

Chapter 12

Malaria in Women and Children

Martin Meremikwu, Emmanuel Ezedinachi and John E. Ehiri

Learning Objectives After reading this chapter and answering the discussion questions that follow, you should be able to

- Explain the global burden of malaria, discuss its clinical manifestations, and appraise its health impact on women and children.
- Analyze the mechanisms and consequences of malaria and HIV co-infection and discuss current treatment, control and prevention strategies.
- Describe the challenges posed by vector resistance to insecticides, parasite resistance to anti-malarials, climate change, wars/conflicts, and HIV/AIDS to malaria control and prevention efforts.
- Evaluate social, cultural, and economic limitations of community-based programs for malaria control and prevention.

Introduction

Malaria is caused by *Plasmodium*, a protozoan parasite transmitted through the bite of infected female anopheline mosquitoes. The four species of *Plasmodium* known to cause malaria in humans are *P. falciparum*, *P. malariae*, *P. ovale*, and *P. vivax*. *Plasmodium falciparum* is the most virulent of these species and is responsible for most cases of malaria infections and malaria deaths in sub-Saharan Africa. *Plasmodium vivax*, the second most common species of the malaria parasite, is more

prevalent in Asia and is rarely associated with acute complications of malaria or fatality. Box 12.1 presents definitions of some of the most commonly used terms in malaria epidemiology.

Figure 12.1 shows the global distribution of malaria transmission risk. Malaria transmission occurs in Africa, Asia, and the Americas, but sub-Saharan Africa bears over 80% of the global burden of malaria mortality (Ehiri et al. 2004). Malaria is still a major public health problem in parts of Southeast Asia with foci of high *P. falciparum* transmission and high incidence of multidrug resistance.

More than 40 species of *Anopheles* mosquitoes transmit malaria. *Anopheles gambiae*, which is the most efficient and resilient vector, is the predominant vector in most parts of tropical Africa, where it finds adequate rainfall, temperature, and humidity to support its breeding. Figure 12.2 provides an illustration of the life cycle of *Plasmodium* in the human and in the mosquito vector.

Spleen rates (percentage of the population with palpably enlarged spleen at any given time) and parasite rates (percentage of the population with malaria parasites in peripheral blood film at any given time) are traditionally used as malario-metric indices to determine whether or not malaria is endemic in a given area. The entomologic inoculation rate (EIR) is believed to be a better measure of malaria transmission and risk of infection than spleen or parasite rates. However, it is more difficult to assess. EIR is the product of human biting rates (the number of mosquitoes biting a person over a given period of time) and the sporozoite rate (the proportion of vectors with sporozoites in the salivary glands) (Snow et al. 2004).

M. Meremikwu (✉)
Department of Pediatrics Institute for Tropical Disease
Research, University of Calabar, Calabar, Cross River
State, Nigeria

Box 12.1 Definition of Terms

Anemia: A reduction in the number of circulating red blood cells or in the quantity of hemoglobin.

Anopheles: A genus of mosquito, some species of which can transmit human malaria.

Artemisinin: A drug used against malaria, derived from the Qinghao plant, *Artemisia annua* L.

Cerebral Malaria: A complication of *Plasmodium falciparum* malaria in which infected red blood cells obstruct blood circulation in the small blood vessels in the brain. When cerebral malaria is present, the disease is classified as severe malaria.

Chemoprophylaxis: Taking antimalarial drugs to prevent the disease.

Chloroquine: A drug used against malaria. A very safe and inexpensive drug, its value has been compromised by the emergence of chloroquine-resistant malaria parasites.

Drug Resistance: Drug resistance is the result of microbes changing in ways that reduce or eliminate the effectiveness of drugs, chemicals, or other agents to cure or prevent infections.

Endemic Malaria: Constant incidence over a period of many successive years in an area.

Epidemic: The occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular period of time.

Erythrocyte: A red blood cell.

Erythrocytic Stage: A stage in the life cycle of the malaria parasite found in the red blood cells. Erythrocytic stage parasites cause the symptoms of malaria.

Gametocyte: The sexual stage of malaria parasites. Male gametocytes (microgametocytes) and female gametocytes (macrogametocytes) are inside red blood cells in the circulation. If they are ingested by a female *Anopheles* mosquito, they undergo sexual reproduction which starts the extrinsic (sporogonic) cycle of the parasite in the mosquito. Gametocytes of *Plasmodium falciparum* are typically banana- or crescent-shaped (from the latin *falcis* = sickle).

Hemoglobin: The red, oxygen-carrying protein found in red blood cells.

Hemolysis: Destruction of red blood cells. Malaria causes hemolysis when the parasites rupture the red blood cells in which they have grown.

Hyperreactive Malarial Splenomegaly (also called “tropical splenomegaly syndrome”): occurs infrequently and is attributed to an abnormal immune response to repeated malarial infections. The disease is marked by a very enlarged spleen and liver, anemia, and a susceptibility to other infections (such as skin or respiratory infections).

Hypoglycemia: Low blood glucose. Hypoglycemia can occur in malaria. In addition, treatment with quinine and quinidine stimulate insulin secretion, reducing blood glucose.

Immunity: Protection generated by the body’s immune system, in response to previous malaria attacks, resulting in ability to control or lessen a malaria attack.

Leukocyte: White blood cell.

Lymphocyte: Leukocyte with a large round nucleus and usually a small cytoplasm. Specialized types of lymphocytes have enlarged cytoplasm and produce antibodies.

Merozoites: A daughter cell formed by asexual development in the life cycle of malaria parasites. Liver stage and blood stage malaria parasites develop into schizonts which contain many merozoites. When the schizonts are mature, they (and their host cells) rupture; the merozoites are released and infect red blood cells.

Monocyte: Leukocyte with a large, usually kidney-shaped nucleus. Within tissues, monocytes develop into macrophages which ingest bacteria, dead cells, and other debris.

Oocyst: A stage in the life cycle of malaria parasites, oocysts are rounded cysts located in the outer wall of the stomach of mosquitoes. Sporozoites develop inside the oocysts. When mature, the oocysts

rupture and release the sporozoites, which then migrate into the mosquito's salivary glands, ready for injection into the human host.

Parasitemia: The presence of parasites in the blood. The term can also be used to express the quantity of parasites in the blood (e.g., 'a parasitemia of 2%').

Phagocyte: A type of white blood cell that can engulf and destroy foreign organisms, cells and particles.

Platelets: Small, irregularly-shaped bodies in the blood that contain granules. These cells are important components of the blood coagulation (clotting) system.

Presumptive Treatment: Treatment of clinically suspected cases without, or prior to, results from confirmatory laboratory tests.

Protozoan: Single-celled organism that can perform all necessary functions of metabolism and reproduction. Some protozoa are free-living, while others, including malaria parasites, parasitize other organisms for their nutrients and life cycle.

Residual insecticide spraying: Treatment of houses by spraying insecticides that have residual efficacy (i.e., that continue to affect mosquitoes for several months). Residual insecticide spraying aims to kill mosquitoes when they come to rest on the walls, usually after a blood meal.

Resistance: The ability of an organism to develop strains that are impervious to specific threats to their existence.

Schizogony: Asexual reproductive stage of malaria parasites. In red blood cells, schizogony entails development of a single trophozoite into numerous merozoites. A similar process happens in infected liver cells.

Schizont: A developmental form of the malaria parasite that contains many merozoites. Schizonts are seen in the liver-stage and blood-stage parasites.

