

## 6 | LEARNING FROM HISTORY

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### 6.1 | Introduction to Malaria Elimination: Lessons from Yesterday for Today and Tomorrow

Malaria has accompanied mankind since the origin of *Homo sapiens*. The cause of malaria, parasites of the genus *Plasmodium*, and the mechanism of transmission by mosquitoes were discovered before the end of the 19th century, followed by the development of the armamentarium of malaria control, namely, methods of personal protection, advances in the discovery of therapeutic and prophylactic drugs, and methods of vector control directed against larval breeding sites and adult mosquitoes. These developments set the scene for attempts to eliminate malaria through the Global Malaria Eradication Program (GMEP), which considered elimination feasible in countries with malaria of low or intermediate stability. However, after only 14 years, WHO downgraded the GMEP to malaria control because many countries had experienced difficulties in initiating or sustaining national programs, often because of inadequate national commitment. Nevertheless, several countries successfully eliminated malaria, demonstrating that this goal remains a feasible option for other malaria-endemic countries. This chapter analyzes the lessons learned from both successful and unsuccessful attempts to eliminate malaria, as well as

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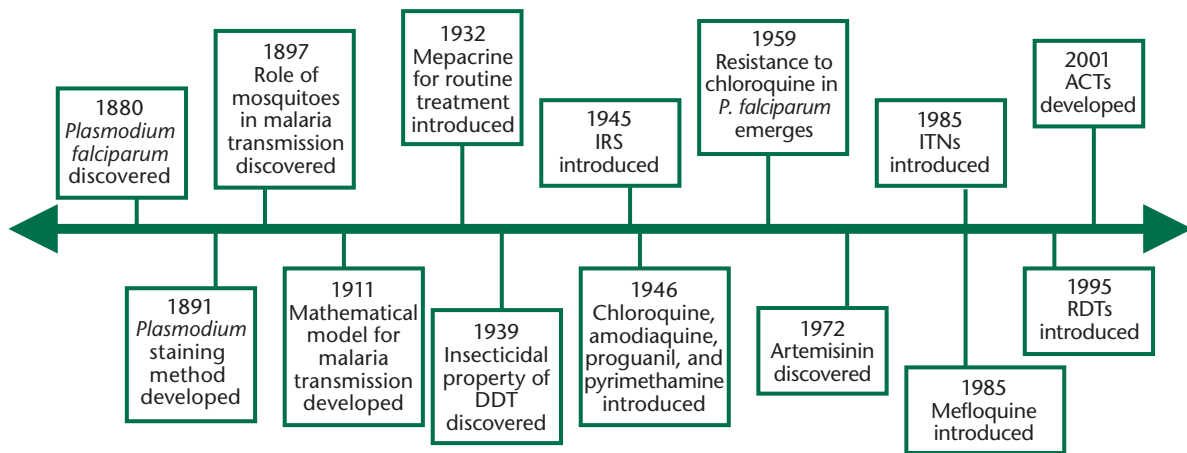


FIGURE 6.1 | Timeline of the development of the malaria armamentarium

factors that have contributed to a constant shrinking of the malaria map from 1955 to today.

## 6.2 | Chronology: Development of Tools for Malaria Control

Since *Plasmodium falciparum* was first discovered in 1880, many important discoveries have been made, and tools have been developed that enable endemic countries to control and/or eliminate malaria. A time line of major discoveries and the development of technologies in use for diagnosis of malaria and for parasite and vector control is given in Figure 6.1.

Drugs that today are essential for the treatment of malaria (quinine and artemisinins) were first used in their native form for treatment of periodic fevers long before the malaria parasites were discovered in the 19th and early 20th centuries.<sup>1, 2, 3</sup> The demonstration of the natural mode of transmission through anopheline mosquitoes around the same time led to the development of vector control measures against the larval and adult stages.<sup>4</sup>

## 6.3 | History of Conceptual Changes: Malaria Control to Elimination

The concept of eradicating malaria was first proposed by Fredrick L. Hoffmann in 1916 in his “plea for malaria eradication in the Western Hemisphere.”<sup>5</sup> At

