Applied Research on Child Health Project
Harvard Institute for International Development
Harvard University

In collaboration with
The New England Medical Center
Gorgas Memorial Institute, University of Alabama

Funding from
United States Agency for International Development
Highlighted are some of the countries in which the ARCH Project is conducting and plans to conduct research activities.
The Applied Research on Child Health Project

Annual Report 1998

Harvard Institute for International Development
In collaboration with
The New England Medical Center
and
Gorgas Memorial Institute, University of Alabama
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This report summarizes the ARCH Project activities for the year ending December 31, 1998.

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Executive Summary

Mission Statement

The Applied Research on Child Health (ARCH) Project at the Harvard Institute for International Development (HIID), Harvard University, along with its collaborators at the New England Medical Center and the Gorgas Memorial Institute, University of Alabama, seek to reduce the global burden of mortality and morbidity from common childhood illnesses. To accomplish this, we support clinical and behavioral applied research on high priority, child health research questions. Using a small grants program that fosters international collaboration, and research and policy advising skill development, the ARCH Project builds long-standing research collaborations between U.S. research universities, and developing country research institutions. It also fosters an environment for greater communication and interaction among the researchers and research institutions within developing countries, so-called South – South collaboration. The ARCH Project focuses on producing program and policy relevant research that can more easily be presented to government program and policy personnel and facilitates greater utilization of research results. The ARCH Project is a component of the USAID Global Bureau, Center for Population Health and Nutrition, Office of Health and Nutrition’s Child Health Research Project. The Project has evolved from the Applied Diarrheal Diseases Research (ADDR) Project, which operated from 1985-1996.

Goals

The ARCH Project has three primary goals:

- To use applied research to improve existing child survival approaches and technologies;

- To identify, develop, and test new cost-effective interventions to improve child health and facilitate their incorporation into health policies and programs; and

- To broaden, strengthen, and sustain global and national capacity to conduct high quality, policy-relevant research by improving the research skills of selected scientists and institutions from the developing world.
Scientific Focus

The ARCH Project is currently organized around five scientific themes and six special initiatives:

Scientific themes:
- Studies to improve case management of acute respiratory infections (ARI Portfolio);
- Studies on zinc nutriture and its relationship to child health (Micronutrient portfolio);
- Intervention research to change professional and consumer practices, particularly concerning the appropriate use of medicines (Drug portfolio);
- Intervention research to change household behaviors to improve child health (Household portfolio);
- Community-based research in support of the Global Eradication Initiative to identify factors underlying participation in routine immunization, supplemental immunization and surveillance activities. This research will form the bases for intervention research to increase participation in these activities (Polio portfolio).

Special Initiatives:
- Innovative research fund to support research opportunities not related to the core scientific themes above (El Niño and diarrheal epidemiology, for example)
- Malaria Initiative in Zambia;
- Support for the USAID Infectious Disease Initiative with a focus on antimicrobial resistance; and improving the professional and consumer use of antibiotics and antimalarials;
- Country-specific research activities (El Salvador and Zambia);
- Research on strengthening linkages between health research and policies or programs;
- Research on health research capacity strengthening;

This Annual Report will describe the research rationale and focus for each of the themes and special initiatives, and highlight the current research activities.

Research Outputs

By the end of 1998, the ARCH Project has made funding commitments to 33 research studies in 18 countries. The total value of the research monies committed is approximately $1,078,720. An additional $678,000 has been allocated for country specific and special initiative activities. The research network consists of over 75 researchers from 35 institutions. These researchers are added to the ADDR Project network of over 400 researchers from eighteen countries that connect the ARCH Project to an extensive and highly valuable network of developing country researchers from many of the premier research institutions in the developing countries. This network is invaluable for disseminating research results, for getting input into research priority setting exercises, and for identifying scientists and institutions for future research collaborations.
Collaborations

The ARCH Project has extensive collaborations with a number of multilateral institutions, other U.S.-based institutions working on child health research, and the network of host country institutions. In the ARI portfolio, we work closely with the World Health Organization/Department of Child and Adolescent Health and Development (formerly WHO/CHD). The Drug portfolio is a joint initiative in a consortium consisting of ARCH Project, WHO Drug Action Programme (DAP), International Network for the Rational Use of Drugs (INRUD), and the Rational Pharmaceutical Management (RPM) Project. The Polio portfolio has developed collaborative relationships with WHO, UNICEF, Rotary International, local USAID missions and other partners in the Global Polio Eradication Initiative (PEI). The Zinc portfolio studies are connected to a larger, loosely coordinated program on zinc research involving Johns Hopkins University and the ICCDR,B from the CHR consortium. The household research is focused largely around issues arising from the implementation of the Integrated Management of Childhood Illness (IMCI) approach and communicates with the ongoing IMCI research activities of WHO, UNICEF, and the BASICS Project. We expect to continue, deepen, and expand our research collaborations in the coming years.

Conclusion

The past year has provided us the chance to make our research portfolios fully operational and award most of our available research funds. The coming year will be focused largely on data collection, with some early analysis and dissemination. Published results from some earlier research awards (ADDR Project related) continue to emerge and efforts to improve health programs and policies continue. We have initiated a major new effort to support the malaria control program in Zambia and establish an applied research agenda to complement the program.

The researchers with whom we have the privilege to work have exhibited a profound commitment to addressing high priority issues that directly affect child survival. The opportunity to develop the ARCH Project research network, which includes several of the research teams from the ADDR Project initiatives but brings in many new colleagues, has been both a challenge and a pleasure. The success of the ARCH Project depends on the creativity, hard work, and perseverance, amidst difficult conditions, of the researchers themselves. Along with the children and their families who enroll in the research studies, the researchers are central to global efforts to reduce childhood mortality and morbidity. With deep respect for their efforts, we present the 1998 ARCH Project Annual Report.
ARCH Project Research Portfolios
Acute Respiratory Infections (ARI)

Background

Acute respiratory infections (ARI) account for a large number of childhood deaths in developing countries, often exceeding the mortality due to watery diarrhea and dysentery. Recognition of ARI as an important target for child survival programs over the past decade has prompted the development and implementation of management guidelines which are based on a diagnostic algorithm and treatment plan that includes the use of antimicrobial agents early in the course of presumed pneumonia. This approach has reduced case fatality rates markedly for the children that are able to access and afford appropriate antibiotics prescribed in a timely fashion. The benefit of decreased ARI mortality realized from the widespread application of these guidelines has been partially offset by the potential hazard caused by the more widespread use of antimicrobials. There is concern that this may result in the selection, amplification, and spread of antibiotic-resistant pathogens, as well as a higher rate of adverse drug reactions in children treated with antimicrobials that may not be necessary in every case of ARI.

The ARCH Project has therefore focused a significant part of its resources on ARI for a clinical research program designed to address these concerns. The initial focus has been on the improvement of the WHO/UNICEF IMCI algorithm and management guidelines for pneumonia. This research stream is being pursued in close collaboration with the Department of Child and Adolescent Health and Development, (formerly Child Health and Development, CHD) division at WHO.

The intent of this research portfolio is to develop a series of clinical research projects which will help refine the globally recommended treatment algorithms in order to reduce both morbidity and mortality due to ARI and to minimize the development of antimicrobial resistance through more judicious use of antibiotics. Each of the three degrees of ARI acuity—non-severe (simple), severe and very severe disease—has been or will be addressed by this portfolio.
I - New ARI Management Algorithm (NARIMA) Proposal Development Workshop

The first proposal development workshop was held during July 1997 in Canberra, Australia and produced two multi-center research protocols, NARIMA I and II. This was followed by a second protocol development workshop in Durban, South Africa in May 1998 from which another multicenter protocol was developed (APPIS) and is currently being implemented across 9 countries. The third protocol development workshop is scheduled for spring, 1999 and will result in an international efficacy protocol comparing standard treatments of very severe pneumonia.

Table 1: A Multi-Center Prospective Observational Study of Clinical Outcome Following Amoxicillin Treatment of Non-Severe Acute Respiratory Infection (NARIMA I)

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<th>COUNTRY</th>
<th>PRINCIPAL INVESTIGATOR</th>
<th>INSTITUTION</th>
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<tr>
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<tr>
<td>Viet Nam</td>
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<td>Pediatric Hospital #1, Ho Chi Minh City</td>
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July 12-17, 1997, Canberra, Australia

In collaboration with WHO/CHD

The objective of the first workshop was to design a study to determine the necessity of antibiotic therapy in the treatment of mild pneumonia in children as defined by the WHO/IMCI diagnostic algorithm. This condition, also termed non-severe or simple pneumonia, is based on the presence of an elevated respiratory rate, lower chest indrawing, and the absence of clinical signs (danger signs) of very severe disease. The premise of the workshop was that the current algorithm was highly sensitive but not specific enough to distinguish between children whose respiratory symptoms resulted from bacterial infection from those without a bacterial etiology. Because this category of pneumonia accounts for 85-90% of all cases seen, application of these guidelines may be a major contributor to the overuse of antibiotics and the resultant emergence of antimicrobial resistance. This workshop produced two multicenter research proposals (described below) which are designed to systematically investigate the validity of the current approach and to identify risk factors for, and frequency of, complications resulting from a change in the antibiotic use recommendations.

The objective of the initial protocol (NARIMA I) is to determine the clinical failure rate of children with non-severe pneumonia who are treated with oral
amoxicillin according to the WHO/IMCI algorithm. In order to do this however, the definition of treatment failure used in prior studies of ARI treatment efficacy, which is the absence of respiratory improvement at 48-72 hours of therapy, will need to be redefined. This definition of treatment failure does not account for bronchiolitis, commonly due to Respiratory Syncytial Virus (RSV). The symptoms for this frequent cause of respiratory disease often persist well beyond 48-72 hours, especially if the clinical presentation includes an episode of wheezing in a child who has never experienced this symptom. Therefore, the workshop redefined clinical failure at these early time points as progression of clinical manifestations, including an increase in respiratory rate or the development of lower chest wall indrawing or other signs of deterioration.

Considerable scientific evidence is required to support a change in the WHO recommendation especially removing the use of antimicrobials in mild pneumonia. It is therefore necessary to conduct the most rigorous kind of clinical study; a randomized placebo controlled clinical trial comparing usual supportive therapy with and without an effective antibiotic. However, before such a trial can be mounted, preliminary information on the frequency of failure of standard therapy at the study sites will need to be collected with the initial observational study. The observational study will be a four-site (India, Peru, South Africa, Vietnam) examination of the failure rate (as defined above) of standard amoxicillin therapy at 48-72 hours among children fulfilling the WHO criteria for non-severe pneumonia. Included in this study will be a determination of the prevalence of RSV infection in these children, and an assessment of clinical parameters that will allow us to identify clinical risk factors that may predict clinical worsening.

The objective of the second protocol (NARIMA II) is to compare the outcome of non-severe pneumonia in the presence or absence of acute wheezing, treated according to the WHO algorithm with or without the use of amoxicillin by means of a randomized, placebo-controlled clinical equivalence trial. This study has been designed to determine if antibiotics provide any benefit in the treatment of non-severe pneumonia beyond that provided by the standard supportive therapy. It will be hospital-based in order to ensure that regular and frequent clinical observations are made in order to permit intervention with antimicrobials in the event that the child does not respond to the protocol regimen. In order to determine the number of children necessary to include in this equivalence trial, a good estimate of the clinical failure rate of amoxicillin therapy in this setting is required, and will be generated by the observational study mentioned above. ARI research proposal one and two are inter-related investigations focused on the same questions, and targeted to the same goal.
Table 2: A Randomised Double-blind Trial of Amoxicillin Compared with Placebo for Treatment of Non-severe Acute Respiratory Tract Infection. (NARIMA II)

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July 12-17, 1997, Canberra, Australia

In collaboration with WHO/CHD

**A - Accomplishments to Date:**

**NARIMA I**

The first study has passed the ARCH/WHO external scientific and Institutional Human Subjects Reviews, funding is in place and enrollment has begun at three of the four sites (Peru, Vietnam and South Africa). The fourth site, India did not receive institutional approval from the Indian Council for Medical Research and will not be implemented. Patient accrual will thus have to be extended at the remaining three sites to achieve the necessary sample size.

**NARIMA II**

Implementation of the second study is dependent on the results which will be available from NARIMA I. The protocol for NARIMA II has been written and will be submitted for approval once the results of NARIMA I are available and it is clear that sample size considerations can be met. All of the sites that participated in the protocol development workshop will participate in the implementation of the NARIMA II study, including the sites that are currently implementing NARIMA I.
B - Goals for 1999-2000

It is expected that patient enrollment will continue throughout the summer for the NARIMA I study but accrual at the remaining three sites will need to be increased somewhat from 100 to 134 each because of the withdrawal of the India site. It is expected that this will cause only a minor delay and the results needed to calculate adequate sample size and mount NARIMA II will be available by Fall, 1999. We anticipate that NARIMA II will be finished with the approval and funding process and ready for implementation by winter, 2000.

II - Amoxycillin Penicillin Pneumonia International Study Proposal (APPIS) Workshop

Table 3: A Multi-Center Randomized Controlled Study, Comparing the Use of Oral Amoxycillin versus Injectable Penicillin in the Treatment of Severe Pneumonia in Children

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May 3-10, 1998, Durban, South Africa
In collaboration with WHO/CHD

The objective of this workshop, held during May 1998 in Durban was to design a protocol to compare the efficacy of an oral regimen of amoxycillin with injectable penicillin, the standard treatment of severe pneumonia recommended by the WHO management algorithm for ARI. As with the NARIMA, this project is collaboratively funded and managed by both the ARCH Project and WHO/CAH. The goal of the APPIS protocol is to demonstrate that oral therapy may be safely substituted for parenteral therapy in the treatment of children with this condition. This would allow a new standard for community treatment of severe pneumonia to be established with three important public health consequences. First, it would
provide an acceptable treatment alternative for children with severe pneumonia who cannot be transferred for in-patient therapy at a regional or District Headquarter health facility. Second, non-hospital based management of this condition would be expected to produce significant cost savings compared with hospitalization. Third, it would decrease the exposure risk associated with the use of dirty needles in areas where sterilization procedures are not readily available or maintained.

A - Accomplishments to Date:

This multicenter study is being conducted over three continents, making the results locally applicable as well as globally relevant. The protocol has been approved by a panel of external scientific reviewers, and the Harvard, WHO, and host country institutional review boards. As of January 1, 1999, patient enrollment has begun at the Pakistan site and is expected to begin at all sites by the end of February 1999. Patient accrual will continue for approximately 250 children per site, which is anticipated to be completed in 18 months.

B - Goals for 1999-2000:

This study will accrue patients throughout the 1999-2000 funding period. Once data entry has been established at each site (projected March 1999), cleaned and verified data files will be sent on a regular basis to the Data Coordinating Center located within the ARCH Project offices from which patient accrual and interim progress reports will be generated. These reports will be used to provide study sites with information about data accuracy and consistency, patient accrual progress and also for the production of interim efficacy and safety reports to be reviewed by the Data Safety and Monitoring Board (DSMB). We expect to have the first interim efficacy analysis by the DSMB after 500 patients have been enrolled which should occur by Fall 1999.

C - Cost Effectiveness Analysis Of Oral Amoxicillin

A - Background

In addition to establishing whether children with severe pneumonia can be safely and effectively treated with oral medication at the community level, it is important to assess the cost differences for both treatments. A regimen of oral amoxicillin therapy for severe pneumonia, which may be administered as an outpatient, could reduce expenses through the avoidance of costly hospitalization and injectable therapy costs. It would have the added benefit of avoiding the costs associated with nosocomial infections and transmission of diseases through the use of contaminated needles.
It is therefore of interest to assess at least two aspects of the treatment of children with pneumonia simultaneously within this clinical trial. First, to compare the clinical consequences of the use of oral treatment with those observed using injectable therapy. Second, to determine the total costs of treating an episode of severe disease with each approach.

Outcomes Measurement

Ideally, effectiveness data should be used as the source of clinical evidence regarding the impact of oral amoxycillin vs. injectable penicillin for the treatment of severe pneumonia in children. Because this type of data is not available, we accept that it will be necessary to extrapolate from trial efficacy data to estimate utilization effectiveness.

The main objective of the APPIS trial is to determine if the percent of children that improve after 48 hours of treatment is the same in both groups. It is also of interest to compare the percent of children that improve by day 5 of treatment, and are cured by day 14. Therefore, the primary outcomes of interest are:

- number of pneumonia cases improved at 48 hours and 5 days of treatment
- number of cases cured at 14 days
- number of deaths avoided
- number of adverse events avoided
- number of treatment failures avoided

Cost Comparison between Oral Amoxycillin vs. Injectable Penicillin

The main purpose of the study will be to compare the overall costs of oral amoxycillin vs. injectable penicillin. As both therapeutic approaches are hospital-based and the expected length of stay is the same, it is expected that differences in costs for each therapy will arise mainly from cost difference between oral and parenteral therapy during the first 48 hours of hospitalization. We also will measure costs associated with complications of parenteral therapy use, and from possible differences in adverse drug events. A secondary objective of the study will be to identify the non-drug-related costs of management of severe pneumonia in children. For this purpose, we have determined three main stages in the clinical management of severe pneumonia with their respective resource categories. Protocol driven costs will be excluded.

Limitations

The major limitations of the cost effectiveness and cost identification study are the following:

- We can expect higher compliance rates since patients will be closely followed
- It is likely that the study will detect adverse events that would otherwise have gone undetected
- Economic results are highly dependent upon the setting in which care is being delivered.
In Colombia, for example, severe pneumonia in children is also managed in first and second level hospitals; therefore, the results obtained at Hospital San Ignacio might not reflect the costs of other settings of care.

These issues will be addressed by testing the assumptions of the study through sensitivity analysis.

**B - Accomplishments to Date:**

This study will be conducted in conjunction with the APPIS study at the India, Colombia, Mexico, and two South African sites (Durban and Cape Town). A research protocol has been written and case report forms are being prepared.

