

## Prophylactic Control of the Spread of Venereal Disease through Prostitutes in Japan

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In Japan, as in many other countries, the most important factor in the spread of venereal disease is the prostitute. The control and identification of prostitutes, however, is a matter of considerable difficulty and represents one of the greatest obstacles to the conduct of an effective venereal disease control campaign.

According to a report issued in 1957 by the Ministry of Health and Welfare, the number of prostitutes in Japan in September 1956 was estimated at 150 000. During the year 1956, 144 273 cases of venereal disease were traced to 14 294 contacts, and it was found that 72% of the infections were attributable to prostitutes or their male partners.

The entry into force of the new anti-prostitution law in April 1958 has brought about the dissolution of the system of collective prostitutes which had been in existence for many years. However, for a variety of sociological reasons, it is not expected that the actual number of prostitutes will decrease rapidly or that the prostitute will cease in the near future to play the most important role in spreading venereal disease. Moreover, with the scattering of the prostitutes their management and the early detection and prompt treatment of infection becomes very much more difficult than in the past.

It would therefore appear reasonable to place the main stress in venereal disease control on the guidance and education of prostitutes towards the practice of self-prophylaxis in order to reduce the likelihood both of their acquiring venereal infection and of their spreading it.

At present the best prophylactic measure against venereal disease is the use of antibiotics. In the use of antibiotics by prostitutes, however, it must be considered that the amount of antibiotics necessary to inhibit the growth of the invading organisms must be maintained over prolonged periods because of their frequent exposures to venereal infections.

There are three ways of administering antibiotics for prophylaxis against venereal disease—namely, oral administration, injection and local application. In the two former ways the growth and multiplication of invading organisms are inhibited or killed in the tissue immediately by effective blood concentrations of antibiotics administered beforehand, and both methods have proved excellent if performed correctly, with a complete knowledge of the therapeutic effect, pharmacodynamics and toxicology of the drugs administered. However, the continued use of antibiotics in these ways may cause some side-effects, such as the appearance of antibiotic-resistant strains of bacterial organisms in the body. Therefore, these methods of administration are not desirable as means of self-prophylaxis for prostitutes.

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**Prophylaxis by means of vaginal foaming tablets of antibiotics.** Since 1952, experiments in prophylaxis by means of vaginal foaming tablets of antibiotics have been conducted in our hospital, and it has been found that an astonishingly high concentration of antibiotics can be obtained in the vagina and cervix with the application of vaginal tablet. In spite of the small dosage, effective antibiotic concentrations have been maintained in the genital organs for a prolonged period with almost no absorption into the blood system. It is felt, therefore, that the continued use of antibiotics in this manner would have the least effect on the susceptibility of bacteria to antibiotics in other parts of the body.

Our basic and clinical tests on the prophylaxis of gonorrhoea by this means were conducted with penicillin tablets in 1952 and extended in 1953 to tablets of chlortetracycline, chloramphenicol and oxytetracycline.

*Basic tests.* The vaginal foaming tablets studied were composed as follows:

Sodium bicarbonate . . . . .	0.1633 g
Tartaric acid . . . . .	0.1 g
Boric acid . . . . .	0.005 g
Glucose . . . . .	0.1 g
Talc . . . . .	0.02 g
Starch . . . . .	0.082 g

In addition, 50 000 units of penicillin G were included per penicillin tablet, or 100 mg of the other antibiotics in the corresponding tablets.

In the tests on prostitutes, one tablet was inserted deeply into the vagina after vaginal irrigation following the last sexual intercourse each night. No more irrigation was done for at least several hours following the insertion. The next morning, the antibiotic concentrations at the vaginal fornix and the external uterine orifice were measured by the following method:

A sheet of filter paper was moistened by placing it upon the mucous membrane of the vaginal fornix and the uterine orifice. Where penicillin tablets were used, two further sheets of filter paper were moistened with a solution of 5 units/ml and of 50 units/ml of penicillin respectively for comparison. Similarly, contrast papers were moistened with 25  $\mu\text{g}/\text{ml}$  and 100  $\mu\text{g}/\text{ml}$  of chlortetracycline, 250  $\mu\text{g}/\text{ml}$ , 500  $\mu\text{g}/\text{ml}$  and 1000  $\mu\text{g}/\text{ml}$  of chloramphenicol, or 50  $\mu\text{g}/\text{ml}$  and 200  $\mu\text{g}/\text{ml}$  of oxytetracycline. These moistened papers were placed upon a double-layer agar plate containing FDA 209 strain. This plate was left in a refrigerator for 4 hours, and then incubated for the following 24 hours at 37°C. The concentrations of each antibiotic in the vagina and cervix were calculated by measuring the diameter of the inhibition-zones around the papers in comparison with those around the contrast-papers.

The concentration of *penicillin* at the vagina and the uterine orifice examined 6-8 hours after insertion of one penicillin tablet is shown in Table 1. In these cases, irrigation was performed once between 2½ and 4 hours after insertion.