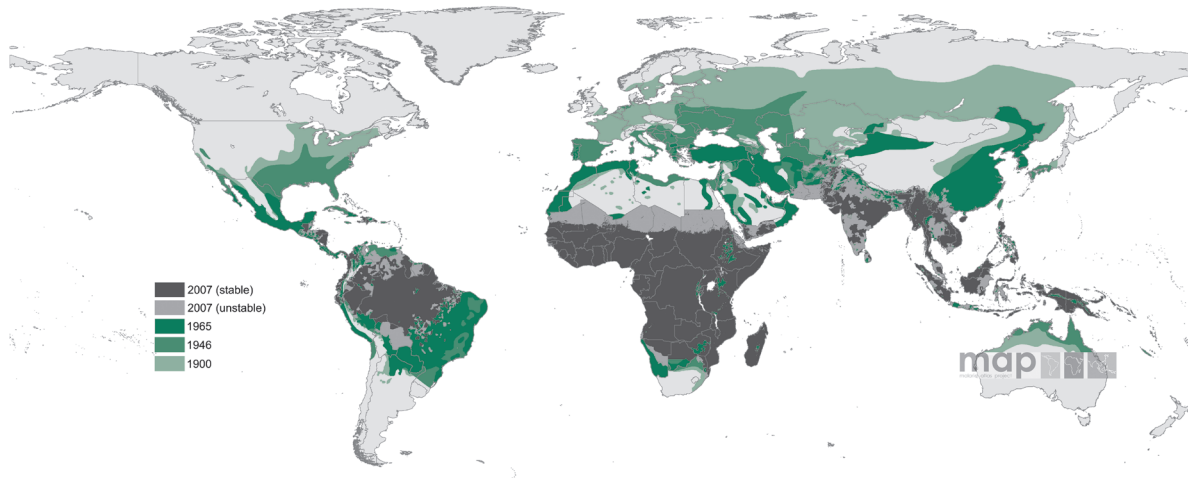
that time, however, controlling malaria was the priority, and eradication was not yet considered a feasible goal.

New tools such as indoor residual spraying (IRS), chloroquine, amodiaquine, proguanil, and pyrimethamine were developed at the end of World War II and radically improved the prospects for intensifying malaria control. International attention directed toward control of malaria became stronger, as demonstrated by the establishment of disease control institutions such as the Centers for Disease Control and Prevention (CDC) in the United States in 1946, which was founded to limit the impact of malaria and which eventually achieved elimination of the disease in 1952 in the 13 states where malaria was still endemic.

Devastating postwar malaria epidemics in southern Europe highlighted the need to design and implement effective malaria control programs. Cyprus, Greece, and Italy strengthened their health systems to cope with diagnosis and radical treatment of malaria, with transmission controlled by residual spraying of DDT. After the Greek government suspended DDT spraying, the expected resurgence of malaria did not occur, indicating that in similar eco-epidemiological settings, *P. falciparum* and *P. vivax* can be eliminated if transmission is fully suppressed for 4 years for *P. falciparum* and 5 years for *P. vivax*.

Successful elimination campaigns such as those in Greece and Italy gave hope for a malaria-free world. The GMEP was launched at the eighth World Health Assembly in 1955, when the following announcement was made: "The World Health Organization should take the initiative, provide technical advice, and encourage research and coordination of resources in the implementation of a program having as its ultimate objective the worldwide eradication of malaria."<sup>6, 7</sup>

This new strategy was heavily dependent on employing long-lasting pesticides, primarily DDT, to kill adult vectors and interrupt malaria transmission. The countries and regions where elimination seemed feasible were initially targeted, which at the time included the Americas, Europe, the Mediterranean countries, western and eastern Asia, and the western Pacific and Australia. Malaria elimination in sub-Saharan Africa and New Guinea was not considered feasible with available tools and means, a perception that remained fundamentally unchanged until recently, despite the fact that very large swaths of both regions experienced low endemicity.<sup>8</sup>



**FIGURE 6.2** | Geographical distribution of all-cause malaria 1900, 1946, and 1965 (modified from Hay et al.<sup>9</sup>) with the overlay of the 2007 spatial limits of *P. falciparum* malaria transmission (modified from Guerra et al.<sup>8</sup>). The 2007 bounded areas were defined as stable (dark gray areas, where *P. falciparum* annual parasite index, or PfAPI,  $\geq 0.1$  per 1,000 per year) or unstable (lighter gray areas, where PfAPI  $< 0.1$  per 1,000 per year).

#### 6.4 | Shrinking the Map: Geographical and Chronological Progression of Malaria Elimination

The geographical and chronological progression of malaria elimination between 1900 and 2007 is shown in Figure 6.2 and summarized in Table 6.1.

