Peripatetic Epidemiology

In the Service of Global Health

Center for Population Health Sciences
Stanford University

Alfred Sommer M.D. M.H.S
Johns Hopkins University
Evidence-Based Medicine

“...medical science will advance not by opinions and assertions but by registering facts... by applying that mighty instrument of natural science — arithmetic”

William Farr, 1837
“Research is formalized curiosity.”

Zora Hurston
African-American
Writer and Anthropologist
10 Lessons in Public Health
Inspiration for Tomorrow's Leaders
ALFRED SOMMER, M.D., M.H.S.
GO WHERE THE PROBLEMS ARE

The world is very different now. For man holds in his mortal hands the power to abolish all forms of human poverty and all forms of human life.

JOHN F. KENNEDY
Would the use of a “protected” water supply reduce the risk of cholera?

(In East Pakistan – not in John Snow’s London)

{thank you Billy Woodward}
## Risk of Cholera by Proximity to Tube Well

<table>
<thead>
<tr>
<th>Proximity to Tube Well</th>
<th>Classical</th>
<th>El Tor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inaba</td>
<td>Ogawa</td>
</tr>
<tr>
<td>Near</td>
<td>1/27 (3.7%)</td>
<td>13/43 (30.2%)</td>
</tr>
<tr>
<td>Far</td>
<td>19/75 (25.3%)</td>
<td>31/106 (29.2%)</td>
</tr>
<tr>
<td>RR</td>
<td>6.8</td>
<td>1.0</td>
</tr>
<tr>
<td>(Far)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
THE INFLUENCE OF PROTECTED WATER SUPPLIES ON THE SPREAD OF CLASSICAL/INABA AND EL TOR/OGAWA CHOLERA IN RURAL EAST BENGAL

ALFRED SOMMER* WILLIAM E. WOODWARD

Center for Disease Control, U.S.P.H.S., Atlanta, Georgia 30333, U.S.A.; and the Epidemiology Division, Cholera Research Laboratory, Dacca, Bangladesh

Summary Randomly selected children of a rural village in East Bengal had daily rectal swabbing and pre and post epidemic vibriocidal-antibody titrations performed during two successive cholera epidemics. During the first epidemic (1968–69), caused by the Classical/Inaba strain, participants living in the immediate vicinity of tube-wells had a much lower rate of infection (1 out of 27, or 3.7%) than those living farther away (19 out of 75, or 25.3%). During an epidemic the following year (1969–70), caused by the El Tor/Ogawa strain, there was no the countryside, but these drilled artesian wells with pitcher-type pumps remain in short supply. When operated properly their water has generally been found safe and free of V. cholerae 3; even so, their effectiveness as a general prophylactic agent, especially in areas like rural Bengal where alternative sources of unprotected water abound, has never been adequately demonstrated. The greatest difficulties in getting such proof have been the relatively low clinical attack-rate of the disease and the scarcity of villages with significant numbers of tube-wells.

The present study was conducted as part of a broader comparative investigation of Classical/Inaba and El Tor/Ogawa cholera. Making use of the recent demonstrations that clinical cases of cholera represent only a small percentage of total infections,6–9 we obtained daily rectal swabs and pre and post epidemic sera during two successive cholera epidemics and were thus able to accumulate information on sufficient numbers of cases to allow comparisons between groups within a single, relatively homogeneous, village population. In addition, the data obtained...
Public Health

Efficacy of Vaccination of Family Contacts of Cholera Cases

Alfred Sommer*  Moslemuddin Khan
Wiley H. Mosley

Epidemiology Program, Center for Disease Control,
U.S. Public Health Service, Atlanta, Georgia 30333,
U.S.A., and Epidemiology Division,
Cholera Research Laboratory, Dacca, Bangladesh

Summary 742 family contacts of 149 cholera patients with bacteriologically confirmed Vibrio cholerae Inaba infection were given either placebo (vaccine diluent) or monovalent Inaba vaccine of proven efficacy within 12 hours of hospital admission of the index case. Rectal swabs and histories of diarrhea obtained daily for 10 consecutive days revealed no appreciable difference in subsequent rates of infection, date of onset of positive stools, duration of vibrio shedding, or clinical expression of the disease. Although protection did seem to begin by the 9th day of observation, the numbers were too small to be statistically significant. Given the close temporal clustering of secondary infections among family contacts near the onset of the index case (well over 95% had occurred by day 8), tetracycline remains the prophylactic agent of choice.

