# DISEASE PREVENTION & ANTIMICROBIAL USE REDUCTION: IMPACT OF VACCINATION


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# VACCINE ACHIEVEMENTS

**"At the end of the 20th century the US Centers for Disease Control and Prevention (CDC) cited vaccination as the number one public health achievement of that century"**

"The elimination in 1977 of smallpox as a human disease must rank as one of the major achievements of modern medicine"

# VACCINE ACHIEVEMENTS

- With sanitation and nutrition, vaccines are hailed as one of the most important public health achievements of the 20th century.
- Once only targeted against serious childhood diseases, vaccinology has become a tool for preventing infectious diseases or their complications and outcomes in all age groups.
- This has seen the number of vaccine-preventable diseases rising to around 26.

# VACCINE ACHIEVEMENTS

- Currently, it is estimated that immunization saves the lives of 3 million children a year but another 3 million more lives could be saved by use of existing vaccines
- Seen the eradication of smallpox and the near eradication of polio
- Elimination of measles and neonatal tetanus

# Decrease in cases of vaccine-preventable diseases in the USA through 1998 as reported by the US Centers for Disease Control and Prevention

**(MMR 48: 243-248, 1999)**

| DISEASE | CASES Baseline | CASES 1998 | REDUCTION % |
|---|---|---|---|
| Smallpox | 48,164 | 0 | 100 |
| Diphtheria | 175,885 | 0 | 100 |
| Pertussis | 147,271 | 7,405 | 95 |
| Tetanus | 1,314 | 41 | 97.9 |
| Paralytic Polio | 16,316 | 0 | 100 |
| Measles | 503,282 | 100 | 100 |
| Mumps | 152,209 | 666 | 99.6 |
| Rubella | 47,745 | 364 | 99.3 |
| *H influenzae* B | 20,000 | 63 | 99.7 |

# VIRAL VACCINES

| DISEASE | VIRUS TYPE | CONSTITUENTS | EFFICACY |
|---|---|---|---|
| SMALLPOX | Variola virus | Vaccinia virus | 100 |
| POLIO | Picornavirus | Oral: live attenuated<br>Parenteral: inactivated | >95%<br>>95% |
| HEPATITIS A | Picornavirus | Killed virus | >90% |
| HEPATITIS B | hepadnavirus | Recombinant antigen | >80% |
| INFLUENZA | Orthomyxovirus | Inactivated virus | 50-70% |
| MEASLES | Paramyxovirus | Live, attenuated virus | >95% |
| MUMPS | Paramyxovirus | Live, attenuated virus | >90% |
| RUBELLA | Togavirus | Live, attenuated virus | >95% |
| CHIKEN POX | Varicella zoster | Live, attenuated virus | >80% |
| RABIES | Lyssa virus | Inactivated virus | 100 |
| YELLOW FEVER | Flavivirus | Live, attenuated virus | >90% |
| JAPANESE ENCEPHLITIS | Flavivirus | Inactivated virus | >90% |

# BACTERIAL VACCINES

| DISEASE | ORGANISM | VACCINE | EFFICACY |
|---|---|---|---|
| **DIPHTHERIA** | *Corynebacterium diphtheriae* | Inactivated exotoxin | >95% |
| **TETANUS** | *Clostridium tetani* | Inactivated exotoxin | >95% |
| **MENINGITIS** | *H influenzae*<br>*Neisseria meningitidis* | Polysaccharide protein congugate/ purified polysacc | >90% for <2yrs |
| **PNEUMONIA** | *Strep pneumoniae* | Purified polysaccharide<br>Polysac-protein congugate | 60% for >2 yrs<br>> 95% |
| **WHOOPING COUGH** | *Bordetella pertussis* | Acellular components – incl inactvated toxin, fimbriae | 80-90% |
| **PLAGUE** | *Yersinia pestis* | Inactivated bacteria | uncertain |
| **ANTHRAX** | *Bacillus anthracis* | Inactivated bacteria | uncertain |
| **TUBERCULOSIS** | *Mycobacterium tuberculosis* | Live attenuated BCG | Disseminated disease protection |
| **CHOLERA** | *Vibrio cholerae* | Inactivated bacteria | 50% (short) |

# TARGETED PARASITIC DISEASES

- **Malaria**
  - Life cycle, antigenic variation, CMI vs HI
  - Sporozoites (CS), merozoites (MSP-1)

