

lysin-producing cells. The demonstration of the existence of "antigen-sensitive" cells provides strong support for the view that cell proliferation is involved in the generation of hemolysin-producing cells.

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Naturally Occurring Fatal Disease of the Pregnant Golden Hamster.* (30679)

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Eclampsia is a disease which occurs only during or immediately after pregnancy. It is characterized by convulsions on a background of hypertension, edema and albuminuria and it is attended by a high mortality. *Abruptio placentae* is a common accompaniment. Some pre-partum cases develop fibrin thrombi in the renal glomerular capillaries which may lead to bilateral renal cortical necrosis, anuria and uremia(1).

It is believed that eclampsia is peculiar to man and possibly the higher primates since its spontaneous occurrence in other species is not well documented, although syndromes resembling human pre-eclamptic toxemia are known to occur in several animals, most notably the sheep(2).

The generalized Schwartzman reaction (GSR), an experimentally induced disease of certain laboratory animals, bears a striking resemblance to the type of human eclampsia associated with renal cortical necrosis(3). It

has recently been shown that during late pregnancy, the Syrian (golden) hamster regularly develops the generalized Schwartzman reaction in response to a single intraperitoneal injection of colchicine(4). A similar reaction sometimes follows devitalization, by arterial occlusion, of the appendix or of a short segment of the small intestine(5).

Since the pregnant golden hamster appears particularly susceptible to such experimentally induced episodes of disseminated thrombosis, the possibility was examined that similar spontaneous disease processes might occur naturally in this species.

Materials and methods. The tissues were examined of hamsters which became ill during late pregnancy or shortly after delivery at a large commercial hamster production establishment, the Lakeview Hamster Colony, Newfield, N. J. The colony consists exclusively of the golden hamster, *Mesocricetus auratus* Waterhouse, 1839. It has been a closed breeding colony since its foundation from 3 breeding pairs in 1949 and a fourth in 1951. Animals are housed in polypropylene cages bedded with white pine shavings.

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The diet consists of a 4:1 mixture of Purina laboratory and rabbit chows (Ralston Purina Co., St. Louis, Mo.), supplemented with carrot for one week before weaning, and water *ad libitum*. Systematic breeder rotation is employed. There are approximately 280 deliveries a week and an average of 2,200 breeding females at any time.

During the 2-year period of observation from September 1963 to August 1965 approximately 100 pregnant hamsters became ill and died, a maternal mortality of roughly 1 in 300 pregnancies. The tissues were examined of 16 hamsters found either dead or severely prostrated in the last 2 days of pregnancy (8 hamsters), in the process of delivering (6 hamsters) or immediately after delivery (2 hamsters). This number includes all deaths except those taking place over weekends and therefore it constitutes an otherwise unselected sample of the 20-25% maternal mortality occurring on or after day 14 of the 16-day gestation period.

Results and discussion. Incomplete data concerning maternal age and parity indicate an age range of 8 to 30 weeks and from 0 to 3 previous litters. Cases occurred randomly throughout the year, with no suggestion of a seasonal cycle. Apart from the obvious prostration, no other clinical signs, such as convulsions, were observed.

Histologic examination showed that in 7 of the 16 hamsters there were disseminated renal glomerular capillary fibrin thrombi and bilateral renal cortical necrosis, characteristic of the GSR in this species (Fig. 1) (4,5). In 4 other hamsters there was marked lower nephron nephrosis but there were no glomerular thrombi. The kidneys were normal in the remaining 5 hamsters. Of the 7 hamsters displaying the GSR, 5 were found dying during delivery, one was at term and one was at 15 days of pregnancy.

The adrenals, liver, spleen, small intestine and lung were also examined. The histologic findings suggest that one of the 5 hamsters with normal kidneys suffered from peritonitis and another from acute hepatic necrosis. No pathologic lesions of consequence were noted in the tissues examined of the other 3 hamsters in this group.