INTRODUCTION

Cholera, the scourge of the Indian subcontinent for millennia, has in the past century become a worldwide problem. While the installation of proper sanitation facilities remains the most important means of epidemic control, this is too costly a solution for many underdeveloped countries. Instead, they rely heavily on vaccination—a technique first described in 1884. Microscopic examination with type-specific sera was done on the initial stool specimens of all patients admitted to the Cholera Research Laboratory in Dacca. The families of patients with confirmed infections with Inaba serotype of Vibrio cholerae and with at least 3 symptom-free contacts at home were alternately assigned to receive either placebo or vaccine.

Each family was visited daily for 10 consecutive days. The first visit was made within 12 hours of the index case being admitted to hospital (day 1), at which time a census was taken and vaccine or placebo was administered. Rectal swabs were obtained and each member's medical status was noted daily; fingertip blood specimens were collected on days 1, 5, and 10 for vibriocidal antibody determination. The entire study was double-blind.

Vaccine

The vaccine, of proven efficacy, was prepared from V. cholerae Inaba strain NIH 35A3 as described by Mosley et al. Before use, it was reconstituted with sterile isotonic phosphate-buffered saline solution containing 0.25% phenol, to contain $8 \times 10^6$ bacteria per ml., and put in a vial labelled "vaccine B". The placebo consisted of the diluent only in an identical vial labelled "vaccine A". Field teams were unaware of the vials' contents.

All family contacts received a single 0.5 ml dose of either vaccine or placebo from foot-operated jet injectors ('Pedojet'). Separate, clearly marked jet injectors were used for the different preparations.

Bacteriological and Serological Methods

The techniques of obtaining and culturing rectal swabs and of handling fingertip blood specimens have already been described. The vibriocidal antibody titres against Inaba organisms were determined by the microtechnique of Berenson et al.

Blood specimens were tested in doubling dilutions from 1/20 to 1/2560. The results are presented as mean tube dilutions.

RESULTS

Of the 174 index cases, 149 proved to be infected
<table>
<thead>
<tr>
<th>Date</th>
<th>Vaccine/prophylactic drug</th>
<th>Dose</th>
<th>Physician's signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Tetanus-Dip</td>
<td>1st</td>
<td></td>
</tr>
<tr>
<td>1992</td>
<td>Hepatitis B series</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/94</td>
<td>Meningococcal (2-tecensis &amp; Booster in past)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/94</td>
<td>Typhoid Tip20 oral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/96</td>
<td>HAV/HBV Hep A</td>
<td>Off</td>
<td></td>
</tr>
<tr>
<td>9/96</td>
<td>HAV/HBV Hep A</td>
<td>Off</td>
<td></td>
</tr>
</tbody>
</table>

Johns Hopkins Travel Medicine
601 N. Caroline Street
Baltimore, MD 21287 USA
Tel: 410.955.8931
Email: travelmedicine@hopmi.edu
MODERN STAMP MFG. CO. BALTIMORE

WILMER CLINIC BALTIMORE 301 - 955-5000
CHOLERA VACCINATION
Anyone who has spent a few nights in a tent during a storm can tell you: The world doesn’t care all that much if you live or die.

