Elicitation of Shwartzman Reaction in Hamsters[1] (35586)

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It became desirable to establish the criteria for the elicitation of the Shwartzman reaction during the course of study of hypersensitivity phenomena in the hamster (1). The local reaction previously had been produced in the cheek pouch (2) and a feeble generalized reaction (GSR) had been reported as occurring only in the pregnant hamster (3). The present report indicates that the local Shwartzman reaction can be elicited in the Syrian and Armenian but not in the Chinese hamster, under the conditions of these experiments.

Materials and Methods. Animals.[2] Chinese (*Cricetulus griseus*), Armenian (*Cricetulus migratorius*), and Syrian (*Mesocricetus auratus*) hamsters of mixed sexes, weighing approximately 38, 40, and 90 g, respectively, were maintained on Purina Laboratory Chow with water allowed *ad libitum* during the course of the experimentation.

Local reaction. After shaving the recipient skin area, 8 Chinese, 9 Armenian, and 24 Syrian hamsters each received 0.1 ml of 0.85% saline solution (ss) containing 20 μg of *Escherichia coli* endotoxin $Co08_{2158}S_5$[3] (ECE) injected intradermally. Twenty-four hr later, a provocative dose of 0.5 ml (100 μg) of the ECE solution was administered via the femoral vein. A positive reaction, when it was elicited, was evident after about 3 hr and reached its maximum not later than 5 hr after challenge. The reaction maintained its magnitude for about 2 days before starting to fade. For purposes of histological examination, a biopsy of the site was taken 24 hr after the challenge, the skin sections were preserved in Tellyesniczky's fixative, then cut and stained with hematoxylin and eosin.

The reaction was compared with that occurring in animals "prepared" by intradermal inoculation of ss followed by either intravenous ss or ECE solution, or "challenged" by ss following ECE solution preparation.

Generalized reaction. An attempt was made to elicit this reaction by the intravenous challenge of hamsters prepared by the intravenous inoculation of 0.1 ml (50 μg) of the ECE solution. The challenge dose was the same as that used to evoke the local reaction. The 9 Syrian hamsters used in this study were sacrificed by ether inhalation 24, 48, or 72 hr after the challenge dose. Blocks of kidney were removed at that time, fixed, sectioned, and stained as above.

Kidney blocks were taken also from hamsters receiving only the preparative dose and "challenged" by ss.

Results and Discussion. Significant local Shwartzman skin reactions were noted in 87% of the Syrian hamsters 3 hr after the provocative dose of ECE. The positive reaction was indicated by a purple hemorrhagic area which extended to about 2 cm in diameter at maximum. A typical lesion, as contrasted to a negative control, is depicted in Fig. 1. Histologically, Fig. 2, positive reactions were characterized by edema and leukocytic infiltration into the interstitial spaces and occlusion of small blood vessels by masses of leukocytes and platelets. A positive reaction of lesser intensity, was elicited in 7 out of 9 of the Armenian hamsters. Figure 3 illustrates the characteristic histological findings. It is of interest that no lesions were observed in the Chinese hamster.

The GSR has been produced by colchicine in pregnant Syrian hamsters (3), but, appar-

[1] Supported, in part, by U.S. Public Health Service, NIH Grant FR-05526.

[2] We thank Dr. G. Yerganian of this Foundation for the Chinese and Armenian hamsters.

[3] Generously donated by Dr. Otto Westphal, Max-Planck-Institut für Immunobiologie, Freiburg, Germany.

