Summary: (1) Weights of liver and spleen obtained at all months of the year on 499 male and 444 females, healthy, adult ring doves demonstrate that a true sex difference exists. Though the male body weight is slightly larger, the male livers and spleens are smaller, 9.4%, and 23.5%, respectively. (2) A true seasonal increase in size of liver and spleen occurs in spring and summer in both sexes (10.4% and 12.0% in ♂♂; 6.1% and 4.3% in ♀♀). (3) These changes in spleen and liver are positively correlated with size changes in testis and ovary; and negatively correlated with size changes in the thyroids of these animals.

[1] Donaldson, H. H., *The Rat*, Philadelphia, 1924.
[2] Latimer, H. B., *J. Agr. Res.*, 1924, xxix, 363-397.
[3] Riddle, O., *Am. J. Physiol.*, 1925, lxxiii, 5-16.

3909

Significance of Female Sex Hormone Reaction in the Male Blood.

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In 1925, simultaneously and independently, Loewe of Dorpat[1] and one of us with collaborators[2] demonstrated the presence of the female hormone in the circulating blood of females by means of the rodent vaginal spread test.[3] Since then, in numerous publications we have attempted to simplify and standardize the method of extracting and testing human blood for the female sex hormone.[4] Among other applications we advocated the use of this test to determine the sex of pseudo-hermaphroditic individuals in whom we regarded a positive reaction, appearing cyclically, as a proof of the presence of functioning ovaries and feminine sex.[5] Our preliminary work had shown that large quantities of bull's blood (150-100 cc.) gave a negative reaction when extracted by our method. The same applied to concentrated lipoid, HCl, saline and watery extracts of bull's testes, as well as extracts of the hypophysis, thyroid and adrenal, liver, muscle, various proteins, etc.[6] The work of Dohrn,[7] who claimed to have obtained a positive reaction with male urine first called our attention to the possible non-specificity of the Allen and Doisy reaction. After our investigation on male bloods had been completed, the short article of Hirsch,[8] who used our method,

appeared. In the 4 male bloods which he examined, he has found a positive reaction.

To date we have obtained 70 bloods from 55 males. Of these, 10 had to be discarded because the injected mice died early. The technic was that mentioned in our last article,[4] in which 40 cc. of blood were dried with sodium sulphate, extracted with ether, the dry ethereal extract taken up in 2 cc. of water and injected. Our readings are: 0 to —2 = no reaction; 2 to 2+ = weak reaction; —3 to 3 = threshold reaction; 3 to 4 = strong reaction.

Our results are, therefore, based on 60 bloods from 47 patients. Of these, 4 showed a weak reaction (2 to 2+) 3 showed a threshold reaction (—3 to 3), 40 showed a negative reaction.

Two of the individuals investigated were healthy young males from whom weekly, over a period of four weeks, 80 cc. of blood was obtained, permitting us to run a double test (40 cc.). No cyclical reaction was noted, although one test gave a 2, the second sample obtained on the same day reading 0. Neither the age or the fertility of the positive subjects appears to play any rôle. Age 19-22-24-25-45-53-55 years. Children 0-0-0-0-3-5-3.

We extracted 12 urines obtained from males, injecting the concentrates into test mice. No positive results were obtained even with total quantities of 450 to 570 cc., although 5 cc. of urine from pregnant women similarly extracted gave positive results.

We tested the effect of the female sex hormone on capons by injecting a lipoid solution containing 2 rat units daily for 40 days and 5 rat units for 8 days without noticeable effect on the comb, wattles, spurs, or behavior.

The findings may be variously interpreted: (1) The vaginal spread reaction may not be specific. (2) The male and female sex hormone may produce the same reaction in the castrate rodent. (3) Certain males, though apparently normal, may be latent hermaphrodites (ovotestis).

The question naturally arises as to whether these findings in the male in any way diminish the applicability or nullify the interpretations of our findings obained in females. In the hundreds of blood tests we have made, our results have been amply confirmed by the clinical course after prolonged observation or after operation.. The occasional and as yet unexplained positive results in males do not reduce the value of our test, even as much as the occasional positive outcome of the Wassermann reaction in a non-syphilitic renders this widely used test less valuable.

We desire, however, to caution against the use of our blood test

in the determination of sex[5] until further study assures us that the *cyclical* appearance of a positive reaction is unquestionably limited to females.

[1] Loewe, S., *Klin. Wchnschr.*, 1925, iv, 1407.

[2] Frank, R. T., Frank, M. L., Gustavson, R. G., and Weyerts, W. W., *J. Am. Med. Assn.*, 1925, lxxxv, 510.

[3] Allen, E., and Doisy, E. A., *J. Am. Med. Assn.*, 1923, lxxxi, 819.

[4] Frank, R. T., and Goldberger, M. A., *J. Am. Med. Assn.*, 1926, lxxxvii, 1719; *J. Am. Med. Assn.*, 1928, xc, 106; *J. Am. Med. Assn.*, 1928, (February 4).

[5] Frank, R. T., and Goldberger, M. A., *J. Am. Med. Assn.*, 1926, lxxxvii, 554.

[6] See 2; also Frank, R. T., Gustavson, R. G., Holloway, J., Hyndeman, D., Kreuger, H., and White, J., *Endocrinology*, 1926, x, 260.

[7] Dohrn, M., *Klin. Wchnschr.*, 1927, vi, 359.

[8] Hirsch, *Klin. Wchnschr.*, 1928, vii, 313.

3910

Immunity in Guinea Pigs to the Virus of Vesicular Stomatitis.

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It is known that the injection of immune serum into guinea pigs prevents generalization of the lesions but not the primary vesicles of foot-and-mouth disease. In studying a strain of the virus of vesicular stomatitis, a disease of horses closely related to foot-and-mouth disease of cattle,[1] we have found that the virus, when injected into guinea pigs, loses its original feeble power to produce the characteristic secondary lesions in the pad, and that only primary lesions arise after pad inoculation. Notwithstanding this fact, the virus receives a general distribution since it can be recovered, 48 hours after pad inoculation into guinea pigs, from the apparently normal tongue. On the other hand, when the virus is injected into the muscles or the skin (intradermal) elsewhere than in the pad, no local lesion whatever follows, and 10 days after the inoculation it is found that the pigs are immune to reinoculation.

In the preliminary experiments, no attempt was made to titrate the strength of the virus, because present methods are crude, and once the infectivity of a given sample of virus has been determined, it is impossible to estimate the rate of its deterioration. Guinea pig pad vesicle fluid, obtained 24 to 48 hours after inoculation, diluted 1:10 and 1:20 with phosphate buffer at a pH of 7.5; and filtered