Anthony Doerr
(unexpected) things happen……

= new opportunities!
Pakistan government requests 12 field hospitals and 25 x-ray machines

What is an appropriate “First Response”? 
Fig. 2—Cyclone mortality by union.
Fig. 3—Age-specific mortality rates in cyclone-affected area.
EAST BENGAL CYCLONE OF NOVEMBER, 1970

EPIDEMIOLOGICAL APPROACH TO DISASTER ASSESSMENT

Alfred Sommer  
Wiley H. Mosley*

Epidemiology Program, Center for Disease Control, U.S. Public Health Service, Atlanta, Georgia 30333, U.S.A., and Epidemiology Division, Cholera Research Laboratory, Dacca, Bangladesh

Summary  Two medical relief assessments were carried out in the southern coastal region of East Bengal affected by the cyclone and tidal bore of November, 1970. The first, a rapid 18-site survey, documented the adequacy of existing water supplies and absence of significant post-cyclone morbidity or exceptional levels of epidemic diseases. The second, wider in scope, was done 2 months later, between Feb. 10 and March 4, 1971. Seventy-nine unions in the nine most affected thanas were visited, and 2973 families, comprising 1.4% of the area's Dacca. When news did reach the outside world, relief supplies and volunteers poured in, but no-one knew the magnitude or geographic distribution of losses and needs. Newspapers reported widespread famine, cholera, and smallpox¹; if these had been true, they might have meant an even greater disaster than the cyclone. East Bengal is one of the most densely populated and impoverished areas in the world (average per-caput income is less than $70). Medical resources are scarce and, although the soil is surprisingly fertile, the population has long outstripped the area's agricultural capacity.²

To permit more rational planning of relief operations, teams from the Epidemiology Division of the (Pakistan-SEATO) Cholera Research Laboratory (C.R.L.) conducted two surveys of the cyclone-affected region. The first, between Nov. 28 and Dec. 2, 1970, was concerned with water supplies and immediate medical needs. It also provided rough estimates of cyclone mortality and housing and livestock losses. The second survey was done between
How should one STOP a smallpox epidemic?
Smallpox Outbreaks

Khulna Municipality, Bangladesh - 1972

Calendar weeks of 1972

Cases

Area 1
Area 2
Ebola Vaccine Trial

(NYT 8/1/15)

“This was the first time in memory that a vaccine’s effectiveness has been studied with a so-called ring vaccination approach”.

(“memory” = < 40 years)
SMALLPOX VACCINE!... HOW DID YOU KNOW?
Another unsought Opportunity!
(of little practical value until 30 years later)

{and a chat with Josh Lederberg}
Onset of Smallpox in Family of Initial Case

<table>
<thead>
<tr>
<th>Day vaccinated</th>
<th>Rash in Vaccinated</th>
<th>Rash in Unvaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post Infection*</td>
<td># rate/ 1000</td>
<td># rate/ 1000</td>
</tr>
<tr>
<td>12 (2)</td>
<td>3 1.7</td>
<td>1 3.6</td>
</tr>
<tr>
<td>10 (4)</td>
<td>2 1.7</td>
<td>1 3.6</td>
</tr>
<tr>
<td>8 (6)</td>
<td>6 3.4</td>
<td>2 3.4</td>
</tr>
<tr>
<td>6 (8)</td>
<td>3 1.7</td>
<td>2 7.3</td>
</tr>
<tr>
<td>4 (10)</td>
<td>—</td>
<td>2 7.3</td>
</tr>
<tr>
<td>2 (12)</td>
<td>—</td>
<td>1 3.6</td>
</tr>
<tr>
<td>0 (14)</td>
<td>1 0.6</td>
<td>2 7.3</td>
</tr>
</tbody>
</table>

*Assumes 14 day incubation period

A. Sommer, AJE, 1974
THE 1972 SMALLPOX OUTBREAK IN KHULNA MUNICIPALITY, BANGLADESH

II. EFFECTIVENESS OF SURVEILLANCE AND CONTAINMENT IN URBAN EPIDEMIC CONTROL

ALFRED SOMMER

(Received for publication August 27, 1973)