TABLE 1. PENICILLIN CONCENTRATION 6-8 HOURS AFTER INSERTION OF PENICILLIN TABLET

Case *	Concentration at uterine orifice (units/ml)	Concentration at vaginal fornix (units/ml)
1	240	300
2	280	300
3	150	250
4	140	200
5	100	180
6	180	220
7	130	400
8	200	420
9	100	150
10	180	250
Average	170	267

\* In these cases, vaginal irrigation was performed once 2½-4 hours after insertion of a tablet.

The concentrations 24 and 48 hours after the insertion are shown below:

24 hours after the insertion { uterine orifice, 50 units/ml  
vaginal fornix 200 units/ml

48 hours after the insertion { uterine orifice, 5 units/ml  
vaginal fornix, 30 units/ml

In these cases, no irrigations were done after the insertion.

The concentrations of *chlortetracycline* at the vagina and the uterine orifice examined 8-9 hours after insertion of one tablet were found to be 400-500 µg/ml at both sites. Where no irrigation was performed, 25-100 µg/ml were still demonstrable 30-35 hours after the insertion.

1000-2000 µg/ml of *chloramphenicol* were demonstrated 15-24 hours after insertion of one tablet of 100 mg chloramphenicol in the cases where no irrigation was performed.

500-1500 µg/ml were found 8-10 hours after insertion of a 50-mg tablet in cases where no irrigation was done.

The concentration of *oxytetracycline* at the vagina and the uterine orifice 8 hours after insertion of one tablet was 500  $\mu\text{g/ml}$  in the cases of no irrigation. Even when irrigation was done once 3-7 hours after insertion, 200  $\mu\text{g/ml}$  were demonstrable 13 hours after the insertion.

The blood concentrations of penicillin before and after insertion of one tablet of 50 000 units, 100 000 units, or 200 000 units of penicillin G are shown in Table 2.

TABLE 2. PENICILLIN CONCENTRATION IN BLOOD SERUM BEFORE AND AFTER INSERTION OF VAGINAL PENICILLIN TABLET

Case	Concentration of penicillin in tablet	Time of collection of serum after insertion	Serum concentration before insertion (units/ml)	Serum concentration after insertion (units/ml)
1 2 3 4	50 000 units	1 hour	0 0 0 0	0 0 0 0
1 2 3 4 5 6 7	100 000 units	$\frac{1}{2}$ hour	0 0 0 0 0 0 0	0 0 0 0 0 0 0
1 2 3 4 5	100 000 units	1 hour	0 0 0.03 0 0	0 0 0.03 0 0
1 2 3 4 5 6	200 000 units	$\frac{1}{2}$ hour	0 0 0 0.3 0.05 0	0 0 0 0.3 0.05 0.015
1 2 3 4	200 000 units	1 hour	0.3 0 0 0	0.3 0 0 0

When no vaginal irrigation is performed for a few hours after insertion of a tablet, and even if irrigations are repeated a few times thereafter, the concentration of the antibiotic does not decrease so much as it does when irrigation is carried out shortly after insertion.

*Clinical tests.* The persons in the clinical tests, who were divided into two groups—a test group and a control group—were all selected from among collective prostitutes who were confirmed to be negative for gonorrhoea and who had also been negative in consecutive serological examinations for syphilis prior to these tests.

The results of clinical trials in 1953 for the prophylaxis of *gonorrhoea*, in which one penicillin tablet was used daily for one month, were as follows:

	<i>Number treated</i>	<i>Number of male contacts during month</i>	<i>Number of attacks of gonorrhoea during month</i>	<i>Number of attacks of gonorrhoea during 3 months before test</i>
Test group	10	360	1 (urethral gonorrhoea)	19
Control group	20	666	9	29

The results of similar clinical tests in 1953 in which one tablet of penicillin, chloramphenicol or oxytetracycline was used daily for a 3-month period were:

<i>Tablet</i>	<i>Number treated</i>	<i>Number of attacks of gonorrhoea during 3-month test period</i>
Penicillin	20	2 (urethral gonorrhoea)
Chloramphenicol	9	0
Oxytetracycline	5	2

By contrast, 45 persons in the control group contracted gonorrhoea 118 times during the test period.

Another series of tests with chloramphenicol tablets during a 4-week period in 1957 gave the following results:

	<i>Number treated</i>	<i>Number of attacks of gonorrhoea during 4-week period</i>	<i>Number of attacks of gonorrhoea during 3 months before test</i>
Test group	24	2 (1 urethral gonorrhoea)	25
Control group	20	8	22

A clinical test was also conducted in 1953 for the prophylaxis of *syphilis*, using one tablet of penicillin, chloramphenicol or oxytetracycline daily for 3 months, and the subjects were given a monthly serological examination for 4 months. The results were:

<i>Tablet</i>	<i>Number treated</i>	<i>Number of seropositive patients</i>
Penicillin	20	0
Chloramphenicol	9	1 (in 3rd month)
Oxytetracycline	5	0

Six of 106 subjects in the control group were seropositive within the 4 months. Chancres or other symptoms suggestive of infection were not, however, found in all the seropositive cases.