



Global
**Antibiotic
Resistance**
Partnership

CDDEP THE CENTER FOR
Disease Dynamics,
Economics & Policy
WASHINGTON DC • NEW DELHI

Opportunities for Reducing Antimicrobial use Through New Vaccines

Robert F. Breiman
Global Disease Detection Division
CDC-Kenya
Nairobi, Kenya

Premise and a Question

- Antibiotic use drives resistance
- How can vaccines contribute to the reduction of antimicrobial use?

How are Antimicrobials Generally Used in Infants and Children?

- Appropriately (10-20%) and inappropriately (80-90%) as coverage for:
 - Painful ear (some is bacterial otitis media, a lot is non-bacterial)
 - Respiratory symptoms (some is bacterial pneumonia, but most is viral)
 - Diarrheal disease (some is dysentery, but most is rotavirus or other non-treatable)
 - Febrile illness (some is typhoid or malaria, but most is a wide array of viruses)
 - Skin rash (some is impetigo or cellulitis, but a lot of exanthems)

Where do vaccines come in?

Relevant New (and not so new) Vaccines

Haemophilus influenzae type B (Hib)—prevents pneumonia, febrile illness, otitis media

Pneumococcal—prevents pneumonia, febrile illness, otitis media

Influenza— prevents seasonal flu and pneumonia

Rotavirus— Prevents dehydrating diarrhea

Typhoid— Prevents febrile illness with and without complications

Measles, Mumps, Rubella (MMR)

Varicella— Prevents chicken pox and secondary skin infections

Effectiveness/Impact

- Hib vaccines: 22-34% reduction in pneumonia
- Pneumococcal vaccine: 23-35% reduction in pneumonia
- Influenza vaccines: Depends upon year—maternal immunization → 29% reduction in febrile respiratory illness in infants
- Rotavirus vaccines: 40% efficacy against all cause diarrhea hospitalizations (L. America and N. America—African data pending)
- Typhoid vaccines: 70% efficacy— incidence as high as 1%-2%/year in children in urban slums
- MMR-V: Highly efficacious (each associated with fever and rashes)

How does universal pneumococcal immunization potentially affect clinical management of febrile child?

- Children with fever without localizing signs in UK after introduction of pneumococcal vaccine
 - When compared with pre-vaccine period, dramatic reduction in pathogens isolated from blood culture
 - Urinary tract infection now most prevalent bacterial infection in kids 3-36 months of age

Pneumococcal Vaccine Impact on Antimicrobial Use—Findings from Blinded Studies (1)

- 264 kids (12-35 months) received either pneumococcal conj vaccine or a mening vaccine in Israel
 - 15-17% reduction in respiratory infections
 - 17% reduction in antimicrobial use
 - 10% in URIs
 - 20% for otitis
 - 47% for lower respiratory illness

Pneumococcal Vaccine Impact on Hospitalizations and Clinic Visits, Children <2 years—United States

- 47% reduction in all-cause pneumonia hospitalization rates
- 41% reduction in all-cause pneumonia clinic visits

Infant Pneumococcal Conjugate Vaccination and Antimicrobial Use

- N California Kaiser P III trial (35,000 kids immunized)
 - Reduction in overall antibiotic use in immunized kids by 5.7% (95% CI=4.2-7.2)
 - Reduction in 3 visits over 6-month period by 26%
 - Reduction in 10 visits over 6-month period by 10%
 - 24% reduction in tube (ear) placement

Influenza vaccination in a day care setting-impact on household contacts*

- Unvaccinated child-Contacts of vaccinated children when compared with those of unvaccinated children
 - 50% reduction in any resp illness
 - 80% reduction in cough with fever
 - 80% reduction in cough with fever $\geq 38^{\circ}\text{C}$
 - 88% reduction in antimicrobial use

*In children 5-17 years of age, during influenza season

Rotavirus vaccines

Pentavalent (Merck) and Monovalent (GSK)

- Efficacious in N American, European and Latin American studies
- Studies of GSK vaccine in Malawi and S Africa completed
- Studies of rotavirus vaccine in Kenya, Mali, Ghana completed and undergoing data analysis
 - Kenya component will look at impact on antimicrobial (inappropriate) use.
 - Behavioral research in Kibera and Nyanza showed that

Belief in effectiveness of treatments for watery diarrhoea, by health worker category

	Medical officer / nurse / clinical officer (N=28)	Community health worker (N=118)	Herbalist / traditional healer (N=125)
ORT is among 5 most effective	89%	89%	42%
ORS is among 5 most effective	71%	73%	5%
Antimicrobial agents are among 5 most effective	71%	49%	26%
ORT is <u>most</u> effective	64%	59%	5%
ORS is <u>most</u> effective	57%	31%	2%
Antimicrobial agents are <u>most</u> effective	7%	4%	10%



Barriers to taking full advantage

- Cost
- Cost
- Cost
- Recognition of the value—direct and indirect
 - Direct disease prevention
 - Herd/community indirect effect
 - Reduction in health care associated costs
 - Including antimicrobial use
 - Reduction in sequelae
 - Reduction in antimicrobial use



Final Considerations

- Strategies to address emerging antimicrobial resistance should include optimal use of vaccines
- Studies (including P IV post-marketing studies) should be configured to provide data on impact of vaccination on antimicrobial use patterns
- Rapid diagnostic, affordable tests need to be available/used so that appropriate antibiotic use can be optimized
- Ultimately, a balanced holistic approach to emerging and re-emerging diseases focused on overall public health benefit, especially in light of limited public health resources (for the foreseeable future)