INFORMATION CIRCULAR

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PUBLIC HEALTH PROBLEMS OF GONORRHOEA AND SYPHILIS

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1. INTRODUCTION

Within the South Pacific, gonorrhoea is common in occurrence and has become increasingly so, as has happened in other parts of the world. Neisseria gonorrhoeae has increased its resistance to penicillin, creating difficulties in treatment; and efforts to control the infection have been unsuccessful. On the other hand, syphilis is very rare indeed at the present time and, while there has been a slight increase, this has been small. Its very rarity, however, presents a problem from a public health point of view, for, with the changes occurring in the area, it is possible that the infection may become very much more common. (For incidence figures see Annex 2.)

The purpose of this circular is: for gonorrhoea, to examine the possible reasons for failure of control; for syphilis, to examine the reasons for its low incidence and its potential as a future problem and, for both, to describe current methods of treatment.

2. GONORRHOEA

The basic causes for the increase in incidence are mainly the characteristics of the infection itself, with the difficulty of identifying sources of infection, the emergence of treatment-resistant strains and the social changes involved in travel, immigration and urbanization.

2(a) The Characteristics of the Infection

The combination of high infectivity, the mode of transmission and the short incubation period of three to five days makes it impossible to evolve epidemiological methods effective against its very rapid spread. The reason being that it is not possible to bring a sufficiently large number of cases and contacts to treatment quickly enough to overtake this rapid spread in the community or, indeed, to interrupt transmission effectively.

While infection usually, but not invariably, gives rise to symptoms in the male which will make him seek treatment, a considerable proportion of infected females are completely free of symptoms and examination does not always yield the organism. Thus, even if all contacts of male urethritis are examined, diagnosed and treated within the short incubation period of the disease, some asymptomatic infected females will escape diagnosis, will continue to be present in the community and will have no reason to seek treatment on their own account.

The fluorescent antibody method of detecting organisms has facilitated laboratory diagnosis and has reduced the number of asymptomatic females escaping diagnosis. Even using this technique, however, asymptomatic infected females will still evade detection unless swabs from at least two of the three usual sites (cervix, vagina, urethra) are examined and that on more than one occasion.

A certain number of asymptomatic males with infection do occur but the greater number of "carrier" males consist of those with chronic infection as the result of inadequate or partial response to treatment.

Identification of the sources of infection therefore presents particular problems. Contact training in its usual form is not always satisfactory as the patient may not provide the names of all contacts, especially at first interview. Second interview is often worthwhile, can be combined with follow-up of treatment and will frequently produce information on additional contacts. In one series 45 out of 100 patients provided additional names as the result of a second interview. Not all patients return, of course, and not all can provide the name of contact or contacts. To overcome this, in some areas, it may be more useful to request the names of habitual associates of the patients and to screen them for infection. This, the so-called "cluster testing", may not be too readily acceptable, but it may become necessary in order to limit spread in a practical manner.

There is no doubt that, where prostitution exists, the prostitute constitutes a fairly large segment of the pool of infected females and every effort should be made to identify this group. Investigations lead only to the identification and treatment of an individual episode of infection and there is no system which will ensure continued freedom from infection.

To identify the infected asymptomatic female and the male with chronic infection there is considerable need for a serological or screening test which could be applied to vulnerable groups or in "cluster testing". This might result in less resistance to contact-tracing and a higher rate of detection, but no satisfactory test has so far been produced.

2(b) Emergence of Drug Resistant Strains

One of the factors responsible for increasing incidence is the remarkable capability of N. Gonorrhoeae of acquiring resistance to chemotherapeutic agents to which it is at first susceptible. This has not only created treatment and control problems by itself but the initial ready response to treatment, when the organism is at first susceptible, has given rise to the common attitude that infection is of no importance - one shot of penicillin and that's that. There are, therefore, two factors at work - increasing casualness regarding infection, as the result of treatment and the emergence of insusceptibility to infection.

When the sulphonamides and penicillin were first used, both were extremely effective but resistance to sulphonamides developed rapidly and resistance, or rather, reduced susceptibility to penicillin became increasingly frequent after 1957. Streptomycin, which was used effectively in those who did not respond to penicillin, became increasingly ineffective about the same time. Similarly, tetracyclines, also used in those who did not respond to penicillin, has been shown to produce resistant strains.