- **Trypanosomiasis**
- **Leishmaniasis**
- **Toxoplasmosis**

DEPARTMENT OF HEALTH AND HUMAN SERVICES • CENTERS FOR DISEASE CONTROL AND PREVENTION

# Recommended Immunization Schedule for Persons Aged 0–6 Years—UNITED STATES • 2008

| Vaccine ▼ / Age ▶ | Birth | 1 month | 2 months | 4 months | 6 months | 12 months | 15 months | 18 months | 19–23 months | 2–3 years | 4–6 years |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Hepatitis B[1] | HepB | HepB | | *see footnote 1* | HepB | | | | | | |
| Rotavirus[2] | | | Rota | Rota | Rota | | | | | | |
| Diphtheria, Tetanus, Pertussis[3] | | | DTaP | DTaP | DTaP | | DTaP | | | | DTaP |
| *Haemophilus influenzae* type b[4] | | | Hib | Hib | *Hib*[4] | Hib | | | | | |
| Pneumococcal[5] | | | PCV | PCV | PCV | PCV | | | | PCV / PPV | |
| Inactivated Poliovirus | | | IPV | IPV | IPV | | IPV | | | | IPV |
| Influenza[6] | | | | | Influenza (Yearly) | | | | | | |
| Measles, Mumps, Rubella[7] | | | | | | MMR | | | | | MMR |
| Varicella[8] | | | | | | Varicella | | | | | Varicella |
| Hepatitis A[9] | | | | | | | HepA (2 doses) | | | HepA Series | |
| Meningococcal[10] | | | | | | | | | | MPSV4 | |

Range of recommended ages

Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 0–6 years. Additional information is available at http://www.cdc.gov/nip/recs/child-schedule.htm. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event

# GAVI SCHEDULE EVOLUTION

| AGE | VACCINE |
|---|---|
| birth | BCG + OPV0 + (HB0) |
| 6 weeks | DTP-HepB/Hib1 + OPV1 |
| 10 weeks | DTP-HepB/Hib2 + OPV2 |
| 14 weeks | DTP-HepB/Hib3 + OPV3 |
| 9 months | measles/MR/MMR + (YF) |

health

Department:
Health
REPUBLIC OF SOUTH AFRICA

# Expanded Programme on Immunisation – EPI (SA)
## Revised Childhood Immunisation Schedule from April 2009

| Age of Child | Vaccines needed | How and where is it given? |
|---|---|---|
| At Birth | BCG Bacillus Calmette Guerin | Right arm |
| | OPV (0) Oral Polio Vaccine | Drops by mouth |
| 6 Weeks | OPV (1) Oral Polio Vaccine | Drops by mouth |
| | RV (1) Rotavirus Vaccine | Liquid by mouth |
| | DTaP-IPV//Hib (1) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined | Intramuscular / Left thigh |
| | Hep B (1) Hepatitis B Vaccine | Intramuscular / Right thigh |
| | PCV7 (1) Pneumococcal Conjugated Vaccine | Intramuscular / Right thigh |
| 10 Weeks | DTaP-IPV//Hib (2) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined | Intramuscular / Left thigh |
| | Hep B (2) Hepatitis B Vaccine | Intramuscular / Right thigh |
| 14 Weeks | RV (2) Rotavirus Vaccine* | Liquid by mouth |
| | DTaP-IPV//Hib (3) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined | Intramuscular / Left thigh |
| | Hep B (3) Hepatitis B Vaccine | Intramuscular / Right thigh |
| | PCV7 (2) Pneumococcal Conjugated Vaccine | Intramuscular / Right thigh |
| 9 Months | Measles Vaccine (1) | Intramuscular / Left thigh |
| | PCV7 (3) Pneumococcal Conjugated Vaccine | Intramuscular / Right thigh |
| 18 Months | DTaP-IPV//Hib (4) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined | Intramuscular / Left arm |
| | Measles Vaccine (2) | Intramuscular / Right arm |
| 6 Years (Both boys and girls) | Td Vaccine Tetanus and reduced strength of diphtheria Vaccine | Intramuscular / Left arm |
| 12 Years (Both boys and girls) | Td Vaccine Tetanus and reduced strength of diphtheria Vaccine | Intramuscular / Left arm |

* Rotavirus Vaccine should NOT be administered after 24 weeks.

# IMPACT OF EXPANDED PROGRAMME OF IMMUNISATION (EPI)

- BCG, DPT, Hep B, Hib, rotavirus, PCV, OPV, combined vaccine (IPV),
- *Haemophilus influenzae* type B (Hib)
- *(Neisseria meningitidis)*
- *Streptococcus pneumoniae*

MINI REVIEW Clinical Microbiology and Infection, Volume 15, Supplement 3, April 2009 10.1111/j.1469-0691.2009.02726.x

