Hematologic Changes Associated with Specific Infections in the Tropics

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KEYWORDS

• Anemia • Malaria • Leishmaniasis • Schistosomiasis • Trypanosomiasis
• Hookworm • Bartonellosis

KEY POINTS

- Malaria is responsible for approximately 600,000 deaths each year, although the epidemiologic picture over the last decade has been one of a substantial reduction in the burden of malaria.
- Malaria causes severe and life-threatening anemia by reducing erythropoiesis and increasing red cell destruction.
- Blood transfusion is beneficial in the group of children with malaria who have both anemia and respiratory distress, but bolus fluid supplementation of severely ill children on admission may result in higher mortality.
- Ill children should be carefully assessed clinically, and appropriate fluid or blood transfusion should be given to correct hypovolemia or severe anemia.
- Visceral leishmaniasis can cause considerable diagnostic difficulty and may be mislabeled as leukemia or myelodysplasia when the diagnosis of leishmaniasis was not considered.

Anemia frequently accompanies and plays a minor role in the presentation and course of parasitic, bacterial, or viral infection. However, a variety of infections, many of which are common in Africa and Asia, cause specific hematologic syndromes. The pathophysiology of these syndromes is complex and, to some extent, reduced red cell production may form part of an innate protective host response to infection. Across the world and in endemic areas, malaria, the most important among this group of infections, forms a major part of everyday practice across all clinical specialities and laboratory work. Several other parasitic diseases and bacterial infections, including visceral leishmaniasis, schistosomiasis, trypanosomiasis, hookworm, and bartonellosis, may present with major hematologic syndromes. These diseases may have restricted geographic distribution, but through travel, may present anywhere and must be recognized, diagnosed, and treated.

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MALARIA

Malaria is the most important parasitic illness of humans.[1–3] The total burden of disease in 2013 was estimated to be 200 million episodes annually, and malaria is responsible for approximately 600,000 deaths each year.[4,5] Despite the huge number of cases and deaths, the epidemiologic picture over the last decade has been one of a substantial reduction in the burden of malaria. The prevalence of infection and malaria-related mortality decreased dramatically in sub-Saharan Africa during the period 2000 to 2013. Across Africa, the average infection prevalence in children aged 2 to 10 years decreased from 26% in 2000 to 14% in 2013, a relative decline of 46%.[2,5] Nevertheless, substantial problems remain for successful malaria control. There remains the perennial problem of increasing drug resistance of the malarial parasite and of resistance of the mosquito vector to insecticides used to impregnate bed nets, and malaria still remains one of the major global problems of public health.

The Life Cycle of Malaria Infection and Human Infection

Because of its peculiar life cycle (**Fig. 1**), the malarial parasite is particularly prone to cause hematologic manifestations. Female anopheline mosquitoes inject sporozoites that enter liver parenchymal cells, where they proliferate into thousands of merozoites. Merozoites rupture from liver cells, pour into the bloodstream, and invade erythrocytes. Further development of the intraerythrocytic parasite follows 1 of 2 pathways: asexual differentiation or differentiation into sexual parasites called gametocytes. Asexual parasites develop from young ring forms through trophozoites to dividing forms called schizonts. On rupture of infected erythrocytes, forms called merozoites are released, invade other erythrocytes, and thus continue the erythrocyte cycle. When billions of schizonts rupture simultaneously and release cytokine-inducing toxins, they cause paroxysms of malarial fever.

When a child is infected with malaria for the first time, the result is usually an intermittent febrile illness lasting a few weeks, although a significant proportion of children and a high proportion of nonimmune adults experience severe disease (see later discussion). In the phase between cessation of the fever and final resolution of the infection, the child may appear well, but the destruction of red cells continues. From a hematologic viewpoint, the major question is how soon will the child be reinfected, for in some communities reinfection occurs almost every day, and immunity to malaria is slowly acquired and never complete. In regions of high transmission, children eventually acquire the ability to maintain a parasite density below the level that causes fever, but chronic or repeated infections cause a state of chronic anemia.

Four species of Plasmodium infect humans—*Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, and *Plasmodium malariae*—and a fifth species, *Plasmodium knowlesi*, normally restricted to macaque monkeys, has recently been discovered in the human population in Borneo.[6] *P falciparum* is the predominant cause of clinical malaria in Africa and much of Southeast Asia, whereas *P vivax* tends to predominate in Central America and the Indian subcontinent. *P vivax* is essentially absent in populations of Central and West Africa because their erythrocytes fail to express the Duffy antigen or interleukin-8 (IL-8) receptor, to which the merozoites of this species attach during invasion.[7]

Another peculiarity of *P vivax*, shared also with *P ovale*, is the ability to form hypnozoites, which can remain dormant in cells for months or years. This ability results in relapsing infections that are often associated with mild chronic anemia. However, profound anemia and other grave complications are almost always seen with *P falciparum* malaria, and the following sections apply mainly to this particular species.