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Gaps and Priorities in U.S. Contributions to Global Disease Challenges: What has the U.S. done well and not as well?

Diarrheal Disease and Acute Respiratory Infection

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Challenges

- ❑ All children everywhere are susceptible to a variety of non-vaccine preventable diarrheal disease (DD) and acute respiratory infection (ARI) pathogens – huge burden of disease
- ❑ Failure to fully deliver available vaccines in low and middle income countries (LMIC) impacts ongoing morbidity/mortality
 - still limited understanding of the immunology of protection
 - problem of serotype specificity or antigenic variation
- ❑ The burden of mortality is overwhelmingly in LMIC's (> 3 ½ million/yr) in the 0-5 yo group, ARI > DD, with little difference between males and females (M sl > F)
- ❑ Over 130 million DALY's are attributable to these infections, ARI > DD, primarily in sub Saharan Africa and South Asia
- ❑ Increasing antimicrobial resistance; continued inappropriate use of antimicrobials; limited access to affordable products
- ❑ Support for surveillance (esp lab based) and health information systems is limited and usually via non-sustainable mechanisms
- ❑ Etiology specific DX tools for household or health post level
- ❑ Clinical assessment tools for household or health post level



Major Findings: Diarrheal Diseases

- What works?
 - DD results in 3 syndromes: dehydration, inflammatory diarrhea/dysentery, and malabsorption/malnutrition
 - Causes and responses differ significantly
- What is highly effective?
 - Dehydration: appropriate method, early use, and thoroughness of rehydration
 - Inflammation: appropriate antibiotics
 - Malabsorption: nutritional rehabilitation
 - Water and sanitation interventions – primary prevention but cost, maintenance
- What is cost-effective?
 - ORS reduces or may preclude the need for IV fluids
 - Cost/DALY adversely affected by the huge number of episodes to be treated
 - Removes morbidity due to complications of IV therapy – systemic, local
 - Choice and duration of antibiotic treatment – when and what (resistance)?
 - Are there inexpensive, safe and effective etiology-appropriate oral drugs available?
 - Can short course therapy be used (is there evidence?)
 - Vaccines – rotavirus works and by itself could reduce dd mortality by over 50%
 - Age appropriate locally available calorie and protein-rich food
- What tools are available?
 - Etiologic diagnostic methods exist but these can be costly, take time, and require technical expertise, laboratory facilities and maintenance not readily available
 - Syndromic and epidemiological algorithms



Major Findings: Acute Respiratory Infection

- What works?
 - Four separable processes – treatment depends on process/likely causative agent
 - Upper respiratory illness (URI) – primarily viral, complications may require antibiotics
 - Pharyngitis – mostly viral, need to identify Group A strep infection to treat
 - Acute otitis – mostly viral, usually do not need antibiotics
 - Acute lower respiratory tract infections (LRI) +/- pneumonia – timely use of antibiotics
- What is highly effective?
 - Vaccines (measles, diphtheria, pertussis, Hib, pneumococcus, ? influenza)
 - URI/pharyngitis/acute otitis: Supportive care, reserve antibiotics for suspected bacterial complications
 - Reducing indoor air pollution due to cooking/heating fires
 - LRI – appropriate choice/duration of antibiotics; oxygenation for hypoxemia
- What is cost-effective?
 - Vaccines – routine EPI administration, but Hib, Pneumo, Influenza still too costly
 - Clinical diagnosis of pneumonia and implementation of treatment algorithm
 - Choice and duration of antibiotic
 - Is there an inexpensive, safe and effective cause-specific oral drug available?
 - Can short course therapy be used (are there data?)
 - Oxygenation restricted to hypoxemic patients
- What tools are available?
 - Etiologic diagnostic methods exist but these cost too much, samples not easily obtained, and require technical expertise and laboratory facilities
 - Syndromic and epidemiological algorithms (can be useful)
 - Pulse oximetry and imaging but restricted to higher level health facilities



