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Biochemical Studies of Human Semen.* II. The Action of Semen on the Human Uterus.

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In the treatment of human sterility, one of us (R. K.) has made many attempts to secure pregnancy by means of artificial insemination. Of the dozens of attempts, only 2 were probably successful. In a number of cases it was observed that when 0.5 cc. of semen was injected into the uterine cavity, the semen was promptly expelled, even though the patient was kept in an extreme Trendelenburg position. A similar quantity of Ringer's solution similarly injected was invariably retained. The patient always gave the same reaction, apparently independent of the phase of the menstrual cycle. These observations led to the following questions: What is the action of human semen upon the human uterus? Do 2 human uteri ever react differently to the same semen? Does one uterus react differently to the semens of 2 different individuals? The answers to these questions can be found in the following observations.

All material (uteri and semen) used for these experiments is of human origin. The uteri were obtained from the operating rooms of the Sloane Hospital, through the kindly cooperation of Dr. Benjamin P. Watson. Immediately after the removal of the uterus from the patient, adjacent strips were cut from it, and dropped into iced Ringer's solution, and placed in the refrigerator until required for an experiment. The strips were cut parallel to the fibers of the external muscular layer.

The semen specimens were obtained from private and clinic patients. Many were delivered directly into sterile jars; a few were condom specimens. The specimens were brought to the laboratory immediately after collection, and placed in the ice-box, at 5° C. The experiments were done as soon as possible after the collection of the semen; usually within 3 hours. The uterine strips were suspended in 100 cc. of warm, oxygenated Ringer's solution, and 1 cc. of the warm semen was added. In all cases, contraction of the uterus caused ascent of the lever.

* Mucin of the Cervix Uteri. I. R. Kurzrok and Edgar G. Miller, Jr., PROC. SOC. EXP. BIOL. AND MED., 1927, **24**, 670.

