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Two measles clusters in connection with short inner-European air travels indicating impediments to effective measles control: A cluster analysis

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ABSTRACT

Importation and transmission of measles via air travel is a public health concern to countries, which are close to or have achieved elimination, i.e., to the majority of countries in Europe. In 2018, two measles cases occurred in Berlin residents, who flew within Europe while being infectious. In addition to contact tracing through passenger manifests, we contacted national authorities in flight destination countries or embarking countries and inquired about epidemiologically linked measles cases to the two Berlin index cases. We identified eight epidemiologically linked cases (six males, median age: 32 years) from three countries associated with three air-travels. Consequently measles was imported to Germany (Bavaria), Denmark and possibly Sweden. Our investigations revealed impediments to an effective public health response indicating the need to revisit current guidelines and methods to better control transmission of measles related to air travel.

1. Introduction

Measles is a highly transmissible, vaccine-preventable viral disease spread through direct contact or air [1]. The disease typically begins with a prodromal phase of fever and cough, coryza or conjunctivitis, in any combination. A generalized maculopapular rash develops 3–7 days later. The infectiousness usually extends from four days prior to rash onset to four days after rash appearance. While measles cases have been gradually declining since 1980 [2], all regions of the world have reported increasing numbers in 2018 a trend which is also continuing in 2019 [3]. Importation of measles from endemic regions to countries that are close to or have achieved elimination are thus becoming more likely and are contributing to the recurrent spread [4] Transmission can occur during air travel [5]. Cases travelling while being infectious are of special concern as they usually have many contacts, possibly from different regions or countries. Postexposure prophylaxis (PEP) with measles containing vaccine (MCV) within 72 h or human immunoglobulin within 6 days may prevent or alleviate clinical disease. Depending on the progress of measles elimination, different regions or countries have published guidelines for the handling of contact tracing in the case of exposure to measles during air travel. For the European Union the European Center for Disease Control and Prevention has published guidelines on risk assessment for diseases on aircraft, "RAGIDA" [6], that have been principally endorsed in Germany. Briefly, if the flight of a probable or laboratory-confirmed measles patient during the infectious period was within the previous 5 days, offering PEP to all susceptible flight passengers and staff should be considered. That is, vaccination with MCV of all susceptible and eligible passengers > 6 months of age if the flight was within two days, and giving human normal immunoglobulin for vulnerable persons, i.e. immunocompromised persons, pregnant women and infants below the age of six months, otherwise. Of note, these time cut-offs were explicitly chosen to allow one day for organizing the intervention. Afterwards, as long as the incubation period for potential secondary cases has not elapsed and measles elimination is achieved or within reach in the country of arrival, contact tracing may still be warranted to identify

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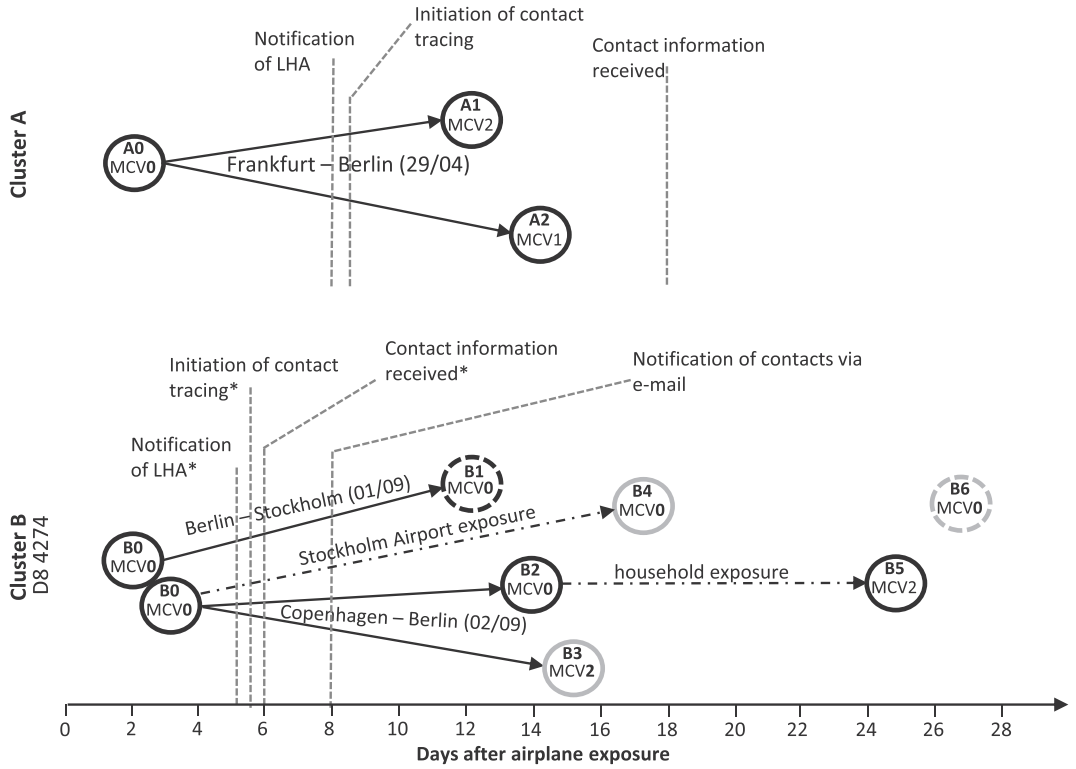

