

which the neuroinvasiveness of W.E.E. virus is differently affected: first, at the very early age of 15 days when certain vessels still permit the virus to traverse and spread in the CNS by some definite pathway;⁸ second, at the age of 21 days when the virus can no longer do this in the majority of mice but now progresses along the nerves supplying the inoculated muscle; and third, between the 21st and 30th days of life when the appearance of some change in the muscle or specialized nerve endings in the great majority of mice (it is important to remember the few exceptions) now prevents invasion of the CNS altogether. Intramuscular injections of as much as 10^8 M.C.L.D. of the mouse-passage W.E.E. virus finds practically all old guinea pigs (800-1000 g) resistant with only an occasional one exhibiting flaccid paralysis.

Conclusions. Studies of the conditions which permit or prevent the viruses of vesicular stomatitis and equine encephalomyelitis to invade the CNS of mice and guinea pigs have thus far disclosed that depending upon the age or species of the host there may be changes or variations in localized sites, *e.g.*, in terminal, specialized nerve endings, in special areas of the CNS, blood vessels, etc., which can prevent the virus from invading or progressing in the CNS—changes in different tissues functioning as barriers for different viruses depending upon the mode of CNS invasion utilized by the virus.

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Inhibition of Estrogenic Effects on the Skeleton by Testosterone Injections.*

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Hypercalcification of the skeleton involving a partial or complete obliteration of the marrow cavities occurs in immature rats and chickens¹ and in mice² following extended treatment with large amounts of estrogens. Simultaneously with this, the pubic and ischial bones are reabsorbed at the symphysis and the former carti-

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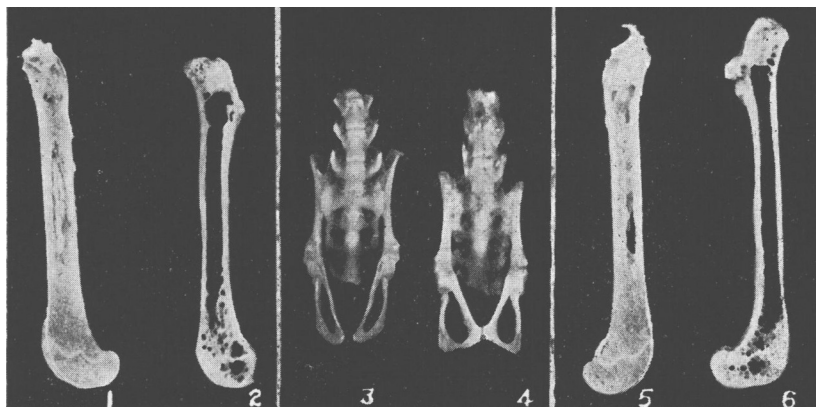
¹ Zondek, B., *Folia Clin. Orient.*, 1937, **1**, 1.

luginous union is replaced by an interpubic ligament.^{2,3} Similar pelvic changes occur during normal pregnancy.

Untreated old virgin females show only a slight loosening of the pelvis. However, ovarian grafts produce slight pelvic changes in males but are more effective in castrated than intact animals. Also in over 100 mice treated with estrogens the bone changes occurred more slowly in the intact males than in the females, indicating that the male hormone may exert an inhibiting effect. Therefore, testosterone propionate was injected along with the estrogen.

Six mice from 2 inbred strains were given weekly injections of 500 or 1000 i.u. of estradiol benzoate† and of 1.25 or 2.5 mg of testosterone propionate (Table I).

The femoral marrow cavities of mice receiving testosterone and estrogen were similar to those of normal untreated mice of comparable ages or showed only a slight increase in endosteal cancellous bone. (Figs. 2 and 6). Mice of the same strains receiving similar amounts of estrogen but no testosterone for comparable periods showed an extensive hyper-calcification of the femurs (Figs. 1 and 5), compact and cancellous bone largely replacing the marrow cavities.



Figs. 1 and 5. Femurs of a female (1) and a male (5). ($7\text{C}_3\text{H}$ and $6\text{C}_3\text{H}$ respectively. See table. Alizarine was injected during the last 24 days.

Figs. 2 and 6. Femurs of mice $91\text{C}_3\text{H}$ and 61N respectively (see table). These bones were similar to those of normal animals.

Figs. 3 and 4. Pelvises of (3) 56A and (4) of $24\text{C}_3\text{H}$ (see table).

² Gardner, W. U., and Pfeiffer, C. A., *Proc. Soc. Exp. Biol. and Med.*, 1938, **37**, 678.

³ Gardner, W. U., *Am. J. Anat.*, 1936, **59**, 459.

† The estrogen (Progynon B) and testosterone propionate (Oreton) were generously supplied by Drs. E. Schwenk and M. Gilbert of the Schering Corporation.

TABLE I.

	Sex	Days treated	Estrogen weekly, i.u.	Total estrogen, i.u.	Testosterone propionate, weekly, mg	Total testosterone propionate, mg	Pelvis	Femur
24C ₃ H	F	232	500	16,000	2.5	80	Firm (Fig. 4)	Normal
38C ₃ H	M	128	1000	18,000	1.25	21.25	"	"
89C ₃ H	M	127	1000	18,000	1.25	22.25	"	"
91C ₃ H	F	161	1000	23,000	1.25	27.50	"	" (Fig. 2)
61N	F	162	500	11,500	2.5	55	Measurable, 0.5 mm lig.	" (Fig. 6)
55N	F	163	500	11,500	1.25	27.50	Firm	Normal
60C ₃ H	M	142	500	10,000	—	—	2 mm lig.	Fig. 5
70C ₃ H	F	142	500	10,000	—	—	4 mm lig.	Fig. 1
56A	M	153	500	10,500	—	—	3 mm lig. (Fig. 3)	—

The mice were 24-75 days of age when the injections were started.

The pubes of all mice receiving testosterone and estrogen, except 61N, were firmly united at the symphysis (Fig. 4). The pelves of the mice receiving estrogens alone in similar amounts had interpubic ligaments of 3 to 5 mm (Fig. 3). The pubes of 61N were movable but were separated by a ligament of less than 0.5 mm.

Conclusion. Testosterone propionate inhibits the skeletal changes (pubic resorption and hypercalcification of the skeleton) which occur when estrogens are injected over extended periods.