Practically all malaria-endemic countries in the Americas joined the GMEP, and most endemic countries in Europe continued to move toward elimination. In tropical Africa, only two offshore islands declared national malaria eradication programs. Australia, the Solomon Islands, and Vanuatu joined the program, as did the majority of southern Asian countries, from Turkey in the west to Taiwan in the east.

In the Americas, 22 countries achieved malaria elimination from 1950 to 1978, among them the majority of Caribbean countries. With the exception of the United States and Chile, none of the malaria-endemic continental countries in the Americas reached this goal. In the European region, 37 of the remaining 43 malarious countries became malaria free during the same time period. Small foci, or limited areas of continued transmission, persisted in Greece beyond 1970, but malaria was eliminated in the late 1970s. Australia, Japan, and Singapore all succeeded in eliminating malaria by 1978. Brunei, Israel, and Réunion followed suit soon after.

**Table 6.1 | Malaria status of countries and territories 1900, 1949, 1978, and 2009 by WHO regions**

Parameter	Africa	Americas	S.E. Asia	Europe	E. Med.	W. Pacific	Total
Total number of countries	48	45	10	58	20	27	208
Malaria free in 1900	1	2	0	3	1	13	21
Malaria free 1900-1949	0	0	0	9	0	0	9
Malaria free 1950-1978	2	22	0	37	4	4	68
Malaria free 1979-2009	1	1	1	1	6	0	10
Total malaria free	4	25	1	50	11	17	108

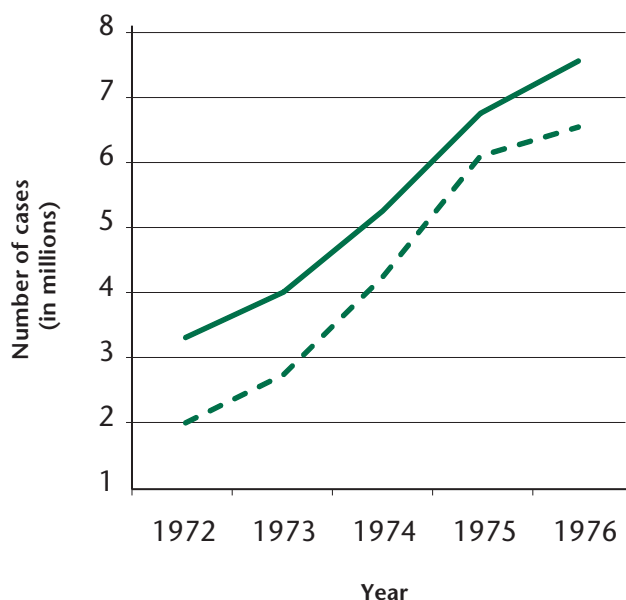
Sources: Wernsdorfer,<sup>10</sup> WHO,<sup>11</sup> Packard,<sup>12</sup> Bruce-Chwatt and Zulueta,<sup>13</sup> and "Malaria in the Southwest Pacific"<sup>14</sup>

Although mortality and morbidity from malaria decreased significantly in most countries during the GMEP, the initiative failed to reach the ultimate goal of eradication. Consequently, in 1969, the WHO General Assembly reexamined the strategy<sup>15</sup> and recommended a reversion to malaria control for the countries that were clearly unable to achieve elimination within the foreseeable future; however, it failed to provide guidelines and recommendations for a systematic strategy to achieve control. After 1972, the malaria situation worsened as a result of political factors, insufficient national support, and withdrawal of external assistance. This was marked by a substantial increase in the number of autochthonous malaria cases recorded in areas under surveillance between 1972 and 1976 (Figure 6.3).

Nevertheless, several countries continued on the path to the elimination of malaria, as shown in Table 6.1, and ten countries achieved elimination between 1979 and 2009, among them six Eastern Mediterranean countries, including Bahrain, Morocco, Oman, Syria, Tunisia, and the United Arab Emirates. Kazakhstan, Maldives, and Seychelles were also successful.

Remarkable success in spatially progressive elimination in large parts of endemic countries has been achieved in Argentina, Brazil, China, Paraguay, the Philippines, and Thailand. By the year 2000, an estimated 60% of the world's population resided in malaria-free areas, a great increase from 20% in 1950. In 2007, 35% of the world's population lived in areas still endemic for malaria,<sup>8</sup> with about 66% of those protected by some form of organized malaria control. Tropical Africa and the island of New Guinea are still considered the last epicenters of endemic stable malaria.