Sequelae: Morbid conditions following as a consequence of a disease.

Severe Malaria: occurs when *P. falciparum* infections (often in persons who have no immunity to malaria or whose immunity has decreased) are complicated by serious organ failures or abnormalities in the patient's blood or metabolism, resulting in cerebral malaria, with abnormal behavior, impairment of consciousness, seizures, coma, or other neurologic abnormalities, severe anemia due to hemolysis (destruction of the red blood cells), hemoglobinuria (hemoglobin in the urine) due to hemolysis, pulmonary edema (fluid buildup in the lungs) or acute respiratory distress syndrome (ARDS), which may occur even after the parasite counts have decreased in response to treatment, abnormalities in blood coagulation and thrombocytopenia (decrease in blood platelets), cardiovascular collapse, shock, acute kidney failure, hyperparasitemia, where more than 5% of the red blood cells are infected by malaria parasites, metabolic acidosis (excessive acidity in the blood and tissue fluids), often in association with hypoglycemia (low blood glucose).

Splenomegaly: Enlargement of the spleen, found in some malaria patients. Splenomegaly can be used to measure malaria endemicity during surveys (e.g., in communities or in school children).

Sporozoite Rate: The proportion of female anopheline mosquitoes of a particular species that have sporozoites in their salivary glands (as seen by dissection), or that are positive in immunologic tests to detect sporozoite antigens.

Sporozoite: A stage in the life cycle of the malaria parasite. Sporozoites are produced in the mosquito and migrate to the mosquito's salivary glands. They can be inoculated into a human host when the mosquito takes a blood meal on the human. In the human, the sporozoites enter liver cells

where they develop into the next stage of the malaria parasite life cycle (the liver stage or exoerythrocytic stage).

Stable Malaria: A situation where the rate of malaria transmission is high without any marked fluctuation over years though seasonal fluctuations occur.

Strain: A genetic variant within a species.

Sulfadoxine–pyrimethamine: A drug used against malaria.

Trophozoite: A developmental form during the blood stage of malaria parasites. After merozoites have invaded the red blood cell, they develop into trophozoites (sometimes, early trophozoites are called “rings” or “ring stage parasites”); trophozoites develop into schizonts.

Uncomplicated Malaria: The classical, (but rarely observed) uncomplicated malaria attack that lasts 6–10 hours. It consists of a cold stage (sensation of cold, shivering), a hot stage (fever, headaches, vomiting, seizures in young children), and finally a sweating stage (sweats, return to normal temperature, tiredness).

The classical (but infrequently observed) uncomplicated malaria attacks occur every second day with the “tertian” parasites (*P. falciparum*, *P. vivax*, and *P. ovale*) and every third day with the “quartan” parasite (*P. malariae*). More commonly, the patient presents with a combination of symptoms that include fever, chills, sweats, headaches, nausea and vomiting, body aches, general malaise.

Unstable Malaria: A situation where the rate of malaria transmission changes from year to year.

Vaccine: A preparation that stimulates an immune response that can prevent an infection or create resistance to an infection.

Vector: An organism (e.g., *Anopheles* mosquitoes) that transmits an infectious agent (e.g. malaria parasites) from one host to the other (e.g., humans).

Source: Malaria Glossary – Centers for Disease Control and prevention

<http://www.cdc.gov/malaria/glossary.htm>

Malaria transmission can be perennial (occurring throughout the year), high, intense, and/or stable, low, unstable, and seasonal. High stable transmission of mostly *P. falciparum* associated with high incidence of severe illness and mortality among preschool children is the predominant pattern of malaria in most of sub-Saharan Africa. The average malaria incidence rates across several parts of Africa with high transmission are estimated at 1.4 per persons per year, 0.59 per persons per year, and 0.11 persons per year for age groups <5 years, 5–14 years, and ≥15 years, respectively (Snow et al. 2003). In low transmission areas, incidence rates of malaria are much lower, and differ only marginally between the young and older age groups. Malaria epidemics are more likely to occur in areas with seasonal and unstable transmission.

Burden of Malaria

Figure 12.3 illustrates the various pathways by which malaria contributes to poverty, under-development, malnutrition, and maternal and infant mortality. Some 300–500 million malaria episodes occur annually. Children under 5 years of age in sub-Saharan Africa and women who are pregnant for the first or second time bear the heaviest burden of malaria morbidity and mortality. An estimated 250 million episodes of clinical malaria occur in young sub-Saharan African children annually. About 1 million cases are cerebral malaria, 4 million cases are severe anemia, and approximately 1 million result in death. Estimates of malaria mortality show wide variation. A review of the literature on this subject shows that the number of deaths due to malaria in African children aged less than 5 years

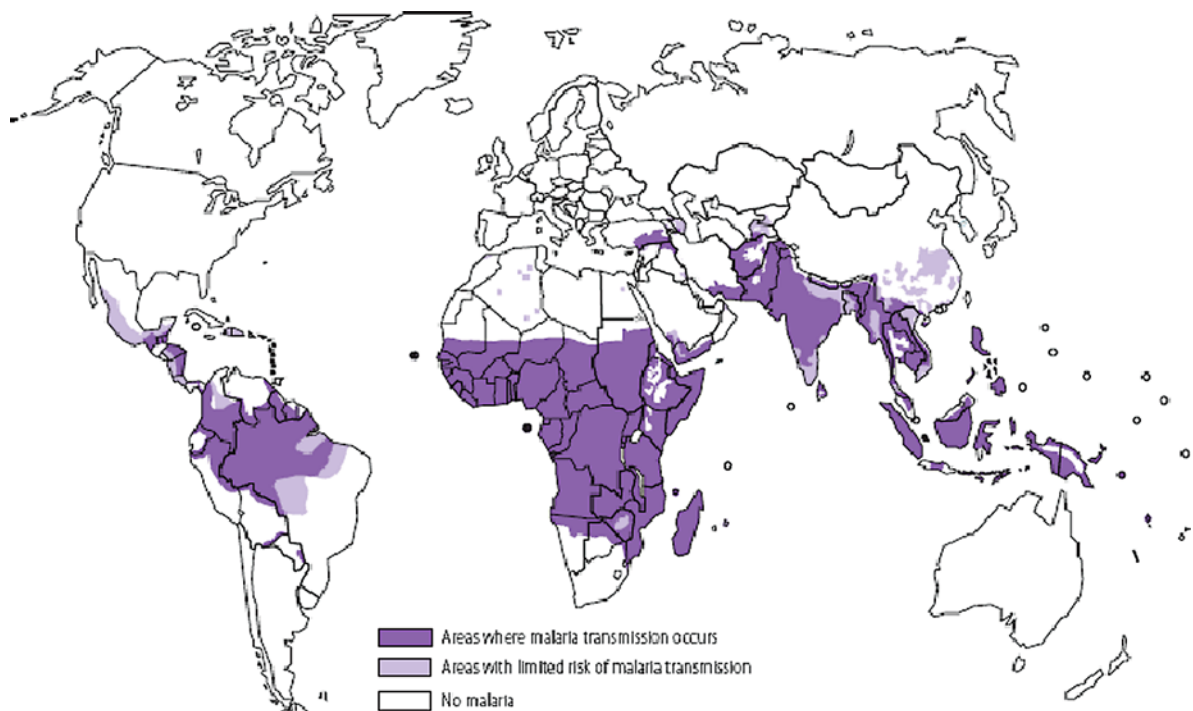


Fig. 12.1 Global distribution of malaria transmission risk, 2003. Source: WHO (2007)

could be between 625,000 and 1,824,000 annually (Breman et al. 2004).

