TABLE II. Ascitic Fluid in Rabbits with Thoracic Caval Constriction Following Two-Stage Portal Ligation.

Exp.	Onset of ascites (days)	S.G.	T.P. (g/100 cc)	A/G
1	3	1.012	3.6	0.9
2	4	1.013	3.5	0.8
3	4	1.016	4.2	1.0
4	4	1.016	4.0	1.1
5	3	1.015	4.4	1.0
6	4	1.015	3.9	0.9
7	4	1.013	4.1	0.9
8	3	1.014	4.0	0.9
			Avg 3.9	0.9

with silk. In none of these animals was ascites demonstrable by frequent paracentesis.

One week following the second-stage portal ligation, thoracic inferior caval constriction was performed on these rabbits, using the same technic as was used in the control series. The formation of ascites was usually demonstrated by paracentesis within 4 days. This fluid was examined for total protein and A/G ratio every 7 days for a period of 3 months. No appreciable change in average total protein or A/G ratio was noted in comparison with the animals with thoracic inferior caval constriction alone. Total protein averaged 3.9 g per 100 cc, A/G ratio 0.9, and the specific gravity varied from 1.012 to 0.016. Table II outlines the results obtained in this group of animals. These rabbits did not show clinical jaundice. There was no evidence that 2-stage ligation decreased the total volume of ascitic fluid.

Conclusion. 1. Constriction of the thoracic vena cava in rabbits produces ascites. 2. 2-stage portal ligation in rabbits does not cause demonstrable ascites. 3. In rabbits, the ascitic fluid formed by caval constriction in the chest is not affected by previous 2-stage portal ligation.

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Effects of Administration of Gonadotropic Hormone on Vitamin A Deficient Rats. (18419)

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It had been shown by Mason(1), in particular, that the effect of vit. A deficiency on the male rat amounted to a virtual castration as far as secondary sexual characters are concerned. This could be interpreted as meaning that in vit. A deficiency target organs did not respond to circulating androgens or it could mean that androgens were not synthesized or released. To answer this point, Mayer and Truant(2) administered testosterone to vit. A deficient castrates and noncastrates and to their controls. It was found that the response of target organs of the deficient animals to injected androgens was essentially normal. In particular, the secondary sex organs became extremely hypertrophied even while severe losses of weight due to the deficiency were taking place. It was concluded that in vit. A deficiency, synthesis or release of androgens was interfered with. In order to find out whether this was due primarily to a testicular lesion or to a pituitary hypofunction, it was decided to study the effects of administration of gonadotropic preparations on vit. A deficient animals and their controls.

Method. The animals used were male Wistar albino weanlings, of the Harvard-Hisaw colony, 22 days of age. Their average weight was 50.75 g. These animals were kept in an air-conditioned room (about 26°C) at constant humidity and were alternately 12 hours in darkness and 12 hours in artificial light. The diet used had the following composition: Casein 25%, "Salt IV" mixture 4%, Corn

1. Mason, K. E., *Am. J. Anat.*, 1933, v52, 153.
2. Mayer, J., and Truant, A. P., PROC. SOC. EXP. BIOL. AND MED., 1949, v72, 436.

TABLE I. Effect on Body and Organ Weight of Gonadotropic Hormone Administration.*

	Controls	Controls and hormone	Deficient	Deficient and hormone
Final† wt gain	186 g	177 g	117 g	115 g
Max. wt gain	id	id	119 g	121 g
Testes	2.65 (11.2)‡	2.30 (10.4)	1.92 (11.5)	1.46 (9.2)
Seminal vesicles§	0.39 (1.7)	1.595 (7.2)	0.33 (1.9)	1.46 (9.2)
Kidneys	2.51 (11.2)	2.65 (12.0)	1.92 (11.4)	1.92 (12.1)

* Each set of values corresponds to 7 animals. Statistical treatment is not given, as the differences observed between groups, even when small, derive their significance from the fact that they duplicate numerous classical results (*loc. cit.*) obtained with testosterone.

† The difference between "Final" and "Maximum" gain weights is due to the fact that when the animals were sacrificed, the degree of deficiency reached was such that several animals had already lost weight.

‡ Figures in parentheses represent ratio: $\frac{\text{organ wt}}{\text{body wt}} \times 10^3$.

§ Prostates and epididymes showed size changes in the same direction as seminal vesicles.

oil 5%, Sucrose 65.9%, Choline 0.1%, and contained supplements of thiamine, riboflavin, calcium pantothenate, pyridoxine, biotin, folic acid, α-tocopherol, menadione (vit. K) and viosterol (vit. D). Control animals received orally 1200 I.U. vit. A every 7 days. The animals receiving hormone were injected every other day subcutaneously with 0.025 cc of "APL" chorionic gonadotropin* in saline solution corresponding to 100 international units gonadotropic activity. The other animals received control saline injections. Two weanlings were sacrificed at the start of the experimental period to provide a baseline for histological examination. Forty-four other animals were used on the experiment. They were divided into equal groups: control animals, control animals receiving hormone, deficient animals, deficient animals receiving hormone. Two animals per group were sacrificed for histological examination after 10 and 20 days respectively. All other animals were sacrificed after 30 days, by which time about one-fourth of the deficient animals were losing weight, with another fourth "plateaued." Body weights, as well as the weights of organs which have been shown to be affected by androgens(3-7) were recorded. Histological examination of the testes was conducted.

