Antimalarial Drug Supply Issues During the Second World War

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Abstract

Malaria was a major cause of casualties during World War II in the Southwest Pacific, and drug supply issues were acute strategic concerns. The capture of the cinchona plantations of Indonesia by the Japanese Imperial Army and the lack of manufacturing capacity for synthetic substitutes were significant logistical constraints that limited Allied combat operations in the Indo-Pacific Region. Tens of thousands of soldiers were infected with malaria due to inadequate treatment and chemoprophylaxis. In Milne Bay, Papua New Guinea, military operations halted for several months at the end of 1942 due to poor malaria discipline compounded by inadequate medications. Sufficient drug supplies only became available in 1943 when daily quinacrine suppression was enforced. Drug supply disruptions during the COVID-19 pandemic are a reminder that specialist anti-infective medications could have an outsized, modern impact on military operations.

Keywords: malaria, chemotherapy, logistics, Indo-Pacific, World War II

Medical officers and others kept on their feet by taking increased suppressive doses of quinine. Had this alarming increase in rate continued, bounding upwards in geometrical progression as the parasite reservoir grew, the whole force (Milne Bay) *would have been lost in less than two months.*[1]

During the COVID-19 pandemic, supply chain interruptions massively disrupted the world's medical logistical systems. Interestingly, one of the drugs most in demand in 2020 was the antimalarial chloroquine because it was mistakenly thought to work against coronavirus infections.[2] This anomaly reflects the historical reality of 1942 during World War II in the Southwest Pacific when antimalarial drugs were a critical strategic shortage that caused limitations to combat operations, particularly in Papua New Guinea and the Solomon Islands. The global supply of cinchona bark centred in the Dutch East Indies (now Indonesia) had been captured by the Japanese Empire, and the bark processing industry yielding quinine in the Netherlands had fallen to the Nazis. Most of the production capacity of synthetic antimalarials (pamaquine, quinacrine) was in Germany. The Allies had never planned to fight a major war on highly malarious islands and were faced with the prospect of unsustainable disease casualties due to malaria. 'Just-in-time' logistics do not work for events like global pandemics and unexpected tropical campaigns. The Allies rose to the challenge and eventually used superiority in malaria control as a crucial war-winning advantage against the Japanese Imperial Army, but not without great loss and delay. Malaria is one of the few infectious diseases with a well-established capacity to disrupt military campaigns across centuries.[3] Given the Australian Defence Force's (ADF) regional focus and faltering malaria control programs in Melanesia, it is worth re-examining the historical record for future medical logistics lessons, particularly regarding antimalarial drug supplies (e.g., drugs, insecticides).

The Japanese centrifugal offensive after Pearl Harbor captured most of the Australian, British, French, Dutch and USA colonial outposts in the Pacific and Southeast Asia in the first half of 1942.[4,5] One of the worst Australian debacles was the capture of Rabaul, Papua New Guinea in January 1942 with elements of the 2/22 Battalion Australian Imperial Force (AIF) retreating across the mountains of New Britain. Approximately 400 men of Lark Force fled across the southern coast, pursued by both the Japanese and malaria. Approximately 250 men escaped the Tol Plantation massacre and became progressively degraded by malaria as their limited quinine stocks ran out.[4] It is estimated that one-fifth of these survivors died of malaria before being evacuated by boat to Australia; a grim reminder of the lethal character of falciparum malaria.[6] Their pursuers from the 1st Battalion/144 Regiment of the Japanese Imperial Army only fared a little better against malaria as they had come from Guam with no preparation against the parasite. It is estimated that nearly the entire battalion became infected with malaria and 5% died.[7] This battalion was subsequently committed to the Kokoda Campaign and was nearly exhausted by malaria even before arriving in Papua. Disease and starvation accounted

for most of the soldiers on either side in New Guinea once they were cut off from logistical support.[3,8]

The US situation in the Philippines was a larger-scale disaster that occurred in April/May 1942, leading to the greatest surrender in the history of the US Army at Bataan/Corregidor.[5] Malaria played a prominent role in this defeat, with nearly a battalion's worth of men being hospitalised for malaria each day in Bataan.[9] There was insufficient quinine to suppress infections and keep men well enough to fight. Tragically, there were 100 000 kg of cinchona bark in Mindanao from Philippine plantations that could not be turned into useful medication for the troops in Luzon.[9] The lethal aftermath of the surrender was the 'Bataan Death March' to Camp O'Donnell, where 29 589 US and Filipino soldiers died in 1942; one-fifth were estimated to have died directly from malaria.[10] The huge mortality dropped acutely in August of 1942 when their Japanese captors made some quinine available for malaria treatment.[11] The last US Army medical officer (COL Arthur Fischer) leaving the Philippines from Del Monte field in a B-17 carried cinchona seedlings on his lap to re-establish quinine production in Brazil (Figure 1). Unfortunately, this great effort was superseded by better synthetic antimalarial drugs and timed out by the five years required for a tree to yield useful alkaloids.[12]

Figure 1: Cinchona seedlings growing in Washington DC, USA, in November 1943 taken from Mindanao in the Philippines to re-establish quinine production in the Americas.

