Frontiers in Global Health, 15.232, Management Briefing - Malaria

Disease Definition: Malaria is a parasitic disease caused by protozoa from the genus *Plasmodium* that invade red blood cells and is characterized by an intermittent and reoccurring fever.

Disease life cycle (adapted from NIH, 2013):
The classic infection vector to humans is via female *Anopheles* mosquitos:

1. A female *Anopheles* mosquito carrying infectious malarial sporozoites feeds on human and injects sporozoites into the blood stream
2. In 1 – 2 weeks the sporozoites reproduce in the liver and form merozoites. Merozoites can reside dormant in the liver for extended time periods
3. The merozoites exit the liver and enter the blood stream and invade red blood cells (RBCs). The merozoites reproduce asexually in the RBCs over a 72 hour period. The RBCs accumulate merozoites and eventually the lyse to release the merozoites and cell waste into the blood stream:
    a. The immune system responds to the lysed RBCs and creates the malarial symptoms such as shaking chills, high fevers, low body temperature, sweating, headache, vomiting, diarrhea, and paroxysm
    b. Some merozoites develop into sexual forms called gametocytes that circulate in the blood stream
4. Uninfected mosquitos feed on an infected human. The infected RBCs burst in the mosquito's gut that releases the gametocytes that reproduces sexually into infectious malarial sporozoites.

Malaria symptoms can be difficult to differentiate from other diseases without laboratory testing. Thus the co-morbdity of malaria shows conflicting data:

- Meningitis and severe invasive bacterial infections are associated with severe malaria deaths in children. HIV and anemia are also associated with malaria in children (Gwer, Newton, Berkley 2007).
- Fenn, Morris, and Black (2005) show a *negative* co-morbidity exists with diarrhea, dysentery, and pneumonia. The hypothesis is the additional conditions disrupt the malaria life cycle. However the authors do caution that the sample size lacks enough power

Affected Population Groups

- 219 million cases of malaria and up to 917,000 deaths as of 2010 (WHO 2013)
- 70% of malaria deaths are children in Sub-Saharan Africa (Roll Back Malaria 2013)
    - Nigeria and the Democratic Republic of the Congo account for 40% of malaria deaths (Roll Back Malaria 2013)
- At risk populations are:
    - Children in Sub-Saharan Africa (SSA) are most afflicted, especially in poor rural areas. WHO estimates a child dies each minute in SSA (WHO 2012)
    - Pregnant women (CDC 2012)
    - HIV/AIDS patients (CDC 2012)
    - People traveling to/from malaria endemic areas with no immunity (CDC 2012)

Treatment Options

- Primary mode of prevention is mosquito vector control with indoor residual spraying (IRS) and insecticide treated nets (ITN) (WHO 2012)
- Early diagnosis and course of anti-malarial drugs are required to stop illness (Pearson 2008)
- No vaccine options exist (Pearson 2008)
- Recommended first treatment is artemisinin-based combination therapy (ACT) (WHO 2012)
- Chemoprophylaxis is recommended for people with no innate immunity (Pearson 2008)
- Resistance to antimalarial drugs and insecticides are increasing worldwide (WHO 2012)
- Fevers persist and may create severe malaria infections and death (WHO 2012)
- Common to prescribe anti-malarias without proof and misdiagnosis fails to treat disease (Gwer et al 2007)

Patient Care Differences

- Malaria is virtually eradicated in richer nations and can be treated effectively with an outpatient visit and a course of anti-malarial combination therapy (Gates 2013)
- Malaria accounts for 20 – 30% of hospital admissions and 30 – 50% of outpatient visits in SSA (WHO 2008)
- Malaria is strongly associated with poverty. Countries with per capital earnings less than US $1.25 per day have higher mortality rates (WHO 2012)
- Vector control measures like insecticide treated nets are used more in wealthier, urban areas and diminish in use in rural areas (WHO 2012)