Of the 4 hamsters with lower nephron nephrosis 2 displayed perivascular hemorrhages in the lung and one of these also exhibited massive hemorrhage in the lumen of the small intestine from an undetermined source. Hemorrhage into the lumen of the small intestine was also present in 4 of the 7 hamsters with renal involvement characteristic of the GSR, and in one of these 4 the presumed site of hemorrhage, a large benign ulcer, was included in the section. Perivascular pulmonary hemorrhage was evident in another of these animals.

Except for the hamster with acute hepatic necrosis, the liver, spleen and adrenal were normal in the entire series. In contrast, the adrenal in the experimentally-induced GSR is frequently involved with hemorrhage and thrombi (5).

The occurrence in 7 of the 16 spontaneously ill hamsters of renal pathologic lesions resembling those characteristic of one variety of human eclampsia raises the possibility that similar etiologic mechanisms might be operative in both man and the hamster. Unfortunately, the absence of observed prodromal symptoms in the hamster makes it very difficult to conduct a more intensive study of the early stages of the disease in this species; it would be interesting to know whether the fatal thrombotic episode is preceded by hypertension, albumenuria and edema.

Approximately 1-5% of hamsters shipped in early pregnancy from Newfield, N. J. to Hanover, N. H., a 2-day journey, fail to thrive and become increasingly lethargic, dehydrated and wasted. Death follows an illness of several days duration. In most cases, autopsy failed to show significant lesions although the fetuses were invariably undergoing resorption. The renal lesions characteristic of the GSR were present in only one such animal out of the 27 studied. Possibly the stress of transportation resulted in fetal death; toxic products entering the mother during the ensuing fetal resorption may have contributed to the maternal illness, but other factors, such as viral or bacterial infection, were not excluded. The rarity of renal involvement in these cases may indicate a more complicated etiology of the GSR than intra-

