yields a curve from which the plasma free fatty acid concentration may be obtained. Use of 0.5 ml of plasma per determination gives optimal results, but the method may be employed with 0.1 ml plasma or less.

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Received November 16, 1964. P.S.E.B.M., 1965, v118.

Modification of Sucrose Adaptation in the Rat. (29913)

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Rats injected intraperitoneally (IP) with hypertonic sucrose solutions adapt to subsequent reexposures to the disaccharide by increasing 1) volume output of urine, 2) sucrose concentration of urine and 3) fraction of the injected load excreted within a 6-hour test period(1). Similar experiments employing intraarterial (IA) loading of the sugar demonstrated that the adaptation generated under these circumstances is qualitatively different from that induced by IP administration. Under conditions of IA infusion, reexposure to sucrose causes a reduction in both total urine volume and the fraction of the load excreted in 6 hours, with no demonstrable difference in sucrose concentrations of urine(2). To determine whether the reductions in urine volume and sucrose excretion after a second IA infusion persist beyond the 6-hour period, experiments were conducted to examine the completeness of sucrose excretion over 24 hours. In addition a series of repeated IA loadings was performed to determine if the adaptive response, once established, was further modified.

Methods. Three groups of male albino rats (Holtzman, 188-239 g) were infused with 2.0 ml/100 g body weight (b.w.) of a 1.46 M solution of sucrose through a chronically indwelling catheter. The tip of the catheter rested in the aortic arch. Prior experiments demonstrated that this load given IA produced a maximum adaptive response with respect to total urine and sucrose excreted. At the time of loading animals were unanesthetized and under moderate restraint(3). All urine voided within the 24-hour period following infusion was collected and analyzed for sucrose(4). Infusions of the same relative load were repeated in each group at 6-day intervals and totaled 4 exposures per group. Urine volumes excreted and urinary sucrose concentrations were measured following each exposure. Data were treated by analysis of variances of independent group means.

Results. A comparison of the sucrose excretion after 6 and 24 hours in unadapted and adapted rats is given in Table I. Unadapted rats (first exposure) excreted most of the load (92.8%) within the 6-hour period following the infusion and increased the fraction of the total load excreted in 24 hours by merely 0.7%. In contrast, adapted animals (second exposure) excreted only 78.5 ± 4.1% (S.D.) of the infused load within

TABLE I. Recovery of Sucrose from Urine as Percentage of Infused Load.*

	Time from infusion		Δ
Exposure	6 hr	24 hr	6-24 hr
1	92.8 ± 6.2† (13)‡	93.5 ± 4.7 (33)	.7
2	78.5 ± 4.1 (12)	85.9 ± 4.2 (30)	7.4
ΔExposure 1-2	14.3	7.6	

* 2.0 ml/100 g body weight of 1.46 M sucrose (50%); intraarterially.
† Mean ± S.D.
‡ No. of animals infused.

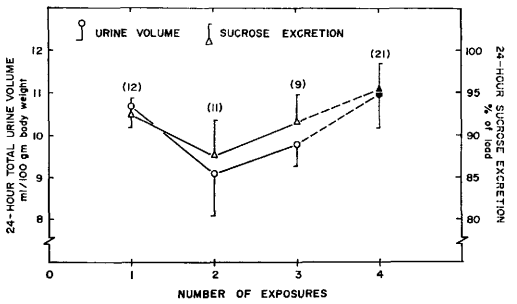

FIG. 1. 24-hr urine output and sucrose excretion as a function of number of exposures to 2.0 ml/100 g body wt of 1.46 M sucrose given intra-arterially. Number of animals in each group is given in parentheses. Exposures 1-3 were conducted on different groups of animals; values for exposure 4 were obtained by pooling data from all animals given the load 4 times.

6 hours and 85.9 ± 4.2% within 24 hours of infusion. Twice exposed animals therefore excrete a standard load more slowly and less completely than do unadapted rats.

Total sucrose excreted (as a percentage of the infused load) and total urine output over 24 hours (ml/100 g b.w.) are shown in Fig. 1 as a function of number of exposures to the load. Animals exposed for the first time excreted 92.5 ± 2.0% of the total sucrose load. After a second exposure the fraction of the load excreted was reduced to 87.7 ± 4.2%, but increased to 91.7 ± 3.2% following a third exposure. This pattern of response in sucrose excretion was statistically significant ($P<0.01$). After a fourth exposure the mean sucrose excretion of all animals tested was 95.4 ± 3.2% of the infused load. The latter data are tentative, however, since they do not meet the requirements for independency and are not included in the statistical treatment.

Changes in total volume of urine excreted in the 24 hours following infusion show a similar pattern to that characterizing the total sucrose excretion. This pattern of response was also significant ($P<0.01$). Combined data for all groups during a fourth exposure suggest a further slight increase in urine output to near initial levels, although these data must also be regarded under those restrictions indicated above.

