

PROTEUS INFECTIONS SUCCESSFULLY TREATED IN GENERAL PRACTICE WITH BICILLIN AND STREPTOMYCIN

DAVID PELKOWITZ, M.B., B.Ch., Johannesburg

Case 1. About 6 years ago (1952) a case of very severe vaginitis and inguinal adenitis was seen (Mrs. V.R.). Fever was present and evidence of toxæmia. The patient was listless and weak and had a profuse vaginal discharge with pains in both groins. As this was an unusually severe vaginitis, swabs were taken; culture showed a profuse growth of *B. proteus*. The swabs were repeated and again a culture of *B. proteus* was obtained. As a result of the sensitivity tests, treatment with erythrocin was suggested, though the tests showed the organism to be only slightly sensitive to this antibiotic. The patient had already been started on Bicillin, 1,200,000 units daily. For a few days, her condition remained unchanged; then after the 5th day there was a slow but steady improvement and in 2 weeks the case had cleared up. The only antibiotics used were Bicillin and erythrocin.

In view of the heavy penicillin dosage (a total of about 17,000,000 units of long-acting penicillin in daily doses over 2 weeks) I thought it would be worth while to test the *B. proteus* against stronger quantities of penicillin in the routine sensitivity tests. My idea was that heavy dosage with long-acting penicillin maintained for a long spell (about 2 weeks) would destroy *B. proteus*, even though routine sensitivity tests always showed *B. proteus* to be insensitive to penicillin. The clinical pathologist was therefore asked to use up to 500 units in the test instead of the routine 100. I wished to determine which of the antibiotics used was responsible for the satisfactory result achieved. The modified sensitivity test showed that *B. proteus* was extremely sensitive to the 500 strength penicillin used.

It is commonly recognized that *B. proteus* is a highly resistant organism, and it was a surprise to find it sensitive to the 500 unit penicillin test. The Bicillin treatment was therefore followed up in later cases of *B. proteus* infection. It was hoped that massive dosage would assist body defence mechanisms (enzymes, phagocytes and antibodies) which are absent in the *in vitro* test, to fight against this highly resistant organism. It is known what trouble this organism can cause, and how difficult it is to eradicate, especially in vaginitis and adenitis.

Case 2. The next case was seen about 5 months later—an elderly lady (Mrs. L.M.) with a chronic intractable colitis of long standing and apparently incurable. She gave a history of severe attacks of diarrhoea, colic and pruritus. X-rays had previously revealed diverticulitis. Stool culture gave profuse growth of *B. proteus* and a further specimen confirmed the existence of the organism. A course of Bicillin therapy was instituted. The first week the improvement was slow, but during the second week the patient was much more comfortable, and symptoms settled down; the number of stools was much less and colic and pruritus were much improved. Culture now gave a scanty growth, and the next culture no growth at all. The organism was not sensitive to penicillin in the usual *in vitro* sensitivity tests, but when 500 units were used it was definitely sensitive.

Case 3. A further case of vaginitis and inguinal glands then cropped up (Mrs. J.P.). Treatment with pessaries and sulphonamides failed to achieve an improvement. Swabbing revealed *B. proteus* and the 2-week course of Bicillin was started. Once again the result was very good.

As in the previous cases most headway was made during the second week.

Case 4. The next case (Miss R.M.) had colitis, with nausea, diarrhoea and colic, which did not clear up with the usual anti-diarrhoea and colic mixtures. Culture gave a profuse growth of *B. proteus*. No marked improvement resulted from an intensive and prolonged oral course of streptomycin (it is known that some *B. proteus* bowel infections will clear up under this treatment by mouth). Once again a course of Bicillin daily for 2 weeks proved effective; the nausea disappeared, the diarrhoea was now under control, and the colic was minimal. This patient suffered a relapse about 6 months later. The Bicillin was then repeated, but a culture still showed a scanty growth of *B. proteus*.

If a case showed a profuse growth during the first 24 hours and after treatment the culture was scanty, this, in my view, showed a definite response to therapy. In order to achieve a negative culture, it was considered advisable to add another antibiotic in cases where the stool was still positive and minor symptoms persisted. As with Bicillin, *B. proteus*, though insensitive to streptomycin in the usual maximum strength of 100, was found to be sensitive to 500 units of streptomycin.

Miss R.M.'s slight relapse was accordingly now treated by adding streptomycin by injection, Bicillin and streptomycin (1 g.) being given daily. The result was very satisfactory, and culture was now negative. The conclusion appeared to be that in a relapsing case streptomycin and Bicillin for about 2 weeks led to a cure.

