

ARTIFICIAL PRODUCTION OF STERILITY

WITH SPECIAL REFERENCE TO EXPERIMENTAL TEMPORARY STERILITY
BIOLOGICALLY INDUCED IN THE FEMALE

BY JULIUS JARCHO, M.D., F.A.C.S., NEW YORK

*(Attending Gynecologist and Obstetrician, Sydenham Hospital; Attending
Gynecologist, Beth David Hospital and Home of Daughters of Abraham;
Consulting Gynecologist, Hastings Hillside Hospital)*

THE present-day method of defeating fertility in civilized communities is by the induction of abortion or the practice of contraception. That many pregnancies are prevented or terminated by artificial means is a well-recognized fact. Changing social conditions, by giving woman a definite status in the business world, have done much to discourage the natural function of childbearing. Many women who continue to work after marriage feel that their economic status will not allow them to resign their positions and therefore sacrifice or postpone motherhood. Another type of woman who frequently resorts to contraception or abortion, or both, is the mother of a large family who is weary of the obligations of rearing children and feels that she is entitled to a respite. Usually some one of the various methods of contraception is utilized; but, when this fails, abortion is generally induced.

The frequency with which abortions are performed is appalling. Professor V. S. Gruzdev,¹ of the University of Kazan, states that there is actually a pandemic of abortions spread all over the world, invad-

do not believe that their findings indicate that a diagnosis of "immunity to spermatozoa" can be made by serologic methods in cases of sterility.

Oslund,²¹ in 1926, claimed that the delay in pregnancy occasionally found after sperm injection is of short duration and is probably caused by physical disturbances of the body rather than antibody reactions, also that some of the delayed pregnancies reported in the literature were probably due to breeding conditions. This view, however, is contrary to the work of most investigators.

Perhaps the most exhaustive experiments with reference to the biologic induction of temporary sterility in female animals have been performed by Kostromin and Kartashev,²² of the Perm Institute of Bacteriology, in East Soviet Russia.

As this paper is very difficult to obtain and appears only in Russian, I thought it desirable to quote it at great length for the benefit of the average reader, to whom the material would not otherwise be available.

The government of Soviet Russia recognized economic distress as an indication for the prevention of conception and is sponsoring a considerable amount of research for the purpose of devising a biologic method of contraception applicable to women. In the United States, of course, we are not in sympathy with such a liberal use of contraceptive technic and believe that impregnation should be prevented only when the health of the woman demands this course. Nevertheless, while we cannot countenance the far too liberal application of the prevention of conception by biologic means advocated in Soviet Russia, we must admit that the results of the research work done for this purpose have great scientific value and that we may possibly utilize them to advantage for the control of impregnation under conditions set forth by the physician.

Kostromin and Kartashev began their experiments in 1924 and completed them in 1927. They injected female rabbits and guinea pigs with heterogenous spermatozoa, both living and dead, and obtained positive results in both cases. However, the results were better when living spermatozoa were used. They used spermatozoa from the bull for immunization of rabbits and guinea pigs; and from rabbits for the immunization of guinea pigs; and from guinea pigs for the immunization of rabbits. The experimental results reported by Kostromin and Kartashev are most impressive and offer much encouragement for the clinical application of biologic sterilization in the practice of gynecology. Certainly the results of the investigations so far reported are sufficiently convincing to justify further study with the hope of eventually placing at the disposal of the physician a simple, safe, and convenient method of inducing temporary sterility under circumstances when the onset of pregnancy would endanger the health of his patient. But we must be conservative. To quote an editorial²⁴ in the *Journal of the American Medical Association*, "Whether injection of spermatozoa or spermatoxic serums may be used as a method of sterilization in human biology is a question of the future." Credit is due to Kolpikov²⁵ for the preparation of a standardized vaccine containing a definite number of spermatozoa.

STERILITY DUE TO OVARIAN TRANSPLANTS AND HORMONE INJECTIONS

Haberlandt²⁶ in 1921 attempted to produce temporary sterilization in female animals by transplanting the ovaries of gravid animals. Also experiments performed showed that it is possible to produce a hormonal sterilization of the females by subcutaneous injection of extract of ovaries of pregnant animals.²⁶ The sterile periods lasted one and a half to three months in rabbits and three to four weeks in guinea pigs. Haberlandt considers that this form of sterilization may be applied

as a therapeutic measure by employing injections of extract of ovary of pregnant animals in order to provide temporary sterilization for prophylactic or hygienic reasons. The ovaries of the treated animals contained numerous small follicles but no large mature ones. It therefore appeared that the treatment had brought about a great inhibition in the maturation of the follicles. Treatment with Abderhalden's placenta option had the same effect, especially when the material was taken in the second half of pregnancy.

