# THE SPERMICIDAL POWERS OF CHEMICAL CONTRACEPTIVES. I.

## INTRODUCTION, AND EXPERIMENTS ON GUINEA-PIG SPERMS.

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(With Plate II.)

### Introduction.

The spermicidal powers of the various chemical contraceptives sold to the public have never previously been compared, and no one has been in a position to say that one spermicide is preferable to another. The only literature on the subject consists of the pamphlets issued by the makers of the different pessaries, and these give little or no information on the length of time taken to kill sperms at stated concentrations. The Birth Control Investigation Committee therefore asked me to undertake this investigation. The work was financed by the Committee, and carried out, with Prof. Goodrich's permission, in the Department of Zoology and Comparative Anatomy at Oxford.

It must be understood that in this investigation no observations were made to find whether any of the contraceptives tested have harmful effects upon the vagina or uterus. This question is being studied by other workers under the auspices of the Birth Control Investigation Committee. Some of the makers of the contraceptives studied regard their *germicidal* powers as a recommendation; but this was not considered in this investigation.

Only solid pessaries were investigated, since it seems probable that the semi-liquid ones will be less used owing to their requiring special appliances for their introduction into the vagina. Four contraceptives (quinine, chinosol, semori and speton) were studied in detail. A standard method of comparing the spermicidal powers of chemical contraceptives was elaborated, and by this means two more contraceptives (double-strength quinine and finil) were investigated. New contraceptives can readily be compared with these six by using the standard method of comparison. The standard method will be described in Part II of this report. The characteristics of the six contraceptives studied are given below. Plate II shows what happens when each of these six pessaries is placed in 7·5 c.c. of distilled water in a specimen tube and left for $2\frac{1}{2}$ hours at body temperature.

*Quinine.* The pessary is shaped like a solid flattened thimble. It weighs 2·08 grm. It is stated by the makers to consist of cocoa-butter and 5 grains of quinine bisulphate. When placed in water at the temperature of the body, the pessary retains its shape unless the tube containing it is shaken (see Plate II). It seems probable that the quinine would take a long time to find its way to all parts of the vagina. Possibly the cocoa-butter itself interferes

with the free movement of the sperms with which it comes in contact. Quinine pessaries are manufactured in England.

*Chinosol.* The pessary is of the same shape and weight as the quinine pessary. It is stated by the makers to consist of cocoa-butter and 3 grains of chinosol. The cocoa-butter melts and floats at the surface of water at the temperature of the body (see Plate II). Chinosol pessaries are manufactured in England.

*Semori.* The pessary is a tablet weighing 1·04 grm. It is stated by the makers to consist of sodium bicarbonate, tartaric acid, boric acid and "ortho-oxychinolin sulf." When placed in water at the temperature of the body, the pessary at once starts to make a foam of small bubbles. The purpose of the sodium bicarbonate and tartaric acid is presumably to make this foam by the production of carbon dioxide. The foam probably finds its way to all parts of the vagina, and it is thus rendered unlikely that sperms could pass into the uterus without coming into contact with it (unless the end of the penis were introduced into the cervix, which is said sometimes to occur). Semori is manufactured in Germany.

*Speton.* The pessary is a tablet weighing 1·20 grm. It is stated by the makers to consist of "natrium dichlorylsulfamidbenzoic," "dioxybernstein acid," and sodium bicarbonate, and to give off oxygen in the vagina. When the pessary is placed in water at the temperature of the body, a rather violent effervescence takes place at once, resulting in a foam of large bubbles (presumably of oxygen and perhaps carbon dioxide). The foam occupies a greater space than that formed by the semori and finil pessaries (see Plate II). A large precipitate is formed, which would appear to be rather disadvantageous. Speton is manufactured in Germany.

*Double-strength Quinine.* This pessary resembles the ordinary quinine pessary in every way, except that it may be presumed to contain 10 instead of 5 grains of the bisulphate. It is manufactured in England.

*Finil.* The pessary is in the form of a thin tablet. Two are directed to be used at the same time. The weight of the two pessaries is 1·30 grm. The pessary is stated by the makers to consist of "dioxyquinolin sulf.," boric acid, burnt alum, potato-starch, tartaric acid, sodium bicarbonate and dried egg-albumen. The composition of the pessary resembles that of semori, with the addition of alum, starch and egg-albumen. When placed in water at the temperature of the body, a dense foam of small bubbles is formed at once, together with a small precipitate. Finil is manufactured in Germany.

