THE SPERMICIDAL POWERS OF CHEMICAL CONTRACEPTIVES.

III. PESSARIES.

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CONTENTS.

Introduction.

My first paper (1930) in this series contained a general introduction and an account of a preliminary investigation of a few pessaries with guinea-pig sperms. The second paper (1931) was concerned not with pessaries, but with chemically pure substances, free from any vehicle. In this third paper I return to pessaries. First I describe some experiments performed with guinea-pig sperms in continuation of those reported on in my first paper. I then present an account of a technique for pessaries using human sperms, and of the results obtained with it. Finally, experiments on the foam-producing pessaries in the absence of the foam-producing substances are described. The next paper in the series will deal with more pure substances.

I wish to thank the Hon. Mrs Marjorie Farrer and the Birth Control Investigation Committee once more for continued support. The work described in this paper could not have been performed had not Dr C. P. Blacker given invaluable help in many ways. Prof. E. S. Goodrich, F.R.S., has kindly allowed the whole of this investigation to be carried out in the Department of Zoology and Comparative Anatomy at Oxford. I want to thank him for his interest in the work.

The pessaries investigated.

Some of these were described in the first paper, but it will be convenient to describe them all here, especially as I now have more accurate information as to some of them. The makers of all the pessaries have most kindly communicated the quantitative analyses of them to me, but they do not allow me to make these analyses known to anyone else, except in the case of the quinine and chinosol pessaries.

The qualitative analyses are not secret.

Quinine. The pessary is shaped like a solid flattened thimble. It weighs 2·08 grm. It consists of 0·324 grm. of quinine bisulphate in cocoa-butter. It is made by Messrs Lambert.

Double-strength quinine. This is the same as the quinine pessary, except that it contains 0·648 grm. of quinine bisulphate. It is made by Messrs Lambert.

Chinosol. This is the same as the quinine pessary, except that it contains 0·195 grm. of potassium oxyquinolin sulphate (chinosol) instead of quinine. It is made by Messrs Lambert.

Lactic acid. The pessary is shaped like a solid flattened thimble. It weighs 1·58 grm. It consists of lactic acid in cocoa-butter. It is made by Messrs W. H. Martindale.

Contraps. This is a large spherical pessary weighing 10·9 grm. It consists of magnesium sulphate, lactic acid, quinine bisulphate, glycerine, tragacanth and water. There is no cocoa-butter nor foam-producing substances. It is made by Messrs Docker.

Quinine urea hydrochloride. This is a minute tablet weighing 0·17 grm. It contains only quinine urea hydrochloride and sodium chloride. There is no cocoa-butter nor foam-producing substances. It is made by Messrs Parke, Davis.

Semori. This is a foaming tablet weighing 1·04 grm. It consists of dioxyquinolin sulphate, potassium borotartrate, sodium bicarbonate and tartaric acid. It is made by Messrs Luitpold Werk in Munich.

Speton. This is a foaming tablet weighing 1·20 grm. It consists of sodium dichloryl-sulphamidbenzoate, lactose, starch, French chalk, sodium bicarbonate and tartaric acid. It is made by Messrs Temmler in Berlin.

Finil. This is a thin foaming tablet. Two are directed to be used together. The weight of two is 1·30 grm. The constituents are dioxyquinolin sulphate, boric acid, burnt alum, starch, egg albumen, sodium bicarbonate and tartaric acid. Finil is made by the Pharmazeutische Fabrik in Munich.

Monsol. This is a foaming tablet weighing 0·97 grm. It contains powdered quillaia bark, monsol fluid, gum extract, sodium bicarbonate and potassium hydrogen tartrate. Monsol fluid contains substances allied to cresol. This tablet is made by the Mond Staffordshire Refining Co., but is not yet on the market.

Experiments with guinea-pig sperms.

