

The investigation was carried out on male CBA mice using the casein model of amyloidosis. After simultaneous transplantation of fragments of spleen from intact and amyloid donors beneath the capsule of opposite poles of the kidney into intact and amyloid recipients, deposits of amyloid both in the endogenous spleen and in the graft from intact donors were found in 40% of intact animals. In amyloid recipients under observation for periods of between 5 days and 6 months, deposits of amyloid in the intact graft were observed in only 5% of cases. It is postulated that amyloidosis is "transferred" through migration of cells participating in amyloid formation and that this mechanism is inhibited in animals with amyloidosis.

KEY WORDS: experimental amyloidosis; "transfer" of amyloidosis; transplantation.

Several investigators have described the development of amyloidosis in syngeneic recipients after injection of a suspension of spleen cells or transplantation of fragments of spleen from an amyloid donor – the

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(Presented by Academician of the Academy of Medical Sciences of the USSR E. M. Tareev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 6, pp. 754-757, June, 1978. Original article submitted July 27, 1977.

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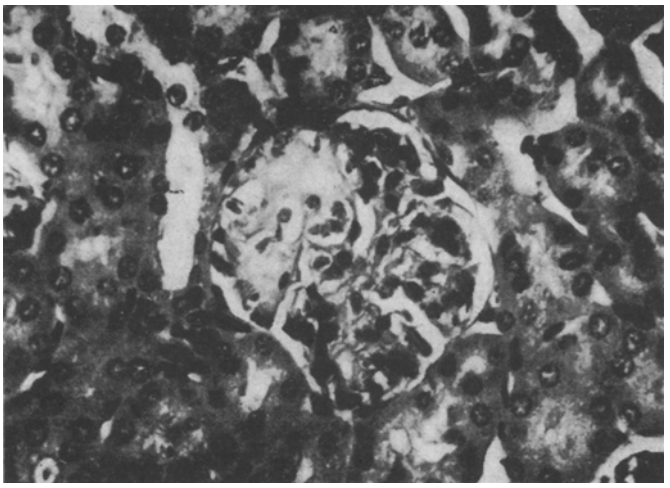

Fig. 1. Transfer of amyloidosis into kidney of intact mouse from graft of amloid spleen. Deposition of amyloid in glomeruli. Congo red, 300×.

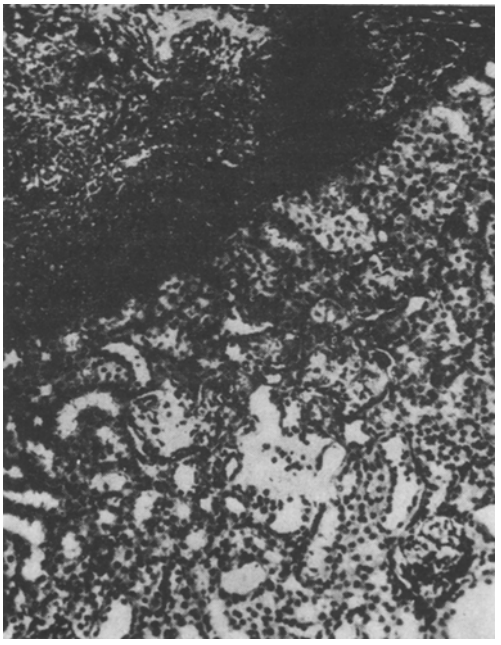

Fig. 2. Absence of transfer of amyloidosis into intact graft in amyloid recipient: top part of section shows intact splenic graft, lower part amyloidosis of kidney. Hematoxylin–eosin, 100×.

so-called transfer of amyloidosis. If immunodepressive factors subsequently act on the recipients, the development of amyloidosis is intensified [3-6, 8].

In the present investigation the transfer of amyloidosis and the pattern of resorption of amyloid in a syngeneic graft of amyloid spleen were studied in intact and amyloid recipients [1].

EXPERIMENTAL METHOD

Experiments were carried out on CBA male mice weighing 18-20 g. Amyloidosis was induced in the donors and recipients by subcutaneous injection of 5% casein solution in 0.25% NaOH solution in doses of 1 ml

6 times a week for 7 weeks. In accordance with the primary aim of the investigation, fragments of spleen 2.5-3 mm in diameter from amyloid (upper pole) and intact (lower pole) donors were grafted simultaneously beneath the capsule of opposite poles of the kidney. The state of the grafts, the kidneys with the grafts, and the spleens of the recipients were investigated morphologically by staining with hematoxylin–eosin, with Congo red, and with thioflavine T between 5 days and 6 months after the operation. Altogether 36 amyloid and 32 intact recipient mice were used.

EXPERIMENTAL RESULTS

Intact Recipients. Throughout the experiment marked resorption of amyloid was observed in the amyloid graft in the intact recipients, similar to that discovered previously in experiments with transplantation of fragments of spleen only from amyloid donors [1]. Deposits of amyloid in the endogenous spleen at the periphery of the follicles and in the graft of intact spleen, also at the periphery of the folicles or as focal concentrations, were found in 13 of the 32 recipients of this group. In addition, "transfer" of amyloidosis into the recipients' kidney also was found. In the group of intact recipients after syngeneic transplantation of the spleen from amyloid and intact donors the "transfer" of amyloidosis thus took place from the amyloid graft both to the host's own spleen and kidney and also to the donor's intact grafted spleen.

