To the Editor:

I would like to consider a few points in Dr. Brown's letter. He does not tell us why he dislikes the word "controlled." The trial was certainly not under double-blind control—perhaps he would tell us how to arrange this in a drug whose high dosage pigments the skin. The following paragraphs refer to paragraphs in his letter.

(1 and 2) I believe that even a "guarded and tentative suggestion" should be logical. I do not think that the pilot trial which he mentions went on long enough. He says "some of the patients" were treated for 12 months. If my memory serves, more were treated for six months. I am not persuaded by the logic of an assumption drawn from two groups with differing lengths of treatment.

(3) Browne says his early report was concerned with the prevention of ENL. Such success would not necessarily prove that the drug used was anti-inflammatory, but, as this claim was made, albeit tentatively, it seemed to me that the reasonable extension of this work was to use B.663 in the treatment of ENL.

(4) It is indeed unfortunate that my patient did not like to be turned red. I do not believe that I said 100 mg. produced this effect. I am well aware that low dosage of B.663 produces satisfactory bacteriologic improvement in lepromatous leprosy.

(5) If Browne tries to reconcile two dissimilar statements he will necessarily meet with difficulties. My statement on page 12 was concerned with five cases, and that on page 15 with 15 cases. I have already pointed out in my reply to Dr. Fowler's letter that out of 13 cases receiving steroids when B.663 was started, eight still needed such hormones seven or more months later.

Further workers to attempt controlled trials and not rely too much on a small collection of case reports such as the paper by Williams et al., which he quotes. He will then realize that my "rigidity" in dosage is perhaps not so blameworthy as he implies, and that variation in drug dosage has no place in a controlled trial and would indeed even further confuse the problem of analysis.

To turn to a more important matter, that of the place of sulfone therapy while a patient has ENL. I believe that my figures show that ENL does not stop significantly after the cessation of sulfone. Out of 13 cases still being treated with ACTH when sulfone was stopped, Cases A-5 and C-2 needed two months' further treatment and Cases A-1, A-2 and B-3 needed 3, 4 and 6 months respectively. Eight of the 13 cases were still being given ACTH seven or more months after the cessation of sulfones. This does not convince me that there is a post hoc-propter hoc relationship between the two. Indeed of the only two cases not being treated by steroids when the sulfone was stopped, one relapsed temporarily a few months later.

Authors writing about ENL tend to overlook the fact that almost all cases ultimately get better even if sulfone is continued (2), and are often prepared to draw conclusions from coincidentals occurring near the time of remission. It was hoped that this paper would "go some way toward encouraging studies (into ENL) of an accurate and controlled nature."

—J. H. S. Pettit

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13 June 1967
Maybe I am wrong in my use of the word "anti-inflammatory," but to my mind drugs like ACTH and prednisolone are anti-inflammatory. I have seen no comparable effect following the use of B.663 at a dose of 100 mgm. daily.

(6) As to the use of higher doses, I must emphasize that when a trial is started there is no place for variation in dosage. The authorities that Browne cites did not, to the best of my remembrance, even attempt a controlled study. So I do not understand how Browne can "state with assurance" that higher dosage would be successful. I am frightened by this reliance on uncontrolled investigations and can only reiterate that I hope my paper will stimulate a more scientific approach to a disease in which, in Browne's own words, patients suffer from "recurrent crops" of lesions and where there is a tendency to "subside spontaneously."

(7) On the problem of ENL and sulphones, I will say no more until experienced leprologists read the paper by Waters and myself (7), which bases our conclusions on a larger and more representative series.

As to the rest of Browne's letter, I am afraid that I do not always follow the reasoning. Earlier he stated that he would not expect a majority of patients to improve on "inadequate amounts," i.e., 100 mgm. of B.663, but later he stated that in cases comparable to those in my paper, 100 mgm. was sufficient in some patients. I look forward to hearing more of the hitherto unpublished work of Dr. Imkamp and particularly I will be interested to learn of his methods of control.

I must perhaps make it clear that in my experience, using the dosage described, B.663 does not work convincingly. In my reply to Dr. Fowler's letter I asked for evidence of the anti-inflammatory effect of B.663 in other diseases. In a personal communication Dr. Fowler stated that he has tried to get other people interested in this project without much success. Perhaps this implies that others, like myself, are not impressed by the claims that B.663 has an anti-inflammatory effect.

Browne fears that a potentially valuable drug may fail to be investigated because of my paper. I feel that he may be safely reassured on this matter; I have personally written papers claiming success for B.663 in low doses against lepromatous leprosy (1), against sulfone-resistant M. leprae infections (1), and against M. ulcers infections (2). I do not believe that my work will cause the drug to fall into disrepute.

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REFERENCES

ENL in Borderline Leprosy

To the Editor:

We have carefully read the comments from Dr. Kwittken and Dr. Harter regarding our paper.

With reference to Dr. Kwittken's remarks on our paper we have two comments. First, our paper was submitted for publication on 15 August 1966, his on 5 October 1966. Second, in his paper he gives a clinical description and diagnosis of ENL but fur-