Malaria in Pregnancy

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Sir Ronald Ross – Nobel Prize winner
for discovering
life cycle of malaria in mosquito

Sir Ronald Ross Institute of Tropical Diseases, Hyderabad

Lecture Outline

- Epidemiology
- Significance of malaria in pregnancy
- Patho-physiology
- Severe malaria
- Treatment
- Prevention
- Malaria in Asia-Pacific region
- Comorbidities

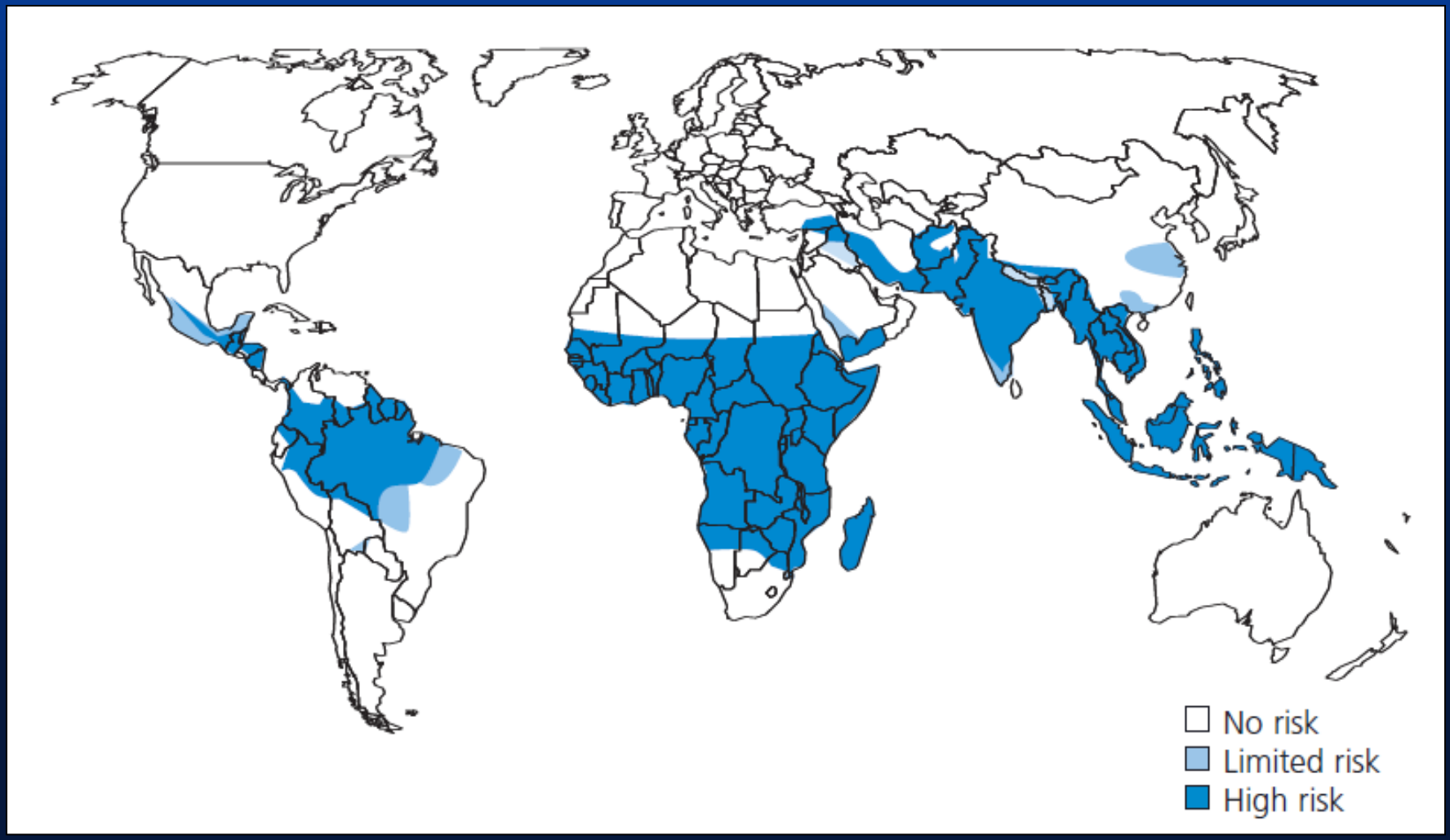
Epidemiology

Introduction

- Human malaria – five species of Plasmodia
  - Vivax, Falciparum, Ovale, Malariae, Knowlesi

