Parasites and their vectors

A special focus on Southeast Asia
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Yvonne Ai Lian Lim • Indra Vythilingam
Editors

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Chapter 1
Southeast Asia: Hotspot for Parasitic Infections

Yvonne A.L. Lim and Indra Vythilingam

1.1 Brief Overview

Southeast Asia (SEA) is a vibrant subregion of Asia located between the two mega Asian powers, India and China. This region is blessed with high diversity of flora and fauna, covering an area of approximately 4 million km², and is inhabited by an estimated 600 million people [1]. For the purposes of this book, we adopt the definition of SEA as the 11 member countries of the Association of Southeast Asian Nations (ASEAN) which was established in 1967 by founding member countries, namely Indonesia, Malaysia, Philippines, Singapore and Thailand. Besides these founding members, the current ASEAN countries also consist of neighbouring countries such as Brunei Darussalam, Cambodia, Timor-Leste (observer), Lao PDR, Myanmar and Vietnam. The pivotal aims of ASEAN are to promote regional economic growth, political stability, social progress and cultural developments (http://www.asean.org/asean/about-asean/overview).

Historically, this region was once plagued with political conflicts, uncertain economies and ethnic and social inequities. However, in recent times, this diverse cultural region is experiencing thriving economic, environmental and sociodemographic transformations. As a region with increasing geopolitical influence in view of Asia’s global economic ascendancy, it is not surprising that the global focus is now on SEA as an emerging economic market.

The dynamic processes of rapid urbanisation, exponential population growth and mobility which SEA is undergoing have also led to the intensification of food production, agriculture, livestock and land use resulting in deforestation and inevitably climatic change. As the ecological balance is disturbed, new niches emerge encouraging infectious agents (e.g. parasites) to adapt and change. Evidences of these sometimes subtle adjustments between parasites and their ecologies are
unfolding in SEA as reports on the emergence of zoonotic parasitic infections are appearing to be more common [2]. The problem of controlling parasitic infections is further augmented as drug resistance develops due to indiscriminate usage of antiparasitic agents enabling the parasites to thrive, thus compromising on the progress of malaria control programmes [3].

These interconnected driving forces have vital impact on human health and recent articles in Lancet (2011) alerted the global community of the significance of SEA region as an emerging hotspot for global health [4, 5]. Granted its rich biodiversity, SEA is at the focus of attention with regard to parasitic infections, in particular, zoonotic and vector-borne diseases (i.e. Plasmodium knowlesi infection) where the burden of these diseases can be substantial. Although many countries in this region are experiencing economic development, pockets of impoverished populations still exist, and these populations play significant roles in the propagation and transmission of neglected tropical diseases (e.g. soil-transmitted helminthiasis) [6].

Limited available financial resources and rapid urbanisation often results in insufficient clean water supply or proper waste disposal. These factors, coupled with the HIV/AIDS pandemic the region is facing and the conducive tropical or subtropical climate, facilitate the transmission of waterborne/foodborne and opportunistic parasites [7]. With advancing modes of transportation, increasing transboundary migrations and a burgeoning tourism trade, the potential for the spread of these infectious diseases will be borderless and immeasurable.

In 2015, the ASEAN Economic Community (AEC) with a goal of regional economic integration will be established. The AEC aspires to transform ASEAN into a region with borderless trade. There will be free movement of goods, services, investment, skilled labour and freer flow of capital (http://www.asean.org/communities/asean-economic-community). When this materialises, there will be greater transboundary movement amongst these neighbouring countries. Hence, it is crucial to assess and have an enhanced understanding of the current status of the epidemiology and clinical impact of parasitic infections in these 11 SEA countries.

Thus far, there has been no collective systematic appraisal of parasitic infections and their vectors in SEA. For these reasons, this book attempts to present a comprehensive review of all the accessible information/data and publications for individual SEA countries. Coverage of parasites in this book includes Plasmodium, Entamoeba, Giardia, Cryptosporidium, Toxoplasma, Blastocystis, free-living amoeba, filarial worm, soil-transmitted helminths, cestodes, trematodes, Sarcocystis, pentastomes and vectors for malaria and filariasis. For those who have always been intrigued by the diversity of the SEA communities, may this book inject some interest into the health aspects, in particular, the epidemiology of parasitic infections in this region. On a more serious note, it is hoped that the collation of these data will provide an extensive baseline information with crucial highlights on the significant gaps of knowledge. It is hoped that this understanding could then assist in formulating a solid scientific framework/platform for future integrated research in the field of infectious diseases, in particular, parasitic
infections amongst member countries. In short, may it spearhead a consolidated regional effort in public health and prepare the region as it launches into a borderless trade.

