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Review

Historical review: Does falciparum malaria destroy isolated tribal populations?

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Summary Many isolated populations of tribal peoples were nearly destroyed when they first contacted infectious diseases particularly respiratory pathogens such as measles and smallpox. Surviving groups have often been found to have declining populations in the face of multiple social and infectious threats. Malaria, especially *Plasmodium falciparum*, was thought to be a major cause of depopulation in some tribal peoples isolated in tropical jungles. The dynamics of such host parasite interactions is unclear especially since most such populations would have had long histories of exposure to malaria. Three groups are individually reviewed: Meruts of Borneo, Yanomami of Amazonia, Jarawas of the Andaman Islands. The purpose of this review is to examine the role of falciparum malaria in the depopulation of some isolated tribal groups in order to understand what measures, if any, would be likely to prevent such losses.

> *It is not often that the exact fashion in which malaria affects a native tropical community has been described.*
> S R Christophers 1912 [1].

Plasmodium falciparum is likely to have coevolved with humans and our primate ancestors in tropical Africa [2]. This understanding is based on the discovery in gorillas of parasites indistinguishable from *P. falciparum* [3–5]. It is not obvious that malaria was a major cause of primate mortality in pre-historic tropical Africa or in gorillas today. Human mortality due to malaria may have been greatly magnified as part of the agricultural revolution that brought the three species of plasmodium parasite, human host and anopheles vector into effective combination [2]. The resulting mortality shift generated by lethal falciparum malaria may have occurred only during the last few millennia of co-evolution as marked by the selection of balanced genetic polymorphisms in West Africa such as that seen in sickle cell anemia caused by hemoglobin S.

Populations with long histories of exposure to lethal malaria have adapted over time. This includes such isolated tribes as the various Pygmies (Yaka, Bawta etc) of central Africa who have genetic markers of malaria resistance such as glucose-6-phosphate dehydrogenase deficiency (G6PD) and Hemoglobin S [6]. Although more isolated than their Bantu neighbors, Pygmies do not appear to have comparatively increased mortality due to malaria [7]. Malaria parasites migrated down the Melanesian island archipelago

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with their human hosts more than ten millennia ago. Malaria risk is partitioned in Melanesia away from coral islands without *Anopheles* mosquitoes and mountainous areas where cold temperatures limit parasite development [8]. Coastal populations on volcanic islands (e.g. Solomon Islands) have coevolved with falciparum malaria with the isolated populations developing a wide range of polymorphisms such as Southeast Asia ovalocytosis [9]. In Vanuatu on the edge of Melanesia, G6PD forms a north-south gradient reflecting the decreasing malaria evolutionary pressure [10]. So for some tribal groups that have long co-existed with malaria, falciparum extracts its mortality toll from the young but does not cause destabilizing population losses. Figs. 1–3.

There are exceptions to the long coevolution of man with malaria in Melanesia. Ontong Java is a Polynesian outlier north of Santa Isabel in the Solomon Islands. It is a coral archipelago and not volcanic like the rest of the Solomon Islands. It is said that malaria was only introduced on Ontong Java in the 1880s and was a major if not primary cause of reducing the peak population by 80% in 1939 [11]. Malaria was considered holoendemic on Ontong Java based on spleen surveys in the 1940s and parasite surveys in the 1950s. Once malaria control measures through residual insecticide spray were initiated, malaria decreased and the population returned to near pre-contact levels by 2000 [11,12].

But does falciparum malaria kill truly isolated tribal groups that have no previous history of malaria exposure? Since it is impossible to be sure what pathogens might have existed in a pre-contact situation, it is necessary to examine historical records of isolated groups soon after the end of their relative separation from global pathogen circulation. In three cases such information exists and will be reviewed in order to gain insight into what may have happened more broadly across the tropics. See figure for approximate geographic locations.

1. Meruts of Borneo

The Meruts of North Borneo are a jungle Dyak tribal group related to their near neighbors the more agriculturally settled Dusuns. Depopulation labeled as "racial extinction" was an acute concern of the colonial era government by a chartered company when it was found that the number of Meruts were rapidly decreasing compared to the Dusuns [13]. Early investigators of the Merut long-house environment in the deep jungle identified several health problems associated with isolated tribes but thought that chronic ill health due to malaria was the primary cause of their falling population. The plausible hypothesis put forward was that imported Javanese rubber plantation workers had brought *P. falciparum* into close contact with a disturbed jungle eco-system causing localized malaria epidemics in the previously isolated Meruts [13]. Introduction of a new lethal pathogen had destabilized the population and in the absence of any effective chemotherapy (e.g. quinine) the Meruts were in danger of disappearing as a discrete people.

Figure 1 Map showing approximate location of tribal groups discussed as examples of falciparum malaria in tribal peoples.

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Figure 2 Example of an Andaman Islander from the Wellcome Images collection M0005591.

