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Potential impact of chemical prophylaxis on the incidence of gonorrhoea

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One of the major world-wide public health problems today is the rapidly rising incidence of venereal disease combined with the increase in unwanted and casual pregnancies.

For example, in the U.S.A., an incidence of 137 cases of gonorrhoea per 100,000 in 1957 had risen to 307·5 per 100,000 in 1971. The current epidemic has made gonorrhoea the leading reportable communicable disease in the U.S.A. Also, it is well known that the actual number of cases of gonorrhoea is almost four times the total number reported to health authorities by all sources.

For years, attempts at 'controlling' gonorrhoea were abandoned in favour of 'treating' it out of existence with increasingly larger doses of penicillin. A decade ago, the less sensitive strains requiring 0·1 unit of penicillin per ml. for inhibition *in vitro* were extremely rare in clinical practice, but strains requiring 0·5 unit of penicillin per ml. are now common. Today, many strains of gonococci are so resistant to penicillin, that a dose so large as to approach the outer limits of safety is required to effect a cure (Goldstein, 1972). Another major problem in controlling gonorrhoea is the existence of a large number of unidentified asymptomatic females (estimated as 640,000 to 1 million). A small change in the percentage of these females will produce significant changes in the prevalence of gonorrhoea. The task of eliminating gonorrhoea can therefore be simplified by making prophylactic measures as well as medical treatment available to those at risk. Parallel examples are smallpox and measles which have been brought under control by surveillance and vaccination. There are, however, fundamental obstacles to the development of an effective vaccine against gonorrhoea.

Recent work has shown that some of the intravaginal birth control compounds used by women also kill *N. gonorrhoeae* and *T. pallidum* (Arnold and Cutler, 1970; Singh, Cutler, and Utidjian, 1972; Cutler, Utidjian, Singh, and Arnold, 1973). At the 1971 American Public Health Association meeting in Minneapolis, it was reported that many such compounds 'show promise' of being extremely useful in the battle to bring venereal disease under control.

The purpose of this paper is to illustrate by using a theoretical model that a dramatic change in the prevalence of gonorrhoea is possible if topical V.D. prophylaxis is incorporated into existing V.D. control programmes and is accepted by the population at risk. In an attempt to evaluate the expected effectiveness of a prophylactic intravaginal compound in reducing the incidence of infection, a stochastic statistical model has been constructed. This model predicts the change in the national incidence of gonorrhoea for various degrees of effectiveness of the compound and for different proportions of usage by potential subjects at risk.

Method

THE MODEL

The reported total number of cases of gonorrhoea in the U.S.A. in 1957 was 216,476, and since then the figure has increased exponentially to 624,371 in 1971, with an average rate of increase of from 8 to 15 per cent. per year. Dynamic modelling theory indicates that any exponentially growing quantity is somehow involved with a positive feedback loop which is sometimes described as a "vicious circle" (Meadows, Meadows, Randers, and Behrens, 1972). For example, an increase in new gonorrhoea infections will lead in turn to a further increase in the incidence of new infections.

Several definitions must be presented to comprehend the model which is to be described:

(1) Define *a generation* for a patient with gonorrhoea as the interval between the time at which the individual acquires an infection and the time that the individual becomes potentially infectious to another through sexual contact. The average incubation period for *N. gonorrhoeae* in the male is about 3 to 5 days. It, can, therefore

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reasonably be assumed that *a generation* is about 7 days (incubation + average time for next sex act) for the male.

The *generation time* for the female may be shorter. The term 'incubation period' is scarcely applicable to the female with respect to gonorrhoea, in that 80-85 per cent. of females show no symptoms for many months—if at all. Moreover, the female may transmit infection as a passive mechanical vehicle of infectious material within minutes of the deposition of fresh material (*i.e.* by coitus with an infectious male) in the vaginal vault. This passive transmission may operate for several hours and may be significant in the case of a prostitute or highly promiscuous female.

(2) Let x (t) = total national cases of gonorrhoea at time t, where $0 \leq t < \infty$. Then x (0) = the total cases of gonorrhoea at the time prophylaxis is initiated.

(3) Define λ as the average risk of an uninfected person acquiring gonorrhoea by sexual contact with an infected person during *a generation.*

(4) Define μ as the overall rate of loss of infectiousness whether by treatment or spontaneous cure during *a generation.*

(5) Define k as the proportion of individuals at risk prevented from acquiring a gonococcal infection in *a generation* by a prophylactic compound, assuming that each individual uses the compound before each act of coitus.

