portant, if not decisive role in the genesis of amyloid deposits. The results of our study, utilizing indices of reticuloendothelial activity other than morphological, tend to support this theory.

Summary. 1) A group of 8 rabbits was shown to have significantly higher rates of phagocytosis when young and small than when fully matured. However, after the animals achieved a weight of 3.5 kg, further gains in weight did not significantly decrease phagocytic activity. 2) Two groups of 8 and 6 rabbits respectively were given casein injections as used previously to induce amyloidosis. Both groups showed a pattern of accelerating and then decelerating phagocytic activity over many weeks. One group was sacrificed while phagocytic indices were still quite high. The animals in this group showed no evidence of amyloidosis. The second group of animals, sacrificed only after phagocytic indices had returned to control levels, showed definite amyloid deposition. 3) The possible relationships between amyloidosis and the R.E.S. were discussed.

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Effect of Sensitization to BSA on Adjuvant Disease in Normal and Neonatally Thymectomized Rats.* (30269)

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It has been noted that rats are readily sensitized to tuberculin by a single footpad injection of tubercle bacilli suspended in mineral oil(1). This sensitization is reduced or suppressed entirely when a competing antigen, bovine serum albumin (BSA), is included in the adjuvant mixture employed for sensitization. Adjuvant disease, a complex of polyarthritis, ocular, and mucocutaneous lesions occurring in rats sensitized with tubercle bacillus-oil mixtures(2,3,4), was also found to be inhibited when the mixtures contained BSA(5). The suppressive effect of BSA on these forms of immune response appeared related to the development of sensitivity to the BSA itself, and was not noted when amounts insufficient to sensitize were employed. It was supposed that this suppressive effect depended on antigenic competition analogous to that described in a number of systems involving humoral antibody(6,7).

Comparative data have been obtained on the incidence and severity of adjuvant disease

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TABLE I. Effect of Sensitization to BSA on Development of Arthritis in Normal and Neonatally Thymectomized Rats.

Treatment	Antigen	Sensitization to BSA*	Intensity of arthritis: No. of rats	Day of onset†	Peak disease†: Day	Peak disease†: Degree
Sham-operated	Tbc-oil	—	9/9	9.1	13.9	2.7
"	BSA-adjuvant	+	2/65	—	—	.5
Thymectomized	Tbc-oil	—	15/16	10.1	15.6	2.4
"	BSA-adjuvant	0	10/10	15.2	18.3	1.5
Thymectomized, cells‡	BSA-adjuvant	+	20/35	15.3	20.0	1.4

* Details in references (8, 9). † Average in positive animals. ‡ 0.6-1.2 × 10^9 lymph node cells injected intravenously on days 0, 1, and 2 or 2, 3, and 4.

in presence and absence of sensitization to BSA in a recent study of neonatally thymectomized rats(8). These data appear to provide additional support for our earlier conclusion.

Methods. Lewis rats were thymectomized or sham-operated within 24 hours of birth. At 8 weeks they were sensitized with a single footpad injection of killed tubercle bacilli in oil, 0.3 mg/0.1 ml, or with a BSA-adjuvant mixture containing 500 μg BSA and 0.3 mg of tubercle bacilli in 0.1 ml. The latter animals were skin tested at 7 and 14 days with BSA 30 μg. Some of these received intravenous infusions of normal adult lymph node cell suspensions on days 0, 1, and 2 or 2, 3, and 4. The methods have been given in detail earlier(3,4,8,9). All rats were observed for development of arthritis; and the disease was evaluated in terms of day of onset, day on which arthritic manifestations reached their peak, and intensity of the disease process, graded on a scale of 0 to 3.0(3,4).

