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The Breaking Strength of Femurs of Mice Receiving Estrogens.*

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The femurs and other bones, especially of the appendicular skeleton, of mice which received estrogens had greatly thickened walls. Following prolonged treatment the marrow was largely or completely replaced by new osseous tissue.[1, 2, 3] The new bone was well organized and fully calcified. The percentage of ash was increased and the calcium-phosphorus ratio was higher than in the bones of untreated mice.[4] The above observations indicated that the breaking strength of the bones might be increased.

The strength was determined by ascertaining the weight required to fracture the bone. An apparatus was constructed by which weight was progressively and regularly added to the center of a uniform length of bone supported at both ends. Recently dissected femurs were placed over 2 blunted upright steel supports set 1 cm apart. A third freely movable blunted steel knife, attached to a container into which lead shot was delivered, rested upon the bone equidistant between the 2 uprights. The apparatus was so constructed that the addition of shot was prevented as soon as the bone broke. The strength of the bone was determined as the weight in grams required to fracture the femurs. Both femurs of each animal were used.

The breaking strengths of the femurs of 30 estrogen-treated and 9 control mice were determined. The mice were all F_1 hybrids of the C_{57} and CBA strains. They were maintained on a diet of Purina Fox Chow. Weekly subcutaneous injections of 16.6 or 50 μg of estradiol benzoate† were started at weaning and continued throughout life in the test animals. Only 3 mice received the larger amount

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1 Gardner, W. U., and Pfeiffer, C. A., PROC. SOC. EXP. BIOL. AND MED., 1938, **37**, 678.

2 Gardner, W. U., and Pfeiffer, C. A., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 599.

3 Gardner, W. U., *Anat. Rec.*, 1940 suppl., **76**, 22.

4 Wentworth, J. H., Smith, P. K., and Gardner, W. U., *Endocrin.*, 1940, **26**, 61.

† The estradiol benzoate (progynon-B) was generously supplied by the Schering Corporation by Dr. E. Schwenk.

of estrogen. The smaller amount was insufficient to result in extreme osseous changes in all of the hybrid mice.

The estrogen-treated mice were killed at ages ranging from 322 to 555 days (average 478) and the controls at ages ranging from 375 to 553 (average 479). The weight required to fracture the femurs under the above conditions ranged from 1599 g to 3542 g (average 2499) for the test animals and 1244 to 2102 g for the controls (average 1655). The breaking strength was closely correlated with the amount of bone present as determined by direct observation and by density as demonstrated by X-ray photographs (Fig. 1). The femurs of 25 of the 30 test mice fractured at weights exceeding that of the strongest control. The average breaking strengths of the femurs of the estrogen-treated mice was over 800 g more than that of the control mice. The average ages of mice of the 2 groups were practically the same.

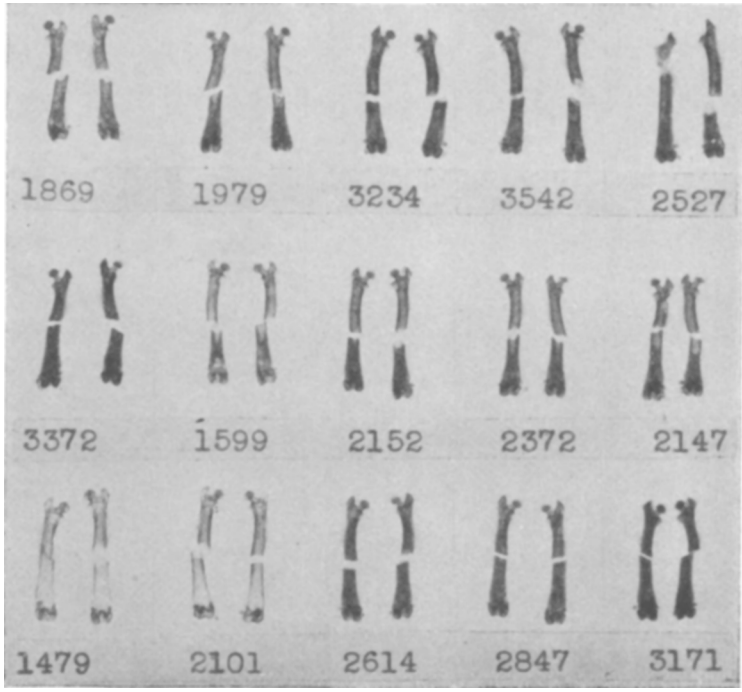

FIG. 1.

X-ray photographs of the femurs of 15 mice (C_{57} ♀ × CBA ♂). Photographed and printed under identical conditions. The figures indicate the average breaking strengths of the pairs of femurs. The upper 2 rows were from mice which had received 16.6 μg of estradiol benzoate weekly. The 3 groups at the right in the bottom row were from mice which had received 50 μg weekly and the 2 at the left from untreated controls of comparable ages. X-ray photographs taken by Department of Radiology, Yale University.

The weight required to fracture the two femurs of the same mouse varied in most animals. These variations probably represent technical inaccuracies and biological fluctuations. The differences in breaking strength of the 2 femurs of individual estrogen-treated mice averaged 207 g and of the individual controls 147 g, ranging from 0 to 455 and 15 to 275 g.

The length and smallest diameter of the bones were determined by micrometer measurements prior to fracture. The bones of the test mice were approximately 1 mm shorter than those of the controls. The diameters were similar. All the control mice were in excellent general health. The treated mice showed the usual toxic effects of chronic estrogenic stimulation and most of them had tumors of the mammary glands, pituitary gland or both.

Summary. The average breaking-strength of femurs of estrogen-treated mice was 2499 g or 844 g greater than that of untreated controls.

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Influence of Sterile Inflammation on Susceptibility to Experimental Poliomyelitis.*

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Since neither the serum antibodies nor specific neutralizing substances in the nasopharynx[1] seem to present an adequate basis for the relatively high immunity to poliomyelitis, a further study of the mechanism of this resistance might be made by approaching the problem from the point of view of possible elements, other than the virus, as determining factors in establishing the infection. Is some symbiotic agent, a state of allergy, or an inflammatory condition of the mucosa with resulting increased permeability, a contributory factor in producing clinical cases of the disease?

Flexner and Amoss[2] reported that poliomyelitis could be produced successfully in monkeys with subinfective doses of the virus given

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1 Park, W. H., *J. A. M. A.*, 1932, **99**, 1050; Howitt, B. F., *J. Inf. Dis.*, 1937, **60**, 113.

2 Flexner, Simon, and Amoss, H. L., *J. Exp. Med.*, 1914, **20**, 249; Flexner, Simon, and Amoss, H. L., *J. Exp. Med.*, 1917, **25**, 1525.