In the first paper in this series it was shown that if a quinine or cocoa-butter pessary is thrown into 7·5 c.c. of guinea-pig sperm suspension at the temperature of the body, and left there for a quarter of an hour, the activity of the sperms is affected little or not at all.

This gave rise to the supposition that the inefficiency of the pessary might be due simply to the slowness of the diffusion of the quinine or chinosol out of the cocoa-butter. Accordingly a series of experiments was performed, in which the pessary was left in glucose-saline solution for 12 hours at the temperature of the body, with occasional shaking, before the introduction of the

sperms. As before, one pessary was allowed to 7·5 c.c. of fluid. Although the pessary was of course melted, the sperms were scarcely or not at all affected in a quarter of an hour.

The conclusion reached was that the inefficiency of the pessary was due to the low spermicidal power of quinine bisulphate and chinosol. Since the first paper was written, I have disproved this conclusion, as follows.

A series of experiments was carried out in exactly the same way as in the first series, except that instead of introducing one pessary into 7·5 c.c. of sperm suspension, 0·324 grm. of finely powdered quinine bisulphate or 0·195 grm. of finely powdered chinosol was introduced instead. These are the actual amounts contained in one pessary. The results, which are most remarkable, are recorded below. The activity of the sperms, after a quarter of an hour with the quinine or chinosol, is indicated by a system of grading which is explained at length in my second paper. III indicates that the majority of the sperms were active; 0 indicates that not a single active sperm was seen in ten microscopical fields of a $\frac{1}{6}$ in. objective with No. 2 eyepiece. I, I+, II and II+ indicate intermediate grades of activity. In the experiments recorded below, the control sperms were III or III+ in each experiment.

The results were as follows:

Quinine	0	0	0
Chinosol	0	0	0

Not a single movement in a single sperm was seen in any of the six experiments.

This experiment was performed at *S* (standard) concentration, *i.e.* in the proportion of one pessary to 7·5 c.c., which is postulated as being the usual amount of fluid in the vagina after coition. The next series of experiments was performed on *S*/10 concentration. The technique was the same, except that 0·032 grm. of quinine bisulphate and 0·02 grm. of chinosol were used instead of the 0·324 grm. and 0·195 grm. respectively. Three experiments were again performed with each pessary, the control sperms being III or III+ in each case. The results were as follows:

Quinine	0	0	0
Chinosol	0	I	I+

This shows that although a pessary of quinine or chinosol has scarcely any or no effect on sperms, even when it has been melted for 12 hours, yet it contains ten times as much quinine as suffices to kill every sperm in a quarter of an hour, or ten times as much chinosol as suffices to kill the great majority of the sperms. I cannot account for this paradoxical result. It would be understandable if quinine bisulphate or chinosol were more soluble in cocoa-butter than in water; but they are quite insoluble in cocoa-butter, and are only suspended in it.

The following table shows the results of all the experiments which have been performed by the standard technique for comparing pessaries, using

guinea-pig sperms. Most of these results were recorded in my first paper, but they are all brought together in one place for convenience. The pessaries are arranged in the order of their spermicidal powers. The control sperms were III or III+ in each case. The result of the experiment was not recorded if the control sperms were less active than this.

	At S concentration				At $S/10$ concentration		
Quinine urea hydrochloride	0	0	0	0	I	I	I+
Semori	0	0	0	0	I	II	II+
Speton	0	0	0	0	I	II+	II+
Chinosol	I+	III	III	III+	Not tested		
Quinine	II+	III	III	III	Not tested		

Experiments with human sperms.

Brief description of the technique.

Guinea-pig sperms are extremely convenient to work with, but it was felt to be essential to carry out a series of experiments using human sperms. This was made possible by two men who volunteered as donors. Both men are of young middle age and the fathers of families, so their sperms may be regarded as normal.

