MALARIA

[Descriptive Epidemiology of Malaria]

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Malaria is a mosquito-borne infectious disease of humans and other animals caused by the genus *Plasmodium*. It is transmitted all year round (CDC, 2012). Malaria kills a child somewhere in the world every 30 seconds infecting 350-500 million people annually, killing one million, mostly children in Africa. In Africa, malaria accounts for one in five of all childhood deaths, 99% of childhood death in Africa attributable to malaria (UNICEF, 2012). According to the World Health Organization, in the year 2010 there were 219 million episodes of malaria and 660,000 deaths worldwide which is equivalent to 2000 deaths daily 91% in Africa, 6% in South-East Asia and 3% in East Mediterranean (86% of which was in children and 65% in children less than 15years). An average of 1,500 malaria cases is reported annually in the United States though malaria has been eliminated from the US since the early 1950’s. In most of the affected countries, malaria is a leading cause of illness and death. In areas with high transmission where malaria is endemic, the most vulnerable groups are young children, who have not developed immunity to malaria yet and pregnant women who have reduced immunity because of pregnancy. The cost of malaria to individuals, families, communities and nations are enormous (CDC, 2012). Approximately 125 million pregnant women are at risk of malaria infection annually. In malaria endemic countries, pregnant women have increased susceptibility to *Plasmodium falciparum*. Malaria contributes to 8-14% of still birth, low birth weight and infant mortality (200,000 estimated infant deaths in Sub Saharan Africa annually) (Hartman T., Rogerson S., Fischer P., 2010; CDC, 2012).

Immigrants in the US from malaria-endemic countries returning to their "home" countries to visit usually do not use appropriate malaria prevention measures predisposing themselves to malaria infection (CDC, 2012). Annually, 125 million international travelers visit these countries and more than 30,000 are infected with malaria (Kajfasz P., 2009). According to the WHO, 3.3 billion people live in areas at risk of malaria transmission in 106 countries and territories (CDC, 2012). Malaria parasites belong to the genus *Plasmodium* (phylum Apicomplexa). In humans, malaria is caused by *P. falciparum, P. malariae, P. ovale, P. vivax* and *P. knowlesi* (Mueller I., Zimmerman P., Reeder J., 2007). *P. falciparum* is the commonest specie that causes infections (approximately 75%) then, *P. vivax* (approximately 20%) (Nadjm B., Behrens R., 2012). *P. falciparum* accounts for majority of malaria deaths, (Sarkar P., Ahluwalia G., Vijayan V., Talwar A., 2009). *P. vivax* malaria is associated with life-threatening conditions (Baird J., 2013) and it is commoner outside Africa (Arnott A., Barry A., Reeder J., 2012). Only female mosquitoes feed on blood and transmit malaria. Male mosquitoes do not transmit malaria they feed on plant nectar. The females *Anopheles* mosquito prefer to feed at night they start searching for a meal at dusk, and continue throughout the night until they have taken a meal (Arrow K., Panosian C., Gelband H., 2004). Malaria is endemic in a broad band around the equator, in areas of Central and South America, Haiti and the Dominican Republic, some Pacific islands, such as Papua New Guinea and some parts of Middle East many parts of Asia, and much of Africa. In Sub-Saharan Africa, 85–90% of malaria morbidity and mortality occur (Layne S., 2006). Rainfall, consistently high temperatures and humidity, stagnant waters in which mosquito larvae matures, provides mosquitoes with the environment they need for continuous breeding this contributes to malaria prevalence in tropical and subtropical regions (Jamieson A., Toovey S., Maurel M., 2006). In cooler regions where transmission is less intense and more seasonal, *P. vivax* might be more prevalent because it is more tolerant of lower ambient temperatures. *Plasmodium falciparum* (which causes severe
malaria) cannot complete its growth cycle in the *Anopheles* mosquito and cannot be transmitted at temperatures less than 20°C (68°F) (CDC, 2012). Malaria is not commonly seen in the United Kingdom. In the United States around 1,500 cases of malaria are reported annually. Worldwide about 3.3 billion people live in areas at risk of malaria transmission in 106 countries and territories (Mandal A., 2013).