**C - Goals for 1999-2000:**

It is expected that data collection will begin shortly after actual patient enrollment begins at each of the APPIS sites participating in this study. Patient accrual will continue for the duration of the APPIS study and be completed after 18 months. Data analysis will begin immediately upon completion and a data analysis workshop will be held with all the research teams.
III - Multi Center Study of Optimal Treatment of Very Severe Pneumonia in Children

STUDY PROPOSAL AND WORKSHOP

Date: April 1999
Location: To be determined
Organizer Sponsors: ARCH Project/WHO/CAH
Participants: To be determined

The objective of this workshop will be to develop a clinical efficacy study protocol comparing the combination of penicillin plus gentamicin with chloramphenicol for the treatment of very severe pneumonia in children.

Many children assessed as having very severe pneumonia may in fact also have or develop bacterial meningitis or septicemia, and data have shown that, in the presence of antimicrobial resistance, a number of these children may not respond to injectable chloramphenicol. Although there is evidence that H. influenzae and S. pneumoniae are the common bacterial organisms causing bacterial meningitis and pneumonia, there is limited data on the actual etiology of patients categorized as having very severe pneumonia. Some data suggest that other bacteria may also be responsible for very severe pneumonia and that those bacteria may be less susceptible to chloramphenicol. Many pediatricians do not believe chloramphenicol is the right treatment for these very severely ill children and use a combination of penicillin and gentamicin instead.

Because there is very little scientific data to support either choice, we believe research is needed to:

- Identify the bacterial etiology of very severe pneumonia and document antimicrobial resistance patterns
- Compare the clinical efficacy of injectable chloramphenicol with that of injectable penicillin plus gentamicin for very severe pneumonia cases in children less than five-years-old

It is intended that this would be a randomized, controlled efficacy study of very severe pneumonia cases among 2-59 months old children. One group will be randomized to injectable chloramphenicol for 7 days and the other group will be randomized to a combination therapy of injectable penicillin and gentamicin for 7 days. Pre-treatment blood cultures will be obtained to document the etiology and susceptibility patterns. Nasopharyngeal swabs will be obtained to document carriage and resistance rates in children with very severe pneumonia.

As with NARIMA and APPIS studies, this study will be designed as multicenter and international in scope to achieve the greatest generalizability of the findings.
is hoped that this study will lead to the development of revised recommendations for the management of children with very severe pneumonia, to be included in the IMCI case management guidelines, and will result in more appropriate antimicrobial use at the referral level facilities.

A request for comments on the importance of such a study has been circulated among ARI opinion leaders who have indicated near unanimous approval for the timeliness and relevance of such a study.

**IV - Multi-Center Study on Antibiotic Resistance of Streptococcus Pneumoniae - Caribe Study**

The ARCH Project is collaborating with WHO/CAH and the Pan American Health Organization (PAHO) in a multicenter study on antibiotic resistance of *Streptococcus pneumoniae* isolated from children with severe pneumonia. ARCH Project is supporting the Peru site for this collaborative project. Other participating sites and funded by the WHO or PAHO are: Brazil, Colombia, Argentina and the Dominican Republic.

Antimicrobial drug resistance, a global problem, is well documented in several countries where increasing levels in both community-acquired and nosocomial infections have led infectious disease experts to declare the situation a crisis that could lead to a post-antibiotic era. Although less well-documented, the detection of significant levels of antimicrobial drug resistance is increasing in Latin America where over 25% of strains of *S. pneumoniae* have diminished susceptibility to penicillin in some selected countries.

The strategy set forth by WHO and PAHO to reduce the burden caused by ARI among children under five years of age, based on standard IMCI case-management, has saved lives but contributed to the emergence of antimicrobial resistance, and made the choice of empiric therapy for pulmonary infections more difficult. Surveillance data have shown a 10-26% reduction of streptococcus in the susceptibility to penicillin. With the emergence and spread of the drug-resistant strains of *S. pneumoniae* and *H. influenzae*, treatment options for invasive bacterial disease may become considerably more limited.

Controversy exists, however, about the clinical relevance of *in vitro* resistance. No prospective study has been conducted to evaluate the impact of drug-resistant *S. pneumoniae* on the clinical outcome of pneumococcal pneumonia in Latin America.

This multicenter prospective observational study is designed, therefore, to investigate the relationship between *in vitro* penicillin resistance of *S. pneumoniae* and the clinical outcome of current recommended therapy for severe pneumonia as defined by standard ARI case management. In addition, this study will generate data...
to guide ARI therapy policy for the countries of the region, and will strengthen the regional antimicrobial resistance surveillance networks.

**Accomplishments and Goals for 1999-2000:**

This study is in its pilot phase at the Peru site. Enrolment criteria and case report forms have been pilot tested at the Recife and Buenos Aires sites. Patient accrual for the main study is expected to begin within the first several months of 1999. The projected enrolment is 200 children, which will occur over the ensuing 12 months.

**V - Future Strategic Plans for the ARCH Project ARI research portfolio:**

These studies relating to current management issues in ARI are designed to systematically explore the guidelines for the use of antimicrobial agents in ARI in order to sharpen the specificity of treatment and maintain the sensitivity of the recommendations. We believe that a change in the treatment recommendations contained in the WHO management guidelines for Integrated Management of Childhood Illness (IMCI) could reduce the use of antibiotics for ARI by up to 75%, and that this will substantially decrease pressure on the selection and spread of antibiotic-resistant ARI pathogens. These studies are linked with others in the ARCH Project research portfolios that address the prescribing behavior of practitioners and the expectations of the consumers. The ARCH Project ARI portfolio will continue to expand in areas that will be determined following the completion of the described studies. Subsequent projects will focus on the implementation of new recommendations resulting from the original studies, as well as continued surveillance of issues of importance to child health including the emergence of new respiratory pathogens and clinically important antimicrobial resistance.

**VI - Surveillance of Antibiotic Resistance of Pneumococcal Surface Protein A in South America and Central America**

The ARCH Project at HIID has a subcontract to the Gorgas Memorial Institute at the University of Alabama, Birmingham (UAB). The Gorgas Institute, in turn, is using some of the funds to subcontract to the Pan American Health Organization (PAHO) to provide partial support for a research project entitled, “Surveillance of antibiotic resistance and diversity in pneumococcal surface protein A in South and Latin America”. The goal of this project is the surveillance of antibiotic resistance and documentation of the diversity of PspA in pneumococcal isolates from South and Central America. PspA is a pneumococcal surface protein which has been shown to elicit protection against fatal infection and nasopharyngeal carriage in mice. Although the protein is variable in structure, most PspAs are cross-reactive. The various PspAs
are classified into four major families. It is anticipated that a PspA vaccine for humans would contain representatives of each of the four families.

In order to ensure that a future vaccine would be effective in the region, it is important to learn the diversity of this molecule within disease isolates from this region. It will be especially critical that any anticipated vaccine be able to elicit cross-reactive protection against strains that are multiply resistant to antibiotics. The proposed surveillance will be accomplished by tying the proposed program to an ongoing study supported by the Pan American Health Organization (PAHO). The PAHO surveillance study has been collecting *S. pneumoniae* isolates from invasive disease in children under the age of 5 since 1993. They run a surveillance network that includes over 70 hospitals in 30 cities in Argentina, Brazil, Colombia, Chile, Mexico, and Uruguay. Recently, Cuba and the Dominican Republic have joined the network.

**Accomplishments to date:**

The preliminary tests were recently completed to determine which PCR primer and antisera would be used to determine the clades and family of PspA. In February 1999, a two-week training period will be initiated at UAB for seven Latin and South American scientists (estimated time of two weeks). During the training, each site will be provided with an identical set of reference strains to insure uniformity of typing assignments.

**Goals for 1999-2000**

Typing will begin during the training on a subset of the 2000 isolates already available and will continue at each of the three sites after training. Throughout the study a quality control program will be set up at UAB to which a percentage of all strains will be shipped for comparison typing. In addition, the staff at UAB plan to make at least one trip to the three South American sites after they are set up to help them resolve problems with techniques and to facilitate data collection and data exchange from site to site. The implementation of this quality control program will insure that the data obtained are of maximal value.
Micronutrients

A - Background

Adequate micronutrient nutrirture has been widely recognized as important in normal growth and development in children. It has been shown to have a significant role in determining immunologic competence and resistance to infection. Malnutrition and micronutrient deficiencies are common place complications of childhood diseases. The vitamin A experience has shown that micronutrient supplementation can be a relatively easily implemented intervention to improve child survival.

Zinc is an essential trace element in human nutrition that plays an integral role in the development and function of the immune system, and which is required for normal growth and development in children. Zinc deficiency may have many adverse consequences including growth retardation, hypogonadism, and impaired cell mediated immunity with a consequent increase in the susceptibility of children to diarrheal disease, acute respiratory infections, and possibly malaria.

Field intervention studies in the last decade have evaluated the effect of zinc supplementation on the morbidity due to infectious diseases of young children in developing countries. The largest group of studies looked at the impact of zinc supplementation on morbidity associated with acute diarrhea, and consistently demonstrated a reduction in the duration of diarrhea, with the greatest effects seen in children with underlying malnutrition or biochemical evidence of zinc deficiency. Investigations of zinc supplements for persistent diarrhea also showed reductions in the mean duration of diarrhea.

Experimental studies with mice have shown that zinc deficiency leads to higher levels of malarial parasitemia. A recent study suggests that zinc may have important clinical benefits for children in malaria-endemic regions. This small placebo-controlled study of a twice-weekly zinc supplement in rural Gambia, reported that the supplement appeared to be associated with a trend towards a reduction in the incidence of malaria. In a community-based study in Papua New Guinea, long-term zinc supplementation in children reduced malaria-attributable health center attendance by 30 to 35% in preschool children. These findings suggest a potential role of zinc in the reduction of malaria-related morbidity.

Given the known beneficial effects of zinc on the immune system, and evidence of a therapeutic effect of zinc in acute and persistent diarrhea, the ARCH Project nutrition research portfolio seeks to improve our understanding of some of the potential benefits of zinc and other micronutrients for child health.
The current focus of micronutrient research activities within the ARCH Project is a placebo-controlled study of the use of zinc supplementation as a therapeutic adjuvant in the management of uncomplicated acute malaria in children. Several additional studies on individual or micronutrient cocktails in the treatment or prophylaxis of childhood diseases are being reviewed for funding.

A total of 15 pre-proposals were submitted in response to a request for proposals sent out in September 1997. Pre-proposals were submitted from investigators based in Burkina Faso, Cameroon, Ecuador, Ghana, Indonesia, Pakistan, Tanzania, Uganda and Zambia.

Protocol Development Workshop:

After careful review of the study pre-proposals by the ARCH Project core staff, five research teams were invited to the protocol development workshop held in Mukuno, Uganda from April 27 to May 3, 1998:

Table 4: The Effect of Zinc as an Adjuvant to Standard Therapy for Uncomplicated Plasmodium Falciparum Malaria in Children

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PARTICIPANT</th>
<th>INSTITUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ecuador</td>
<td>Fernando Sempertegui</td>
<td>Corporacion Ecuatoriana De Biotecnologia, Quito</td>
</tr>
<tr>
<td>Ghana</td>
<td>Kojo Yeboah Antwi</td>
<td>Kintampo Health Research Centre, Kintampo</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Zul Premji</td>
<td>Institute of Public Health, Muhimbili U. College of Health Sciences, Dar es Salaam</td>
</tr>
<tr>
<td>Uganda</td>
<td>Freddie Ssengooba</td>
<td>Institute of Public Health, Makerere University, Kampala</td>
</tr>
<tr>
<td>Zambia</td>
<td>Victor Mwanakasale</td>
<td>Tropical Diseases Research Centre, Ndola</td>
</tr>
</tbody>
</table>

April 27-May 3, 1998
Mukuno, Uganda

A common protocol with standardized design, inclusion and exclusion criteria, and clinical endpoints was developed for the five sites. By combining the results from multiple sites, the study is able to demonstrate potentially beneficial effects of zinc as an adjunct to the therapy of malaria. Given the potential differences in the epidemiology and ecology of the disease between the African sites and Ecuador, the study is powered based on the African sites. It will also provide the opportunity to examine the efficacy of the supplement on different subsets of children, such as those with baseline zinc deficiency or malnutrition. Genotyping of P. falciparum strains in children who develop recurrent episodes of malaria during the 28-day follow up period will also be performed to gain insight on the epidemiology of chloroquine-resistant falciparum malaria at the participating sites.
B - Accomplishments to Date:

Pilot studies were completed in late December 1998 and the enrollment of patients will begin in early January 1999 in Tanzania and Uganda. The pilot study began in Ecuador in early January and will start in Ghana and Zambia in early February. If patient enrollment proceeds as planned, the full cohort of 1300 children will have completed the study by the fall of 1999.

C - Goals for 1999-2000:

Patient accrual and follow-up for this 6-month study should be completed by fall of 1999. A data analysis workshop will be convened in late fall 1999 with the generation of a draft manuscript by winter 2000.
Drug Use Intervention

A - BACKGROUND

The International Conference on Improving Use of Medicines (ICIUM), held in Chiang Mai, Thailand in 1997 marked a milestone in international efforts to promote quality use of medicines by health providers and consumers, and to develop appropriate pharmaceutical policies. Through over 120 presentations of previous research and active discussion in small groups, participants identified substantial progress over the last decade in improving the use of medicines in developing countries, developed guidelines for disseminating proven strategies, and highlighted important priority areas for future research.

The overall goal of the post-ICIUM initiative is to increase the capacity for drug use intervention research and to stimulate research projects in the priority areas. The larger the number of well-designed research projects, the greater the overall impact on knowledge about means to improve use of medicines under different circumstances. For the first time, there exists a publicly accessible database of summaries of previous experience in these areas, as well as an agreed agenda of priority policy implementation and intervention research topics. Four organizations (WHO/DAP, INRUD, RPM and ARCH) are collaborating to promote this agenda through individual and joint activities over the next 2-3 years.

The ARCH Project portfolio on drug intervention research is being developed and co-funded with the other sponsors of the ICIUM initiative. In September 1997, submissions were requested for intervention pre-proposals, especially ones on the priority topics of improving drug-prescribing practices in hospital and primary care settings, as well as pharmacies and drug stores. Eighty-eight proposals were submitted in response to this request, an indication of the widespread interest in this area.

The major topics of investigation for which proposals were submitted are summarized below. The first three topics have proposals under review, or research projects underway. The fourth topic, nosocomial infections, will be proposed for funding to the USAID AMR Initiative in 1999. The last topic, household adherence to therapy, is being developed and a call for applications and a proposal development workshop are planned in the future.

1. Improving pharmaceutical use in primary care settings

Inappropriate pharmaceutical use in primary care settings is widespread, and irrational use of antimicrobials – the most widely prescribed class of drugs - is felt to be one of the major forces driving the development of community-acquired antimicrobial resistance. Numerous studies have shown both over-prescribing as well as
inappropriate selection and dosing by health providers, unfettered access to prescription drugs by consumers, and a failure to adhere to clinically desirable treatment regimens. Work presented at the ICIUM suggested promising approaches for improving the use of antibiotics in treating children with diarrhea and ARI in public-sector health facilities. Proposals from several researchers propose to follow up on these promising studies by extending them to other geographic environments; other categories of primary health care workers, including drug sellers; other types of infections; and to private sector health practitioners. In addition, a number of innovative approaches to behavior change were suggested, including group interactions with drug sellers involving community members, or the use of local hospital specialists as influential opinion leaders in educational efforts to facilitate change among primary health care physicians.

2. Improving antimicrobial use in hospitals

Antibiotics are a mainstay of hospital therapy but are by far the most expensive category of drugs in a hospital budget. Although unnecessary use of antibiotics in hospitals appears to be as widespread as in primary care settings, even appropriate use can drive the rapid development of resistance because of the intensity of pressure in a relatively enclosed ecosystem. The consequences of this intense selective pressure can include both treatment failures in community-acquired infections treated in hospitals, as well as dramatic increases in nosocomial infections, especially in high-use environment such as intensive care units or surgical wards. Little research exists from developing countries on how to improve the use of antibiotics in hospital settings. In response to this topic in the call for proposals, a number of proposed studies target nosocomial antibiotic use. The venue of these studies range from teaching hospitals to district hospitals; public to private to mission institutions; neonatal intensive care units to pediatric outpatient departments; and specialists to general medical officers. A number of researchers focus on improving and expanding the role of Pharmacy and Therapeutics Committees (P&T Cs), the mainstay in many developed countries of efforts to improve the quality of prescribing.

3. Improving malaria case management

Despite the importance of malaria as a cause of mortality and morbidity, especially in Africa, we know very little about effective and cost-effective strategies for improving malaria case management. Malaria is typically managed in its early manifestations in the home, often using anti-malarials that are available in drug shops and pharmacies in most malaria endemic countries. Improved case management of severe malaria on hospital wards is one mechanism for reducing rates of child mortality. Ineffective treatment in all these settings increases clinical risk, wastes resources, and promotes the development of resistance. Several proposals from African researchers focus on improving malaria case management. These studies vary widely in focus and include treatment practices in teaching hospitals or district hospitals, guideline compliance and effective dosing; primary care case management in the public and private sector; and household case management practices.
4. Reducing nosocomial infections

Hospitals worldwide are presently confronted with the rapid emergence and spread of multi-resistant microorganisms. In addition, limited resources combined with a poor understanding of how antibiotic-resistant bacteria spread within the hospital environment have resulted in numerous nosocomial outbreaks and the spread of resistant microorganisms from hospitals into the community. The ARCH Project has therefore established a nosocomial infection control research initiative. This effort will have several components:

- establishing infection control committees in hospitals that currently lack them;
- developing systems for monitoring specific infections, antibiotic sensitivities, infection control practices, and antibiotic usage;
- establishing programs and policies to reduce the incidence of infections and limit the use of expensive, broad spectrum antibiotics;
- evaluating the effects of these interventions on the incidence and treatment of common childhood infections.

These initiatives will be coupled with improvements in pre-existing systems for monitoring bacterial resistance, i.e., microbiology laboratory capacity strengthening.

