EXPERIMENTAL BIOLOGY

Regeneration of the Spleen in Intact Animals and Radiation Chimeras

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Regeneration of the splenic tissue after partial splenectomy is incomplete in adult non-irradiated mice and lethally irradiated animals reconstituted with donor syngeneic bone marrow. Transplantation of the splenic tissue to intact adult animals after partial splenectomy resulted in virtually complete regeneration of the spleen. In chimeras recovery of the splenic tissue was decreased; autotransplantation of the whole spleen or its part did not lead to appreciable changes in the weight and cellularity of this organ. No more than 30% splenic tissue is restored after complete splenectomy and transplantation of the splenic tissue in intact and chimeric mice.

Key Words: *radiation chimeras; splenectomy; regeneration; spleen transplantation*

Loss of the spleen can lead to severe bacterial infection, particularly in children [6]. The presence of even 5% splenic tissue protects the organism from sepsis often developing after splenectomy [8]. The spleen well regenerates after partial splenectomy or splenic tissue transplantation to a splenectomied recipient. The size of this organ (in contrast to bone marrow stroma) is regulated at a total systems level: if several spleens are transplanted into the greater omentum of a recipient, they will take, but their total size will not surpass the size of one spleen [3,4]. Subcutaneous transplants from newborn donors are always larger in splenectomied recipients than in controls [2]. Regeneration of the spleen depends on animal age. In young rats splenic parenchyma regenerates after 2 weeks, while in adult animals it is not over even after 3 weeks [1]. The weight of the spleen transplanted from young donors 3-4-fold surpassed that from adult animals [10]. The capacity of the spleen to regeneration in larger mammals is still not proven. The weight of the organ in splenectomied rabbits 6 months after autotransplantation reached only 11% of the normal organ [9].

Autotransplantation of the splenic tissue was suggested for preventing negative consequences of splenectomy [7]. Transplanted tissue in such cases was not connected to blood vessels. Splenic fragments transplanted into the greater omentum undergo the phase of complete necrosis: all cells except some fibroblasts die. After regeneration the red and white pulp develop in autotransplantates, marginal zone and lymphoid follicles form [6]. The size of autotransplantates in rats is usually 30% less than the normal organ [11]. In mice regeneration of the spleen after partial splenectomy is very effective, though incomplete. Regeneration of the spleen in chimeric mice exposed to lethal irradiation and transplanted donor bone marrow is little studied. However, these data are essential for the study of the clonal composition of the myeloid and lymphoid constituents of hemopoietic tissue in the spleen and, moreover, for evaluating the clinical possibility of its restoration after splenectomy. We studied splenic regeneration after complete and partial

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TABLE 1. Weight and Cellularity of the Spleen after Partial or Complete Splenectomy and Transplantation of Additional Tissue* (*M±m*)

Group		Weight of spleen, mg	Cellularity of spleen, $\times 10^6$
Intact mice		114±10	178±20
Partial splenectomy in intact mice	no transplantation of the spleen	69±10	99±15
	transplantation of half of spleen	105±13	149±13
	transplantation of whole spleen	106±26	174±30
Complete splenectomy in intact mice	transplantation of half of spleen	29±7	12±6
	transplantation of whole spleen	37±5	22±8
Partial splenectomy in chimeric mice	no transplantation of the spleen	54±5	140±16
	transplantation of half of spleen	68±20	124±31
	transplantation of whole spleen	65±4	89±19
Complete splenectomy in chimeric mice	transplantation of half of spleen	33±5	23±3
	transplantation of whole spleen	35±6	23±9

Note. *Data of two independent experiments are presented.

splenectomy in intact and lethally irradiated mice reconstituted with bone marrow transplantation.

MATERIALS AND METHODS

Experiments were carried out on 9-26-week-old female and male (CBA×C57BL/6)F_1 mice. In order to study regeneration of the spleen in chimeras reconstructed with labeled bone marrow, the animals were divided into 10 groups. Chimeric mice were obtained by irradiation of recipient females on an IPK device (Hematology Research Center) with ^{137}Cs in two equal doses at 3-h interval (total dose 10 Gy). Donor bone marrow cells from males were transplanted intravenously in a dose of 8×10^6 cells per mouse. Partial and complete splenectomy were carried out in chimeras 3 months after restoration and in intact mice of the same age under ketamine narcosis (5 mg/kg). For complete splenectomy the vascular pedicle of the spleen was ligated with a silk thread, after which the organ was removed. For partial splenectomy half of the spleen was ligated with a silk thread and the part not connected to vessels was removed. The tissue was autotransplanted into the greater omentum. The weight and cellularity of the spleen were evaluated 3 months after the operation.

RESULTS

The total weight of the spleen and its cellularity virtually did not change after transplantation of additional splenic tissue. Our study just partially confirmed previous [3,4] data. Neither the weight, nor cellularity of the remaining part of the spleen could be completely restored without additional transplantation of the spleen both in intact and chimeric mice (Table 1). The weight of the remaining part of the spleen in reconstituted mice was the same as in non-irradiated mice. After autotransplantation of the removed spleen the weight and cellularity of the splenic tissue increased; in reconstituted mice autotransplantation restored both the weight and cellularity of the organ. This is in line with D. Metcalf's data [2,3] obtained on newborn animals. The regeneration parameters were worse in the group of lethally exposed and reconstituted mice in comparison with intact animals. The bulk of the organ virtually did not increase irrespective of the volume of transplanted splenic tissue. No differences between transplantation of a half of the spleen or the whole organ were detected. Transplantation of a part or the whole organ after complete splenectomy led to recovery of no more than 30% tissue in both intact and irradiated animals.

The difference between our results and Metcalf's data [2,3] can be due to the fact that we transplanted tissue from adult, but not newborn, animals. In our experiments the splenic tissue in small rodents was restored just partially, which was confirmed in experiments on rats: all components of the spleen (red pulp, white pulp, marginal zone) were restored partially after tissue autotransplantation, and functional reactions were not normalized [5]. Lethal irradiation did not inhibit regeneration of the spleen.

Hence, partial and complete splenectomy in adult animals was not followed by full-value regeneration of the spleen. Autotransplantation of the splenic tissue is insufficient for increasing the regeneration and functional potential of this organ. It seems that other approaches to replacing splenic functions after splenectomy should be searched for.

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