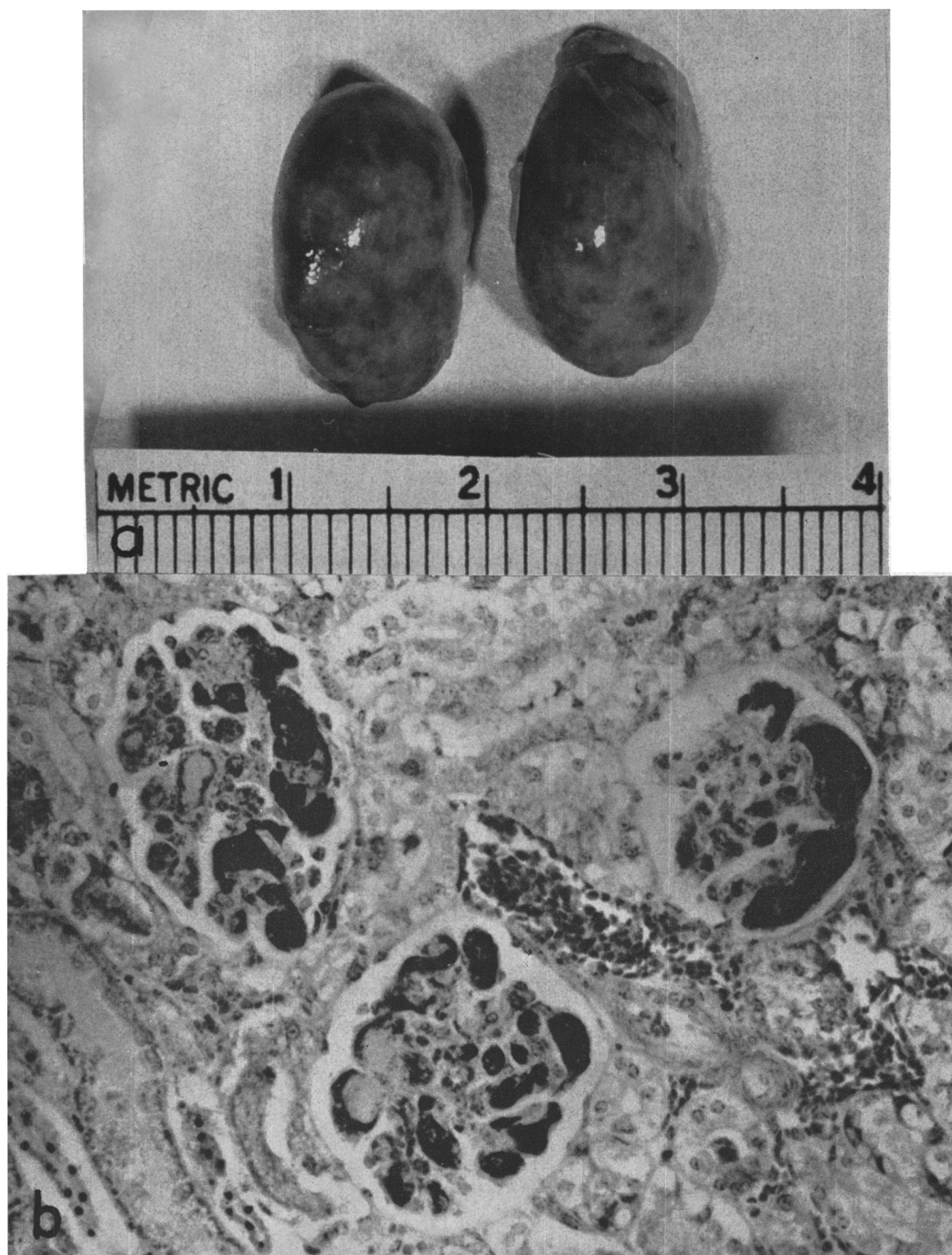


FIG. 1. The kidneys of a golden hamster (LAK 4) which died during delivery. a) Gross appearance: renal surface displays mottling and irregularity characteristic of the generalized Shwartzman reaction. b) Microscopic appearance: the glomerular capillaries are occluded by masses of fibrin and there is extensive tubular necrosis, typical of the generalized Shwartzman reaction. (Phosphotungstic acid hematoxylin; $\times 327$.)

uterine fetal death alone, although the consideration remains that the hamster in the earlier stages of pregnancy might be as resistant to toxic products of fetal resorption as it is to colchicine(5). In man, septic abortion may lead to renal glomerular fibrin thrombosis and renal cortical necrosis(6). In the present study there was no histologic evidence of bacterial infection. Furthermore, the hamster appears to be quite resistant to the Shwartzman-provoking activity of endotoxin (5).

Graded vit E deficiency provokes the GSR during late pregnancy in the rat(7). Although it is unlikely that a similar deficiency is prevalent in the Lakeview Hamster Colony in view of their animals' excellent reproductive performance, occasional hamsters might require greater amounts of this vitamin and such an idiosyncrasy could account for the sporadic occurrence of the spontaneous disease. Similarly, other dietary or hormonal factors may be involved in the rare occurrence of the disease in peculiarly sensitive individuals since it is known that manipulation of such factors is capable of producing the GSR in the rat(8).

Until it can be more intensively studied, the spontaneous disease of the pregnant hamster which features bilateral renal glomerular fibrin thrombosis and renal cortical necrosis remains as much an enigma as human eclampsia. However, the knowledge that a disease

of this type occurs in an otherwise eminently healthy colony might stimulate the search for similar diseases of other species. Comparative study of diseases of pregnancy, particularly those resembling some varieties of human eclampsia might serve a useful purpose in defining the factors responsible for this human disease.

Summary. There is a spontaneous maternal mortality of approximately 1 in 300 pregnancies at a commercial colony of Syrian hamsters. Twenty to 25% of deaths occur on or after the 14th day of the 16-day gestation period. Nearly half the number of hamsters dying at this time exhibits the renal lesions characteristic of the generalized Shwartzman reaction.

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