5. Improving household caretakers adherence to therapeutic regimens

Intervention research to identify cost-effective ways to improve household caretaker's adherence with appropriate advice regarding the use of antimicrobials is a high priority for development in the coming year. This work will investigate how to influence the private sector, over-the-counter purchases of medicines as well as propensity to seek prescriptions. The focus research agenda will incorporate ideas presented at the recent IUALTD meeting. It is hoped that a call for proposals will go out in late spring 1999.
B - PROPOSAL DEVELOPMENT WORKSHOPS

After competitive review of 88 submissions to the request for pre-proposals, the 18 highest ranked teams were invited to submit full proposals, either independently or after attending a proposal development workshop. Except for one research team from Mexico, the remaining high priority projects were evenly split between Asia and Africa. For this reason, a decision was made to carry out separate proposal development workshops in the two regions, one in Yogyakarta, Indonesia, and one in Kampala, Uganda.

Additional support for interventions focused on improving antibiotic use was received from the USAID Antimicrobial Resistance Initiative. This has made it possible to expand the first phase of the initiative to include a total of 21 research teams.

1. Asia Regional Workshop

The Asia Regional Proposal Development Workshop was held in Yogyakarta, Indonesia, from April 18-25, 1998 in collaboration with WHO, RPM and INRUD. The workshop was attended by 20 professionals representing ten research teams (three from Philippines, two from Indonesia, two from Thailand, and one each from Nepal, Vietnam, and a team consisting of a Pakistani working collaboratively with a New Zealander). (Please see Table 5 on page 23)

Two projects focus on improving the treatment of acute respiratory infections (ARI) in district hospitals. In Vietnam, the behavior change intervention consists of adaptation of a national guideline for ARI to the local setting by representatives from six hospitals combined with active dissemination of the resulting guideline at each institution. In Indonesia, the research works through Pharmacy and Therapeutics Committees (P&TCs) to disseminate the national ARI guideline to hospital pediatric staff, and sets up a system of regular feedback regarding their adherence to the guideline.

Two interventions in Thailand are also set in hospitals. The research team in one large teaching hospital in Bangkok uses a variety of interactive seminars and printed materials to inform ENT staff about pharmaceutical cost issues, and suggests therapeutically equivalent, lower cost substitutions, while prospectively analyzing the impact of the intervention. Twelve rural Thai hospitals participate in an intervention to strengthen P&TCs by providing a set of tools to improve drug use in specific therapeutic areas. In the experimental stage, six hospitals will target antibiotic prophylaxis in clean surgery, while the other six hospitals focus on treatment of lower respiratory tract infections.
One project in Nepal and one in Indonesia aim to improve practice in public sector primary health care facilities. The team in Nepal will test the impact of interactive group training with and without regular self-monitoring and supervision on treatment of four common primary health care problems in health posts staffed by paramedics. In Indonesia, the intervention consists of small group discussions among medical and paramedical staff at health centers about the national guidelines for treatment of ARI, combined with feedback of data about their own practices in relation to the guidelines.

Two research proposals focus on physicians in the private sector. The research group in Philippines, in collaboration with the Society for Microbiology and Infectious Disease, are testing two strategies alone and in combination for dissemination of new national guidelines for treating urinary tract infection. One strategy involves interactive learning seminars facilitated by opinion leaders, while the other will provide physicians with feedback about their own practice patterns in relation to peers and to the guidelines. The second project from Pakistan tests the impact on knowledge and practice of private physicians of an article in a popular drug bulletin that provides targeted clinical recommendations for managing commonly mistreated health problems.

The final pair of proposals, both from the Philippines, is concerned with improving drug use through innovative small group seminars. One project targets specific problems in advising and dispensing by drug sellers, including inappropriate antibiotic use for respiratory infections, using small group seminars of drug store clerks facilitated by clinical experts and representatives from the Bureau of Food and Drugs of the Department of Health. The final project attempts to increase budget allocations for essential drugs and improve the efficiency of drug purchasing by municipal mayors and village leaders. The intervention will include specially designed materials on the importance of health services and key concepts in efficient drug purchasing, an interactive seminar for mayors with local health officials to introduce these materials, and supportive services and reinforcement during the process of drug procurement.

2. Africa Regional Workshop

The Africa Regional workshop was held from September 14-23, in Kampala, Uganda. Nineteen professionals representing ten research teams (three teams from Uganda, two each from Kenya and Tanzania, and one each from South Africa, Ghana, and Zambia) participated in the 10-day workshop. The studies under development include the following: (Please see Table 6 on page 24)

Two proposals focus on improving drug prescribing in teaching hospitals. One study in South Africa will focus on the ordering of restricted antibiotics for inpatient care. In the teaching hospital at the University of Ghana, senior consultants will be actively engaged in the process of improving prescribing by their junior residents and house staff. After reviewing pneumonia case management guidelines and agreeing on acceptable criteria, consultants receive audit reports every two months summarizing
prescribing indicators for each six-month rotation of house staff; the intervention will continue for four staff rotations.

Two studies in Kenya will also focus on hospital care. One project combines development of P&TCs in mission hospitals where they do not exist with a targeted educational intervention aimed at improving outpatient treatment of ARI and malaria. The second Kenya intervention targets quality of care for inpatients with pneumonia in both government and mission hospitals. A detailed audit tool will be used to collect data on the quality of treatment decisions made throughout the course of inpatient care, examining therapy at admission, as well as response to subsequent laboratory and clinical data. These audits are carried out by existing P&TCs, and coupled with an in-service education program targeting improved decision-making in areas of identified divergence from national clinical guidelines.

One study from Uganda will examine the impact of decentralization of health services on patient access to government services (measured as utilization rates of outpatient, MCH, and inpatient services), availability of key drugs, and prescribing practices for malaria and ARI.

Private sector prescribing is the focus of a second project from Uganda. In collaboration with the Uganda Medical Association, the research team conducts targeted educational sessions for private physicians on malaria, respiratory infections, and diarrhea. Impacts are measured both through physician interviews of knowledge about treatment conducted under the guide of a medical student project, and through visits to these physicians by simulated patients.

Two studies carry out interventions to improve the quality of service in pharmacies and drug shops. Both projects use small group training of counter attendants and supportive materials for customers (such as posters) as the mode of intervention, and measure effects using simulated customers. In Uganda, the focus for the work will be improving referral, dispensing, and advising for ARI, while in Tanzania, the focus will be both ARI and malaria treatment.

The final pair of studies in the workshop are concerned with the inappropriate treatment of young children with malaria in the community, and specifically, with non-adherence to the national treatment regimen with respect to drug selection, dosing. These projects will first conduct a formative phase to identify the prevalence and reasons for inappropriate treatment at the household level, available drug outlets (public and private) in the study communities, and the knowledge and treatment practices of personnel working in these outlets. The intervention phase will combine a treatment aid in the form of a card indicating correct dosing and regimen for children of different ages, active education of dispensing personnel, and community education programs for community members.
### Table 5: Drug Use Intervention

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PRINCIPAL INVESTIGATOR</th>
<th>INSTITUTION</th>
<th>TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vietnam</td>
<td>Pham Huy Dung</td>
<td>Hanoi Medical University, Hanoi</td>
<td>Improving community drug use through peer review and implementation of clinical guidelines</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Rustami</td>
<td>Gadjah Mada University, Yogyakarta</td>
<td>Reducing the use of expensive antibiotics for ARI in children utilizing small group face-to-face intervention.</td>
</tr>
<tr>
<td>Thailand</td>
<td>Witmon Anansakunwatt</td>
<td>Mahidol University, Bangkok</td>
<td>Improving clinical and economic rationality of prescribing in a teaching hospital.</td>
</tr>
<tr>
<td>Thailand</td>
<td>Sayomporn Srinavin</td>
<td>Ramathibodi Hospital, Mahidol University, Bangkok</td>
<td>Responsible factors for successful hospital pharmacy and therapeutic committees in improving use of antimicrobial agents for surgical prophylaxis and lower respiratory tract infection treatment in provincial hospitals.</td>
</tr>
<tr>
<td>Nepal</td>
<td>Kumud Kafle</td>
<td>INRUD, Kathmandu</td>
<td>Test of strategies for implementing STG in improving use of drugs.</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Sri Hidayati</td>
<td>Faculty of Medicine, Gadjah Mada University, Yogyakarta</td>
<td>Small group discussion among paramedics at health centre level to improve compliance to acute respiratory tract infection standard treatment guidelines.</td>
</tr>
<tr>
<td>Philippines</td>
<td>Mediadora Saniel</td>
<td>Philippines Society for Microbiology and Infectious Diseases, Manila</td>
<td>Improving private physicians' prescribing practices in the diagnosis and treatment of uncomplicated urinary tract infection (UTI) through clinical practice guidelines (CPG).</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Zafar Mirza</td>
<td>Association for Rational Use of Medication in Pakistan, Islamabad</td>
<td>To establish a methodology suitable for the evaluation of independent drug bulletins.</td>
</tr>
<tr>
<td>Philippines</td>
<td>Rainier Galang</td>
<td>University of the Philippines, Manila</td>
<td>The effect of an educational activity on the dispensing practices of drug store clerks.</td>
</tr>
<tr>
<td>Philippines</td>
<td>Isladora Sia</td>
<td>University of the Philippines, Manila</td>
<td>The effect of an educational activity on the drug use purchasing practices of village heads.</td>
</tr>
</tbody>
</table>

*April 18-25, 1998
Yogyakarta, Indonesia.*
### Table 6: Drug Use Intervention

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PRINCIPAL INVESTIGATOR</th>
<th>INSTITUTION</th>
<th>TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>Rob Summers</td>
<td>Medical University of Southern Africa, Medunsa</td>
<td>The impact of an antimicrobial policy on the use of antimicrobials at Ga-Rankuwa Hospital.</td>
</tr>
<tr>
<td>Ghana</td>
<td>David Ofori-Adjel</td>
<td>University of Ghana Medical School, Accra</td>
<td>Improving doctors' prescribing habits at a teaching hospital.</td>
</tr>
<tr>
<td>Kenya</td>
<td>Lilian Gitau</td>
<td>Mission for Essential Drugs and Supplies (MEDS), Nairobi</td>
<td>The effect on treatment of ARI cases after introducing clinical guidelines and pharmacy and therapeutics committees in mission health facilities in Kenya.</td>
</tr>
<tr>
<td>Kenya</td>
<td>Michael Thuo</td>
<td>Faculty of Pharmacy, University of Nairobi, Nairobi</td>
<td>Influencing prescribing behavior: the use of drug audit as an intervention tool.</td>
</tr>
<tr>
<td>Uganda</td>
<td>Willy Anokbonggo</td>
<td>Makerere University, Kampala</td>
<td>The impact of decentralization on access to health services, use and availability of drugs in two district hospitals in Uganda.</td>
</tr>
<tr>
<td>Uganda</td>
<td>Paul Waako</td>
<td>Makerere University, Kampala</td>
<td>Improving rational drug use by the private physicians in Uganda: An educational intervention study.</td>
</tr>
<tr>
<td>Uganda</td>
<td>Winifred Tunwikirize</td>
<td>Makerere University, Kampala</td>
<td>Drug utilization review program targeting private pharmacists and drug retailers in Uganda.</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Stephen Nsimba</td>
<td>Muhimbili University College of Health Sciences, Faculty of Medicine, Dar Es Salaam</td>
<td>Assessment of knowledge and attitudes on use of drugs for treating malaria in Kilosa District, Morogoro region, Tanzania: A preliminary drug stores/ordinary shops survey.</td>
</tr>
<tr>
<td>Zambia</td>
<td>Frederick Kaona</td>
<td>Tropical Diseases Research Centre, Ndola</td>
<td>Improvement of utilization of malarial drugs at household level in Zambia.</td>
</tr>
</tbody>
</table>

**September 14-23, 1998**  
**Kampala, Uganda**

This study team did not attend the proposal development workshop

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PRINCIPAL INVESTIGATOR</th>
<th>INSTITUTION</th>
<th>TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mexico</td>
<td>Hortensia Rewes Morales</td>
<td>Instituto Mexicano Del Seguro Social (IMSS), Mexico</td>
<td>Effectiveness of an educational strategy, based on critical analysis of clinical practice, to improve appropriateness of treatment of common diseases in family medicine clinics.</td>
</tr>
</tbody>
</table>
C - Accomplishments to date
Participants in the two regional workshops and the one team from Mexico are currently working on finalizing 21 research proposals. As of this time, eight final proposals from the Asia workshop have been submitted for technical review to the Joint Initiative secretariat; funding has been committed for 6 of these projects pending minor revisions, one study in Philippines is already under way, and one team has withdrawn its proposal.

D - Future Strategic Plans
There are as many as thirty additional studies from the 88 submissions that the review panel considered potentially worthy of support pending development of a full proposal. The Joint Initiative has also received additional funding to conduct a Spanish-language proposal development workshop in 1999 for Latin American investigators whose proposals did not receive the highest ranking.

Once the current wave of interventions is underway, it is planned that a second request for proposals will be issued emphasizing patient and community-oriented interventions, as well as evaluations of economic incentives and pharmaceutical policies. Support will be sought from additional donors to expand the scope of the research initiative, in terms of both the number of funded projects and the focus of the research.

In light of these facts, the eventual growth in this portfolio will depend on the ability of the consortium members to secure additional funding for the research and their ability to provide coordination and technical assistance.
In 1988, the World Health Assembly resolved to eradicate polio from the world by the year 2000. As the millennium approaches, the World Health Organization is optimistic that the transmission of wild poliovirus can be interrupted by 2000, and the eradication of polio certified by 2005. One of the key strategies for eradication is the administration of polio vaccine through mass immunization campaigns called National Immunization Days (NIDs). The effectiveness of NIDs in interrupting wild poliovirus transmission depends on achieving and maintaining uniformly high coverage rates among all children under five. For this reason, pockets of unimmunized children that may remain after a series of annual NIDs become critical, as this is where outbreaks tend to occur. Often, these pockets are densely populated urban or peri-urban areas with inadequate health services.

The ARCH Project has received global USAID funds to assess missed opportunities for polio immunization in Africa in support of the global Polio Eradication Initiative (PEI). Initially, the project is centered in poor urban neighborhoods of five West African countries that represent a mix of vaccination strategies, coverage rates, and success with NIDs.

The project has adopted the following five principles:

- to concentrate on a few selected West African countries, both anglophone and francophone;
- to focus within these countries on low-income neighborhoods in major cities;
- to develop the understanding of “demand side” factors at the household level;
- to encourage the development of the capacity for the evaluation and elaboration of immunization strategies by mixed teams of health professionals, civil servants and social scientists;
- to support South-South collaboration across the language divide.

The project’s initial contribution to the PEI will be to increase the reach of NIDs by 1) identifying children not reached by NID campaigns and 2) exploring the social factors affecting participation in NIDS and developing community mobilization strategies that take into account these factors. The rationale behind the ARCH Polio Project is that, with appropriate strategies, polio immunization coverage can be improved through mobilization of households to participate in routine immunization programs and NID campaigns. Study findings will be used to enhance the effectiveness of supply-side eradication strategies that include vaccine delivery, acute flaccid paralysis (AFP) surveillance, and mopping up activities. The ARCH strategy includes close collaboration with the National Interagency Coordinating Commit-
tees (ICCs) of host countries, the committees responsible for polio eradication activities.

Analysis of the success stories in some low-income but well vaccinated populations (The Gambia, for example) reveals that routine immunization with trekking teams providing outreach within a Primary Health Care (PHC) framework has lifted immunization levels to over 90 percent overall. The PHC system, however, is not working well in all urban areas, especially in poor, "spontaneous" neighborhoods, where the contacts between families and the public health services are weakest. Unfortunately, even with good delivery of the vaccines either through routine services or NIDs, we find significant numbers of children not receiving polio vaccine. As immunization coverage improves throughout West Africa, the need to reach urban poor areas and other "pockets" of low coverage will increase, as polio outbreaks typically involve unvaccinated or inadequately vaccinated subgroups within highly immunized communities. In response to this need, The ARCH Project has decided to adopt a demand-side strategy to first discover the barriers to routine and supplemental immunization at the household and community level, and then to develop appropriate community mobilization strategies to ensure that the missing children appear for immunization in the future.

An important aim of the ARCH Project is to build global and national research capacity. To this end, we have developed a regional network of multi-disciplinary teams of health professionals and social scientists to ascertain key factors affecting participation in immunization programs. It is anticipated that these teams will continue to work on such problems even when polio cases are very rare since this capacity is needed to deal with the control of other infectious diseases in the future. Our assessment is that other groups (WHO, UNICEF, Rotary International and many bilateral donors including Australia, Canada, Denmark, Germany, Japan, UK, and the USA) are providing solid support for the production and distribution of the polio vaccine and the development of laboratory networks and surveillance systems. The ARCH Project will contribute to these efforts by developing the local research capacity and the South-South cooperation needed to break poliovirus transmission and control other infectious diseases.
B - Proposal Development Workshop

The ARCH Project contribution to the Polio Eradication Initiative was developed in 1998 and announced publicly to partners and scientists active in Africa. The call for proposals was also publicized at the EPI Manager’s Meeting in March 1998, in Abidjan, Côte d'Ivoire. Expressions of interest were received from 38 countries in 16 African nations. Taking into account the ARCH Project's limited resources, the strong response from West African countries, and the “poliovirus reservoir” status of the region, the Project decided that in its initial phase, it would focus on West Africa. ARCH Project technical staff reviewed 28 pre-proposals from 9 West Africa countries. Ten teams from West Africa were invited to attend the proposal development workshop held in Banjul, The Gambia, from June 14th - 20th, 1998. Of these ten teams, nine attended the workshop (Please see table 7).