# Impact of pneumococcal conjugate vaccine on infections caused by antibiotic-resistant *Streptococcus pneumoniae*

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## Abstract

Studies have shown that vaccination with seven-valent pneumococcal conjugate vaccine (PCV7) results in a decline in nasopharyngeal carriage of penicillin-resistant *Streptococcus pneumoniae*, in carriage of vaccine-type pneumococci, and in replacement by non-vaccine serotypes. Vaccines can reduce pneumococcal resistance in vaccinated and unvaccinated populations by reducing the carriage of antibiotic-resistant serotypes, which protects the vaccinated population and prevents spread of disease to others, and by decreasing antibiotic resistance through overall reduction in antibiotic use. However, while reducing the level of vaccine serotypes and drug-resistant serotypes in the nasopharynx, PCV7 also causes non-vaccine pneumococci replacement. The impact of serotype replacement on disease is not clearly understood. Pelton *et al.* surveyed two communities shortly after the introduction of the PCV7 immunization programme and found that while colonization with vaccine serotypes declined from 22% to 2% from 2000 to 2003, prevalence of non-vaccine serotypes increased from 7% to 16%. Although penicillin-resistant colonizing *S. pneumoniae* isolates initially declined, penicillin-intermediate isolates increased 2 years following PCV7 introduction. The change was primarily accounted for by an increase in penicillin-intermediate serotype 19A. Serotype 19A is the only serotype not affected by PCV7 that is prevalent worldwide, clinically important, and highly multidrug-resistant. A study by Hicks *et al.* established serotype 19A as the predominant post-PCV7 cause of invasive pneumococcal disease (IPD) in children and the elderly. An increase in IPD rates caused by antibiotic-resistant serotype 19A isolates can also occur without vaccination; reports indicate increases in regions characterized by extensive antibiotic use, underscoring the importance of strategies to contain antibiotic resistance.

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# Emerging diseases, zoonoses and vaccines to control them

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ABSTRACT

Vaccination, when available, is undoubtedly the most cost-effective means of preventing and controlling, and even eradicating, infectious diseases. In recent years vaccination has also been used for other purposes in animal health, production and welfare, e.g. immunocastration.

Vaccination of animals serves many different purposes, such as controlling animal infections and infestations, thus improving animal health and welfare; controlling anthropozoonoses and food poisoning in humans, thereby protecting public health; solving problems associated with antibiotic and anthelmintic resistance; helping to leave food-producing animals free of chemical residues; protecting the environment and biodiversity and ensuring animal farming sustainability. The problem is nevertheless more complex when facing emerging or re-emerging infections particularly zoonotic ones.

# Emerging diseases, zoonoses and vaccines to control them

**PP Pastoret Vaccine 2009; 27: 6435-38**

- **VACCINATION OF ANIMALS**
  - Controlling animal infections and infestations
  - Improving animal health & welfare
  - Controlling antropozoonoses & food poisoning in humans
  - Protecting the environment & biodiversity
  - Solving problems with antibiotic & anti-helminthic resistance
  - Ensuring animal farming sustainability

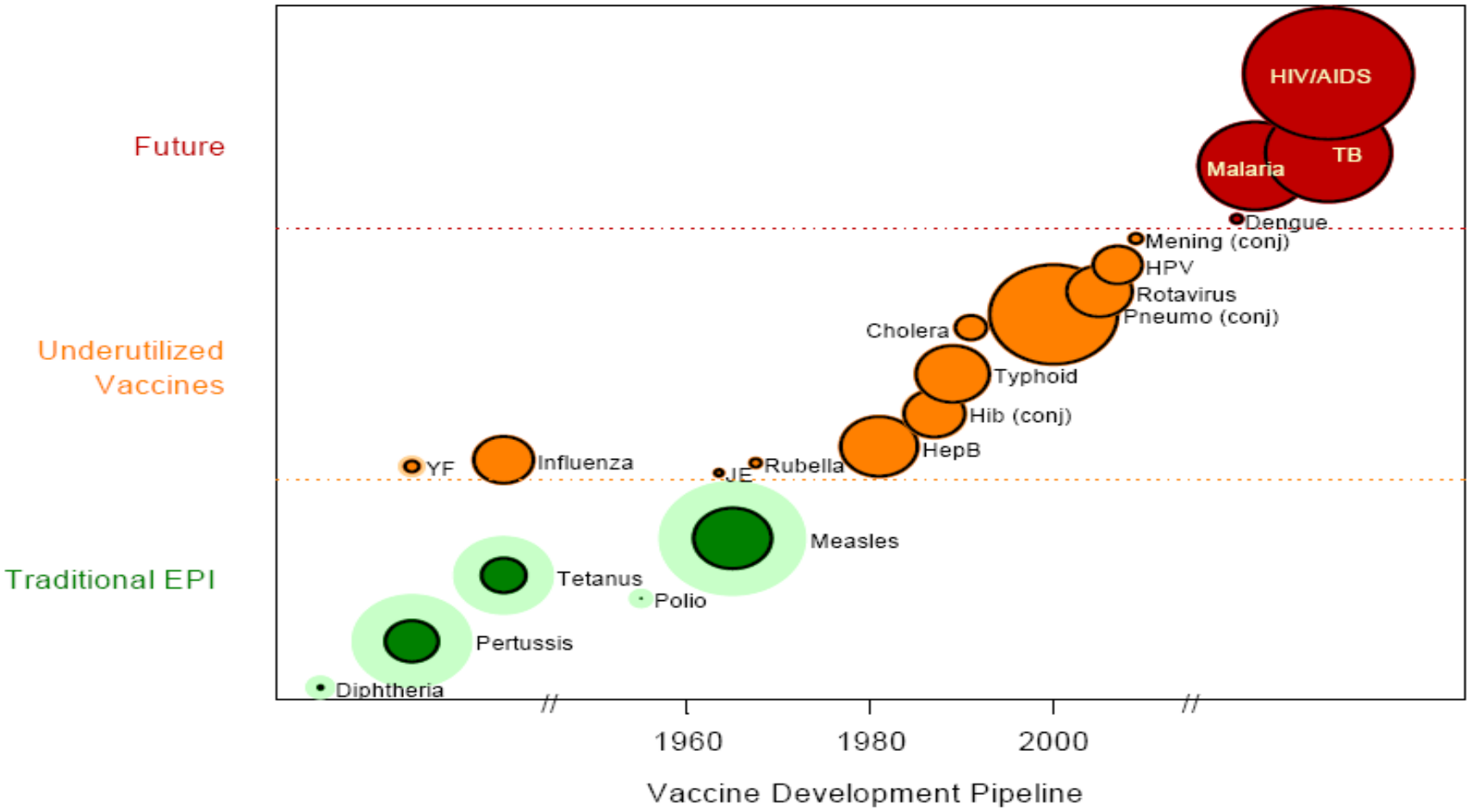
# Emerging diseases, zoonoses and vaccines to control them