(6) Define p as the proportion of population at risk using the prophylactic compound before each act of coitus. Therefore $[(1 - pk)\lambda]$ is the risk of acquiring gonorrhoea by sexual contact per *generation*, taking into account the effectiveness of the prophylactic compound used and the proportion of those at risk using it.

(7) From the above descriptions, the expected total number of cases of gonorrhoea at the time t is derived as

$$E[x(t)] = x(0) \cdot \exp[(1 - pk)\lambda - \mu]t.$$

RISK OF ACQUIRING GONORRHOEA BY SEXUAL CONTACT WITH INFECTED CASES IN A *GENERATION*

A recent paper (Holmes, Johnson, and Trostle, 1970) reported that the estimated average risk to crewmen from an aircraft carrier while on 6 days shore leave in the Philippines of acquiring gonorrhoea from infected females was approximately 22 per cent. According to other investigators (Cutler, 1971; Boulton, 1970; Fiumara, 1971), the risk of contracting gonorrhoea on sexual exposure with an infected partner ranges from 5 to 40 per cent. Therefore, for both sexes, the overall average risk of acquiring gonorrhoea by sexual contact with an infected partner is estimated to be 27 per cent.

OVERALL RATE OF LOSS OF INFECTIOUSNESS BY TREATMENT AND SPONTANEOUS CURE DURING A *GENERATION*

It is known that the rate of loss of infectivity by treatment and spontaneous cure varies considerably between the sexes. However, when this rate is considered from the point of view of the prevalence rate and in terms of a *generation* as defined above, it is estimated to be approximately 26·7 per cent. per *generation.*

Results

By employing the model $E[x(t)] = x(0) \cdot \exp[(1 - pk)\lambda - \mu]t$, the significant effect of prophylaxis when merged into the existing venereal disease programme can be seen from Tables I, II, and III.

Table I shows that, if there is no significant change in VD control programme and the rate of increase remains the same as in the past several years, there will be 1,169 cases by the end of 52 *generations* (that is 1 year), a 17 per cent. increase over that of 1 year ago. On the contrary, if there is a prophylactic

TABLE I *Expected total number of cases of gonorrhoea at the end of different generations (starting with* 1,000 *cases*)*

Effectiveness of product (k)	*Proportion of usage* (p)	*Generation*[a]									
		1	5	10	20	30	40	52	*2nd Year*	*3rd Year*	*4th Year*
	0	1,003	1,015	1,031	1,061	1,094	1,127	1,169	1,366	1,597	1,860
	0·20	976	886	786	618	486	323	286	82	24	7
0·50	0·25	969	856	733	537	394	289	199	39	7	1
	0·30	963	831	690	477	329	227	146	21	3	0
	0	1,003	1,015	1,031	1,061	1,094	1,127	1,169	1,366	1,597	1,860
	0·20	970	860	740	548	406	301	210	44	9	2
0·60	0·25	963	831	690	477	329	227	146	21	3	0
	0·30	955	794	631	398	251	158	91	8	1	0
	0	1,003	1,015	1,031	1,061	1,094	1,127	1,169	1,366	1,597	1,860
	0·20	965	839	704	496	349	246	162	26	4	0
0·70	0·25	956	802	644	414	267	172	101	10	1	0
	0·30	947	763	582	339	197	115	60	4	0	0

*$x(0)$ = 1,000 is an arbitrary figure chosen for convenience
[a]The 52nd generation means the end of 1970. $\lambda = 0{\cdot}27$ $\mu = 0{\cdot}267$
2nd year means the end of 1971
3rd year means the end of 1972
4th year means the end of 1973

TABLE II *Expected total number of cases of gonorrhoea in the U.S.A. at different times (reported cases*)*

Effectiveness of product (k)	*Proportion of usage* (p)	*Generation*[a]										
		1	5	10	20	30	40	52	*2nd Year*	*3rd Year*	*4th Year*	*5th Year*
	0	495,482	501,410	508,820	524,134	540,436	566,738	577,486	674,804	788,918	923,286	1,077,661
	0·20	482,287	438,128	388,580	305,637	240,429	189,103	141,531	40,952	11,707	3,359	938
0·50	0·25	478,883	423,061	362,299	265,722	194,883	142,914	98,741	19,735	3,902	780	148
	0·30	476,018	410,563	341,206	235,687	162,798	112,434	72,420	10,512	1,531	197	29
	0	495,482	501,410	508,820	524,134	540,436	556,738	577,486	674,804	788,918	923,286	1,077,611
	0·20	479,377	425,186	365,955	271,107	200,811	148,743	103,789	21,785	4,544	938	197
0·60	0·25	476,018	410,563	341,206	235,687	162,798	112,434	72,420	10,512	1,531	197	29
	0·30	471,770	392,483	311,813	196,859	124,241	78,447	45,250	4,100	346	34	3
	0	495,482	501,410	508,820	524,134	540,436	556,738	577,486	674,804	788,918	923,286	1,077,611
	0·20	477,006	414,633	348,072	245,271	172,850	121,771	80,028	12,943	2,074	336	54
0·70	0·25	472,708	396,435	318,136	204,861	131,947	84,968	49,992	5,038	494	49	5
	0·30	468,015	377,070	287,853	167,713	97,713	56,958	29,738	1,778	99	6	0