Table 7: Polio Workshop

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PRINCIPAL INVESTIGATOR</th>
<th>INSTITUTION</th>
<th>TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bénin</td>
<td>Dismand Houinato</td>
<td>Groupe de Recherche d’Action de Dévelopement (GRAFED-Bénin, Cotonou)</td>
<td>Study of the missed opportunities of polio vaccination in the health zone of COTONOU-1.</td>
</tr>
<tr>
<td>Côte d'Ivoire</td>
<td>Sékou-Victor Sangaré</td>
<td>Ministry of Health, Abidjan</td>
<td>Immunization coverage and its determinants in Boribana and Cité Fermont. Two quarters of the commune of Attecoube in Abidjan in Côte d'Ivoire.</td>
</tr>
<tr>
<td>Ghana</td>
<td>John Gyapong</td>
<td>Ministry of Health, Accra</td>
<td>An exploratory study to help develop specific interventions to improve routine EPI and NID coverage in the Accra Metropolis of Ghana.</td>
</tr>
<tr>
<td>Ghana</td>
<td>Edmund Browne</td>
<td>School of Medical Sciences, University of Science and Technology, Kumasi</td>
<td>Factors influencing participation and non-participation in immunization programs, including polio, in the city of Kumasi, Ghana.</td>
</tr>
<tr>
<td>Guinea</td>
<td>Momo Camara</td>
<td>Ministry of Health, Conakry</td>
<td>Study of the factors which influence the vaccine coverage in the urban commune of Matam.</td>
</tr>
<tr>
<td>Mali</td>
<td>Abdel Karim Kouraré</td>
<td>Association pour la Recherche, l'Evaluation, la Formation Continue (AREFOC), Bamako</td>
<td>Study of the vaccine coverage and the national days of vaccination in a peri-urban quarter of Bamako in Mali.</td>
</tr>
<tr>
<td>Mali</td>
<td>Soumaré Absatou N'Diaye</td>
<td>Institut National de Recherche en Santé Publique, Bamako</td>
<td>Study of socio-economic and cultural factors influencing the vaccine coverage in children of less than 5 years in a peri-urban area of Bamako in Mali.</td>
</tr>
<tr>
<td>Sénégal</td>
<td>Salif Ndiaye</td>
<td>Services d'Etudes pour la Recherche et pour le Développement Humain en Afrique (SERDHA), Dakar</td>
<td>Study of the vaccine coverage against poliomyelitis and its determinants in the urban zone of Dakar, Sénégal.</td>
</tr>
</tbody>
</table>

June 13-23, 1998
Banjul, The Gambia
The overall aim of the workshop was to produce a set of fundable research proposals assessing the country, household, and individual level factors that determine the NIDI/routine immunization coverage rates among children in urban areas, with an emphasis on hard-to-reach children. Study findings will be used to develop strategies to achieve uniform immunization coverage in urban and peri-urban areas. At the workshop, the participants, representing a mix of program managers, researchers and physicians, developed a set of proposals designed to achieve three main goals:

- to measure polio immunization coverage levels in low-income neighborhoods of major cities in West Africa, including coverage through routine immunization and NID campaigns;
- to ascertain the main household-level obstacles to wider participation in these programs at the family and community level;
- to solicit the views of caretakers, vaccinators and other health professionals about the reason affecting participation in the polio elimination activities (i.e., immunization and case reporting).

The study design and survey instruments reflect a sharing of each research team's contributions to the project as well as a consensus view of needs and opportunities in the West African context. At the workshop, an attempt was made to standardize the approaches so that the results would be internationally comparable, and at the same time, allow sufficient scope for the teams to investigate problems particular to their own communities. Local investigators chose to employ two linked approaches to assess factors underlying participation in NID campaigns and routine immunization programs: a household survey of mothers and a qualitative research component targeting consumers and providers.

The household survey has been designed to 1) document the level and distribution of NID/EPI immunization coverage at the local level and to 2) assess attitudinal and motivational factors and background characteristics underlying participation in routine immunization programs, NID campaigns and AFP case reporting. Several qualitative research approaches will be used to gather more insight from both the consumer and the immunization provider. Information will be obtained from open-ended interviews with key informants, semi-structured interviews with selected individuals, and focus group discussions. In addition, a community study will describe the institutions and power structures found within the chosen urban community as well as the formal political structure (administrators, police etc.) in the district. This inventory of institutions will insure that health planners are aware of formal and informal institutions and associations that might either hinder or help the drive to full immunization coverage and that key associations are not by-passed in the next campaign.
C - Accomplishments to Date

As a first step, the Project has funded seven studies in West Africa. The first series of studies will be conducted in Benin, Ghana, Guinea, Mali, and The Gambia and are scheduled to begin fieldwork early in 1999. Researchers agreed with the strategy set out by the project and further developed at the workshop in Banjul. The research approach finalized at the workshop allows sufficient scope for the teams to investigate problems particular to their own communities, while maintaining some comparability across sites.

The research teams supported by the Polio Portfolio have coordinated their activities with their National Inter-Agency Coordinating Committees (ICC). These committees, with representation from the ministry of health, international agencies, donors, Rotary International, and NGOs, and other partners in the global eradication initiative, coordinate and monitor PEI activities. In addition, the portfolio has worked to establish collaborative relationships with UNICEF, WHO, and local USAID missions in the region. As a result, The ARCH Project has been working with the Polio Eradication/EPI Regional Social Mobilization Advisory Group to develop social mobilization and communication strategies and the portfolio has been invited to present at the 1999 EPI Managers Meeting for West Africa. In addition, UNICEF/The Gambia has agreed to co-finance the Gambian study and WHO-AFRO would like to expand the network by inviting additional countries to the ARCH Project workshop scheduled for June 1999.

D - Goals for 1999-2000

A second workshop is scheduled for June, 1999, in one of the partner countries where preliminary results will be shared and interventions and evaluation plans based on study findings prepared. Detailed dissemination strategies that include follow up on the implementation of recommendations, will also be finalized during the workshop. Through its focus on urban poor communities and in collaboration with other Polio Partners, the ARCH Project will contribute to the development of targeted social mobilization and service delivery strategies, and facilitate their incorporation into health policies and programs.

Another aim of this initial stage of the work is to be able to compare issues and strategies across the different countries and to produce some collective articles for the scientific literature and partners and agencies active in the eradication initiative. Using a semi-standardized questionnaire and similar field methods, we hope to produce a consolidated report in addition to the separate country analyses.
At the June 1999 workshop, in addition to hearing about the results of the studies, we will develop a new set of proposals for the implementation of the new strategies based on the research findings. The aim is to produce for each case a revised intervention strategy that will be implemented and evaluated during the next round of the NIDs in late 1999. By introducing the new approach in a controlled manner and only in selected neighborhoods, we hope then to be able to assess more scientifically the effects of the new strategy.

**E - Future Strategic Plans**

In the coming year, we hope to continue work with the research teams to extend and deepen this research capacity; to further refine the intervention strategies; and to develop a rapid response mechanism for dealing with outbreaks. One of the difficult tasks ahead is the development of a community-based surveillance systems that will complement facility-based AFP surveillance. The need for effective surveillance intensifies as eradication nears. Surveillance is used to identify these pockets where mopping up activities (house-to-house immunization campaigns) or localized immunization days (SNIDs) need to be conducted in order to eliminate transmission, and ultimately, to certify polio-free areas. Polio eradication, therefore, requires that sensitive surveillance systems capable of picking up polio cases be established in every country.

Within the framework of current eradication activities, future strategic plans for the polio project will focus on the following areas:

- expansion of the ARCH Project research network to include other countries
- identification of approaches at the family and community level to encourage AFP case reporting in order to enhance overall effectiveness of facility-based surveillance activities
- strengthening the ARCH Project network of researchers and practitioners to foster cooperation and the exchange of information within and across countries
- continued collaboration with other partners in the eradication initiative, including National Interagency Committees.
Health-Related Behavior of Households and Communities

A - Background

The discovery and development of new preventive and therapeutic health measures are necessary but not sufficient to achieve progress in public health. For progress to occur, these new technologies must be successfully brought to the community or household and used appropriately. Social and psychological factors play an important role in decisions people make regarding their health and the health of their children. For this reason, applied public health research must address the context in which household decisions are made about health seeking behavior. The Household and Health-Related Behavior portfolio of the ARCH Project addresses these wider issues in the following areas:

- use of preventive measures;
- illness recognition;
- seeking expert advice; and
- management of treatment.

Building Capacity to Conduct Social Research on Health-Related Behavior

The ARCH Project is using two approaches to build the capacity to conduct research concerning the health-related behavior of households and communities: encouraging social scientists to become involved in research on health topics; and encouraging physicians to carry out research on household and community behaviors.

The first element of the capacity building strategy is to develop a general framework for considering interventions to change household behavior. Households and individuals can engage in two kinds of activities related to illness. First, they can prevent it, either by decreasing exposure to the pathogens or important cofactors. Second, once disease occurs, households and individuals can act to minimize its consequences. In this latter category of disease management, there are four relevant categories of actions: recognition of the illness; home management; solicitation of "expert" advice; and finally, application of that advice. Each of these categories of action may comprise a variety of discrete behaviors and possibilities for intervention.

During the later months of 1997, letters of intent were sent out to scientists emphasizing the above areas of research.
The first ARCH Project Proposal Development Workshop for Behavioral Sciences was held in Pretoria, South Africa during January 1998. The workshop focus was household behavior related to illness prevention and treatment. Six teams, four from Uganda and two from South Africa were invited to participate in the workshop.

Table 8: Household Behavior

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PRINCIPAL INVESTIGATOR</th>
<th>INSTITUTION</th>
<th>TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uganda</td>
<td>Harriet Birungi</td>
<td>Makerere Institute of Social Research, Kampala</td>
<td>Are Caretakers Reached: A Study of Advice-giving through the Integrated Management of Childhood Illness Approach in Uganda</td>
</tr>
<tr>
<td>Uganda</td>
<td>Charles Karamagi</td>
<td>Makerere University, Kampala</td>
<td>Assessment of the Implementation of the Integrated Management of Childhood Illness in Uganda</td>
</tr>
<tr>
<td>Uganda</td>
<td>Xavier Nsabagasani</td>
<td>Makerere University, Kampala</td>
<td>Factors Influencing Caretaker Behavior in the Management of ARI. A Study of Mothers with Under Fives in Uganda</td>
</tr>
<tr>
<td>Uganda</td>
<td>Stella Neema</td>
<td>Makerere Institute of Social Research, Kampala</td>
<td>Caretaker's Behavior in the Management of Childhood Diarrhoeal Diseases. A Study of Iganga and Mbarara Districts in Uganda</td>
</tr>
<tr>
<td>South Africa</td>
<td>Petro Esterhuyse</td>
<td>University of the Orange Free State, Bloemfontein</td>
<td>The Dynamics of Household Decision-Making Concerning the Health Care of Small African children</td>
</tr>
<tr>
<td>South Africa</td>
<td>Mxolisi Mankazana</td>
<td>Health Development Institute and Oral Health Centre, Cape Town</td>
<td>An Assessment of the Health Needs of Children in Unregistered Creches in Mitchells Plain, Cape Town, South Africa</td>
</tr>
</tbody>
</table>

The first two proposals from Uganda are attempts to measure the impact of the Integrated Management of Childhood Illness (IMCI) counseling approach on the caregiver's child caring behaviors. The first addresses counseling in health centers, an essential element of the IMCI approach. This team's research will assess the amount, quality and content of counseling that is being done, and examine its effectiveness through interviews with people who have been recently counseled. This research has the potential to help policy makers refine IMCI training to improve the counseling component and to help implementers develop tools for monitoring counseling.

The second proposal will compare caretakers in communities served by facilities where providers have been using IMCI for more than a year with communities where it has not yet been implemented. This research has the potential of helping policy makers decide whether the content of counseling is appropriate and whether other, community-based efforts to promote certain behaviors should also be considered.
The third study from Ugandan investigators evaluates household management of ALRI. This team will compare communities where IMCI has been implemented with communities where it has not yet been implemented to assess the extent to which caretakers recognize ALRI, using the IMCI approach and other signs. They will also analyze factors that determine caretaker choices in the management and treatment of ALRI, and identify factors that facilitate or impede appropriate care seeking. The results of this research should help improve household management of ALRI.

The fourth Ugandan proposal examines the effect on household behavior, specifically on the use of ORT, of face-to-face health education activities at health centers. They determine household knowledge of proper ORT use within the catchment areas of two health centers - one where there has been good promotion of ORT and one where it has been lacking. This research should help policy makers understand the importance of face-to-face promotion at the point of delivery.

The proposal from Blantyre, South Africa will examine household decision-making concerning the use of free medicines for childhood illnesses and whether they are supplemented with other, non-free treatments. South Africa recently established a policy that all medicines dispensed through government services would be free. Concern exists that over-utilization of free medicine may exist.

The sixth proposal, also from South Africa, addresses the health of children placed in unregistered crèches in Mitchell's Plain, a lower-income area in Cape Town. This topic is of great interest to the South African Ministry of Health, since unregistered crèches serve more children than registered crèches. The research has the potential of changing policy on crèche registration and on provision of government health services to children in unregistered crèches.

**C - Accomplishments to Date.**

Data collection on these set of studies will begin in February-March 1999 and continue for up to 18 months. A data management and manuscript preparation workshop is planned for early fall of 2000.
D - Future Strategic Plans

The ARCH Project portfolio on health-related behavior of households and communities has developed slowly relative to the other portfolios. It has been problematic finding bona fide social researchers keen to undertake community-based applied health research for many years. Using clinicians interested in social medicine has its limitations as most researchers trained in clinical medicine lack research training in the social sciences.

The ARCH Project will continue to expand this portfolio focused on two main areas:

- Evaluation and operations research related to the implementation of the IMCI approach;
- Household recognition and management of fever.

With staffing changes and additions, we are optimistic that we will be able to markedly expand this portfolio of activities in 1999.
Country Specific Activities
Zambia

The ARCH Project is working with the Zambian Central Board of Health (CBoH) and key national research institutions to support a program for expanding and strengthening the applied child health research capacity in Zambia. The research will be consistent with the principles of the ongoing health reform and contribute to the further development of evidence-based health policy. The applied research will be conducted in close collaboration with the strategic objectives of the USAID Mission and the BASICS Project and potentially, in collaboration with the Population Council, UNICEF, the World Bank Study Fund, and other donor organizations actively supporting research and health sector development activities in Zambia.

The research program will be driven primarily by the needs of the emerging health reform process. The creation of the Central Board of Health (CBoH), the financial and programmatic decentralization to districts, and the de-linking of personnel from the public sector civil service constitute key parts of the reform effort. The CBoH will be highly streamlined and will depend on other national institutions for technical support in developing policy applied research (analysis, formulation, including the need for new information), technical guidelines, and supporting districts in the implementation of promotive, preventive and curative services.

The ARCH Project has three related technical components in Zambia. First, we are encouraging Zambian researchers and institutions to compete for funds allocated to the research agenda developed by the ARCH Project using USAID Global Bureau/HPN/HN funds. Second, we are developing a Zambia-specific research agenda in collaboration with our national partners. Third, we are supporting the Zambian National Malaria Control Program.

Area 1 - Global Research Awards -

Zambian research teams from the Tropical Diseases Research Center in Ndola have successfully competed in global research competitions and are participating in two international clinical studies, the ZAP and APPIS trials. One additional research team has participated in the African Regional Workshop held in Uganda and currently is revising its protocol.
Area 2 - National Research Agenda and Research Competition -

The second major area of ARCH Project sponsored activity is to assist in the development of a national health research agenda for Zambia. In working closely with the CBoH and key national research institutions, the ARCH Project is supporting a program to expand and strengthen the applied child health research capacity in Zambia.

Siavonga Workshop

On October 8 and 9, 1998, a conference and symposium to establish Zambian health research priorities was held in Siavonga, Zambia. The goals of the conference were:

1. To foster a national network of both social and behavioral researchers interested in priority national health research and policy issues.
2. To produce an inventory of health research studies conducted in the past decade by Zambian or other health scientists working with problems among Zambian populations.
3. To clarify the essential national health research agenda for the GRZ and donor investments over the next five years.

In preparation for the conference, the first national bibliography of Zambian-based health research reports was collected from individual researchers throughout the country, organized into broad thematic areas and distributed as background for the meeting. It is the single most comprehensive collection of information on Zambian health research ever collected. In addition, commissioned papers covering twelve technical areas were presented by leading Zambian researchers and policy makers. These papers serve as a summary of the research work to date, identify areas requiring additional investments, and highlight the policy linkages and gaps. The ARCH Project, in collaboration with CBoH will produce and disseminate the bibliography and commissioned papers in a bound form so that it can serve as a permanent reference for researchers, program and policy personnel, and the donor officials in the future.

The national meeting was successful in developing and promoting a set of health research priorities and allowing Zambian scientists from several health disciplines to interact with senior health policy officials. Based on the priorities generated at the meeting and further refined by an expert panel, the ARCH Project will distribute a call for proposals to Zambian scientists, and will initiate a proposal development workshop, probably in collaboration with the Horizons Project, Nairobi.

The ARCH Project will focus its capacity strengthening and small grants program on three institutions — the Tropical Disease Research Centre (TDRC), the National Food and Nutrition Commission (NFNC), and the University of Zambia (UNZA) Faculties of Medicine and Arts and Sciences. These three institutions were selected as they can make major contributions to the applied research needs of the
country and support the CBoH.

**Area 3 – Support to the National Malaria Control Program**

**Background:**

The ARCH Project was awarded funds from the USAID Global Bureau, Africa Integrated Malaria Initiative, to provide core support for the development and expansion of the National Malaria Control Program in Zambia. The National Malaria Control Center (NMCC) in Lusaka is responsible for the organization of a significant scaling-up of the current Integrated Malaria Initiative (IMI) in Eastern Province and an extension of the program into two additional provinces Luapuala (LIMI) and Copperbelt (CIMI)). Specifically, the ARCH Project support will permit the NMCC to expand core staff, improve control facilities, and cover basic operating costs necessary to implement these activities.

With technical assistance from the BASICS program, the Eastern Province Integrated Malaria Initiative (EPIMI), was developed last year. It represents an approach to malaria control that is highly integrated with community participation, other basic public health measures (e.g. IMCI) and contains plans for sustainability. We believe that this approach constitutes an alternative model for malaria control that is applicable worldwide and affords the best possibility of providing an authentic and sustainable possibility to decrease malaria transmission and associated morbidity and mortality.

The new Zambian National Malaria Control Program is, in large part, consistent with the stated malarial control strategies being planned by the worldwide Roll Back Malaria campaign recently announced by the WHO. For this reason it constitutes an important test site for these planned global interventions. While the ARCH Project funds will support core administrative activities within the NMCC and at selected field sites, substantial amounts of additional funding will be required in the next 12 months for this ambitious project to be successful. Complimentary support in the form of commodities (insecticide treated bednets [ITNs], antimalarials, diagnostic reagents, etc.) and equipment (vehicles, microscopes, computers, etc.) has been promised by the Japanese Government.