**Life cycle of malaria parasites**
(adapted from the Centers for Disease Control and Prevention, 2012)

Mosquito causes infection by taking a blood meal. Sporozoites enter the bloodstream and migrate to the liver infecting liver cells and mature into schizonts, which rupture and release merozoites (*P. vivax* and *P. ovale* a dormant stage [hypnozoites] can persist in the liver causing relapses). After this initial replication in the liver (exo-erythrocytic schizogony), the parasites undergo asexual multiplication in the erythrocytes (erythrocytic schizogony). Merozoites return
to the blood stream infecting red blood cells where they develop into ring forms, the ring stage trophozoites mature into schizonts, which rupture releasing merozoites. Blood stage parasites are responsible for the clinical features of malaria. Some parasites differentiate into sexual erythrocytic stages (gametocytes). Sexual forms are produced, when taken up by a mosquito; it infects the insect and continues the life cycle (CDC, 2012).

The female Anopheles mosquito (the definitive host and vector is not affected by the parasite) transmits a motile infective form (the sporozoite) to a vertebrate host (human who is the secondary host). A sporozoite travels through the blood vessels to liver cells (hepatocytes), where it reproduces asexually (tissue schizogony) and produces thousands of merozoites. These infect new red blood cells and initiate a series of asexual multiplication cycles (blood schizogony) that produce 8 to 24 new infective merozoites, the cells then burst and the infective cycle begins anew (Schlagenhauf-Lawlor P., 2008).

During a blood meal, the gametocytes, male (microgametocytes) and female (macrogametocytes), are ingested by an Anopheles mosquito and mature in the mosquito’s gut. The parasites’ multiplication in the mosquito is known as the sporogonic cycle. While in the mosquito’s stomach, the microgametes penetrate the macrogametes forming zygotes. The zygotes in turn become motile and elongated (ookinetes) which invade the midgut wall of the mosquito where they develop into oocysts. The oocysts grow, rupture, and release sporozoites, which make their way to the mosquito’s salivary glands ready to infect another host. Inoculation of the sporozoites into a new human host perpetuates the malaria life cycle (CDC, 2012). The sporozoites are injected into the skin, alongside saliva, when the mosquito takes a subsequent blood meal (Cowman A., Berry D., Baum J., 2012).

Malaria infection develops through two phases. A phase that involves the liver (exoerythrocytic phase) and another that involves red blood cells (erythrocytic phase). When an infected mosquito takes a blood meal, sporozoites in the mosquito’s saliva enter the bloodstream and migrate to the liver infecting the hepatocytes, multiplying asexually and asymptptomatically for 8–30 days (Bledsoe G., 2005). After a dormant period in the liver, they differentiate to yield thousands of merozoites, which rupture their host cells, escape into the blood, infect red blood cells and begin the erythrocytic stage of the life cycle (Bledsoe G., 2005). Within the red blood cells, the parasite continues to multiply asexually, breaking out of their host cells periodically to invade fresh red blood cells. This occurs cyclically resulting in fever waves (Bledsoe G., 2005). A period of time after the female anopheles mosquito bites (the “incubation period”) goes by before the first symptoms appear. The incubation period is usually 7 to 30 days. With P. falciparum the incubation period may be shorter and longer with P. malariae (CDC, 2010).

Some P. vivax sporozoites do not develop into exoerythrocytic-phase immediately. They produce hypnozoites that remain dormant for long (typically, 7 to 10 months to years). They then reactivate and produce merozoites. Some P. vivax infections have long incubation periods and late relapses due to hypnozoites (White N., 2011). Malaria prophylaxis by travelers can delay symptoms of malaria for weeks or months. This can happen with P. vivax and P. ovale, both of which can produce dormant liver stage parasites; the liver stages may reactivate and cause disease months after the infective mosquito bite (CDC, 2010).
Malaria parasite is protected from attack by the body's immune system because it lives within the liver and red blood cells in humans making it relatively invisible to immune surveillance. The spleen destroys circulating infected blood cells hence, *P. falciparum* parasite displays adhesive proteins on the surface of the infected blood cells which makes blood cells to stick to the walls of small blood vessels preventing the parasite from passage through the general circulation and the spleen (Tilley L., Dixon M., Kirk K., 2011). The blockage of the microvasculature causes symptoms such as in placental malaria (Mens P., Bojtor E., Schallig H., 2012). Sequestered red blood cells can pass through the blood–brain barrier causing cerebral malaria (Rénia L., Wu Howland S., Claser C., Gruner A., Suwanarusk R., Hui Teo T., Russell B., 2012).

