

# **Child Health Research Project**

## Challenges for Child Health

### **Acute Respiratory Infection (ARI)**

#### **The Challenge**

ARI remains one of the leading causes of morbidity and mortality in children under the age of five in developing countries. Even with significant progress in addressing the burden of disease due to ARI, pneumonia claims approximately 2 million lives annually of children under the age of five.

#### **CHR Approach**

The CHR partners seek to increase recognition, prevention, and treatment of ARI by:

- Improving health care provider's recognition and treatment approaches through refinement of the treatment strategies for the three categories of pneumonia: non-severe (simple) pneumonia, severe pneumonia, and very severe pneumonia;
- Reducing the spread of antibiotic resistant pathogens and adverse drug reactions by:
  - o Assessing the necessity of antibiotic therapy for non-severe pneumonia (e.g. NARIMA Study);
  - o Determining the etiology of very severe pneumonia, documenting antimicrobial resistance patterns, and identifying best treatment practices, (e.g. SPEAR Study);
- Demonstrating that oral therapy may be safely substituted for parenteral therapy in the treatment of children with severe pneumonia (e.g. APPIS Study);
- Developing improved diagnostics to identify co-morbidity and recognition of pneumococcal infections (meningitis, pneumonia, bacteremia, and otitis media), and malaria;
- Adapting treatment strategies in areas with endemic malaria and HIV/AIDS; and
- Evaluating and introducing promising vaccines, e.g. pneumococcal, HiB, and RSV.

## **Selected CHR Achievements**

- A 7-valent pneumococcal conjugate vaccine demonstrated an estimated efficacy of 77% among all children who received at least one dose of the vaccine prior to 24 months.
- Showed that improved nutrition in developing countries (including breastfeeding and reduction of low-birth weight) would greatly reduce pneumonia mortality.
- After the introduction of Haemophilus influenzae type b (Hib) conjugate vaccine into The Gambia, the annual incidence of Hib meningitis has fallen from more than 200 per 100,000 before vaccination to 21 per 100,000 in less than 1 year.
- Showed that ARI could be prevented in the developing world through improved nutrition and increased breastfeeding.
- A 45% reduction in pneumonia incidence with zinc supplementation in India.
- Determined that cotrimoxazole is effective for non-severe pneumonia, but amoxicillin is better for severe cases.
- 95% efficacy of Haemophilus influenzae type-b (Hib) conjugate vaccine in The Gambia.
- Improved case management of ARI and reduced antibiotic use by 26% and case fatality rate by 27% in Pakistan.
- Showed that maternal immunization against Streptococcus pneumoniae elevated infant serum antibody levels 2 to 3 fold higher than control infants.

## **Diarrheal Disease**

### **The Challenge**

An estimated 2.2 million diarrheal deaths occur annually in developing countries in children under five. Thousands of deaths could be averted through interventions such as Oral Rehydration Therapy, appropriate drug therapy, optimal breastfeeding practices, improved nutrition, increased access to clean water and sanitation facilities and improved personal and domestic hygiene.

## **CHR Approach**

CHR seeks to improve diagnosis and assessment and increase prevention, and treatment by:

- Advancing the understanding of causes and risk factors of diarrheal diseases;
- Developing new revised guidelines for management of diarrhea;
- Evaluating new and alternate drug treatments and rehydration therapies; and
- Contributing to the prevention of diarrhea through evaluation of new vaccines (e.g. rotavirus and shigella) and improved nutrition and micronutrient status.

## **Selected CHR Achievements**

- Developed a standardized approach for ORS rehydration for treatment of children with severe malnutrition and diarrhea that resulted in fewer episodes of hypoglycemia, less need for intravenous fluids, and a 47% reduction in mortality. These findings were incorporated into new WHO guidelines.
- Determined that El Nino increased hospital admissions due to diarrhea over 200% during the last season.
- Showed that approximately 40% of all hospitalized diarrhea cases are due to rotavirus in urban and rural Bangladesh. In addition, reanalysis of the efficacy of the past rotavirus vaccine trials in Peru and Brazil has demonstrated that a safe vaccine would have a significant public health impact.
- Characterized newly emergent pathogen *Vibrio cholerae* O139 and designed rapid diagnostic tests.
- Characterized a new toxigenic clone of *Vibrio cholerae* O1 El Tor.
- Designed a surveillance system to detect *Vibrio cholerae* O1 by sampling potable water and sewage in Peru.
- Designed an algorithm, using locally-available foods, that is up to 89% effective in treating persistent diarrhea (1996), and is now incorporated into the IMCI guidelines in over 79 countries around the world.

## **Nutrition**

### **The Challenge**

In 1995, WHO identified that 56% of global child deaths were attributed to malnutrition, and that most of this mortality was the result of infectious complications of mild to moderate, rather than severe malnutrition. Recent nutrition research has demonstrated that: micronutrients sustain and improve child health; malnutrition is a major risk factor for disease and death; and low birth weight impacts adult health and the health of subsequent generations.

