oestrus or, less frequently, by prolonged dioestrus. If killed during the oestral period the uteri were found distended, though not fully to the size of normal controls. The histological picture of the hypophyses is essentially normal. Untreated females in parabiosis with females of this group stay in constant oestrus for periods of several months.

Females of Group II, 17 cases, according to their vaginal smears either stay in constant oestrus or in constant dioestrus (observed duration 2 to 5 months). The uteri are slightly stimulated in the first case and of the castrate type in the second case. In the anterior lobe of the hypophyses large vesicular castrate cells are present in varying numbers. Parabiotic untreated females stay in constant oestrus.

The untreated parabiont in constant oestrus always possesses a histologically normal hypophysis. Her ovaries are crowded with cystic follicles of mature size or slightly larger. Corpora lutea are entirely absent. Evidently only the follicular growth stimulating hormone of the sterilized twin is carried over in quantities surpassing the threshold value. Since this reaction appears already in Group I it is obvious that castrate cells are not necessarily responsible for the excess production of the follicle stimulating hormone.

The fact that cyclical oestrus changes are observed only as long as parts of the follicular apparatus are retained does not necessarily prove that the rhythmical phenomena depend on these morphological formations. Parkes'[2] observations on mice rather seem to suggest that our 2 groups are only differing in a quantitative way.

While the ovary deprived of all germ cells still is able to produce hormones controlling secondary sex characters and even to maintain cyclical phenomena, it appears that in all cases the output is quantitatively reduced.

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Further Studies on Copper and Iron.

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Waddell, Steenbock, Elvehjem, and Hart[1] showed that rats fed milk exclusively developed nutritional anemia and that the ingestion

[1] Hart, E. B., Steenbock, H., Elvehjem, C. A., and Waddell, J., *J. Biol. Chem.*, 1928, **77**, 777.

of pure iron salts failed to cure it. However, normal regeneration of hemoglobin was obtained with small additions of copper sulphate along with the iron salt. These results have been confirmed by Keil and Nelson.[2] Myers and Beard[3] found that higher doses of zinc and magnesium retarded blood regeneration. If this is the case, anemia should develop more rapidly on milk and $FeCl_3$ if these elements are included. The slope of the curves obtained with and without zinc or magnesium demonstrate that anemia resulted as readily with or without these elements.

Prior to this work on hemoglobin regeneration, Daniels and Hutton[4] demonstrated that rats failed to reproduce on milk and iron, but reproduction was a success when a mineral mixture of NaI, NaF, $KAl(SO_4)_2$, $MnSO_4$, and Na_2SiO_3 was added. They concluded that all of these salts were necessary in the milk for reproduction. The work of Hart, Steenbock and associates[1] and Keil and Nelson[2] is so conclusive, that it is certain animals cannot grow and reproduce normally without copper. There must have been contamination of this element either in the milk or salt mixture used by Daniels and Hutton. The minimum amount of copper required for regeneration of hemoglobin is extremely small. The minimum amount of copper as $CuSO_4$, when injected intraperitoneally, is shown to be 0.002 mg. daily. The milk used in these experiments was collected directly into glass containers in order to avoid contamination with copper. Milk *ad lib* and 0.5 mg. of Fe as $FeCl_3$ daily were fed to the rats. 0.05 mg. of Fe as $FeCl_3$ injected intraperitoneally with 0.002 mg. Cu as $CuSO_4$ daily does not result in normal regeneration. When the iron as $FeCl_3$ was increased to 0.1 mg. daily there was further stimulation of hemoglobin formation; but regeneration was not normal as shown by the plateau of the hemoglobin curve. At this point 0.15 mg. of colloidal Fe was administered intraperitoneally daily, and as a result regeneration to the normal level of hemoglobin occurred. Injections intraperitoneally of 0.05 mg. and 0.1 mg. of Fe as $FeCl_3$ caused necrosis and sloughing off of the skin at the point of application; hence colloidal Fe was used. The colloidal Fe was free from dialyzable Fe.

Rats on milk collected in glass together with $FeCl_3$ and $CuSO_4$ grew at a rate considerably slower than rats on our stock ration. The addition of Na_2SiO_3 to the above ration did not improve the growth curves. However, $KAl(SO_4)_2$ in place of the silicate gave

[2] Keil, H. L., and Nelson, V. E., *J. Biol. Chem.*, 1932, **97**, 115.

[3] Myers, V. C., and Beard, H. H., *J. Biol. Chem.*, 1931, **94**, 89.

[4] Daniels, A. L., and Hutton, M. K., *J. Biol. Chem.*, 1925, **63**, 143.

better results than the other 2 rations. Sodium fluoride when added to the milk, Cu and Fe ration gave results which surpassed those on $KAl(SO_4)_2$ for the first 4 months; then the fluoride exhibited toxicity. Rats on milk, $FeCl_3$, and $CuSO_4$ and the Daniels and Hutton salt mixture, exclusive of NaI, grew satisfactorily and performed equally well as rats on our stock ration. Rats on milk, $FeCl_3$, $CuSO_4$, and $MnSO_4$ performed better than any of the previous lots and even surpassed those on the stock ration. Reproduction on milk, $FeCl_3$, $CuSO_4$, and the Daniels and Hutton salt mixture was very good, during 3 generations studied. The rats on milk, copper, and iron in the first generation reproduced equally well with the animals on the Daniels and Hutton salts, but the mortality of the young was considerably greater in the former case. Furthermore, the weight of the young at birth and weaning time was considerably less in the former case than on the Daniels and Hutton salts. Male and female rats of the first generation on milk, copper, and iron proved fertile for at least 20 months and are still active in this respect. However, rats on this same diet do not reproduce in the second generation. The animals of the second generation failed to reproduce in 8 months; but with the addition of the Daniels and Hutton salt mixture reproduction occurred, and the per cent mortality of the young was low. Infection of the middle ear, *otitis media,* was very prevalent in the second generation rats receiving milk, iron, and copper; but it was not nearly so common in the first generation. Only 2 of the 88 animals on milk, Cu, Fe, and Mn as $MnSO_4$ showed this pathological condition. 6 to 12 rats were employed in each experiment.

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Cardiovascular System in Acute Experimental Peritonitis.

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The purpose of this work is to determine the reaction of the cardiovascular system to experimental peritonitis. Holzbach[1] in his review on circulatory failure in infectious conditions states that functional heart failure appears early in peritonitis, but this opinion

[1] Holzbach, E., *Wurzb. Abhandl. a. d. Gesamtgeb. d. Med.*, 1931, **27**, 1.