Conclusions

Because of the high rate of cross reactivity in flavivirus serology, a positive screening test should be interpreted with caution. Specific tests for other flavivirus infections such as Kokobera are not routinely requested. If the patient had had a travel history consistent with vector contact in Queensland, he would have been notified as a case of dengue. However, if he had not travelled to Queensland dengue serology would not have been requested in the first place. This case is a reminder to consider a wide range of diagnostic possibilities when determining the cause of an arboviral infection.

This case also reinforces the importance of ensuring that all factors; laboratory tests, clinical symptoms and epidemiologic data, are consistent before making a diagnosis that has considerable public health implications. This case of 'dengue' was suspect because the clinical illness was inconsistent and there was no entomological evidence that the vectors were present in Darwin. The assumption that this was not dengue was borne out by reference laboratory testing. In the Northern Territory it justified the approach of waiting for the results before vector surveys and control strategies, including human health service alerts, were implemented.

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Three cases of dengue 1 virus infection from islands in the Gulf of Thailand

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Abstract

Three Australian tourists who recently travelled to islands in the Gulf of Thailand developed febrile illnesses associated with myalgias, thrombocytopenia, and atypical lymphocytosis. Dengue 1 virus was isolated from all three patients. The patients' clinical features and serological and virological investigations are presented. These cases highlight the need for awareness of dengue amongst travellers and the preventive precautions required when visiting endemic regions. After the urgent exclusion of malaria, dengue should be considered in the the differential diagnosis of febrile persons who have recently returned from endemic regions. *Comm Dis Intell* 1998;22:107-109

Introduction

Dengue fever is endemic throughout southeast Asia. Over the past three years, increased dengue activity has been reported from Malaysia, where over 19,500 cases of predominantly dengue 1 and 2 were notified during 1997,[1] Indonesia,[2] Cambodia,[3] India[4] and the western Pacific.[3,5,6,7] Although the north and central areas of Queensland, which correspond to the distribution of *Aedes aegypti*,[8] are potentially receptive to the establishment of endemic dengue, the virus is not endemic in Queensland. Epidemics are assumed to have arisen from viraemic travellers.[9] Recent outbreaks in Queensland have included an outbreak of dengue 2 in Cairns, commencing in December 1996, and resulting in 201 confirmed cases,[10] and an outbreak of dengue 3, which commenced in December 1997 and has resulted in 165 confirmed cases up to 25 May 1998 (J. Hanna and S. Ritchie, personal communication). Sequencing data of the dengue 3 isolates has shown that the most likely source of the virus was Thailand (D. Phillips, unpublished data)

This report presents three cases of dengue 1 in Australian tourists who recently travelled to islands in the Gulf of Thailand, and discusses the implications of these cases for travellers to endemic areas and for dengue control in Australia.

Case 1

A 57 year old male developed a febrile illness associated with myalgias on 17 October 1997, three days after returning from Ko Chang. He had spent one week on the

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island and sustained numerous mosquito-bites. Over the preceding 6 months he had travelled through southern Spain and northern India without medical problems, apart from self-limited diarrhoea in India. Upon presentation to hospital on the 20 October 1997, investigations revealed mild leucopenia (total white cell count 2.3 $\times 10^9$/L, neutrophil count 1.47 $\times 10^9$/L). Four days later significant thrombocytopenia (platelet count 56 $\times 10^9$/L) and mild atypical lymphocytosis (5% of 2.7 $\times 10^9$/L) developed.

Arboviral serology was performed on serum collected on 21 October and 24 October. Flavivirus IgG was reactive by enzyme immunoassay (EIA) on both specimens. Dengue IgM by EIA was initially nonreactive, but reactive on the second specimen. Cross reactive IgM antibody to the four dengue serotypes was detected following ultra-centrifugation separation and haemagglutination inhibition assay (UC/HI) of the second specimen. Dengue 1 virus was isolated from both specimens.