About 250,000 of those that survive develop sequelae from neurological complications of *P. falciparum* malaria. Pregnant women are more vulnerable to adverse consequences of malaria than other adults. An estimated 10 million infections occur in pregnant women annually, resulting in 500,000 cases of severe maternal anemia and 500,000 low birth weight babies (Greenwood et al. 2005). In malaria-endemic countries of Africa, up to 40% of all outpatient clinic visits and between 20 and 50% of all hospital admissions are due to malaria (WHO 2003). Although the incidence of uncomplicated malaria is lower in adolescents aged 10–19 years than younger school aged and preschool children, the burden of malaria in this age group could be substantial in areas with high and stable transmission. A recent review of the epidemiology and pattern of malaria in adolescents estimates the clinical malaria rate in African adolescents aged 10–20

years to be 0.252 attacks per adolescent per year (Lalloo et al. 2006). Results of analyses based on rainfall and temperature data and geographic information system (GIS) population databases in areas with high and stable malaria transmission put the yearly estimate of the number of malaria attacks in children aged 0–4 years, 5–9 years, and 10–14 years at 81.3 million, 16.0 million, and 13.4 million, respectively.

Clinical Manifestation of Malaria

The clinical pattern and deleterious consequences of malaria infection vary, depending on the level of acquired malaria immunity of the individual and the pattern of malaria transmission in an area. In areas with high and stable malaria transmission, resident adults and older children acquire sufficient partial immunity to reduce the

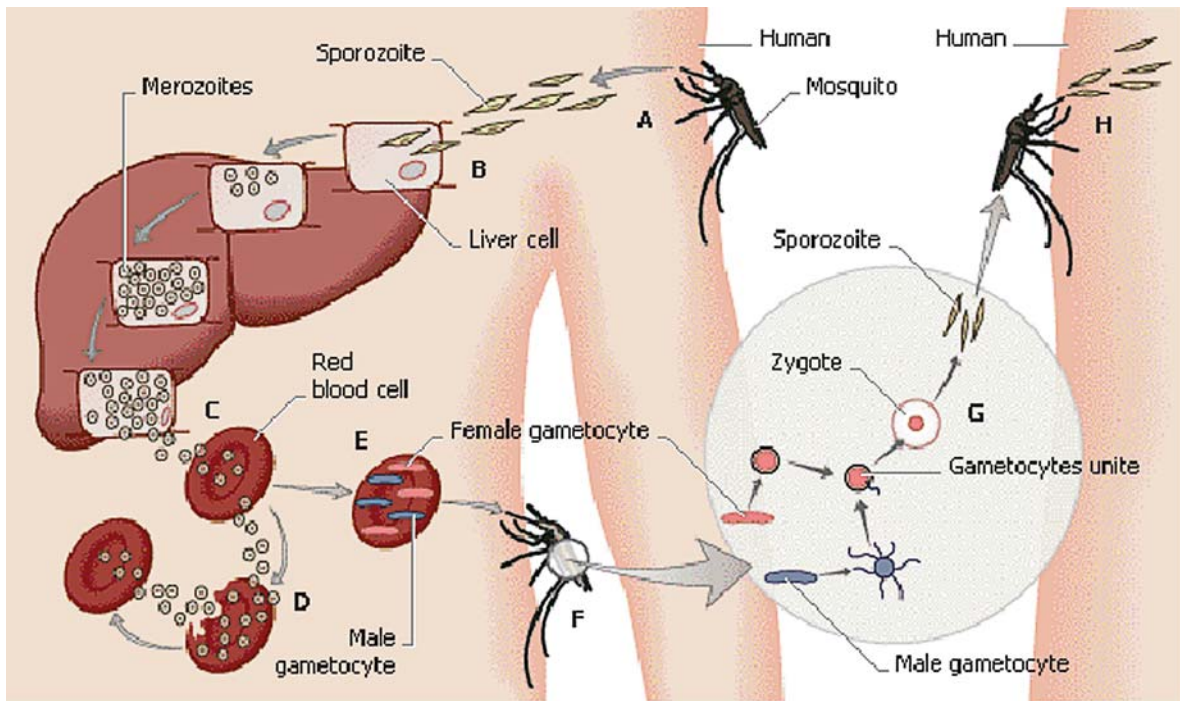
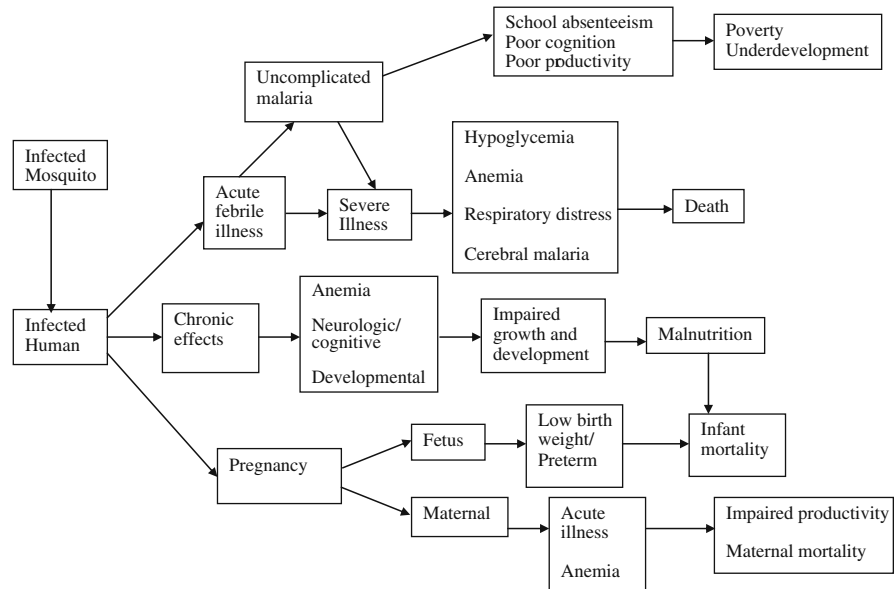


Fig. 12.2: Life cycle of *Plasmodium* parasite. Key: (A) Mosquito infected with the malaria parasite bites human, passing cells called sporozoites into the human's bloodstream. (B) Sporozoites travel to the liver. Each sporozoite undergoes asexual reproduction, in which its nucleus splits to form two new cells called merozoites. (C) Merozoites enter the bloodstream and infect red blood cells. (D) In red blood cells, merozoites grow and divide to produce more merozoites, eventually causing the red blood cells to rupture. Some of the newly released merozoites go on to infect other red blood cells. (E) Some merozoites develop into sex cells known as male and female gametocytes. (F) Another mosquito bites the infected human, ingesting the gametocytes. (G) In the mosquito's stomach, the gametocytes mature. Male and female gametocytes undergo sexual reproduction, uniting to form a zygote. The zygote multiplies to form sporozoites, which travel to the mosquito's salivary glands. (H) If this mosquito bites another human, the cycle begins again. Source: Microsoft Encarta (2008), http://encarta.msn.com/media_461541582_761566151_-1_1/life_cycle_of_the_malaria_parasite.html

Fig. 12.3 Pathways by which malaria contributes to morbidity, mortality, and under-development. Source: Adapted from Breman (2004)



risk of severe and fatal malaria but younger children and pregnant women remain vulnerable to severe and complicated malaria. Malaria infection may be asymptomatic or symptomatic. The majority of malaria infections in areas where transmission is high and stable are asymptomatic. Even when malaria infection is asymptomatic, it is believed that the high prevalence of low parasitemic and asymptomatic malaria infections contribute to the high prevalence of mild and moderate childhood anemia. In these settings, young children who are less immune to the disease are more likely to have clinical malaria following infections.