Case 5. This was confirmed in the next case (Mrs. K.W.), who suffered from nausea, upper abdominal cramp, diarrhoea and urinary symptoms (burning and frequency). Stool culture gave a profuse growth of *B. proteus*. Bicillin daily was effective, but the stool remained positive. After a rest of about 1 week, the combined therapy of daily Bicillin and streptomycin once again met with success. This case, and all the others, have kept particularly well since the stools became negative.

Case 6. Mrs. T.R. had an unusual type of relapsing colitis. As there was no definite response to simple treatment, stool cultures were made and a profuse growth of *B. proteus* was obtained. This case was treated in the same way as the others and a very good result was achieved. As there was depressive psychosis present and institutional therapy was necessary, it was not possible to follow up the stool cultures. When asked to have repeat tests done, she refused, insisting that she had been cured. This is the only case where a final culture was not done. She was seen about 6 months after treatment was begun and then stated that there was no sign of any relapse.

Case 7. The next case was a child (M.P.) aged 6 months, with severe diarrhoea, vomiting, colic, and abdominal distension. Culture gave a profuse growth of *B. proteus*. Oral therapy with streptomycin was contra-indicated by the vomiting, and the child was therefore given Bicillin (half the adult dose) daily for 2 weeks. During the second week the condition was much improved and stool culture towards the end of the second week showed a scanty growth of *B. proteus*. Accordingly, 1/3 g. of streptomycin was added daily, and the stools when re-checked were found to be negative. No relapse occurred for several years.

Case 8. The last case to report was a child aged 4 months

(H.P.). The story was one of profuse diarrhoea, severe colic, insomnia, and mucus in the stools. This child had been subjected to all forms of therapy in an attempt to cure the infection. He had been given streptomycin, penicillin, tetracyclin and sulphatriad at different times, orally. These treatments met with no success at all, and diarrhoea, vomiting and colic, with abdominal distension, persisted. Another treatment which failed was oral streptomycin, freshly prepared. The stool culture gave a profuse growth of *B. proteus*, and a repeat specimen showed the same. A course of daily Bicillin was started (half the adult dose). After a week there was an improvement, but the stools were still positive. Combined therapy was therefore instituted ($\frac{1}{2}$ vial of Bicillin and $\frac{1}{3}$ g. of streptomycin daily) and continued for one week. There was a remarkable recovery, and, after a further week, the stools were negative, and the child was very much improved. A repeat stool culture made 2 months later was also found to be negative.

CONCLUSIONS

In 7 cases a cure of *B. proteus* infection was obtained by the treatment described. In these cases the *B. proteus* was shown on culture to have been eradicated, and in one other case, apparently cured, a final culture test could not be made. The cure rate with this treatment in my cases has been 100%.

The treatment is the daily injection of Bicillin for 2 weeks, and in resistant cases streptomycin (by injection) is added. Heroic dosage of an antibiotic hitherto regarded as useless against *B. proteus* has produced the successful results. A possible explanation is that the penicillin, long-acting and used in massive dosage, assists enzymes and body defence mechanisms which are not a factor in *in vitro* sensitivity tests. This method of therapy, and sensitivity tests modified in the manner described, may lead to further successes in the treatment of bacterial infections. It will be interesting to see what results are obtained with *B. proteus* infections in the bladder by courses of long-acting penicillin plus a bladder antiseptic or another antibiotic. This treatment is to be applied in the urological and neurological units of a Johannesburg hospital.

Bicillin by itself produces a cure in certain cases, but in others the combination of Bicillin and streptomycin (by injection) is needed to obtain a negative stool culture, making relapse unlikely. The use of streptomycin by itself, orally or by injection, has marked limitations. Massive streptomycin therapy by injection would be attended by dangers, especially vestibular.

Since certain antibiotics, such as streptomycin and neomycin, have but restricted use in the treatment of *B. proteus* infections, intensive therapy with long-acting penicillin may be applied in any type of infection at any site. For instance, in gynaecological infections associated with secondary glands, topical therapy may not be of great use, and parenteral antibiotic therapy as here described is then indicated. Gynaecological infections with *B. proteus* are very resistant to other forms of therapy.

Although Bicillin need not be given in such frequent doses for other infections, in *B. proteus* infections daily Bicillin injections are strongly indicated. It would appear that daily injections of a long-acting penicillin produces and maintains a higher blood level. The addition of an anti-allergic with each injection is suggested as a routine.