In the experiments with human sperms every effort was made to represent actual conditions as closely as possible. The whole experiment was carried out on the scale of one-fifth, in order to economise semen. Thus, instead of trying one pessary to 2·5 c.c. of artificial vaginal fluid and 5 c.c. of semen, which is postulated as being the standard (S) concentration, one-fifth of a pessary was used with 0·5 c.c. of artificial vaginal fluid and 1 c.c. of semen.

The following is a brief description of the technique, for the benefit of those who do not care to follow the detailed description.

0·5 c.c. of artificial vaginal fluid (a neutralised glucose solution) is placed in a glass specimen tube in a damp chamber in a thermostat maintained at the temperature of the body. 1 c.c. of human semen is placed in another tube in the same damp chamber. When the fluids have warmed up, one-fifth of a pessary is thrown into the artificial vaginal fluid. A quarter of an hour later the warm semen is transferred to the same tube as the artificial vaginal fluid and the one-fifth pessary. Half an hour later the sperms are examined under the microscope. The result of the experiment is not recorded unless the control sperms are active (II+, III or III+).

This experiment was performed four or five times with each make of pessary. Those pessaries which were shown by this experiment to be effective were tested again at $S/10$ concentration.

The details of the general technique and of the special techniques required for certain of the pessaries are given below.

Results.

The following is a summary of the results of the experiment. The pessaries are arranged in the order of their spermicidal powers.

	At S concentration					At $S/10$ concentration				
Semori	0	0	0	0		0	0	I	I	I+
Quinine urea hydrochloride	0	0	0	0		0	I	I+	I+	
Monsol	0	0	0	0		I	I	I	I	I+
Speton	0	0	0	0		0	I+	II	II	II
Finil	0	0	0	I		I	I+	I+	II	II
Chinosol	0	0	0	I						
Double-strength quinine	II+	II+	III	III						
Quinine	II+	III	III	III	III					
Lactic acid	II+	III	III	III+						

A complete investigation of contraps was not made, as its very large size introduced difficulties. Only a minute part dissolves when one-fifth of it is placed with 0·5 c.c. of artificial vaginal fluid. In two experiments at S concentration it reduced the activity of the sperms to I. It would have been equally effective at $S/10$ concentration, for the same amount of it would have dissolved.

It seems worth mentioning that the mean amount of semen produced at each ejaculation by one of the donors was 6·7 c.c. This is based on the measurement of 23 ejaculates. The maximum amount was 10·5 c.c. and the minimum 4·5 c.c.

Full description of the technique.

The following is a detailed account of the technique, which may be applied, with the specified modifications, to all pessaries of reasonable size. In order to shorten this account, several references are made to the second paper in this series, in which a very detailed account is given of a somewhat similar technique, for comparing the spermicidal powers of pure substances.

(1) A thermostat is maintained at 37° C. It contains coverslips, pipettes and a damp chamber. The latter, which contains a rack of small specimen tubes, is described and figured in my second paper.

(2) A hot stage, regulated thermostatically to 37° C., is arranged on a microscope.

(3) The average weight of the pessary to be investigated is determined.

(4) One-fifth of a pessary is weighed out, and set aside in a corked specimen tube, sealed with wax, until semen is available.

(5) Some ice and a corked specimen tube are placed in a vacuum flask, the cork of the specimen tube having been impregnated with paraffin wax.

(6) Semen is caught in a rubber sheath at coition.

(7) The contents of the sheath are shortly afterwards transferred to the corked specimen tube, and left within the vacuum flask until required for the experiment.

(8) A neutral fluid, isotonic with mammalian blood, is prepared by adding sufficient 6 per cent. aqueous sodium hydrogen phosphate ($Na_2HPO_4.12H_2O$)

solution to 5·2 per cent. aqueous glucose solution to cause a sample of it to give a yellowish-green colour with the "Universal" Indicator of Messrs British Drug Houses. The amount of phosphate solution required depends on the length of time that the glucose solution has been made up. Since the vaginal fluid is sometimes acid, sometimes neutral and sometimes alkaline, it was thought best to use a neutral fluid. Since the vaginal fluid is a very complicated and variable one, it was obviously impossible to represent its chemical composition accurately in a laboratory investigation.