The common symptoms of uncomplicated malaria are fever, poor appetite, aches, malaise, nausea, and vomiting. Uncomplicated malaria is the most common reason for which children and adults use the health service in sub-Saharan Africa. Uncomplicated malaria accounts for about 40 and 30% of outpatient attendance and hospital admissions, respectively. Malaria is also a leading cause of absenteeism and poor performance at work and school. Uncomplicated malaria is rarely fatal when treated promptly with effective antimalarial drugs. In preschool children, delayed treatment or failure to treat uncomplicated falciparum malaria could lead to rapid disease progression to severe and potentially fatal malaria within a period often less than 48 h from onset of illness. *Plasmodium falciparum* causes severe malaria through complex processes that involve immunological substances known as cytokines (John et al. 2000) leading to impaired perfusion and damage to tissues and organs. These pathological changes lead to clinical and laboratory features that are characteristic of severe and complicated malaria, namely cerebral malaria that is associated with impaired consciousness, repeated convulsions, severe malarial anemia, hypoglycemia, respiratory distress, and circulatory collapse. Children that die from malaria would have one or more of these signs. The risk of death is higher in patients with multiple signs (Schellenberg et al. 1999). Case fatality rate of complicated falciparum malaria is 10–50%. About 10–17% of those that survive cerebral malaria have residual neurological problems such as dyskinesia, cortical blindness, seizures, and learning disorders (Meremikwu et al. 1997). Most of these disorders are resolved

within 6 months but about 2% persist for longer periods of time causing varying degrees of disability and impaired intellectual development (Murphy and Breman 2001).

Consequences of Malaria in Children and Adolescents

Anemia

Childhood anemia in low-income countries is caused by multiple factors including poor nutrition, malaria, intestinal parasites, HIV/AIDS, and inherited blood disorders (e.g., glucose-6-phosphate dehydrogenase (G-6-P-D) deficiency and sickle cell disease). In areas with high transmission, malaria is the leading etiological factor for anemia. The processes by which malaria causes anemia are not yet fully understood; however, malaria-related toxins and immunological factors are believed to cause increased hemolysis, increased splenic clearance of infected and uninfected red blood cells, and impaired production of red blood cells in the bone marrow (dyserythropoiesis). In areas of Africa with high malaria transmission, surveys have shown high prevalence rates of anemia (hemoglobin <11 g/dL) among infants and children under 5 years of age (as high as 50–80% in several areas). Most of these cases of anemia go unnoticed and untreated because they are mild and cause no symptoms. Although children with mild and chronic anemia do not feel distinct symptoms of illness, mild anemia is associated with chronic debility. It can cause such adverse effects as reduced activity and impaired cognition and learning. These chronic effects of malarial anemia in concert with malaria-related school absenteeism and neurological complications from cerebral malaria, adversely affect childhood development and education in sub-Saharan Africa (Mung'Ala-Odera et al. 2004).

Severe anemia (hemoglobin <5 g/dL) is a common acute complication of falciparum malaria. It is responsible for high case fatality and often follows massive hemolysis from a single episode of falciparum malaria. Repeated episodes or poorly treated episodes of uncomplicated malaria are fairly

common pathways to severe anemia in infants and young children who are residents of areas with high and stable malaria transmission. In many communities in Africa where there are high levels of *P. falciparum* resistance to chloroquine and sulphadoxine–pyrimethamine, the continued use of failed drugs has resulted in an increase in the incidence of severe malarial anemia. Case fatality from severe malarial anemia varies from 1% in treated cases to over 30% when associated with other complications of falciparum malaria, especially respiratory distress and deep coma (John et al. 2000). Many more children with life-threatening severe malaria anemia do not have access to formal health care where adequate treatment and blood transfusion are possible. This indicates that overall case fatality from severe malarial anemia is likely to be much higher than reported. Blood transfusion for severe malaria-related anemia accounts for a remarkable proportion of new pediatric HIV infections in Africa (Crawley and Nahlen 2004).

Given the multifactorial nature of the etiology of childhood anemia, interventions to prevent or treat it should involve several approaches. For instance, mass de-worming of children and micronutrient supplementation programs are interventions that have the potential to reduce the burden of childhood anemia in developing countries (Briand et al. 2007). Insecticide-treated nets, chemoprophylaxis, and intermittent preventive treatment are malaria-specific interventions that have been shown to significantly reduce morbidity and mortality from malaria-related anemia (Briand et al. 2007). Malaria is a leading cause of hemolytic and vaso-occlusive crisis in African children and adolescents with sickle cell disease. Sickle cell disease is the most common inherited hematological disease among Africans. The prevalence of the sickle cell trait (heterozygous inheritance on an abnormal and a normal gene) can be as high as 25–40% in some parts of Africa with 1–3% affected by the disorder (inheritance of a pair of abnormal gene). A paradoxical relationship exists between the sickle cell gene and malaria. The sickle gene is believed to confer some measure of protection against malaria to those with the trait (one abnormal gene); however, it is a leading cause of morbidity and mortality among those with the disorder (two abnormal genes).

Malaria Nephropathy and Splenomegaly

Two other notable chronic effects of malaria in children and adolescents include malarial nephropathy and hyperactive malarial splenomegaly. Malarial nephropathy results from gradual damage of kidney cells by an antigen–antibody complex that is caused by previous malarial infection. There are no reliable data on the magnitude of renal morbidity which are caused by this malaria-induced pathology. However, it is believed that the problem is substantial. Hyperactive malarial splenomegaly (also called tropical splenomegaly syndrome) is another chronic, but less common presentation of malaria among children and adolescents in the tropics. This condition is characterized by an enlarged spleen, high levels of malarial immunoglobulin (IgM), sinusoidal lymphocyte infiltration, and resolution with prolonged antimalarial therapy.

Malaria in Pregnancy

Plasmodium falciparum and *P. vivax* are known to cause significant effects on maternal and child health during pregnancy. *Plasmodium falciparum* exerts the worst effects among all the species of malaria parasite. In sub-Saharan Africa, the transmission of *P. falciparum* is predominantly high and intense with high levels of morbidity and mortality among infants and pregnant women. The major consequences of malaria infection during pregnancy are clinical episodes of malaria, maternal anemia (hemoglobin concentration <11 g/dL), or severe anemia (hemoglobin concentration <8 g/dL), placental parasitemia, intrauterine growth retardation, preterm births, and low birth weight.