- Pregnancy - P. *falciparum*
  - Predominant species
  - Heightened morbidity and mortality

Map of Risk of Malaria Transmission



2005 report on progress towards the MDGs by the United Nations Statistics Division

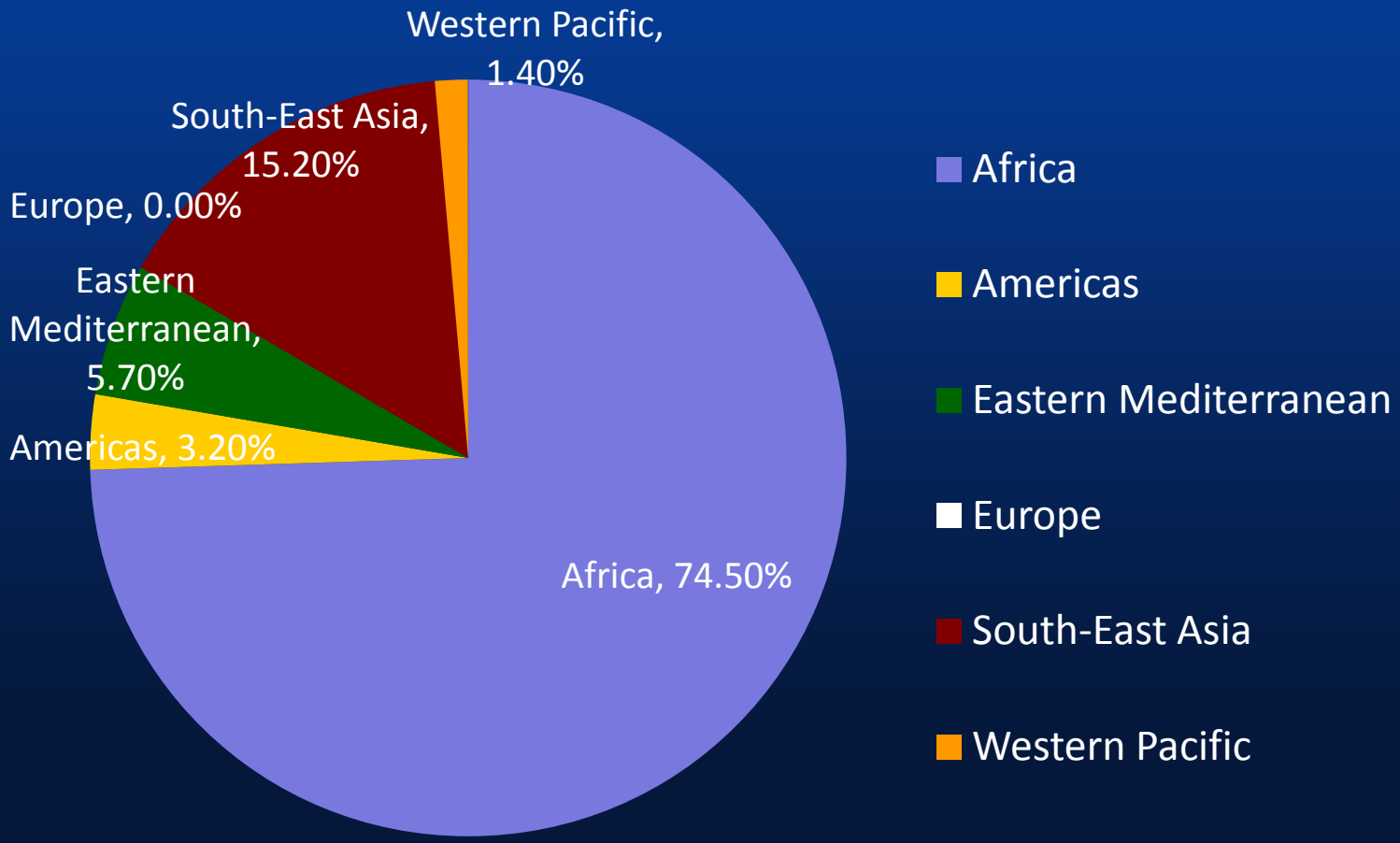
Malaria : Global Situation

- **3.3 billion – at risk**
- **Cases : 216 million (2010)**
- **Deaths : 655,000 (2010)**

Mortality rates : 25% reduction since 2000

http://www.who.int/malaria/world_malaria_report_2011/WMR2011_factsheet.pdf

World Malaria Report 2011 Cases



http://www.who.int/malaria/world_malaria_report_2011/WMR2011_factsheet.pdf

Malaria in Pregnancy – Mortality

- **10,000 – pregnant women**
- **200,000 – infants**
- **Anaemia – half of these deaths**

WHO Malaria Report April 2012

Why is the Issue of Malaria During Pregnancy Important?

