PENICILLIN RESISTANCE IN GONORRHOEA*

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About a decade back, with the advent of new therapeutic methods, the conquest of the disease was sighted in distent horizon, but we must now confess that we have been deluded. The number of gonorrhoea cases has shown a progressive rise ever since the inception of the V. D. Department of this Hospital in 1954. This steady rise in gonorrhoea cases during the last six years, after an initial steep fall during the post war period, is almost a global phenamenon. It seems that several factors have been responsible for this increase; but possibly the most important is the emergence of strains of gonococci which have increased resistance to penicillin.

The treatment schedule for uncomplicated gonococcal urethritis in this clinic up to 1958 was a single intramuscular injection of 6 lacs units of PAM. With this treatment schedule, it was observed that a few male patients with uncomplicated gonococcal urethrities, continued to show persistent urethral discharge, which occasionally showed gonococci. At this stage, the treatment of uncomplicated acute gonorrhoea was changed to 2 intramuscular injections of PAM, 6 lacs units each, on alternate days. But it was observed that mere increase in the dosage of PAM from 6 lacs units to 1.2 megaunits, did not solve the problem, as some male patients of acute gonorrhoea still showed gonococci In urethral discherge.

Obviously, the gonococci which in the early forties of this century, were extremely sensitive to pencillin even in as great a dilution as in 1:50,000,000 had now become less sensitive to penicillin. Curtis and Wilkinson (1958) studied and observed that 19.5 per cent strains were sensitive to penicillin at levels of 0.125 to 0.5 units per ml. This has been confirmed by Cradock-watson, Shorter & Nicol (1958); Alice Reyn, Bent Korner and Michael Weis Bentzon (1958) and Alice Reyn (1961).

Curtis and Wilkinson have suggested that it would be worthwhile to devise a preparation of penicillin which would give a blood concentration of not less than 1 unit per ml. for at least 24 hours. On this basis Hilton (1959) conducted a pilot study by using 1.2 megaunits of PAM intramuscularly and 0.5 gms of oral probenecid 6 hourly for 24 hours in the treatment of acute gonorrhoea and did not observe failures in the series. Probencid (P (di-n-propylsulphamyl) benzoic acid) retards the excretion of penicillin from the kidney tubules. Hilton also studied in the series the mean serum penicillin level and found it to be 1.27 units per ml. 21 to 30 hrs. after the injection of 1.2 megaunits of PAM.

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It was therefore decided to observe the effects of 2 intramuscular injections of crysta.line penicillin, 5 lacs units each, at 12 hrs. interval, in those cases of accute uncomplicated gonococcal urethritis which continued to show gonococci in the urethral discharges even after the administration of 1.2 megaunits of PAM. Serum penicillin levels were not estimated because of lack of facilities and the patients were also not hospitalized. The treatment was completely effective and confirmed the work of Curtis and Wilkinson (1958) referred to above. The following two cases which illustrate this point may therefore be of interest;

CASE REPORT I

History. An unmarried male aged 32 years attended the clinic on 15-2-61 with urethral discharge and dysuria of 2 days duration. He gave history of exposure to infection a week earlier.

Examination. There was urethritis with profuse mucopurulent discharge. Scrotal contents were normal. Urine 1st glass hazy; 2nd glass clear. Urethral smear showed gonococci intracellular, almost every field 1/12 objective. The blood STS was negative.

Treatment. PAM 6 lacs units interamuscular stat.

Progress and follow up. The patient was next seen on 17-2-61 and 18-2-61. Urethral discharge persisted though slightly less and urethral smear examination showed the same findings as on 15-2-61. Subjective symptoms of dysuria much less.

18-2-6. He was given second injection of PAM 6 lacs units.

20-2-61. No subjective symptoms at all, but on examination profuse mucopurilent discharge persisting, microscopic exam. of which showed gonococci intracellular almost every alternate field of 1/12 objective. At this stage, he was given 2 intramuscular injections of crystalline penicillin 5 lacs units each at 12 hours interval.

21-2-61. Scanty thin serous discharge per urethra. Microscopic exam. of smear did not show any gonococcus and even pus cells were very few.

He was subsequently examined daily, till 27-2-62. There was no urethral discharge. Urine was clear with few floating threads microscopic examination of which did not show any gonococcus. He was followed up for 2½ months and all tests of cure were negative. His blood STS was also negative.

CASE REPORT II

History. An unmarried male 22 years reported to the Clinic on 25-4-61 with similar complaints of dysuria and urethral discharge of 1 month duration, for which he had some indigenous treatment. He admitted exposure to infection about one month back.