The organism itself appears to possess innate capability to tolerate different chemotherapeutic agents but this is greatly aided by the practice of giving medication by one injection at one time. There are few infections caused by even susceptible organisms where reliance would be placed on this type of treatment and, from this point of view, it is surprising that this practice has persisted. It is, of course, well known that patients with gonorrhoea are reluctant to return for further treatment or for follow-up unless symptoms persist. Unfortunately, relief from immediate symptoms does not mean cure from the infection and this, again, has assisted in the emergence of resistant strains.

2(c) Treatment

In spite of the reduced susceptibility of many strains of N. Gonorrhoeae to penicillin, this remains as the drug of choice. It is the least toxic, the most generally effective and the cheapest, but it must be given in adequate dosage to prevent further increase in partial resistance.

2(c.1) Penicillin

In place of long acting penicillins (such as P.A.M.) there is now general acceptance that those administered should achieve high and persistent blood levels and that slow release preparations are unsuitable. The U.S. Public Health Service advises a dose of 2,400,000 units of aqueous benzyl penicillin (penicillin G) given intramuscularly at one time, but even this can result in a failure rate of about 10 to 20%. Benzathine

penicillin or benethamine penicillin and mixtures of long and short acting penicillins such as benzyl, procaine and benethamine penicillins are effective in similar dosage and have been stated to give failure rates of only 2%.

Another approach which has been successful has been the use of probenecid (used in gout) in association with penicillin at the dosages stated, as this inhibits the renal tubular secretion of penicillin thus maintaining higher tissue levels. The use of this regime in strains particularly resistent to penicillin resulted in a failure rate of 2% in one study. This method, however, has the disadvantage that the probenecid requires to be given orally 1g, one hour before injection and o.5g, six, twelve and eighteen hours later.

"Penicillin resistance" of the gonococcus is usually, in fact, reduced penicillin sensitivity and, with adequate dosage, organism sensitivity is increased. Opinion is divided on the best product to use. Benzathine penicillin is favoured by one French author while an American counsels that it should not be used at all.

The concensus is that penicillin should be given in a dose of 2,400,000 units at one single time and that, in order of priority, the best forms are:

(1) aqueous procain benzylpenicillin (This may be combined effectively with 2,400,000 units of oily procain penicillin, but this represents a massive and virtually impracticable dosage.)

(2) benzyl, procaine, benethamine penicillins mixture (Triplopen).

(3) benzathine penicillin (Benzylpenicillin).

In those who do not respond to procaine benzylpenicillin, a repeat dose of one of the other two may be successful.

In some areas of Europe, gonococcal resistance to penicillin is becoming less and this is considered to reflect the fact that with adequate dosage there is a tendency for the organism to revert to penicillin sensitivity.

2(c.2) Other antibiotics

For those patients who cannot tolerate penicillin, have failed to respond to penicillin treatment or in an effort to avoid penicillin failure, broad spectrum antibiotics are used. As with penicillin, none are completely satisfactory and many have the disadvantage that they have to be taken by mouth over some days.

Those that can be given in a single dose are:-

Kanamycin 2.0g I/M	- failure rate about 4%
Spectinomycin Sulphate 2 to 4g. I/M	- failure rate about 10%
Ampicillin 250-500mg 1/M	- failure rate about 28%
Lymecycline 250mg orally	- failure rate about 7%
Rifampicin 900mg orally	- failure rate about 11%

Those which require to be given over several days are:

Tetracyclines: 1,500mg then 500mg six-hourly for sixteen doses
failure rate 0% (limited series)

Ampicillin 0.5 to 1G - failure rate about 15%.

Sulphonamide with trimethoprim* over four days - failure rate about 10%.

The choice of antibiotic to be used will depend largely on those which are available and on their cost. Drugs capable of administration in a single dose are the most useful but, in selected patients, there is obvious advantage in the use of tetracyclines and the combination of sulphonamide with trimethoprim when used as indicated above.

Streptomycin is now of little value as almost all penicillin resistant strains are also completely resistant to it. It is now the least recommended of anti-gonococcal agents. Tests have also shown that the cephalosporins as well as spiramycin and erythromycin, all chemically related to penicillin, have gonococcal resistance patterns similar to penicillin.