More Severe Disease

- **Hypoglycemia (58% vs 8%)**
- **Cerebral malaria**
  - **20% case – fatality**
  - **3% – permanent neurologic sequelae**

50% Mortality

Hypoglycaemia in pregnant women with malaria.
Trans R Soc Trop Med Hyg 1990; 84:349
White NJ. The treatment of malaria. N Engl J Med 1996; 335:800

Other Adverse Maternal and Perinatal Outcomes

- **Miscarriage**
- **Preterm birth**
- **Congenital infection**
- **Perinatal death**

Sholapurkar et al, Trans R Soc Trop Med Hyg 1988
Singh et al, Southeast Asian J Trop Med Public Health 1998
McGready et al, Lancet Infect Dis 2011. Newman et al, J Infect Dis 2003
Espinoza et al, J Matern Fetal Neonatal Med 2005

Why Is the Issue of Malaria during Pregnancy Important?

- In malaria-endemic settings : may account for

Maternal anemia	3 – 15%
Low birth weight newborns	8 – 14%
Growth restriction	13 – 70%
Infant deaths	3 – 8%

Steketee RW et al Am J Trop Med Hyg 2001; 64:28.
Guyatt HL, Snow RW. Clin Microbiol Rev 2004; 17:760.

Why Is the Issue of Malaria during Pregnancy Important?

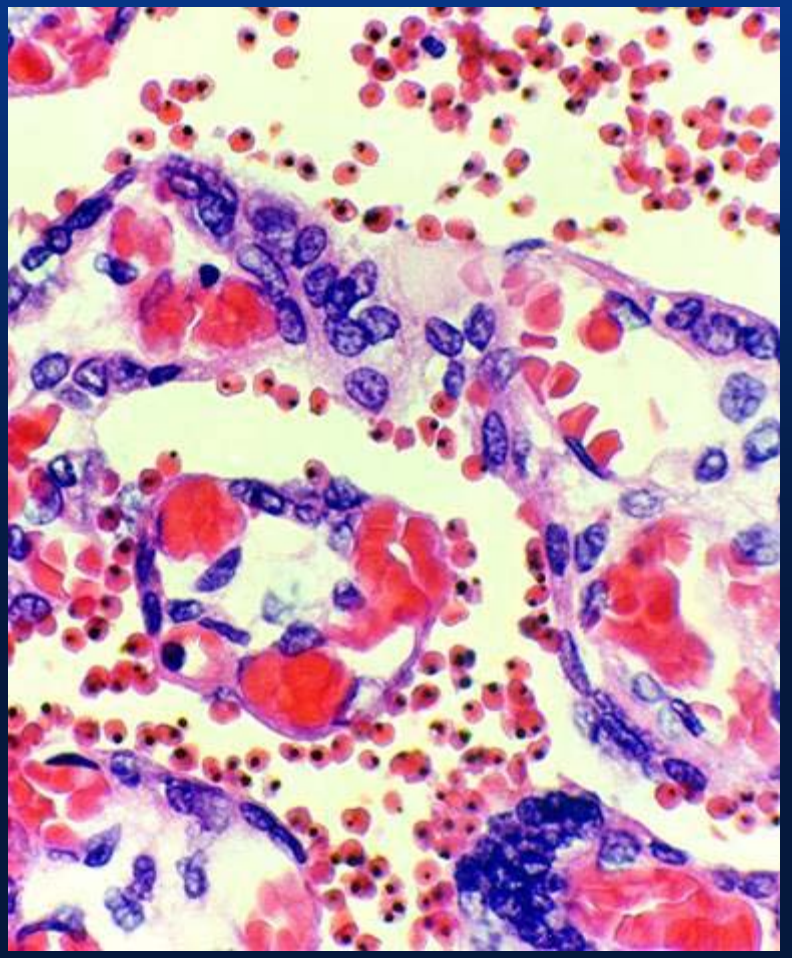
- **60 – 70 days postpartum**
  - **Acquiring infection**
  - **Severe disease**

