# CHOLERA SEVERITY AS RELATED TO NUTRITIONAL STATUS AND ANTIBIOTIC THERAPY

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## Introduction:

Several studies (1,2,3) have demonstrated the efficacy of antibiotic therapy (particularly tetracycline) in decreasing the duration and rate of stool-fluid loss in cholera, both in adult and pediatric illness. However, there has been relatively less attention to the possible effect of malnutrition on cholera severity(4) or to possible regional differences, or variations with time at the same locale(5), in clinical disease presentation. It has been felt that current illness severity (as estimated by stool volume and duration) may be less than previously seen and may be appreciably shortened by antibiotic therapy. Also, much of the cholera currently seen is found in quite malnourished children and adults, leading to the speculation that severity may also be related to nutritional status. These relationships need further precise analysis. In addition, since tetracycline has a relatively high cost and may be in short supply in areas of critical need, the ability to define which patients are most likely to benefit from its use would be of value.

## Goals:

The goals of the proposed study would be to:

A) make careful clinical observations, especially as regards to stool volume and duration, of patients in the current epidemic, with observations on serotypes and biotypes, in order to quantify an impression of a less severe clinical presentation.

B) make appropriate measurement of nutritional status both in children and adults in the same groups in order to determine the possible effects of malnutrition on cholera severity.

C) administer antibiotics in a controlled sequential fashion so as to determine practical efficacy in the current cholera epidemic and evaluate any possible interaction with nutrition.

Materials and Methods.

All patients, both children and adults, entering the Cholera Research Hospital in whom a clinical diagnosis of cholera is entertained, will be potential trial subjects. Those with prior antibiotic or fluid therapy during the proceeding week will not be used and only those with subsequent isolation of V. cholerae will be retained. Those with isolation of other potential diarrheal pathogens (Shigella, Amoeba, other parasites or NAG) either alone or in combination with cholera, will also be excluded, as will patients currently receiving iron supplement (Fesoy) therapy. Patients will be stratified by admission impression into two groups, those severely and those moderately dehydrated. Within each severity-group, alternate patients will be given tetracycline in standard dose proportionate to age.

All patients will have age, sex, time of onset and character of diarrhea, prior food intake and current place of residence recorded in the usual fashion as well as the usual physical examination. At admission serum specific gravity by refractometer and electrolyte concentration will be determined as well as temperature and blood pressure. In addition, all study patients will have stool culture and microscopic exam for parasites prior to therapy and laboratory determination of biotype, serotype and antibiotic sensitivity of V. cholera.

Subsequent sequential determinations will include the usual stool and urine volume, daily weights, mid-arm circumference at admission and discharge; and serum albumin, specific gravity and height at the second day after full rehydration.

Dehydration severity will be determined by initial impression (pulse, skin turgor, mentation) plus serum specific gravity, electrolyte concentrations and weight gain on rehydration. Nutritional status will be determined by a modification of the McLaren system(6) using age, weight to height measures based on Bengalee standards(7). Type of (P.C.M.) nutritional deficiency i.e. Kwashiorkor or Marasmus, will be by serum albumin concentration and the presence or absence of edema, dermatosis, hair changes or hepatomegaly (8). These will be estimated only after rehydration. The cholera vibrio biotypes, serotypes and antibiotic sensitivity will be determined in the usual fashion from isolates of stool collected at the time of admission.

Stool output will be measured every eight hours from the time of admission to the end of diarrhea, defined as the last eight-hour period with a liquid stool. If less than 4 hours exists in the initial admission 8 hour period, this period will be ignored; otherwise the stool volume will be prorated over the initial interval.

Facilities.

The currently available facilities of the Cholera Research Hospital and its attached clinical laboratory will be used for this project. Patients will be stratified into two severity groups (severe and moderate) and alternatingly assigned to antibiotic or no antibiotic sub-groups, while all will have nutritional assessment. Thus, there will be four sub-groups examined. To ensure a similar age distribution in each sub-group, all subjects admitted to the study in any one week will be of approximately the same age, starting with adults in the first 2 weeks and progressing to younger patients thereafter. With approximately 50 patients for each sub-group, 200 patients in total should be adequate for statistical comparison. If these can be entered into the study at approximately 10 new patients per day for a 5 day week, the observations to be made and facilities occupied should not be excessive at any one time yet the total should be rapidly reached.

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