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U.S. Contribution

- What has the U.S. done well in the last few decades?
 - Building local research capacity (NIH, CDC)
 - Building epidemiological capacity (CDC)
 - Building local health services capacity (USAID, Foundations, NGO's)
 - Ongoing vaccine research coupled with immunology studies of host response to infection and protective immune mechanisms, field trials
 - Global health career development pathways for US investigators – much less so in the past 20 yrs
- How:
 - Training partnerships between US and LMIC institutions –
 - But are we spending enough to train the next generation of US research/global health workforce?
 - Ongoing research support for vaccine development – especially via NIH intra and extramural funding
 - Field epidemiology and operational research – especially via CDC and USAID, also Fogarty ICOHRTA
 - BOD, etiology, case management strategies and effectiveness, implementation and evaluation
 - Career development programs and awards – via Fogarty International Center, CDC's EIS
 - Product development PPP's – especially via Foundations
- Financing – some unique programs have been (are being) supported
 - D-43 training grants for developing country researcher training (NIH) (ongoing)
 - IRSDA award (K-99) and Clinical Research Training Scholars and Fellows award (R24)
 - Board of S&T for International Development (BOSTID, NAS) ARI program 1985-1990
 - International Centers for ID Research (ICIDR's) (NIAID) (ongoing) – set aside funds
 - Indo-US Vaccine Action Program (ongoing) – no set aside funds on US side
 - Extrabudgetary support for WHO programs – ideally based on scientific objectives
 - USAID Child Survival program
 - ADDR/ARCH research capacity building program – USAID



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U.S. Contribution

- ❑ Solo efforts vs. global cooperation- needed or not?
 - Global cooperation is essential
 - ❑ The agenda from discovery through development to delivery is complex, requires many players, and is distorted by frequent gaps or unnecessary overlaps because of solo efforts
 - ❑ Institutional mandates and mechanisms for funding often do not mesh, let alone wasteful/mindless competition
 - ❑ Organizational competition too often overrides collaboration
- ❑ Missed opportunities for the US? Why?
 - Vaccine development – competitive, proprietary (more PD-PPP's?)
 - ❑ Why don't we have a serotype independent Pneumococcal vaccine?
 - ❑ Why is the cold chain still essential?
 - ❑ Alternative routes of administration?
 - Drug resistance as a global concern – clonal nature of strains
 - ❑ sustainable global surveillance – expense, multi-country, dissemination
 - ❑ improved/controlled use of drugs – norms, regulation, enforcement
 - ❑ linking veterinary and human health – pathogen emergence/spread, drug resistance – sectoral conflicts, funding constraints, who's in charge?
 - Emergency response (H5N1) vs. sustained efforts for surveillance and control
 - ❑ health benefits for US, improved image internationally
 - ❑ leadership role vs when and how to collaborative competently
 - ❑ Rational decision making based on reliable burden, laboratory and outcome data
 - Information and knowledge management systems – local, regional, internat'l



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Gaps in Knowledge

- What are the key gaps in knowledge?
 - There is a huge knowledge to action gap for DD and ARI for prevention, diagnosis and case management
 - Improving access, availability, affordability of care and interventions
 - Mechanisms of drug resistance (new insights) and their implications for new strategies for drug development
 - The immune system – how does it really work? how do you target vaccines for effective protective responses? how do you identify common vaccine antigens?
 - What interventions really work to improve outcomes at the different levels of care?
 - How to “educate” the public about effective options to improve health that require behavior changes



Recommendations

- What should be the priorities and recommendations for U.S. action
 1. Improve communication and collaboration between diverse government agencies, and between them and the academic and private sectors while allowing different perspectives to guide action
 2. Identify and prioritize areas for research and implementation, and disseminate these widely –balance upstream basic science and downstream implementation/operational science and provide sustainable support based on reviews of progress
 3. Develop mechanisms that encourage and “reward” innovation and scientific risk taking – ie Gates Grand Challenges
 4. Include resources for scale up from the lab, to local pilot projects, to national programs, to regional/international implementation efforts as a necessary process
 5. Invest in capacity building at the local level for research and program management, information systems with connectivity nationally and internationally
 6. Identify ways to co-fund with other national and international organizations, avoid wasteful competition, and prevent distortion of the job market for local health workers by salary or other incentives
 7. Build programs together with local health authorities, academics, NGOs and ensure they address, meet and support local priorities

Strengthening Health Systems

- How does the structure of health systems in developing countries affect/exacerbate the health challenge you're addressing?
 - Can the system use health information effectively?
 - Is there a functional referral system of care?
 - Is Integrated Management of Childhood Illness effective? Are minimally trained health workers trained to diagnose and treat DD and ARI at the household level?
- How do the proposed recommendations for U.S. action strengthen or affect national health systems?
 - Upstream research targeting downstream needs
 - Working through the health system to conduct epidemiology and clinical trials, including capacity building for local action
 - Working within locally set priorities
- Are there interventions outside the traditional health sector which are important for the success of the identified set of interventions (i.e. hunger, water and sanitation)?
 - DD and ARI susceptibility and outcomes are conditioned by nutritional status
 - Breast feeding, complementary feeding and weaning strategies
 - Micronutrient status
 - Water and sanitation are primary prevention strategies for DD – low tech solutions are available and can be implemented with international financing and support
 - Market/financing strategies to improve access, affordability, and appropriate use of drugs and vaccines