Diagne et al. N EJM 2000;
Ramharter M et al. J Inf Dis 2005;

Pathophysiology

Placental Malaria

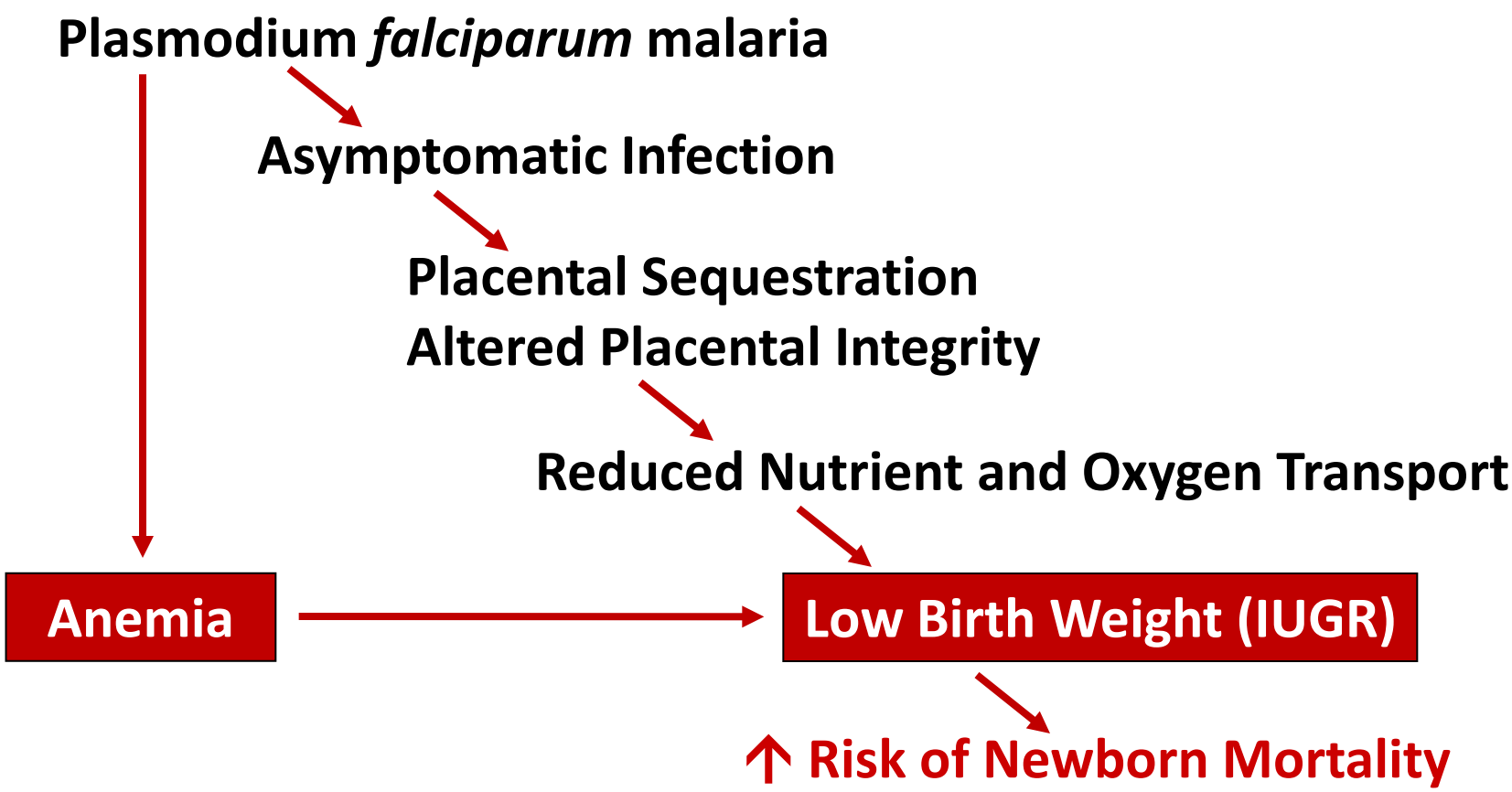
- P. *falciparum*
- Primigravidae



Endemicity

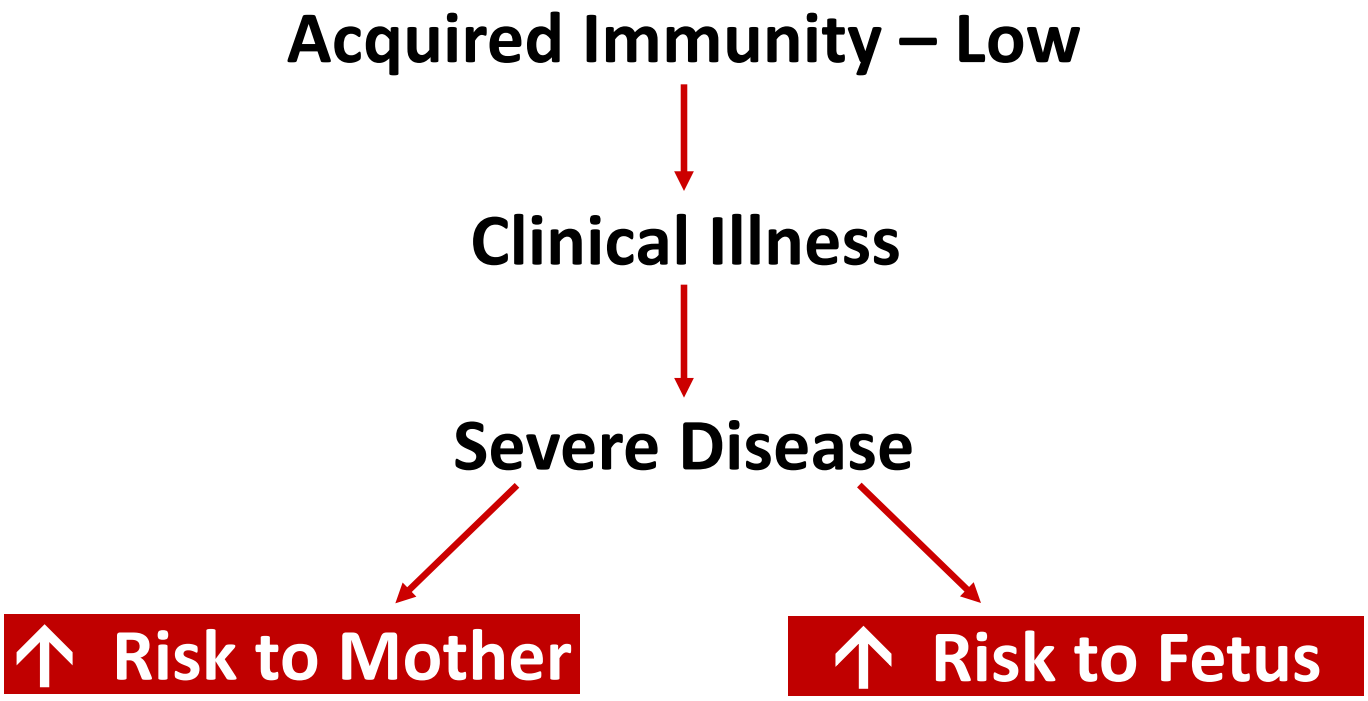
	Holoendemic	Mesoendemic
Children < 5 yrs of age affected	> 60%	< 20%
WHO regions	Sub-Saharan Africa	Endemic areas outside Africa
Median prevalence of maternal malaria	28%	1.8% - 17.4%
Parasite exposure	Stable	Unstable