### **CHR Approach**

CHR seeks to improve nutrition in children by:

- Conducting research on the use of zinc and other micronutrients to treat and prevent disease;
- Fostering innovations in successful breastfeeding counseling;
- Research and consensus building within the scientific and programmatic community to reduce low birth weight;
- Increasing the quality of complementary feeding practices in at-risk populations; and
- Promoting the use of a child's nutritional status in the re-estimation of the Global Burden of Disease.

### **Selected CHR Achievements**

- Daily zinc supplementation in small for gestational age babies documented a 66% reduction in mortality.
- Demonstrated that oral zinc supplementation in children under 5 reported a 24% reduced probability of continuing diarrhea and a 42% reduced probability of treatment failure or death in children with persistent-diarrhea.
- The use of zinc to prevent infectious diseases showed that zinc had a significant preventive effect on incidence and prevalence of diarrhea and pneumonia.
- Established the safety of vitamin A when administered with childhood immunizations.

- Established that a single, large postpartum dose of vitamin A raised breastmilk retinol levels in women, and reduced duration of ARI and febrile illness in their infants.
- Among young mothers with infants hospitalized for diarrhea, exclusive breastfeeding levels were increased significantly to 75% through the use of community lactation counselors.

## **Infectious Diseases**

### **The Challenge**

Infectious diseases account for 63% of deaths in children ages 0-4 years. Unfortunately, ARI, DD, TB, malaria, and other diseases have been shown to develop some degree of resistance to commonly used antimicrobial drugs. As a result, the decreasing effectiveness of these drugs has contributed to persistent infections, higher morbidity and mortality, prolonged hospitalization and increased health expenditures. The emergence of drug resistance and new infectious agents presents a serious challenge to global public health.

### **CHR Approach**

CHR-funded research has assisted USAID in accomplishing its goals by conducting research in and building capacity to:

- Combat AMR by addressing its major causes and consequences, establishing a global strategy and action plan, contributing to the understanding of mechanisms of antimicrobial resistance, developing methods to detect resistance, responding to data on antimicrobial resistance and drug-use, and preventing and slowing the spread of antimicrobial resistance;
- Support the work of the USAID Zambia mission strategy in combating malaria;
- Respond to a congressional earmark to provide regional and national training to improve tuberculosis control programs committed to the WHO DOTS strategy, with special attention to issues concerning high-risk and marginalized populations; foster development of local and national TB control program capacities to utilize operations research as a program tool; and implement and evaluate new and innovative approaches to community-based interventions for TB control; and

- Conduct research to develop delivery strategies and identify impediments to the successful completion of the global strategy to eradicate polio.

### **Selected CHR Achievements**

- Demonstrated that steroid therapy did not improve outcome in bacterial meningitis allowing WHO to make a clear recommendation against the use of steroids in this disease.
- Developed emergency response system for a dengue outbreak at the request of the Bangladesh government and mission. This approach has been adopted by WHO for use globally.
- Developed an innovative and field-appropriate education process involving immediate feedback and small group discussions, followed by self-assessment meetings. These efforts have reduced the number of children inappropriately treated with antibiotics for simple ARI from 70% to 23%.
- An ongoing effort to strengthen tuberculosis control and establish effective DOTS campaigns in rural areas of Rio de Janeiro, Brazil. This work has demonstrated that 82% completion of all doses is achievable and that patient cure rates in a country with a 40% default rate of DOTS interventions can be improved. The program has already moved treatment success rates from 60% to 84% in its first year of existence.
- Trained key officials in Russia's Kemerovo region in the control of MDR-TB and assisted in the development of an action plan.
- Field testing of an innovative, rapid, and inexpensive technique for diagnosing TB in an urban slum of Lima, Peru that has some of the world's highest prevalence of TB and morbidity and mortality for HIV/MDR-TB.
- In Cambodia, the CHR project has developed and implemented a cross-training effort for the country's HIV and TB care programs. This has been accomplished by adding a TB component to an existing HIV-care program that provides home care to about 700 symptomatic patients in the greater Phnom Penh area.
- Implementation of a DOTS program in Indonesian hospitals and then linking them to the national TB program.
- A large multi-center study in India to document the etiology and antimicrobial resistance of *S. pneumoniae* and *H. influenzae* invasive infections. This study has found up to 85% resistance to routinely used antimicrobial drugs. Higher levels of drug resistance were found in urban areas (78% cotrimoxazole

resistance) vs. 39% in rural areas, and identified pneumococcal serotypes that should optimally be included in vaccine formulation for India.