Failure of Treatment

Apparent failure of treatment may result from the insensitivity of the organism, inadequate dosage or inadequate absorption of the antibiotic used It may, however, result from re-infection and, if symptoms recur or if follow-up examination remains positive, it should not be assumed that the organism is necessarily resistant, as it may be a new organism.

Further causes of apparent failure of treatment may result from misdiagnosis of urethritis from other causes such as penicillinase-producing staphylococci, mimaea or foreign body.

It cannot be stressed too much that diagnosis and assessment of the result of treatment should be made on the basis of clinical examination with supporting laboratory procedures.

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* Trimethoprim is a sulphonamide potentiator, British trade name "Beptrin".

2(d) Complications of Treatment

Most complications which arise in the course of treatment result from the antibiotic rather than from the infection. In spite of the large doses used these are not common.

Treatment may be followed by post-gonococcal urethritis (P.G.U.) more commonly after penicillin than other antibiotics. This is postulated to be attributable to mycoplasma infection and is best treated with tetracyclines.

The third complication, if it may be so called, is the effect that the antibiotic may have on co-existing syphilis infection. Some penicillin in the types and doses described is considered to be treponemicadal and, in a sense, prophylactic. The effect of other antibiotics is variable with the exception of kanamycin which is without effect on the treponema.

2(e) Implications for Control

To attempt to offer a control programme in a circular of this type would be presumptuous, however, there are some indications from the material presented above which have bearing in a control programme:

(a) The importance of identification of the asymptomatic infected female and of the chronically infected male as the result of inadequate treatment;

(b) In females, the importance of examining swabs from at least two of the three sites: urethra, vagina or cervix;

(c) The importance of second interview for assessment of treatment and additional contact information;

(d) The importance of adequate penicillin and other antibiotic dosage;

(e) The importance of increased source infection detection by the use of "cluster testing" for some groups, if necessary.

Identification of those infected can never be complete and chemotherapy by itself will not bring gonorrhoea under control.

Any control programme therefore requires to include a considerable amount of education so that those in susceptible groups are aware of the nature of symptoms and know where to go for treatment.

3. Syphilis

In gonorrhoea, it is the high incidence which creates problems, while in syphilis it is its relative absence for, throughout the territories of the South Pacific, syphilis is of very rare occurrence at the present time. As the result of medical, social and economic changes, however, this situation may not continue and it is possible that circumstances are being created which are favourable to the introduction of syphilis and its emergence as an important problem.

3(a) Yaws and Syphilis Inter-relationship

The organisms responsible for yaws, Treponema pertenue, and that of syphilis, T. pallidum, are indistinguishable in the laboratory and it has been postulated that they are in fact one and the same organism and that the differences in clinical and epidemiological behaviour between the two diseases occur as the result of differing environmental circumstances. Yaws appears in tropical areas where most of the body surfaces are constantly moist and where scant clothing facilitates skin contact while syphilis appears in colder climates were skin surfaces are not constantly moist and clothing prevents casual skin contact.

Whether there is one organism or two, however, is not really important. What is important is the immunity relationship which occurs after infection. In areas where yaws has been endemic, syphilis is rare and where yaws is not prevalent, venereal syphilis is usually found. This observation, along with other immunologic information, makes it clear that yaws infection results in immunity to syphilis, explaining the low incidence of syphilis which this area enjoys at the present time. Such a situation, however, can only exist as long as there is sufficient incidence of yaws to maintain infection in the community.

3(b) Effect of Mass Yaws Eradication Programmes

Mass yaws eradication programes were commenced in the South Pacific area in 1955, most territories were covered by 1960 and the last was completed by 1962. Population coverage was excellent and these campaigns resulted in the reduction of yaws incidence to very low levels. The few cases which occur now are usually promptly diagnosed and treated.

As a result, those in the population between eight and fifteen years of age (depending on the date of termination of the programme) have not been exposed to yaws infection and, if the theory is true, have therefore no immunity to syphilis. The extent to which this has occurred could only be

determined by serological survey and this is an area for investigation which could yield important information in estimating future possible developments. If immunity is not in fact present, this group has reached, or will shortly reach, sexual maturity and is susceptible to syphilitic infection.