The first necessity in an investigation into the spermicidal effects of chemical contraceptives is that the conditions of the experiments should approximate as closely as possible to the conditions within the vagina. Unfortunately the vaginal fluid is a complex one, formed of the secretions of the labial glands, Bartholin's glands, the vaginal epithelium and the cervical glands, and varies in amount, composition and *p*H according to whether the woman is sexually aroused and whether she has borne children before. It is clear that a fluid of this sort cannot be exactly reproduced under the conditions of a laboratory investigation.

For this reason, and because in other ways it is impossible to reproduce the actual conditions precisely in the laboratory, it was thought best to perform two series of experiments, as different from one another as could be arranged. Then, if anyone were to criticise one of the series of experiments on the ground that in a certain point the conditions differed materially from vaginal conditions, he could be referred to the other series. One series of

experiments was carried out on guinea-pig sperms, the other is being carried out on human sperms. Some critics may object to the use of guinea-pig sperms at all, when the purpose of the experiments is to find out the effect on human sperms, but there are two reasons why they were used in one series. The first is that they are always obtainable at a few moments' notice. The second is that critics might object to general conclusions being drawn from experiments on the sperms of one man; but if it were shown that even guinea-pig sperms behave to the various spermicides in the same way as the human sperms used, then it might reasonably be concluded that the sperms of other men behave like the human sperms used in the experiments.

Although every effort was made to represent vaginal conditions as closely as is possible in glass vessels, yet it must be recognised that the experiments might have had somewhat different results if they could have been carried out in the human vagina.

Before describing the series of experiments on guinea-pig sperms, it will be convenient to mention three features which are common to this series and to the series on human sperms.

(1) *The concentration of the contraceptive.* In man, about 5 c.c. of seminal fluid are passed into the vagina at a single ejaculation. It is very difficult to know how much fluid is already present in the vagina before the ejaculation. This varies very greatly according to the state of sexual excitement of the woman. No records of measurements of the amount of fluid in the vagina exist, but 2·5 c.c. cannot, I think, be very far from the average amount. After ejaculation there are, then, about 7·5 c.c. of fluid. One pessary to 7·5 c.c. of fluid is therefore the standard concentration of contraceptive used in both series of experiments. For brevity, this concentration is termed the "$S$" concentration throughout, and dilutions are termed $S/10$ (one-tenth of a pessary to 7·5 c.c. of fluid) and so on.

(2) *Examination of sperms under the microscope.* It was necessary to have a hot stage for the microscope, in order that the sperms might not become torpid through cold while being examined. For this purpose a constant stream of water at approximately 37° C. was kept running through a hollow microscope stage. The stream of water was produced by a thermostatic heater, working by gas, regulated to a few degrees above 37° to allow for the cooling which takes place during its passage through a rubber tube to the hot stage.

Two or three drops of the fluid containing sperms are placed in a hollow-ground microscopical slide, and covered. The hollow of the slide is sufficiently large to ensure that a large bubble of air is present when only two or three drops of fluid are used, so that there is no danger of the sperms becoming less active from lack of oxygen during their examination. A $\frac{1}{6}$-inch objective is used for examination.

(3) *Estimation of the activity of the sperms.* This is a subject to which I have given a great deal of consideration. After a comparison of the activity

of a very large number of slides of sperms under all sorts of conditions, I have decided upon the following grades of activity:

III. The majority of the sperms moderately or very active.

II. Ten per cent. of the sperms moderately active, *or* feeble movement in the majority of the sperms, *or* any greater amount of activity that is less than Grade III.

I. Any amount of movement that is less than Grade II (including the slightest movement in a single sperm).

0. No movement whatever observed.

It will be understood that no counts of active and inactive sperms are made, but a general impression is gained by observation of several microscopic fields.

Small differences in activity are shown by the use of the plus sign. Thus II + indicates greater activity than II. But this symbol is used sparingly.

### Experiments on guinea-pig sperms.

The experiments in this series are carried out on sperms suspended in a fluid which I have elaborated for the purpose. This fluid, which may be called buffered glucose-saline, is designed to give maximum sperm activity at the temperature of the body. Its composition is as follows:

| | | |
|---|---|---|
| Acid potassium phosphate ... ... | 0·03 grm. | (Dissolve this first.) |
| Sodium hydrogen phosphate ... ... | 0·6 ,, | |
| Sodium chloride ... ... ... ... | 0·2 ,, | |
| Glucose ... ... ... ... ... | 3·0 ,, | |
| Water ... ... ... ... ... | 100·0 c.c. | |

The standard technique is as follows:

The following are placed in a thermostat at 37° C.: 1 small covered glass capsule containing 17 c.c. of buffered glucose-saline; 2 small covered glass capsules, empty; 1 measuring cylinder; pipettes; hollow-ground microscopical slides and cover-slips.