Effect of Malaria on Pregnancy in Stable Transmission Areas



Source: WHO 2002

Effect of Malaria on Pregnancy in Unstable Transmission Areas

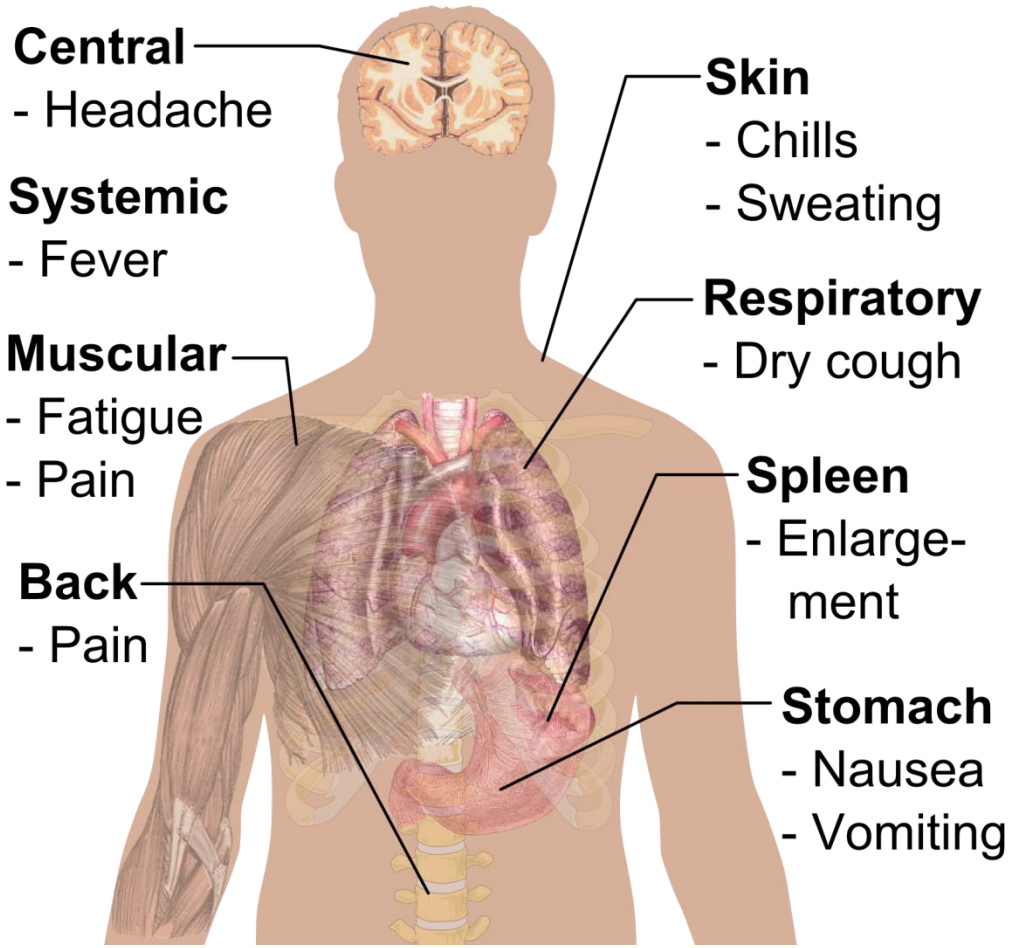


Source: WHO 2002

Clinical Features, Diagnosis and Treatment of Malaria

Signs and Symptoms of Malaria

- Fever
- Jaundice
- Pallor
- Tachycardia
- Hypotension
- Splenomegaly



Severe Malaria (WHO Definition)

- Coma (cerebral malaria)
- Convulsions (> 2 in 24 hr)
- Spontaneous bleeding
- Prostration, failure to feed
- Shock (SBP < 70 mmHg)
- Jaundice or other vital organ dysfunction
- Metabolic acidosis plasma bicarb < 15 mmol/l

Severe Malaria (WHO Definition)

- Hemoglobinuria
- Blood glucose <2.2 mmol/l; 40 mg/dl
- Pulmonary oedema (X-ray)
- Severe anemia (Hb < 5 g/dL PCV < 15%)
- Hyperparasitaemia (> 2% low transmission areas; > 5% in high transmission areas)
- Lactate > 5 mmol/l
- Serum creatinine > 265 µmol/l

Fetal Distress in Severe Malaria

- **Before and during labour**
  - **Falciparum malaria**
  - **Severe anaemia**

Cardiotocography or meconium stained liquor

Mola Get al, Aust NZ J Obstet Gynaecol 1999;
Looareesuwan S, et al,Lancet 1985

Diagnosis of Malaria

- Microscopy: gold standard for diagnosis
  - Rapid; species identification
  - If negative : repeat
- Antigen Capture or Rapid Diagnostic Tests (RDT)
  - Simple; 95% sensitivity and specificity; species
- PCR Test
  - More sensitive; species; 48 – 72 hours
  - Expensive; availability; research

Source : WHO

Anti-malarial Drug Resistance

- Indiscriminate use – selective pressure
- All classes of antimalarials
- Artemisinin-based monotherapies banned (2007)
- Artemisinin-based combination therapies
  - highly effective
  - partner drug : locally effective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Treatment of Malaria in Pregnancy