3(c) Implications of Loss of Immunity

With the rapid social and economic changes occurring throughout the area, there is a break away from older patterns of living, greater population mobility and increasing urbanization. To meet the needs of industry in some territories, there is considerable migration of single men from one place to another. Tourism is being introduced on a large scale, bringing not only tourists but the crews of ships and aircraft. Where prostitution has been uncommon, it is already present in some areas and, as a result of other changes mentioned, is likely to increase.

The position is, therefore, one where there is an increasing proportion of the population which has no immunity to syphilis and which is going to be exposed to imported infection within the next few years. All the factors involved are those which favour the introduction and spread of syphilis within the communities of the South Pacific.

3(d) Possible Action to Control and Limit Spread

The cross immunity between yaws and syphilis and the immunity which occurs in cases of syphilis whose treatment has been delayed would indicate that it should be possible to produce an agent which would induce "artificial" immunity. As yet, however, no such agent has been produced and, while some advocate that, were it available, its use could make good the loss of immunity consequent on yaws eradication, it is far from certain that such immunization on a wide scale would be acceptable.

The only possible method of control is the creation of an acute awareness that an increase in syphilis incidence is likely in the next few years, together with the development of diagnostic and follow-up procedures which will detect such an occurrence.

The possibility of syphilis must be considered when a genital lesion is present and should be considered as suspect until ruled out clinically and by specific procedures. The chancre of primary syphilis can, of course, occur on other than genital areas and again, there should be constant suspicion when limited lesions are found about the mouth or nipple. Secondary syphilis can mimic a wide varity of skin conditions and there must be constant awareness that these might be syphilitic. At this stage serological tests are generally positive but diagnosis can easily be missed due to the similarity of signs with other conditions.

Early treatment is, as always, essential in control and, fortunately, penicillin is still very effective and no problems of resistance analagous to those in the treatment of gonorrhoea exist as yet. However, care is needed in the choice of penicillin for its use in gonorrhoea or concealed syphilis infection may delay identification and therefore result in spread.

3(e) Treatment

1. Penicillin

P.A.M. is still effective in syphilis but it is not recommended for use in gonorrhoea. Benzathine penicillin, benethamine penicillin and mixtures of benethamine, benzyl and procaine penicillin are fully effective in treating primary syphilis in a dose of 2,500,000 units given at one time. Since these are also effective in most cases of gonorrhoea, it would appear that the use of one of these preparations routinely in gonorrhoea will provide one barrier to the spread of syphilis in a particularly prone sector of population. Although one dose at one time is effective, many prefer to give the dose on two or three consecutive days.

Aqueous benzylpenicillin is not satisfactory in syphilis when given in one dose of 2,400,000 units as it may suppress signs of infection without eliminating it. In the treatment of syphilis, 4,800,000 units are required in daily doses spread over eight days.

Penicillin in the same form and dosage should be given prophylactically to contacts with or without symptoms as delay for symptoms to appear will only result in further spread.

3(e) Other antibiotics

Oral broad spectrum antibiotics are effective but these are not preferred to penicillin as they have less spirochaeticidul action, absorption is variable and follow-up studies still leave some doubt as to the efficacy of treatment. There is also the usual difficulty of patient co-operation as all require to be taken over some days.

When patient sensitivity to penicillin precludes its use, erythroymycin, tetracycline, chlortetracycline (all 30 to 40g total) or demethylchlortetracycline (20 to 30g total) may be given in divided doses four times daily over ten to fifteen days. Close follow-up is essential and this should include spinal fluid examination.

