There was no change in the biochemical reactions. All the other organisms used, including 2 other strains of *Staphylococcus,* showed no variation from normal when grown in the presence of colchicine. The growth of *Streptococcus hemolyticus* was inhibited by 1% of colchicine; 0.50% and 0.25% had no apparent effect. There was marked but not complete inhibition of growth of *M. catarrhalis* in 2% colchicine, some inhibition in 1% but none in 0.50% and 0.25%. The staphylococci and *B. megatherium* grew equally well in all concentrations of colchicine used. There was no evidence of any stimulating effect on the growth of any of the organisms.

Blakeslee[2] says that colchicine affects only the cell division of the chlorophyl-bearing plants and that the fungi including the bacteria are not affected. Jennison[3] could detect no change in the rate of reproduction or colony morphology of bacteria in the presence of colchicine. With the exception of one strain of Staphylococcus which showed a temporary variation in cell and colony morphology when grown in the presence of colchicine, our results are in accord with these observations but further indicate that colchicine does not affect the cell metabolism of bacteria.

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The Liver and Endogenous Androgens.*

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It is well known that most androgens and estrogens are either inactive when administered orally, or are less potent than when administered subcutaneously. In the case of the estrogens, experimental evidence has been offered to explain this phenomenon. All workers agree that the lack of effectiveness with oral administration is due to inactivation of estrogens in the liver. When natural estrogens are incubated *in vitro* with liver,[1,2] their potency is lost.

2 Blakeslee, A. F., *Science,* 1939, **89**, 10.

3 Jennison, M. W., *J. Bact.,* 1940, **39**, 20.

* Supported in part by a grant from the Josiah Macy, Jr., Foundation.

1 Zondek, B., *Skand. Arch. f. Phys.,* 1934, **70**, 133.

2 Heller, C. G., *Endocrin.,* 1940, **26**, 619.

When ovaries are implanted intra-mesenterically so that the venous drainage is through the liver, the animal manifests changes characteristic of castration but, when the same ovary is later regrafted into the axillary region, the castration effects disappear.[3] Talbot[4] showed that impairment of liver function by CCl_4 apparently increased the concentration of endogenous estrogen in the blood stream as evidenced by increase in uterine weight.

Concerning the possible inactivation of androgens by the liver, only two reports have been offered. Biskind and Mark[5] showed that pellets of testosterone propionate are ineffectual when implanted into the intact spleen, but not when implanted into the spleen after the original blood supply of this organ has been altered. This indicates that inactivation of the testosterone propionate occurs only when it passes from the site of absorption directly through the portal system. Biskind,[6] by the same type of experiment, showed that methyl testosterone is also inactivated when it passes first through the portal system. In view of the known oral effectiveness of methyl testosterone, in contrast to all other androgens, it seems probable that this substance is removed from the gastro-intestinal tract by some route other than the portal system.

The present report is concerned with the possible rôle of the liver in the inactivation of testicular androgens. The transplantation method devised by Golden and Sevringhaus was used.

Twenty-five males, 20 to 23 days old, were castrated and, in each case, one-half of a testis was sutured into the gastro-splenic mesentery. At the same time 21 males of the same age were castrated and one-half a testis was implanted subcutaneously into the groin of each.

One or two months after implantation the surviving animals were killed. In each case the size and appearance of the penis was noted, the general character and vascular relationships of the implant were established, and the ventral prostates and seminal vesicles were removed and weighed. In some of the animals the thymus was also weighed. It was thought that the thymus might present an additional check for the presence or absence of androgens, inasmuch as thymic hypertrophy after castration has been mentioned in the literature.

[3] Golden, June B., and Sevringhaus, E. L., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 361.

[4] Talbot, N. B., *Endocrin.*, 1939, **25**, 601.

[5] Biskind, G. R., and Mark, Jerome, *Bull. Johns Hopkins Hospital*, 1939, **65**, 212.

[6] Biskind, G. R., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 259.

Part of the graft tissue from each animal was preserved in Bouin's fluid.