## PP Pastoret Vaccine 2009; 27: 6435-38

- Vaccination in the face of emergence & re-emergence of diseases
  - Slaughter
  - Vaccination

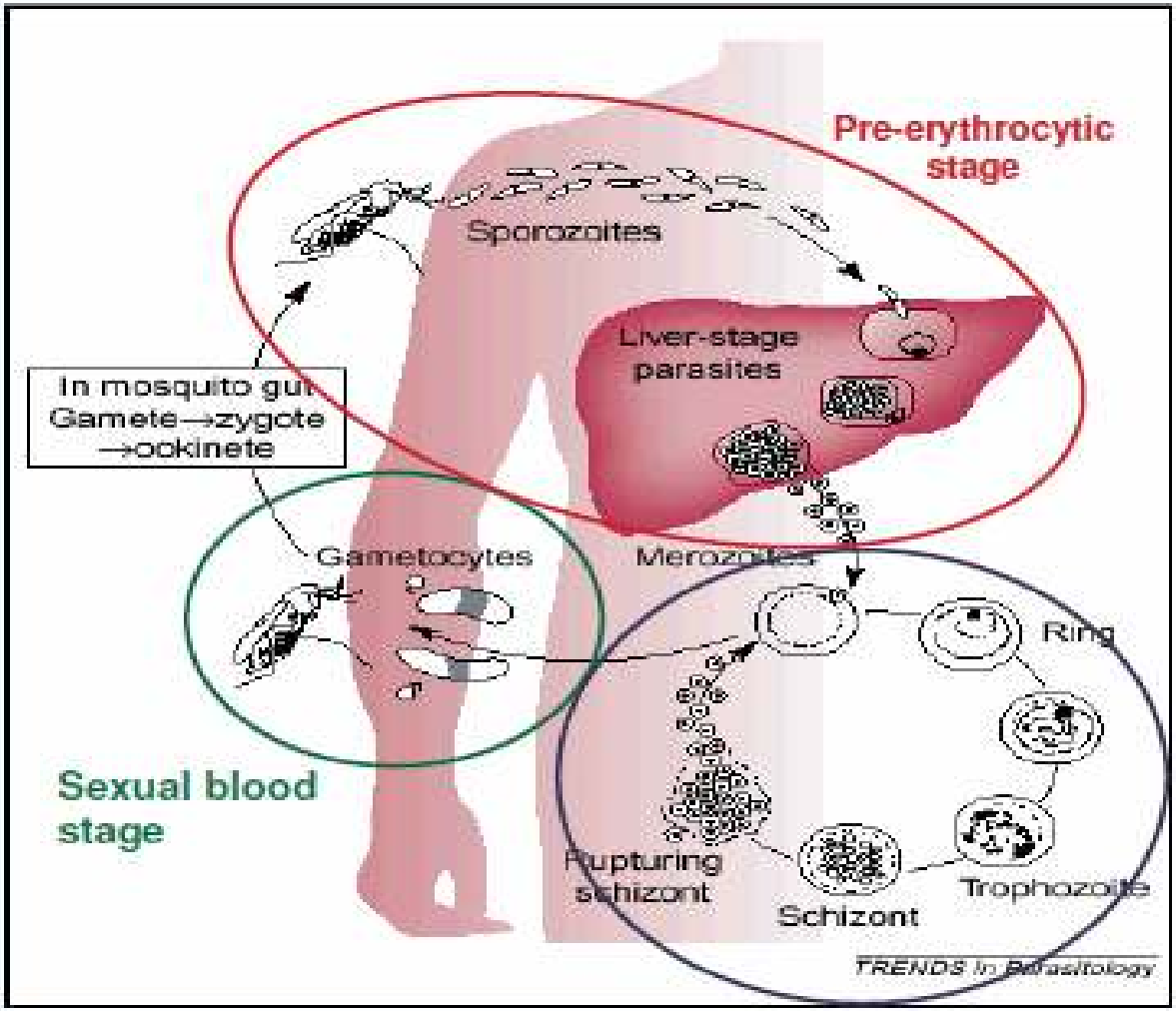
- Vaccination against zoonoses
  - Concerns about food-borne infections, the presence of drug residues following treatment of food-producing animals and the possible transfer of antibiotic resistance from bacteria causing disease in livestock to those which affect man
  - Vaccination of wildlife against rabies goal was not to protect wildlife species from rabies but to prevent human exposure and the disease in human populations
  - Veterinary vaccines can be used to prevent food poisoning as demonstrated by the "*in ovo*" vaccination of poultry against salmonellosis
  - A vaccine against *Escherichia coli* 0157:H7 has been conditionally approved for cattle in the United States.
  - A vaccine against sheep cysticercosis has been developed experimentally and may lead to the development of similar vaccines to control bovine cysticercosis and thus *Taenia saginata* infestation In humans.