Sommer, A. (Wilmer Institute, Johns Hopkins Hospital, Baltimore, Md. 21205). The 1972 smallpox outbreak in Khulna Municipality, Bangladesh. II. Effectiveness of surveillance and containment in urban epidemic control. Am J Epidemiol 99:303–313, 1974.—Between April 28 and June 22, 1972, 1384 smallpox cases and 372 deaths were detected in Khulna Municipality, Bangladesh. Within three weeks of instituting surveillance and containment activities the entire city-wide epidemic was under control. Active surveillance detected over 84% of all new cases, as estimated by dividing the number of cemetery registered "pox" burials by the observed case fatality rate. Ninety per cent of family contacts of detected cases were vaccinated in the
Anthropometry
(circa 1970)

• height-for-age
• weight-for-age
• weight-for-height
“QUAC” Stick
(Quaker-Arm-Circumference)

• Arm Circumference for Height
• Three “cut-offs”:
  lower 9\text{th} percentile
  10\text{th} – 50\text{th} percentile
  > 50\text{th} percentile
Is the QUAC Stick a valid and useful index of nutritional status?

Is any anthropometric index?
### Mortality RR and Duration Since Measurement

(1 to 4 years old)

<table>
<thead>
<tr>
<th>Months since Assessment</th>
<th>Category 1</th>
<th>Category 2</th>
<th>Category 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>19.8</td>
<td>1.3</td>
<td>1.0</td>
</tr>
<tr>
<td>1 - 3</td>
<td>12.2</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>4 - 6</td>
<td>4.5</td>
<td>1.8</td>
<td>1.0</td>
</tr>
<tr>
<td>7 - 9</td>
<td>3.2</td>
<td>1.7</td>
<td>1.0</td>
</tr>
<tr>
<td>10 - 12</td>
<td>3.0</td>
<td>1.3</td>
<td>1.0</td>
</tr>
</tbody>
</table>

% of all deaths

- Category 1: (56%) (38%) (19%)
- Category 2: 8%

% of all children

- Category 1: (56%) (38%) (19%)
- Category 2: 8%
- Category 3: 100%
“...one is unconvinced that the AC for height categories were reasonably predictive of death...”

“These results refer only to the 1-4 year old age group...”

“...lack of appropriate standards of AC for height limits the use of this anthropometric measurement...”

New England Journal of Medicine
"I must ask you to forgive us for having decided in the end – and with great reluctance – against accepting your paper. The *Lancet* is most awkwardly situated..."
Nutritional status and mortality: a prospective validation of the QUAC stick

Alfred Sommer, M.D., M.H.S. and Matthew S. Loewenstein, M.D.

ABSTRACT In December 1970, 8,292 rural Bengali children between the ages of 1 and 9 had their height and arm circumference measured. Eighteen months later the fate of 98.8% of these children was ascertained. Overall, 2.3% of the children had died. Those below the 9th and between the 9th and 50th percentiles of arm circumference for height were at 3.4 and 1.5 times greater risk of dying, respectively, than those above the 50th percentiles. A gradient was present at every age, although it was greatest for the vulnerable 1- to 4-year age group, for whom the relative risks were 4.5, 1.6, and 1.0, respectively. The discriminant efficiency of these categories was greatest immediately following measurement and decreased with time. During the first postmeasurement month the risk of dying in the poorest nutritional category was 19.8 times that of the best, and for the first 3 months, 12.2 times. By the last 3 months of followup it was only twice that of the best. Females in all three categories fared slightly worse than males, being at 1.1 times the risk of dying. This same vulnerable group of 1- to 4-year olds could be identified without knowing their age. Limiting the analysis to children whose heights were between 65 and 89 cm resulted in relative risks, for the three categories, of 4.1, 1.6, and 1.0, respectively. These arm circumference to height categories and the QUAC stick survey technique for which they were devised appear to be valid tools for identifying nutritionally disadvantaged individuals and populations at high risk of death. Am. J. Clin. Nutr. 28: 287–292, 1975.
METHODOLOGY
OF
NUTRITIONAL SURVEILLANCE