With a few exceptions, the findings were fairly uniform. In almost all cases the implanted tissue appeared to be fairly healthy, seminiferous tubules were visible under the dissecting microscope. In the intra-mesenteric location, the grafted tissue was usually spread out over a considerable area, closely associated with the pancreas, so that the tubules in these grafts were somewhat more dispersed than in the subcutaneous grafts.

The animals with intra-mesenteric implants gave no evidence of androgenic stimulation. The penis was small, poorly developed and barely evertable; the prostates and seminal vesicles were small and atrophic in appearance. The animals with subcutaneous implants, however, showed some degree of androgenic stimulation in that the penis was generally normal in size and structure and the prostates and seminal vesicles were well above the castrate level in weight.

The weight findings in those animals having healthy implants are recorded in Table I. In the first set of experiments, the number of animals was small, therefore no attempt at statistical analysis was made. In the second set of experiments the prostate and seminal vesicle weights of the subcutaneous group were significantly larger than those of the intra-mesenteric group. The thymus weights were not significantly different.

The implants from all animals were sectioned and examined microscopically. In most cases the implanted tissue appeared to be well established and well vascularized. Regions of lymphocytic

TABLE I.
Prostate and Seminal Vesicle Weights in Rats with Testicular Implants.

Situation of implants	No. operated	No. survived to autopsy	No. with healthy implants	Avg body wt	Avg prost. wt	σ	Avg S.V. wt	σ	Avg thymus wt	σ
Operated at 22-23 days of age. Implants resident for 2 months.										
Intra-mesen.	10	7	5	213	4.92		5.93			
Subcut.	10	4	4	187	29.37		29.37			
Operated at 20 days of age. Implants resident for 1 month.										
Intra-mesen.	15	13	12	146	5.26	0.29	7.03	0.26	509.6	31.9
Subcut.	11	11	10	142	23.77	4.19	17.85	2.89	433.9	45.0

σ derived by the formula $\sqrt{\frac{\Sigma\delta^2}{n(n-2)}}$

Significant difference $> 3\sqrt{(\sigma_1)^2 + (\sigma_2)^2}$

infiltration and fibrosis were observed. The seminiferous tubules which were found in all healthy implants resembled those of experimental cryptorchid testes in that generally Sertoli cells alone were present, although occasionally a few spermatogonia were observed. Interstitial cells were present in all implants. The number of interstitial cells varied from a few scattered cells between the tubules to fairly large areas of densely packed cells. The latter condition may be regarded as true interstitial cell hypertrophy. Generally the grafts which were *in situ* for 2 months exhibited better development of interstitial cells than those which were only one month old.

One fact has been shown by these experiments. If viable testicular tissue is situated so that its venous drainage passes directly through the liver, there is no evidence of androgenic stimulation or maintenance in the accessory structures. If, however, the testicular tissue is located so that it is associated with the peripheral circulation, there is some androgenic activity registered in the accessories. The conclusion that the liver is responsible for the lack of androgenic effect in the case of the intra-mesenteric grafts is valid only if it can be shown that the graft tissue in this location is actually producing androgens. Jeffries[7] and others have shown that testes rendered cryptorchid continue to produce androgens, in normal or nearly normal amounts, for a considerable period, even when the germinal elements are completely degenerate. In the grafted tissues from the animals reported here, interstitial cells were present and, in some cases, hypertrophied. This finding cannot be regarded as absolute proof of secretory function in the grafted tissue, but is strongly indicative of such function.

Summary. When testicular tissue was implanted into the immature rat so that its venous drainage passed through the liver, there was a lack of androgenic stimulation evident in the castrate condition of the penis, prostate and seminal vesicles after a period of one to 2 months. When the testicular tissue was implanted subcutaneously, some androgenic effect on the penis and accessories was obtained. Interstitial cells in varying numbers were present in all grafts. This finding indicates probable endocrine function by the implanted tissue. It is tentatively concluded that the lack of androgenic stimulation in animals with intra-mesenteric implants of testicular tissue is due to inactivation of testicular androgens by the liver. This is in agreement with similar experiments using implanted crystals of testosterone propionate and methyl testosterone.[5,6]

[7] Jeffries M. E., *Anat. Rec.*, 1931, **48**, 131.