**Program Description:**

The ARCH Project financial support will lead to three main achievements:

1. Provide NMCC with funds for expansion of core staff, increase the facilities needed to run a National Malaria Control Program and provide funds to cover operating costs.
2. Provide funds for NMCC to run the Eastern Province Integrated Malaria Initiative (EPIMI).
3. Provide funds to establish and maintain two additional provincial Integrated Malaria
Initiatives. These will be the Luapula Integrated Malaria Initiative (LIMI) and the Copperbelt Integrated Malaria Initiative (CIMI).

Overall Description and Expected Outputs of Integrated Malaria Initiatives (IMI)

In order to improve the present Zambian malaria control program a new approach to strengthening the delivery of malaria control was conceived and termed the Integrated Malaria Initiative (IMI). This initiative was developed to implement decentralized malaria control that is based at a district level with central coordination. The district level IMI’s will have a supervisory role and aim to increase the capacity of the district public health systems to implement malaria control in the future. The IMI’s are expected to improve distribution routes for ITN’s and drugs relating to malaria prevention and treatment, support training activities in health, and facilitate the spread of IEC materials to improve community participation in improving health.

IMI Initiatives

These initiatives will be undertaken in all target communities using an array of methods and tools. They can be broadly categorized as follows:

- early recognition, care-seeking, and treatment of malaria, including community-based growth monitoring and promotion of appropriate case management with effective drugs at health facilities through the integrated management of childhood illness (IMCI)

- provision of effective antimalarial chemoprophylactic agents to pregnant women, distribution of insecticide-treated mosquito nets (ITNs) for children < 5 years old and pregnant women, and strengthening of health system epidemic preparedness and response.

All interventions are delivered as part of the MoH’s essential health care package and are designed to strengthen the Zambian government (GRZ) structures and systems.

Expected Outputs of the IMIs during 1999

Further strengthening of the decentralised District Health System, including the establishment of:

- District Partnership Committees
- Health Centre Committees
- Neighbourhood Health Committees
- Cost-sharing Schemes/ITN Revolving Fund
Expansion/Initiation of an Insecticide-Treatment Mosquito Net (ITN) Intervention programme with POWERNET/POWERCHEM

- Improved facility-based case management through:
  - Improved availability and rational use of drugs, including FANSIDAR
  - Improved health worker performance following IMCI training
  - Improved supportive supervision
  - Improved laboratory diagnosis

- Improved community-based prevention and management through:
  - Trained community-based volunteers who are implementing promotive, preventive, and curative cost-effective interventions
  - Expansion/introduction of community-based growth monitoring and promotion.
  - Development of plans for an intervention to provide chemoprophylaxis of pregnant women
  - Implementation of multiyear monitoring and evaluation plan, and completion of all baseline studies.

El Salvador

SALVADORENOS SALUDABLES (SALSA)

Policy Analysis and Applied Research

I - Background and Focus

The ARCH Project was invited by the USAID/San Salvador Mission to develop specific policy analysis and applied research in support of the Salvadoran health reform process. The principal government clients are the National Assembly Health Sub-Committee, the Ministry of Health, and the Presidential Commission on Health Reform.

The research that the HIID/ARCH team and Salvadoran counterparts proposed, focused primarily on delineating the options for health system reform. Much of the research work related to health sector financing issues. A system of sound financial support for health care does not currently exist in El Salvador, making reform of health care finance a key element in improving access to health care by Salvadorans who currently lack it.

A workshop amongst major institutions of the public health sector was held in October of 1998 in San Salvador to discuss (1) priorities for health policy research, and (2) proposals for research priorities put forward by local partner institutions. The institutions invited to state their priorities were the Legislative Assembly Commission on Health and the Environment (LA/CHE), the Ministry of Public Health
and Social Assistance (MSPAS), the Colegio Médico (CM), and the National Commission on Health (NCH). The local partner institutions were FUSADES, Funda Unago, FUNDE, and the Univ. of El Salvador Medical School. Over fifteen research proposals were submitted by the various institutions.

II - Completed Research

The ARCH Project and UCA, working with data supplied by the Instituto Universitario de Opinion Publica (IUDOP), undertook a secondary data analysis of several existing data sources. The purpose of the analysis is to aid health policy in two ways. First, by looking at public opinion towards the health care system, privatization, cost-recovery, etc., areas have been identified where likely obstacles to change may arise and where there is likely to be support for new policies. Second, an analysis of the available data on personal health care spending, and patterns of usage will provide a comparative point and complement the new research on health care financing.

The report includes information on health care spending in rural areas and attitudes towards privatizing the health system, as well as other themes chosen in consultation with the BASICS group and relevant political actors such as the Legislative Assembly, the Presidential Commission on Health, and the MSPAS. The report will be submitted in early 1999.

III - Ongoing activities

The USAID/San Salvador Mission decided not to fund the research proposals presented at the national workshop described above. With elections pending in March 1999 and the end of the mandate of the National Commission on Health at the close of 1998, the Mission is re-considering the directions of their support for the health reform process in El Salvador. The HIID team withdrew from ongoing technical support activities with the completion and submission of the public opinion secondary data analysis.
Jamaica
ARCH Project in collaboration with the Gorgas Memorial Institute

A - Background

In 1992, the Jamaican perinatal mortality rate (including stillbirths and deaths before one week of age) was 33.6 per 1,000 live births, and in 1990, 12.0 percent of babies born had low birth weight. The highest morbidity rate among women (107.9 per 10,000) in 1991 was due to complications of pregnancy, and the third highest morbidity rate among women (27.6 per 10,000) was due to genito-urinary disorders including STDs.

Chlamydia, gonorrhea and syphilis accounted for 97 percent of communicable diseases reported to the Ministry of Health, Jamaica, in 1993. These conditions can result in severe complications that adversely affect the outcome of pregnancy and are a major cause of perinatal morbidity and mortality. In addition to these STDs, vaginal infections such as trichomoniasis and bacterial vaginosis (BV), can also adversely affect the fetus in a number of ways, causing abortion, ectopic pregnancy, intrauterine death, stillbirth, premature delivery, low birth weight, congenital malformation and other neonatal disease.

STD SYNDROMIC MANAGEMENT IN JAMAICA:

Reproductive tract infections (RTIs) include syndromes such as syphilis, gonorrhea, chlamydia, HIV, candidiasis, trichomoniasis, and bacterial vaginosis (BV). RTIs facilitate HIV transmission and result in increased frequency of ophthalmia neonatorum (ON), preterm deliveries and low birth weight (LBW) infants. Prenatal screening of women for RTIs is not routinely done in Jamaica.

In June 1997, an intensive one-week training course in RTI diagnosis, management, prevention, and standards of care for RTIs using a syndromic management approach substantiated with basic laboratory tests was conducted in Jamaica. Public health nurses from four antenatal clinics in Kingston were enrolled in this course. The objectives of the training program included principles of syndromic diagnosis, appropriate methods for laboratory sample collection, basic laboratory tests, accurate interpretation of test results, practice of universal precautions during patient examination and processing of laboratory samples, treatment, patient treatment and follow-up, and management of sex partners for RTIs.

A cross-sectional study was conducted in four facilities delivering prenatal care to assess the actual prevalence of RTIs (syphilis, gonorrhea, chlamydia, trichomoniasis, HIV and BV) among a cohort of pregnant women. The study was started in June 1997 and ended in September 1997. A sample of 371 pregnant women, attending
one of the four prenatal clinics in Kingston, Jamaica, was screened. Using the TRUST test, 5.7% of our sample tested positive for syphilis, 17.8% tested positive for chlamydia using EIA, 5.4% tested positive on gonorrhea cultures, 27.2% tested positive for candidiasis with the yeast test, 17.8% tested positive for trichomoniasis with the Pouch test, 6.2% tested positive for bacterial vaginosis and 1.3% of our sample tested positive for HIV using Western Blot confirmation of ELISA.

**B - Accomplishments to Date:**

While the laboratory samples were collected, women received prenatal care according to the syndromic case management based on the WHO algorithms in which readily obtained historical variables, physical findings, and low cost laboratory tests guide therapeutic interventions. The results of the clinical assessment were then compared to the results of a laboratory assessment in order to measure the impact of syndromic case management on RTI prevalence. A statistically significant difference was observed between clinical assessment and laboratory assessment for vaginitis (trichomoniasis and bacterial vaginosis, p = 0.04), candidiasis (p = 0.006), cervicitis (gonorrhea or chlamydia, p = 0.015), and vaginitis and cervicitis (p = 0.001). No significant difference was observed between clinical assessment and laboratory assessment for candidiasis and cervicitis (p = 0.6).

The women were also enrolled in a study looking at risk predictors for syphilis, gonorrhea, chlamydia and HIV (STDs). A specific questionnaire including details on medical history and specific risk factors was administered to each woman before taking samples for the laboratory analysis to evaluate risk predictors among Jamaican pregnant women. The variables found to be significantly associated with the presence of an STD by univariate analysis included clinical algorithm (p = 0.003), friable cervix (p = 0.001), cervical erosion (p = 0.027), blood transfusion (p = 0.001), presence of past STD infections (p = 0.005) and number of partners (p = 0.032). Predictor variables for STDs will be derived from these associations with a multivariate analysis. The findings of this study will be critical in predicting the presence of STDs and RTIs among pregnant women in Jamaica.

**C - Goals for 1999-2000**

Further analysis of these data will continue and lead to publication in the peer-reviewed literature.
Special Initiatives
Effects Of El Niño On Diarrheal Incidence In a Shantytown In Lima, Peru

Background and focus

During the last twelve to eighteen months, El Niño has had a profound effect on weather conditions in Peru. As a consequence, there have been increases in air temperature and the relative humidity in Lima, a city that normally has an arid climate. Understanding the effect of climate changes on the epidemiology of diarrhea will allow affected countries to focus surveillance activities and to better prepare health services for potential outbreaks. Although there has been a lot of press describing an association between El Niño and disease outbreaks, there have been no well-done, prospective studies designed to evaluate this possible association. The above proposal is one of the first prospective studies worldwide to undertake the field epidemiology necessary to understand the impact of El Niño on infectious diseases of public health importance.

The study, proposed by scientists from Proyectos de Informatica, Salud, Medicina, y Agricultura (PRISMA), in collaboration with the Universidad Catolica de Chile, Santiago, and the U.S. Naval Medical Research Investigation Detachment based in Peru, has been designed to provide high quality surveillance of the effects of El Niño on the epidemiology of diarrheal disease. The investigators seek to examine the effect of climate changes (increased air temperature and relative humidity) caused by El Niño on the risk and severity of diarrheal disease in children in a shantytown in Lima.

The study took place in Las Pampas de San Juan de Miraflores, a shantytown on the outskirts of Lima, Peru. Active surveillance for diarrheal disease has been taking place in this community since 1995 as part of a NIH-sponsored trial.

This prospective study was an extension of observations of a cohort of 270 children under the age of 2 years. The goal of the study was to compare the incidence, prevalence, and duration of diarrheal disease before, during, and after El Niño in order to determine whether this powerful climatic phenomenon has had any effect on the epidemiology of diarrheal disease. The final patient observations took place in December 1998. The investigators are presently completing the microbiologic studies and preparing to analyze their data.
Multi-Center Low Osmolarity ORS Clinical Trials

A major clinical effort for which ARCH has provided consultative and technical assistance has been the Multi-Center Low Osmolarity ORS Clinical Trials. These trials have been designed to evaluate the safety and efficacy of new formulations of Oral Rehydration Solutions (ORS) in comparison to the WHO-ORS. The ORS under study contains 75 mEq/L of sodium and 75 mmol/L of glucose, so that its osmolarity is approximately 245 mOsm/L (vs 311 mOsm/L for the WHO-ORS). Two trials took place: one in children with acute diarrhea, and another in adults with cholera.

Summary of findings

A controlled clinical trial was conducted in 300 adult patients with severe cholera to compare the efficacy of a reduced osmolarity ORS solution (Na\(^+\)75, glucose 75 mmol/L and osmolarity 245 mosm/L with the WHO/UNICEF recommended standard ORS.

147 patients received reduced osmolarity ORS and 153 received WHO/UNICEF standard ORS. No advantage was observed of the reduced osmolarity ORS solution compared to the standard ORS in terms of stool reduction (initial 24hr and total stool output, RO-ORS vs standard ORS; 212±99 vs 207±101 and 284±162 vs 273±156), ORS intake, and duration (h) of diarrhoea RO-ORS vs standard ORS, 46.4±18 vs 43±16. The proportion of patients who required unscheduled IV infusion and the proportion of patients vomiting during the initial 24 hours were similar between groups.

The incidence of hyponatraemia (serum sodium <130 mmol/L at 24 hours was greater among the patients receiving RO-ORS compared to standard ORS (OR, 2.15; 95%CI, 1.06 to 4.38; P=0.02). However, all hyponatraemic patients in both groups were asymptomatic.

Reduced osmolarity ORS solution in the treatment of adult cholera did not show any benefit in clinical course of diarrhoea. The risk of asymptomatic hyponatraemia was greater with the reduced osmolarity ORS solution than the standard ORS solution.
Data Coordinating Center (DCC)

The Data Coordinating Center has been established in the Health Office of the Harvard Institute for International Development, Cambridge, Massachusetts to provide overall administrative, statistical and data management support for international multi-center clinical trials. This facility will be the central repository of the primary data sets produced by individual sites participating in multi-center clinical trials and will be responsible for coordinating all aspects of data management, data maintenance, data and study quality control, and report writing. It will also act as the primary source of those safety and efficacy data that need to be regularly reviewed by the Study Steering Committees and Data Safety and Monitoring Boards. Coordinating center staff will also be responsible for the establishment and maintenance of a secure email or internet-based communication system for the dissemination of statistical and performance reports to members of the steering committee, DSMB and site participants.

Capacity Strengthening

Meeting on Research Capacity Development and Indicators
WHO/HQ/Geneva, October 6-7, 1998

The ARCH Project/HIID staff participated in a meeting convened at WHO/HQ, Geneva, October 6-7, 1998, to exchange information and organizational perspectives in relation to evaluating health research capacity development (HRCD). The meeting was a follow-up to similar consultations, previously held in Boston and Ottawa, which focused on methods to evaluate HRCD in developing countries.

In preparation for the meeting, a paper by ARCH Project staff entitled, “Health Research Capacity Strengthening: Framework and Indicators for Assessment” was developed to focus the discussion. This paper served as a basis for further development of the framework for evaluating HRCD.

The suggested goals of research capacity development included developing competencies and requisite research skills in areas critical to local, national or international needs and ensuring that these skills are used to solve priority health problems. The importance of taking the research results into programmes and policies was highlighted, though different opinions persist as to the appropriate role of the individual researcher in this process. Discussions were held on the role of the research environment in sustaining and enhancing research at the institutional level, the need for continued training of new researchers, and at the national level, a recognition of research as an integral part of health system development.
Future Plans:

- Selection and field testing of common indicators of research capacity development for evaluation with input from developing countries.
- Assessment of research capacity needs at the country level; development and evaluation of an assessment tool based on materials developed to date including COHRED materials and the Research Capacity Indicator Framework paper.
- Field testing of the assessment tool at the country level in southern Africa (initially). Outputs from the field tests to inform further development of the assessment and evaluation tools.
- Communication of content/outcomes of Research Capacity Development Meeting (date to be set) to interested partners.

Some of the above activities will be completed by, and reported on, at the Global Forum, June 8-10, 1999. In addition, interested parties will reconvene at that time, Monday, June 7, 1999.
Publications
ADDR/ARCH Project 1997-98 Publications

The following is a list of the 1997-1998 publications and abstracts of the ADDR and ARCH Projects. The ADDR Project scientific network is continuing to publish results and findings from their research studies, and we anticipate that more publications will continue to appear in national and international journals.

A complete listing of the ADDR and ARCH Project publications is available in “Publications of Applied Diarrheal Disease Research (ADDR) and Applied Research on Child Health (ARCH) 1985-1998.” The list is also available on the ARCH Project web site: http://www.hiid.harvard.edu/projects/arch.

The publications are listed in order of ADDR Project grant. The title of the grant and the contact information for the Principal Investigator are also included.
Publications

A Study of the Dietary Management of Persistent Diarrhea in Severely Malnourished Children

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Bhutta ZA, Nizami SQ, Isani Z.

Lactose intolerance is frequently encountered in children with persistent diarrhoea (PD). Selection of an appropriate milk-based formulation is a major management problem in the developing world. In a consecutive series of studies, we evaluated the role of feeding a traditional rice-lentil (khitchri) diet alone (KY) or in combination with either soy formula (KY-Soy) or a dilute buffalo milk (KY-B), in children (age 6 months-3 years) with PD. Serial observations of stool output, caloric intake and weight gain of these children over a 14 day period indicated satisfactory tolerance of the KY diet with adequate weight gain. The weight gain and stool output was however, higher in lactose intolerant children, with the worst results seen with KY and buffalo milk combination. While lactose intolerant children with PD do have higher rates of therapeutic failure, our data indicates that a traditional diet and yogurt combination can be used satisfactorily for nutritional rehabilitation in over 80% of such children.

Bhutta ZA, Nizami SQ, Thobani S, Isani Z.

We evaluated factors associated with mortality among a cohort of malnourished children with persistent diarrhoea (PD) admitted for nutritional rehabilitation with a defined rice-lentil (Khitchri) and yoghurt diet. Of 302 children consecutively admitted with PD, 13 (4%) died, mostly (62%) within 72 h of admission. Univariate analysis of risk factors at admission associated with mortality indicated significantly increased risk of death with severe stunting [relative risk (RR) 3.1, 95% confidence interval (CI) 1.1-9.0], hypoalbuminaemia (RR 4.3, 95% CI 1.5-12.3), stool frequency > 12/day (RR 6.0, 95% CI 2.0-17.6), stool volume > 100 g/kg/day (RR 10.7, 95% CI 3.0-37.6) and severe dehydration (RR 7.5, 95% CI 2.6-21.8). Children who died also had comparatively shorter duration of diarrhoea at admission, and were also associated with higher rate of bacteremia at admission (Fisher's exact test P < 0.01). The logistic regression model evaluating multivariate risk of mortality identified weight-for-age z-score and sepsis as significant risk factors. Our data suggest that severe malnutrition and sepsis are associated with significantly increased...
risk of mortality in children with PD. Stringent screening for infections and recognition of subgroups with severe malnutrition and severe diarrhoea may improve screening and case management strategies for this disorder.