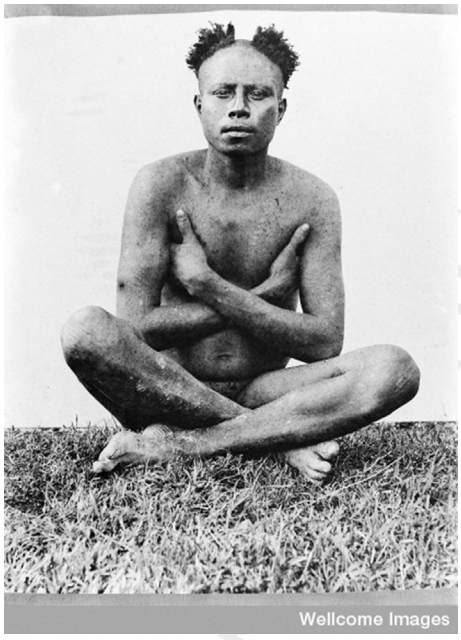

Figure 3 Murut tribeswomen at a feast in Sarawak circa 1896 photo by Charles Hose from the Wellcome Images collection V0037457.

The Meruts were thought to be "doomed to slow but inevitable extinction, unless given systematic and energetic medical aid" [13].

In this area of Malaysia today, the primary lethal malaria is *Plasmodium knowlesi* a monkey malaria parasite spread to humans by the jungle mosquito *Anopheles leucosphyrus* [14–16]. How much malaria mortality in the Meruts of the early 20th century was due to *P. knowlesi* as compared to the more familiar *P. falciparum* is uncertain. The earliest malaria surveys of the area identified *Plasmodium malariae* as a surprisingly common parasite with up to 40% of all positive blood films [17]. *P. knowlesi* is often mistaken microscopically for *P. malariae* so this may be early evidence of monkey malaria's impact in North Borneo [15]. Deforestation around the Merut long-house targeted at eliminating *A. leucosphyrus* was a remarkably effective malaria control measure with 95% of the vector disappearing while also reducing child splenomegaly rates from 86% to 45% [16,18].

Continued studies of the Meruts suggested that infertility likely caused by introduced sexually transmitted diseases was perhaps a greater problem than malaria in terms of the inability to maintain the tribal population [19,20]. Additional retrospective studies in the 1960s when the Merut population losses had been reversed showed that part of the problem was how one counted a transient population that moved freely between jungle and a more settled agricultural life style [21]. The differential mortality compared to the Dusuns and the recovery of the Meruts during the execution of a nearly successful malaria elimination program in the 1960s indicated that malaria was likely a part of a multi-factorial population loss. Today *P. knowlesi* infections remain a major challenge in rural areas of the island of Borneo and are likely to remain so for the foreseeable future due to the macaque monkey reservoir living in the forest fringe areas [15].

2. Yanomami of the Amazon

The Yanomami Amerindians have until recently been small groups of hunter-gathers in the depths of the Amazon rainforest largely disconnected from contact with the rest of society. The earliest medical reports of the Yanomami by Ranke in 1898 indicated there were numerous cases of malaria and "malaria cachexia" in children but how these

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diagnoses were determined is uncertain. Yanomami were hit by multiple lethal infectious diseases epidemics on first contact with the external human pathogen pool largely due to respiratory viruses such as measles [22]. As illegal mining and timber operations have moved into the forest reserves of the Yanomami, falciparum malaria has grown as an important medical problem of these now less-isolated tribal peoples. When members of the Kren-Akorore tribe moved into the Xingu National Park in the mid-1970s they began to suffer frequent severe attacks of malaria and some developed what was described as tropical splenomegaly syndrome necessitating prolonged periods of malaria chemotherapy [23]. Falciparum malaria was the leading cause of death (5 of 11 deaths) documented in this small vulnerable group that had been transferred from one part of the Amazonian rainforest to another in order to move them away from road construction which was certain to eliminate their isolation. Good intentions to protect isolated tribal people may only change the pathogens which eventually kill them such as malaria quickly or tuberculosis more slowly.

There are relatively few observations which describe what must be a dynamic malaria situation in the Yanomami, however it is known that malaria is a major cause of ill health especially anemia [24]. A series of reports over the 1990s indicate that malaria transmission has become a stable part of the Yanomami environment with infections taking the greatest toll among the children [24–27]. Chronic ill health is combined with poor access to medical care which compounds the many challenges faced when isolated peoples begin to move towards the civilized world.

The most plausible reconstruction of the ancient malaria environment of the Amazon has no malaria parasites in the Americas prior to the 16th century when malaria was likely introduced by Spanish and Portuguese explorers and their African slaves [2]. The best evidence of this hypothesis is the total lack of any genetic polymorphisms known to provide protection against malaria in indigenous Americans. Even the American monkey malarias appear to be due to recent human to monkey transmission and not the reverse as is known to occur in Asia and Africa. Therefore, lethal falciparum malaria has to be considered one of several exogenously introduced human pathogens which have devastated isolated tribal groups in the Americas such as the Yanomami. It is not possible to assign relative importance to malaria as compared to other infectious agents and any explanation of isolated Amerindian population loss would almost always be multi-factorial.

