have a completely formed penile urethra. In eight animals (all from different litters) the testes were in abnormally high position and in three, the testes were in the typically female position, at the base of the kidney.

Eight of these new-born males (each from a different litter) have been serially sectioned to date. One animal (0.5 mg estradiol dipropionate) showed marked inhibition of the ventral prostatic diverticula and a moderate inhibition of the posterior diverticula. In another animal (1.0 mg estradiol dipropionate) the ventral prostatic diverticula were absent and the posterior diverticula were scanty. In six animals (2.0 to 4.0 mg estradiol dipropionate) the prostatic diverticula were entirely absent. Furthermore, in each of these six animals there was a vagina which was comparable in development to that found in the normal new-born female. In four of these six cases marked inhibition of the right vas deferens was found. The lumen of the vas was absent throughout most of its length and, in some regions, even the epithelial cells had apparently completely degenerated. In all animals the seminal vesicles exhibited some inhibition or departure from normal development in that the cranial flexure which is typical of this organ at this stage was absent. The epididymides also showed evidence of inhibition inasmuch as the convolutions of the ducts were less numerous than in the normal males.

On the basis of the few animals observed, it seems that the amount of development of female structures (vagina and nipples) and inhibition of male structures has a fairly definite relationship to the dosage given.

The females in these litters have not been examined microscopically to date. However, some changes from the normal have been grossly visible. Large nipples have been present in the new born. Normally nipples do not appear in the female rats of our colony until the fifth to tenth day. Usually in the same litter the females had more and better developed nipples than the males. The uteri were grossly enlarged and apparently distended. The development of the ovarian capsule had been inhibited; with the higher dosages no ovarian capsule was present.

CONCLUSIONS

The administration of large amounts of an estrogenic substance to the pregnant rat has so modified sexual development of genetic male fetuses that feminized males or intersexed animals have resulted.

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XANTHINE OXIDASE: AN ALLOXAZINE PROTEID

A XANTHINE oxidase preparation has been obtained that is 500 times more active per unit dry weight than the whole milk used as a source. The activity has been determined by measuring manometrically the oxygen consumption, usually with hypoxanthine as the substrate, though xanthine and aldehydes may also be employed. Solutions of this enzyme preparation containing 6 mg/cc have a strong golden brown color and possess an absorption spectrum with a band in the visible lying between λ400–500 mμ. This band disappears if hypoxanthine is added to a solution from which air is excluded. The original color can then be rapidly restored by the admission of air. If the spectrum of the reduced enzyme preparation is subtracted from that of the oxidized form, a spectrum is obtained which is similar to that of the "gelbe ferment" in having two bands centered at λ370 mμ and λ465 mμ, respectively. The prosthetic group may be split off from the protein by the addition of acid or alcohol. Such solutions are pure yellow in color, fluoresce strongly and possess the characteristic absorption spectrum of a flavin with two bands centered at λ450 mμ and λ375 mμ. Definite proof of the flavin nature of the prosthetic group is furnished by the fact that it can be quantitatively converted by the method of Warburg and Christian[1] into a lumiflavin, the absorption spectrum of which is identical with that given by these workers. Complete separation of the flavin part from the protein without destruction of the latter has not yet been accomplished. It is, however, possible to obtain a partial separation. The protein part so obtained shows a 3–4 fold increase in activity on the addition of the flavin component. The flavin alone is inactive. If the flavin containing co-ferment of the amino acid oxidase recently isolated by Warburg and Christian[2] or lactoflavin phosphate is substituted no increase in activity is obtained. It therefore appears that xanthine oxidase is to be classified as an alloxazine proteid whose active group is of a different composition from those flavins hitherto known. Further details will be published elsewhere.

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[1] O. Warburg and W. Christian, *Biochem. Zeits.*, 266: 377, 1933.
[2] O. Warburg and W. Christian, *Biochem. Zeits.*, 296: 294, 1938.