Discussion. Other studies from this laboratory have suggested that the failure of the adapted rat (2 exposures) to excrete a standard load of sucrose as rapidly and as completely as the unadapted animal may derive from changes in the sensitivity of receptors involved in stimulation or inhibition of antidiuretic hormone (ADH) release(2). Considering the present data it further appears that the adaptations so elicited are only transient, despite continued periodic loading with hypertonic sucrose. Although the process of deadaptation is commonly understood to involve the restoration of initial function subsequent to removal of the stimulus inducing the original adaptation(5,6), these findings suggest that modifying processes may originate during application of the adapting stressor. With specific regard to the sensitivity changes in intravascular volume receptors and osmoreceptors postulated to account for the adaptations characterized, it may be concluded that original function of these receptors is eventually restored, despite the uniform stresses (multiple loadings) imposed on the animals.

The question may be raised at this point whether changes in volume excretion of urine and in total sucrose excretion are merely coincident with or are representative of an overall adaptation to sucrose. Iampietro found that rats, exposed to a single IP load of sucrose which was adapting (in terms of urine volume excretion, urinary sucrose concentration, and total sucrose excretion), better tolerated sucrose loads at levels lethal to unadapted rats(1). It was therefore suggested that adapted animals are able to maintain a greater "tissue tolerance" for the disaccharide than were unadapted animals. These observations have been confirmed in our laboratories with intraarterial loadings. Integration of this information suggests that the process of adaptation to sucrose (tolerance) may be independent of the urine volume and sucrose excretions characterized. Likewise, the same adaptagent (sucrose load) may simultaneously induce 2 processes or adaptates, one that may be further modified with periodic application of the adaptagent (urine volume, total sucrose excretion), while the other continues to be reinforced (sucrose tolerance). The validity of this hypothesis remains to be tested.

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Received November 30, 1964. P.S.E.B.M., 1965, v118.

The Immunoglobulins of Mice. 4. Serum Immunoglobulin Changes Following Birth. (29914)

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A characteristic pattern of serum changes in 3 immunoglobulins, *i.e.*, the IgG (7S γ_2-globulin, IgA (γ_{1A}-globulin) and IgM (γ_{1M}-globulin), has been described following birth of the human infant(1-3). Quantitative studies of individual immunoglobulin changes after birth, however, have not been described in other species. Four major immunoglobulin classes, the 7S γ_2-globulins, 7S γ_1-globulins, γ_{1A}-globulins and γ_{1M}-globulins were recently identified in mice(4). The present studies were undertaken to determine the serum levels of these immunoglobulin components in the newborn and to characterize the immunoglobulin changes following birth of the normal mouse. Three mouse strains were studied and found to be similar. Both similarities and differences between man and mouse were observed.

Methods. C57BL/6JN, C3H/HeN, and GP (general purpose, white Swiss mice maintained in a closed colony at the NIH) mice were obtained from the Animal Production Section of the NIH at one day of age, one week of age, or at weekly intervals thereafter. Animals were weaned at 3 weeks of age. Ten or more animals were bled at each date to obtain enough serum for the various experiments. All animals were housed and fed in a similar manner throughout the study.

Quantitative serum levels of 7S γ_2-globulin, 7S γ_1-globulin, γ_{1A}-globulin and γ_{1M}-globulin were measured in antibody-agar plates using essentially the same method described elsewhere for measuring the human serum immunoglobulins(5). Briefly, addition of antigen (mouse immunoglobulin) to wells in an antibody-containing agar plate results in antigen-antibody precipitate rings, the diameter of which reflects the concentration of antigen.

Specific antiserums were prepared from antiserums produced in rabbits by immunization with 7S γ_2-myeloma protein (5563), 7S γ_1-myeloma protein (MPC-25), γ_{1A}-myeloma protein (MPC-1) and normal γ_1-macroglobulin(4).

Antibody-agar plates were prepared by pouring a solution containing 8 ml of diluted antiserum and 8 ml of 3% Noble agar onto a 3¼ × 4 inch glass plate. The antiserum dilution for the individual immunoglobulin determinations varied from 1:10 to 1:60 depending on the potency of the antiserum. The highest dilution of antiserum which gave distinct end points (precipitation rings) was used. Thirty-six antigen wells were cut in the antibody-containing agar plates using a plastic template(5). Six of the wells in each plate were used for standard reference samples of known protein concentration. In practice a single serum sample was used as a reference on all antibody-agar plate tests. The level of each immunoglobulin in this serum was determined by comparison with the following purified immunoglobulin preparations: two 7S γ_2-myeloma proteins, two 7S γ_1-myeloma proteins, two $\gamma_{1A}(\beta_{2A})$-myeloma proteins and a preparation of normal mouse γ_{1M}-globulin.