- Uncomplicated falciparum malaria (first trimester and later gestation)
- Uncomplicated vivax malaria
- Uncomplicated malaria with other plasmodium species
- Severe malaria

Uncomplicated P. *falciparum* Malaria in Pregnancy : Treatment

First trimester:

- **Quinine + Clindamycin for 7 days**
- Artesunate + Clindamycin for 7 days
  - In treatment failure
  - if quinine unavailable

WHO Recommendations 2010

Uncomplicated P*. falciparum* Malaria in Pregnancy : Treatment

Second and Third trimesters and Lactation:

- ACT known to be effective in the region for 7days
  - **Artesunate + Clindamycin: for 7 days**

WHO Recommendations 2010

Uncomplicated P. *vivax* Malaria in Pregnancy : Treatment

- **Chloroquine-sensitive**
  - Oral Chloroquine
- **Chloroquine resistant**
  - ACTs (Artemesinin based combination treatments); partner medicines with long half-lives

? prevent relapses until radical treatment

WHO Recommendations 2010

Anti malarials with Long Half Life

- **Sulfadoxine- pyrimethamine**
  - **(7 – 9 days; 3 – 4 days)**
- **Mefloquine (2 – 3 wks)**

Other Malarial Species (Uncomplicated) – Treatment

- Chloroquine – drug of choice
  - P *knowlesi*
  - P *malariae*
  - P *ovale*

Coldrenet al, Am J Trop Med Hyg 2007

Severe Malaria in Pregnancy : Treatment (P. *vivax* / P. *falciparum*)

- Medical emergency
- Rapid assessment
- Confirm diagnosis
- Parenteral anti-malarials
- Monitor – fetal distress, hypoglycemia

Treatment of Severe Malaria (P. *vivax* / P. *falciparum*)

- Parenteral for minimum 24 hr then oral
- Total 7 days with Clindamycin
- Artesunate IV or IM
  - Artemether / Quinine (acceptable alternative)

WHO Recommendations 2010

Artemisinine Compounds

- Rapid schizonticidal; Gametocidal
- Artesunate – water soluble; unstable; given IV/IM

Dose adjustment not needed in vital organ dysfunction

Other Anti-Malarials – Safety in Pregnancy

- Chloroquine
- Quinine and Quinidine
- Amodiaquine
- Mefloquine
- Atovaquone + Proguanil
- Lumefantrine
- Sulfadoxine-pyrimethamine

Drugs that should NOT be used during Pregnancy and Lactation

- Tetracycline
- Doxycycline
- Primaquine
- Halofantrine


Prevention

Prevention of Malaria in Pregnant Women in Holoendemic Areas

- Intermittent Preventive Therapy (IPT)
  - sulfadoxine-pyrimethamine (SP)

- Insecticide-Treated Nets (ITNs)

Malaria Guideline, WHO 2010

Sleeping under Long-lasting Insecticidal Nets Protects Against Malaria

Intermittent Preventive Therapy (IPT) in Holoendemic Areas

- 2 doses of Sulfadoxine-Pyrimethamine
  - at quickening and at 28 – 34 wk
- Prevents 23 – 86% severe maternal anemia
- New recommendations : 4 doses

Malaria Guideline, WHO 2010

Advise to Pregnant Women Travelling to Malaria Endemic Areas

- Avoid travelling if possible
- Use insecticide sprayed nets / repellent sprays
- Prophylaxis : local drug resistance patterns
- Drug used for chemoprophylaxis should not be used for treatment

WHO Recommendations 2010

Chemoprophylaxis of Malaria in Pregnant Travelers

Mefloquine

- Sub-Saharan Africa
- Once weekly
- 2.5 – 3 weeks before entering malaria area
- Avoid in T1

Chemoprophylaxis of Malaria in Pregnant Travelers

Chloroquine + Proguanil

- Only if no chloroquin resistance
- CQ weekly, PG daily
- 24 hr before entering malaria area till 1 week after returning

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Malaria in Pregnancy - Our Experience

Our Experience

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- 16 cases – 10 years
- Uncomplicated – 11
- Complicated – 5 (30%)
- Vivax – 6, falciparum – 5, data not available – 5
- Artesunate received – 6, Chloroquine received – 8