Results and discussion. Table I gives the final and maximal weight gains of all groups as well as the weights of kidneys, testes and seminal vesicles, and the ratios of the weights of these organs to body weight. In the control animals, the classical effects of androgen administration can be noted. Body and testes weight are slightly decreased, kidney weight is slightly increased. The considerable hypertrophy of the secondary sex organs—seminal vesicles as well as prostates and epididymes—obtainable by testosterone injection is, as could be expected, duplicated by gonadotropic hormone administration. In the deficient animals the weight response of testes, kidneys and especially seminal vesicles follows that of the controls. From consideration of organic weights alone no qualitative or, (when the differences in body weight are taken into consideration) quantitative differences appear between the reactions to gonadotropic hormone of controls and deficient animals. This can be taken to demonstrate that the primary "castrating" lesion in vitamin A deficiency is the decrease of the secretion of pituitary gonadotropic hormone rather than the inability of the testes to produce androgens upon gonadotropic stimulation.

Histological examinations proved fruitful.

* We wish to thank Ayerst, McKenna and Harrison, Ltd. for their generous gift of gonadotropic hormones.

3. Selye, H., PROC. SOC. EXP. BIOL. AND MED., 1941, v46, 142.

4. Selye, H., *J. Endocrinol.*, 1939, v1, 208.

5. Korenchevsky, V., and Ross, M. A., *Brit. Med. J.*, 1940, v1, 645.

6. Paschkis, K. E., Shay, H., Gershon-Cohn, J., and Fels, S. S., *Am. J. Physiol.*, 1940, v129, 191.

7. Pfeiffer, C. A., Emmel, V. M., and Gardner, W. U., *Yale J. Biol. Med.*, 1940, v12, 493.

As classically described administration of gonadotropic hormone had little detectable effect on seminiferous tubules and spermatogenesis in normal animals. It had a striking effect on the interstitial tissues, more than doubling the number of Leydig cells. Vitamin A deficiency alone, as previously indicated(1,8) decreases the number of spermatozoa and spermatides. The number of first and second order spermatocytes was normal, with the spermatogonias somewhat smaller and generally quiescent. The picture in simple vitamin deficiency is therefore one of decreased spermatogenesis, but, at least in the relatively early stage, without radical, generalized pathology. On the other hand, when gonadotropic hormone was administered to vitamin A deficient animals, very definite lesions were observed. Striking increases in the number of Leydig cells (interstitial tissue) were obtained as in normal animals, but many cells appeared to be in a state of lysis and presented abnormally shaped nuclei. Delicate interconnective tissue fibrils could be observed between many cells (early collapse fibrosis). While gonadotropic hormone administration had practically no effect on spermatogenesis in the normal animal, it had definitely inhibitory effects in the deficient animal. No ripe spermatozoa were visible. Spermatides were also totally absent. The number of spermatocytes of the first and second order was decreased, but many of them presented mitotic figures; the "block" appeared therefore to be between the second order spermatocyte and the spermatide stages. At the level of the spermatocytes many agglutinated and partially lyzed cells with vacuoles were to be seen. Spermatogonias, although somewhat fewer and smaller than normal, presented many mitotic figures, thus confirming the localization of the block, and indicating that a new series of spermatozoa production would be possible if vitamin A became again available. The number of Sertoli cells was increased. Administration of gonadotropic hormone to vitamin A deficient animals, while it must still elicit production of androgens by the interstitial tissue, thus also results in effects not only quantitatively but qualitatively different from those produced in normal animals. Decrease in pituitary gonadotropic activity in vitamin A deficiency could thus perhaps be considered one of the defense mechanisms of an organism which lacks an essential tissue nutrient. Differential effects of follicle stimulating (FSH) and luteinizing (LH) hormones are being studied.

Summary. 1. To find out whether degeneration of secondary sex organs in vit. A deficient male rats is due to the inability of the testes to produce androgens or to a decrease in the activity of the pituitary, gonadotropic hormone was administered to vit. A deficient animals and to their controls and the effects compared with control conditions. 2. The weight response of "target organs," *e.g.* kidneys and seminal vesicles was found to be essentially normal in vit. A deficient animals, thus showing that androgens could still be produced by the testes. 3. On the other hand, it was observed that gonadotropic hormone had a definitely injurious effect on vit. A deficient animals, in particular producing a block at the spermatocyte level with consequent arrest of spermatide production.

8. Wolbach, S. B., and Howe, P. R., *J. Exp. Med.*, 1925, v42, 753.

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