thrombi in capillaries and venules are a key histopathologic feature of the reaction(1); Gram-negative endotoxin promotes coagulation both *in vitro*(13) and *in vivo*(14); anticoagulants, either heparin(15) or Dicumarol® (16), prevent the reaction; and, finally, fibrinolytic agents also prevent the reaction(17). But clearly, the ability to trigger diffuse intravascular coagulation can not be the sole essential requirement—the least common denominator— of all agents capable of provoking the local Shwartzman reaction. Diffuse intravascular coagulation did not cause thrombi to localize at the prepared site, which strongly suggests that all of the factors needed for localization were not provided by the preparatory agent. Apparently, the provoking agent must also contribute to the processes which localize the platelet-white cell-fibrin thrombi at the prepared site with the consequent production of the hemorrhagic necrosis of the local Shwartzman reaction.

Summary. An infusion of thrombin will not provoke the local Shwartzman reaction in rabbits prepared with an intradermal injection of Gram-negative endotoxin. Therefore, the ability to trigger an episode of diffuse intravascular coagulation can not be the sole requirement of a provoking agent for the local Shwartzman reaction.

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Neonatal Cortisol Administration and Immunological Impairment In the Adult Rat.* (31842)

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The consequences of neonatal hormonal imbalance may not become apparent until long after correction of the brief abnormality. Thyroxine deficiency in early life, for example, will lead to mental retardation unless exogenous hormone is administered within the first 6 to 12 months of life(1); in the rat, the critical period for thyroxine treatment is the first 14 days(2). Similarly, in the female rat, neonatal testosterone propionate adminis-

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TABLE I. Effects of a Single Injection of Cortisol on Postnatal Day 1 upon Immunological Capacity of the Adult Rat at 60 to 70 Days of Age. (Number of animals indicated in parentheses.)

		Immunological response				Thymus wt (mg)‡
		S. typhosa		Sheep RBC		
Group	Body wt (g)	Agglutinin titer*	%†	Hemolysin titer*	%†	Body wt (g)
Cortisol	144 (12)	.42 ± .29 (12)	8 (1)	2.6 ± 1.4 (8)	25 (2)	3.93 ± .15
Control	190 (13)	3.4 ± .8 (13)	75 (9)	10.0 ± .7 (10)	100 (10)	4.11 ± .32
Significance		<.01		<.001		N.S.

* Number of serial 2-fold serum dilutions (averages with S.E.) which gave a 3+ agglutinin response to *Salmonella typhosa* H antigen, or a 3+ hemolysin titer to sheep red blood cells.

† Percentage and number of animals giving 3+ agglutinin titer at 3 2-fold serial serum dilutions or greater, or a 3+ hemolysin titer at 7 2-fold serial dilutions or greater.

‡ Data for thymus/body weight taken from previous publication(3).

tration during the first 5 days of life will induce permanent sterility and interfere with normal cyclic gonadotropin secretion(3). Several workers have reported that neonatal cortisol administration to the mouse will cause a complex of symptoms similar to that produced by neonatal thymectomy(4,5). These animals are characterized by runting, loss of hair, early death, and altered brain DNA concentration. In the rat, the symptoms of neonatal thymectomy and of cortisol treatment are less severe. The cortisol treated animals remain somewhat runted up to at least 3 months of age, are fertile and have a normal pituitary-adrenal response to stress(6). The similarity in symptomatology between neonatal cortisol administration and thymectomy and the well known thymolytic effects of the adrenal-cortical hormone suggest(6,7) that the hormone treated animals have been, in effect, functionally thymectomized in early infancy. As neonatal thymectomy interferes with the normal development of the immunological response mechanism(8,9,10), neonatal cortisol administration might also have a deleterious effect on the immunological capabilities of the adult organism.