Report of a
Joint FAO/UNICEF/WHO Expert Committee

WORLD HEALTH ORGANIZATION
GENEVA
1976
Public Health

INCIDENCE, PREVALENCE, AND SCALE OF BLINDING MALNUTRITION

ALFRED SOMMER  IGNATIUS TARWOTJO
GUSTI HUSSAINI  DJOKO SUSANTO
TIMO SOEGIHARTO


Summary 4595 pre-school-age children in six villages of West Java were examined every 3 months. The incidence of active corneal xerophthalmia was 5 per 1000 per year (95% confidence limits, 2.6-7.5), and the average prevalence during each round of examinations was 12 per 10 000. In a randomised, multistage cluster survey of 27 084 rural children throughout Indonesia the population-weighted prevalence of active corneal disease among pre-school-age children was 6.4 per 10 000 (95% confidence limits 3.2-9.6), 53% of that in the longitudinal study areas. At an adjusted incidence rate of 2.7 per 1000 per year, over 60 000 Indonesian children become xerophthalmic every year. By extrapolation of these findings about 500 000 new cases of xerophthalmia, half of which lead to blindness, occur xerophthalmia (Bitot's spots or night blindness) were carefully followed up.

The randomised multistage cluster probability survey (the cross-sectional study), done in 23 of the 27 provinces of Indonesia, covered 96% of the country's population. 36 060 pre-school-age children were examined in 254 sampling areas. Only the rural sample of 27 084 children was truly representative of the rural pre-school-age population and will be considered in this report. Examinations were carried out by three teams of similar composition and training to those of the team for the longitudinal study; periodic checks were made to see that observations made were standardised. All children with xerophthalmia received 200 000 IU vitamin A orally. The survey period, October, 1977, to May, 1978, was dictated by political considerations and a desire to avoid Ramadan, with its attendant effect on dietary patterns.

All data were entered on self-coding forms, checked twice (once in the field and once at study headquarters, Bandung), transferred to 80 column IBM cards, and analysed on an IBM 370 computer. Standard diagnostic criteria for xerophthalmia were employed, and all corneal lesions were drawn and photographed.

RESULTS

Incidence

To minimise the influence of seasonal variations, calculation of annual incidence was based on data from the 12-month period covered by rounds 2 to 5 (July, 1977—June, 1978), inclusive, of the longitudinal study. 16 study children had active xerophthalmic corneal disease (X2/X35) during this period (table 1). Incidence was calculated in two ways. A
Vitamin A Deficiency and Blindness

63,000 new cases of corneal ulceration in Indonesia annually.

500,000 new cases of corneal ulceration each year in Asia.

One 2 cent capsule, twice a year, would prevent it.
Vitamin A Deficiency and Blindness?

No One Cared!
Xerophthalmia and Risk of Death

1. XN, XB
   Non X
   Alive
   Alive

2. II
   Alive
   Alive

3. III
   Alive
   Alive

6. VI
   Alive
   Alive

7. 
   Alive
   Alive
INCREASED MORTALITY IN CHILDREN WITH MILD VITAMIN A DEFICIENCY

ALFRED SOMMER
GUSTI HUSSAINI
IGNATIUS TARWOTJO
DJOKO SUSANTO

International Center, Dana Center for Preventive Ophthalmology of the Wilmer Ophthalmologic Institute and Johns Hopkins School of Hygiene and Public Health, Baltimore, Maryland; Indonesian Nutritional Blindness Prevention Project, Bandung, Indonesia; and Helen Keller International, New York, USA

Summary
An average of 3481 preschool-age rural Indonesian children were re-examined every 3 months for 18 months. The mortality rate among children with mild xerophthalmia (night blindness and/or Bitot's spots) was on average 4 times the rate, and in some age groups 8 to 12 times the rate, among children without xerophthalmia. Mortality increased, almost linearly, with the severity of mild xerophthalmia (night blindness, Bitot's spots, and the two combined). These relations persisted after stratification for respiratory disease, wasting, gastroenteritis, pedal oedema, and childhood exanthems. Mild vitamin A deficiency was directly associated with at least 16% of all probably several times greater. However, the overall proportion of childhood deaths associated with severe xerophthalmia is small, and their excessive mortality is commonly attributed to the severity of concurrent illnesses responsible for high childhood mortality in general (eg, protein-energy malnutrition, diarrhoea, respiratory infections, and childhood exanthems).

