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Chemotherapeutic Trials in Leprosy

5. A Study of Methods Used in Clinical Trials in Lepromatous Leprosy[1]

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Outline

STANDARD CONTROLLED CLINICAL TRIALS OF CHEMOTHERAPY

I. Clinical Type of Patient Required, and Methods of Classifying Leprosy

II. Methods of Assessing Progress

(a) Clinical assessments.

(b) Bacteriologic assessments.
- (i) *Bacterial index.*
- (ii) *Morphologic index.*

(c) Histologic assessments

III. Conduct of a Trial

(a) Selection of patients.
- (i) *Significance of prior sulfone or other specific therapy.*
- (ii) *Severity of the leprosy.*
- (iii) *Age, sex, race, and duration of the disease.*
- (iv) *Other factors.*

(b) Number of patients.

(c) Random allocation of patients to the treatment series.

(d) Aspects of trial design.
- (i) *Stratification.*
- (ii) *Matched pairs.*
- (iii) *Analysis of covariance.*

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(e) Assessment of progress.
  (i) *Clinical assessments.*
  (ii) *Bacteriologic assessments.*
  (iii) *Histologic assessments.*

(f) Interruptions in treatment and losses from observation.
  (i) *Causes other than leprosy.*
  (ii) *Toxicity and nonacceptability of the trial drug.*
  (iii) *Leprosy.*
    (1) *Worsening of the primary leprosy condition.*
    (2) *Losses due to secondary complications.*
    (3) *Erythema nodosum leprosum.*

PILOT TRIALS

TRIALS IN ERYTHEMA NODOSUM LEPROSUM

OTHER TRIALS AND OBJECTIVES

SUMMARY

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The Leprosy Research Unit, Sungei Buloh Leprosarium, Malaysia, has been principally concerned since 1957 with the trial of new drugs and of new drug regimens in the treatment of leprosy ([41, 43, 44, 46, 65, 66]). The cumulative experience gained from these trials has enabled us to consider critically how controlled clinical trials should be performed in leprosy, especially with regard to their general design, the type of patients to be admitted, the ways of assessing progress, and the methods of analyzing the results. Furthermore, we have been greatly influenced by recent major experimental advances, in particular the discovery of limited multiplication of *Mycobacterium leprae* in experimental animals ([55]) and of the significance of the different morphologic forms of the bacilli ([48, 57]). We believe that the application of these fundamental advances has already provided new understanding of the efficacy and mode of action of drugs on the leprosy bacillus ([45, 47, 56, 67]), which will without doubt influence the methods employed in convincing as possible. Leprosy is a chronic disease in which assessment is especially difficult. It would therefore be expected that controlled trial methods would have been introduced early and applied meticulously in the study of its treatment. However, apart from the series sponsored by the Leonard Wood Memorial ([13, 15–20, 26, 60]), controlled clinical trials have been frequently neglected by leprologists. Thus Noordeen ([40]) states that of 104 drug trials reported during the 10 years 1954-1963, only 25 included adequate controls. Indeed, the majority of studies have been based on small groups of patients without adequate controls, only assessed clinically and by the bacterial index. Histologic examination has rarely been included, and therefore patient selection has been inadequate, resulting in nonuniform groups. In addition, in some trials, including those of the Leonard Wood Memorial, previously treated patients have been admitted.

In conjunction with the general neglect of controlled trial methods, there has been little consideration of the