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SHORT REPORT
Measles transmission in immunized and partially immunized air travellers

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SUMMARY

Most cases of measles in Australia are associated with travel or acquired from travellers from overseas. This study presents a series of three secondary cases of measles acquired through contact with a case of infectious measles acquired in China. Two of the cases were fully immunized siblings sitting eight rows behind the index case on a $4\frac{1}{2}$-h flight from Singapore. The third case was acquired in the airport where the index case was in transit. The report highlights the travel-associated risk of measles and discusses the heredity of vaccine-induced measles immunity.

Key words: Disease susceptibility, disease transmission, measles, transportation, vaccination.

In Australia, a high proportion of measles cases are either imported or linked to an imported case, as for other countries which have achieved measles elimination [1]. This association with travel together with the high infectivity of measles, highlights the risk of transmission during travel, both in-flight and in transit at the airport, and complicates the public health response to imported cases. As more countries approach elimination, it is likely that a larger proportion of the public health response will be directed towards travel-associated infections. In particular, given that contacts of an infectious traveller may be ill-defined, numerous and difficult to trace, a risk-based approach to contact tracing taking into account local resources may be required. Current national guidelines in Australia recommend contact tracing of just those passengers seated in the row of the case and two rows in front and behind [2]. Despite measles' high infectivity, there are few documented cases of transmission under these circumstances [3–7] and other reports have suggested that the risk of in-flight transmission of measles is low [8].

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The efficacy of the measles vaccine following two doses is estimated to be 99% [9]. Nevertheless, cases in fully vaccinated individuals have been reported, occurring both sporadically [10] and during outbreaks in highly vaccinated populations [11, 12]. We report a cluster of three measles cases resulting from air travel exposure to an overseas-acquired case; two of these cases were in fully vaccinated siblings.

The index case was a 16-year-old female student who developed a fever and cough on the day she left Cheng Du in south-west China for Melbourne, Australia in January 2008. She transited through the airports of Guangzhou, Singapore and Darwin (Nothern Territory, Australia) before arriving in Melbourne the following morning. The Singapore–Darwin flight was of $4\frac{1}{2}$ h duration and arrived at Darwin Airport at 00:20 hours local time. The case collected her luggage, checked in for the domestic flight to Melbourne and then waited in the domestic lounge until boarding at 02:20 hours.

The following day, she developed a rash and testing revealed a positive measles-specific IgM, fulfilling the national case definition for measles [13]. Following the national guidelines [2], passengers on the Singapore–Darwin and Darwin–Melbourne flights who sat in the same row or in the two rows ahead and behind the case were followed up. Forty-two contacts from the flights were traced and no further cases identified. The majority of contacts were found to be immune either due to their age ($n=18$) or documented vaccination ($n=13$) (K. Simpson, personal communication). Eight required further action, receiving either normal human immunoglobulin or a second dose of measles-containing vaccine and the remainder ($n=3$) were not contactable. Passengers seated elsewhere were not contacted and no media statement was made. Interestingly, several of the contacts remembered a passenger fulfilling the description of the case and commented on the extent to which she was coughing.

Cases 2 and 3 were siblings, a 13-year-old boy and an 11-year-old girl, who were Australian residents, returning from Singapore to Darwin on the same flight as the case, seated together eight rows behind the index case.

Ten days after arrival, the boy developed fever, a mild cough and conjunctivitis followed 4 days later by a mild papular rash, predominantly on the face and trunk. Serology detected both measles-specific IgM and IgG and a throat swab and urine sample were positive for measles RNA by PCR. Further studies revealed that the strain was H1.

His sister became ill 12 days after arrival with a similar but milder illness, including a mild papular rash starting 2 days later, the same day as her brother's onset of rash. Her measles-specific serum IgM was equivocal, IgG positive and a throat swab PCR for measles RNA was negative. She fulfilled the national case definition for measles on epidemiological grounds.

Both children were fully immunized according to their immunization records and the Australian Childhood Immunisation Register. The boy received a measles-mumps-rubella (MMR) combination vaccine at ages 12 months and 5 years, his sister was vaccinated with the same vaccine at ages 12 months and 4 years. Neither child had any significant past personal and family medical history, and were completely well prior to this illness. Their parents who were sitting in the same row, were not considered susceptible to infection (born before 1966) and neither became unwell after the flight. Their mother recalled hearing a passenger, sitting towards the front of the aeroplane, coughing loudly and persistently throughout the flight. Of the 87 contacts of these cases, 69% had had two validated doses of measles-containing vaccine while a further 20% had had one dose. All but two of the remainder were considered immune by virtue of their date of birth. Those who could not validate their status or were unvaccinated were excluded from school and subsequently vaccinated.

Case 4 was a 17-year-old male who was travelling from Darwin to Brisbane on the morning the index case was in transit at Darwin Airport. He boarded his flight at Darwin Airport at 01:00 hours after waiting in the same departure lounge as the index case, who was about to board the flight to Melbourne. He returned 3 days later and developed fever, cough and conjunctivitis 7 days after his initial visit to the airport. Four days after the onset of fever he developed a confluent maculopapular rash that commenced on the face and inner arms. He had measles virus RNA detected by PCR in urine and a positive measles-specific IgM serology, with a negative IgG. Further studies revealed that the strain was also H1. His mother thought she recalled one measles vaccination as a child but there was no record to confirm this. He was not infectious during his return trip from Brisbane. The timing of all the cases is illustrated in Figure 1.

A measles outbreak of eight cases in and around Cairns in far North Queensland a few weeks after this cluster and caused by the same genotype raised the possibility of an additional airport-acquired measles case [14]. The outbreak investigators proposed a possible 'missing link', an unidentified case who acquired the disease in Darwin Airport or on the Singapore–Darwin flight on the morning in question before travelling to Cairns 3 h after the index case's Darwin–Melbourne flight. The H1 genotype has been associated with outbreaks and importations from China in the past [15].