These remain in the thermostat for 10 minutes or more, to warm up. A male guinea-pig is then killed by a blow on the head, and the tails of both epididymes are removed and placed in the glass capsule containing 17 c.c. of buffered glucose-saline, which has been temporarily removed from the thermostat. The tail of each epididymis is now cut in two and the halves are pressed with forceps to cause the sperms to come out. The fluid is stirred to form an even suspension, and the remains of the epididymes are removed. All this is done rapidly to avoid much cooling. 7·5 c.c. of the suspension is now placed in each of the empty capsules in the thermostat, the warm measuring cylinder and one of the warm pipettes being used. (The remaining 2 c.c. of sperm suspension are thrown away.) Ten minutes or more are now allowed to elapse, in order to be certain that the fluids may have attained the temperature of the thermostat after the slight cooling which occurred during the preparation of the suspensions.

One pessary is now placed in one of the covered glass capsules in the thermostat, the other serving as a control.

Five minutes later both capsules are shaken ten times, the covers being held firmly in position. This is repeated 5 minutes later, and again 5 minutes later. After the third shaking, when the pessary has acted for a quarter of an hour, a microscopical slide of the sperm suspension containing the pessary and another of the control suspension are made, as explained before. Different pipettes are of course used for the two suspensions. The activity of the sperms in each slide is now estimated according to the system of grading explained before, and the result recorded.

It will be observed that in these experiments the concentration of the contraceptive is "*S*."

Four experiments were made with each spermicide. The results are given in tabular form below.

| | Activity of sperms with spermicide at *S* concentration | | | | Activity of corresponding control sperms | | | |
|---|---|---|---|---|---|---|---|---|
| Quinine | III | II+ | III | III | III | III | III+ | III |
| Chinosol | I+ | III | III | III+ | III | III | III | III |
| Semori | 0 | 0 | 0 | 0 | III | III | III | III |
| Speton | 0 | 0 | 0 | 0 | III | III | III | III |

The conclusion is that semori and speton are far more spermicidal than quinine and chinosol, which have hardly any effect in a quarter of an hour[1].

*Note on special technique for speton.*

Such a dense precipitate is formed by the speton pessary used at *S* concentration, that it is impossible to observe the sperms properly under the microscope. A special technique has therefore to be used with speton. In essentials the technique is the same as the standard technique, but it differs in that the pessary is thrown into the fluid and allowed to act for 5 minutes, after which the fluid is filtered and the sperms are introduced into it.

The details of the experiment with the speton pessary are as follows: The following are placed in a thermostat at 37° C.: 1 large covered glass capsule containing 15 c.c. of buffered glucose-saline; 1 small covered glass capsule containing 7·5 of ditto; 1 small covered glass capsule, empty; *1 small glass funnel with glass receptacle and filter-paper; 1 measuring* cylinder; pipettes; hollow-ground microscopical slides and cover-slips.

These remain in the thermostat for 10 minutes or more, to warm up. Two speton pessaries are then placed in the capsule containing 15 c.c. of buffered glucose-saline. After 5 minutes the contents of this capsule are shaken and filtered. 7·5 c.c. of the filtrate are pipetted into the empty capsule.

There are now two small capsules in the thermostat, each containing 7·5 c.c. of buffered glucose-saline; one of them contains speton as well in *S* concentration. These are left for 5 minutes or more to regain the temperature of the thermostat.

A male guinea-pig is next killed by a blow on the head, and tails of both epididymes are removed. Each is divided into two with scissors. One-half of each is placed in each capsule and squeezed with forceps. When the sperms have been pressed out and stirred into an even suspension, the halves of the tails of the epididymes are removed. The suspensions are prepared inside the thermostat, to prevent much loss of heat.

[1] Experiments will be performed to find whether sperms are actually killed, or only temporarily immobilised by the carbon dioxide which is produced by certain contraceptives.

Five minutes after the preparation of the suspensions, both capsules are shaken ten times. From this point onwards the technique is precisely the same as with the other contraceptives. (The three shakings are only given to make the experiment as similar as possible.)

