THE ROLE OF A DIAGNOSTIC REFERENCE LABORATORY IN MALARIA SURVEILLANCE

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Abstract

Australia was declared free of malaria by the World Health Organization in 1981, but the infection has been endemic here in the past. Some tropical regions of the country are still considered to be receptive to its reintroduction. Although the risk of reintroduction is small, it cannot be dismissed. About 700-800 imported cases of malaria are notified in Australia each year. Most of these are imported from neighbouring countries such as Papua New Guinea and the Solomon Islands. A person who had arrived from the Solomon Islands was believed to be the source of a small outbreak of *Plasmodium vivax* at Cape Tribulation in north Queensland in 1986. There were at least four introduced cases and, almost certainly, one indigenous infection. The clustering of cases was detected because of the existence of a national surveillance system based on notified laboratory diagnoses. Without such a system, the relationship between a number of infections diagnosed in different parts of the country would almost certainly have gone unrecognised. Apart from supporting a surveillance system, reference laboratories can also provide a system of quality assurance for routine laboratories, many of which have difficulty in diagnosing infrequently seen infections such as malaria.

Background

With the inclusion of New South Wales in 1969, malaria became notifiable in all States and Territories of Australia. At the time, a national register of cases was established and maintained by the late Professor R. H. Black at the School of Public Health and Tropical Medicine (SPHTM), University of Sydney. An important function of the register was the checking of all malaria diagnoses by the medical parasitology department of the SPHTM. Because of the impossibility of unequivocally diagnosing malaria clinically, no case could be included in the register unless it was based on a verified blood film identification. This checking also ensured that the data on malaria species in the annual reports of the register were accurate. As will be discussed later, Australian laboratories can make significant errors in malaria diagnosis (Walker, unpublished data on New South Wales register of malaria cases).

An important function of the register, which is now maintained at the Tropical Health Program, University of Queensland, is to provide the World Health Organization (WHO) with data on the number of cases of malaria occurring in Australia. As a result of an assessment based mainly on these data, WHO declared Australia to be free of endemic malaria in 1981[1]. This status has important connotations for tourism and development projects in the north, and its maintenance is in the national interest. In the past, epidemics of malaria, some with significant case mortality, were associated with mining projects in the Northern Territory and Kimberley region[2].

Malaria cases at Cape Tribulation, 1986

At least four cases of introduced malaria and one possible case of indigenous malaria were reported from Cape Tribulation in north Queensland in 1986. The cluster was detected because of the existence of a national register of cases.

The original case in this outbreak (probably case 5) would be classified as *imported*, as the infection was acquired outside Australia. The cases involving individuals infected by mosquitoes which had fed on the original case (cases 1,2,3 and 6) would be classed as *introduced*. Any cases derived by mosquito transmission from one of the introduced cases would be defined as *indigenous*.

The cases are discussed in chronological order with reference to the dates of the blood film diagnosis.

Cases 1, 2 and 3

Plasmodium vivax infections in three patients who had not travelled outside Australia were diagnosed at Cairns and Mossman in north Queensland between 6 and 9 November 1986. These patients had been living at Cape Tribulation for several months before becoming ill. Because of delays in the case details reaching the central register in Sydney, it was not immediately clear that they were related. At the time, the checking of blood films from Queensland cases was not being performed at the SPHTM.

Case 4

This 21 year old male had become ill on 17 October 1986 at Cape Tribulation in north Queensland, where he had been living for at least several months, and possibly for a number of years. No blood films were made at the time, but following travel to Sydney, a diagnosis of *Plasmodium vivax* infection was made by a private pathology laboratory on 14 November 1986. The blood films were examined at the SPHTM on the same day and the diagnosis was confirmed. As there was no

history of recent travel out of Australia, authorities in Queensland were immediately notified of a possible case of local transmission of malaria at Daintree River, near Cape Tribulation.

Case 5

This man, who arrived in Brisbane from the Solomon Islands on 1 September 1986, is thought to have been the primary source of the outbreak. He had been taking Fansidar prophylaxis when in the Solomon Islands. He visited Cape Tribulation for one week from 3 October. On the 10th he left the area and was treated in Cairns with quinine for a febrile illness, clinically diagnosed as malaria. *P. vivax* was subsequently diagnosed by blood film at Katherine in the Northern Territory on 17 November 1986.

There is uncertainty about case 4 mentioned above. His febrile illness began on 17 October 1986. If this was due to the malaria infection that was diagnosed in Sydney on 14 November, it was too early to have resulted from mosquito-borne infection originating from case 5. It is possible that the initial illness was not malaria, or that it was a relapse from an infection acquired outside Australia months or years before. If the latter possibility is correct, this individual could have been the source of the subsequent infections.

Case 6

The most significant case in this series was that of a 22 year old woman whose *P. vivax* infection was diagnosed at Gosford, New South Wales on 8 December 1986[3,4]. This patient had spent one night at Cape Tribulation on 21 October 1986 and had become ill at Cairns on 3 November. She had never been out of Australia. When the blood films were reviewed at the SPHTM, Queensland authorities were immediately notified of a definite case of introduced malaria originating in the Daintree River area. An epidemiological investigation of the region identified the most probable site of transmission. Larvae of *Anopheles farauti* were found nearby[3].