(9) 0·5 c.c. of this artificial vaginal fluid is transferred with a graduated pipette to each of two test-tubes in the damp chamber, and is left to warm up. One tube is the control tube, the other the experimental tube.

(10) 1 c.c. of semen is transferred with a graduated pipette to each of two other tubes in the damp chamber in the thermostat, and left to warm up. If the semen is stringy, it is difficult to measure 1 c.c. accurately when cold. Under these circumstances it is best to warm the semen slightly before transferring it to the tubes in the damp chamber.

(11) A quarter of an hour later, one-fifth of a pessary of the contraceptive to be investigated is placed in the experimental tube. If necessary it is pushed below the surface of the fluid.

(12) A quarter of an hour later again, the semen from one of the two tubes containing it is transferred with a pipette to the control tube.

(13) Air is bubbled through the contents of the control tube with a pipette. This mixes the fluids and promotes respiration by the sperms.

(14) The contents of the other tube of semen are transferred to the experimental tube.

(15) Air is bubbled through the experimental tube. If the fragment of pessary is caught in the froth, it is pushed down into the fluid again.

(16) The time is recorded as the start of the experiment.

(17) Two hollow-ground microscopical slides are labelled with a grease-pencil. One is labelled *C* (control), the other with letters denoting the name of the pessary under investigation.

(18) Over the grease-pencil lettering on each slide is fixed a blank gummed-paper label, stuck down at one side in such a way that it may be turned back to disclose the grease-pencil lettering. The object of this arrangement is explained in section 24.

(19) The labelled slides are placed in the thermostat.

(20) Ten minutes after the start of the experiment, air is again bubbled through each tube. A clean pipette is of course used for each tube. The repeated bubbling of air through the fluids not only promotes respiration, but also ensures that all the sperms present are acted upon by the spermicide at the same concentration. This is important, for only three drops are examined under the microscope, and inconclusive results would be obtained if it were not certain that the sperms in these three drops were representative of all the sperms in the tube.

(21) Twenty-five minutes after the start of the experiment (section 16), air is again bubbled through the control tube, and with the same pipette three drops of the fluid are transferred to the hollow of the slide marked *C*. (If the fluid does not form readily into drops, an equivalent amount is transferred.)

(22) A coverslip is applied. The slide is left on the floor of the thermostat. Three drops of fluid do not fill the hollow of the slide. A large bubble of air is included below the coverslip, which prevents the sperms from becoming inactive quickly from inability to respire.

(23) The process described in the last section is applied to the contents of the experimental tube and to the slide labelled with the name of the pessary under investigation.

(24) The slides are shuffled together, till the observer does not know which is which. Bias, conscious or unconscious, is thus avoided. The shuffling is particularly valuable when two or three different pessaries are being tested at the same time. (See section 30.)

(25) As exactly as possible half an hour after the start of the experiment (section 16), the slides are removed one by one from the thermostat and examined under the microscope with a $\frac{1}{6}$ in. objective and No. 2 eyepiece, on the hot stage mentioned in section 2. The sperms in the peripheral part of the hollow of the slide are observed. If the sperms in the deep part of the hollow of the slide were examined, a different impression of the percentage active would be likely to be gained. Living human sperms have a marked tendency to apply themselves to surfaces. One may focus a long way up and down in the region of the deep part of the hollow without seeing many active sperms, while crowds of active ones are present in the shallow peripheral part.

(26) The activity of the sperms is recorded on the blank labels on the slides, in accordance with the system of grading which is explained at great length in the second paper. Here it must suffice to say that III indicates that the majority of the sperms are moderately active, II+ indicates that it cannot quickly be decided whether the majority are moderately active or not, and 0 indicates that not a single active sperm was seen in ten microscopical fields of view, while I, I+ and II indicate intermediate degrees of activity.