Table 12.1 shows the contribution of malaria to adverse maternal and child health outcomes. Malaria in pregnancy is estimated to account for up to 25% of cases of severe anemia, 10–20% of babies born with low birth weight, and 5–10% of neonatal and infant deaths are due to malaria-induced LBW (Greenwood et al. 2005). The effect of malaria in pregnancy is influenced by the level of malaria immunity acquired by the mother before pregnancy. This depends on the pattern and intensity of malaria transmission. The parasite species,

Table 12.1 Contribution of malaria to anemia, low birth weight, and infant deaths

Adverse health events	% of total
Maternal anemia	2–15
Low birth weight	8–14
Preterm birth	8–36
Intrauterine growth retardation	13–70
Infant death	3–8

Source: WHO-AFRO (2004)

the number of previous pregnancies, and the presence of human immunodeficiency virus (HIV) also remarkably impact malaria morbidity and mortality during pregnancy. In areas with high and stable malaria transmission, the prevalence and intensity of *P. falciparum* parasitemia are higher in pregnant women than in non-pregnant women. The majority of malaria infections in pregnant women living in high transmission areas are asymptomatic because of immunity acquired from repeated exposure to malaria before pregnancy. The adverse consequences of malaria during pregnancy in areas of high transmission are anemia, placental malaria, intrauterine growth retardation, and low birth weight. In areas of low or unstable transmission, acquired malaria immunity is low in all age groups. Pregnant women with malaria in this area are vulnerable to severe manifestation of the disease including cerebral malaria.

HIV and Malaria Co-infection

The evidence that malaria and HIV co-infection increases morbidity associated with both conditions has been confirmed by several studies (Snow et al. 2003). Impact of the complex interaction between malaria and HIV appears to be most profound in pregnancy and children. HIV infection in pregnancy is known to increase the risk of malaria infection (population attributable risk (PAR), 10–27%), maternal anemia (PAR, 12–15%), and low birth weight (PAR, 11–38%) (Steketee et al. 2001). The mechanism by which HIV infection alters malaria morbidity is not well understood. It is believed to be due to systemic and placental immunologic changes that are induced by HIV. In a Rwandan cohort study that included 228 HIV-positive and 229 HIV-

negative participants, the incidence of malaria was almost twice as high in the HIV-positive group (6.2 per 100 women-months) than in the HIV-negative group (3.5 per 100 women-months) (Ladner et al. 2002). A review of studies on malaria and HIV co-infection shows that HIV infection in pregnancy significantly increases the risk of peripheral and placental malaria parasitemia. Malaria in pregnant women infected by HIV is more likely to cause higher parasite densities, febrile illness, severe anemia, and low birth weight than malaria in those without HIV infection (Snow et al. 2003). In the absence of HIV infection, the deleterious effects of malaria in pregnancy, notably low birth weight and maternal anemia, were significantly worse in those pregnant for the first or second time than in those who have been pregnant for three or more times (Ter Kuile et al. 2004). With HIV co-infection, the pattern of malaria morbidity is similar across all categories of pregnant women (Ter Kuile et al. 2004).

A review of studies in areas of sub-Saharan Africa with high and stable malaria transmission shows that HIV-1 infection and clinically diagnosed AIDS increased the incidence of malaria 1.2-fold and 2-fold, respectively (Korenromp et al. 2005). In these high transmission areas, HIV-1 infection in children increased hospitalization for malaria and malaria case fatality 6-fold and 9.8-fold, respectively. At the same time in low transmission areas, the incidence of severe malaria and malaria case fatality increased 2.7-fold and 3.6-fold, respectively. The effect of HIV on malaria incidence is worse in HIV patients with lower CD4 counts. In adult patients living in high malaria transmission areas, HIV increased the malaria incidence 1.2-fold, 3-fold, and 5-fold when CD4 counts were ≥ 500 , 200–499, and $< 200/\mu\text{L}$, respectively (Korenromp et al. 2005).

The increase in morbidity and mortality associated with HIV and malaria co-infection, both of which are highly prevalent in most parts of sub-Saharan Africa, calls for more focused research in this area and for integration of service delivery. One way of achieving greater impact is the integration of malaria and HIV/AIDS control activities within maternal and child health programs. Achieving high coverage of insecticide-treated bed nets (ITNs) use and prompt access to treatment with artemisinin-based combination treatments (ACTs) would contribute to the reduction in the morbidity and

mortality attributable to HIV co-infection with malaria in high transmission areas. In areas of low intensity and unstable transmission, widespread and effective indoor residual spraying combined with effective treatment using artemisinin-based combination therapy (ACT) is cost-effective and has been shown to significantly reduce malaria morbidity and mortality (Snow et al. 2003).

Strategies for Global Malaria Control

The following section provides a summary of the three-pronged approach to malaria control recommended by the World Health Organization's malaria control program (WHO 2005).

Vector Control

Indoor residual spraying, environmental management to eliminate mosquito breeding sites, and use of larvicides are known to be effective in reducing malaria when used in combination. Aerial and terrestrial spraying of insecticides is used in parts of South America and Asia to control malaria. This intervention strategy is cost intensive and low in effectiveness. It is therefore, not an appropriate control measure for sub-Saharan Africa given the complex terrains and weak economies of these malaria-endemic countries.

Prevention of Human–Vector Contact

Insecticide-treated bed nets (ITN) have been shown by studies in a variety of settings to be effective in reducing the incidence of clinical malaria by half and fatalities by about a third (Snow et al. 2003). Population coverage for ITN in most parts of Africa remains low (<20%). The low re-treatment rate at the expiration of the usual period of potency (6 months) was a major challenge, even in areas that achieved high ITN coverage. The development and widespread deployment of factory-treated nets with lifelong protective effects (LLINs) has eliminated the need to re-treat insecticide-treated nets. The persisting challenge is how to improve access to

ITNs by poor women and children who need to be protected from severe and fatal malaria. The Global Fund for Tuberculosis AIDS and Malaria is providing funding to countries in endemic low and middle-income countries to support this intervention. A systematic review of randomized controlled trials conducted in Africa showed that ITNs used in pregnancy compared to “no nets” significantly reduced the risk of placental malaria in all pregnancies (relative risk 0.79, 95% confidence interval 0.63–0.98). The review also showed that ITNs significantly reduced the risk of low birth weight (relative risk 0.77, 95% CI 0.61–0.98) and fetal loss in the first to fourth pregnancy (relative risk 0.67, 95% CI 0.47–0.97). However, this was not the case in women with more than four previous pregnancies (Gamble et al. 2006). In a large randomized controlled trial in communities with intense and perennial malaria transmission, ITN use significantly reduced the risk of severe malaria anemia, placental malaria, and low birth weight among those pregnant for the first to fourth time, but not in those pregnant for five or more times (Ter Kuile et al. 2003). The adherence to ITN use in pregnancy was shown to be significantly lower in adolescent and young women, who are most at risk for the deleterious consequences of malaria (Browne et al. 2001). This observation and the known risk of higher malaria morbidity associated with first pregnancy (involving mostly adolescent women) make it necessary to specially target this age group for intervention.

In summary, the limited risk assessments undertaken so far with regard to the safety of ITNs suggest that they are relatively safe. However, a cautionary note regarding the need to monitor the health effects of long-term exposure to insecticides in resource-poor settings has been presented by Ehiri et al. (2004). Although the use of mosquito nets is not new, mass use of ITNs as a population-based malaria control tool is a relatively new technology, and some uncertainty remains about the potential for problems as their use expands (Hirsch et al. 2002).

Treatment and Prevention with Drugs

Prompt treatment of malaria with efficacious and affordable antimalarials is a key component of the Global Malaria Control Strategy. The emergence

and spread of malaria parasites (especially *P. falciparum*) resistant to the commonly used affordable antimalarials, like chloroquine (CQ) and sulphadoxine–pyrimethamine (SP), hampered malaria control in Africa and has deteriorated the malaria situation on the continent. The emergence of these multidrug-resistant malaria parasites led to the adoption of combination treatment options as the gold standards for treating malaria. The WHO (2006) recommends that the ideal drug combination should contain two drugs that are individually effective against the blood stages of the parasite and use completely different mechanisms to kill the parasite. Based on results from several well-conducted studies, the WHO recommended that combinations that contain artemisinin (a drug derived from the Chinese plant *A. annua L.*) or its derivatives and another structurally unrelated and more slowly acting drug provide the best therapeutic effects and are safe. This category of drug combinations is collectively known as artemisinin-based combination treatments (ACTs).