US Army Photograph, now in the public domain.[12]

The Australian Army had also been making vigorous efforts to secure the last cinchona stocks of Java. COL N. Hamilton Fairley RAAMC paid in advance for the last 100 tons of cinchona bark loaded into a tramp freighter on the Surabaya docks in February 1942.[6] The civil/military collapse of Dutch control of the East Indies resulted in these last precious stocks never arriving in Australia leaving the AIF with less than a year's supply of quinine as a major conflict continued in the highly malarious New Guinea. Synthesising quinacrine (atabrine) was felt to be infeasible not because of a lack of chemical expertise in Australia but because 20 times the amount of precursors would have to be imported to yield a single unit of drug product.[1] COL (later BRIG) Fairley left for Washington on the eve of the Battle for Milne Bay to plead with US and UK Allies for priority access to antimalarial drugs for the Australians because there was no other alternative. Allied medicine stocks fell into an even more critical deficit when the troopship *USS Coolidge* ran upon a mine sinking in the harbour at Espiritu Santo in the New Hebrides (now Vanuatu). The 591 pounds of quinine that went down with the ship represented nearly the entire Allied stock in the Southwest Pacific at the time. In retrospect, it can be stated that it is a very good thing that the Japanese Naval Landing Force landed in Milne Bay in August 1942 to be defeated by the AIF.[13] Had the Japanese waited until December of the same year when the Australian Army was nearly completely combat ineffective from malaria the outcome might have been very different.[14] At one point, 10% of the Allied force in Milne Bay was developing malaria each week.[1]

In truth, the war against malaria could not be won using quinine as it was too short-acting, and the much-reviled but longer-acting quinacrine was essential to eventually asserting malaria control in the combat zones of the Southwest Pacific. Thirty percent of all US Army hospitalisations in the Southwest Pacific in 1943 were from malaria (estimated 50 000). More than 80% of US Marines who initially landed on Guadalcanal were hospitalised for malaria within nine months and 67% of the 32nd US Army Division from Papua developed malaria in ten months. As an example of the continuing casualties from malaria, one needs to consider the four US military Divisions that operated in Melanesia in 1942 (1st and 2nd US Marines, 24th and 32nd US Army Divisions). All required four to six months rehabilitation in non-malarious areas (NSW, VIC, New Caledonia, Fiji) on medication to at least minimise the nearly constant relapses of malaria the soldiers were experiencing before being redeployed for further service.[15] Daily quinacrine use sufficient to turn most soldiers' skin yellow was required, and sufficient medication for this only became available when the American pharmaceutical production capacity caught up with Allied demand in mid-1943 when quinine was largely discontinued except for acute treatment. Due to the unpopular nature of the quinacrine from rumours

Figure 2: Daily quinacrine (atabrine) ingestion enforced by officers (LT J.J. Garrick) in an AIF Commando Unit (2/6th Cavalry) near Wewak, Papua New Guinea, in July 1945.

Australian War Memorial AWM photo 094177, now in the public domain.

and enemy propaganda, enforced drug compliance by subunit officers was necessary[16] (Figure 2).

After 1943, the worst malaria burden was carried by soldiers who were either prisoners of war (POWs) or bypassed Japanese units in New Guinea that expired in the jungle from disease and starvation.[8] Quinine continued to be the only drug available to the Japanese or their prisoners. However, it was strictly rationed in its distribution, causing it to become a medium of exchange (like tobacco) in the Thai-Burma railway camps[10,17] (Figure 3). Quinine's very intermittent use due to supply issues likely caused many to relapse/recrudesce from inadequate treatment or develop the feared complication of blackwater fever (massive haemolysis with hemoglobinuria). Blood for transfusion to treat acute anaemia and antimalarial drugs were key supplies taken by all the medical teams sent to recover POWs in the Southwest Pacific and Southeast Asia.[10,13]

Today, the ADF has three main antimalarial drugs (doxycycline, atovaquone/proguanil, tafenoquine) available in adequate stocks for prevention, but what might happen if there are sudden and unusually high demands for a single product? Examples of epidemic malaria due to inadequate drug stocks have occurred in the 21st century in modern military forces deploying into West Africa with little advanced notice.[18] Although the ADF could manage a battalion's worth of soldiers on antimalarial drugs, a brigade-sized deployment similar to East Timor might once again force a painful re-learning

Figure 3: Lieutenant Ronald Hall of the 9th Division Salvage Unit holding bottles of captured Japanese quinine tablets from a box of abandoned medical stores on the Huon Peninsula in Papua New Guinea in January 1944.

Australian War Memorial AWM photo 070075, now in the public domain.

experience involving preventable casualties and stock-outs of medication.[19] Supply disruptions from concentration of synthesis and formulation of specialised pharmaceuticals in China and India occurred during the COVID-19 pandemic. Let us learn from the historical experience of World War II to avoid such problems in the future.

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