3. Jarawas of the Andaman Islands

The Andaman Islands in the Bay of Bengal, south of Myanmar have a uniquely detailed malaria epidemiology studied since the mid-19th century when an open prison colony was started in what became Port Blair [28,29]. Intermittent lethal epidemics of malaria were seen in the Andaman Islands prison colonies which in retrospect were being driven by construction works creating mosquito habitat in the coastal swamps. Rickard Christophers studied malaria around Port Blair in 1911 and determined that nearly all transmission was due to brackish-water breeding *Anopheles sundaicus* and that inland villages were largely malaria free [1]. Interestingly a large proportion (up to half) of the prisoners who were forest workers with positive blood smears were infected with *P. malariae* then labeled as quartan malaria. As in Borneo this is suggestive of *P. knowlesi* or monkey malaria but although monkeys are common in the nearby Nicobar Islands, the potential primate reservoir population of the Andaman Islands is uncertain; it appears that Indian macaques were introduced sometime in the 19th century [30]. Human malaria such as *P. falciparum* was likely introduced to the Andaman Islands by prisoners brought from India in the 19th century but it is unknown whether *P. knowlesi* had been circulating in the jungle monkey population before then [31]. It is possible that recent tsunami destruction of coastal mangrove swamps may have increased the current vector mosquito breeding areas but this would have had no effect on the jungle transmission of monkey malaria [32,33].

The Jarawas are a Negrito tribe of the Andaman Islands that are thought to have been part of the original *Homo sapiens* wave of immigration out of Africa in the very distant past as their genetic composition is quite distinct from others in the area [34]. Although other Andamanese tribes were largely destroyed in the 19th century by a series of epidemics of pneumonia (1868), syphilis (1876), measles (1877) and influenza (1892), the Jarawas maintained a hostile distance from later immigrants to the Andaman Islands [35]. It has been the policy of Indian Government for many years to leave the Jarawas in their isolated areas of the southern Andaman Islands. Decimated by measles in the 1980s, the first known malaria infections occurred in the Jarawas in 2001 as marked by an epidemic of lethal febrile disease [36]. A survey carried out identified only *P. falciparum* in 30 of 179 (17%) blood films despite the primary malaria species in the other island populations being *Plasmodium vivax* (80% of total). Males were infected at twice the rate of females suggesting that the male hunters who ventured farther into the forest and nearer to other groups may have thus been more exposed to infection. The investigators felt it was likely that *P. falciparum* had only recently begun to infect the isolated Jarawas and represented a distinct mortality risk to this very vulnerable, small population [36].

The Jarawas would seem to be roughly equivalent to the Meruts in terms of their potential exposure to *P. knowlesi* but it remains unknown whether such infections occurred prior to any scientific observations. Certainly the jungle mosquito vector is present and some cases of *P. knowlesi* have been reported in the current population of the Andaman Islands [31]. It seems likely that *P. falciparum* was a new lethal infection to the Jarawas due to their very isolated status until the very recent past [35,36].

4. Discussion

Mass mortality is often the result when isolated tribal groups first contact the global pathogen pool; that falciparum malaria might be one of several pathogens contributing to the deaths seems plausible [22]. The evidence is at best incomplete due to the lack of data from uncontacted populations and the often multifaceted aspect of falling

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populations even when they can be studied. For the three tribal groups discussed it appears that they had not co-evolved with falciparum malaria, the record is mixed [13,23,36]. Malaria was thought to be the major reason for population loss in the Meruts but subsequent studies gave a more nuanced picture including infertility due to sexually transmitted diseases and demographic shifts. At least some Yanomami groups do appear to have suffered greatly from recently introduced falciparum malaria by other groups participating in mineral and timber extraction from the Amazon jungle [24,25,37]. The Jarawas of the Andaman Islands have at least one epidemic of documented falciparum malaria but it is unclear whether this is a new event or whether they may have been subject to *P. knowlesi* in the past [36].

Epidemic falciparum malaria has the potential to kill many people quickly even in groups long accustomed to episodic malaria exposure such as during recent highland malaria epidemics in Kenya and Ethiopia or during the Rwandan refugee crisis [38–40]. Normally falciparum malaria extracts an on-going mortality cost on an endemic society's children, but during epidemics in hypo-endemic areas people of all ages die of malaria. This is likely also true in isolated tribal populations but malaria may be only one of many causes of infectious disease mortality when such groups are being incorporated into the global circulation of pathogens. Isolated tribal or island groups appear to be uniquely vulnerable to infectious disease mortality for about one to two generations and then quickly adapt suggesting that this is not entirely caused by classical Darwinian evolution [41].

Very few, if any, extremely isolated human populations still exist today. Historical information tested against plausible hypotheses may be the only remaining method to reconstruct the reasons why such isolated tribal groups had such devastating population losses when initially contacted by other societies with different microbiota and parasites. Isolated tribal groups appear to be a special case of lethal falciparum malaria epidemics in hypo-endemic areas and as such may best be protected by local malaria elimination removing the risk of infection. Prevention of similar episodes will remain difficult based on society's past inability to protect such isolated tribal groups from encroachment by other groups seeking to extract resources from the jungle.

Conflict of interest

None.

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