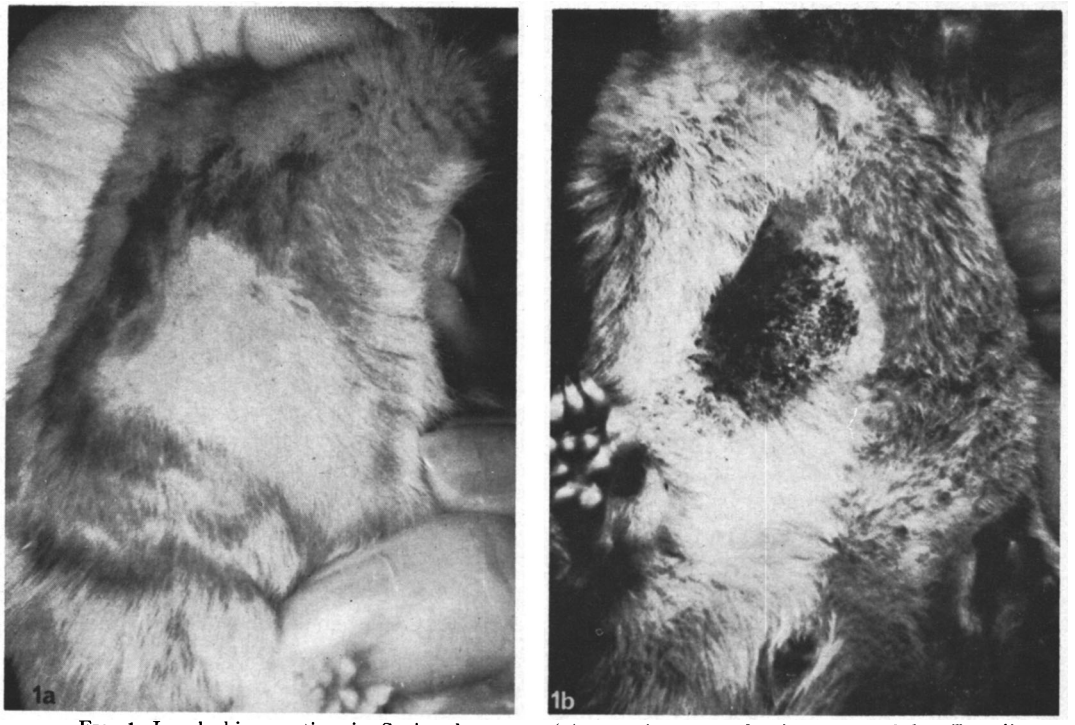

FIG. 1. Local skin reaction in Syrian hamster: (a) negative control: site prepared by *E. coli* endotoxin (ECE) id and challenged by ss iv. (b) hemorrhagic lesion: ECE id and ECE iv.