Our Experience

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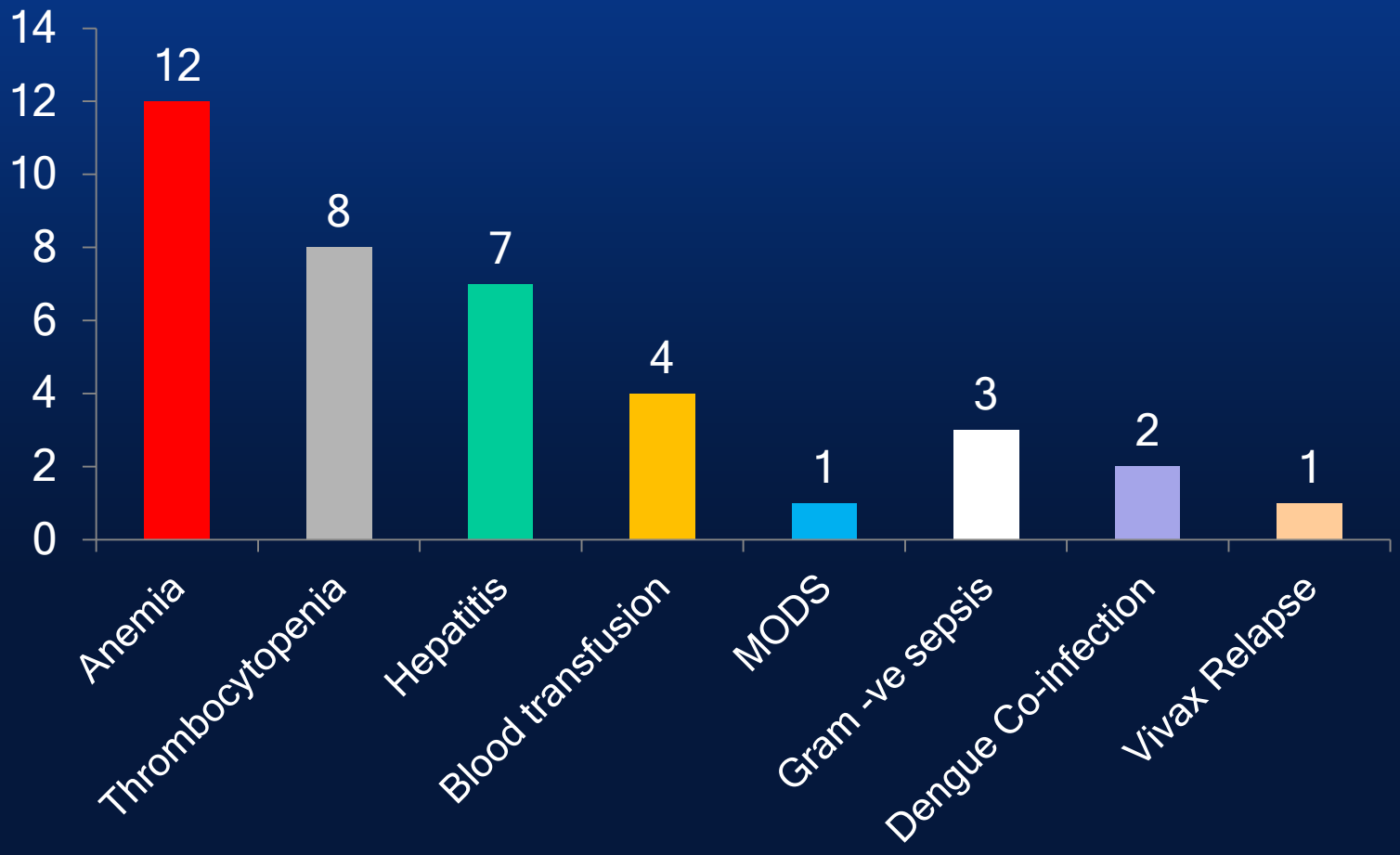

Our Experience

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- **Maternal deaths – none**
- **Neonatal outcomes – good**

  – despite 3 preterm births

Conclusion – Malaria in Pregnancy

- Threat both to mother and to pregnancy
- Management can be challenging
- Endemic areas : often not suspected; not treated
- Non endemic areas : severity is under-estimated
- Priority : data on safety of anti-malarials

Never delay treatment with effective drugs

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