# VACCINE DEVELOPMENT




*Area of circle is proportional to number of deaths (2002 data)*
*Shaded area is proportional to number of deaths prevented by vaccination.*

# *Plasmodium falciparum* life cycle




Asexual blood or erythrocytic stage

# MEFLOQUINE, QUINIDINE, AND QUININE

- Form toxic complexes by binding to heme
- Mefloquine resistance may be associated with mutations in the P-glycoprotein homolog-1 gene *pfmdr1*
- ↓ quinine sensitivity associated with resistance to structurally related drugs (mefloquine and halofantrine)
- Implies resistance mechanisms may *share* genetic determinants
  - *pfmdr1* mutations in mefloquine, quinine, and halofantrine resistance
  - *pfcrt* mutations in quinine and quinidine responses
- Slow rate of quinine resistance - a complex phenotype and is probably affected by other genes in addition to *pfmdr1* and *pfcrt.*

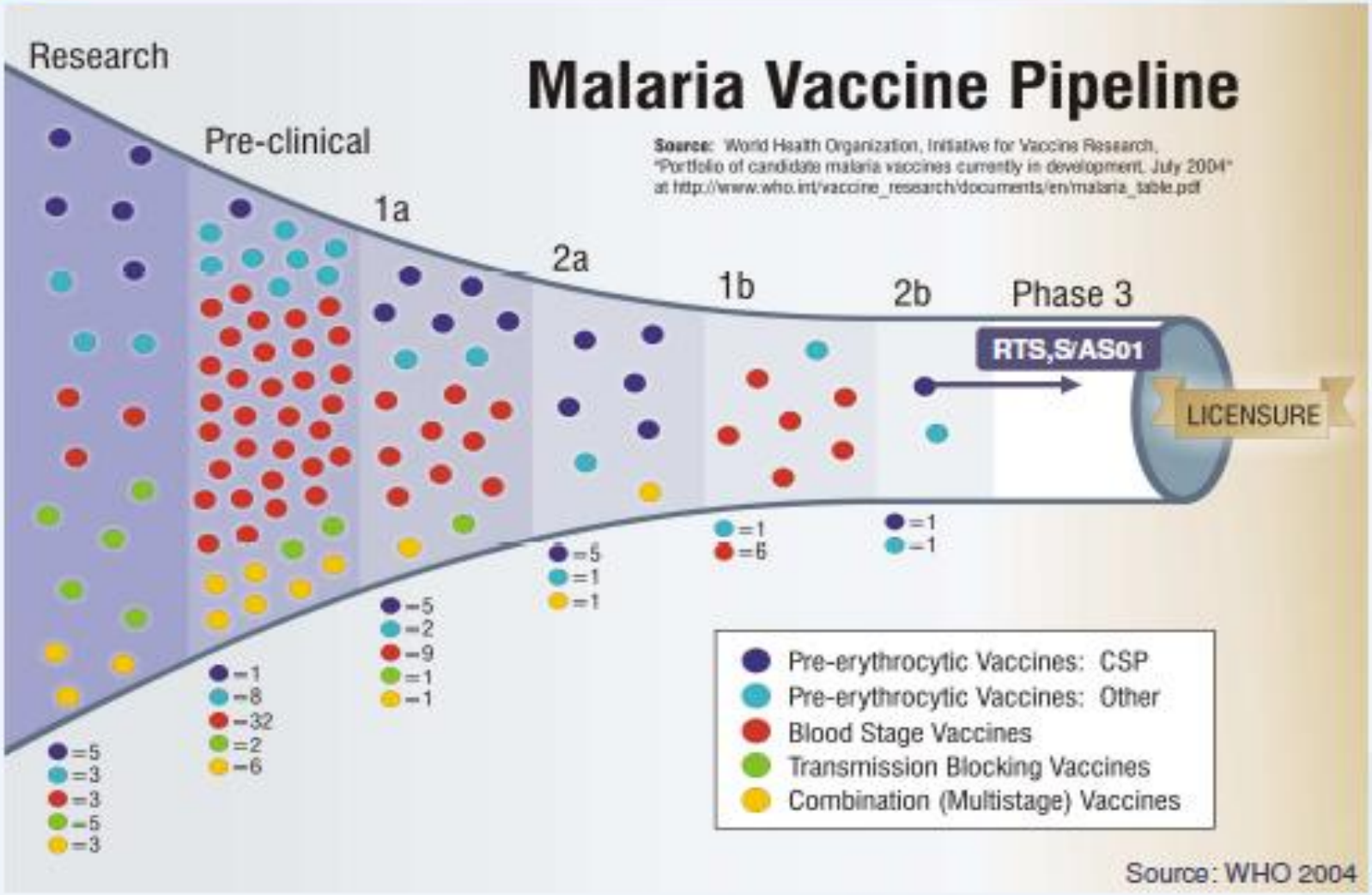
# Artemisinin Resistance in *Plasmodium falciparum* Malaria