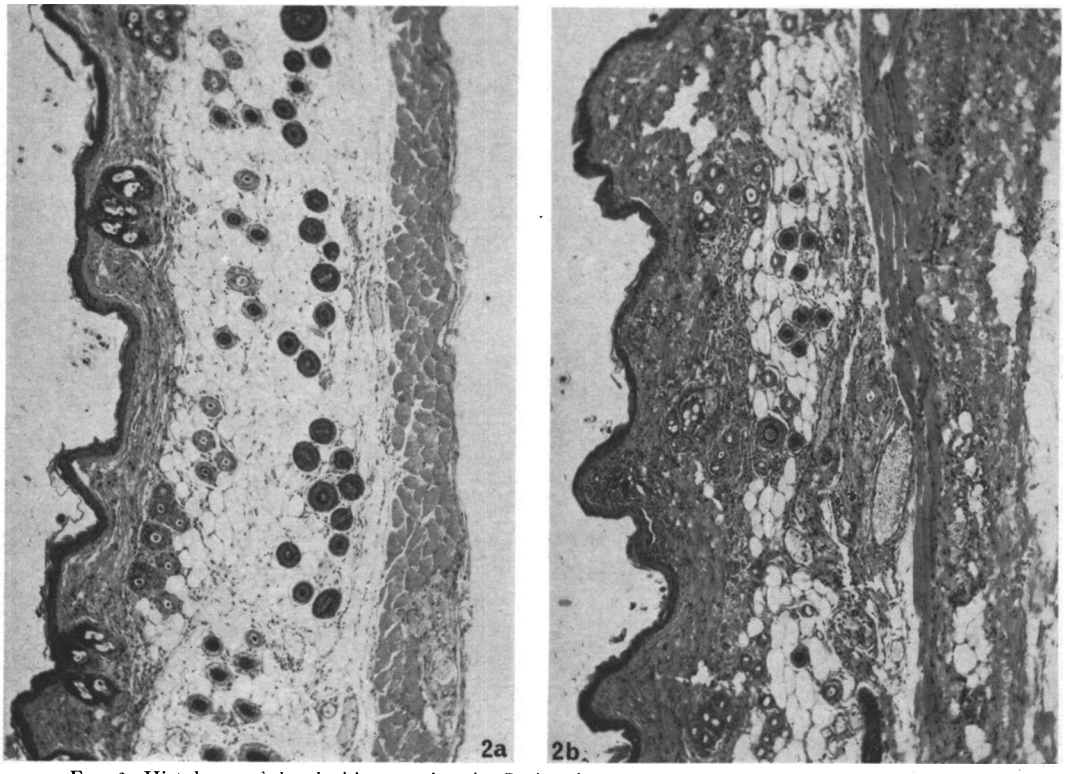

FIG. 2. Histology of local skin reaction in Syrian hamster; ×130: (a) negative control: site prepared by *E. coli* endotoxin (ECE) id and challenged by ss iv. (b) positive reaction: ECE id and ECE iv.

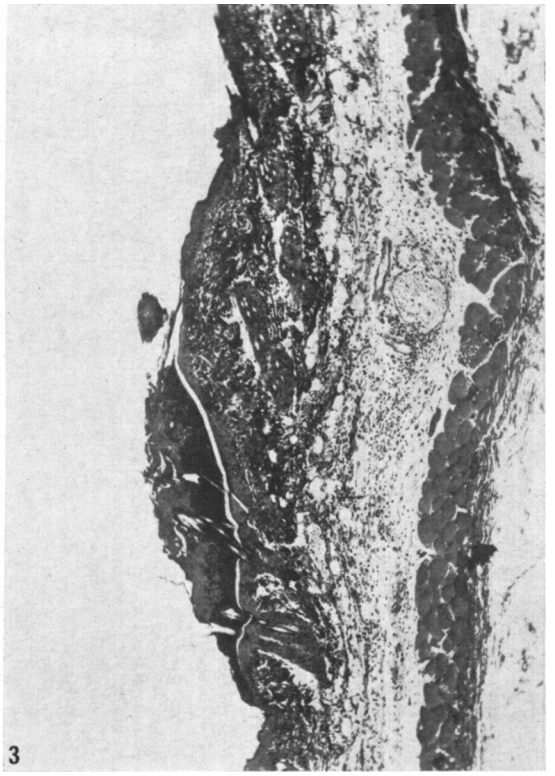

FIG. 3. H stology of local skin reaction in Armenian hamster; ×130: ECE id and ECE iv.

ently, not by bacterial endotoxin (4). The gross appearance of the kidneys of the Syrian hamsters in the present studies was essentially normal in contrast to the mottled pattern of cortical necrosis and hemorrhage described for the kidneys of rabbits with a GSR (5). Histologically, the hamster kidneys (Fig. 4) showed a consistent distal tubular lesion, with focal necrosis of lining cells and polymorphonuclear leukocytes in the lumen. These lesions were located in the regions where the tubules rejoin their glomeruli. The findings were consistent whether the sections were taken at 24, 48, or 72 hr after challenge. Control animals, injected with only the preparative dose, failed to show any microscopical lesions in the kidney. Even though renal cortical necrosis has been considered a necessary prerequisite for a diagnosis of a GSR in the rabbit (5), it may be that the pathological reaction to endotoxin administration affects a different locus in the kidney of the hamster.

Without offering any details, Shwartzman (6) indicated that both local and generalized tissue reactivity in response to bacterial filtrates, etc., could be elicited in Syrian hamsters with equal regularity as compared to rabbits, the animal of choice. However, Galton (7) and Merritt and Galton (4) were not able to demonstrate these reactions in either male or nonpregnant female hamsters following *E. coli* lipopolysaccharide. Previously, Galton (3) did report a feeble response to the endotoxin in the pregnant Syrian hamster. These negative results were consistent regardless of the type of endotoxin, dose, route, or immunological status of the recipient. The procedure in the present study where the reaction was produced with regularity apparently differed only in that a smaller preparative dose was used and a different strain of *E. coli* was used to prepare the endotoxin.