- Microbiological methods, rapid tests, and effective anti-malarial drugs are more likely to be administered within the recommended 24 hours after start of symptoms with proximity to urban centers (WHO 2012)
- There is a lack of rapid diagnostic tests in malaria endemic rural areas (CDC 2012)
- Patient care focuses on chemoprophylaxis for pregnant women (IPT) and short case preventive treatment for children (WHO 2012)
- In rural areas patients visit local medical provides based on low costs, price negotiation, short waits, family elder recommendations, and longer open hours (Kizito, Kayendeke, Nabirye, Staedke, Chandler 2012)

Important Inputs to Treat

The cause and spread of malaria depends on the *Anopheles* mosquito and its human host. Inputs to stopping this cycle are:

- Vector Controls
    - Continued development and deployment of effective insecticides (WHO 2012)
    - New mosquito repellant "stealth" or invisibility technology (Sturrock 2013)
- Human Controls
    - Education and Surveillance
        - Increased acceptance of established microbiological methods (WHO 2012)
        - Standard training and increased quality control in healthcare providers (Roll Back Malaris 2008)
        - Increased funding for increased health care coverage and supplies (WHO 2013)
        - Development of reporting systems in poorer nations with historically low malaria reporting (WHO 2013)
        - Universal rapid diagnostic testing availability and use for 100% of suspected malaria cases (WHO 2012)
    - Prevention
        - Continued development of vaccines (Gates 2013)
        - Adoption of WHO recommendations for malaria control by providing ITN and IRS (WHO 2012)
        - Provide basic sanitation and health care services for all high risk malaria areas (Kizito, et al 2012)
    - Treatment and Prophylaxis
        - A reliable supply chain of anti-malarial drugs to ensure full course of anti-malarial treatment for all infected persons (WHO 2008)
        - Reduction of counterfeit drugs (WHO 2008)
        - Increased availability and deployment of rapid diagnostic testing for malaria (WHO 2012)
        - Confirmation of malaria diagnosis for accurate treatment (WHO 2012)
        - Continued development of anti-malarials in the face of growing drug resistance (WHO 2008)

Conclusion

The science of treating malarial infections and preventing the occurrence of infection between humans and mosquitos are well known. The complexity lies in providing effective prevention and treatment amongst the poorest countries in the world in the Sub-Saharan section of Africa where it is among the leading causes of death (WHO 2012). The burden of fighting malaria is high when viewed through human and financial lenses. Malaria tends to strike a family five to six times year around harvest time, decreasing productivity. A low income African family with a yearly income of US $68 will spend US $19 a year on malaria treatments. The Roll Back Malaria (2012) and the Global Malaria Action Plan (2008) groups of the WHO found:

- Disease burden of malaria to be 35.4 million Disability Adjusted Life Years. (GMAP 2008)
- US $6.8 billion is required to tackle malaria between 2013 and 2015 with a funding gap of US $3.6 billion (Roll Back Malaria 2012)
- US $12 billion in direct losses and 1.3% of lost GDP growth in Africa (Roll Back Malaria 2012)
- ITN with a three year life span costs US $1.39 per person per year of protection (Roll Back Malaria 2012)
- ACT for an adult costs US $0.90 - $1.40 (Roll Back Malaria 2012)
- ACT for a child costs US $0.30 – 0.40 (Roll Back Malaria 2012)
- Rapid diagnostic test costs US $0.50 (Roll Back Malaria 2012)
- Global reduction in malaria rates is 25% and 33% in Africa (Roll Back Malaria 2012)

At the start of the 20th century, malaria was prevalent across the world. The reduction of malaria in temperate areas is nearly complete and there is a worldwide belief that malaria can become an eradicated disease like smallpox (Gates 2013). However, the natural resilience of malaria and insecticides to our current tools is reversing our advances against malaria. As a result, the means to detect, to prevent, and to treat malaria is decreasing. The ability to respond to the challenge of treating malaria will be heavily contingent on continued funding by global partners, development of effective tools and drugs, and the will to execute the policies required against the disease.

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