The advantages of artemisinin-based combination treatments (ACTs) have been outlined by the WHO to include the following (WHO 2006):

- Rapid substantial reduction of parasite biomass
- Rapid resolution of clinical symptoms
- Effective action against multidrug-resistant *P. falciparum*
- Reduction of gametocyte carriage, which may reduce malaria transmission
- No parasite resistance documented as yet with the use of artemisinin and its derivatives
- Few reported adverse clinical effects (note that pre-clinical data on artemisinin derivatives are limited)

Monotherapy with artemisinin derivatives requires multiple doses given for 7 days due to their characteristic short half-life. The other key advantage of artemisinin containing combination treatments (ACTs) is the shortened duration of treatment (3 days), with expected improvement in patient compliance to treatment. If the partner drug is effective, ACTs ensure prompt recovery and high cure rates. They are generally well tolerated. Replacing the older failing or failed monotherapies with effective drugs will reduce morbidity and mortality. The challenge, however, remains how to deliver

these drugs to the people that need them. Implementation of this policy would put significant cost burdens on national malaria control programs. However, the costs of failing to change, such as an increase in childhood deaths and high cost of hospitalization, make it a necessary and cost-effective program.

Affordability of ACTs is a major issue affecting their effective deployment in malaria control programs in sub-Saharan Africa. ACTs are generally too expensive for most people in low-income settings where malaria is endemic. While drugs such as chloroquine and sulphadoxine–pyrimethamine (SP), which were previously used for treating uncomplicated malaria, cost only a few US cents, the new ACTs cost about \$2–\$3.5 and even higher when not discounted. International efforts to address this issue championed by the Roll Back Malaria (RBM) partnership have yielded some positive results, especially through the Global Fund for Tuberculosis, AIDS and Malaria (Brundtland 2002). However, huge gaps still exist. Unfortunately access to prompt treatment with effective antimalarial drugs remains very low in many sub-Saharan countries, leading to the persistence of high malaria mortality rates. The reasons for poor access to treatment are mainly due to weak health systems that are poorly patronized by the populace and a lack of funds to procure and effectively deliver expensive artemisinin-based combination treatment (ACTs). ACTs are necessary since high levels of *P. falciparum* resistance have rendered chloroquine and sulphadoxine–pyrimethamine ineffective. These were the cheaper treatment options that have been used for several decades. Most children who become ill with malaria in these areas are usually treated at home with poor quality or inappropriately administered medicines that were purchased from local, often untrained drug vendors.

Antimalarial treatment policies, adopted by each country, depend on the epidemiology of the disease, including patterns of transmission, drug resistance, political environment, and economic context. The adoption of ACTs in sub-Saharan Africa was preceded by establishment of local evidence on the effectiveness of existing first- and second-line drugs which have demonstrated consistently high treatment failure rates due to parasite resistance (Snow et al. 2003). The WHO (2006) also

Box 12.2 Challenges of Community Delivery of Malaria Chemotherapy Through the Primary Healthcare System

Limitation of outreach capacity to geographically remote areas, and particularly to nomadic populations

Inability to make efficient use of community resources (both human and material)

Difficulty in achieving full community acceptance of chemotherapy

Insufficient training of local health workers

Lack of understanding of health problems and their solutions

Potential ineffectiveness of the curative drug or drug dosage used, usually through the emergence of parasite resistance to the drug

Undesirable side-effects of the drug

Source: Jeffery (1984)

recommends that countries developing antimalarial treatment policies should strive to ensure that

- all populations at risk have access to prompt treatment with safe, good quality, effective, affordable, and acceptable antimalarial drugs and
- there is rational use of antimalarial drugs in order to prevent the emergence and spread of drug resistance induced by unduly high selection drug pressure on mutant malaria parasites.

Delivery of effective and safe antimalarial treatment to poor rural populations and those in difficult, hard-to-reach settings poses enormous challenges to malaria control programs in Africa. In many endemic countries, the formal health system is weak. Often the health system consists of a few ill-equipped health facilities run by inadequately trained and/or poorly motivated health personnel. The proportion of the people that access these services is so low that successful malaria treatment programs in Africa would be impossible without community-based delivery mechanisms including adequately trained and equipped informal community-based providers and caregivers who provide treatment and preventive services as close as possible to where people live and work. Delivering community health care such as malaria treatment services through primary healthcare centers has long been identified a big challenge by Jeffery (1984) as summarized in

Box 12.2. A careful appraisal of these factors in the context of the current situation of malaria control efforts in most endemic countries in sub-Saharan Africa shows situations that are as pertinent today as they were over two decades ago when they were highlighted by Jeffery (1984).

Home management of malaria (HMM), the strategy currently recommended by the WHO (Mendie et al. 2003) as an effective community delivery mechanism for antimalarial treatment, is likely to address some of the limitations highlighted in Box 12.2. The HMM strategy entails educating community health workers, volunteers, mothers, and caregivers to recognize symptoms of malaria and treat with appropriate antimalarial drugs (Mendie et al. 2003). Its goal is to ensure early recognition and prompt and appropriate response to malarial illness in under-5 children in the home and community by enabling health workers, mothers, and caregivers to recognize malarial illness early and take appropriate action. The WHO HMM strategy consists of four strategic components:

1. Ensure access to effective and good-quality anti-malarial drugs (preferably pre-packed) at community level.
2. Ensure that community drug or service providers (e.g., patent medicine vendors, volunteer village health workers, community health extension workers) have necessary skills and knowledge to manage malaria.

3. Ensure an effective communication strategy to enable caregivers to recognize malarial illness early and take appropriate action.
4. Ensure good mechanisms for supervision, monitoring, and communication activities.

As shown in [Chapter 27](#), integrated management of childhood illness (community IMCI) also addresses both preventive and curative aspects of malaria control by seeking to improve community and family practices.

Using Drugs to Prevent Malaria

Giving prophylactic antimalarial drugs to prevent malaria is a routine practice for non-immune persons visiting malaria-endemic areas. Malaria prophylaxis refers to daily or weekly administration of antimalarial drugs at a dose that is usually smaller than the therapeutic doses with a view to preventing clinical malaria. Intermittent preventive treatment (IPT) refers to full therapeutic doses of an antimalarial given at specified time points to presumptively cure asymptomatic malaria and prevent clinical malaria or such other adverse consequences as anemia or placental malaria. Usually, sulphadoxine–pyrimethamine (SP) is used for IPT as it requires a single dose and has a long half-life. The rationale is that intermittent treatment is likely to have fewer adverse events than prophylaxis because it is taken less often, and it is easier to deliver through clinics, reducing poor adherence with self-administration.