Rarely, malaria parasites are transmitted by blood transfusions (Owusu-Ofori A., Parry C., Bates I., 2010).

The World Health Organization (WHO) classifies malaria into either "severe" or "uncomplicated". (Nadjm B., Behrens R., 2012; WHO, 2012). Malaria is diagnosed as severe or complicated when any of the following criteria listed below are present, (WHO, 2012).

- Significant weakness such that the person is unable to walk
- Inability to feed
- Breathing problems
- Circulatory shock
- Pulmonary edema
- Hypoglycemia, blood glucose less than 2.2 mmol/L (or 40 mg/dL). It may occur as a side effect of quinine treatment or in pregnant women with uncomplicated malaria (CDC, 2010).
- Metabolic acidosis, acidosis or lactate levels of greater than 5 mmol/L. It often occurs with hypoglycemia.
- A parasite level in the blood of greater than 100,000 per microlitre (µL) in low-intensity transmission areas, or 250,000 per µL in high-intensity transmission areas (Andrej T., Matjaz J., Igor M., Rajesh M., 2003; Nadjm B., Behrens R., 2012; WHO, 2012).
- Cerebral malaria (abnormal behavior, abnormal posturing, nystagmus, conjugate gaze palsy (failure of the eyes to turn together in the same direction), opisthotonus, seizures, coma, impaired consciousness, convulsion or other neurologic abnormalities).
- Hemoglobinuria due to hemolysis
- Malarial hepatopathy (malaria hepatitis), Liver dysfunction from malaria. A rare condition usually a result of a coexisting liver condition such as viral hepatitis or chronic liver disease. Liver compromise in people with malaria correlates with a greater likelihood of complications and death (Bhalla A., Suri V., Singh V., 2006).
- Acute respiratory distress syndrome (ARDS), an inflammatory reaction in the lungs that inhibits oxygen exchange. May occur even after parasite load has reduced in response to treatment due to respiratory compensation of metabolic acidosis, noncardiogenic pulmonary oedema, concomitant pneumonia, and severe anaemia.
- Abnormalities in blood coagulation resulting in bleeding problems
- Hypotension caused by cardiovascular collapse, blood pressure (less than 70 mmHg in adults or 50 mmHg in children)
- Acute renal failure, a feature of black water fever (hemoglobin from lysed red blood cells leaks into urine).
- Hyperparasitemia, when more than 5% of the red blood cells are infected by malaria parasites
- Neurologic defects (ataxia, palsies, speech difficulties, deafness, blindness) may occur following cerebral malaria especially in children.
- Severe anemia due to hemolysis following recurrent infections with *P. falciparum* which are inadequately treated.
- Malaria during pregnancy (especially *P. falciparum*) may cause severe disease in the mother, and may lead to preterm delivery or delivery of a low-birth-weight baby.
- Neurologic defects (ataxia, palsies, speech difficulties, deafness, blindness) may occur following cerebral malaria especially in children.
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- Malaria during pregnancy (especially *P. falciparum*) may cause severe disease in the mother, and may lead to preterm delivery or delivery of a low-birth-weight baby.
- Nephrotic syndrome (a chronic, severe kidney disease) which can result from chronic or repeated infections with *P. malariae*.
- Tropical splenomegaly syndrome due to an abnormal immune response to repeated malarial infections. Its features are hepatosplenomegaly, abnormal immunologic findings and a susceptibility to other infections (such as skin or respiratory infections) and anemia.
- With *P. vivax* infection, it can rarely cause rupture of the spleen (WHO, 2012; CDC, 2010).

WHO defines cerebral malaria as “a severe *P. falciparum*-malaria presenting with neurological symptoms, including coma (with a Glasgow coma scale rating of less than 11), or with a coma that lasts longer than 30 minutes after a seizure”. Severe malaria caused by *P. falciparum* can develop from uncomplicated malaria, especially if it is poorly treated malaria or it is caused by a drug-resistant parasite. Young children are at risk of severe malaria. African children are prone to four malaria complications cerebral malaria, respiratory distress, hypoglycaemia and severe anaemia. Even with adequate hospital treatment, up to 20 per cent of these children will die (Cross C., 2004).