In contrast to severe vitamin A deficiency, mild vitamin A deficiency and xerophthalmia (night blindness and Bitot's spots) occur in a substantial proportion of children, many of whom appear to be otherwise healthy and well nourished. The present study demonstrates that even mild xerophthalmia is associated with a marked increase in mortality.

Background and Methods
The organisation of this study has been described elsewhere. In summary, a prospective, longitudinal study of 4600 children aged up to 6 years at entry was conducted in 6 rural villages of Purwakarta District, West Java, Indonesia, between March, 1977, and December, 1978. The six villages were mapped and a census was taken, and all families with at least one child below 7 years of age were enrolled.
ACEH

- 450 villages
- 22,000 children
- capsule versus no capsule
IMPACT OF VITAMIN A SUPPLEMENTATION ON CHILDHOOD MORTALITY
A Randomised Controlled Community Trial

ALFRED SOMMER  IGNATIUS TARBOTJO
EDI DJUNAEDI  KEITH P. WEST, JR
A. A. LOEDEN  ROBERT TILDEN
LISA MELE
AND THE ACEH STUDY GROUP

International Center for Epidemiologic and Preventive
Ophthalmology, Dana Center of the Wilmer Institute and School of
Public Health, Johns Hopkins University, Baltimore, Maryland;
Directorate of Nutrition and National Center for Health
Research and Development, Ministry of Health, Government of
Indonesia; and Helen Keller International, New York, USA

Summary  450 villages in northern Sumatra were
randomly assigned to either participate in a
vitamin A supplementation scheme (n = 229) or serve for 1
year as a control (n = 221). 25 939 preschool children were
examined at baseline and again 11 to 13 months later.
Capsules containing 200 000 IU vitamin A were distributed
to preschool children aged over 1 year by local volunteers 1 to
3 months after baseline enumeration and again 6 months
later. Among children aged 12–71 months at baseline,
mortality in control villages (75/10 231, 7.3 per 1000) was
49% greater than in those where supplements were given
(53/10 919, 4.9 per 1000) (p<0.05). The impact of vitamin A
supplementation seemed to be greater in boys than in girls.
These results support earlier observations linking mild
vitamin A deficiency to increased mortality and suggest that

All members of the two study teams, each consisting of an
ophthalmologist (team leader), a nurse, an anthropometrist, a
dietary interviewer, five enumerators, and a driver, all fluent in
the local dialect received a month’s classroom, hospital, and field
training. The enumerators, responsible for collecting demographic
data, were unaware that mortality was a research question.
Standardisation exercises were done before and regularly throughout the
study. First, each village was visited to identify households
containing children aged 0–5 years and to mark their dwellings.
Within 2 days the village was visited by the full team. Enumerators
visited every house containing preschool children, collected
socioeconomic, demographic, and medical data, and rounded up
children at a central point for their clinical examination. Dates of
birth were ascertained by reference to local events charted on the
Muslim calendar and then translated to their roman equivalent by
the use of a specially prepared conversion table. Eyes were
examined with a focused light and 2X loupes and diagnoses were
made according to standard diagnostic criteria.5,6 Parents
were carefully questioned about the presence of nightblindness.5,7 They
were also asked about a history of diarrhoea (4 or more loose, watery
stools per day), of fever or cough lasting at least 24 h in the previous
7 days, and of “ever having” measles.

Recumbent length (if less than 24 months old) or standing height
(if 24 months or older) to the nearest 0.1 cm, and weight (using a
calibrated Salter scale) to the nearest 0.1 kg, were measured on a
10% subsample of all study children.