ANNEX I

GLOSSARY OF CHEMICAL AND PROPRIETARY NAMES OF MEDICAMENTS MENTIONED IN TEXT

Chemical Name	Proprietary Name
Ampicillin, BP	Penbritin Pollycillin
Benethamine penicillin, BPC	Benapen
Benzathine Penicillin, BP, USP	Bicilin Neolin Permapen
Benzylpenicillin, BP (Penicillin G)	Crystapen G Solupen
Kanamycin Sulphate, BPC	Kannasyn Kantrex
Lymecycline	Armyl Mucomycin
PAM (Procaine penicillin G in oil with alumium monostearate)	Almocillin Lucillin Monocillin Procarist
Penicillin combinations	Triplopen
Probenecid, BP, USP	Benemid Colbenemid Probecid Probenid Prolongine
Rifampicin	Rifampicin
Spectinomycin (Actinospectocin)	Trobicin
Trimethoprim and Sulphamethoxazole	Septrin

Chemical Name Dénominations Communes	Proprietary Name Noms de Spécialistés
Ampicilline	Pénicline
Bénéthamine Pénicilline	Biclinocilline
Benzathine Pénicilline	Extencilline Pénidure
Pénicilline G	Pénicilline G Diamant
Kanamycine	Kamycine Kanamycine
Lymécycline	Tetralysal
PAM (Pénicilline G dans de l'huile avec monostéarate d'alluminium)	PAM
Associations des Pénicillines	Biclinocilline procaïne
Probénécide	Bénémide
Rifamipicine	Rifamipicine
Spéctinomycine	Spéctinomycine

ANNEX 2

TOTAL NUMBER OF CASES OF SYPHILIS AND ITS SEQUELAE

NOMBRE TOTAL DES CAS DE SYPHILIS ET SES SÉQUELLES

Country - Pays	1955	1960	1961	1962	1963	1964	1965	1966	1967
OCEANIA - OCÉANIE									
Australia - Australie	646	...772	873	...	694	611	...	798	+
Fiji - Fidji	48	2	11	16	30	25	13	4	+
French Polynesia - Polynésie française	...	86	202	129	177	104	+	+	+
New Caledonia - Nouvelle-Calédonie	78	28	+	+	+	+	+	+	+
New Zealand - Nouvelle-Zélande	73	...	29	33	62	83	79	+	+

+ Data not yet available

Data presented in Annex 2 has been drawn from World Health Statistics Report, Vol.22, No.5, 1969 "Syphilis and its sequelae and gonococcal infection" 1955, 1960-1967.

NUMBER OF CASES OF GONOCOCCAL INFECTION
NOMBRE DE CAS D'INFECTION GONOCOCCIQUE

Country - Pays	1955	1960	1961	1962	1963	1964	1965	1966	1967
OCEANIA - OCÉANIE									
Australia - Australie	...	4,620	6,105	...	6,790	7,291	+	+	+
Fiji - Fidji	322	380	227	316	445	455	714	785	+
French Polynesia - Polynésie française	...	...	79	71	106	106	+	+	+
New Caledonia - Nouvelle-Calédonie	...	318	284	246	136	134	+	+	+
New Zealand - Nouvelle-Zélande	843	...	1,100	1,127	1,186	1,404	1,822	+	+
Gilbert and Ellice Is. - Iles Gilbert et Ellice	17	...	...	-	-	-	-	+	+
Guam	-	39	66	14	202	+	+	+	+
New Guinea (Trust Territory) Nouvelle-Guinée (Terr.sous tutelle)	...	...	107	251	225	213	326	283	+
New Hebrides - Nouvelles-Hebrides	46	...	59	48	...	94	+	+	+
Niue Is. - Ile Nioué	8	1	5	36	9	11	12	+	+
Pacific Is. (Trust Territory) Iles du Pacifique (Terr.sous tutelle)	599	293	243	227	293	437	+	293	+
Papua Papouasia	...	...	69	12	36	33	84	75	+
Tonga	...	46	18	14	47	42	44	+	+
Wallis and Futuna Is. - Iles Wallis et Futuna	...	...	...	24	+	+	+	+	+
Western Samoa - Samoa-Occidental	8	35	...	19	37	164	168	194	+

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No.		Classification
1.	Annual Conference of O.I.E. Report of S.P.C. Observer, September 1968.	Livestock Production and Health
2.	South Pacific Commission Publications Series October 1968.	Publication
3.	Free Diving Without Breathing Apparatus - Its Accidents - March 1969.	Public Health
4.	"A": Australia's Notification on Bovine Pleuropneumonia Regulations. March 1969.	Plant and Animal Quarantine
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11.	Agricultural Extension Workshop - Western Samoa November 1969.	Agricultural Education and Extension
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