Methods. Complete litters of Sprague-Dawley rats born in this laboratory either were injected subcutaneously within 24 hours of birth with 1 mg cortisol acetate, or were handled briefly. Thereafter they were undisturbed until weaning at 25 days of age. At 60 to 70 days of age they were challenged with 2 separate antigens; a single intraperitoneal injection of .3 ml of *Salmonella typhosa* H antigen (O.D. .29 at .430 mμ) and/or 3 daily intravenous injections of a 10% suspension of washed sheep red blood cells, 0.1 ml/100 g body weight. Blood was removed by heart puncture 8 days later and agglutinin for *S. typhosa* cells and hemolysin for sheep red blood cells were determined on serial dilutions of serum.

Results and discussion. Results are shown in Table I, and indicate that the titers for the cortisol treated animals are considerably less for both types of antibodies. Thymus weights in the rat following neonatal cortisol administration are not permanently compromised since in the adult rat organ weights expressed on a body weight basis are the same for treated and control animals (Table I).

Our results, therefore, do not as yet specifically implicate the thymus; nevertheless, in view of the active thymolytic effects of the adrenal-cortical hormones it is tempting to suggest that neonatal cortisol administration may have produced a functional thymectomy at a critical period in the maturation of the immune mechanism. During such critical periods in late fetal or early postnatal life an excess of adrenal-cortical hormones, produced either endogenously by maternal or neonatal stress, or exogenously by prescribed medication, may interfere with the normal expression of immunological competence at later stages of development. The neonatal block to ACTH secretion in response to stress(11) may, thus, provide for the development of an effective immunological response system.

Summary. Newly born rats, on the first postnatal day of life, received a single, intraperitoneal injection of 1 mg cortisol and 60

to 70 days later their immunological response to 2 different antigens, sheep red blood cells and *S. typhosa* H, was assessed. The hormone treated rat produced less antibodies in response to both these antigenic challenges than did control animals.

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Location of the Estrogen Effect on Uterine Glucose Metabolism.* (31843)

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One of the rapid and most pronounced responses of uterine target tissue to estrogen is an acceleration of the pathways of glucose metabolism. Examples of this effect, including glucose utilization and glycogen synthesis, have been reported by several workers (1,2,3). Recently, Nicolette and Gorski(4) found a relationship between increased glucose metabolism and other estrogen effects when they showed that estradiol-17β increased the incorporation of radioactivity from ^{14}C-labelled glucose into uterine lipid, CO_2, RNA, and protein. These studies imply that some early step in uterine glucose metabolism is involved in the tissue response. Characteristics of this response suggest that the estrogen effect could be located: (1) in the Embden-Meyerhoff pathway, (2) the pentose phosphate cycle, or (3) some step common to both these pathways.

The experiments described here have utilized measurements of $^{14}CO_2$ production and radioactivity incorporation into lipid from labelled substrates to study the pathways in glucose metabolism which are influenced by estrogen. These studies reveal that the estrogen-sensitive step is probably located prior to the formation of glucose-6-phosphate from glucose. This indicates that either the transport step or the phosphorylation step is the site of early estrogen action on uterine glucose metabolism.

Materials and methods. Immature, female, Holtzman rats (21-24 days old) were injected intraperitoneally with 5 μg of estradiol-17β dissolved in .5 ml of 1% ethanol in 0.15 M NaCl. Control animals received only the injection vehicle. Animals were killed 2 hours after treatment, uteri were excised, weighed, and transferred immediately to ice-cold incubation medium in 25 ml Erlenmeyer flasks. Uteria were incubated in an atmosphere of 95% O_2-5% CO_2 at 37°C in 2.0 ml of Eagle's tissue culture medium HeLa (Difco). This medium contains glucose (90 mg%) but does not contain pyruvate. The incubation medium contained 0.1 μc/ml of glucose-1-^{14}C (3.14 mc/m mole) or glucose-6-^{14}C (3.56 mc/m mole) as substrate. Where pyruvate-3-^{14}C was used, the incubation medium contained 0.05 mc/ml (3.12 mc/m mole). Radioactive CO_2 was collected by absorption on hy-

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