**x* (0) = 494,000 = national total of cases reported in 1969. $\lambda = 0{\cdot}27$ $\mu = 0{\cdot}267$
[a]52nd generation means the end of 1970
2nd year means the end of 1971
3rd year means 1972
4th year means 1973 and
5th year means 1974

TABLE III *Expected total number of cases of gonorrhoea in the U.S.A. at different times (including non-reported cases*)*

Effectiveness of product (k)	*Proportion of usage* (p)	*Generation*									
		1	5	10	20	40	52	*2nd Year*	*3rd Year*	*4th Year*	*5th Year*
	0	1,173,375	1,187,414	1,206,132	1,242,164	1,319,024	1,367,456	1,598,154	1,868,744	2,183,321	2,552,062
	0·20	1,141,789	1,037,554	920,216	723,796	447,825	334,581	95,929	27,784	7,955	2,223
0·50	0·25	1,134,068	1,001,873	857,980	629,271	338,442	233,739	46,736	9,242	1,848	351
	0·30	1,127,283	927,276	808,026	558,143	226,261	171,502	24,895	3,720	526	70
	0	1,173,375	1,187,414	1,206,132	1,242,164	1,319,024	1,167,456	1,598,154	1,868,744	2,183,321	2,552,062
	0·20	1,135,238	1,006,904	886,637	642,022	352,352	245,789	51,591	10,844	2,269	468
0·60	0·25	1,127,283	972,276	808,026	558,143	266,261	171,502	24,895	3,720	526	70
	0·30	1,117,222	929,458	738,419	446,192	185,775	107,159	9,815	819	82	6
	0	1,173,375	1,187,414	1,206,132	1,242,164	1,319,024	1,367,456	1,598,154	1,868,744	2,183,321	2,552,062
	0·20	1,129,622	981,985	824,287	580,838	288,372	189,541	30,650	4,972	795	128
0·70	0·25	1,119,445	938,817	753,394	485,143	201,217	118,461	11,991	1,228	124	11
	0·30	1,108,331	892,958	681,681	397,169	134,885	70,425	4,221	234	15	1

**x* (0) = 1,169,866 = national total cases adjusted for under-reporting in 1969. $\lambda = 0{\cdot}27$ $\mu = 0{\cdot}267$

compound which is only 50 per cent. effective against *Neisseria gonorrhoeae* and which is used by 25 per cent. of the subjects at risk before every act of coitus, then it will take a little more than 4 years to eliminate all 1,000 cases to start with. This is a dramatic decrease. Further trends of change under different assumptions of effectiveness of the prophylactic product and the proportion of usage by potential subjects at risk are also presented in Table I.

The same calculations can be carried out for the reported cases of gonorrhoea in the U.S.A. The expected number (Table II) is based on the national total of approximately 494,000 cases reported in the U.S.A. in 1969. Again, assuming no significant changes in venereal disease prevention and treatment programmes, a statistical projection using the model gives totals of 577,486 cases in 1970, increasing to 674,804 cases in 1971. The actual totals reported were 573,200 and 624,371 for 1970 and 1971 respectively. According to the present projection, by the end of 1974 the total cases reported will exceed one million if there is no major change in existing public health prevention programmes.

By contrast, Table II shows the value of prophylactic measures, and the trend towards a decreasing number of infections with different degrees of effectiveness of the prophylactic compound and different proportions of usage. If the reported cases of gonorrhoea were the cases actually existing in the U.S.A. and if an effective prophylactic

programme had been introduced at the beginning of 1969, it might have eliminated virtually all the 494,000 cases by the end of 1974 (assuming 70 per cent. effectiveness of the prophylactic and 30 per cent. usage by subjects at risk).

