

Dr PAUL K. PYBUS

M.D., F.R.C.S., D.R.C.O.G.

CONSULTING HOURS:
MON. TUES. THURS. FRI.
8. 00 A.M. - 5. 00 P.M.
WED. 8 - 12 NOON

404 UNITED BUILDING
181 CHURCH STREET
PIETERMARITZBURG 3201
TELEPHONE 0331-57675

7th February, 1986.

MAY 12 1986

Perry A. Chapdelaine Sr.,
The Rheumatoid Disease Foundation
Rt. 4, Box 137
FRANKLIN
Tennessee 37064
U.S.A.

Dear Perry,

It was good to hear you on the 'phone in spite of the fact that you had rather disturbing news. I think I shall await answers to my letters first before I start 'phoning up as perhaps they will give me some lead as to what I can do.

Sorry to hear that both Fransen and Neff investigations seem to be largely negative. I don't think we need worry about this, however. I have given the whole situation some thought. For some time now I have been worried about the presence of free living amoebae and Davies seems to be convinced that there aren't any. However, one thing is still very certain and that is if you give these various drugs which we say are anti-amoebic, the patients get better. What is more they also have Herxheimer reactions which correlate very firmly with the degree of clinical improvement as I have shown in my last letter which you may have a copy of now. There is no doubt about these two facts.

This is the story as I think it probably happened. I have been in close contact with everybody concerned and I might as well tell you what I think is the real position. I think by far the best book that was written by Roger was the one on the Reticulo Endothelial system. This was all based on the action of trophic nerves and the macrophages which seem to come from these nerves. He had obviously studied this very very closely and was able to show increased macrophage activity in all these various rheumatoid diseases as well as many others. In fact anywhere that showed increased nervous activity had increased numbers of macrophages. He then met up with Stamm and according to Joan, he and Stamm used to work for long hours down in the Cancer Hospital or at the Hospital for Tropical Diseases. Apparently they were always talking and discussing things and of course Stamm, being an amoeba expert, was trying to persuade Roger that they were looking for amoebae and not macrophages. Then Roger tried out his Clotrimazole and got the results that he did which he wrote up in World Medicine which was found by Blount and he, unable to get Clotrimazole, looked at the formula and saw that Metronidazole was similar and so he tried this and we all know what happened. Then we looked for other imidazole groupings and we found that Levamisol, which was used already for rheumatoid arthritis, was also an imidazole. Then we found Tinidazole which also seemed to have an effect - all these seemed to work and they are all anti-amoebics. This all produced huge evidence that Wyburn-Mason was probably correct.

Wyburn-Mason said that he had cultured these amoebae, but unfortunately there is no real figures or evidence that he did. He never mentions what culture medium he used except in the book when he mentions liver fusion agar. I have tried to get hold of this, not only here, but also overseas in England and I have been unable to get any. In any case free living amoebae are supposed to grow very easily on non-nutrient agar already populated by klebsiella. We have tried to do this several times through the Institute of Amoebic Research in Durban with Dr. Jackson as well as myself and Davies and we all failed to get any. Then, as you know, we

Page 5 M.S.S. 109

got Kwang Jeon interested and he tried and also failed to culture them. He did, however, culture macrophages and demonstrated that they were killed by Flagyl. As you know doctors on our foundation sent specimens from all over the United States as well as from as far away as New Zealand and thus enabled Kwang Jeon, his figures showing that treated cases grew nothing whereas non-treated cases he grew macrophages from and these turned into fibroblasts and produced fibrous tissue. This I think is the most significant finding we have got. We might almost say that Davies and I have showed this in another way. We have taken fluid from knee joints which have shown the presence of macrophages. We then put Flagyl into the joint and these macrophages at first move more rapidly for about 5 minutes then become more stationary and finally become crenated and are slowly absorbed. This would also suggest action of Flagyl on macrophages.

Now you have been trying to show the sensitivity of free living amoebae to the various anti-amoebic drugs. This work is largely Perry Chapdelaine's and he found that although many of the anti-amoebics had effects on amoebae, the one which seemed to not have any effect at all was Metronidazole or Flagyl. However, one thing we do know is that Flagyl effects macrophages as proven, not only by Davies and myself but also by Kwang Jeon. (Metronidazole must be metabolized by good intestinal microflora - Not human enzyme system - to be effective!)

Professor Dowdle, in Cape Town, gave a very masterful address on the macrophage and its action in immune response and he came to the conclusion as he put it, the macrophage was the villain in the rheumatoid saga. We know how to deal with the macrophage, namely Flagyl, and this may well account for our good results.

I think, in future, if the free living amoebae story fails to show any scientific proof that we should then concentrate on the macrophage and its reaction in the immune response. It is a bit early to say this but keep this in mind.

All this does not mean to say that Roger was wrong as his interest in macrophages in his original work would show. However, his association with Stamm may have led him into the wrong track. Joan said to me that she remembered one night Roger coming in very late, looking absolutely exhausted, and he sat down and said "Well, I think there must be amoebae after all." He seemed to have been convinced by Stamm that this was so. And, of course, Stamm can't give us any information at all now. (Senile)

Don't be too downhearted about it all, as through our publicity and our work we have cured very many people. It doesn't matter a damn how we do it as long as we have done it, which we have. We do not really have to say why we have done it all we have to say is that it works. Perhaps we should engage some immunology people to look into this action of Flagyl and indeed some of the other anti-amoebics on the macrophage. Perhaps we would get further, but the main thing, as you have always said, is to get people better and Flagyl does it as I'm sure Professor Meyers will find out when he completes his tests at Groote Schuur. The only strong indication that there is an infection going on is the occurrence of the Herxheimer and I have put this to Davies several times and he can never answer it.

I do not think that acanthamoeba are involved for the following reason. When I brought Tony's specimens of acanthamoeba back with me I gave them to Davies and he tried to get them through the filter which was one of Roger's original filters and they didn't go through. He then put some ordinary rheumatoid arthritis joint fluid with macrophages present and these macrophages did go through and they were thermotropic and for this reason Davies feels that amoebae are not involved. No-one has so far cultured these macrophages except Kwang Jeon and he again confirms that they are rendered impotent by Flagyl.