(27) The blank labels are turned aside to disclose the identity of the slides.

(28) If the control sperms show an activity of II+ or more, the result of the experiment is recorded.

(29) If the control sperms show an activity of less than II+, the result of the experiment is not recorded. It would have been more satisfactory if only those experiments could have been recorded in which the activity of the control sperms was III or III+. Unfortunately this was impossible, as the experiment could not be performed immediately after the ejaculation of semen. Indeed, nearly half of the samples of semen used came through the post.

(30) From one to three contraceptives may be tested at the same time against the same control.

(31) If the pessary forms a sediment which renders it impossible to observe the sperms properly under the microscope, or if it is so small or crumbly that one-fifth of a pessary cannot be separated in one piece, modifications of the technique are employed, which are described below.

(32) If the contraceptive under investigation is not sufficiently spermicidal to reduce the activity of the sperms to 0, the experiment described above is performed four or five times (not counting experiments in which the activity of the control sperms is less than II+).

(33) If the contraceptive under investigation is sufficiently spermicidal to reduce the activity of the sperms to 0 in four consecutive experiments, its efficiency is further tested by carrying out the experiment four or five times, using one-fiftieth of a pessary instead of one-fifth. When one-fiftieth of a pessary is used, the sediment is never great enough to necessitate the use of the modified technique. When one-fiftieth of a pessary is used, the contraceptive is at $S/10$ concentration.

Modification of the technique for pessaries which form a sediment (semori, monsol, finil, speton).

In this modification of the usual technique, the following are placed in the thermostat in addition to the objects mentioned in section 1 of the description of the usual technique:

One glass capsule of about 100 c.c. capacity, with a watch-glass, concave side upwards, for a cover. (A watch-glass is used as a cover, because the foam produced by some pessaries will displace a flat cover. The watch-glass may be weighted if necessary.) One glass funnel with filter-paper and glass receptacle.

The procedure is as usual in other respects up to and including section 8, and then as follows:

(i) 10 c.c. of neutralised glucose solution is placed in the glass capsule. It is left to warm up.

(ii) 0·5 c.c. of neutralised glucose solution is placed in a specimen tube in the damp chamber, and left to warm up. This is the control tube.

(iii) A quarter of an hour after the 10 c.c. of glucose solution were placed in the capsule, 1 c.c. of semen is transferred with a graduated pipette to each of two empty specimen tubes in the damp chamber, and left to warm up.

(iv) Four whole pessaries of the contraceptive under investigation are thrown into the 10 c.c. of glucose solution in the capsule. The capsule is shaken. Four pessaries to 10 c.c. are equivalent to one pessary to 2·5 c.c., which is postulated as being the amount of fluid normally present in the vagina before ejaculation of semen. Much more fluid is taken than will be used, because in the subsequent filtration only a small part of it generally manages to pass the filter. Most is retained in the form of foam. (In the case

of finil, eight pessaries are thrown into the capsule instead of four, because two pessaries are directed to be used together at each coition.)

(v) Five minutes later the capsule is shaken again.

(vi) Ten minutes later, when the pessaries have been a quarter of an hour in the fluid, the capsule is shaken again, and the fluid filtered in the warm filter.

(vii) 0·5 c.c. of the filtrate is transferred with a graduated pipette to a tube in the damp chamber. This is the experimental tube. The remainder of the filtrate is discarded.

(viii) The semen from one of the tubes in the damp chamber containing it is transferred with a pipette to the control tube.

(ix) The usual procedure is now adopted, beginning at section 13.

Modification of the technique for the quinine urea hydrochloride pessary.

The quinine urea hydrochloride pessary is so small and powdery that it is not possible to cut off a piece of it exactly one-fifth of the total weight. Its spermicidal power is therefore tested at S concentration as though it were a pessary forming a sediment, since in that technique whole pessaries, not one-fifth pieces, are used. One pessary is dissolved in 2·5 c.c. of neutralised glucose solution at 37° C., and 0·5 c.c. of this is transferred to the experimental tube. The fluid is not filtered, as complete solution takes place.