The main objective of a venereal disease prevention programme should be to prevent the sexually active from contracting gonorrhoea and finally to eliminate this disease from the population. The non-reporting of cases by private physicians always presents a difficult problem for the programme planner organizing various preventive activities. It has been suggested that the number of persons treated for gonorrhoea is three or four times the number reported. Also, despite their value, cultures are positive only in about 70 per cent. of female contacts of known cases of gonorrhoea (Pariser, 1971). A preventive programme can succeed only by treating those exposed to risk of infection, whether clinical symptoms or positive cultures are present or not. Another approach could be tried by making available to subjects at risk pre-coital prophylactic products that will prevent them from becoming infected. With this in mind, Table III was compiled, using as the initial number the cases of gonorrhoea for 1969 (1,169,866)* as obtained by adjusting for under-reporting by private physicians. The merit of the prophylactic approach is self-evident from this Table. If the upward trend remains as it is, there will be over 2·5 million cases of gonorrhoea by the end of 1974. But gonorrhoea could be almost completely eliminated by the same date if only 30 per cent. of the population at risk would use a prophylactic product which was only 70 per cent. effective.

Discussion

All the information used for defining the risk of acquiring venereal disease by sexual contact during a *generation* was obtained indirectly at different places and different times under diverse circumstances. However, it is felt that the range of 5 to 40 per cent. with an average of about 27 per cent. will not differ too much from the true risk. It should be pointed out that a prophylactic programme alone cannot be expected to eliminate the gonorrhoea epidemic. Its greatest value will be obtained only by incorporating it into the existing programme of treatment and education.

Active measures must be taken to encourage a greater sense of responsibility and desire for co-operation on the part of potential patients in protecting themselves through the practice of prophylaxis. If they do not accept this responsibility, our experience suggests that there will be a massive increase in the prevalence of gonorrhoea with a corresponding need for public health manpower for case finding and treatment. Without ever increasing health expenditure, the incidence of gonorrhoea will certainly continue to rise (Cutler, 1972).

*See Appendix

Summary

Research is being conducted at the Graduate School of Public Health, University of Pittsburgh, to evaluate the prophylactic efficacy against the commoner venereal diseases of several vaginal chemical contraceptives in common use.

Using the average risk of contracting gonorrhoea from sexual contact and the estimated true prevalence of gonorrhoea in the total population of the United States, a stochastic model was developed to predict the epidemiological impact of such prophylaxis at various hypothetical levels of effectiveness and of population usage. Even if a topical prophylactic is only 50 per cent. effective and only 25 per cent. of the population at high risk use it for every act of coitus, one can expect a dramatic decrease in the incidence of gonorrhoea within a short period of time. It is apparent from the model that the longer the delay in initiating prophylaxis programmes the longer will it take to bring the disease under control.

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APPENDIX

Total number of cases of gonorrhoea (reported + non-reported) in 1969.

(*a*) The reported number of cases in the U.S. population in 1969 was 494,227.

(*b*) In 1969, about 28 per cent. of reported cases of gonorrhoea were contributed by private physicians.

(*c*) In 1968 a survey by the American Social Health Association revealed that private physicians were reporting only 17 per cent. of cases of gonorrhoea treated by them.

(*d*) Total U.S. cases of gonorrhoea in 1969 adjusted for under-reporting by private practising physicians was derived as:

494,227 × 28 per cent. = 138,384
138,384 ÷ 0·17 = 814,023
814,023 + (494,227 — 138,384) = 1,169,866.

Action possible de la prophylaxie chimique sur l'incidence de la gonococcie

Une recherche a été entreprise à la Graduate School of Public Health, Université de Pittsburg, pour estimer l'action prophylactique, contre les maladies vénériennes communes, de plusieurs contraceptifs chimiques vaginaux d'emploi courant.

En se fondant sur le risque moyen de contracter la gonococcie par contact sexuel et sur la prévalence réelle estimée des gonococcies dans la population totale des Etats-Unis, un modèle stochastique fut établi pour prévoir l'influence épidémiologique d'une telle prophylaxie à des niveaux hypothétiques variés d'efficacité et selon l'usage fait par la population. Même si la prophylaxie des maladies vénériennes par un topique n'a qu'une action de 50 pour cent et même si 25 pour cent seulement de la population hautement exposée l'utilise à chaque coït, on peut s'attendre à une nette et rapide diminution de l'incidence de la gonococcie. Le modèle montre que plus long sera le moment de mise en place des programmes de la prophylaxie de la gonococcie plus longtemps il faudra pour arriver à contrôler la maladie.