The recovery pattern and outcome were analysed in 261 consecutive children (age 6-36 months) with persistent diarrhoea who underwent inpatient nutritional rehabilitation with a rice-lentil (Khitchri) and yoghurt-based diet. Overall, 217 (83%) recovered successfully, as judged by a reduction in stool output and weight gain for a consecutive 3 days. Failures were more commonly febrile at admission [odds ratio (OR) 2.3, 95% confidence interval (CI) 1.1-4.8] and a greater number had culture-proven sepsis (Fisher’s exact test, p < 0.001). Logistic regression analysis identified significantly increased risk of treatment failure with several admission characteristics, including stool frequency > 5 days (-1) (OR 2.9, 95% CI 1.6-5.2), vomiting (OR 2.5, 95% CI 1.1-5.7) and sepsis (OR 2.8, 95% CI 1.1-7.5). Survival analysis revealed significantly longer time-to-recovery among children with stool frequency > 5 days (-1) at admission (p < 0.001), suspected sepsis necessitating intravenous antibiotics (p < 0.001) or oral candidiasis (p < 0.05). These findings suggest that severity of diarrhoea and coexisting systemic infections are key determinants of the response to nutritional therapy in children with persistent diarrhoea.

Epidemiology of Prolonged Diarrhea in Lima

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Although breast-feeding is widely accepted as important for infant health, its benefits during the second year of life have been questioned. We analyzed data from 107 breast-fed and weaned Peruvian children living in a periurban community to determine whether breast milk contributed to improved linear growth between 12 and 15 mo of age. Breast-feeding frequency was self-reported; intakes of complementary foods and animal products were estimated from a food-frequency survey. Multivariate-linear-regression analysis was used to predict the length of the children at 15 mo of age. Determinants of length included length and weight-for-length at 12 mo of age (US National Center for Health Statistics standards), interval between 12- and
15-mo measurements, breast-feeding frequency, incidence of diarrhea, and intakes of complementary and animal-product foods. Complementary foods, animal-product foods, and breast milk all promoted toddlers' linear growth. In subjects with low intakes of animal-product foods, breast-feeding was positively associated ($P < 0.05$) with linear growth. There was a 0.5-cm/3 mo difference in linear growth between weaned toddlers and children who consumed the average number of feedings of breast milk. Linear growth was also positively associated with intake of animal-product foods in children with low intakes of complementary foods. The negative association between diarrhea and linear growth did not occur in subjects with high complementary-food intakes. When the family's diet is low in quality, breast milk is an especially important source of energy, protein, and accompanying micronutrients in young children. Thus, continued breast-feeding after 1 y of age, in conjunction with feeding of complementary foods, should be encouraged in toddlers living in poor circumstances.


BACKGROUND: Child feeding recommendations include breastfeeding beyond 12 months, however, some researchers have reported increased rates of malnutrition in breastfed toddlers. A negative association between growth and breast-feeding may reflect reverse causality; that is, the outcome (growth) is a determinant of the predictor (breastfeeding), and not vice versa. We examined this question with data from 134 Peruvian toddlers.

METHODS: A linear regression analysis predicted length at the age of 15 months by length at 12 months, study interval, and 12-14.9-month breastfeeding, complementary food intake, and diarrhoeal incidence. This analysis defined the association between breastfeeding and linear growth. To elucidate the direction of the effect between breastfeeding and linear growth, logistic regression was used to predict the probability of weaning by the end of 14 months. Determinants included weight-for-age (W/A) at 12 months, complementary food intake at 9-11.9 months, and change in diarrhoeal incidence between 9 and 14.9 months.

RESULTS: There was a significant ($P < 0.01$) interaction of breastfeeding, diarrhoeal incidence, and complementary food intake on length at 15 months. Increased breastfeeding was associated with a 1.0 cm decrease in length gain when dietary intake was low and diarrhoeal morbidity was high, implying that breastfeeding is harmful. The logistic analysis, however, demonstrated that the risk of weaning decreased only when W/A and dietary intake were low and diarrhoeal morbidity was high.

CONCLUSIONS: The negative association between breastfeeding and linear growth reflected reverse causality. Increased breastfeeding did not lead to poor growth; children's poor growth and health led to increased breastfeeding. Children's health must be considered when evaluating the association of breastfeeding with anthropometric outcomes.
Physicians' Practices Related to the Treatment of Childhood Diarrhea in Two Areas of Peru, With Special Emphasis on Nutritional Aspects of Therapy

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Huttly SR, Lanata CF, Yeager BA, Fukumoto M. del Aguila R, Kendall C.  

Sanitary disposal of feces is vital to combat childhood diarrhea, and its promotion is key to improving health in developing countries. Knowledge of prevailing feces disposal practices is a prerequisite to formulation of effective intervention strategies. Two studies were conducted in a shantytown area of Lima, Peru. First, information was gathered through in-depth interviews with mothers and structured observations (4 hours) of young children and their caretakers. Data on beliefs and practices related to feces disposal behaviors were obtained. Excreta were deposited by animals or humans in or near the house in 82% of households observed. Beliefs about feces depended on their source and were reflected in how likely the feces were to be cleared. While 22% of children aged > or = 18 months were observed to use a potty for defecation, 48 defecated on the ground where the stools often remained. Although almost all children were cleaned after defecation, 30% retained some fecal matter on their body or clothes. Handwashing after the child's defecation was extremely rare for both children (5%) and caretakers (20%). The hygienic disposal of feces poses problems in this type of community. Nevertheless existing practices were found that show promise for promotion on a wider scale, including greater use of potties.

Lanata CF, Huttly SR, Yeager BA.  

Abstract not available.
Some Determinants of Outcome of Diarrhea in an Urban Slum in Nairobi, Kenya

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Nazrat M. Mirza, Laura E. Caulfield, Robert E. Black, and William M. Macharia.

To identify child feeding behavior and household hygiene practices that are risk factors for prolonged diarrheal illness, a longitudinal community study was conducted over a 14-month period among 920 children aged 3-37 months who lived in an urban slum settlement in Nairobi, Kenya. Morbidity surveillance was done by home visits every third day in the absence of diarrhea and daily during diarrheal illness until termination of the episode. In-home observations were made to characterize maternal hygiene, cooking, and child feeding practices. Overall, 1,496 episodes of diarrhea were detected. The average diarrheal incidence was 3.5 episodes/child-year, and the incidence of diarrhea>14 days was 3 episodes/100 child-years. Cox regression was used to examine the independent effects of covariates on time to recovery from a diarrheal episode. Adjusted behavioral factors that were observed to influence recovery from diarrhea included: uncovered water containers (rate ratio (RR) = 0.77, 95% confidence interval (CI) 0.64-0.94); giving no fluids (as opposed to oral rehydration solutions (ORS)/sugar salt solutions (SSS)) (RR=1.42, 95% CI 1.14-1.77); and administration of diluted cow’s milk during the first 3 days of an episode (RR=1.23, 95% CI 1.00-1.52). These associations remained significant after adjusting for diarrheal severity. The authors recommend, among other measures, improvement of water storage and promotion of continued feeding with cereal-milk mix during diarrhea.
Dietary Management of Severely Malnourished Infants and Children with Chronic Diarrhea: A Comparative Study of Three Different Formulas

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Nurko S, Garcia-Aranda JA, Fishbein E, Perez-Zuniga MI.  

OBJECTIVE: To evaluate the efficacy of a chicken-based diet for the treatment of persistent diarrhea in severely malnourished children.

STUDY DESIGN: Prospective, randomized, double-blind study that compared a chicken-based diet with elemental (Vivonex) and soy (Nursoy) diets. Hospitalized children with third-degree malnutrition and persistent diarrhea, aged 3 to 36 months, were included. Diets were isocaloric and given nasogastrically at 150 ml/kg per day in progressively increasing concentrations.

RESULTS: Fifty-six children were included (18 received Vivonex, 19 Nursoy, 19 chicken). They had a mean age of 6.4 ± 4.4 months, a mean weight of 3604 ± 1232 gm, and a mean weight-for-age percentage of 51.4% ± 7.2%. Sixty-four percent had associated conditions on admission to the hospital. Forty-one children (73.2%) were successfully treated (13 Vivonex, 13 Nursoy, 15 chicken). There were no differences in diarrheal outcomes, and all groups had significant weight gain. Failure was independent of the diet and was associated with the presence of infection on admission. There was a significantly higher nitrogen balance in the children from the chicken group (358.2 ± 13 mg/kg per day) than in those receiving Vivonex (226.6 ± 61) or Nursoy (291.4 ± 111.6; p < 0.05) groups.

CONCLUSIONS: The chicken-based diet was as effective as Vivonex or Nursoy. It is well tolerated, inexpensive, and widely available and thus represents an effective and inexpensive alternative to the treatment of severely malnourished children with persistent diarrhea.
To identify possible risk factors for persistent diarrhoea, 307 children with acute diarrhoea presenting at the University College Hospital, Ibadan, Nigeria over a 10-month period from July 1993 to April 1994 were followed up prospectively until the resolution of the illness. The children were aged 6-60 months. In 36 (11.7%) of them, diarrhoea became persistent (i.e. lasted more than 14 days). The hospital frequency of 11.7% of persistent diarrhoea is, as expected, higher than the figures from previous community-based studies of diarrhoea in Nigeria. The major factor associated with persistent diarrhoea was poor nutritional status. Mean z scores of weight-for-height and weight-for-age were significantly lower in the persistent diarrhoea group, while mean z scores of height-for-age were similar in the two groups. The frequencies of occurrence of under-nutrition, marasmus and kwashiorkor were also higher in the persistent diarrhoea group. Therefore, in common with studies from other regions of the world, malnutrition is an important risk factor for persistent diarrhoea in this group of Nigerian children. The implication of these findings is that reduction in the prevalence of malnutrition may be associated with reduction in the proportion of acute diarrhoeal episodes that eventually progress to persistent diarrhoea.
Promotion of Breastfeeding as Intervention for the Control of Diarrhea Among Infants

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Breast-feeding Promotion in a Diarrhoea Programme in Rural Communities

Breast-feeding promotion is an important intervention for the control of infant diarrhoea. This study assesses the impact of a breast-feeding counseling programme on the prevalence of exclusive breast feeding in rural communities in Nigeria. Mothers attending primary care facilities because their infants had acute diarrhoea were randomized into two groups. The study group (n=82) received individual, focused breast-feeding counseling, while the controls (n=79) had routine advice for diarrhoea. Both groups were monitored and followed with home visits to determine infant-feeding practices. The results showed marked increases in exclusive breast-feeding prevalence for the intervention group at day 7 (49% vs. 6% control; p<0.0001) and day 21 (46% vs. 8%; p<0.0001). Moreover, diarrhoea re-occurrence at day 21 was less in the intervention group (12%) than controls (18%). It is concluded that focused breast-feeding counseling can increase exclusive breast feeding and reduce the prevalence of diarrhoea in rural communities.

Davies-Adetugbo AA.

Child survival strategies include prolonged and intensive breastfeeding, together with its early initiation, and breastmilk only for the first six months of life. This paper reports on local knowledge and attitudes of breastfeeding and the sociocultural factors that shape its practice in poor rural Yoruba communities of Southwestern Nigeria. The study has conducted 10 focus group discussions among homogeneous groups of grandmothers, pregnant women, lactating mothers, husbands, and community health workers, and a questionnaire survey of 256 third trimester pregnant women. All women in these communities breastfeed their infants on demand, and for up to two years, because breastmilk is universally accepted as the best food for babies, and breastfeeding spaces births. Prelacteal feedings of water herbal infusions and ritual fluids are the norm, and breastmilk is supplemented, from birth, with water and teas. Exclusive breastfeeding is considered dangerous to the infant: the baby has an obligatory requirement for supplementary water to quench its thirst and promote its normal development, and for herbal teas that serve as food and medi-
 Colostrum is discarded because it is dirty, "like pus," and therefore potentially harmful to the infant, although 24% of the survey sample would give it to their babies. Expressed breastmilk is suspect as it can get contaminated, poisoned or bewitched. Complementary foods are introduced as early as two months because of perceived lactation insufficiency. The commonest supplement is a watery maize porridge of low nutrient density. Breastfeeding can also be dangerous, as toxins and contaminants can be passed to the infant through breastmilk. The most serious conflict with the WHO/UNICEF recommendations is the lack of local credibility of exclusive breastfeeding. According to local knowledge, the early introduction of water, herbal teas, and of complementary foods is designed to enhance child survival, while these are supposed to do the exact opposite by the WHO/UNICEF rationale, by exposing the infant to contaminants early, thereby increasing diarrheal morbidity and mortality. Child survival interventions need to address this conflict.

Comparative Study of the Perception and Treatment of Diarrhea Among the Three Major Ethnic Groups in Borno State, Northeastern Nigeria

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Awareness and knowledge of oral rehydration therapy (ORT) and preparation abilities of salt-sugar solution (SSS) were investigated by means of focus group discussions and complemented by a structured questionnaire survey of mothers in rural and urban areas of north-eastern Nigeria. ORT awareness was high with some intra-regional variations. Perception of ORT function was, however, grossly unrealistic, with a third to four-fifth of mothers expecting ORT to stop diarrhoea. At least one quarter of mothers lacked adequate SSS preparation abilities and the materials and ingredients required for its preparation. Re-evaluation of the content and method of imparting health education messages in ORT promotion is recommended. Such messages should emphasize the function of ORT. It is also recommended that standardized cups for water, salt and sugar measurements be provided to households as a ready means of ensuring the correct preparation of SSS in the home-based management of diarrhoea.
Antibiotic Susceptibility Patterns of Bacterial Agents of Diarrhea in Urban and Rural Areas of Nigeria

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Obi CL, Coker AO, Epoke J, Ndip R.

A total of 2,400 stool samples comprising 1,200 from patients with diarrhoea (600 each from urban and rural area) and 1,200 similarly divided controls were obtained from school children and clinic attendants of government and private clinics around three designated study centres of Edo, Lagos and Cross river states, Nigeria. These were screened for the prevalence of bacteria that could cause diarrhoea. Diarrhoea cases in urban areas had a high prevalence rate for Campylobacter spp. (28%), followed by enteropathogenic Escherichia coli (22%), Salmonella spp. (17%), Shigella spp. (14%), Aeromonas spp. (5%), and Yersinia enterocolitica (4%), whereas in rural areas E. coli was the most frequently encountered pathogen (18%), followed by Salmonella spp. (16%), Aeromonas spp. (15%), Shigella spp. (9%), Campylobacter spp. (8%), and Plesiomonas shigelloides (8%). A similar distribution but with lower rates was noted for controls in both urban and rural areas, however, no P. shigelloides was isolated. Results highlight a possible difference between the prevalence of enteric bacteria in rural and urban areas and reveal the strong association of Aeromonas and Plesiomonas species with cases of diarrhoea in Nigeria.

Evaluation of Dowdo as a Diet for Children with Acute Diarrhoea

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Jan A, Rafi M, Mustafa S, Rasmussen ZA, Thobani S, Badruddin S.

Appropriate feeding practices have an important impact on diarrhoeal disease management in developing countries. We evaluated the efficacy of feeding dowdo, a wheat-milk gruel, traditionally used as a weaning food in the Northern Areas of Pakistan. Dowdo was compared with khitchri, a rice-lentil mixture, in acute watery...
diarrhoea through a randomized trial. Seventy-six children between 6 and 36 months of age, with acute watery diarrhoea of less than seven days were recruited. After rehydration with standard World Health Organization (WHO) glucose-based oral rehydration solution or intravenous Ringers lactate, patients were randomly assigned to either diet group. Dowdo and khitchri were found to be equally effective in terms of stool frequency and output, duration of diarrhoea, weight gain and duration of hospitalization. The results indicate that feeding dowdo was as effective as khitchri in children with acute diarrhoea. Additionally, acceptability of dowdo was better than khitchri. It is recommended that dowdo be used for nutritional management of diarrhoeal disease in children in the Northern Areas of Pakistan.

**A Study of the Efficacy of Cereal-Based (Sagodana) ORS Solution in Children with Acute Diarrhea**

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Ibrahim S. Isani Z.  

This study was carried out to compare the efficacy of a cereal based ORS (prepared with 50 G of sagodana (cereal), 3.5 G/L sodium chloride, 1.5 G/L potassium chloride, 2.9 G/L trisodium citrate) with rice based oral rehydration solution (using same amounts of rice and electrolytes) for treatment of diarrhoea. One hundred and twelve children aged 3 months to 2 years with watery diarrhoea of less than 5 days duration with mild to moderate dehydration and no sepsis, were included in the study. The amount of ORS intake, stool volume and frequency were similar in both groups. Clinical success was seen in 79% of rice ORS group and 81% in sagodana group. Both can be used as a cereal based ORS in the management of acute diarrhoea in communities where it is culturally accepted and used as a weaning diet.
Drug Prescribing Practices in Childhood Diarrhea

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S.Q. Nizami, I.A. Khan, Z.A. Bhutta.  

To assess amount of drug overuse we studied drug prescribing for common childhood problems by 65 general practitioners (GPs) and 29 paediatricians. A total of 2433 encounters between GPs or paediatricians and children under five years of age were observed. The presenting complaints were fever in 18%, cough in 9%, both fever and cough in 21%, vomiting in 20% and diarrhoea in 41% of encounters. Antibacterials were prescribed in 49% of encounters, analgesics and antipyretics in 29%, and antiemetics in 8% and injectables in 15%. Antidiarrhoeals were prescribed in 41% encounters with children reported to have diarrhoea. Ampicillin and cotrimoxazole were the two common antibacterials prescribed by both GPs and paediatricians. Antibacterials were prescribed in significantly larger number of encounters with GPs than in those with paediatricians. Mean encounter time of patients with GPs was 3.4 ±2.7 minutes and with paediatricians, 9.7±4.1 minutes.