Arjen M. Dondorp, M.D., François Nosten, M.D., Poravuth Yi, M.D., Debashish Das, M.D., Aung Phae Phyo, M.D., Joel Tarning, Ph.D., Khin Maung Lwin, M.D., Frederic Ariey, M.D., Warunee Hanpithakpong, Ph.D., Sue J. Lee, Ph.D., Pascal Ringwald, M.D., Kamolrat Silamut, Ph.D., Mallika Imwong, Ph.D., Kesinee Chotivanich, Ph.D., Pharath Lim, M.D., Trent Herdman, Ph.D., Sen Sam An, Shunmay Yeung, Ph.D., Pratap Singhasivanon, M.D., Nicholas P.J. Day, D.M., Niklas Lindegardh, Ph.D., Duong Socheat, M.D., and Nicholas J. White, F.R.S.

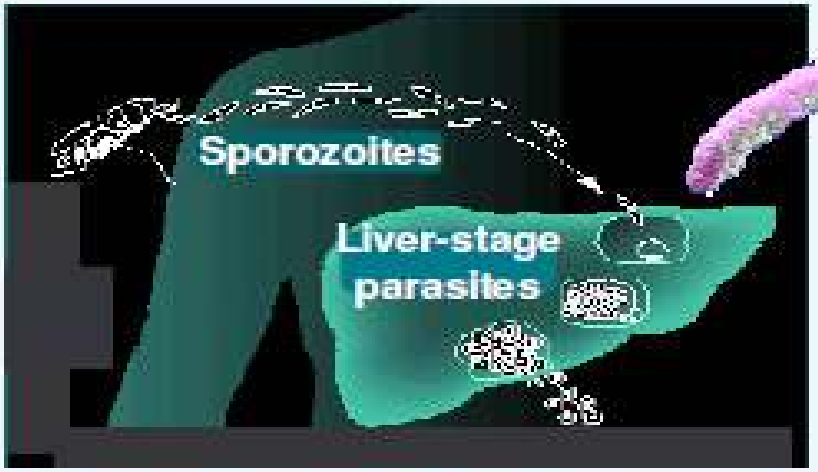
*P. falciparum* has reduced in vivo susceptibility to artesunate in western Cambodia as compared with northwestern Thailand. Resistance is characterized by slow parasite clearance in vivo without corresponding reductions on conventional in vitro susceptibility testing. Containment measures are urgently needed. (ClinicalTrials.gov number, NCT00493363, and Current Controlled Trials number, ISRCTN64835265.)

N Engl J Med 2009;361:455-67.

# Malaria Vaccine Pipeline

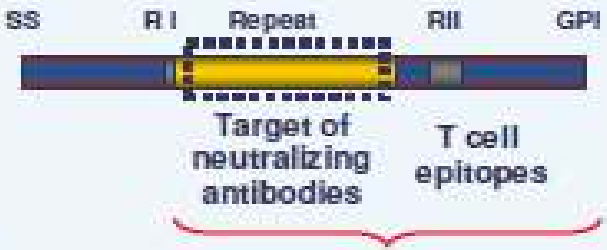


# The RTS,S pre-erythrocytic antigen



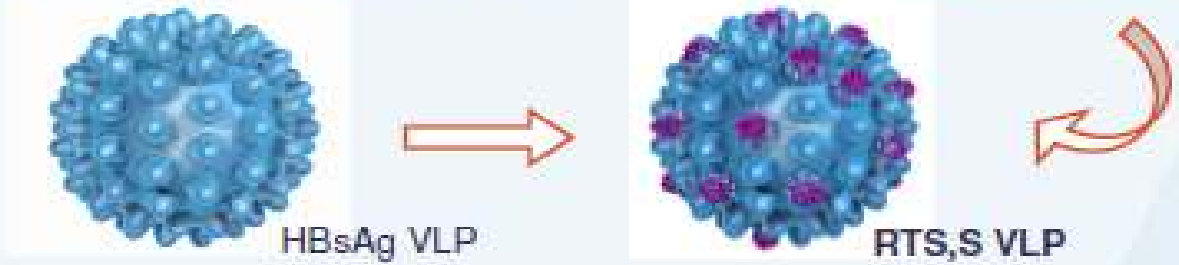

## Circumsporozoite Protein:

- Major surface protein of the sporozoite
- Involved in binding of sporozoite to liver cells