The inhibition took place in three stages: (1) The animal would not allow herself to be covered. (2) The animal could be covered but fertilization did not take place. (3) The animal became pregnant but the number of young was decreased. Haberlandt²⁷ showed that injections of corpus luteum do not have the effect of interfering with impregnation. In 1927 he produced temporary sterility in white mice by feeding them with ovarian or placental extract over a period of one or two months.²⁸ The sterility induced thereby lasted from one to two and a half months, which is a long time considering the short life of the white mouse. In some cases, the animals were rendered permanently sterile.

Köhler²⁹ attributes Haberlandt's experimental results to a nonspecific protein effect rather than hormone action. He injected female rabbits with various organic extracts, including mammary glands, kidney, testicle, and spleen extracts. He observed that the animals resisted intercourse after such injections and did not become pregnant. Whether the organic extract injected was prepared from the ovary or some other gland, temporary sterility was induced thereby in either case.

Greil³⁰ questions Haberlandt's work with reference to the production of sterility in animals by the implantation of ovaries of pregnant animals and the injection of ovarian extract from pregnant animals. He maintains that there is no proof that sterility in these cases was due to the action of a sex gland hormone, believing that it was caused by a toxic element in the extract used. He asserts that toxic doses of the extract must have been used and is unalterably opposed to the use of such extracts in gynecology.

However, Haberlandt³¹ specifically stated that there was no evidence of toxic action in his experiments.

PERSONAL EXPERIMENTS

In the conduct of my experiments, I have largely followed the line of research laid down by Kostromin and Kartashev, believing that confirmation of their findings would be of great value. I employed female rabbits exclusively, as being the most convenient animal with which to work. It is not too small. On the other hand it is cheap, inexpensive to maintain, and easy to house. It copulates readily when mated. There is never any doubt whether copulation has taken place.

A research worker who is not already familiar with rabbits and contemplates repeating similar experiments, should study carefully the books dealing with the care and breeding of rabbits.^{32, 33, 34}

Hygienic housing, proper food, and regularity of feeding are of much importance. Lusk³⁵ states that in undernutrition in rabbits, the reproductive function is one of the first to suffer. Of recent years it has been fully established that a state of infertility may be produced by a diet deficient in vitamin E. Hammond and Marshall³⁶ assert that the percentage of rabbits which will copulate depends upon the temperature at the time as well as on the abundance of good

TABLE I. INTRAMUSCULAR INJECTIONS OF LIVING SPERMATOZOA

NO. OF DOE	RABBIT	VIRGIN OR MATRON	SPERMATOZOA	WASHED OR UNWASHED	COMPUTED DATE OF CONCEPTION	DATE OF GIVING BIRTH	NO. OF OFF-SPRING	DAYS OF STERILITY	REMARKS
1	V		G.P.	U	----	----	--	82	Died 9/28/27
2	V		G.P.	U	----	----	--	208	
3	V		G.P.	U	----	----	--	208	
13	M		G.P.	W	----	----	--	208	
15	M		G.P.	W	----	----	--	---	Died 7/ 7/27
4	V		SHP.	U	11/ 3/27	12/ 3/27	4	115	
5	V		SHP.	U	----	----	--	64	Died 9/10/27
6	V		SHP.	U	10/28/27	11/28/27	4	110	
16	M		SHP.	W	----	----	--	86	Died 10/ 2/27
17	M		SHP.	U	9/ 3/27	10/ 3/27	2	57	
18	M		SHP.	W	6/ 9/27	7/ 9/27	1	---	Pregnant when injected

Each cubic centimeter contained 30,000,000 living spermatozoa, either guinea pig or sheep and either unwashed or washed, as indicated in the table.

Dosage: First on July 1, 1927—1 c.c.; second on July 3, 1927—2 c.c.; third on July 6, 1927—4 c.c.; fourth on July 8, 1927—6 c.c.