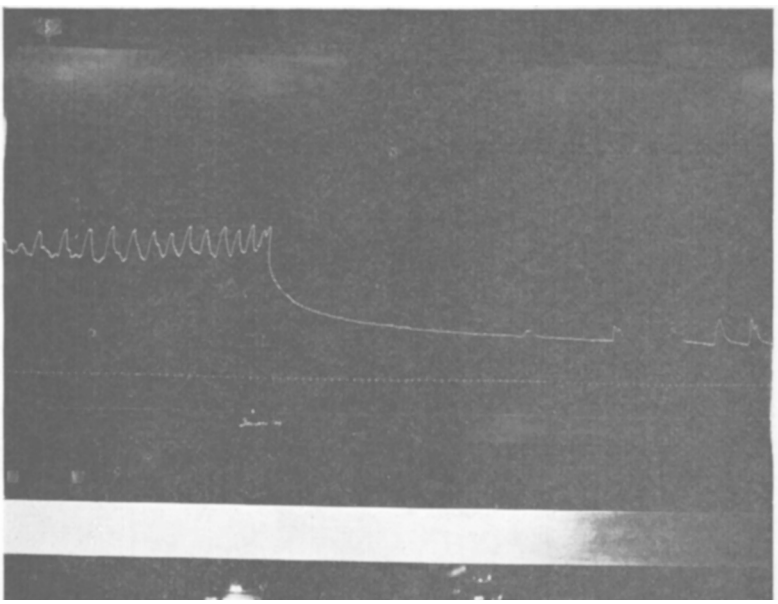


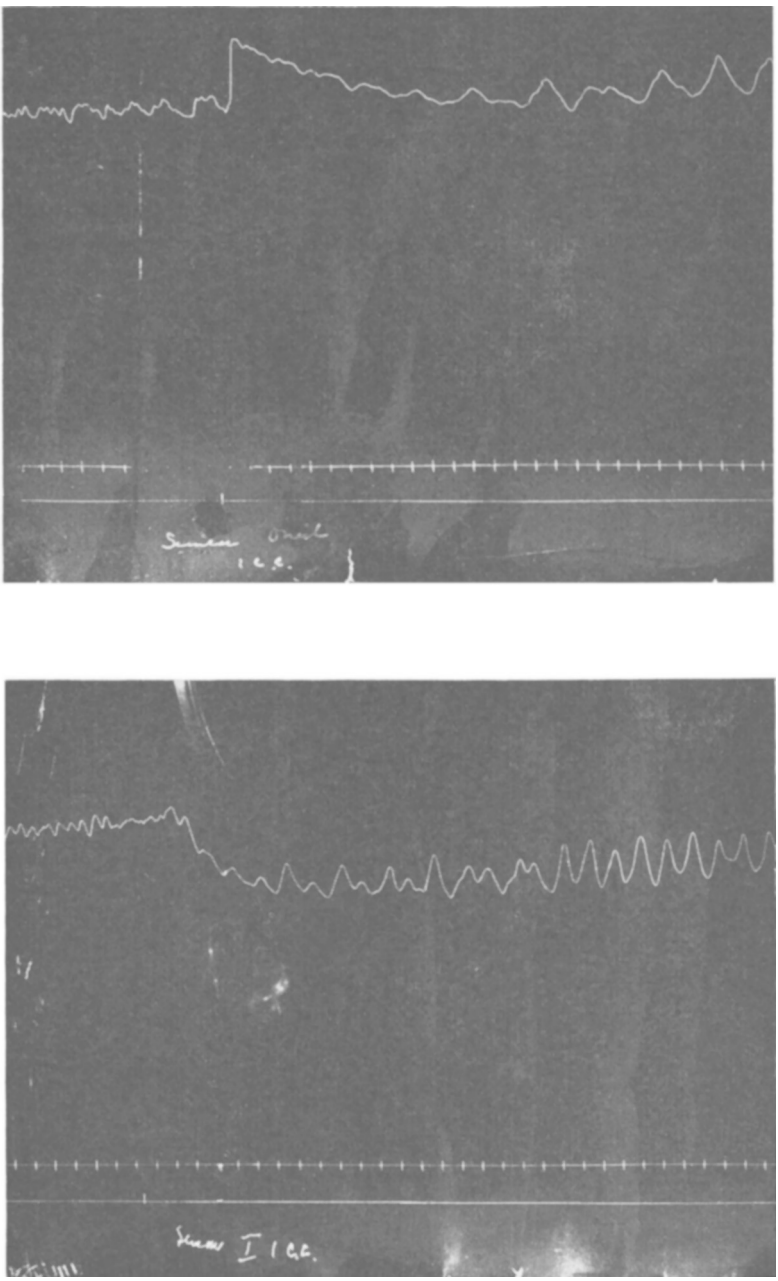
FIG. 1.
A segment of uterus (No. 81753) contracting in 100 cc. oxygenated Ringer's solution. At sequel, 1 cc. of semen was added to cylinder. Contraction-time in this and subsequent figures in minutes.

Fig. 1 shows one typical effect obtained by the addition of semen (No. X) to a contracting uterine strip (No. 81753). The result is a marked relaxation of the uterus, due to loss of tonus. There is marked inhibition of all contractions. This suppression of contraction lasts, on an average, 1 hour, when contractions reappear, develop gradually in strength, but remain in low tonus for several hours more.

Other experiments using different semen and uteri give, not depression but distinct contractions, with a marked rise in tonus, and more or less spasm, during which the individual contractions are extinguished.

Figs. 2 (a and b) show the action of 2 specimens of semen upon the same uterine strip (No. 270079). In Fig. 2a the semen (O.N.) produced a distinct contraction, with temporary spasm. Semen No. 1 caused decrease in strength of contraction, and marked loss of tonus on an adjacent strip of the uterus (Fig. 2b). Later, semen (O.N.) was added to this cylinder, and produced an effect comparable to Fig. 2a.

Fig. 3 is a tracing of 2 strips from 2 different uteri contracting in the same bath; the environment of the 2 strips is, therefore, identical. The addition of semen (No. 1) produced a definite contrac-



FIGS. 2a and 2b.

The graphs were made by 2 adjacent segments taken from the same uterus (No. 270079). In 2a semen (No. 0.N) caused contraction, while in 2b semen (No. 1) caused inhibition of the uterus.