Clinical symptoms of malaria are caused by the asexual erythrocytic or blood stage parasites. When the parasite develops in the erythrocyte, numerous toxic waste substances like hemozoin pigment, glucose phosphate isomerase (GPI) accumulate in the infected red blood cell from the lysed infected cells and releases invasive merozoites. These toxic substances stimulate macrophages and other cells to produce cytokines and other soluble factors which produce fever and rigors and other severe pathophysiology associated with malaria.

Malaria infection can be asymptomatic or present with mild symptoms but it can become a severe disease leading to death. Signs and symptoms of malaria begin 8–25 days following infection but, it may occur later in people on malaria prophylaxis (Nadjm B. et al, 2012). The classical (but rarely observed) malaria attack lasts 6-10 hours. It occurs every 48 hours with the "tertian" parasites (*P. falciparum, P. vivax, and P. ovale*) and every 72 hours with the "quartan" parasite (*P. malariae*) (CDC, 2010).

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 initial symptoms common to all malaria species are unspecific and are similar to flu-like symptoms (Bartoloni A, Zammarchi L (2012), they mimic conditions like septicemia, gastroenteritis, and viral diseases (Nadjm B et al, 2012).

Clinical features of malaria include:

- hyperpyrexia, pyrexia, fever (temperature greater than 38°C/ 100.4F)
- shivering (chills and sweating), intense muscle pain
- blurring of vision, dizziness
- headache
- arthralgia (joint pain),
- Nausea, vomiting, bloody stools,
- hemolytic anemia,
- Hepatomegaly
- Splenomegaly
- Tachypnoea
- jaundice,
- Body aches
- General malaise, general body weakness
- hemoglobinuria,
- retinal damage, (Beare N., Taylor T., Harding S., Lewallen S., Molyneux M., 2006)
- Convulsions.

In non-endemic countries, a high index of suspicion is needed to diagnose malaria. A history of recent travel, clinical findings of splenomegaly, fever without localizing signs, thrombocytopenia and hyperbilirubinemia with laboratory findings of a normal peripheral blood leukocyte count are useful in diagnosing malaria (Nadjm B. et al, 2012). In malaria endemic countries where malaria is frequent, residents often treat themselves presumptively (CDC, 2012). Recurrent malaria can be due to a recrudescence (symptom return after a symptom free period due to parasites surviving in the blood because of poor treatment) (WHO, 2012), relapse (symptoms reappear after parasites have been eliminated from blood because they persist as hypnozoites in liver cells) (WHO, 2012), or re-infection (re introduction of a new parasite despite eliminating the parasite responsible for the initial infection). Relapse commonly seen with P. vivax and P. ovale infections occurs between 8–24 weeks (Nadjm B., et al 2012). Recurrence of infection within two weeks of treatment of the initial infection is due to treatment failure (WHO, 2010).

Severe malaria usually caused by P. falciparum, (a medical emergency) should be treated urgently and aggressively. It occurs when infections are complicated by organ failures or and abnormalities in the patient's blood or metabolism. Manifestations of severe and or complicated malaria were mentioned above.

Diagnosis of malaria depends on laboratory findings which may include;

- Demonstration of parasites in the blood, usually by microscopy.
- Anemia, mild decrease in blood platelets (thrombocytopenia), elevation of bilirubin, and elevation of aminotransferases.
Some genetic factors are resistance to malaria. They include; sickle cell trait, thalassaemia traits, glucose-6-phosphate dehydrogenase deficiency, and the absence of Duffy antigens on red blood cells (Kwiatkowski D., 2005). The red blood cell has a biconcave shape. Sickle cell trait causes a defect in the hemoglobin molecule in the blood. The hemoglobin S molecule causes red blood cell to sickle making it relatively ineffective in taking or releasing oxygen. Infection causes red cells to sickle more so they are removed from circulation sooner. This reduces the frequency with which malaria parasites complete their life cycle in the cell. Homozygous individuals (with two copies of the abnormal hemoglobin beta allele) have sickle-cell anaemia, while heterozygous individuals (with one abnormal allele and one normal allele) experience resistance to malaria (Hedrick P., 2011; Weatherall D., 2008).

When malaria and HIV infections coexist, malaria worsens HIV by increasing viral load in adults and pregnant women, accelerating progression to AIDS and increasing the risk of HIV transmission between adults and a mother and her child. In adults with low CD4 cell counts and pregnant women, HIV infection appears to make malaria worse (UNICEF 2012).