The same technique is used to test the efficiency of this pessary at $S/10$ concentration, except that one pessary is dissolved in 25 c.c. of neutralised glucose solution. As before, 0·5 c.c. of this solution is transferred to the experimental tube.

This modification of the technique could be applied to any pessary in order to test it at very low concentrations. This would be necessary if any pessary were invented which always killed all sperms at $S/10$ concentration. One would then need to test it at $S/20$ or even $S/100$. This could easily be done by dissolving one pessary in 50 c.c. or 250 c.c. of neutralised glucose solution at 37° C., and transferring 0·5 c.c. of the solution to the experimental tube.

TEST OF FOAMING PESSARIES IN THE ABSENCE OF THE FOAM-PRODUCING SUBSTANCES.

It was felt that foaming pessaries should be tested also without the foam-producing substances, for two reasons. Firstly, there is the possibility that carbon dioxide may only temporarily immobilise sperms. Secondly, if a pessary relies too largely on the carbon dioxide which it produces, it will not be effective unless placed in the vagina at precisely the proper time before the ejaculation of semen.

Guinea-pig sperms were used in this part of the work. Semori, finil and speton were tested, but not monsol. It did not seem worth while in the case of monsol, for this pessary is not yet on the market.

The experiments were carried out as follows.

The essential constituents of the pessary, other than the foam-producers, are dissolved in 0·9 per cent. sodium chloride solution, at the concentration at which they exist when one pessary is dissolved in 2·5 c.c., the postulated amount of vaginal fluid. Unessential constituents, such as French chalk, starch, lactose and egg-albumen, are omitted for the sake of simplicity. A sperm suspension is prepared by squeezing the tails of both epididymides of an adult male guinea-pig in 5 c.c. of B.G.S. (Instructions for the preparation of the fluid called B.G.S. are given in the second paper.) 1 c.c. of this is mixed with 0·5 c.c. of the fluid containing the essential constituents of the pessary, after both have been allowed to warm up for a quarter of an hour. The experiment is disregarded unless the control sperms show an activity of III or III+. In all other respects the experiment is carried out according to the usual technique for pessaries with human sperms.

Finil presents the difficulty that the essential constituents will not dissolve completely at the concentration of one pessary to 2·5 c.c. of 0·9 per cent. sodium chloride solution. It was not necessary, however, to invent a special technique for this pessary, for despite this handicap, it always killed all sperms.

The results were as follows:

Pessaries without foam-producers and unessentials, at *S* concentration.

Semori	0	0	0
Finil	0	0	0
Speton	III	III	III

This proves that, even without foam-producers, semori and finil kill all sperms at *S* concentration. Speton, on the contrary, is without effect if the foam-producers are omitted.

It was decided to test semori and finil at *S*/10 concentration, without foam-producers. The experiments were carried out exactly as before, except that the essential constituents of the pessary, other than foam-producers, were dissolved in 0·9 per cent. sodium chloride solution at the concentration at which they exist when *one-tenth* of a pessary is dissolved in 2·5 c.c.

The control sperms showed an activity of III or III+ in each experiment.

The results were as follows:

Pessaries without foam-producers and unessentials, at *S*/10 concentration.

Semori	0	0	0
Finil	I	I	I

This shows that both semori and finil are very spermicidal at *S*/10 concentration even when the foam-producers are omitted. Semori has the advantage both here and in the standard experiment.