Semori and speton at *S* concentration are both so lethal to guinea-pig sperms that it is not possible to decide, from the experiments recorded above, whether one of them is more so than the other. A series of experiments with these two spermicides was therefore carried out in precisely the same way as before, except that one-tenth of a pessary (by weight) was used instead of one pessary. At this dilution speton does not make a very dense precipitate, and therefore it was not necessary to use the special technique.

Three experiments were performed with each spermicide. The results are tabulated below:

| | Activity of sperms with spermicide at *S*/10 concentration | | | Activity of corresponding control sperms | | |
|---|---|---|---|---|---|---|
| Semori | II | I | II+ | III | III | III+ |
| Speton | II+ | I | II+ | III | III | III+ |

The table shows that there is no significant difference between the spermicidal powers of semori and speton, and that one-tenth of a pessary of either of these two spermicides is much more effective than a whole pessary of quinine or chinosol.

A series of experiments was performed to find whether the inefficacy of the quinine and chinosol pessaries was due to their not dissolving sufficiently rapidly. In this series the pessary was placed in the fluid 12 hours or more before the sperms were added, and the fluid was shaken from time to time during this period. In this way it was made certain that the spermicides were acting at the full concentration intended by the manufacturer.

The experiments were carried out as follows:

Two pessaries are placed in a stoppered glass phial in the thermostat at 37° with 15 c.c. of buffered glucose-saline. This is left in the thermostat for 12 hours or more, being shaken occasionally during this period.

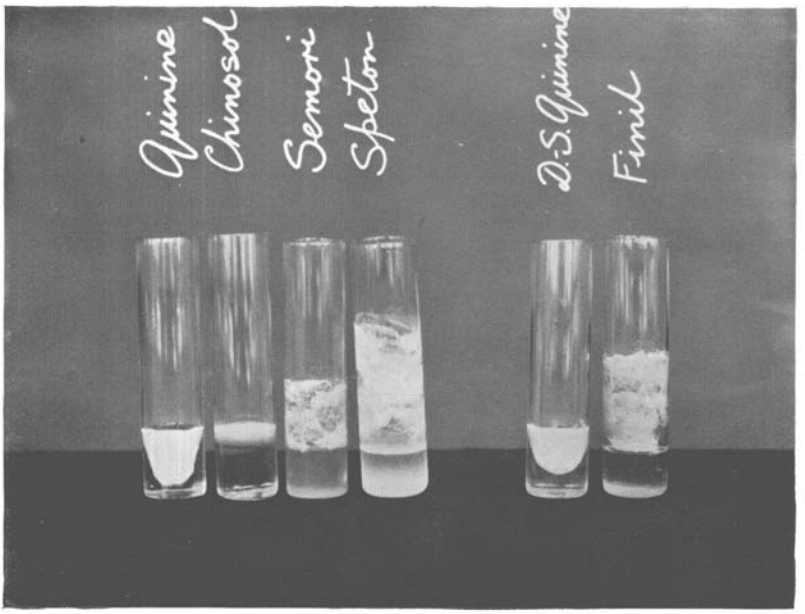
7·5 c.c. of this fluid are then pipetted into one capsule, and 7·5 c.c. of buffered glucose-saline into another. These are covered and left for 10 minutes or more to warm up.

A sperm-suspension is prepared in each precisely as in the "Special technique for speton" (see p. 327), and from now onwards the technique is the same as in that method.

The results are tabulated below:

| | Activity of sperms with spermicide at *S* concentration, after the spermicide has been allowed to dissolve for 12 hours or more | | | Activity of corresponding control sperms | | |
|---|---|---|---|---|---|---|
| Quinine | III | II+ | III | III | III | III+ |
| Chinosol | III | III+ | III | III | III | III |

The table shows that quinine and chinosol pessaries are ineffective even when they have been allowed to dissolve for 12 hours or more, and that their inefficacy is therefore due to the low spermicidal powers of the quinine and chinosol at the standard concentration.




Contraceptives investigated after $2\frac{1}{2}$ hours in water at the temperature of the body.

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## CONCLUSION.

Experiments on guinea-pig sperms show that one-tenth of a pessary of semori or speton is much more spermicidal than a whole pessary of quinine or chinosol. The latter spermicides, in standard concentration, have little or no effect on guinea-pig sperms in a quarter of an hour. This is due to the small spermicidal powers of the active substances, and not simply to their dissolving slowly out of the cocoa-butter vehicle.

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