This cluster of measles cases demonstrates transmission in unusual settings; first, on an aeroplane in passengers seated some distance from the index case, and second, in a passenger on a different flight but in the same airport as the index case. In addition, the acquisition of measles in fully immunized siblings raises the question of a genetic basis of vaccine failure.

Acquisition of measles on aeroplanes and in airports has been previously reported. In 1982 six secondary cases of measles were found to be acquired through travel exposure in the USA [3]. One case had

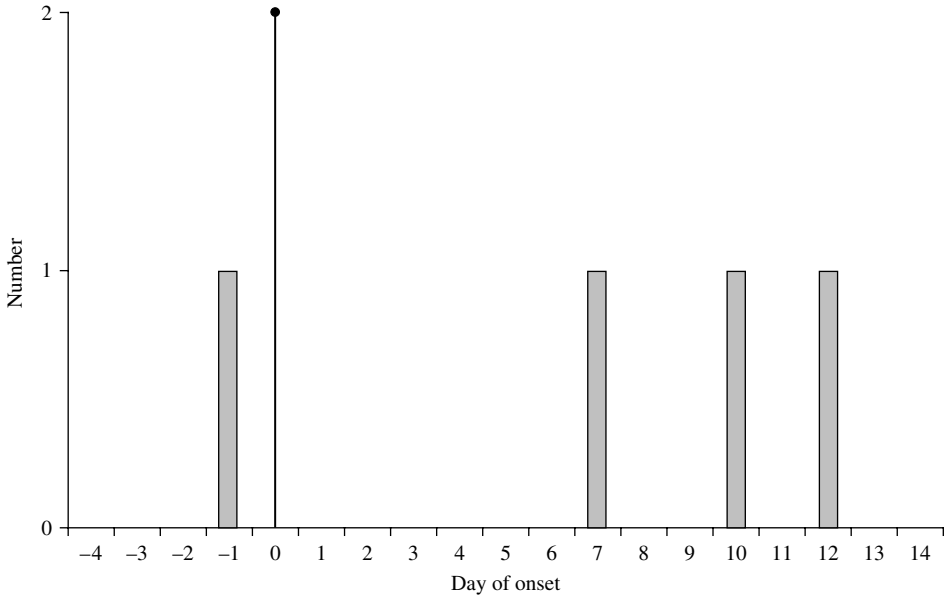

Fig. 1. Cases (▢) of confirmed measles by onset date relative to the Singapore–Melbourne flight. The vertical black line indicates the flight day.

flown on the same flight as the index case, while the remaining cases had left from the same departure lounge. A second report from 1982 identified two possible secondary cases resulting from in-flight exposure during a $3\frac{1}{2}$-h flight [4]. In 1994 the possibility of in-flight transmission leading to eight cases was raised; however, the source or index case was never identified [5]. More recently, two further reports have described measles transmission resulting from travel to or within countries of high incidence. In 2004 a fully immunized passenger who had sat next to a case on a small aeroplane for 2 h developed measles [6], while in Brazil in 2005, two secondary cases arose in unvaccinated individuals seated three and eight rows away from the index case on a domestic flight [7].

Our case series implies transmission across eight rows, a similar distance to that described in the Brazilian case, although it was possible that transmission occurred at other times such as in the airport, boarding or movement during the flight. These cases might suggest that contact tracing of air-flight passengers should be expanded to include more than just those seated two rows either side of the case or tailored to the estimated infectivity of the case. For example, the number rows of contacts traced could be reduced if the case was asymptomatic at the time of travel exposure and expanded if the case had paroxysmal coughing, as was evident in this case. However, the degree of infectivity of the index case in our setting, evidenced by the degree to which she was coughing, may have been at the extreme end of the spectrum and therefore not be considered typical. Ultimately, decisions about the definition of contacts are risk-based and need to be balanced against available public health resources.

Factors which may be associated with vaccine failure include increasing age [10, 12], age at vaccination, number of vaccinations received and the immunogenicity of the vaccine strain [16]. In cases 2 and 3, the presence of measles-specific IgG and their clinically milder illness consistent with vaccine-modified measles, suggests secondary vaccine failure [12, 17]. Given that the vaccinations received by the siblings were over a period of several years it is unlikely that the failure was due to a faulty batch or cold chain problems.

The contribution of genetics to vaccine failure has been investigated, with twin studies suggesting that heritability, i.e. the percentage of variance in measles vaccine-induced antibody levels attributable to genetics, was 88·9% (lower 95% confidence interval of 52·5%) [18]. The authors concluded that genetic influences play a substantial role in the variation of antibody levels following immunization against measles. Both primary and secondary vaccine failure can lead to transmission of measles in highly vaccinated populations and this example emphasizes the need for vaccination coverage targets to allow for these unavoidable failures and so protect, through herd immunity, those who have been vaccinated but

are genetically unable to mount an adequate immune response.

There was no further transmission of measles identified in the Northern Territory from these three cases. Local vaccination coverage rates for the 12-month MMR vaccine (measured at 24 months, first quarter 2008) and the booster at 4 years (measured at 60 months) were 96·4% and 94·3%, respectively [19]. A high proportion of contacts of cases 2 and 3 had been immunized and it is likely that, given the mild nature of their illness due to their partial immunity, they were concomitantly less infectious.

Even in populations with high vaccination coverage, measles continues to impress us with its infectivity. Moreover, the existence of unforeseeable vaccine failures, in particular those which may have a genetic basis, emphasizes the importance of herd immunity in preventing transmission of this highly infectious disease.

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DECLARATION OF INTEREST

None.

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