In South East Asia, India accounts for 66.6% of confirmed malaria cases. In 2008, 96million slides of suspected malaria was examined, 1.5million cases were confirmed. In 2008 malaria cases reduced to 1.5million as a result of malaria control measures half of which was confirmed (World malaria report, 2009).

Table 1: The table below shows population, endemicity and malaria burden in India (World malaria report, 2009).

<table>
<thead>
<tr>
<th>Population in thousands</th>
<th>Year 2008</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>1 181 412</td>
<td></td>
</tr>
<tr>
<td>Less than age 5</td>
<td>126 642</td>
<td>11</td>
</tr>
<tr>
<td>Greater than or equal to age 5</td>
<td>1 054 770</td>
<td>89</td>
</tr>
</tbody>
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Population by malaria endemicity (in thousands)

| High transmission > 1/ 1000 | 307 189 | 26 |
| Low transmission 0- 1/ 1000 | 755 223 | 64 |
| Rural population             | 833 321 | 71 |
| Malaria free                 | 118 999 | 10 |

Figure 1: The graph below shows population, endemicity and malaria burden in India from year 2001 to 2008 (World malaria report, 2009).
Figure 2: The graph below shows trends in malaria mortality in all ages in India from year 2001 to 2008 (World malaria report, 2009).

Malaria control measures have resulted in lower disease burden (CDC, 2012). WHO reported that; “deaths attributable to malaria in 2010 were reduced by 33.3% from a 2000 estimate of
985,000 due to the widespread public health prevention of malaria with the use of insecticide-treated nets and artemisinin-based combination therapies”. Other malaria control measures are intermittent preventive treatment for pregnant women (IPTp), indoor residual spraying (IRS), insecticide-treated bed nets (ITNs) and malaria prophylaxis for travellers (CDC, 2012). No effective malaria vaccine exists. Despite all these measures, malaria epidemics still kill more than 100,000 people of all ages annually, 30% of malaria deaths in Africa occur in the wake of war, local violence or other emergencies (CDC, 2012).

Figure 3: The graph below shows hospitalized malaria cases and malaria mortality in 2 countries (Eritrea, Sao Tome and Principe), all ages, 2001 to 2008. The introduction of malaria control measures has resulted in a reduction in mortality seen in 2002 to 2008 in Eritrea and from 2003 to 2008 in Sao Tome and Principe.

Malaria is associated with negative economic effects in areas where it is endemic. In the late 19th and early 20th centuries, it was a major factor in the slow economic development of the American southern states (Humphreys M., 2001). Malaria is a major hindrance to economic development (Gollin D, Zimmermann C 2007; Worrall E, Basu S, Hanson K 2005). Malaria has huge economic impacts in Africa; it slows economic growth and development and perpetuates the vicious cycle of poverty. It is a disease of poverty, it afflicts the poor who tend to live in malaria-prone rural areas in poorly-constructed dwellings that offer few, if any, barriers against mosquitoes (UNICEF, 2012). It is commoner in rural areas (poor people lack the wherewithal to control malaria), along international borders and forest fringes (Cui L, Yan G, Sattabongkot J, Cao Y, Chen B, Chen X, Fan Q, Fang Q, Jongwutiwes S, Parker D, Sirichaisinthop J, Kyaw M, Su X, Yang H, Yang Z, Wang B, Xu J, Zheng B, Zhong D, Zhou G, 2012). In Africa, malaria is equally
present in both rural and urban areas though, the risk is lower in urban areas (Machault V., Vignolles C., Borchi F., Vounatsou P., Pages F., Briolant S., Lacaux J., Rogier C., 2011). In these rural areas much of the malaria infections are undocumented making accurate data unavailable. Malaria has a heavy burden in some countries, where it may be responsible for 30–50% of hospital admissions, up to 50% of outpatient clinic attendance and approximately 40% of public health budget (RBM + WHO). The economic impact of malaria has been estimated to cost Africa $12 billion US dollars annually; this includes health care costs, working days lost due to sickness, days lost in education, decreased productivity as a result of brain damage from cerebral malaria, loss of investment and tourism (Greenwood B., Bojang K., Whitty C., Targett G., 2005). The economic impact of malaria is enormous it has been estimated to cost Africa $12 billion US dollars (Sachs J., Malaney P., 2002). It is estimated that approximately 3 billion US dollars is required annually to effectively prevent and control malaria worldwide (World Malaria report) (UNICEF, 2012).