Results. Sham-operated rats, injected simply with tubercle bacilli in oil, developed intense arthritis of early onset (Table I). Comparable animals given BSA-adjuvant mixtures (containing the same dose of tubercle bacilli) developed reproducible immune responses to BSA, manifested by delayed sensitization, humoral antibody formation, and Arthus reactivity(1,8,9), but failed completely to develop arthritis. In neonatally thymectomized rats, injection of tubercle bacilli in oil gave arthritis virtually indistinguishable from that in sham-operated rats, as reported earlier(10). BSA mixtures failed to induce any immune response to BSA in thymectomized rats; and it is significant that arthritis was observed in all of these animals, though it was late in onset and the disease was mild. Finally, rats whose immune reactivity to BSA was restored by infusions of normal adult lymph node cells, given intravenously at time of sensitization(8) developed similar mild disease.

Discussion. The marked suppressive effect of BSA on development of adjuvant arthritis is not observed in neonatally thymectomized animals, in whom sensitization to this protein is largely or completely lacking. This finding suggests that a competition of antigens in some unknown sense underlies the suppressive effect. This may mean that the cellular response to BSA effectively interferes with the cellular response to the antigens responsible for adjuvant disease, by preempting either the reactive cells themselves, the space in which they must proliferate, or factors essential to the proliferative process. In the thymectomized rat, there is no sensitization to BSA and there can be no such effect. The occurrence of arthritis in animals responding to BSA as a result of lymph node cell infusions at time of sensitization would at first glance seem incompatible with this interpretation. However, a delay of a few hours or a day or two in initiation of BSA responses in these rats may have sufficed to permit the sensitization responsible for adjuvant disease.

This system is of interest as another example of the poorly understood category of immune events designated as "competition" (6,7). It is anomalous, in that the adjuvant arthritis occurs with its normal intensity in thymectomized rats, in whom other immune responses apparently of similar character are

suppressed(10). No explanation has been advanced to account for this phenomenon, which contradicts evidence that the arthritis depends on an immunologic response of the delayed type(3,11). If a new type of response is involved, any explanation of the apparent competition by BSA must remain highly tentative. If the response is of the delayed type and occurs in thymectomized animals only because of the intensity of the stimulus provided by the (unknown) antigen, it is not clear why the BSA stimulus, insufficient itself to induce a response in these animals, can nevertheless, when it occurs, overwhelm the arthritis response.

Summary. Adjuvant arthritis is suppressed in sham-operated rats sensitized with adjuvant mixtures containing BSA. In neonatally thymectomized rats, in whom sensitization to BSA fails to occur, there is a moderate reduction in the intensity of the arthritis observed. In similar animals given lymph node cells at or just after the time of sensitization, the response to BSA is normal; yet the arthritis response is like that in animals not receiving cells.

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Blood Volume in Alligators During Prolonged Hypothermia.* (30270)

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In previous publications it was shown that lowering the body temperature of an alligator from 25°C to 5°C within a 30-minute period produced a small reduction in plasma volume, no change in cell volume, and a very slight increase in circulatory hematocrit. There was, however, in spite of the reduced plasma volume, a significant fall in the venous hematocrit. The ratio of circulatory (over-all cell percentage) to venous hematocrit, BVR_{cells}, increased while the volume of residual plasma decreased significantly. Therefore, as a result of the rapid cooling, there was a shift of cells from the large to small vessels within the circulation of the alligator. This was confirmed by tissue analysis, the spleen and liver showing a significant increase in the volume of red cells(1). Because these animals had only 30 minutes to equilibrate at the low temperature, it was decided to study animals subjected to deep hypothermia for a longer period to see whether or not the effects were intensified or compensated for with time.

Materials and methods. Young North American alligators, *Alligator mississippiensis* (Daudin), weighing 700-2400 g and measuring 66-86 cm in length were obtained from a commercial dealer and kept in a shallow tank. They were usually used within 3 weeks after their arrival, but those kept for a longer period were fed frozen fish scraps. Approximately equal numbers of males and females were selected for this study, although previous work in this laboratory has indicated that the sexes showed no significant differ-

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