- Developed Invasive Bacterial Infection Surveillance (IBIS) to monitor *Streptococcus pneumoniae* and *Haemophilus influenzae* - b prevalence and antibiotic resistance in India. IBIS found: Significant levels of resistance (up to 85%) to antimicrobial drugs; higher levels of drug resistance in urban areas (78% resistance to cotrimoxazole in New Delhi) than in rural areas (39%), and determined pneumococcal serotypes that must be included in vaccine formulation for India.
- Demonstrated that greater improvements in prescribing practices resulted when problem oriented, small-group educational approaches were used in addition to ongoing discussions among clinical peers that were reinforced by routine supervision and monitoring.
- Determined that physician prescribing practices were influenced by factors other than knowledge of the correct therapeutic choice. Factors, such as duration of practice, and caregivers' expectations have an important influence on physician prescribing practices of antimicrobials.
- Showed that compliance in administering cotrimoxazole preparations was strongly correlated with caregivers' difficulty in administering the medication.

## **Neonatal Health**

### **The Challenge**

The World Health Organization (WHO) estimates that 5 million neonates die each year. A very large proportion of these neonatal deaths (3.4 million) take place in the first week of life. More than 40% of neonatal deaths are caused by infection. Many cases of neonatal infection never reach treatment facilities, and the case-fatality rate for those that do ranges from 13% to 69%.

### **CHR Approach**

CHR supports refinement of the IMCI approach for the health needs of very young infants through:

- Applied research on the cause of disease and death in this age group;
- Documenting the clinical signs to aid in diagnosis; and

- Research on the treatment and prevention strategies to reduce neonatal mortality.

CHR has also been one of the major advocates for focusing attention on neonatal health.

### **Selected CHR Achievements**

- Field research has found that zinc supplements reduce mortality by 66% in low birth weight (SGA) infants.
- A large multi-center study in The Gambia, Papua New Guinea, The Philippines and Ethiopia documented that *S. pneumoniae* and *S. aureus* are the most common causes of severe infections (together comprising more than 40% of infections) in neonates and young children. This emphasizes the necessity to maintain adequate stocks of drug formularies to combat these common neonatal pathogens, and establish an urgent need to deliver conjugate pneumococcal vaccines to the developing world.
- Low birth weight (LBW), not premature birth, was found to be the most important determinant for subsequent poor growth in infants and children. Because most study infants experienced chronic intrauterine undernourishment, catch-up growth was highly restricted and weight, at 12 months, was highly correlated with birth weight. Improvement of LBW is likely to lead to increases in one-year weight and overall infant nutrition
- In the process of developing a new diagnostic tool and treatment approach for Group B Streptococcus and bacterial vaginosis, which are major causes of perinatal/neonatal deaths.
- Validated the verbal autopsy method for determining infant death in a nationwide study in Bangladesh.

### **Integrated Management of Childhood Illness (IMCI)**

#### **The Challenge**

Surveys reveal that many sick children are not properly assessed and treated by health care providers in developing countries, and that their parents are poorly advised. At first-level health facilities in low-income countries, diagnostic supports such as radiology and laboratory services are minimal or non-existent, and drugs

and equipment are often scarce. Limited supplies and equipment, combined with an irregular flow of patients, leave doctors at this level with few opportunities to practice complicated clinical procedures. Instead, they often rely on history and signs and symptoms to determine a course of management that makes the best use of the available resources.

### **CHR Approach**

The three components to IMCI are: improving the skills of health workers; improving the health system, and improving household and community practices. IMCI is considered to be among the most cost-effective interventions in both low- and middle-income countries and most likely to have the greatest impact on the global burden of disease. As of December 2000, over 81 countries around the world have adopted IMCI guidelines. Much of CHR's work supports the refinement and implementation of IMCI. Through research and field tests, the CHR partners have developed, refined, and validated the IMCI guidelines. Implementation of CHR's results through IMCI allows for rapid dissemination of its findings, and to globally increase the quality of illness diagnosis, treatment, and prevention. CHR has 22 completed or ongoing tasks classified specifically as IMCI activities. However, IMCI related activities are also included under the categories of acute respiratory infection and diarrheal disease.

### **Selected CHR Achievements**

- Developed a tool to measure the effectiveness of counseling caregivers in treatment compliance that has been adopted by the Ugandan Ministry of Health as part of nationwide monitoring of worker performance.
- Developed simple guidelines for emergency triage assessment and treatment of patients in the developing world.
- Validated the basic IMCI outpatient guidelines for treatment of pneumonia, diarrhea, malnutrition and need for referral in six countries - these guidelines are the cornerstone of IMCI which are now widely implemented around the world.
- Validated IMCI guidelines were developed for need of referral in young infants and children with pneumonia in Bangladesh.
- Refined the malaria diagnosis guidelines for highly endemic areas.
- Developed an IMCI Course for Health Workers.