Promotion of Exclusive Breastfeeding and Its Effect on Diarrhea Morbidity

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Akram DS, Agboatwalla M, Shamshad S.  

A community-based intervention study was conducted in a katchi abadi (slum area) of Karachi with the objective of improving optimal breast feeding practices, including promotion of exclusive breast feeding and giving of colostrum to newborns. Sixty-seven mothers were registered in the intervention group and 53 in the control group. Health education to promote exclusive breast feeding was provided in the form of flip-charts, videos and photographs. Sixty-six percent mothers in the control group gave prelacteal feeds as compared to 31% in the intervention group (P< .0001). Colostrum was given by 97% of mothers in the intervention group and
3% in the control group. Majority (94%) of intervention group mothers continued exclusive breast feeding till four months of age against 7% in the control group. It was concluded that health education programmes in the antenatal period as well as after birth can promote exclusive breast feeding practices.

**Evaluation of Diarrhea Training Units (DTUs)**

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**Ibrahim S, Isani Z.**

Diarrhoeal diseases are a major contributory factor for high infant mortality and morbidity in Pakistan. To overcome this, Government of Pakistan launched a National Programme for Control of Diarrhoeal Disease. A Diarrhoea Training Unit (DTU) was established at the National Institute of Child Health, Karachi, where apart from proper case management, 17 training workshops were held between July, 1989 to July, 1991. Eighty-five doctors from various facilities in Sindh were trained in proper management of diarrhoea and establishment of Oral Rehydration Therapy (ORT) units in their regions.

Evaluation of DTU training, assessment of the knowledge of trained doctors, case management and function of ORT Units were done between September, 1992 and October, 1993. Two teams each consisting of a doctor and a lady health visitor, visited 30 such facilities. An observation check list was used for assessing the ORT unit and diarrhoea case management and a test questionnaire for the knowledge of facility physician and paramedic. Of the 29 facilities, 17 had DTU trained doctors. ORT corner had been established in 26, weighing scales were used in 21, record keeping in eight and soap and water was available for hand washing in seven centres. The presence of untrained doctors provided an opportunity to compare the two groups. Dehydration assessment was fairly good, weight was recorded in fewer cases than desirable, case management was similar in the two groups, except for infrequent use of antibiotics by the trained group. Prevention was poorly advised. Physicians’ knowledge in both groups was similar but deficient in advising the use of ORS, feeding in diarrhoea and nutritional assessment. The trained ones had significantly better knowledge about drugs and this was reflected in their case management. Paramedic case management was similar to those in doctors. The study thus showed positive and beneficial effects of training.
Assessment of Doctors Trained at Diarrhea Training Unit, Rawalpindi General Hospital, Rawalpindi

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Kundi MZM, Anjum M, Ahmad I.

To promote the use of oral rehydration therapy (ORT), a training programme was launched by the Pakistan National Programme for Control of Diarrhoeal Disease (CDD) by establishing the Diarrhoea Training Units (DTUs). Physicians trained at DTU were designated to establish functioning oral rehydration therapy (ORT) corners at their health centres and train health workers in delivery of facilities on standard diarrhoea case management. The study was designed to evaluate the functioning of ORT corners three years after their establishment. The study revealed that ORT corners have failed to achieve the main objectives of the DTU programme. Twenty-four out of 49 ORT corners were non-functional after three years of their establishment, mainly due to frequent transfers of trained staff. In 22 ORT corners evaluated, performance of health professionals was far from satisfactory, 19 out of 22 doctors were found to have inadequate performance in diarrhoea management and only 3 out of 7 LHVs performed adequately. LHVs could not consistently deliver health education messages to mothers. There seems to be a lack of interest and willingness to participate actively, as more than 50% of both doctors and LHVs did not consider ORT work as their job. We conclude that the ultimate objectives of improved and appropriate diarrhoea case management through ORT corners have not been achieved.

Study of Current Practices and Factors Affecting the Management of Acute Watery Diarrhea in Children Below Five Years by General Physicians in Lahore

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Choudhry AJ, Mubasher M.

Two hundred sixty-two randomly sampled general physicians of Lahore were interviewed to study the current practices and factors affecting the management of
acute watery diarrhoea (AWD) in children below 5 years of age. Among the physi-
cians, 19% prescribed ORS alone, 61% ORS with some drug, 15% drugs alone and
5% increased fluid intake only. Physicians in government sector, recent graduates and
those trained in a paediatrics unit prescribed more on the WHO guidelines (p<0.05).
Attending a diarrhoea training unit (DTU) course, reading WHO guidelines for
management of diarrhoea and total number of patients seen daily had no significant
effect on prescribing practices. Two hundred fifty-five (97%) physicians thought that
majority of other physicians prescribed drugs for the management of acute watery
diarrhoea to satisfy the mothers of the children, their belief in the effectiveness of
drugs and competition in practice.

Impact of Appropriate Breastfeeding Practices on Diarrhea Morbidity and
Nutritional Status of Infants

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Badruddin SH, Inam SNB, Ramzanali S, Hendriks K.
Constraints to adoption of appropriate breast feeding practices in a squatter settlement in Karachi, Pakistan. JPMA 1997; 47(2):63-68.

Appropriate breast feeding practices (ABFP) are important for successful lacta-
tion. Constraints to adoption of ABFP by mothers in a squatter settlement in
Karachi, Pakistan are reported. One hundred and two mother-infant pairs were
followed from birth to 16 weeks of age. Eighty-seven infants received prelacteal feeds
of honey as a quasi-religious ritual, 16 received ghutti for "cleansing of stomach",
other prelacteal feeds were given as substitutes for breast feeding. Twenty nine moth-
ers initiated breast feeding within 4 hours of birth. Supplemental water was given to
53 infants; major reasons being mothers' perception of thirst and diarrhoea in the
infant. Supplemental milk was given to 24 infants. Insufficient milk and work load
of mothers were main reasons for supplementation. Home remedies were given in 36
instances for prevention/treatment of indigestion or colds. Quasi-religious ritual of
giving honey, perception that child birth was a major stress and early initiation of
breast feeding adds to that stress, fear of dehydration and perception of insufficient
breast milk were the major constraints to adoption of appropriate breast feeding
practices.
Assessment of Nutritional Beliefs and Practices in Pregnant and Lactating Women: A Community Study

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Mahmood S, Atif MF.
Assessment of nutritional beliefs and practices in pregnant and lactating mothers in an urban and a rural area of Pakistan. JPMA 1997;47(2):60-62.

Nutritional beliefs and practices in 100 pregnant and 100 lactating women were assessed in an urban and rural area of Lahore. A structured questionnaire was used for the purpose. Seventy seven percent of women and 54% of their husbands were illiterate, 50.5% belonged to a family with a per capita income of more than Rs.300.00 per month, 52.5% had 7 or more family members and 56% were living in nuclear families. The age of mothers, type of family, literacy, family income, parity and gravidity had not significantly influenced the nutritional beliefs and practices, only urban and rural differences were statistically significant. Eight-four percent of mothers had knowledge that diet should be changed by increasing, adding or avoiding some special food items in the diet during pregnancy and lactation, but only 65.5% practiced them. The reasons for this deficient knowledge and practice of dietary intake are lack of nutritional knowledge and poor economy. However, this can be overcome by improving nutritional knowledge and dietary practices of population in general and vulnerable groups in particular through medical and MCH services on the use of locally available low cost nutritious foods and to avoid undue food restrictions. Improvement of applied nutritional knowledge of medical professionals is also necessary.

A Study of Pakistani Mothers’ Knowledge and Management of Acute Respiratory Infection (ARI)

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Hussain W, Mahmood N, Anwar M, Maqbool S.

Home treatments are important in the management of acute respiratory infection (ARI). In order to examine how urban mothers in Lahore managed ARI, a study was carried out within 1 - Km radius of a teaching hospital. A total of 50 mothers
who had at least one child aged 2 months - 5 years with an ARI from each of three settings - a lower class locality, a middle class locality and the outpatient department of the hospital were interviewed during the winters of 1992-93. A substantial proportion of mothers, particularly those from the lower class locality (44%), did not use home treatment for acute respiratory infection. The majority of mothers indicated that they would not use home treatment if their child had an ARI in the future. The importance of home treatment has to be introduced into the community probably by programmes conducted by health professionals.

Role of Community Health Workers (CHWs) in Detection and Management of Pneumonia and Determination of Cost and Time Savings by the Community and Health Care System

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This community based, case management intervention study was done to assess the effectiveness of Community Health Workers (CHWs) in case detection and management of pneumonia in children under five years of age. Twenty-two volunteers (school teachers and students) were selected as CHWs from Rehri village, in Sindh, Pakistan and trained on World Health Organization (WHO) recommended National Acute Respiratory Tract Infection (ARI) guidelines at the Department of Paediatrics, Dow Medical College, Civil Hospital, Karachi. The CHWs had no prior health education. The intervention was the use of CHWs to detect and manage pneumonia in children under five years of age in Rehri village. Two medical officers supervised the post-training activities of CHWs in the village during the study period. Between December, 1992 and May, 1993, 442 episodes of pneumonia (very severe disease 10, severe pneumonia 54 and simple pneumonia 378) were detected and managed by trained CHWs. The medical officers agreed with the CHWs for classification and treatment in 356 (81%) cases. This study suggests that in areas where there is a shortage of trained health care professionals, educated community members such as school teachers can be trained to detect and manage pneumonia in their community.
Assessment of Breastfeeding and Weaning Beliefs and Practices Among Mothers Following their Infants to Four Months of Age in an Urban Community of Lahore, Pakistan

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Kulsoom U, Saeed A.
Breastfeeding practices and beliefs about weaning among mothers of infants aged 0-12 months.

Beliefs and practices related to the feeding of 52 infants were assessed in an urban community of Lahore in a longitudinal study through quantitative and qualitative data during their first year of life. Ninety-eight percent mothers started breast feeding within the first week and 54.3% continued until 12 months; the mean age for exclusive breast feeding was 1.08 (±1.109) months; breast feeding was initiated 47.4 (±32.58) hours after birth and prelacteal feeds were given to 94% infants. In 34 infants (65.4%) colostrum was not given. Water was considered essential from the very first day in 55.4% cases. Forty-eight percent babies were put on supplemental bottle feeding during the first week and by five months of age 97% were bottle fed. The most common reason for starting bottle feeding was perceived “insufficiency” of breast milk (71%). Breast feeding was stopped earlier by mothers who were illiterate and poor and had female children. The mean age of initiating supplemental feeding with semi-solid food was 4.4 (±0.99) months. Weaning occurred earlier in infants of the upper socioeconomic class and literate mothers. Working women reported problems in feeding their children exclusively on breast during early infancy. Advice of health professionals was used by 31% mothers, more in the upper socioeconomic group and literate group than in other groups. Health education interventions are needed to promote use of colostrum, exclusive breast feeding and appropriate complementary feeding practices.
Community Perceptions of ARI in Urban Slums of Karachi

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Childhood pneumonia continues to be the second highest contributor to childhood morbidity and mortality in all ethnic groups in Pakistan. Information on community perceptions and management is largely limited to the Punjabi populace. In this study, ethno-specific illness terminologies, recognition and severity indicators and resort to treatment options for childhood pneumonia are explored among the two main ethnic groups in Sindh. Results are based on focus group discussions with 90 caretakers and 16 case history interviews. The findings indicate that pneumonia recognition is almost universal. The main recognition and severity indicator was pasli chalna (chest indrawing) followed by signs and symptoms relating to the quality of breathing and presence of high fever, lethargy and anorexia. Recognition of rapid breathing was low and mostly associated with fever. Exposure to thand (cold) through a variety of mechanisms was perceived to be the dominant causal model. The concept of contagion was virtually non-existent. Despite this, belief in efficacy of allopathic care was very high. Most caretakers reported seeking outside care within one to three days of the onset of symptoms. However, unrealistic expectations of cure often led to change in physicians and treatment regimen, if no improvement was observed by the second day. On the other hand, the quality of care provided by the physicians (both licensed and unlicensed) left much to be desired. Female autonomy and mobility did not appear to be a major constraint in seeking outside care other than for hospitalization. Implications of these findings for the national acute respiratory infections control programme and future research are discussed.
Impact of Iron Supplementation on Infant Morbidity and Growth Pattern in North West Frontier Province, Pakistan

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Iron deficiency anaemia is a serious problem among Pakistani children. Pre-intervention haematological status of children under two years was assessed as part of a double-blind, randomized controlled community-based study conducted in two semi-urban areas of Peshawar. The primary objective was to assess the impact of iron deficiency anaemia and iron intervention on growth and morbidity. Three hundred and twenty children who met the criteria of a “healthy child” were recruited for the study. Blood samples were drawn from 275 children for haemoglobin (Hb) and serum ferritin (SF) analyses. The children were classified as anaemic (Hb<11g/dl); iron deficient (SF<12ng/ml) and iron deficient anaemic (Hb<11g/dl and <12ng/ml). Ninety percent of the children were anemic, 67% iron deficient and 63% iron deficient anaemic. Anaemia was more prevalent in boys who had significantly lower Hb and SF values than girls. The magnitude of anaemia in these children tended to increase with age. The study demonstrates that iron deficiency is the predominant cause of anaemia (69%) in children under two years. Minimization of iron deficient anaemia should be a public health priority in order to prevent suffering of children and avert the associated cognitive and physical deficits in child development.
Clinical Diagnosis and Case Management of Children with ARI Presenting to General Practitioners

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Iqbal I, Pervez S, Baig S.

A knowledge, attitude and practices (K.A.P.) survey was conducted among doctors working as general practitioners (GP) in Multan, for diagnosis and management of acute respiratory infections (ARI) in children under five years of age. GPs in Multan were not familiar with national ARI control programme and rational drug use guidelines. They rarely asked about symptoms describing severity of disease while taking patient histories and did not look for signs of severe pneumonia during physical examinations. Most patients diagnosed as URTI (upper respiratory tract infection) received oral antibiotics and those with pneumonia received injectable antibiotics. Other drugs prescribed included cough syrups, antihistamines and antipyretics. The average number of drugs prescribed per patient was 3.4. The doctors were deficient in providing home care advice for sick children to the caretakers. Average time spent by doctors on each patient was two minutes and twenty-three seconds. A combination of biomedical and social factors help to perpetuate this irrational prescribing behaviour of the GPs. Continuing education programmes for doctors in general practice about ARI management in children and rational use of drugs and health education of the public may improve the current prescribing practices.
A Randomized Controlled Trial of Zinc Supplementation in Children with Persistent Diarrhea: Impact on Diarrhea and Nutritional Status

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Bhutta ZA.
The role of zinc in health and disease – relevance to child health in developing countries, JPMA 1997;47(2):68-73.

The last few years have witnessed the earnest recognition of the vital role of micronutrients in human health. The pioneering work by Summers et al in Indonesia on the impact of vitamin A supplementation in young children with respiratory infections, has led to a host of experiments evaluating the impact of both clinical and subclinical deficiency of micronutrients on child survival. Of the micronutrients, in addition to vitamin A and iron, zinc stands out as the one with the greatest potential public health impact. Although, compared to other micronutrients, zinc status is considerably more difficult to assess in humans, its biological effects in malnourished children are diverse, ranging from a profound impact on growth, to a significant role in regulation of immunity. This review will focus on current concepts of the biological effects of zinc, with special reference to its potential role in the paediatric age group in Pakistan.

Assessment of Maternal Risk Factors for Birth of Small Gestational Age Babies in Hospital-Based Urban Populations.

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Arif MA, Qureshi AH, Jafarey SN, Alam SE, Arif K.

OBJECTIVES: We assessed the significance of material sociocultural status within the family as a risk factor for low birth weight-small for gestational age (LBW-SGA) births using a novel scoring system and also isolated related medical risk factors.

METHODS: A prospective matched pairs case control study of 396 LBW-SGA infants (cases) and 396 term, appropriate for gestational age infants (controls) was set up.
RESULTS: Low maternal sociocultural status (p=0.02) was significantly associated with LBW-SGA births as were nonregistration for antenatal care (p=0.001), maternal weight at delivery <50kg (p<0.0001), antepartum hemorrhage/preeclampsia (p<0.01), primigravidity and previous small baby (p<0.0001). Other risk factors included birth interval <24m (p<0.001) and poor maternal or paternal education (p<0.05). Conditional logistic regression identified maternal weight at delivery <50kg (OR 4.8, 95% C.I. 3.0-7.6), lack of antenatal care (OR 2.0, 95% C.I. 1.4-2.9), antepartum hemorrhage/preeclampsia (OR 4.3, 95% C.I. 1.7-10.8) and previous small baby (OR 4.3, 95% C.I. 2.1-8.9) as independent risk factors.

CONCLUSIONS: Low sociocultural status of the mother within the family is significantly associated with having a LBW-SGA baby. Further studies are warranted to study this risk factor.

Editorials


According to the UNICEF State of the World's Children 1996 report, 137 Pakistani children out of every 1000 born will die before their fifth birthday. Though the under-five mortality rate has declined from over 221 deaths per 1000 live births during the period 1960 to 1993, managing childhood illnesses remain as a major problem for the medical practitioners of Pakistan. With an estimated 22 million children less than five years of age, and 60 million under age 16, pediatrics and adolescent health is a major component of medical care provided in both the public and private sector facilities. Child survival activities, including immunization, integrated case management of the major childhood killers (diarrhea, pneumonia, and malaria), and nutrition support for the estimated 40% of preschool age children who are underweight (World Health Report, WHO, 1996), draw a substantial portion of the health sector resources. Child survival activities also command a substantial component of the international donor community's financial and technical resources.

The solutions to these major problems need to be found within Pakistan. Though external knowledge and technology may be useful, the key to addressing local problems is the strengthening of national capacities in clinical care, prevention activities, and applied health research. Given the size of the paediatric population and the extent of child health problems, it is a special pleasure to work with the Journal of the Pakistan Medical Association (JPMA) to produce two special issues highlighting child health research. The two issues represent the research efforts of a diverse group of Pakistani scientists from all areas of the country drawn together into a research network by the Applied Diarrheal Disease Research (ADDR) Project at Harvard University. The sixteen articles presented in this issue (and the companion special issue to follow) are the single largest collection of research work to date by Pakistani scientists on the common pediatric ailments of diarrhea, pneumonia, and
malnutrition. The JPMA and the research scientists believe the information generated from this multiple year research effort will serve to improve the health of the children, if it is given the broadest distribution among the medical community of Pakistan.