Examination. Frank Urethritis with profuse mucopurulent discharge. Scrotal contents normal. Urine hazy with threads (both glasses). Microscopic examination of urethral discharge showed gonococci intracellular in position, almost every alternate field 1/12 objective. Blood STS was negative.

Treatment. PAM 6 lacs units, intramuscular stat.

Progress and follow up. Patient next seen on 27-2-61. Clinical condition and microscopic examination of urethral discharge same. Second injection of PAM 6 lacs units given.

29-4-61. No urethral discharge. Urine clear with threads.

1-5-61. Profuse mucopuralent discharge. Microscopic examination of urethral discharge showed 1-2 pus cells packed with gonococci every field 1/12 objective. No history of fresh exposure or any other exciting factor present. Same day he was given 2 injections of crystalline penicillin, :5 lacs each, at 12 hours interval.

2-5-61. Scanty mucoid discharge. Microscopic examination revealed a few Gram negative diplococci extracellular only.

4-5-61. No further discharge. Urine clear with few floating therads, examination of which did not show any gonococcus.

Unfortunately this patient could not be followed up further.

COMMENTS & DISCUSSION

In case No. I, dysuria and the urethral discharge decreased slightly after treatment but the latter rapidly increased in severity upto pre-treatment intensity. It is interesting to note that this patient of post treatment gonorrhoea had no subjective symptoms at all after the second injection of PAM, but examination revealed a purulent urethral discharge with abundant gonococci in it. This apparentiy asymptomatic carrier state is very important in the management of gonorrhoea and all patients should be carefully examined by stripping the urethra and staining the sceretion even though most of the patients may claim that they have completely recovered.

In case II, the signs and symptoms disappeared after the second injection of PAM and reappeared after three days.

Curtis and Wilkinson (1958) have also observed a third group of post treatment gonorrhoea where the symptoms remain unchanged or even increased after treatment.

It would have been ideal to have studied the serum penicillin levels after the injections of PAM and crystalline penicillin and also in vitro demonstration of enhanced penicillin resistance of the two strains of gonococci, but due to lack of facilities, these could not be done. From reports available (W. H. O. 1953

Several graphs) it will be seen that with PAM penicillin levels in blood adequate to kill gonococci where resistance to penicillin in vitro exceeds 0.5 units/ml., are seldom reached for long enough to ensure good therapeutic result. That may be the reason why 1.2 mega units of PAM in these two cases, under report, failed to give good therapeutic response. But when reinforced with heavy doses of crystallinine penicillin given intramuscularly, dramatic improvement was observed. This dramatic improvement can only be attributed to a considerable rise in the serum penicillin level possibly above 0.5 units/ml. which is practically never obtained with PAM. It is thus logical to interpret that these two strains of gonococci were "insensitive" or "partially resistant" to penicillin. As regards, the potency of PAM, used, is concerned, they were all standard products which showed no evidence of deteriotion in their effects upon other cases.

SUMMARY

Two cases of post-treatment gonorrhoea are reported, which did not respond to PAM 1.2 mega units but improved dramatically with heavy doses of crystalline penicillin.

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REFERENCES

1. Cradock Watson, J. E., Shooter, R. A. and Nicol, C. E. (1958), Brit. Med. Journal, Vol. I, page 1091.
2. Curtis, F. R. and Wilkinson, A. E. (1958) Brit. J. Vener. Dis., Vol. 34, page 70.
3. Dollas, Neil L. (1958) Brit. J. Vener. Dis., Vol. 34, page 194.
4. Gjessing, H. C. (1959) Brit J. Vener, Dis., Vol. 35, page 256.
5. Hilton, A. L. (1959) Brit. J. Vener. Dis , Vol. 35, page 249.
6. King, A. J. (1960) Brit J. Vener. Dis., Vol. 36 page 34.
7. King, A. (1958) Lancet, Vol. I, page 651.
8. Laird, S. M. and Morton, R. S. (1959) Brit. J. Vener. Dis., Vol. 35, page 187.
9. Letchner, E. H. and Nicol, C. S. (1961) Brit. J. Vener. Dis., Vol. 37, page 158.
10. Rajam R. V. (1948) Journal Ind. Med. Association, Vol. 17, No. 6, page 186.
11. Reyn, A. Korner. B and Bentzon, M. W., (1958) Brit. J. Vener. Dis., Vol. 34, page 227.
12. Reyn, A. (1961) Brit. J. Vener. Dis., Vol. 37, page 145.