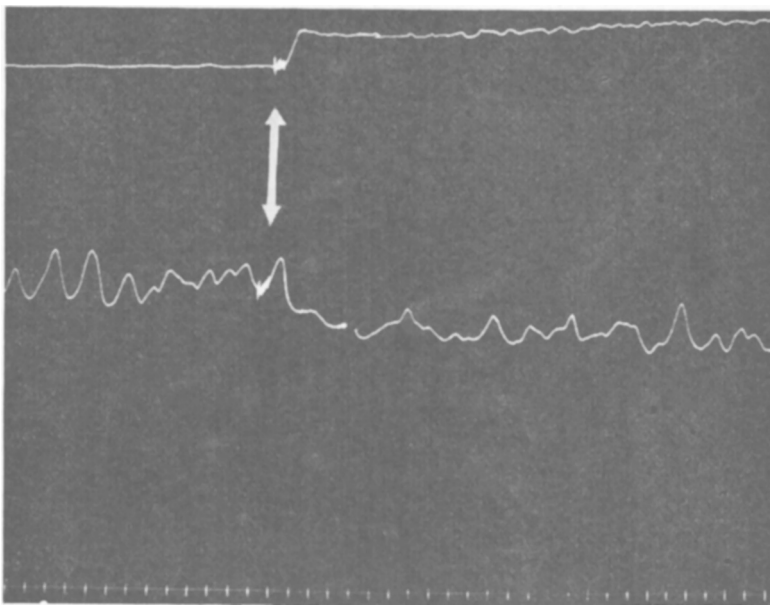


FIG. 3.
Upper tracing made by strip of uterus (No. 271451). Lower graph made by segment of uterus (No. 271839) both segments suspended in same chamber. At arrow, 1 cc. of semen (No. 1) was added.

tion of one uterus (No. 271451), and a well-defined relaxation in the other (No. 271839).

The age of the specimen of semen may influence its action on the uterus; thus a given semen may cause relaxation of a uterine strip, if applied within 3 or 4 hours after collection. If it is kept at 5°C. for 24 hours and then tested on another strip of the same uterus, it may cause a definite contraction. This reversal of action is not due to a change of the pH of the semen. Dr. Edgar G. Miller, Jr., was kind enough to dialize some specimens of semen, and we found that the active agents passed through the collodion membrane.

Spermatozoa are not essential to the reactions described in this paper.

We are indebted to Dr. Harold W. Dudley, of the National Institute of Medical Research, London, for supplying us with some spermine, which he prepared and found relatively non-toxic (personal communication).

Summary. The same uterus may react to one semen by contraction; to another by relaxation. The same semen may contract one uterus and relax another. From this we may draw the tentative conclusions that certain types of sterility are sometimes due to the

female, sometimes to the male. A study of the history of the patients from whom uterine strips were obtained throws an interesting light on our experiments. The uteri from the patients who give a history of successful pregnancy responded to fresh semen by relaxation, while uteri from women who gave a history of complete or long-standing sterility were always stimulated by semen. A tentative deduction is permissible: Uteri are of 2 kinds, receptive and rejective; semina are also of 2 kinds, stimulant and depressant. A large series of carefully selected cases will be studied, with the purpose of criticising these deductions.

We wish to thank Professor Benjamin P. Watson for putting at our disposal the large clinical facilities of the Sloane Hospital and Vanderbilt Clinic.

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Induction of Tetany in Rachitic Rats by Means of a Normal Diet.

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In the study of experimental tetany, removal of the parathyroid glands has generally been resorted to. Following this procedure the calcium concentration of the blood promptly falls and the animal develops tremor or convulsions. Dogs have commonly been used and the thyroid as well as the parathyroids have been extirpated. It is evident that, from a pathogenetic standpoint, this procedure can not be compared with the mechanism of infantile tetany. Another method is to induce tetany by giving large amounts of the phosphates. This procedure likewise can not be considered satisfactory, as it does not reproduce or simulate conditions associated with the development of tetany in human beings. Since infantile tetany comes about almost invariably as a sequel to rickets, it is remarkable that investigators have not more often attempted to induce tetany as a complication of a previously existing rickets. Shohl[1] has clearly recognized the importance of bringing about tetany in rachitic animals and has reported a number of investigations in which this disorder was occasioned by giving phosphates to rachitic rats. More recently Hamilton[2] and his coworkers have induced tetany in rabbits which previously had been rendered rachitic.

[1] Shohl, A. T., and Brown, H. B., 1929, **84**, 501.

[2] Hamilton, B., Kajdi, L., Meeker, D., *J. Biol. Chem.*, 1930, **86**, 331.