Use of a Deficient Ration for Chicks in Bioassay of Gonadotrophic Hormones.* (20658)

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Commercial chick rations are frequently used during the study of gonad response to hormone injections(1). Since the chicks gain weight on this ration, the hormone dosage must be sufficient to elicit a testes weight response over and above the normal increase. Some investigators maintain their chicks without food or water over the experimental period, depending on the unabsorbed yolk to sustain life for 96 hours, after which inanition begins (2). This inhibition of growth results in a significant weight increase at lower levels of hormone dosage. However, the term of the experiment must be short and injections made at frequent intervals. Therefore the full potency of each injection is limited and the overall sensitivity may be reduced.

It was observed that a corn-cob meal ration inhibited growth and caused the endocrine glands to remain infantile in size. These conditions allowed for a maximal dosage response and a longer interval between injections. Based upon these considerations a method for testing pituitary gonadotrophic hormones was devised.

Materials and methods. One-day-old White Leghorn cockerels were kept in an electric brooder and maintained either on commercial chick starter ration or on the corn-cob meal ration. The tested pituitaries, with a mean fresh weight of 11.3 mg (range 10.6-11.8 mg), were obtained from male Rockland rats, 10-12 months of age. They were homogenated and diluted to a volume of 1.25 cc in distilled water. Each volume contained one rat pituitary or fraction thereof. The experimental chicks received 5 daily injections into the axillary region with 0.25 cc of the homogenate. The birds were sacrificed on the sixth day and the testes removed and weighed.

Results. The results are presented in Table I. With the chicks maintained on corn-cob meal ration it was possible to show a graded response of chick testes weight to fractions of whole rat pituitary. There was a significant difference between the 1, ¾ and ½ fractions compared to the response of the non-injected chicks. There was no significant difference in the ¼ group when it is compared with the ½ and 0 groups. Therefore the minimum dosage required to elicit a response in chick testes under these conditions was ½ rat pituitary homogenate per chick.

With chicks maintained on a commercial ration the data show that to elicit a significant gonadotropic response a dosage of at least 1 rat pituitary per chick must be administered.

There was no significant difference between

TABLE I. Graded Response of the Chick Testes to Whole or Fractionated Rat Pituitary Injections.

Group	No. of chicks	Ration	Mean testes wt (mg) ± stand. error	Range (mg)
1 pit/chick	8	Corn-cob*	18.2 ± 1.10	15.6–24.4
¾ "	12	"	14.3 ± .98	8.8–20.6
½ "	10	"	11.5 ± .65	8.6–14.1
¼ "	9	"	10.6 ± .93	7.6–14.0
Saline inj.	10	"	9.4 ± .4	8.2–12.0
"	9	Commercial†	18.4 ± 1.0	12.0–21.8
1 pit/chick	9	"	25.6 ± 1.9	16.4–36.0

* Finely ground yellow corn-on-cob meal.
† Chick Starter Ration, Security Mills, Knoxville, Tenn.

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injections of one or three pituitaries per chick maintained on corn-cob meal ration suggesting that a threshold response to gonadotropic hormones had been reached with injections of one rat pituitary per chick.

Summary. Day-old cockerels were kept on a corn-cob meal ration while testing homogenates of rat pituitaries for gonadotropic hormones. The chicks failure to grow made the testes weight a more sensitive indicator of gonadotropin when contrasted with the cockerels on a balanced ration. With the corn-cob meal ration the chick assay method was significant with ½ of a rat's pituitary.

1. Robinson, G. E., Jr., and Nalbandov, A. V., *J. Ani. Sci.*, 1951, v10, 469.

2. Breneman, W. R., and Mason, R. C., *Endocrinol.*, 1951, v48, 752.

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Formation, Flow, and Reabsorption of Cerebrospinal Fluid in Man.* (20659)

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On the basis of data obtained from multiple simultaneous isotopic tracer studies in man, employing various suitable combinations of Na-24, K-42, Cl-38, Br-86, P-32, HTO, D_2O and radio-iodinated human serum albumin, we have been led to a unified theory of cerebrospinal fluid (CSF) formation, flow and reabsorption which is at variance with the classical and currently held concepts. The textbook teaching(1) is that CSF is formed by the choroid plexuses (Dandy, 2) of the cerebral ventricles whence it flows into the spinal and epicerebral subarachnoid spaces. Here it is considered free to circulate until it is finally reabsorbed, presumably largely or wholly at the arachnoid villi (Weed(3)).

We wish to present evidence that CSF is elaborated throughout the cerebrospinal fluid system independently of flow from one area to another. It is derived both from the choroid plexus in the ventricles, and in the subarachnoid space from the vascular bed of the pia. The reabsorption of CSF, in so far as water and electrolytes are concerned, has similarly been demonstrated by us to occur throughout the system independently of flow. These elements of the fluid enter and leave the ventricles and subarachnoid space by direct molecular capillary exchange, and hence may be considered to be in a state of dynamic equilibrium with plasma, similar to that of other fluid compartments of the body.†

Methods of study. After a large number of tracer studies had been done in patients with normal CSF systems, it became evident that a precise compartmental analysis of the data involved equations of a fair degree of complexity, and more variables than could be adequately measured, the most troublesome in this respect being the rate of flow between compartments. Accordingly we set out to limit the variables insofar as possible and to test the validity of a number of possible compartmental models of CSF physiology in a series of critical experiments. To this end, we sought patients for study in whom it would be possible to isolate the main ventricular compartments from the subarachnoid space. Two such patients were found; and the studies presented below, on which our unified concept of the CSF system rests, were carried out in them. These patients had developed complete blockage of CSF outflow from the large lateral ventricles as the result of tumor encroachment on the third ventricle over five years ago. At that time they were restored to a normal state of CSF pressure and dynam-

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† In this paper, the mechanism of exchange is not considered, i.e., whether by simple diffusion or some form of active transport.