Case 2

A 39 year old male developed a febrile illness associated with myalgias, bone pain, and vague generalised abdominal pain on the 17 October 1997, five days after arriving on Ko Pha-ngan. He sustained numerous mosquito-bites whilst on the island. For the preceding three weeks he had trekked in the Himalayan area of Nepal without medical problems. He presented to hospital in Australia four days after the onset of symptoms. He developed marked leucopenia (total white cell count 1.4 $\times 10^9$/L, neutrophil count 0.58 $\times 10^9$/L) and thrombocytopenia (platelet count 51$\times 10^9$/L). Seven days after the onset of symptoms, his fevers and symptoms subsided, with the subsequent development of atypical lymphocytosis (10% of 2.1 $\times 10^9$/L). Resolution of cytopenias occurred by day 12.

Flavivirus IgG and dengue IgM was detected from serum collected on 23 October. Specific IgM antibodies to dengue 1, but not types 2, 3, or 4, were detected by UC/HI. Dengue 1 virus was isolated from this serum.

Case 3

A 31 year old female, the partner of Case 2 who also visited Ko Pha-ngan, developed a similar febrile illness on the 22 October 1997, approximately five days after that of her partner. She noted a transient erythematous rash over the trunk. Although her fevers and other symptoms settled within five days, she presented to hospital on day 7 of the illness with a faint petechial rash over her ankles and feet. Investigations revealed mild thrombocytopenia (platelet count 81 $\times 10^9$/L), and atypical lymphocytosis (10% of 4.4 $\times 10^9$/L).

Flavivirus IgG was nonreactive and dengue IgM was reactive by EIA. Cross reactive IgM antibodies to all four dengue serotypes were detected by UC/HI. Dengue 1 virus was isolated from this serum.

Discussion

These three recent cases of dengue highlight several important points.

In 1996, 43 cases of dengue were reported in Australia,[11] including both imported and locally acquired dengue, while in 1997 approximately 171 cases were reported.[12] However, given that the south-east Asian region, including the Gulf of Thailand islands where the three patients visited, are both popular destinations for western tourists and areas of dengue endemicity, it is surprising that dengue is not more frequently diagnosed in travellers returning to Australia.

Those visiting endemic regions should routinely be given pre-travel advice regarding dengue. This is particularly important for those travelling to south-east Asia during the late wet season, September to November, which is the peak time for dengue transmission. Emphasis should be given to the importance of avoiding both day-time active mosquitoes that transmit dengue, as well as night-time active mosquitoes that transmit malaria.

Medical officers to whom returned travellers present should be aware of dengue. In addition to malaria, typhoid, HIV, and rickettsial infections, dengue and other arboviral infections should be considered in febrile returned travellers. The incubation period of dengue fever ranges from 3-14 days, usually 5-7 days, and is typically followed by an abrupt onset of fevers, malaise, retrorbital headaches, myalgias, and bone and joint pains. Other specific symptoms include: a bitter, often metallic, taste; itchy skin or sensation of pins and needles in the skin; and vomiting and diarrhoea. The diagnosis may be suggested clinically, although at a minimum, blood films should routinely be performed to exclude malaria. A variety of haematological abnormalities may be encountered, including leucopenia, thrombocytopenia, and atypical lymphocytosis.[13]

Although serology is commonly used to confirm dengue infection, cross-reactive antibodies may prevent identification of the infecting serotype, as occurred in Cases 1 and 3. The definitive diagnosis of dengue infection requires either isolation of virus, or detection of viral RNA by polymerase chain reaction (PCR) in acute-phase serum specimens. These services are provided by reference laboratories.

The period of viraemia extends from shortly before until the end of the febrile stage of the illness,[14] and cases in potentially receptive areas of Australia should avoid being bitten by day-time active mosquitoes, in order to prevent outbreaks of dengue.

The pathogenesis of dengue haemorrhagic fever relates to sequential infection with heterologous dengue serotypes occurring months to years apart,[15] and patients, particularly children, diagnosed with dengue should be counselled regarding the potential risk of dengue haemorrhagic fever if revisiting areas of dengue endemicity.

