COMPARISON OF DIFFERENT ANTIBIOTICS IN THE TREATMENT OF ACUTE GONORRHOEA IN AFRICAN NEGROES *

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Recently it has become apparent that there is a tendency for penicillin to fail in the treatment of gonorrhoea (Curtis and Wilkinson, 1958; King, 1958; Willcox, 1959). This would appear to be due to the development of resistance on the part of the gonococcus. It was decided to compare the effect *in vivo* of two new antibiotics using two series treated with penicillin as controls. In one control series, penicillin was given as a single dose of 1·2 mega units containing the long-acting benethamine penicillin G (Triplopen); in the other, 2·4 mega units procaine penicillin were given in three consecutive daily doses.

One of the two new drugs was actinospectacin ("Trobicin"), a derivative of which has been reported previously to be an effective treatment (Laird and Taylor, 1962; Willcox, 1962). This was given as a "single-shot" treatment, 0·8 g. being injected into each buttock on the same occasion.

The second new drug was the orally administered "Rovamycin" (spiramycin) given in a single dose of ten tablets, very good results having been reported by Siboulet and Durel (1961).

The investigator in tropical Africa is faced with many difficulties, some of which I have outlined previously (Clarke, 1951, 1960). The recent relinquishing of European control over large areas has, if anything, increased these difficulties, the political disengagement usually involving the replacement of experienced personnel by hastily-trained indigenous staff or by new and less experienced expatriates.

Material

An attempt was made to collect four comparable series of young African males, each numbering at least 100, of average age 25 years, 60 per cent. being manual labourers and 40 per cent. in clerical work or unemployed. In the

series using Rovamycin, however, it proved possible to collect only 73 cases. It must be made certain that the patient has actually taken the drug. In Africa patients and nurses may sell the tablets or the nurse (usually male) may inject water and later sell the drug at great profit. So one must watch the patient take tablets and employ a reliable nurse to give injections or give them oneself. The ancillary investigations must be carried out by an honest technician or done by oneself, if one can find the time.

Follow-Up

This is difficult as besides a tendency to give false addresses many patients have no fixed abode. The problem of the interpretation of defaulting is, of course, not confined to Africans, but defaulters will probably form a larger proportion of the whole than in Europe. On investigation of some of the defaulters, it proved that a few had been ill or had left the area, but the vast majority (90 per cent.) had been at least symptomatically cured. It would therefore be legitimate to include this percentage of the defaulters among the cured.

Results

The results obtained with the four treatment schedules are shown in Table I (opposite). The standard error of the difference between "Trobicin" and "Rovamycin" is 5·85 and there is thus no significant therapeutic difference. In ten cases in which penicillin had failed, "Trobicin" cured six and a further three were improved. There were no signs of intolerance to either "Trobicin" or "Rovamycin" and no abscess formation occurred with the former.

The criteria of cure adopted were:

1. Absence of a discharge and of complaints by the patient.
2. Failure to find the gonococcus in the urethra or prostate.
3. No threads, or only very few, in the urine.

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TABLE I
RESULTS IN FOUR SERIES OF CASES

Drug	Penicillin						Newer Drugs					
	Triptopen			Procaine Penicillin			Trobicin			Rovamycin		
	138			126			125			73		
Result	Cured	Failed	Im-proved	Cured	Failed	Im-proved	Cured	Failed	Im-proved	Cured	Failed	Im-proved
No. Followed-up ..	62	22	18	59	24	15	74	12	12	45	5	6
Defaulters	32	4		25	3		24	3		15	2	
Rate per cent. .. .	68.1	18.1		66.6	21.4		77.7	11.9		82.2	9.6	
Mean percentage cure rate	67.4											
Standard error compared with Penicillin ..							4.7			5.35		

Failure implied:

1. Continued discharge and complaint of urethral irritation.
2. The gonococcus still present.
3. Many threads in the urine.

Improvement implied:

1. Less discharge and less complaining by the patient.
2. The gonococcus absent.
3. The urinary threads moderate in number.