The decision taken by the World Health Assembly in 1969 reflected the



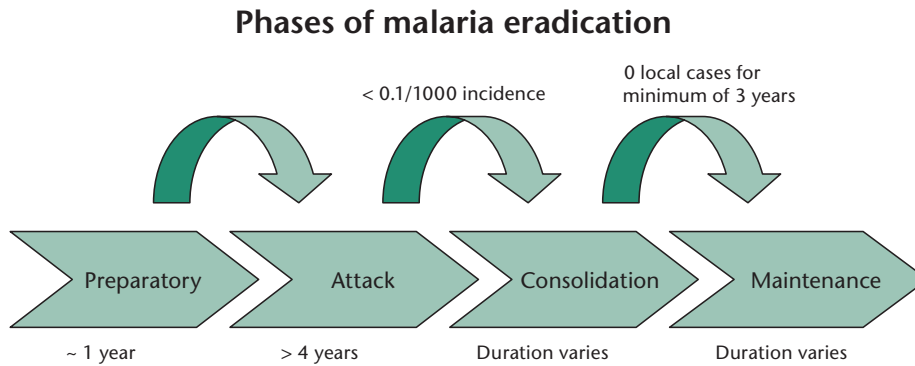
**FIGURE 6.3** | Number of autochthonous malaria cases (in millions) in areas under surveillance outside tropical Africa (solid line) and in Southeast Asia (broken line), 1972-1976 (from Wernsdorfer<sup>10</sup>)

opinion of three separate groups. Those groups were countries not yet able to embark on malaria control or elimination, those that declared the intention of eliminating malaria but failed to implement and sustain efficient programs, and several malaria-free countries that financially supported others in the elimination effort and intended to end these obligations.

## 6.5 | Yesterday's Approach in Malaria Elimination

In countries that successfully eliminated malaria, the disease was predominantly hypo- and mesoendemic, and transmission was of low or intermediate stability. Some countries, including Tunisia and the United Arab Emirates, had hyperendemic areas characterized by intermediate stability.

Before the adoption of WHO's malaria eradication policy in 1955, malaria elimination in the United States relied on vector control to interrupt transmission and reduce the malaria reservoir, organized detection and treatment of residual cases, and complementary focal antivectorial measures that were continued until complete elimination of malaria had been achieved. This model was subsequently adopted by the GMEP. In European countries such as Cyprus, Greece, and Italy, malaria was reduced to low incidence by systematic diagnosis and radical treatment of individual cases before effective



**FIGURE 6.4** | Phases of the Global Malaria Eradication Program (adapted from Pampana<sup>16</sup> and Hay et al.<sup>17</sup>)

vector control became feasible. In Europe, the vector control measures interrupted any residual malaria transmission, and case management through the general health system was responsible for eliminating the remaining malaria reservoir.

The majority of countries that established national malaria elimination programs from 1955 adopted a vertical organizational structure and followed a standard chronological sequence of four phases: preparatory, attack, consolidation, and maintenance (Figure 6.4).<sup>16, 17</sup>

#### PREPARATORY PHASE

The preparatory phase usually lasted a year and did the following:

- established or improved organizational infrastructure
- trained personnel
- established physical facilities for running operations
- carried out geographical reconnaissance and census
- conducted epidemiological and entomological baseline assessment

#### ATTACK PHASE

The attack phase usually lasted 4 or more years and did the following:

- applied attack measures, usually antivectorial intervention
- regularly monitored the impact of the attack measures
- from the second year, established full-scale epidemiological surveillance

- from the second year, conducted active and passive case detection, effective treatment and case follow-up, epidemiological investigation and follow-up of cases and foci, and application of remedial measures

### CONSOLIDATION PHASE

The consolidation phase could start when the surveillance mechanisms, including the general health care system, were functioning smoothly with complete coverage in space and time, and when the malaria incidence had been reduced to a very low level (approximately < 0.1 positive slides per 1,000 population per year). In this phase, antivectorial measures were usually restricted to foci of malaria transmission and particularly receptive areas. The duration of the consolidation phase varied depending on how long it took to reach the qualification for moving into the maintenance phase (below).