## Generation of RTS,S virus-like particles

Co-expression of RTS (fusion protein) and HBS protein in *Saccharomyces cerevisiae*. Spontaneously assemble into mixed virus-like particles (VLP)


*Gordon et al. J Infect Dis 1995*


World TB Day 2009 slogan

# TUBERCULOSIS

- High burden of disease
- Increase in MDR/XDR TB and long duration of treatment
- Convergence of HIV and TB epidemics

# AVANTAGES AND DISADVANTAGES OF BCG

## Pros

- most used vaccine at global level
- very low cost
- recognized protective efficacy against infant tuberculosis (e.g. TB-meningitis)

## Cons

- genetic heterogeneity of different BCG vaccines
- variable efficacy against pulmonary tuberculosis

# Prime vaccines


BCG

rBCG30

Δ*ureC Hly*+ rBCG (VPM1002)

# New boost vaccines

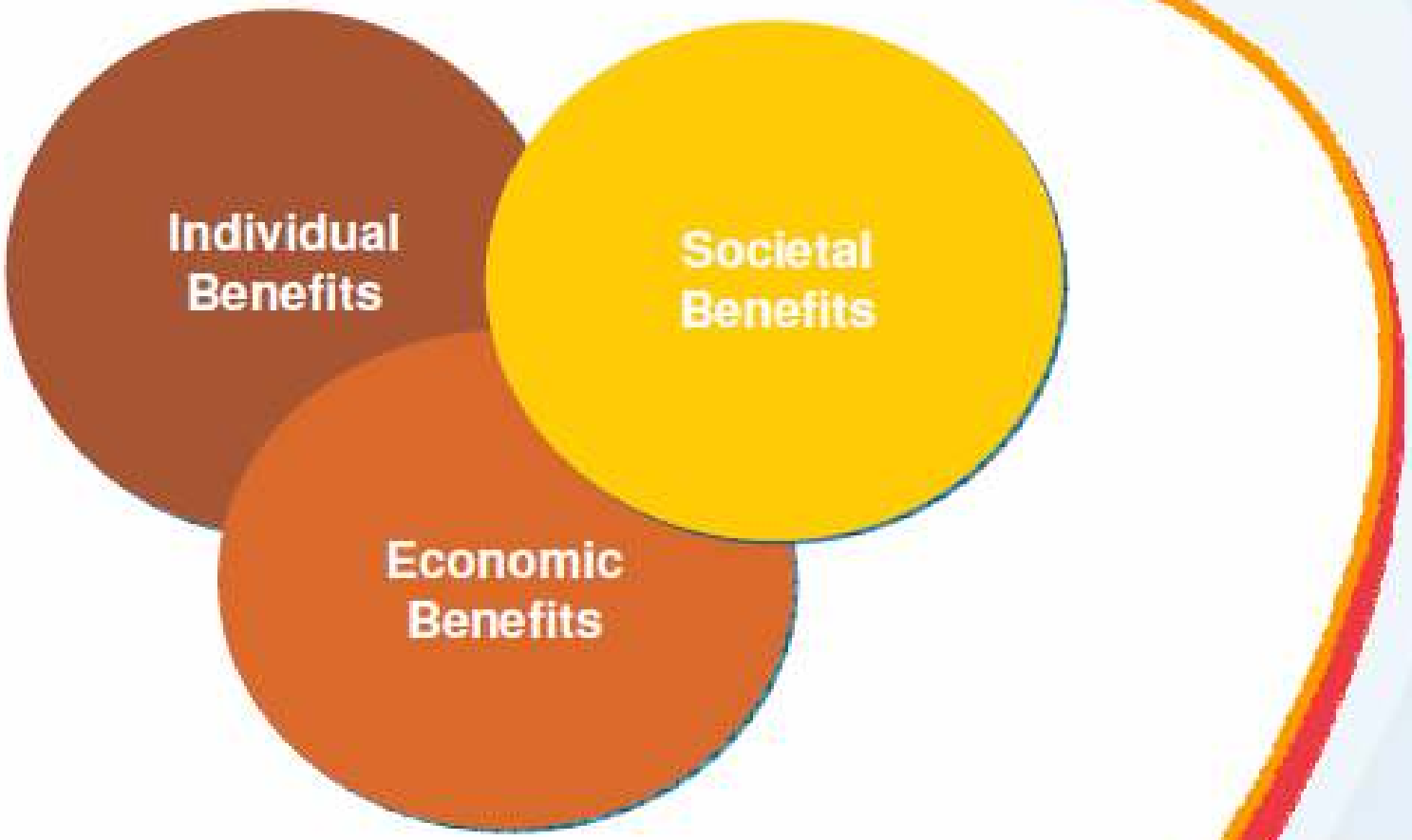

MVA-Ag85A (MVA85A)

Ad35-Ag85A,85b,TB10.4 (A402)

Mtb32,39 in ASO1E (M72)