Displaced persons living in makeshift houses are vulnerable to malaria; they are more likely to be bitten by mosquitoes, lack access to healthcare and are often ill with other infections (CDC, 2012). Malaria epidemics are triggered by factors linked to the human host, the mosquito vector (the environment) and malaria parasites. The change or disruption of the ‘balance’, between these three factors increases the likelihood of an epidemic. There is an increased risk of a malaria epidemic if there is an increase in the susceptible human population (increased vulnerability due to malnutrition and concurrent infections, poor or absent housing and poor coordination among health agencies), increase in the number of mosquito vectors and an increase in the number of people who have the malaria parasite in their blood (CDC, 2012).

Environmental factors affecting the development of mosquitoes and Plasmodium specie parasite are temperature increase (temperatures between 22C and 30C increases lifespan of mosquito, frequency of blood meals, speeds up development of mosquito larvae and shortens the length of time mosquito takes to develop from egg to adult), increase in humidity and increase in rainfall (creates stagnant water which allows mosquitoes to breed in large numbers and increases humidity) (Tarekegn A., Abeku A., 2007; CDC, 2012). Malaria epidemics are also more likely in human populations with low or lack of immunity to malaria (CDC, 2012). Migration also contributes to malaria epidemics. People infected with malaria moving into an area where malaria has been controlled or eliminated will be sources of Plasmodium parasites for local mosquitoes and will precipitate an epidemic. Non-immune persons moving to areas where
malaria is endemic can cause an apparent epidemic because they are more susceptible than the local population to malaria (CDC, 2012).

Naturally acquired immunity to falciparum malaria protects millions of people routinely exposed to *Plasmodium falciparum* infection from severe disease and death. It mechanism of action is unknown. Naturally acquired immunity is virtually 100% effective against severe disease and death amongst heavily exposed adults. Immunity that occurs in exposed infants may be greater than 90% effectiveness. The presence of an adult-like immune status amongst high-risk infants in sub-Saharan Africa reduces disease and death caused by *P. falciparum*. The mechanism of naturally acquired immunity that occurs among adults living in areas of hyper- to holoendemicity should be understood in order to create such protection in infants and young children in endemic areas (Doolan D., Dobaño C., Kevin Baird J., 2009). Immunity or tolerance to *P. falciparum* occurs in response to years of repeated infection. It is postulated that if an individual receives a thousand mosquito bites, the individual can be protected from a *P. falciparum* infection (Tran T., Samal B., Kirkness E., Crompton P., 2012).

Plasmodium vivax is the most widely distributed geographical cause of malaria in people, up to 2.5 billion people are at risk and approximately 80 million to 300 million clinical cases occur annually resulting in severe disease and death. *P. vivax* is overlooked despite its large burden because of the huge problem caused by *Plasmodium falciparum* in sub-Saharan Africa. Technological advances enabling the sequencing of the *P. vivax* genome and a recent call for worldwide malaria eradication have placed an emphasis on *P. vivax* as a major public health problem. Because of *P. vivax*’s biology it is difficult to interrupt *P. vivax*’s transmission. Experts agree that preventive and therapeutic methods available for *P. vivax* infections are inadequate. Development of new methods and strategies should become a priority as well as understanding the biology, pathogenesis, and epidemiology of *P. vivax* (Mueller I., Galinski M., Baird J., Carlton J., Kochar D., Alonso P., Portillo H., 2009).

Further epidemiological research and development is needed in the laboratory and field that focuses on malaria parasite transmission, drug resistance and host immune and pathological responses to malaria. The will give answers to why manifestations of severe disease outcomes differ in various endemic settings (intense transmission versus seasonal transmission), how transmission pressure affects development of immune responses, and factors that determine the acquisition of clinical and parasitological immunity. This can lead to improved or new methods for control and prevention. A person’s genetic factors and the acquisition of immune status can influence the development and outcomes of severe disease states in malaria hence; there is a need for research to develop vaccines effective against malaria parasites, investigations into the genetic complexity of malaria parasites and how this complexity and selection affects drug resistance, immunity, and disease. Understanding immune responses that are active in malaria and how they are destructive to parasites is also an important factor to malaria vaccine development (CDC, 2012). These studies in parasite and human genetics will help develop suitable molecular markers that can be used for tracking parasite populations associated with severe disease outcomes (CDC, 2012).
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