Although it is considered unlikely that dengue will become endemic in Australia,[16] large outbreaks can result from imported cases in the dengue receptive areas. Doctors should be alert to the possibility of dengue in travellers from dengue endemic areas in order to diagnose cases early. Prompt notification of suspected cases occurring in the dengue receptive areas is vital to allow rapid public health action to limit the spread of the virus.

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Dengue 3 in Cairns: the story so far

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In early December last year, the Tropical Public Health Unit (TPHU) was notified of an adult resident of the Atherton Tablelands who had a positive screening-test for dengue. The patient had a non-specific illness that might have been dengue but he had not recently travelled overseas. Because the screening-test gives a number of false-positive results, it is TPHU policy to delay an investigation in these circumstances while a more reliable test is undertaken in Brisbane.

Before this result became available however, the patient subsequently informed the TPHU that he had had substantial contact with a travellers' guesthouse on The Esplanade, Cairns North, and several other people at the guesthouse had developed a similar febrile illness. Blood samples were quickly collected from as many of these other individuals as possible and sent to Brisbane for urgent testing; several of these samples tested positive for dengue 3. Because some of these positive people were staff at the guesthouse and had not recently travelled overseas, it was obvious that they had acquired dengue at the guesthouse. Therefore the outbreak was first confirmed on December 12, eight days after the original notification and 16 days after the onset of his symptoms.

Mosquito investigations were commenced immediately. Numerous adult *Aedes aegypti* were found on the premises including several blood-fed females in the rooms of ill people. The interior of the hostel was sprayed with a commercial pyrethroid aerosol spray. Several pot-plant containers containing *Ae. aegypti* larvae were also found and emptied. Properties within several hundred metres of the guesthouse were also surveyed, containers emptied and (with permission) interiors sprayed.

Although we were not able to identify the traveller who imported the dengue 3 virus from overseas into Cairns, the virus has a very similar nucleotide sequence to a dengue 3 virus isolated from a traveller who returned to Australia from Thailand in 1993. This suggests that the current virus was imported from southeast Asia.

A travellers' guesthouse obviously caters to lots of travellers, and we are aware of eight overseas travellers (two of whom contacted TPHU from Spain and Canada via the Internet!) and two interstate visitors who contracted the virus whilst staying in the guesthouse. Because travellers travel, several turned up in other locations in 'dengue-receptive' North Queensland whilst still infectious to *Ae. aegypti* mosquitoes: Innisfail, Mission Beach, Townsville, Magnetic Island and Proserpine. Fortunately no local transmission occurred in these locations, but the inevitable soon happened: spread to other suburbs in Cairns.

In early February TPHU recognised that local transmission of dengue 3 was occurring in Parramatta Park. This is an older, more central suburb with many old Queenslander cottages on small properties. Most of these residences are not screened, and many properties were found to be effectively breeding large numbers of *Ae. aegypti* mosquitoes in rubbish and garden containers in the backyards. The Parramatta Park outbreak was explosive with 60 confirmed cases occurring in February; a considerable number of these cases were either working from home or unemployed and therefore spending long hours at home exposed to infectious mosquitoes.

Not many travellers stay in Parramatta Park and therefore it was unlikely that the virus would be taken to other travellers' destinations in North Queensland. However residents of Parramatta Park work, visit and convalesce from dengue in other suburbs of Cairns. Therefore further spread within Cairns was inevitable: Westcourt, Earlville had small numbers of cases in late February. There have been more recent, and also small, foci in Stratford and Holloways Beach; it seems that spread has occurred from the latter suburb to a resort Barrier Reef island and to Machans Beach. Fortunately the virus has not spread to the Torres Strait, where a large outbreak of dengue type 2 occurred a year ago.

The outbreak of dengue 3 in Cairns is now in its sixth month. To 25 May 1998, 165 cases have been confirmed. Of these, 31 (19%) have been hospitalised; although some of these only required an overnight stay for IV fluids, two required ICU care. There has been one case of dengue haemorrhagic fever (in an elderly male who fortunately