A possible indigenous case

Case 7

A further infection, which occurred after the investigation was concluded, has not been included in past discussions of this outbreak (Walker,.unpublished data, School of Public Health and Tropical Medicine, University of Sydney). This woman, who had never been out of Australia, became ill at Burnie in Tasmania on 31 December 1986 and *P. vivax* infection was diagnosed on 2 January 1987. She had arrived at Cape Tribulation in late November 1986, after the other individuals had left the area. Either she was infected by a mosquito which had survived from the first week of October to late November, or she was bitten by a mosquito which had fed on one of the other individuals before they left.

On the basis of the time of the onset of symptoms in cases 1,2,3 and 6, it is presumed that mosquitoes were infected on or about 7 October, most probably by feeding on case 5, and that these mosquitoes transmitted the infection to the other individuals on or around 18 October. One person (case 3) became ill at Cape Tribulation on 3 November and his infection was confirmed by blood film at Mossman on the 9th. If there were gametocytes in his blood, he could have been a source of infection for mosquitoes during the first week of November. Around 75% of all cases of *P. vivax* infection diagnosed in Australia have gametocytes in the peripheral blood at the time of diagnosis (Walker, unpublished data on New South Wales register of malaria cases).

It is possible, given the climate at Cape Tribulation, that a mosquito had survived from early October to late November and transmitted the infection to case 7. This is less likely, however, than a second round of transmission involving mosquitoes which had fed on one of the other infected individuals. In studies on the survival of Australian anophelines at Darwin, Russell found that only between 3% and 4.3% of *Anopheles farauti* survived long enough for sporozoite development[5]. Survival of mosquitoes in the rainforest at Cape Tribulation would probably be longer than at Darwin, but even a relatively low daily mortality rate of ten per cent would leave only 0.45% of mosquitoes alive after 50 days, the period involved in this instance.

If this infection was the result of a second round of transmission, it becomes the most recent indigenous case of malaria diagnosed on the Australian mainland. This was previously thought to have occurred at the Roper River Mission in the Northern Territory in 1962[2].

Advantages of a centralised surveillance system

Had it not been for the verification of malaria diagnoses by a single laboratory, the connection between the infections originating at Cape Tribulation would not have been made until the details of the individual cases were collated at the central register. This was often a lengthy process because of the slow return of case information sheets.

In situations where surveillance of an infection is important, and in which the diagnosis of that infection is laboratory based, it is logical to structure the system around a single laboratory or a network of laboratories. A major reason for this is the significant error rate in malaria diagnosis when performed by routine pathology laboratories in Australia (Walker, unpublished data on New South Wales register of malaria cases).

Quality assurance of malaria diagnosis

The error rate in the diagnosis of malaria species by Australian laboratories has been analysed from data collected by the New South Wales malaria register from 1989 until March 1996 (Walker, unpublished data on New South Wales register of malaria cases). Only cases having a definite suggestion of the species identity by the original diagnostic laboratory are included. Infec-

tions initially detected by the State reference laboratory are excluded. Of 1,386 cases which fit these criteria, there were 211 incorrect diagnoses, an error rate of 15%. For diagnoses of *P. vivax*, the rate of incorrect diagnosis was 10%.

For *P. falciparum* infections however, the error rate is much higher. Of 315 cases, 68 were incorrectly diagnosed, an error rate of 21.6%. The most common single error involves the identification of *P. falciparum* as *P. vivax*. This occurred 44 times. There is a highly significant difference (p=0.004) between the error rate for private pathology laboratories (32.5%) and non-private laboratories (17.8%) in the diagnosis of *P. falciparum* infections. The lower error rate for non-private laboratories is influenced by the performance of several large hospitals which diagnose numerous malaria cases. The staff of these hospitals, therefore, have more experience than most in recognition of these parasites. There is no difference between private and public laboratories in the identification of other species. Such a high error rate for *P. falciparum* is unacceptable and needs to be addressed. In five instances involving this species, the infection was missed altogether, although subsequent checking of the films by the reference laboratory revealed parasites.

On this basis alone, it is clear that relying on unconfirmed diagnoses of malaria species would provide extremely inaccurate epidemiological data, with an underestimate of the amount of *P. falciparum* and an overestimate of the amount of *P. vivax*. Even greater rates of error occur when mixed infections and other species are involved.

Climatic factors limit the region of Australia which is considered to be receptive to the reintroduction of malaria in the far north. Bryan, Foley and Sutherst discuss the possible influence of future climate change in extending the range of *Anopheles farauti* down the Queensland coast as far south as Gladstone[6]. This extension of range would include popular tourist destinations such as the Whitsunday Passage. Although the establishment of malaria on the coast of Queensland is unlikely, the experience from Cape Tribulation demonstrates that it could occur and that surveillance is necessary to prevent the reintroduction of an infection which was endemic in Cairns as recently as 1943[2].

References

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