

## Influence of Age on Serosal Tumoral Reaction of the Guinea Pig Towards Estrogens.\*

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Uterine and extragenital peritoneal fibroids have been elicited in almost all castrate adult female guinea pigs given sufficient quantities of estradiol benzoate subcutaneously during a 4-months period.<sup>1</sup> This fact raised the question whether or not *young* animals would react with production of abdominal fibroids as *adult* animals do. Uterine fibromyoma occurs in women before puberty rarely if at all; fibromatogenesis in women is seemingly intimately connected with ovarian endocrine activity. However, in experimental fibromatogenesis elicited by estrogens, extragonadal factors also may be in play, as is demonstrated by the fact that the conjunctive tumoral reaction towards estrogens is less pronounced in the castrate *male* guinea pig than in the castrate *female*.<sup>2</sup> Accordingly, the question of the influence of age irrespective of the gonad on the fibromatogenic reaction of castrate female guinea pigs towards estrogens is of considerable interest. Nelson,<sup>3</sup> who was the first to report uterine fibroids elicited by estrogens, induced them in guinea pigs treated from birth. However, he does not refer to extragenital fibroids, and treatment in his experiments was, with but one or two exceptions, prolonged for 8 to 10 months, so that no judgment is possible as to the moment when these fibroids originated.

In our present work<sup>†</sup> comparison was made between 2 groups of castrate females *very different in body weight* since exact knowledge

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<sup>1</sup> Lipschütz, A., and Iglesias, R., *C. R. Soc. Biol. (Paris)*, 1938, **129**, 519; Iglesias, R., *Pub. Med. Exp. (Chile)*, 1938, No. 1; Lipschütz, A., and Vargas, L., Jr., *Cancer Research*, 1941, **1**, 236.

<sup>2</sup> Koref, O., Lipschütz, A., and Vargas, L., Jr., *C. R. Soc. Biol. (Paris)*, 1939, **130**, 303; Jedlicky, A., Lipschütz, A., and Vargas, L., Jr., *C. R. Soc. Biol. (Paris)*, 1939, **130**, 1466; Lipschütz, A., Vargas, L., Jr., and Palma, J., *Cancer Research*, 1941, **1**, 575.

<sup>3</sup> Nelson, W. O., *Anat. Rec.*, 1937, **68**, 99; *Endocrinology*, 1939, **24**, 50.

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of age was not available. "Aged" animals weighing 700 to 1050 g at beginning of treatment were compared with "young" animals weighing between 180 and 245 g. Subcutaneous injections of 80  $\gamma$  of estradiol given as monobenzoate in oily solution were administered 3 times a week to all animals. Treatment was prolonged for only 2½ to 3 months so as to completely avoid the possibility of a young animal approaching the limit of body weight range of the "aged" group. Part of the young animals even received a smaller number of injections than the aged ones. For a quantitative evaluation of the tumoral effect a system of classification was used as formerly described.<sup>4</sup> Results are given in Table I. Eight of 11 animals of

TABLE I.  
21 Castrate Female Guinea Pigs of High (700 to 1050 g) and Low (180 to 245 g) Body Weight Receiving Subcutaneous Injections of 80  $\gamma$  of Estradiol (Monobenzoate) Three Times a Week.

Series and No.	Initial wt, g	Final wt, g	No. inj.	Days of exper.	Tumoral effect: class				Total tumoral effect
					Subserous or parametrial uterine tumors	"Apical"	Digest. tract and abdom. wall	Spleen	
XV									
10	700	685	38	88	0	0.5 f	0	0	0.5
7	735	720	37	89	2	0	2	2	6.0
19	750	700	38	89	0	0	0.5 f	0	0.5
8	765	790	38	88	1	1	2	2	6.0
9	790	685	37	89	1	2	1	2	6.0
11	900	790	38	88	2	3	3	3	11.0
2	920	795	38	89	0.5 t	0.5 f	2	0.5 s	3.5
3	950	805	37	88	0	0	0.5 f	0	0.5
1	960	720	37	87	0	0.5 f	3	1	4.5
12	980	960	38	88	1	0.5 f	1	0	2.5
6	1050	870	38	90	0	3	3	2	8.0
XV									
24	190	390	38	90	2	2	3	0	7.0
4	200	385	35	91	0	3	2	2	7.0
20	245	410	39	91	1	2	0.5 f	2	5.5
IX									
13	180	460	27	75	0	2	1	2	5.0
16	190	455	30	84	0	3	1	0.5 t	4.5
20	205	490	27	77	0	2	1	0	3.0
15	210	450	27	75	0	1	0	0	1.0
21	220	540	27	77	0	2	0	1	3.5
17	230	460	27	76	0	0.5 f	0.5 f	0.5 t	1.5
19	240	370	30	85	3	3	2	3	11.0

f = fibrous strands only.

t = one or several small tumoral nodules.

s = tumoral seed, *i.e.*, accumulation of minute tumoral nodules.