### MAINTENANCE PHASE

The maintenance phase could start when no autochthonous transmission had occurred for a minimum of 3 years, provided there was a strong surveillance system. Surveillance continued in the form of vigilance through a strong health system, which maintained a designated operational group to monitor outbreak risk and importation risk and to cope with problematic events such as the reintroduction of malaria.

Although the concept of the GMPEP may appear rigid, it did allow considerable leeway in the selection of appropriate tools to be applied in the attack phase. Generally, this required the deployment of vector control measures, namely IRS and/or any of the many forms of larvicidal measures or source reduction. Decisions regarding the selection of intervention methods needed to be based on sound preoperational epidemiological and entomological stratification, an essential task in the preparatory phase, subject to continuous updating throughout the intervention phase.

Activities outlined in the consolidation and maintenance phases should have a firm place in any program aimed at eliminating malaria. When analyzing the GMPEP, it is important to remember that it is useless to adhere to a national uniform operational plan unless the entire country shows homogeneous epidemiological features—a rare situation, even in tropical Africa. Malaria control usually requires different approaches in urban, peri-urban, and rural environments. Updated recommendations for interrupting transmission and preventing reintroduction of malaria are the subjects of Chapters 2 and 3.

**Table 6.2 | Common denominators from the Global Malaria Eradication Program**

Common denominators from successful elimination programs	Common denominators from failed elimination programs
Political stability and absence of internal and/or external conflicts	Political instability, civil unrest, internal and/or external armed conflicts
Firm political and financial commitment to the elimination of malaria	Lack of or fluctuating political and financial commitment
Minor dependence on external financing	Donor fatigue
Good organizational and technical infrastructure	Poor monitoring of operational activities and the epidemiological situation, failure to update the plan of operations, insufficient understanding of the benefits of eliminating malaria
High quality of training and personnel	Inadequate human resources; poor quality of training, staff, and operations; high staff turnover
Fully developed and functional general health system	Weak general health system
Enlightened public that understood and supported the program	Poor public understanding and support of the program
Absence of major cross-border movement from adjacent malarious countries	Major cross-border movement from adjacent malarious countries
Originally unstable or intermediately stable malaria	Originally stable malaria or malaria of high intermediate stability

## 6.6 | Lessons Learned from Past Elimination Programs

Although many factors that assist and enable elimination programs today have changed and improved on those available during earlier global and national programs, it is important to evaluate the lessons learned from the GMEP (Table 6.2) in order to determine the factors that made the difference between success and failure.

### EXAMPLES FROM COUNTRIES THAT SUCCESSFULLY ELIMINATED MALARIA

*Australia, 1960* Malaria was endemic in the tropical part of Australia, affecting the Northern Territory and Queensland. It was predominantly hypo- and mesoendemic malaria, unstable or with low intermediate stability, with several hyperendemic areas in northern Queensland. Systematic malaria control operations started soon after World War II, with IRS, source reduction, and

water management in the sugar plantations as well as case detection and treatment within the framework of the well-developed general health care system. Malaria was eliminated from continental Australia in the 1960s. In the Torres Strait Islands, an integral part of Australia and subject to the introduction of malaria from nearby Papua New Guinea, it took longer to eliminate malaria and to establish effective mechanisms to prevent reintroduction. Nevertheless, malaria was eliminated there in 1978.

*Taiwan, 1965* Taiwan provides an example of an outstanding success of island elimination. Following a DDT spray program starting in 1952, over 20 residual foci of transmission were eventually eliminated with intensive IRS, and courses of chloroquine/primaquine were used for mass drug administration (MDA) in the entire population in each focus of transmission. In Taiwan, MDA was ancillary to the use of insecticides.<sup>18</sup> Finding and eliminating the residual foci was a massive effort of malaria surveillance involving over 5 million blood slides taken from July 1958 to December 1964, which identified and treated 1,023 malaria infections. Taiwan was certified malaria free in November of 1965. The elimination program spanned over 20 years and involved over 7,000 staff and a full research institute, as well as a large logistical establishment.<sup>18</sup>

*The United Arab Emirates, 2007* Until the mid-1950s, malaria was meso- or hyperendemic in most areas in the country, generally with low-grade intermediate stability and an almost equal incidence of *P. falciparum* and *P. vivax*. In the 1960s, the country embarked on malaria elimination, initially using source reduction and IRS. Case detection and treatment were introduced at an early stage, making full use of the strong general health care system in the public and private sectors. During this program, the United Arab Emirates pioneered the use of local larvivorous fish in the main mosquito breeding sites—*Tilapia* for deep wells, and *Aphanius dispar* for shallow wells, irrigation heads, and natural water courses. Despite the annual importation of 2,000 to 3,000 malaria cases from malarious countries, especially Bangladesh, India, Pakistan, and Sudan, transmission was completely interrupted as of 1997, and the country was certified as malaria free in 2007.