The refractoriness of the Chinese hamster toward the Shwartzman reaction is similar to that observed for mice under comparable experimental conditions (8). In many respects

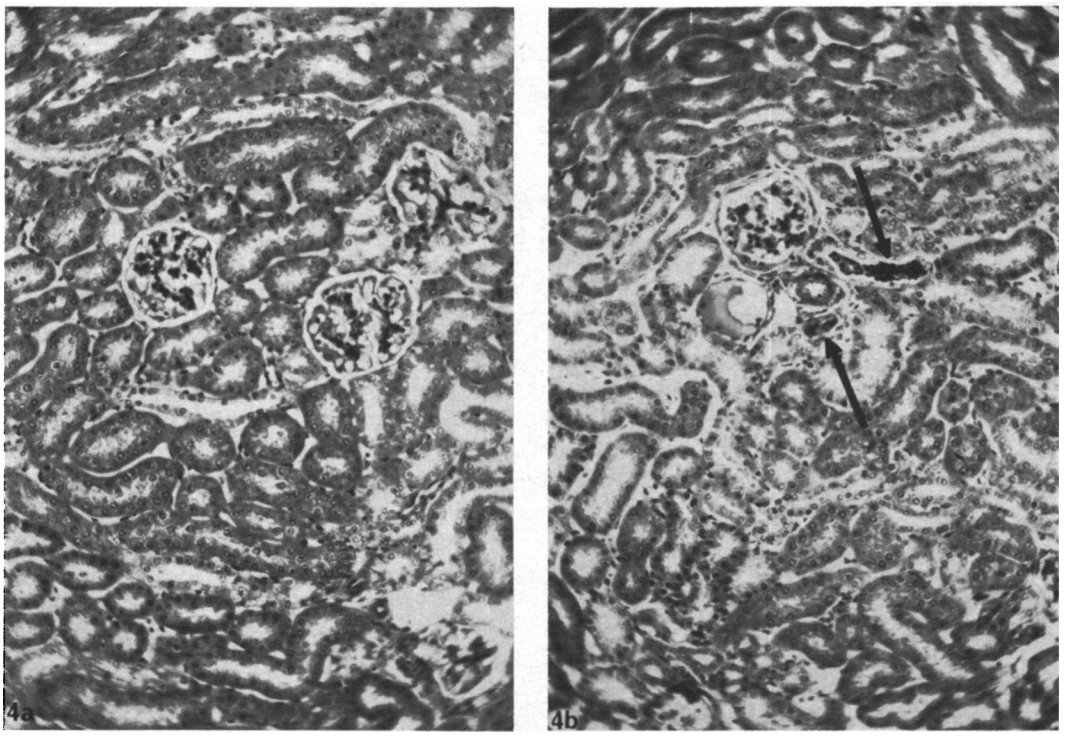

FIG. 4. Histology of kidney in generalized reaction in Syrian hamster; ×250: (a) negative control: ECE iv and ss iv. (b) positive reaction: ECE iv and ECE iv; (arrows) focal necrosis of distal tubules with polymorphonuclear leukocytes in lumina.

the Chinese hamster resembles another member of the same family, *Peromyscus leucopus*, the white-footed deer mouse (9). *P. leucopus*, unlike the laboratory mice tested, was not responsive to anaphylactic sensitization (10). Although there is no definitive explanation for the observed differences among the species of hamster, clearance of endotoxin by the reticuloendothelial system might possibly be implicated. However, preliminary carbon-clearance studies did not reveal any difference among the species of hamster and the mouse (unpublished). It is interesting to note that the Armenian hamster seems to belong somewhere between the Syrian and Chinese hamsters, resembling the former more closely physiologically but being more like the latter in temperament (Yerganian, personal communication) and in chromosome number (11).

Summary. The local Shwartzman reaction was produced in the Syrian and Armenian hamster following preparation and provocation by *E. coli* endotoxin. The Syrian hamster was also shown to manifest a systemic reaction. The Chinese hamster failed to respond by either a local or systemic reaction under identical experimental conditions.

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Received Jan. 20, 1971. P.S.E.B.M., 1971, Vol. 127.