<sup>4</sup> Lipschütz, A., and Vargas, L., Jr., *C. R. Soc. Biol. (Paris)*, 1939, **131**, 27; Lipschütz, A., Bellolio, P., Chaume, J., and Vargas, L., Jr., *Proc. Soc. Exp. Biol. AND MED.*, 1941, **46**, 164.

high body weight (700 to 1050 g) developed uterine or extragenital fibroids of class 1 or more; the remaining 3 animals showed some form of abdominal fibrous reaction. The average total tumoral effect was 4.4. All animals of low body weight treated for the same length of time as those of high body weight (series XV), gave a conspicuous tumoral reaction. Uterine and extragenital fibroids were present even in 5 of those 7 young animals which were treated for a shorter time (series IX) than the aged animals.

Table I gives full evidence that peritoneal fibroids can be elicited not only in the adult, but also in young females when treatment begins at a body weight of less than 200 g and when necropsy is made before a body weight of 500 g is reached. There was no difference in the frequency of abdominal fibroids in the two groups.

Another question also arises here. The average total tumoral effect in young animals, even when treated for a shorter time, as in series IX, was not less than in adult or aged animals. Does this mean that age has no influence on the *degree* of the fibromatous reaction, *i. e.*, on the size and number of fibroids? The number of "resistant" castrate female guinea pigs, *i. e.*, animals which when treated with estrogens for several months showed no conjunctive reaction, was

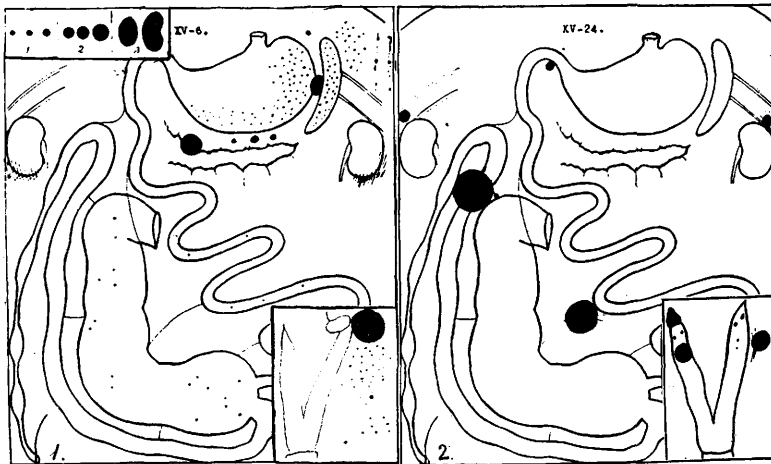


FIG. 1.

Castrate female guinea pig XV, 6. Weight at beginning—1050 g, at end of experiment—870 g. 38 injections of 80  $\gamma$  of estradiol (benzoate) in the course of 90 days. Large apical tumor of left horn and various extragenital tumors. Tumoral seed at different places. In this case there was also considerable development of fibrous strands at different places; they are mostly omitted in the diagram.

FIG. 2.

Castrate female guinea pig XV, 24. Weight at beginning—190 g, at end of experiment—390 g. 38 injections of 80  $\gamma$  of estradiol (benzoate) in the course of 90 days. Large uterine and extragenital tumors.

very low in the work of Lipschütz and fellow workers during the last 4 years. On the other hand, there was considerable individual variation as to the degree of the fibromatous reaction, which may range between 0.5 and 12 according to our classification.<sup>4</sup> For this reason too much importance should not be attributed as yet to the coincidence in the average total tumoral effect in animals of high and low body weight.

*Summary.* Uterine and extragenital fibroids were elicited by subcutaneous administration of estradiol monobenzoate in castrate female guinea pigs weighing no more than 180 to 245 g at the beginning of treatment and autopsied 2½ to 3 months later before they reached a body weight of 500 g. The incidence of abdominal fibroids in these young animals was no less than in a group of adult or aged animals weighing 700 to 1050 g at the beginning of treatment. Whereas this statement referring to the occurrence of experimental abdominal fibroids in young females seems definite, the question remains open whether age may influence the degree of the fibromatous reaction, *i. e.*, size and number of fibroids.

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#### Urinary Excretion of *Trichina* Antigen in Experimental Trichinosis.\*

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The elimination by the kidneys of substances derived from bacterial cells has been noted in several human infections such as the urinary excretion of capsular polysaccharide in pneumococcal infections,<sup>1</sup> and the excretion of scarlatinal toxin in scarlet fever.<sup>2</sup> It is probable that this mechanism is operative in a number of bacterial infections although the field has not been adequately explored. The present note describes an example of the same phenomenon in an experimental disease of parasitic origin.

In this study the urinary excretion of an antigenic substance, or

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<sup>1</sup> Dochez, A. R., and Avery, O. T., *Proc. Soc. Exp. Biol. and Med.*, 1917, **14**, 126.

<sup>2</sup> Trask, J. D., and Blake, F. G., *J. Exp. Med.*, 1924, **40**, 381.