

Diskussion. Auf Grund von tierexperimentellen Befunden wird angenommen, dass unter den ovulationshemmenden Gestagenen zwei Haupttypen zu unterscheiden sind. Einmal Substanzen, welche die Ovulation durch die Blockierung der LH-Freisetzung unterdrücken und für ihre Wirkung weniger Zeit benötigen, zum andern die sogenannten «FSH-Inhibiting»-Typen. Deren Wirkung wird sichtbar in der mangelhaften Reifung der Follikel. Sie benötigen für die Entfaltung ihrer Wirkung mehr Zeit³. Es ist anzunehmen, dass die komplizierten Vorgänge in den Ovarien unter einem längeren Einfluss von Progestagenen nicht unbeeinflusst bleiben. Mehrere klinische und tierexperimentelle Befunde sprechen dafür, dass Progesteron und auch Progestagene auf der Ebene des Ovars ebenfalls eine Wirkung haben können^{4, 5, 8-13}. Weitere Ergebnisse bestätigen eine sichere Wirkung auf das Hypothalamus-Hypophysen-System¹⁴⁻¹⁹. Frühere Untersuchungen über die morphologischen Veränderungen in den Ovarien nach Progesterongabe führten zu der Schlussfolgerung, dass die LH-Freisetzung unterdrückt wird, während die FSH-Freisetzung unberührt bleibt²⁰⁻²².

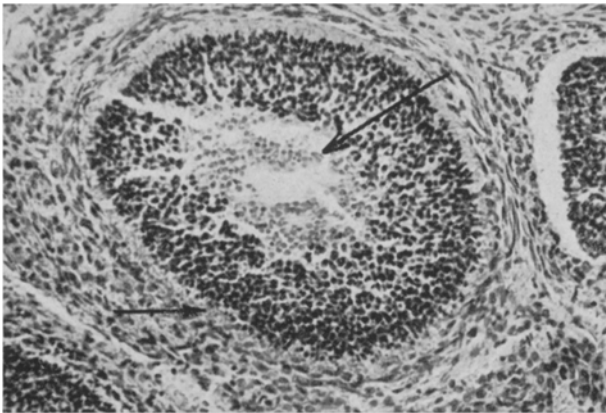


Fig. 4. Haemorrhagische Reaktion eines tertiären Follikels auf Lynestrenol-Behandlung. Zwischen der Theca interna und Stratum granulosum sowie im Cavum folliculi zahlreiche Erythrozyten. $\times 80$.

In unserer Versuchsanordnung konnten wir die LH-Wirkung auf das Ovar unreifer Ratten durch Gestagenbehandlung unterdrücken. Nach NIH-LH-Gabe haben wir in den Ovarien unter Progesteron-, Norgestrel- oder Lynestrenol-Einfluss keine Corpora lutea gefunden. Dies widerspricht Untersuchungsergebnissen mit unveränderter LH-Wirkung unter Progesteron-Einfluss²³⁻²⁵. Nach Norgestrel- und Lynestrenol-Behandlung wurde in den Ovarien das gleiche Bild wie nach einer Progesteron-Behandlung gefunden. Dieser Befund spräche für eine Unterdrückung der FSH-Freisetzung oder für eine Hemmung sowohl der FSH- als auch der LH-Ausschüttung. Die signifikanten Gewichtsverminderungen der Ovarien unter allen drei verabfolgten Gestagenen unterstreichen diese Wirkung. Die oft erwähnte selektive Wirkung dieser Substanzen auf die Hypophyse^{26, 27} konnten wir bei dieser Versuchsanordnung nicht demonstrieren. Es ist bekannt, dass z.B. Progesteron die «Realizingfactor»-Freisetzung nach anfänglicher Sensibilisierung erschwert. Der eigentliche Wirkungsort der von uns benutzten Substanzen ist bei dieser Versuchsanordnung ebenfalls im Hypothalamus zu suchen. Interessant ist, dass die alleinige NIH-LH-Gabe eine signifikante Gewichtsverminderung der Hypophysen hervorruft. Für eine direkte Beeinflussung des Ovars durch Lynestrenol sprach die hämorrhagische Reaktion einiger Tertiärfollikel. Ähnliche morphologische Veränderungen wurden unter Lynestrenoleinwirkung auch beim menschlichen Ovarium beobachtet²⁸. Das Uterusgewicht und das histologische Bild entsprachen den Erwartungen der früheren Untersuchungen^{25, 29}.

Summary. The influence of NIH-LH upon the ovary of infantile rats can be eliminated by treatment with progesterone, norgestrel and lynestrenol. This result suggests suppression of the hypophysary functions of gonadotropines. A direct influence of lynestrenol on the ovary suggests the presumption that some tertiary follicles change haemorrhagically.

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Running Activity of Ovarian Tumorigenic Mice

Sterile female mice of the genic *W* series all develop genetically spontaneous ovarian tubular adenomas by 7 months of age and all have atrophic uteri in adult life. At 2 months of age, the ovaries of the genic *W* series lack ova, follicles and are distinctly atrophic¹⁻³. Mice of the C3B6F1-*W* series in many instances had no hair over the

entire face, so we called them 'bald-faced mice'. Genetically developed tumor-bearing animals exhibited the most extensive hair loss⁴.