All children with active xerophthalmia at baseline examination
received at least one large dose of vitamin A and were referred to the
local health unit. They were excluded from the analyses of
subsequent morbidity and mortality. All children received vitamin
A at the follow-up examination 9–13 months later.

Teams first visited villages between September, 1982, and
August, 1983, and follow-up visits were made by the same team in
the same year—9 to 12 months later. The mortality in follow-up
FETT’ S LAW OF THE LAB:
Never replicate a successful experiment.
NNIPS - Nepal

Mortality Rate Per 1000 Child - Years

Four - Month Trial Intervals

RR = 0.73  RR = 0.67  RR = 0.70  RR = 0.74  RR = 0.82  RR = 1.03

Vitamin A to: Placebo + Rx group
<table>
<thead>
<tr>
<th>Study</th>
<th>Measles</th>
<th>Diarrhea</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamil Nadu</td>
<td>0.58</td>
<td>0.48</td>
<td>0.67</td>
</tr>
<tr>
<td>NNIPS</td>
<td>0.24</td>
<td>0.61</td>
<td>1.00</td>
</tr>
<tr>
<td>Jumla</td>
<td>0.67</td>
<td>0.65</td>
<td>0.95</td>
</tr>
<tr>
<td>Ghana</td>
<td>0.82</td>
<td>0.66</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Post-Measles Ulcers
n = 48
Corneal ulceration, measles, and childhood blindness in Tanzania

ALLEN FOSTER¹ and ALFRED SOMMER²

From the ¹Eye Department, Mvumi Hospital, Dodoma, Tanzania, and the ²ICEPO, Dana Centre for Preventive Ophthalmology, Johns Hopkins Medical Institution, Baltimore, USA

SUMMARY One hundred and thirty Tanzanian children with corneal ulceration were clinically examined to determine the cause of the ulceration. 37% of the ulcers were associated with recent measles infection and 38% of the children had bilateral ulceration. Herpes simplex virus infection was the commonest cause of ulceration in the series, but vitamin A deficiency was the major cause of bilateral ulceration, subsequent blindness, and mortality in this series. Other significant causes of childhood corneal ulceration were the use of traditional eye medicines, confluent measles keratitis, and ophthalmia neonatorum. We discuss the various mechanisms by which measles causes corneal ulceration, and the priorities in prevention and management of corneal ulceration in African children.
<table>
<thead>
<tr>
<th></th>
<th>Routine Therapy</th>
<th>Vitamin A (200,000 IU x 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>0 - 6 Years Old</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>12/ 92</td>
<td>6/ 88</td>
</tr>
<tr>
<td>Mortality</td>
<td>13.0%</td>
<td>6.8%</td>
</tr>
<tr>
<td><strong>RR</strong></td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>
Research from the South

Vitamin A supplements and mortality related to measles: a randomised clinical trial

ANDREW J G BARCLAY, ALLEN FOSTER, ALFRED SOMMER

Abstract
One hundred and eighty children admitted with measles were randomly allocated to receive routine treatment alone or with additional large doses of vitamin A (200 000 IU orally immediately and again the next day). Baseline characteristics of the two groups were virtually identical for age, severity of measles, and vitamin A and general nutritional states. In 91% of the children serum vitamin A concentrations were less than 0·56 μmol/l. Of the 88 subjects given vitamin A supplements, six (7%) died; of the 92 controls, 12 (13%) died (p=0·13). This difference in mortality was most obvious for children aged under 2 years (one death out of 46 children receiving supplements versus seven deaths out of 42 controls; p<0·05) and for cases complicated by croup or laryngotracheobronchitis. Mortality was several times higher in malnourished children to less than those observed in non-infected malnourished children. Measles probably increases utilisation of vitamin A, and children with marginal liver stores of the vitamin may thus develop acute vitamin A deficiency, resulting in eye damage and possibly increased mortality from respiratory and diarrhoeal causes. Indeed, measles is an important risk factor in the development of severe vitamin A deficiency and xerophthalmia in Asia. It is also a particularly virulent disease among African children, accounting for most cases of childhood blindness and for considerable mortality. Recent data suggest that vitamin A deficiency may be prevalent in areas of Africa, including Tanzania.