References

Chapter 2

*Plasmodium knowlesi*: Emergent Human Malaria in Southeast Asia

Kim-Sung Lee and Indra Vythilingam

**Abstract** *Plasmodium knowlesi* is an emerging malaria parasite in humans and is unique to Southeast Asia. Since most countries in Southeast Asia are working towards elimination of malaria, it is important to have knowledge on this emerging simian malaria parasite affecting humans. The first case of simian malaria was reported in Malaysia in 1965. At that time extensive work conducted did not reveal other simian malaria cases in humans. However, in 2004, a large focus of *P. knowlesi* was reported from Sarawak, Malaysian Borneo and that led to many studies and cases being reported from most countries in Southeast Asia. In this chapter, the history, epidemiology, diagnosis, vectors and role of simian host are discussed. Malaria is now a zoonosis and the challenges facing the countries of Southeast in tackling the knowlesi malaria situation and the way forward have been documented.

### 2.1 Introduction

Malaria is a mosquito-borne disease caused by the protozoan parasite of the genus *Plasmodium*. To date, there are nearly 200 species of *Plasmodium* known to infect a wide range of hosts [1]. These include malaria parasite species that infect mammals, rodents, birds and reptiles. There are five species of *Plasmodium* known to infect and cause malaria in humans, namely *Plasmodium falciparum*, *P. vivax*, *P. malariae*, *P. ovale* and *P. knowlesi* [2, 3]. Of these, *P. falciparum* is well known to be the deadliest form of human malaria, whereas *P. vivax* is the most prevalent

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and widely distributed species of human malaria [4, 5]. In general, malaria caused by *P. vivax*, *P. malariae* and *P. ovale* is milder and rarely fatal.

The fifth species of human malaria, *P. knowlesi*, which received much attention only in the last decade, is a malaria species of non-human primate origin [3, 6, 7]. *Plasmodium knowlesi* is prevalent in Southeast Asia and is the cause of human malaria with symptoms ranging from mild to severe disease [8]. Previously, naturally acquired human infections with malaria species of zoonotic origin were considered rare, and it was believed that humans are likely the accidental hosts. This perception changed after it was discovered that a large number of human cases of *P. knowlesi* malaria were routinely misdiagnosed as *P. malariae* in the Kapit division of Sarawak, Malaysian Borneo [2, 9]. Following this first report, it was later discovered that human knowlesi malaria is widespread as human cases were identified throughout Southeast Asia with the exception of Lao PDR.

In this chapter, a special focus is given to the epidemiology and emergence of *P. knowlesi* in Southeast Asia. Several aspects of this simian parasite including its discovery, incidence in countries of Southeast Asia, studies on its natural hosts, vectors, emergence as well as recent development in diagnosis are discussed.

### 2.2 Transmission and Parasite Life Cycle

Transmission of malaria parasites between vertebrate hosts occurs through the bite of infected female *Anopheles* mosquito. The sexual stages or gametocytes (macrogametocyte in female and microgametocyte in male) of the parasite ingested during a blood meal play an important role in this transmission cycle. Fertilization takes place inside the gut of the mosquito to form a zygote. The zygote develops into a motile ookinete, which penetrates the midgut wall of the mosquito before it grows into an oocyst. A matured oocyst contains thousands of infective sporozoites. When the oocyst ruptures, these sporozoites are released into the body cavity of the mosquito and migrate to the salivary gland. The sporogonic phase usually takes between 1 and 2 weeks depending on the species. In the following blood meal from another vertebrate host, the sporozoites are injected into the bloodstream together with the mosquito saliva, thus passing the parasite to the next host. Between ten and a few hundreds of infective sporozoites are usually introduced during the blood meal. Once inside the bloodstream, the sporozoites will reach the liver fairly quickly. Each sporozoite infects the hepatocyte or liver cell individually. The parasite inside each hepatocyte further develops to form merozoites, which forms the liver schizont. When the mature liver schizont bursts, the merozoites are released into the bloodstream and enter into the erythrocytic phase. The duration taken for the parasite to mature inside the liver cells before the merozoites are released into the bloodstream varies depending on the species of the parasite. On average, the pre-erythrocytic phase takes between 5 and 6 days for *P. falciparum*; 8 and 9 days for *P. vivax*, *P. ovale*, and *P. knowlesi*; and 13 days for *P. malariae*. In *P. vivax* and *P. ovale* infections, some of the sporozoite that invades the liver cell