Doe 18 gave birth to one healthy offspring soon after the injections were completed. She was at the beginning of her second half of pregnancy when the injections were begun and it is noteworthy that the injections did not produce abortion, although the possibility arises that they may have been in some way instrumental in preventing a larger litter. In Doe 17 the period of sterility of fifty-seven days is too brief to be considered a successful result. It is interesting that the four pregnancies occurring in this series gave increased litters as the period of sterility was prolonged. The remaining does are still sterile, a period of nearly seven months.

An immunity lasting seven months may not seem significant, unless we consider the relatively short life of the rabbit as compared with the human being. The life of a rabbit is about eight years, and its usefulness as a breeder about four years. Seven months of sterility in a rabbit is therefore equivalent to approximately three years and eleven months in a woman, an appreciable interval of time. It would seem well within the limits of probability that, should biologic sterility prove possible in woman, it will last sufficiently long after the injections to make it of practical value. This state of affairs would apply particularly to such illnesses as tuberculosis, in which a delay of childbirth for several years may be the means of enabling the patient to have a healthy child with relative safety.

In the second series of experiments my aim was to discover whether there is any marked difference when spermatozoa killed with formalin are used instead of the living and active cells. As will be noted in Table II, there were no failures in this series.

The purpose of the third series of experiments was to ascertain whether spermatozoa which were not only dead but whose morpho-

TABLE II. INTRAMUSCULAR INJECTIONS OF WASHED SPERMATOOZOA KILLED WITH FORMALIN

NO. OF DOE RABBIT	VIRGIN OR MATRON	SPERMATO- ZOA— WASHED	NO. OF IN- JECTIONS	INJECTIONS COMPLETED	COMPUTED DATE OF CONCEPTION	DATE OF GIV- ING BIRTH	NO. OF OFF- SPRING	DAYS OF STERILITY	REMARKS
33	V	G.P.	4	7/27	----	----	----	----	Died 7/31
34	V	G.P.	4	7/27	11/ 3/27	12/ 3/27	3	97	
35	V	G.P.	4	7/27	----	----	----	190	
36	V	SHP.	4	7/27	----	----	----	----	Died 8/10
37	V	SHP.	6	9/28	----	----	----	190	
38	V	SHP.	6	9/28	12/28/27	1/28/28	5	151	
39	M	SHP.	4	7/29	----	----	----	----	Died 8/ 8
40	M	SHP.	4	7/29	----	----	----	188	
41	M	SHP.	6	9/28	----	----	----	188	
42	M	RAB.	4	7/29	----	----	----	188	
43	M	RAB.	4	7/29	----	----	----	118	Died 11/27
44	M	RAB.	4	7/29	----	----	----	188	

Each cubic centimeter of the material injected contained 30,000,000 spermatozoa killed with formalin, derived either from guinea pig, sheep, or rabbit. The first injection consisted of 1 c.c.; the second, 2 c.c.; the third, 4 c.c.; and the fourth, fifth and sixth, 6 c.c.

logic integrity had been destroyed as well were capable of inducing sterility on parenteral injection. The four does injected with spermatozoa extracted with alcohol showed a sterility of from one and a half to two months and then gave birth to practically normal litters. The four does injected with spermatozoa extracted with sodium chloride showed a sterility lasting from two and a half to three months and then gave birth to litters decreased in number. The four does injected with spermatozoa extracted with sodium hydroxide showed a sterility lasting to the present, over four months. From these results it may be concluded that injections of spermatozoa extracted with alcohol and spermatozoa extracted with sodium chloride tend to decrease the number in the litters and the short period of sterility is probably due to a nonspecific protein action as Köhler²⁶ has suggested in explanation of Haberlandt's results. Injections of spermatozoa extracted with sodium hydroxide have thus far proved to be effectual. As the spermatozoa employed in the third series of experiments were morphologically destroyed and probably also considerably altered in their chemical construction, it is difficult to attribute their action entirely to true antigenic power.

All of the fifteen control does, coming from the same stock and living under exactly the same conditions as the immunized animals and copulating with the same bucks, became pregnant within a month.

SPERMATOTOXICITY OF THE SERUM

Tests were employed to determine the spermatoxicity of the serum of the immunized does, the control does and also the bucks. Several methods are available for making this test. I employed the simplest, that used by Tushnov. In this test one drop of fresh standardized