

most active participant in the body in the metabolism of manganese. The uptake of labeled manganese by bone was not measurable when the dose was administered orally.

14366

Relaxation of the Pelvic Ligaments of Castrate Hysterectomized Guinea Pigs Induced by Progesterone.*

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Haterius and Fugo¹ showed that in castrate female guinea pigs relaxation of the pelvic ligaments could be elicited by treatment with crystalline progesterone after preliminary conditioning with estrogens. These findings cast some doubt upon the existence of a separate relaxation hormone, or at least its indispensability in the process of pelvic relaxation.

More recently Hisaw *et al.*² confirmed the ability of crystalline progesterone to relax the pelvic ligaments in the spayed and estrogenized guinea pig. But they reported that in castrates which were hysterectomized the estrogen-progesterone treatment did not induce relaxation. The authors concluded therefore that under the conditions of their experiments "the uterus is indispensable for the formation of relaxin."

It would seem from this interesting report that the presence of the uterus in some unex-

plained way facilitates relaxation but is not a necessary factor in the development of this reaction. Similarly progesterone is not indispensable since relaxin alone produces relaxation in the estrogenized hysterectomized castrate. Surprisingly, however, the combination of two factors (uterus and progesterone) each shown to be nonessential, together give a positive reaction.

It was not the intention of this study to analyze the complicated nature of this reaction. Rather it was thought necessary to reinvestigate our earlier conclusion, namely, that progesterone alone was sufficient to produce relaxation when given in combination with estrogen.

Furthermore it occurred to us that perhaps the failure of Hisaw *et al.* to obtain relaxation in castrate hysterectomized guinea pigs might

TABLE I.
Summary of Cases of Relaxation Following Estrogen-progesterone Treatment in Castrated-hysterectomized Guinea Pigs.

Guinea pig No.	1	2	3	4	5	6	7	8	9*	10*	11*	12*
0.5 mg Est. Diprop. daily (days)	7	7	7	7	7	7	7	7	0	0	0	0
0.5 mg Est. Diprop. + 0.5 mg Prog. daily (days)	7	7	7	7	7	7	7	7	0	0	0	0
1.0 mg Est. Diprop. + 1.0 mg Prog. daily (days)	4	2	2	3	0	1	3	0	0	0	0	0
Total mg Est. Diprop.	11.0	9.0	9.0	10.0	7.0	8.0	10.0	7.0	0	0	0	0
Total mg Prog.	7.5	5.5	5.5	6.5	3.5	4.5	6.5	3.5	0	0	0	0
Day Relax. occurred after init. inject.	19	17	17	18	15	16	18	15	N.R.	N.R.	N.R.	N.R.

N.R. = No relaxation.

*Castrated and hysterectomized.

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¹ Haterius, H. O., and Fugo, N. W., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 155.

² Hisaw, F. L., Zarrow, M. X., Talmage, R. V. N., Money, W. L., and Abramowitz, A. A., *Anat. Rec.*, 1942, **84**, 457.

be due to a time factor since their experimental procedure consisted in the injection of 250 mg of estradiol on 4 consecutive days followed by a single injection of 5 to 10 mg of progesterone on the following day.

Consequently 12 virgin guinea pigs weighing approximately 200 g were castrated and hysterectomized under ether anesthesia. A period of 17 days was allowed to elapse between the operation and the initiation of the hormonal injections to assure the complete recovery of the animal and the recession of all sexual characteristics. At this time subcutaneous injections of estrogen were made for 7 days followed by a period of estrogen-progesterone treatment. Dosages and details

of administration are listed in Table I. Relaxation of the pelvic ligaments occurred in all injected animals between the 15th and 19th day of hormone administration.

The last 4 experimental animals were castrated and hysterectomized but received no hormone treatment. None of these animals showed any relaxation during the post-operative period of 37 days.

It appears from this experiment that castrated and hysterectomized virgin guinea pigs when given progesterone after an initial period of estrogen treatment show relaxation of the pelvic ligaments in the complete absence of both ovaries and uteri.

14367

Natural Resistance and Susceptibility to Russian Spring-Summer Encephalitis in Mice.*

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Webster¹ demonstrated that resistance and susceptibility in mice to *B. enteritidis* are inherited independently of resistance and susceptibility to St. Louis encephalitis virus in the same species. Consequently, by inbreeding and selection from a hybrid stock, he was able to derive 4 strains of mice exhibiting the 4 possible combinations of resistance and susceptibility to these two pathogens. For convenience these stable, uniform, inbred strains were designated as follows: Bacteria-resistant-virus-susceptible (BRVS) and, in the same manner, the three remaining strains, BRVR, BSVS, BSVR. These designations were valid as well in terms of the louping-ill virus in the instance of the BSVR and BRVS

lines,² but all strains were uniformly susceptible to mouse passage rabies virus,¹ to vesicular stomatitis virus,³ and to lymphocytic choriomeningitis virus.⁴ At the present time, then, designation of these strains of mice as "virus-resistant" or "virus-susceptible" is restricted to the viruses of St. Louis encephalitis and louping-ill.

Recently, Casals and Webster⁵ have demonstrated the existence of a close relationship between the viruses of louping-ill and Russian spring-summer encephalitis, a relationship based on similarities in (1) pathogenicity for various hosts, (2) complement-fixing antibody formation, (3) neutralizing antibody formation, and (4) cross-resistance following vaccination. The question arose as to whether this relationship could be further defined to include (5) natural resistance. This was

* These investigations were aided through the Commission on Neurotropic Virus Diseases, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Division, Office of the Surgeon General, United States Army.

¹ Webster, L. T., *J. Exp. Med.*, 1937, **65**, 261.

² Webster, L. T., *J. Exp. Med.*, 1933, **57**, 819.

³ Olitsky, Peter K., Sabin, Albert B., and Cox, Herald R., *J. Exp. Med.*, 1936, **64**, 723.

⁴ Casals, J., unpublished data.

⁵ Casals, J., and Webster, L. T., *Science*, 1943, **97**, 246.