

Malaria Vaccine Research

- Malaria is the #1 most devastating mosquito-borne disease in the world.
- 300+ million human cases/year
- 1 million deaths/year – mostly children < 5 years. Malaria kills a child every 30 secs.

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Barriers to Stopping Malaria

- Plasmodia parasites have developed resistance to anti-malarial drugs.
- Mosquito vectors (*Anopheles sp.*) developed resistance to pesticides.
- In-ability to provide adequate prevention supplies (e.g. permethrin impregnated bed-nets, repellents, etc.) to populations at risk.

Barriers to Vaccine Development

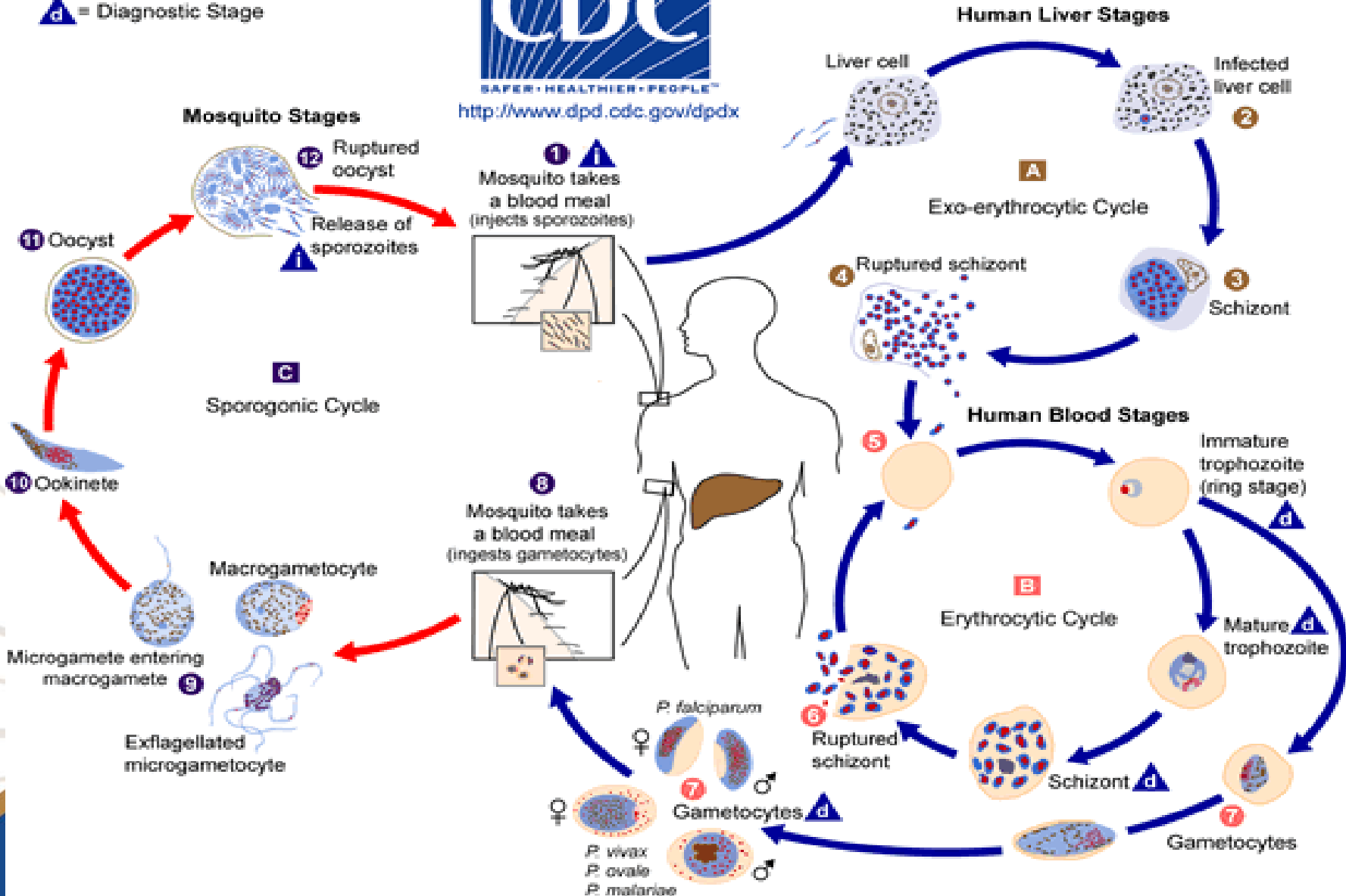
- Four species of plasmodia
 - *Plasmodium falciparum*
 - *P. vivax*
 - *P. malariae*
 - *P. ovale*
- Complex life cycle
- Shifting antigenic makeup
- Unique ability of parasite to evade the immune system



i = Infective Stage
d = Diagnostic Stage



<http://www.dpd.cdc.gov/dpdx>



Malaria Pathogenesis

- Mosquito vectors (*Anopheles* sp.) bites, infects host with sporozoites.
- Sporozoites invade RBCs and liver.
- Multiplication, cells rupture, etc.
- Anemia, liver & kidney damage, brain damage.
- Sx: fever, HA, chills, sweats, anorexia, muscle & joint pain, cough, diarrhea.





Malaria Vaccine Development

- Vaccine R & D has been ongoing for 50+ years!
- Different strategies to interrupt life cycle.
- Immune system response in host (people).
- Interfere with life stages in the mosquito vector.
- Different vaccine approaches:
 - *Live attenuated*
 - *Viral Vectored*
 - *Recombinant proteins*
- Nothing promising has come along, until now.

Malaria Vaccine Development

- RTS,S – originally dvp'ed for military - developed by Glaxo-Smith-Kline® - project initiated 2005.
- Research supported by Gates Foundation
- Vaccine targets a specific protein (circum sporozoite – CS) on surface of the parasite.
- Like other vaccines, RTS,S – the vaccine causes the immune system to recognize the surface protein and produce specific antibodies (Ab) which will target the invaders for destruction by WBCs, or at least inhibit the parasite's ability to multiply.
- It is hoped that vaccine will work in all (or most) plasmodia sp.



Malaria Vaccine Development

- Early clinical trials, smaller scale – human hosts – produced promising results.
- Tanzania – 340 infants vacc.– 3 doses.
- 65% reduction in infections during 6 mos.
- 894 kids (ages 5-17 months) – Tanzania & Kenya – were given 3 doses of vaccine.
- 53% reduction in risk for developing malaria infection (which is a significant improvement in vaccine dev!)



Malaria Vaccine Development

- Results from early studies were publ. in the Dec. 2008 NEJM.
- RTS,S vaccine can be given safely along w/ other childhood vaccines (e.g. diphtheria, tetanus, pertussis, etc.)

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Malaria Vaccine Development

- Expanded human vaccine trials planned in high risk areas/populations– Tanzania, Kenya, Burkina Faso, Malawi & other African countries.
- Labs in 11 hospitals are being equipped for malaria diagnosis (e.g. microscopes, training).
- Goal is to enroll 16,000 high risk people – mostly infants & toddlers.
- Hospitals/labs will look for evidence of infection through (1) blood smears, and (2) clinical sx.
- Compare vaccinated to un-vaccinated.



Malaria Vaccine Development

- Timelines:
- Finish Phase III trials
- GSK hopes to submit vaccine for regulatory approval in 2011.
- Ultimate goal – W.H.O. – include malaria vaccination in the infant immunization programs. Goal to show ↓ trend in malaria by 2015.
- Estimated costs \$500 million.



Questions?



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