Chloroquine was the most widely used drug for malaria prophylaxis in pregnancy. The high prevalence of resistant strains, and the fact that most women adhered poorly to the weekly regimen required to achieve beneficial effects, rendered chloroquine chemoprophylaxis ineffective for malaria control in pregnancy. Meta-analysis included in a Cochrane systematic review of randomized controlled trials showed that IPT with sulphadoxine–pyrimethamine significantly reduced the risk of severe maternal anemia (relative risk 0.60, 95% CI 0.50–0.78; 2,243 participants), placental malaria (relative risk 0.35, 95% CI 0.27–0.47; 1,232 participants), and low birth weight (relative

risk 0.58, 95% CI 0.43–0.78; 1,399 participants) in women who were pregnant for the first or second time (Garner and Gülmezoglu 2006).

IPT with sulphadoxine–pyrimethamine (SP) along with consistent use of ITNS are currently recommended as cost-effective and evidence-based interventions to prevent the deleterious effects of malaria in pregnancy and to reduce the associated maternal and infant morbidity and mortality. Almost all the 35 countries in Africa with stable malaria transmission are already implementing intermittent preventive treatment in pregnancy (IPTp) with SP (Vallely et al. 2007). One of the key challenges with implementation of IPT is the high rate of parasite resistance to SP, and the lack of a safe and effective alternative to this antimalarial. In most parts of Africa SP failure exceeds 20% and surveillance data on the trends are lacking in most cases. The effectiveness of this intervention in areas with high SP failure rates is yet to be adequately studied. The suggestion that two and three doses of SP, respectively, should be used in areas with SP resistance <30 and 30–50% remains to be validated by robust research data. The continued use of IPT with SP in areas where SP resistance exceeds 50% also needs to be justified by research.

There is also the problem of how to handle malaria co-infection with HIV in areas with high prevalence of HIV. A third dose of SP for IPT has been recommended for areas with high HIV prevalence but there is a need to monitor impact on such outcomes as severe anemia and low birth weight, and to study possible drug interactions in those receiving anti-retroviral treatment. In malaria-endemic communities, use of antimalarial drugs for prophylaxis or intermittent preventive treatment (IPT) is recommended for only pregnant women and special vulnerable groups such as children with sickle cell disease. Several randomized controlled trials in malaria-endemic communities have shown consistently that malaria prophylaxis and intermittent preventive treatment of infants (IPTi) and young children are effective. A Cochrane systematic review and meta-analysis (Meremikwu et al. 2005) showed that receiving antimalarial drugs as prophylaxis or intermittent treatment reduced the incidence of clinical malaria episodes and severe anemia by about 50% in preschool children living

in malaria-endemic communities. Two main reasons are commonly given for discouraging widespread use of malaria chemoprophylaxis in pre-school children in endemic communities. The first reason is the concern that giving malaria prophylaxis to infants and young children living in malaria-endemic areas will delay or minimize their chances to acquire protective immunity and result in a rebound rise in the incidence of severe morbidity and mortality later in life.

The second reason is that poor compliance to weekly antimalarial drug prophylaxis could induce drug pressure and selection of mutant resistant strains of *P. falciparum*. Intermittent preventive treatment of infants (IPTi) with treatment doses of SP under direct observation at the time of routine immunization offers a better programmatic option, since it eliminates the problem of non-compliance and is expected to have little or no adverse effect or interfere with the child's ability to acquire malarial immunity. A major challenge to implementation of IPTi, among others, is the rising incidence of SP resistance which is the principal drug currently used for this intervention. There has also been a concern about the possible interaction between SP and the routine infant vaccines but this has not been supported by any strong evidence.

Malaria Vaccines

Timely and efficient deployment of efficacious vaccines is widely accepted as an effective child survival strategy. The development of a successful malaria vaccine especially against *P. falciparum* would contribute remarkably to reduction of the unacceptably high childhood death from malaria. Unfortunately decades of efforts at vaccine development have yet to meet this expected public health success. Developing vaccines against parasitic infections poses greater challenges than developing vaccines for virus and bacterial infections because of their more complex nature and larger genomes. The multiple stages of the malaria parasite and the different proteins they express pose additional challenges to the development of a potent malaria vaccine. An all-stage malaria vaccine capable of inhibiting growth or killing all of these different stages of malaria

poses a complex challenge. Researchers involved in development of malaria vaccine devote their efforts to three key strategies that target the pre-erythrocytic and erythrocytic stages of the life cycle in humans (Fig. 12.2), and vaccines that induce antibodies in humans that can kill or prevent development of viable sexual forms ingested by the mosquito vectors. The pre-erythrocytic stage vaccines aim to prevent sporozoites (the stage of plasmodium that mosquitoes pass to humans) from invading and developing in the liver, while an asexual erythrocytic stage vaccine limits the invasion of erythrocytes or prevents their multiplication in the erythrocytes.

The complete mapping of the *P. falciparum* genome with a better understanding of the organism at sub-cellular and molecular levels coupled with recent advances in genomic and proteomic science has led to a remarkable increase in the number of candidate malaria vaccines. There is no time better than the present to scale up support for malaria vaccine research and development. The goal of most of the initial efforts of malaria vaccine development is complete prevention of the disease with the hope of eliminating malaria. The disappointing results of early malaria vaccine trials appear to have diminished this enthusiasm. Should efforts to develop a malaria vaccine capable of completely preventing clinical malaria fail, most public health experts and vaccine researchers advocate the goal of making malaria vaccines that ameliorate the severity of the disease and reduce the level of fatality. In Africa, where pregnant women and children bear the greatest burden of severe malaria, such a vaccine will be a significant addition to maternal and child health services and will help to reduce the burden of childhood disability attributable to cerebral malaria. The opportunities provided by better research tools and a better understanding of the *Plasmodium* and *Anopheles* genome make the prospects and possibilities of a malaria vaccine better today than ever before. Funding for malaria vaccine development and field trials has increased in recent years. However, it is still far short of the expected investment, given its huge potential for improving child survival and contributing to achievement of the millennium development goals (MDG).

Progress and Challenges of the Global Malaria Control Strategy

The inadequacies of health information systems and vital registration processes in most parts of sub-Saharan Africa make it difficult to obtain reliable records of malaria mortality. Facility-based records of deaths, when available, are not representative of the situation in the larger population given that the majority of sick children do not use health facilities and most deaths occur outside the formal health facilities. Most of the available mortality data from malaria-endemic areas are estimates and prospective mortality data from demographic surveillance systems validated by verbal autopsies (Snow et al. 2004). The inefficiency of health information systems and vital registration processes in sub-Saharan African countries makes it difficult to obtain sufficient and timely information to track the performance of malaria control programs. The malaria situation globally deteriorated in the past three decades. This resulted in increased malaria-related morbidity and mortality, especially in sub-Saharan Africa where emergence and spread of multidrug-resistant malaria parasites and breakdown of malaria control programs were the leading reasons, among others (Korenromp et al. 2003). Greenwood et al. (2005) have given an elaborate summary of the factors believed to

have contributed to the deterioration of the global malaria situation in Box 12.3.

While the discovery of additional malaria control measures such as a highly effective malaria vaccine should be expected to increase the gains of malaria control efforts, several appraisals and overviews of global malaria control efforts agree that the key reasons for the recent decline in the gains of malaria control efforts have not been the lack of effective malaria control measures. There is consensus that the four technical elements of the global malaria control strategy (Box 12.4) affirmed by the international ministerial conference held in Amsterdam under the auspices of the World Health Organization in 1992 have been essentially effective in the years preceding and succeeding the Amsterdam conference.

Careful study of malaria control scenarios (mostly in sub-Saharan Africa) that have failed, or achieved only minimal success with these same strategies, shows that these control programs lacked the pre-conditions for effectiveness of the global strategy (Box 12.5) as also outlined in the Amsterdam Ministerial Conference on Malaria.

