SUPPLEMENTARY REPORT ON THE CASE OF CHRONIC ULCERATION OF THE FOOT DUE TO A NEW PATHOGENIC MYCOBACTERIUM (MACCALLUM)[1]

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The American boy of six and one-half years, the son of missionaries to the Belgian Congo, whose case was reported in a preliminary way by Dr. E. van Oye and Dr. M. Ballion (1), was brought back home to the United States and was referred to us because of our interest in surgical infections.

Although we were told acid-fast organisms had been found in this lesion, it had some of the characteristics of the undermining burrowing ulcers which are not infrequently seen in this country. Our bacteriological studies revealed not only the acid-fast organisms but hemolytic streptococci, hemolytic staphylococci and several different aerobic Gram-negative bacilli. In any bacterial mixture the significance of any one species cannot be immediately determined. The treatment was therefore directed at first toward the hemolytic streptococcus and the hemolytic staphylococcus. Because of the severity and the duration of the infection, the boy was given the maximum dose of systemic bacitracin, namely, 400 units per kilogram of body weight, every eight hours. On this regime the hemolytic streptococcus and the *Staphylococcus aureus* disappeared from the wound and there was some immediate improvement in the appearance of the ulcer, but bacitracin had to be discontinued after six days because of early signs of nephrotoxicity. This rapidly cleared after stopping the drug, which proved to be from a toxic lot. Thereafter penicillin, streptomycin, aureomycin and chloromycetin were tried, both alone and in combination, but there was no real evidence of healing over a period of several weeks. The acid-fast organisms were still present in enormous numbers. The smears stained with the Ziehl-Neelsen

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method revealed innumerable acid-fast organisms that tended to agglomerate in definite masses in a manner similar to that described by MacCallum and his co-workers. The organisms were Gram-positive, but only took the stain when the gentian violet was heated. Gram-negative aerobic rods, including proteus, pyocyaneus and aerobacter, continued to be present as secondary contaminants or associated pathogens. Attention was therefore directed toward these residual bacteria and great significance was assigned to the acid-fast organisms, although they failed to grow on our culture media.

Consultation with Dr. René Dubos of the Rockefeller Institute revealed the fact that he was aware of the observations of MacCallum and his co-workers in Australia and had obtained the cultures of their acid-fast strains; and one of his associates, Dr. Gardner Middlebrook, was making a special study of the characteristics of these organisms. We asked Dr. Middlebrook to see the patient and try to grow the organisms. He agreed that the case resembled in its essential details those described by the Australians. Unfortunately, he did not succeed in recovering the organisms.

On the basis of the fact that these organisms were reported by MacCallum to grow best at 32°C. and to be killed by temperature of 37°C., we decided to keep the foot under a warm cradle above 40°C. This simple expedient resulted in an immediate improvement in the wound. Within a few days the exudate and swelling decreased and new skin began to grow in from one of the margins. The number of acid-fast organisms rapidly diminished from the surface of the wound, but in certain areas where there was a considerable amount of slough beneath the skin, they still persisted.

Streptomycin was given again with the hope that with the heat it would complete the elimination of the organisms, but no beneficial effect could be observed. The physical state of the wound with its densely adherent subcutaneous slough seemed to prevent contact with the acid-fast organisms, either by the systemic or local administration of any of the antibacterial agents. The local application of streptokinase and streptodornase did not result in separation of the slough.

It therefore became necessary to remove the dead tissue surgically. The involvement of the fourth metatarsal bone required its removal and that of the corresponding toe. Thereafter, granulations grew up very rapidly and new skin grew in from all margins. Within a relatively short time it was possible to

plant small Thiersch grafts in the denuded surface. During the period of general improvement, however on two occasions when we compromised with the heating and permitted more activity, the organisms became active again beneath the margin of the wound and two supplementary excisions were required. In due course the whole area became covered with skin and all evidence of infection disappeared. The patient finally left the hospital after four and one-half months with the wound completely healed.

At the time of surgical excision, we made a second attempt to grow the acid-fast organisms. When the necrotic tissue was digested and then inoculated onto Lowenstein's medium and duplicate slants were incubated at 32°C. and at 37°C., acid-fast bacilli grew at the lower temperature only. Injections of digested material into the groin and into the peritoneum of guinea pigs did not result in any tuberculous lesions. This would seem to rule out the possibility of these acid-fast organisms being *Mycobacterium tuberculosis.* Until further animal work, now in progress, has been concluded, we are not prepared to say that this bacillus belongs to the same species as the strains isolated by MacCallum and his co-workers.

The associated Gram-negative rods could not be completely eliminated by any of the anti-bacterial agents employed, but their activity was held in check by combinations of streptomycin, polymyxin B, and parachlorophenol. Bacitracin was also used locally to prevent the reappearance of streptococci and staphylococci. When once the acid-fast organisms had been eliminated, these secondary contaminants did not seriously interfere with wound healing.

We believe that the course of events indicates that this is a case similar to those described from Australia, and we believe that the proper treatment for such cases should be early surgical removal of all dead tissue, maintenance of the part at a temperature above 40°C., and early repair of the defect with skin grafts. Secondary contaminants can be controlled by the appropriate effective antibiotics after testing the sensitivities of the organisms.

RÉSUMÉ

Les auteurs ont pu continuer l'observation du cas rapporté par E. van Oye et M. Ballion. Il s'agissait d'un jeune garçon blanc au Congo Belge, porteur d'une ulcération étendue résistant à tout traitement et dans laquelle des bacilles acido-résistants étaient présents.

A New-York le garçon fut traité de diverses façons. Les antibiotiques: bacitracine per os ou localement, streptomycine, auréomycine, chloromycétine, polymixine B et aussi parachlorophénol se montrerent sans action sur les acido-résistants, mais limitèrent plus ou moins la flore associée. La disparition des acido-résistants (germs thermophobes) fut obtenue par des applications chaudes puis le nettoyage chirurgical, et enfin des greffes activèrent la guérison que la flore associée n'entrava du reste pas. Les premiers essais de culture furent infructueux mais ultérieurement des cultures sur Loewenstein furent obtenues à 32° (négatif à 37°). Les recherches bactériologiques continuent.

Les auteurs croient se trouver devant l'affection décrite en Australie par MacCallum et Col.

REFERENCE

1. VAN OYE, E. & BALLION, M. Faudra-t-il tenir compte d'une nouvelle affection à bacilles acido-résistants en Afrique? (Note préliminaire.) Ann. Soc. belge Méd. trop. **30** (1950) 619-627.