Two special issues of the Journal of the Pakistan Medical Association (JPMA) focusing on child health are an attempt to make applied research more accessible to policy makers and practitioners. This issue, focusing on acute respiratory infections and malnutrition in Pakistani children, is a companion special issue to the previous JPMA issue that focused on diarrhoeal disease and prescribing practices. The two issues represent research from a geographically diverse group of Pakistani scientists drawn together into a research network by the Applied Diarrhoeal Disease Research (ADDR) Project of Harvard University. Strengthening national capacity to conduct high quality research that is relevant for health policy development is important for Pakistan. It is equally important, however, that research results translate into improved health policies, health programmes and clinical practice.

The work of the research teams presented in this issue (and the companion special issue) represents a two to three years investment by highly motivated professionals committed to the goal of improving child health.
OTHER ARTICLES


Duggan C, and Nurko S.
"Feeding the gut": The scientific basis for continued enteral nutrition during acute diarrhea. The Journal of Pediatrics 1997;12;801-808.

We review the laboratory and applied scientific evidence for continued enteral feeding in the face of acute diarrhea in an effort to place this arm of illness management on as firm a foundation as that for ORS… Diarrheal diseases are a significant cause of pediatric mortality in developing countries and in industrialized countries, diarrhea is an important cause of office visits to physicians, hospitalizations and preventable mortality. Therefore, there remain significant incentives to optimize the management of diarrhea. It is now clear that depriving the body of nutrition in general and the gut of enteral nutrients in particular entails a variety of adverse consequences. Optimal nutritional therapy, with continued feeding during illness, should be considered a crucial aspect of diarrhea management.


Hamer D, Simon J, Thea D, Keusch J.

Diarrheal disease remains a leading cause of mortality and morbidity of children in Sub-Saharan Africa, a region where unique geographic, economic, political, sociocultural, and personal factors interact to create distinctive continuing challenges to its prevention and control. Whereas childhood mortality rates from diarrhea are expected to decrease by 30 to 50% in most areas of the world between 1990 and 2000, the decline in Sub-Saharan Africa is estimated to be only 3%. Consequently, approximately 40% of childhood deaths from diarrhea worldwide will occur in Sub-Saharan Africa by the year 2000, although only 19% of the world’s population under the age of 5 years will live in this region. This continuing epidemic deserves sustained programmatic and research attention as international public health moves on to confront newer issues in infectious disease and the changing burdens of disease associated with the demographic transition.

A number of different social, political, and economic factors are present in Sub-Saharan Africa which contribute to the constant morbidity from acute and
persistent diarrhea as well as intermittent epidemics of cholera and dysentery common to this region of the world. Morbidity and mortality from childhood diarrhea, whether due to invasive enteropathogens such as Shigella or the more commonplace rotavirus, are further compounded by inappropriate household case management and the frequent misuse of antibiotics. Limited knowledge among many health care providers of the proper treatment of diarrhea also contributes to poor outcomes. The overuse of antimicrobials exerts a selective pressure for the development of antimicrobial resistance throughout the continent. Antimicrobial resistance will increasingly limit practitioner’s ability to successfully manage cholera and dysenteric diarrheas.

This report on childhood diarrhea in Sub-Saharan Africa is intended to provide an overview of the current state of this problem and to highlight key areas for future research. Given the continued importance of diarrheal disease as a major contributor to childhood morbidity and mortality in Africa, there is a clear need for vigorous efforts to implement the new Integrated Management of Childhood Illness (IMCI) approach to improve diarrhea case management. There is also an urgent need to develop interventions to limit the development and spread of antimicrobial resistance among bacterial enteropathogens.

Hamer DH, Gorbach SL:

Hamer DH.

Hamer DH.

Hamer DH.

Hamer DH, Despommier DD:

Hamer DH, Despommier DD:

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Hamer DH, Gorbach SL.
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Appendices
Appendix 1: Contact List

This list contains contact information for the ARCH Project Principal Investigators of the research studies, listed in alphabetical order.

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Appendix 2: ARCH Project Staff

The ARCH Project is a principal component of the child health research program of the USAID Global Bureau, Office of Health and Nutrition's Child Health Research Project.

The ARCH Project core staff is based at the Harvard Institute for International Development (HIID) at Harvard University and is supplemented by faculty from the New England Medical Center. The staff is comprised of public health professionals, both clinical and social scientists, who collaborate as a multi-disciplinary technical assistance team. Through its core staff and consultants, the ARCH Project is able to provide technical support to Ministries of Health, NGOs, research institutions, medical schools, USAID Missions, and USAID cooperating agencies throughout the world. The Gorgas Memorial Institute at the University of Alabama, Birmingham has a sub-contract for specific activities in Central and Latin America.

Principal Investigator and Project Director

Jonathon Simon, M.P.H., is Principal Investigator of the ARCH Project. He has been involved in applied child health research activities at HIID since 1986. He served as Co-Director of the ADDR Project from July 1994 to the Project end in May 1996. Previous to that, he was the ADDR Project Resident Advisor in Islamabad, Pakistan from June 1992 to June 1994. Mr. Simon’s research interests include research capacity strengthening and urbanization and health issues.

Project Scientific Director

Donald M. Thea, M.D., M.Sc., is the Scientific Director of the ARCH Project, where he is particularly involved in studies designed to improve the use of antimicrobials in case management of acute respiratory infections and to revise the current management guidelines of WHO. He is trained in infectious diseases and tropical medicine, and has considerable experience in HIV infection and AIDS. Dr. Thea was the field director of a longitudinal research project in Kinshasa, Zaire, supported by the U.S. National Institutes of Health from 1988-1992, to investigate the causes and significance of diarrheal disease and malnutrition in the progression of HIV infection to AIDS in children and adults. He was subsequently Director of the Maternal and Child HIV Research Program in New York City, a Centers for Disease Control and Prevention supported study of perinatal HIV transmission from 1992 until 1998.

Scientific Staff

Richard A. Cash, M.D., M.P.H., was one of the original developers of oral rehydration therapy at the Cholera Research Laboratory in Bangladesh. He has developed diarrheal disease treatment centers and conducted research on cholera vaccines and vitamin A deficiency. He served as Principal Investigator of the ADDR Project from 1985 – 1996. As Senior Scientific Advisor to the ARCH Project, he brings a wealth of knowledge and experience to the direction of the Project.

Christopher Duggan, MD, M.P.H. is an Assistant Professor at the Harvard Medical School and Director of the Clinical Nutrition Service at Children's Hospital, Harvard's primary pediatric teaching
hospital. He is a pediatric gastroenterologist whose main clinical and research interest is the determination of the nutritional requirements of sick and catabolic infants and children. He has worked on a number of clinical trials - oral rehydration solutions and Vitamin A clinical trials. Dr. Duggan provides technical assistance on a number of projects for ARCH, including 1) the multicenter trials of reduced osmolarity ORS, 2) the ZAP trial (zinc therapy in children with acute malaria). He also co-authored a widely quoted review article on the benefits of continued feeding children with acute diarrhea.

Wafae Fawzi, MD, DrPH is an Assistant Professor of International Nutrition and Epidemiology at the Harvard School of Public Health. His research focuses on the relationships between nutrition, infectious disease, and health outcomes, particularly among women and children. Dr. Fawzi's research is carried out mainly in sub Saharan Africa and the US. He provides technical assistance to the ARCH Project's Zinc and Malaria portfolio (ZAP) providing input into the design, implementation, management, and analyses of the trial.

Patricia L. Hibberd, M.D., Ph.D., provided technical assistance with scientific design and analysis of the clinical research studies. Dr. Hibberd is an expert in the design of multi-center clinical trials and observation studies and assists with manuscript development and performs data analysis for the Project. Dr. Hibberd left the Project in June 1998 to assume the position of Director of Research at the Children's Hospital, Boston in October 1998.

Mary Hilderbrand, Ph.D., was a Project Scientist, she worked with the ARCH Project staff in developing a preliminary set of indicators of research capacity strengthening that integrated research capacity, leadership, and capacity for policy relevance. She carried out research in Pakistan on linkages between applied health research and health policy, looking particularly on diarrheal disease, acute respiratory infection, and iodine deficiency. In connection with that study, Dr. Hilderbrand made a presentation on the role of research in policy in Pakistan at the National Consultation on Health and Development, sponsored by the Pakistan Medical Research Council.

Allan Hill, Ph.D., is the Andelot Professor of Demography at the Harvard School of Public Health. He has extensive and long-standing interests in West Africa and the Arab countries. Much of his work has centered on the development of low cost and sustainable methods for measuring childhood mortality trends and differentials in poor countries. He has worked extensively on fertility and health in the Sahelian countries. Dr. Hill provides technical lead support for the ARCH Project polio portfolio, is a member of the Harvard University Africa Committee and is working with HIID on a series of workshops supported by the Economic Development Institute of the World Bank on health sector reform and reproductive health. Dr. Hill is also engaged in a major effort to understand male and female fertility at the household level in the Gambia and has just completed a book on the health transition in the Sultanate of Oman.

Nancy Pollock, M.S., is a Project Scientist. She developed the ARCH Polio Portfolio and provides technical support planning, implementing, and monitoring the Portfolio's research activities. Ms. Pollock previously worked with the Data for Decision Making Project (DDM) assessing the integration of STD/HIV services into existing health services. More recently, at the National Technical Center, she developed and monitored studies assessing the need and demand for substance abuse treatment among women.

Dennis Ross-Degnan, Sc.D., is an Assistant Professor, at the Harvard Medical School and Harvard Pilgrim Health Care. As a member of the Drug Policy Research Group, he conducts an active program of quantitative and qualitative research on the evolution and impacts of pharmaceutical policies, factors underlying appropriate use of medicines, and behavioral strategies to improve quality of care. Dr. Ross-Degnan is a co-founder of the International Network for Rational Use of Drugs, an active consortium of academics, health managers, and policymakers in Africa and Asia involved in developing and testing interventions to improve pharmaceutical use in developing countries.
Pramila Vivek, M.A., M.Ed, M.S. is the ARCH Project Manager. She also coordinates and provides technical support to the drug use intervention and household behavior portfolios. Prior to this position, Ms. Vivek was a senior policy analyst at the Division of Health Care Finance and Policy and at the Women's Health Unit at the Department of Public Health, Commonwealth of Massachusetts.

Susan Zimicki, PhD was a Project Social Scientist and provided technical support for the household behaviour initiative in 1997 and 1998. Dr. Zimicki previously worked for ICDDR,B and the Center for International Health and Development Communication and has consulted in Africa and Asia for numerous institutions, including WHO, USAID, and UNDP on interventions concerning diarrheal and respiratory disease, immunizations, malaria, and the appropriate use of drugs, and on measurement of mortality and morbidity. Dr. Zimicki left the Project to join the Academy for Educational Development as Research Director of the CHANGE Project in December 1998.

Administrative Staff

Carolin Dudumian, B.S. was the coordinator of scientific workshops, conferences, and travel; and layout and design of Project presentation materials. Ms. Dudumian has left the Project since October, 1998.

Jeremy Deutchman, B.A. provides general administrative support for the Project.

Wendy Mallari, B.A. provides administrative support for the Micronutrients and ARI portfolios and assists in the general administration of the Project.

Deirdre Pierotti, M.A. is the ARCH Project Grants Manager and is responsible for the administrative and financial management of the Project's research grants program. She is also the Group Manager for the HIID Health Office, and has been with HIID since 1995 when she joined the ADDR Project team. Ms. Pierotti has a background in Energy and Environmental Studies and International Relations.

Bénédicte Visonneau, B.A. provides administrative and translation support for the polio, household behavior and drug use intervention portfolios and assists in the general administration of the Project.

Collaborating Institutions

New England Medical Center

Gerald T. Keusch, M.D., Scientific Director (on leave), Professor of Medicine and Chief of the Department of Geographic Medicine and Infectious Diseases, was responsible for the overall scientific progress of the Project, and had lead technical support responsibilities on the acute respiratory infection research portfolio. Dr. Keusch is on leave as Associate Director for International Research, and the Director of the Fogarty International Center at the National Institutes of Health.

Davidson H. Hamer, M.D. is a specialist in infectious diseases, with a particular interest in tropical infectious diseases, who has both laboratory and field experience. He is the Director of the Traveler's Health Services at New England Medical Center. As Project Scientist for the ARCH Project, technical support for the diarrheal disease, respiratory disease, emerging infections, and antimicrobial resistance programs.
Gorgas Memorial Institute of Tropical and Preventative Medicine, University of Alabama

Dr. Sten Vermund, M.D., Ph.D. is the Principal Investigator overseeing the Gorgas subcontract and is responsible for the scientific progress of the Jamaica RTI studies.

Dr. David Briles, Ph.D. is the Project Director and is responsible for the scientific progress of the Latin American ARI studies.
Appendix 3: Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ADDR</td>
<td>Applied Diarrheal Disease Research</td>
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<tr>
<td>AFP</td>
<td>Acute Flaccid Paralysis</td>
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<tr>
<td>ALRI</td>
<td>Acute Lower Respiratory Infection</td>
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<tr>
<td>AMR</td>
<td>Antimicrobial Resistance</td>
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<tr>
<td>APPIS</td>
<td>Amoxycillin Penicillin Protocol International Study</td>
</tr>
<tr>
<td>ARI</td>
<td>Acute Respiratory Infection</td>
</tr>
<tr>
<td>ARCH</td>
<td>Applied Research on Child Health</td>
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<tr>
<td>BASICS</td>
<td>Basic Support for Institutionalizing Child Survival</td>
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<tr>
<td>CBoH</td>
<td>Central Board of Health</td>
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<td>CHR</td>
<td>Child Health Research</td>
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<tr>
<td>COHRED</td>
<td>Council on Health Research for Development</td>
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<tr>
<td>CPG</td>
<td>Clinical Practice Guidelines</td>
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<tr>
<td>CHD</td>
<td>Child Health and Development</td>
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<tr>
<td>DAP</td>
<td>Drug Action Programme</td>
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<tr>
<td>DCC</td>
<td>Data Coordinating Center</td>
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<tr>
<td>DSMB</td>
<td>Data Safety and Monitoring Board</td>
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<tr>
<td>ELISA</td>
<td>Enzyme-Linked Immuno-Sorbert Assay</td>
</tr>
<tr>
<td>EIA</td>
<td>Electro Immuno Assay</td>
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<tr>
<td>EPI</td>
<td>Extended Programme on Immunization</td>
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<tr>
<td>FUNDE</td>
<td>Fundacion Nacional para el Desarrollo</td>
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<tr>
<td>FUNDAUngo</td>
<td>Fundacion Dr. Guillermo Ungo</td>
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<tr>
<td>FUSADES</td>
<td>Fundacion Salvador Para el Desarrollo Economico y Social</td>
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<td>GRZ</td>
<td>Government of Republic of Zambia</td>
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<tr>
<td>HRCDD</td>
<td>Health Research Capacity Development</td>
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<tr>
<td>ICC</td>
<td>Inter Agency Coordinating Committee</td>
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<tr>
<td>ICCDRI,B</td>
<td>International Centre for Diarrheal Diseases Research, Bangladesh</td>
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<td>ICIUM</td>
<td>International Conference on Improving Use of Medicines</td>
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<tr>
<td>IMI</td>
<td>Integrated Malaria Initiative</td>
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<td>IMCI</td>
<td>Integrated Management of Childhood Illness</td>
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<tr>
<td>INRUD</td>
<td>International Network for Rational Use of Drugs</td>
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<td>ITN</td>
<td>Insecticide Treatment Mosquito Net</td>
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<tr>
<td>IUALTD</td>
<td>International Union Against Lung and Tuberculosis Disease</td>
</tr>
<tr>
<td>IUDOP</td>
<td>Instituto Universitario de Opinion Publica</td>
</tr>
<tr>
<td>MCH</td>
<td>Maternal and Child Health</td>
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<td>MSPAS</td>
<td>Ministry of Public Health and Social Assistance</td>
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<td>NARIMA</td>
<td>New ARI Management Algorithm</td>
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<td>NGO</td>
<td>Non-Governmental Organization</td>
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<td>NFNC</td>
<td>National Food and Nutrition Commission</td>
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<td>NIDs</td>
<td>National Immunization Days</td>
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<td>NMCC</td>
<td>National Malaria Control Centre</td>
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<td>ORS</td>
<td>Oral Rehydration Solution</td>
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<tr>
<td>ORT</td>
<td>Oral Rehydration Therapy</td>
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<td>PAHO</td>
<td>Pan American Organization</td>
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<td>PCR</td>
<td>Polymerase Chain Reaction</td>
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<td>PEI</td>
<td>Polio Eradication Initiative</td>
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<td>PHC</td>
<td>Primary Health Care</td>
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<td>P&amp;TC</td>
<td>Pharmacy and Therapeutic Committees</td>
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<td>RPM</td>
<td>Rational Pharmaceutical Management</td>
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<td>RTI</td>
<td>Reproductive Tract Infection</td>
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<td>SNIDS</td>
<td>Sub-National Immunization Days</td>
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<td>STD</td>
<td>Sexually Transmitted Disease</td>
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<td>STG</td>
<td>Standard Treatment Guidelines</td>
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<td>TDRC</td>
<td>Tropical Diseases Research Centre</td>
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<td>TRUST</td>
<td>Trancetrical Ultra Sonography Test</td>
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<td>UAB</td>
<td>University of Alabama</td>
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<tr>
<td>UCA</td>
<td>Universidad Centro Americano</td>
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<tr>
<td>UNICEF</td>
<td>United Nations Childrens Fund</td>
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<td>UNZA</td>
<td>University of Zambia</td>
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<td>USAID</td>
<td>United States Agency for International Development</td>
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<tr>
<td>UTI</td>
<td>Urinary Track Infection</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>ZAP</td>
<td>Zinc Against Plasmodium</td>
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