This hospital based study sought to determine the effect of high dose vitamin A supplements taken during early infection with measles on subsequent mortality in African children.

Introduction
Recent reports from Indonesia have shown that children with clinically mild vitamin A deficiency have a fourfold increase in mortality from all causes and a threefold increase in the incidence of respiratory and diarrhoeal diseases. Vitamin A supplements nourished children to less than those observed in non-infected malnourished children. Measles probably increases utilisation of vitamin A, and children with marginal liver stores of the vitamin may thus develop acute vitamin A deficiency, resulting in eye damage and possibly increased mortality from respiratory and diarrhoeal causes. Indeed, measles is an important risk factor in the development of severe vitamin A deficiency and xerophthalmia in Asia. It is also a particularly virulent disease among African children, accounting for most cases of childhood blindness and for considerable mortality. Recent data suggest that vitamin A deficiency may be prevalent in areas of Africa, including Tanzania.

This hospital based study sought to determine the effect of high dose vitamin A supplements taken during early infection with measles on subsequent mortality in African children.

Patients and methods
Mvumi Hospital is a rural general hospital in central Tanzania related to the church. Paediatric patients are drawn almost entirely from the local population, which comprises subsistence farmers living in a fairly arid environment. The staple diet is millet eaten with a green vegetable relish.

There is only one harvest a year, in April to May, and that is dependent on good rains. The rains in 1982 were very bad, leaving conditions of near
USE DATA TO SET POLICY

Research is like peeling an onion. You’re ignorant at the start, you take off more layers, and you find it more and more concentrated; a denser and denser node of ignorance. And all the time you’re weeping about how much it costs to get there.

FRANCIS D. MOORE
Bellagio Meeting on Vitamin A Deficiency & Childhood Mortality

Proceedings of—

“Public Health Significance of Vitamin A Deficiency and Its Control”
Bellagio Study and Conference Center of the Rockefeller Foundation
February 3 – 7, 1992
JOINT WHO/UNICEF STATEMENT

EXPANDED PROGRAMME ON IMMUNIZATION

PROGRAMME FOR THE PREVENTION OF BLINDNESS

NUTRITION PROGRAMME

VITAMIN A FOR MEASLES
Countries categorized by degree of public health importance of vitamin A deficiency

The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city, or area of its authority, or concerning the determination of its frontiers or boundaries. Dotted lines represent approximate border lines for which there may not yet be full agreement.
### Vitamin A Deficiency Disorders

**VADD**

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimated Number</th>
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<tbody>
<tr>
<td>Children:</td>
<td>~150 - 200 million</td>
</tr>
<tr>
<td><strong>Xerophthalmia:</strong></td>
<td></td>
</tr>
<tr>
<td><em>children</em></td>
<td>~3 million</td>
</tr>
<tr>
<td><em>pregnant women</em></td>
<td>~3 million</td>
</tr>
<tr>
<td><strong>Blindness:</strong></td>
<td>~1/2 million/ year</td>
</tr>
<tr>
<td>Preventable deaths:</td>
<td>~1 - 2.5 million/ year</td>
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</tbody>
</table>
## Cost-Effectiveness

<table>
<thead>
<tr>
<th>Public Health Intervention</th>
<th>$ per Death Averted</th>
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<tbody>
<tr>
<td>Vitamin A Px</td>
<td>$23</td>
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<tr>
<td>TB</td>
<td>$50</td>
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<tr>
<td>Malaria Chemo Px</td>
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<tr>
<td>Bed nets</td>
<td>$188</td>
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<tr>
<td>Measles immunization</td>
<td>$243</td>
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<tr>
<td>ORT</td>
<td>$3,835</td>
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</tbody>
</table>
“Life is either a daring adventure, or nothing at all.”

Helen Keller