## EXAMPLES FROM COUNTRIES THAT FAILED TO ELIMINATE MALARIA

*Colombia, since the Late 1950s* Malaria was originally mesoendemic with some hyperendemic zones and low-grade intermediate stability. After initial success and near elimination, the program became increasingly affected by civil strife

and illicit activities, thus barring access to large malarious areas. These conditions continue to persist, with little likelihood of change in the near future.

*Sri Lanka, Mid-1960s* Malaria was originally mesoendemic with some hyperendemic areas and an incidence of 2.8 million cases in 1946. Malaria was generally of low-grade intermediate stability. The malaria program had well-trained, highly motivated, and competent staff. The program ran smoothly through the consolidation phase in the mid-1960s. In 1966, the number of autochthonous cases was reduced to 18 when parliament and government decided to disband the entire malaria program and to transfer its activities to the general health services, which were unprepared for this task. Following 3 years of moderately rising incidence of malaria, the country was struck by a major and widespread malaria epidemic, resulting in a half million cases widely distributed throughout the island.<sup>19</sup>

Among the countries that declared a policy of malaria elimination but failed to implement or achieve it, the most important adverse factors have been lack of political will, inadequate and unsustainable financial commitment, infrastructural deficiencies, insufficient availability and appreciation of epidemiological information, and administrative rigidity. In some countries, bureaucratic procedures repeatedly delayed the timely allocation of public funds for malaria elimination, delaying the performance of seasonal IRS beyond the limits of usefulness. Similarly, the allocation of external financial assistance was often delayed, resulting in the late arrival of essential commodities, such as insecticides for IRS. Also, as is occurring today, some countries declared the goal of malaria elimination apparently without true evaluation of their readiness or any serious intention of implementing such a program.

## 6.7 | Recommendations: Eliminating Malaria Today and Tomorrow

As 39 countries pursue malaria elimination, with strong indications that many, if not all, will achieve their goal, it is appropriate to take note of a passage from the Second General Report of the Malaria Commission of the League of Nations, a statement that is as valid today as it was when it was issued in 1927: “The Commission has always insisted that the fight against malaria must be waged not as a separate and isolated task but as part of a general social, economic and sanitary campaign by an enlightened public health service which is

able to obtain assistance from other Government departments and from unofficial agencies, and to secure continuity of action and unity of purpose.”<sup>20</sup>

Observing which countries having achieved and maintained their elimination of malaria supports the Commission’s statement. Equally, it was inadvertent or intentional disregard of the Commission’s views that was responsible for failure in the countries with national malaria elimination programs that did not reach the elimination goal.

Whenever a country considers eliminating malaria, it should carefully examine the lessons learned from past successes and failures, and it should take preemptive remedial action to eliminate any weaknesses. For instance, it is futile to attempt malaria elimination if the country has an active military conflict on a substantial part of its territory or lacks stable political or financial commitment.

Retrospectively, innovative research suffered during the malaria eradication program. Moreover, the unresolved issue of malaria in tropical Africa was overlooked. The pharmaceutical industry was unwilling to invest in developing drugs principally to address the problems of largely insolvent economies. Continued research and development of innovative tools must always be a priority to sustain a program through the inevitable challenges inherent in any process as complex as malaria elimination.

Nevertheless, the comparison of the geographical distribution of malaria in the years 1900, 1946, 1965, and 2007 (Figure 6.2) indicates remarkable success in the fight against malaria, even if the stated goal of malaria eradication was not achieved. Moreover, many countries have a considerable potential for eliminating malaria in the near future.

## 6.8 | Conclusion

With over 3 billion people still at risk for malaria, much needs to be done to control and eliminate malaria from the areas still affected by the disease, and we are still facing the most difficult part of the campaign. As today’s spatially progressive elimination program continues to shrink the global malaria map, we must remember the many important lessons learned from the GMPE and past attempts to eliminate malaria, yet look forward with new hope and commitment to reach a malaria-free world.

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