When the RBM strategy was established in 1998, it was in response to these deficiencies. The RBM is a partnership between the WHO, other UN agencies, bilateral aid agencies, non-governmental organizations, and governments of

Box 12.3 Factors Contributing to Deterioration of the Malaria Situation

- Climate instability: drought and floods increased malaria transmission in different epidemiological circumstances
- Global warming may have led to increased malaria transmission especially in some highland areas
- Civil disturbances and unrest have resulted in the collapse of malaria control programs and refugee situations with attendant effects on malaria transmission across epidemiological areas and increased risk of epidemics
- Changes and increase in travel patterns within endemic areas and from non-endemic areas to endemic areas putting many non-immune people at risk
- HIV increases susceptibility to malaria and increases the burden on the health service
- Emergence and spread of drug resistant *P. falciparum* has been a key reason for deterioration of malaria situation in especially Africa and Southeast Asia
- Insecticide resistance: resistance to pyrethroids used for treated bed-nets has emerged in *Anopheles gambiae* (in West Africa) and *Anopheles funestus* (in southern Africa). High vector resistance to *Anopheles funestus* diminished the use of DDT for household spraying in southern Africa.

Source: Greenwood et al. (2005)

Box 12.4 Basic Technical Elements of the Malaria Control Strategy

- To provide early diagnosis and treatment
- To plan and implement selective, multiple and sustainable preventive measures: including vector control; personal protection (notably insecticide treated nets); and chemoprophylaxis/intermittent preventive treatment.
- To detect early, contain or prevent epidemics;
- To conduct focused research, and to regularly assess the country's malaria situation, including ecological, social and economic determinants of the disease.

Source: WHO (1992)

Box 12.5 Conditions for Effective Implementation of the Global Malaria Control Strategy

- Political Will: sustained political commitment from all levels and sectors of government
- Integration: malaria control should be an integral part of health systems, and be coordinated with relevant development programs in non-health sectors
- Community participation: communities should be full partners in malaria control activities
- Resource mobilization: adequate human and financial resources should be mobilized

Source: WHO (1992)

malaria-endemic countries. The RBM has a long-term goal of reducing malaria morbidity and mortality by at least half by 2010. RBM was not meant to be a new malaria control strategy but rather an organized global effort to facilitate the effective implementation of the global control strategy.

Conclusion

The evidence that large-scale and effective use of ITNs can reduce the incidence of malaria and malaria-related deaths is both strong and consistent (Lengeler 2000). Insecticide-treated mosquito nets (ITNs) can reduce all-cause childhood mortality by about a fifth; with about 6 lives saved for every 1,000 preschool children protected with ITN (Lengeler 2000). It is estimated that full ITN coverage in sub-Saharan Africa could prevent 370,000 child deaths per year (Lengeler 2000). Insecticide-treated nets are cost-effective, but endemic poverty and inadequate sensitization of people in malaria-endemic areas remain the major reasons for low use (Snow et al. 2003). The cost-effectiveness of ITNs (US \$19–85 per disability-adjusted life year

(DALY)) is similar to most childhood vaccines (WHO 2003). When community coverage is high, ITNs not only protect those who sleep under them, but also those in the same dwelling (the home effect) and those living nearby (the community effect) (Snow et al. 2003).

The year 2005 marked the end of the target set by African Heads of State to achieve at least 60% access to prompt and effective treatment of malaria and 60% ITN coverage for under-5 children and pregnant women. However, most countries in sub-Saharan Africa fell far short of these targets. It was also in the same year that RBM set the landmark target of halving malaria mortality by 2010. Appraisal of malaria control efforts at the end of 2005 uniformly indicated that resources available for procurement of malaria control commodities (ACTs, ITN, and diagnostic kits) were grossly inadequate. The appraisal also showed that malaria control personnel at national and regional levels was inadequately equipped.

Donors and governments should develop effective mechanisms to monitor the access that children, adolescents, pregnant women, and children in difficult circumstances have to evidence-based

treatment and preventive interventions for malaria. Donor funds specifically tagged to providing resources and infrastructure for effective management of severe and complicated malaria have been grossly inadequate. Supportive care for women and children with severe malaria is

grossly impeded by weak health systems in malaria-endemic countries. Funds meant for providing adequate infrastructure and personnel for managing severe malaria should be tagged to bilateral and multilateral health system support grants.

Key Terms

Acquired malaria immunity	Impaired consciousness	<i>Plasmodium malariae</i>
Anemia	Infant mortality	<i>Plasmodium ovale</i>
<i>Anopheles funestus</i>	Insecticide-treated bed nets (ITNs)	<i>Plasmodium vivax</i>
<i>Anopheles gambiae</i>	Integrated management of childhood illnesses (IMCI)	Poor appetite
<i>Artemisia annua</i>	Intermittent preventive treatment (IPT)	Population attributable risk (PAR)
Artemisinin-based combination therapy (ACT)	Intermittent preventive treatment of infants (IPTi)	Poverty
Artemisinin-based combination treatments (ACTs)	Intrauterine growth retardation (IUGR)	Pregnancy
Blood transfusion	Learning disorders	Preterm births
Case fatality rate	Lifelong protective effects (LLINs)	Relative risk
Cerebral malaria	Low birth weight	Repeated convulsions
Chloroquine	Malaise	Residual spraying
Circulatory collapse	Malaria-endemic countries	Respiratory distress
Cortical blindness	Malaria vaccine	Roll Back Malaria (RBM)
Cytokines	Malarial nephropathy	Seizures
Dyserythropoiesis	Malariometric indices	Severe anemia
Dyskinesia	Maternal malaria	Severe malaria
Entomologic inoculation rate (EIR)	Maternal mortality	Sickle cell disease
Fetal loss	Monotherapy	Sinusoidal lymphocyte infiltration
Fever	Mosquito	Splenomegaly
Global Malaria Control Strategy	Multidrug-resistant malaria parasites	Sporozoite
Glucose-6-phosphate dehydrogenase (G6PD) deficiency	Nausea	Sporozoite rate
Hemoglobin	Parasite resistance	Stable malaria transmission
Hemolytic crisis	Parasitemia	Sulphadoxine-pyrimethamine (SP)
Home management of malaria (HMM)	Perennial malaria	Tropical splenomegaly syndrome
Hyperactive malarial splenomegaly	Placental malaria	Uncomplicated malaria
Hypoglycemia	<i>Plasmodium falciparum</i>	Under-development
		Vaso-occlusive crisis
		Vector control

Questions for Discussion

- 1 Globally, women, children, and adolescents in sub-Saharan Africa are known to bear the greatest burden of malaria morbidity and mortality. List any six factors most peculiar to the region that account for this high burden.
- 2 List five consequences of malaria infection in children and pregnant women.
- 3 An integrated approach is advocated as an efficient and cost-effective strategy for the management of malaria co-infection with HIV/AIDS. Briefly discuss what you understand by integrated management and describe how such an integrated approach might be operationalized in practice.
- 4 What are artemisinin-based combination treatments (ACTs) and what are the advantages of their use in the treatment of malaria?
- 5 What are the challenges of community delivery of malaria treatment through existing primary healthcare systems? Is home treatment of malaria a better option? Discuss the reasons for your position.
- 6 List six factors that contribute to the worsening of the global problem of malaria? How can these be addressed? What should be the role of Roll Back Malaria initiative in global malaria control?

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