It was thought possible that the inefficiency of speton without foam-producers at *S* concentration might be due to the fact that sodium dichlorylsulphamidbenzoate (the only essential constituent other than foam-producers) is only effective when freshly dissolved. Accordingly the experiment was performed as before, except that the sodium dichlorylsulphamidbenzoate was

only dissolved at the last possible moment, 5 minutes before the start of the experiment (*i.e.* 5 minutes before section 16 in the standard technique). This substance dissolves almost immediately. Directly it had dissolved, 0·5 c.c. of the solution was transferred to the experimental tube. It had thus less than 5 minutes in which to warm up instead of a quarter of an hour, but this could not affect the result, as the 1 c.c. of sperm suspension was warmed for the usual quarter of an hour. The control sperms showed an activity of III or III+ in each experiment.

The result was as follows:

Pessary without foam-producers and unessentials, at *S* concentration, dissolved immediately before the experiment.

Speton	III+	III

This proves that sodium dichlorylsulphamidbenzoate is not spermicidal even when freshly dissolved, and the spermicidal power of speton is wholly due to its foam-producers.

DISCUSSION.

It is clear that the cocoa-butter pessaries are less effective than the foam-producing ones and the quinine urea hydrochloride pessary, when tested by the techniques described in this paper. Chinosol, the most effective of the cocoa-butter pessaries, is shown by the standard experiments on human sperms to have the same spermicidal power as the least effective of the pessaries not containing cocoa-butter, namely finil.

There is some reason to think that cocoa-butter may have a mechanical effect in actual use, which renders it helpful rather than the reverse. This point is about to be studied under the auspices of the Birth Control Investigation Committee. Nevertheless these experiments show that cocoa-butter prevents the active substances (quinine or chinosol) from acting, in a way that can only be described as astounding. There is plenty of quinine or chinosol in a cocoa-butter pessary, but the cocoa-butter in some way prevents it from affecting sperms, even when the pessary has had 12 hours at the temperature of the body in which to melt and dissolve.

The great spermicidal power of the minute quinine urea hydrochloride pessary is noteworthy. The absence of any foam-producers in this pessary must nevertheless weigh against its use. It is usually placed on the upper (cervical) side of a rubber occlusive pessary.

The complete lack of spermicidal power in the supposedly essential constituent of speton is very remarkable. The pessary as a whole is quite effective, on account of the foam-producers. It is perhaps reasonable, however, to distrust a pessary which relies for spermicidal power wholly on its foam-producers.

Semori emerges from the test as the most effective pessary sold in England. It is effective with or without foam-producers.

SUMMARY.

1. A technique is described for comparing the spermicidal powers of pessaries, using human sperms.

2. Those pessaries which do not contain cocoa-butter are more spermicidal than those that do.

3. Quinine and lactic acid pessaries, in cocoa-butter vehicles, are almost without effect upon sperms.

4. There is more than ten times as much quinine bisulphate in a quinine pessary as suffices to kill all sperms in half an hour, but the cocoa-butter prevents its action in some way which is not at present understood.

5. Semori is the most spermicidal pessary of the nine investigated. Even at one-tenth of the concentration at which it is normally used, it kills every sperm or nearly every sperm in half an hour.

6. Even if the foam-producing substances are omitted, semori remains effective.

7. The minute quinine urea hydrochloride pessary is nearly as effective as semori, but the absence of foam-producing substances in this pessary limits its usefulness.

8. Speton relies for its spermicidal power wholly upon its foam-producing substances. Its supposedly active substance, sodium dichlorylsulphamid-benzoate, is without effect upon sperms.

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POSTSCRIPT. I have recently tested another foaming tablet, called "bircon," by the standard technique with guinea-pig sperms. This tablet weighs 0·64 grm. It consists of zinc sulphocarbolate, chinosol, starch, sodium bicarbonate and tartaric acid. It is made by Messrs Bircon Laboratories in London. The results were as follows:

At *S* concentration	0	0	0
At *S*/10 concentration	0	0	I

These results should be compared with those for other pessaries given on p. 312 of this paper. Bircon is seen to be more effective than the other pessaries tested: but no experiments have yet been performed to find to what extent it relies upon its foam-producers, nor has it been tested with human sperms.