One cause of the apparent failures is that some patients will come back within the week with a fresh infection from either the same or another source, having been relieved of the acute pain of the previous infection.

It was noticeable that with penicillin the patient frequently continued to complain but the gonococcus could no longer be found. These cases were classified as "improved", but such cases are not "cured" and must, therefore count as failed.

Table II shows that there was no significant difference in the cure rate between the sedentary and manual workers.

TABLE II
CURE RATE BY TYPE OF WORK

Work	Sedentary		Manual	
Result	Cured	Failed	Cured	Failed
No. of Cases ..	163	47	181	72
Cure Rate (per cent.)	77.6		71.5	
Standard Error ..	4.04			

Table III shows that delay in treatment did not affect the rate of cure,

TABLE III
CURE RATE BY DELAY IN TREATMENT

Delay (days)* ..	2 or less		11 or more	
Result	Cured	Failed	Cured	Failed
No. of Cases ..	100	30	57	16
Cure Rate (per cent.)	76.9		78.0	
Standard Error ..	6.1			

* There were 260 cases for which the delay was 3 to 10 days.

Table IV shows that first infections numbered 159 (34.4 per cent.), while multiple infections (that is one or more previous attacks) numbered 304 (65.6 per cent.); this may be compared with Watt's figures of 54.6 per cent first infections and 45.4 per cent. repeat infections (Watt, 1958).

TABLE IV
CURE RATE BY NUMBER OF ATTACKS

Number of Attacks*	One		Three or More	
Result	Cured	Failed	Cured	Failed
No. of Cases ..	127	32	69	30
Cure Rate (per cent.)	79.8		69.6	
Standard Error ..	5.6			

* There were 205 cases who had had one attack and were then having a second attack.

The standard error of the difference between two percentages is given by the expression

$$\sqrt{\frac{p_1 \times q_1}{n_1} + \frac{p_2 \times q_2}{n_2}}$$

p_1 and p_2 are the percentages cured in the two samples and q_1 and q_2 are the percentages not cured, while n_1 and n_2 are the numbers present in each sample. If the difference between the two percentages is not twice the standard error or more, then it is not statistically significant. Judged by these criteria, both new drugs are

superior to penicillin, but there is no significant difference between them. Manual labourers do not appear to suffer by being kept working. Delay in seeking treatment does not appear to have any serious effect. Subsequent attacks are as easily cured as first ones.

Summary

If penicillin is to be used, the "one-shot" treatment is by far the most convenient. The percentage of cures with penicillin was low compared with that in Europeans, and confirmed the suspicion that penicillin is less effective in Negroes (Willcox, 1958). Both "Trobicin" and "Rovamycin" were superior to penicillin, but in view of the high cost of "Rovamycin" it would be expensive to use it routinely. The production of "Trobicin" has now been discontinued by the makers, owing to its comparative lack of effective action on bacteria other than the gonococcus.

The higher figure for repeat infections possibly reflects a higher level of promiscuity among Negroes than among Europeans. Neither continuing at manual labour nor delay in seeking treatment appeared to influence the cure rate, which was as high in persons with a history of previous attacks as in those first infected with gonorrhoea.

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La blennorrhagie chez les nègres africains traitée par la pénicilline, la Trobicine (actinospectacine), et la Rovamycine

RÉSUMÉ

S'il faut employer la pénicilline, le traitement par une seule dose est le plus facile. Le nombre de cas guéris fut plus petit parmi les nègres que parmi les européens, ce qui renforce l'idée que la pénicilline est moins efficace chez les nègres (Willcox, 1958).

La Trobicine et la Rovamycine furent toutes les deux supérieures à la pénicilline, mais la Rovamycine coûte trop cher et on ne produit plus la Trobicine parce que ce médicament n'est guère efficace que contre la gonorrhée.

Le plus grand nombre de rechutes indique que les nègres sont plus libres dans leurs rapports sexuels que les européens. Ni la continuation du travail manuel ni le délai avant de commencer le traitement ne sembla influencer le nombre de cas guéris, qui fut aussi grand parmi les récidives que parmi ceux qui furent atteints pour la première fois.