Amyloid Recipients. Changes of the same type as in the analogous graft in the animals of the previous group were observed in the amyloid graft in the amyloid recipients. In the amyloid recipients' own spleen at all times an abundance of amyloid was found, with replacement of many of the follicles and of the red pulp ("lardaceous spleen"). Meanwhile some decrease in the quantity of amyloid and in the infiltration of amyloid by cells was noted in the late stages of the experiment. In the intact graft in the amyloid recipients, by contrast with the analogous graft in the mice of group 1, amyloid deposition was observed in only two of the 36 mice. Morphologically, the structure of the splenic graft as a rule corresponded to that of the normal spleen, even though in the adjacent kidney tissue marked amyloidosis was present with deposition of amyloid in the glomeruli or even their total replacement (Fig. 2).

However, in some cases the pattern in the grafts of intact spleen corresponded to the preamyloid stage of development of experimental amyloidosis: hyperplasia of the follicles, reticulocyte and plasma cell transformation of the red pulp, accumulation of PAS-positive cells. The results obtained in this group of animals thus showed that after syngeneic transplantation of the spleen from intact and amyloid donors into recipients with amyloidosis, deposition of amyloid in the intact graft is observed much less frequently than in intact recipients with parallel grafting of amyloid spleen.

The results of these experiements, demonstrating that amyloid may be deposited in the endogenous spleen of intact recipients after syngeneic transplantation of fragments of spleen from amyloid donors beneath the capsule of their kidney, are in agreement with the observations of Hardt [2, 4], who under similar conditions found the "transfer" of amyloidosis in most recipients, but after administration of nitrogen mustard to the animals.

Amyloid formation in spleen grafted from intact donors, i.e., in what amounts to an accessory spleen, evidently takes place by the same mechanism as the "transfer" of amyloidosis into the recipient's own spleen. The problem of the mechanism of "transfer" of amyloidosis by living cells of the amyloid donor has not yet been settled. However, results obtained with donors' cells labeled with [^{3}H]thymidine suggest that at least in the early stages after injection of a suspension of amyloid spleen cells, amyloid production takes place by these donors' cells [6]. Evidence has also been obtained of stimulation of the development of experimental amyloidosis induced by an antigen by the preliminary injection of extracts from the spleen or the serum of animals or patients with amyloidosis, pointing to the role of humoral factors in the development of amyloidosis. According to one hypothesis of the origin and mechanism of action of humoral factors participating in the development of amyloidosis in the body, lymphocytes under the influence of amyloidogenic antigen form and release a factor which, by binding with the antigen, acts like MIF (macrophage migration inhibition factor) at the intercellular level, and has the power to inhibit migration of macrophages and to stimulate the production of the glycoprotein amyloid in them [2].

The deposition of amyloid in the recipients' own spleen and in the transplanted (accessory) spleen of intact recipients discovered in these experiments may perhaps arise as a result of the entry of amyloid-producing cells of the amyloid graft into the spleen through their migration into the blood stream and subsequent hematogenous transport into other organs. The absence of deposition of amyloid in the graft of intact spleen found in these experiments in amyloid recipients of an amyloid graft suggests that conditions preventing the migration of the cells participating in amyloid formation are created in the body of animals with amyloidosis.

All that can be suggested as yet is that these conditions are connected with the presence of the hypothetical factor, mentioned above, inhibiting migration of the cells producing amyloid (amyloidoblasts), a factor which not only acts at the intercellular level, but is also secreted in the blood stream. When the migration activity of the cells was estimated by the method of Soborg and Bendixen [7], the results obtained indicated that the ability of spleen cells to migrate falls progressively in the course of the induction of amyloidosis.

From the standpoint of the phenomenon just described above, the following clinical observation is interesting. Two patients with amyloidosis of the kidneys, developing as a complication of osteomyelitis and periodic disease, were treated by transplantation of a kidney because of the onset of chronic renal failure. Morphological investigation 2 years after the operation showed no amyloid deposits in the graft, despite amyloidosis of the other organs [1]. The authors who described this case consider that it may be due to the intensive immunodepressive treatment given to these patients. However, this seems unlikely in view of the many experimental and clinical observations indicating that amyloid production is stimulated by immunodepressants. The absence of deposits of amyloid in an intact spleen grafted into recipients with marked systemic amyloidosis is evidently an experimental model of the case just described.

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MORPHOLOGY AND FUNCTION OF THE DUODENAL CHOLINERGIC NERVOUS SYSTEM UNDER NORMAL CONDITIONS AND AFTER SUBDIAPHRAGMATIC VAGOTOMY

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UDC 612.338-06: 612.819.941-089.85

A histochemical investigation was made of the intramural nervous system of the albino rat duodenum under normal conditions and after bilateral subdiaphragmatic vagotomy. Morphometric and microspectrofluorometric observations showed a decrease in the number of detectable nerve fibers and in acetylcholinesterase (AChE) activity in them after a transient rise in these indices on the first day after vagotomy, followed by a return to their original levels.

KEY WORDS: cholinergic nerve fibers; acetylcholinesterase; subdiaphragmatic vagotomy.

Histochemical investigations have shown reasonably clearly that adrenergic and cholinergic components of the nervous system participate in duodenal innervation [1, 4, 15]. The structural organization of the intramural ganglia of the duodenum has also been shown to be heterogeneous: neurons of qualitatively different nature have been found in their composition [1, 4, 12]. However, there is still very little information on the response of nerve cells of the intramural ganglia when isolated from the CNS. Yet the solution to this problem is important, for knowledge of the principles governing the morphological reorganization of the duodenal nervous system under these conditions is essential to the understanding of the development of the morphological changes in the tissues of the organ after denervation.

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(Presented by Academician of the Academy of Medical Sciences of the USSR Yu. M. Lopukhin.) Translated from Byulletin' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 6, pp. 757-760, June, 1978. Original article submitted November 15, 1977.