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Endocrine Reactions in Female Rats after X-Ray Treatment of the Ovaries.*

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X-ray sterilized rats with completely destroyed germ cells but well preserved somatic elements of the testis, fully maintain their secondary sex characters.[1] They react like total castrates when united in parabiosis with untreated females. This was taken as evidence that the X-ray sterilized male, like the castrate, produces large amounts of follicle stimulating hormone of the anterior pituitary. So-called castrate cells are found in the hypophyses of X-rayed males, though in smaller numbers than in surgical castrates. Parkes[2] first observed that X-ray sterilized female mice in many instances maintain fully their secondary sex characters including the cyclical oestrus changes. Ford and Drips[3] later reported experiments on rats which led to similar general conclusions. We endeavored to correlate the ovarial changes with the hypophyseal reactions. The main results and conclusions can be summarized as follows:

According to the extent of damage of ovarial structures observed at 4 to 7 months after irradiation the females can be divided into 2 groups. In both the germ cells have completely disappeared but the follicular apparatus—cystic follicles, corpora lutea—is partly preserved in the ovaries of the first group and completely destroyed in those of the second group. Ovaries of the second group show a profuse proliferation of epithelial cells from the germinal epithelium which never become organized into follicular structures. In addition, small "anovular follicles" may arise from the same source, though they soon disintegrate without ever exhibiting cystic transformations.

Females of Group I, 12 cases, observed over periods up to 7 months after irradiation, maintained fairly well the cyclical oestral changes observed in vaginal smears. Periods of 3 to 6 cycles of normal lengths usually were alternating with periods of prolonged

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1 Witschi, E., Levine, W. T., and Hill, R. T., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1024.

2 Parkes, A. S., *Proc. Roy. Soc.*, B., 1926, **100**, 101.

3 Ford, F., and Drips, D., *Radiology*, 1929, **12**, 393.

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.