The 4 genotypes of the C3B6F1-*W* series were studied for the relationship between running activity and ovarian tumorigenesis. Ovarian tumor-bearing mice (*W*⁺*W*⁺)

seemed to move around their cages more slowly than control littermates of the genotypes W^xw , W^vw and ww . Initially we felt that the difference in movement was due to a variation in body weight between the control and tumor-bearing animals. However, we calculated no significant differences in body weight between the genotypes. The present work shows that genetic ovarian tumorigenesis of the genotype W^xW^v mice is associated with inhibited wheelrunning activity.

Materials and methods. Adult female mice of the C3B6F1- W series were obtained from crosses of strains C3H/HeJ- W^x /+ with C57BL- W^v /+ which gave rise to C3B6F1 hybrids segregating only for W -alleles. The animals were then divided into 4 genotypes: W^xW^v -black eyed whites (ovarian tumor bearers); W^xw -agoute, white tip tail; W^vw -agoute, all white tail; and ww -agoute, all black tail. The agoute animals served as controls, while the black eyed whites were the experimental genetically developed ovarian tumor-bearing animals. We weighed the animals and placed each mouse in a tread wheel for 2 h. The number of revolutions per h was recorded and averaged for each genotype. We calculated the standard error for each mean by using the formula, $S.E. = \sqrt{\sum d^2 / N(N-1)}$ and the probability values (P) were determined by Student's t -test⁵.

Results. The W^xW^v ovarian tumor-bearing mice had mean running activity significantly less than the running activity of any control agoute genotype. Animals with ovarian tumors ran 212.5 ± 13.6 revolutions per h. This running activity was significantly slower than the slowest running genotype W^vw which had an activity of 271.7 ± 12.6 revolutions per h ($P < 0.05$). On the other hand, the fastest running activity was recorded by W^xw mice.

Discussion. Ovarian tumorigenesis as well as genetics appear to be contributing factors in the slower running of ovarian tumor-bearing mice. The spontaneous motor activity of the 3 control groups appear to be genetically determined. The adrenals of mice with ovarian tumors commonly contained cells simulating luteal cells, and we interpreted their presence as a stimulating effect from the

ovarian tumors⁶. The remarkable modification of the adrenal glands may in turn produce an altered hormonal secretion which along with decreased estrogen secretion and overproduction of gonadotropin may be responsible for the inhibited running of the ovarian tumorigenic mice. In rats, spontaneous motor activity was greater during estrus⁷ at a time when sexual receptivity and estrogen levels reached the highest point⁸ suggesting that running behavior depends upon sex-related hormone action. Since the uteri of ovarian tumor-bearing animals manifested atrophy, a decrease in endometrial glands and subtle metaplasia of the normal stroma⁶, we feel that low estrogen levels occur in genotype W^xW^v mice.

The faster running control animals all showed signs of a more mature and stimulated exterior vaginal orifice in contrast to experimental ovarian tumor-bearing animals⁶. The ovaries and uteri of control animals were of normal size. The uteri of control animals were red, vascular, had a normal myometrium, and commonly exhibited cystic hyperplasia of the endometrial glands. Individual differences in running activity of control genotypes may be due to genetic differences in the ability to utilize or secrete estrogen. Future studies will be needed to clarify this point.

Résumé. Les ovaires de souris C3B6F1, génotype W^xW^v développent des adénomes tubulaires à l'âge de 7 mois. Dans l'essai du «tread wheel» l'activité spontanée de ces animaux était plus petite que celle des contrôles.

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Spontaneous running activity of C3B6F- W series adult female mice 7-9 months of age

Genotype	No. of mice	Body wt. (g)	P	Revolutions per h	P
W^xW^v	45	29.7 ± 0.5	—	212.5 ± 13.6	—
W^vw	23	30.3 ± 0.7	>0.5	271.7 ± 21.6	<0.05
ww	30	30.3 ± 0.5	>0.1	289.6 ± 24.2	<0.01
W^xw	19	31.3 ± 1.0	>0.1	308.8 ± 26.2	<0.01

P = Probability value; $\pm$ = standard error.

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Sex Ratio and Geographic Parthenogenesis in *Macrobiotus* (Tardigrada)

The cell number in the Tardigrades is not absolutely fixed, because mitoses can be detected in various tissues¹. But a constant number of cells being secondarily attained, it must be deduced that some cells have a short lifetime². Previous observations have also given interesting hints about the sex ratio and the sexual dimorphism.

It is well known that in the Tardigrades the males are generally very few or absent^{3,4}; sometimes they are

frequent in springtime but they are always absent in the other seasons⁵⁻⁷. This suggested a parthenogenetic behaviour which was afterward proved by cytological observations on *Hypsibius dujardini*^{8,9} and by culture methods on *Milnesium tardigradum*¹⁰.

A sex ratio near to 1:1 is observed in collections of Tardigrades belonging to the genus *Macrobiotus* (Table); populations without males are observed in other territories, as in the case of *M. hufelandii* found near Ravenna