Ag85B,TB10.4 in IC31 (HyVac4)

# BENEFITS OF VACCINATION



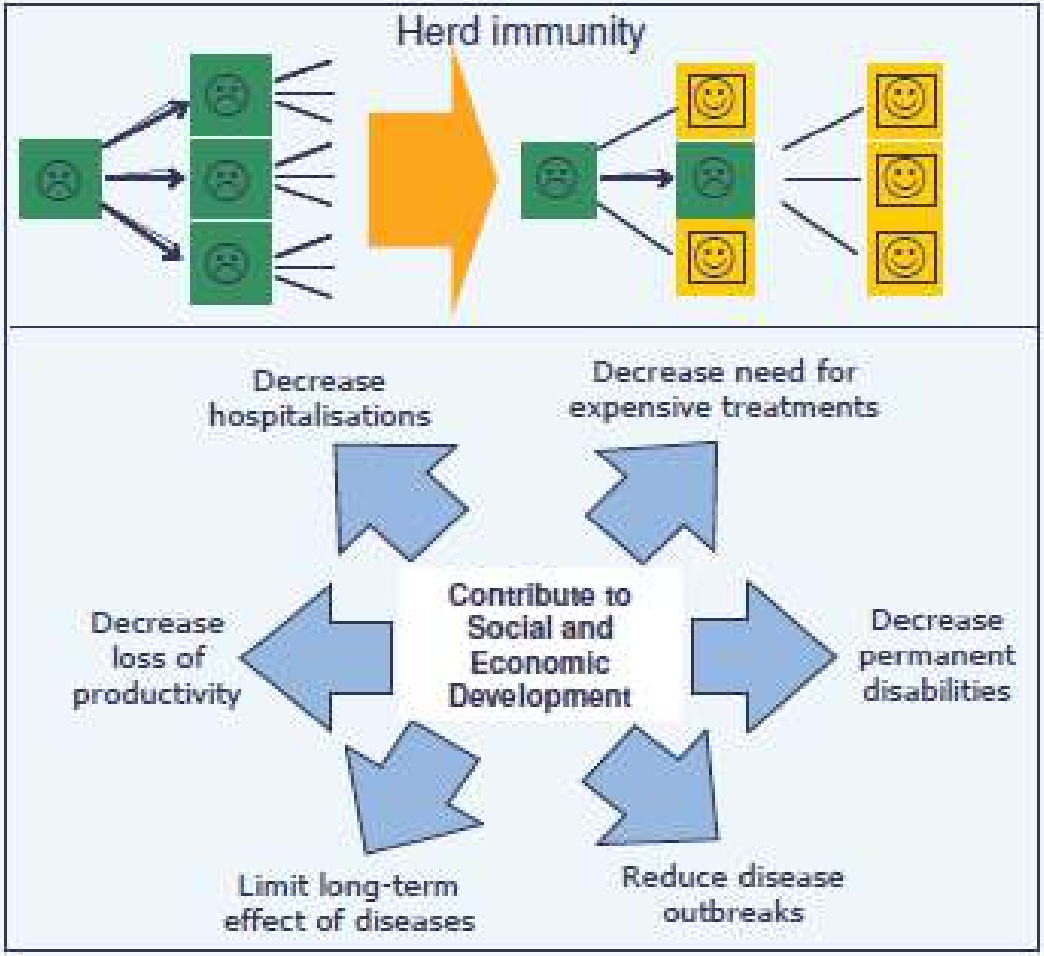
# Individual Benefits

- Today there are 27 vaccine preventable diseases
- Every year, 3 million deaths are prevented and 750,000 children are saved from disability by vaccines
- Immunised children had significantly higher scores in IQ, language (5% level) and maths (10% level)

Individual Benefits

Bloom DE *et al. World Economics* 2005; 6(3): 15–39

# Societal Benefits




Societal Benefits

# Economic Benefits

**Economic benefits**

**In the developing world**

- With the exception of clean drinking water, vaccines are the most cost-effective intervention for economic development*
- A 10 year gain in life expectancy translates into nearly additional 1% of annual growth of income per capita**

**In the developed world**

- For each birth cohort vaccinated, the US saves:
  - $10 billion in direct medical costs
  - $33 billion in indirect costs

*UNICEF 2007; ** D Bloom, ESPID May 2006
***Roush SW, Murphy TV. JAMA 2007; 298:2155-2163

# CHALLENGES

- Despite the great value of vaccines, there is an uphill battle to get vaccination coverage figures high
- A growing proportion of so-called educated minorities leading anti-vaccination campaigns thus endangering disease conrol & elimination
- Emphasis still placed on therapy in preference to prevention in medicine leading to a perception that vaccines are expensive
- Some vaccines are still " packed in shelves" with no near prospects of introducing them to public health programs in a large number of countries
- Exploding costs of R&D of new vaccines, including manufacturing

# CONCLUSION

*"It is a field that is heavily overshadowed by uncertainties, but can be conquered by persistent rational pursuits and by selective choices needed to surmount the hills and mountains in the quest."*


THANK YOU