Fig. 1. Two measles clusters related to inner-European air travel in 2018, detected in Berlin.
Circles indicate the day of rash onset for each case. Black cases are from Germany (solid line Berlin, dashed line Bavaria), grey solid from Denmark, grey dashed from Sweden. Vaccination status is indicated within the circles. MCV0 = unvaccinated, MCV1: vaccinated once with a measles containing vaccine, MCV2: vaccinated twice with a measles containing vaccine; LHA: local health authority.
*Dates of measures taken by LHA for contact tracing are related to the first flight of B0 on 01 September.

secondary cases (early) and limit further spread.

2. Cluster investigation

In Germany, laboratory detection of measles virus and clinical suspicion or diagnosis of measles is notifiable to the local health authority (LHA), which is the competent authority for case investigation and management, including contact tracing. We first describe two measles clusters where transmission occurred in connection with air travels (Fig. 1) of infected persons residing in Berlin and the pertaining contact tracing investigations, and subsequently discuss the implications for current guidelines. To elucidate the extent of transmission chains, the State Health Office (SOHSA) contacted federal public health authorities in flight destination countries or embarking countries. Laboratory-confirmed measles cases were considered epidemiologically linked to an air travel related measles case, or a case secondary to it, if a spatial proximity between the two cases was known (e.g., same flight) or likely (e.g., presence on the same airport) during the infectious period of the air travel related case, and the disease onsets were 7–21 days apart from each other. If only the latter applied, but in addition the identical measles strain was detected, the case was considered possibly epidemiologically linked. Additionally, to assess the practicability of the current guidelines, we reviewed contact tracing efforts of the LHA for both events and computed the time interval between date of rash onset and date of diagnosis or notification, respectively, in Berlin measles cases between 2016 and 2018.

Cluster A: The index patient (case A0), a 40-year-old unvaccinated male, flew from Frankfurt to Berlin on 29 April 2018. His symptoms started on 26 April (rash developed on 01 May). He was diagnosed on 03 May and notified on 07 May. The following day, the LHA requested contact information for flight passengers from the airline using the request form provided by the International Air Transport Association. Although the airline agreed on releasing the requested personal data the next day, it was only provided after 9 days (17 May). The manifest included contact details of passengers and seat numbers but no information on the age of the passengers. At this point, 18 days after the flight, contact tracing was no longer recommended [6]. In connection with the flight from Frankfurt to Berlin, two more measles cases were notified in Berlin. Both cases were airline employees, between 30 and 45 years old, and travelling as passengers. Case A1 had one and case A2 two doses of MCV documented on their vaccination card; all vaccines were received in their childhood. These secondary cases were sitting 6 and 9 rows apart from the index case and both worked afterwards on aircrafts while being potentially infectious. Because at least one of them, potentially both, was likely re-infected after vaccination (secondary vaccine failure), the risk of further transmission was considered minimal. No samples for genotyping could be obtained from patients in this cluster.

Cluster B: The index patient (case B0) was a 34-year-old unvaccinated male, who reported symptom onset on 31 August 2018 and developed rash on 04 September 2018. The case flew from Berlin to Stockholm 01 September and returned to Berlin on 02 September via Copenhagen. The LHA was notified about the case on 06 September and initiated contact tracing the following day. Manifests from all three flights (two different airlines) containing contact information were obtained the same day. The provided information differed between the two airlines. The manifest from airline X contained contact details of all passengers, seat number as well as the information if the passenger was an infant, child or adult. Manifests from airline Y only contained contact details of passengers. For some passengers (ranging from 6% to 16% depending on the flight), no information at all or only information of the travel agency, through which the flight was booked, was provided. As information about the nationality or place of residence of the passengers was missing, the LHA in Berlin informed directly all

passengers with available information (n = 476) via e-mail about the possibility to have become exposed to an infectious measles case. Three further cases (B1–B3), all adults younger than 35 years of age, were identified that shared the same flight as the index case; one (B1) on the flight from Berlin to Stockholm, who was diagnosed in Bavaria where the case resided, and two (B2 and B3) on the flight from Copenhagen to Berlin, diagnosed in Berlin (B2) and Denmark (B3). All cases had received the e-mail from the LHA in advance of disease onset. Two of these secondary cases were unvaccinated. The third (B3), a Danish citizen travelling to Berlin, had documentation of two doses of MCV in his childhood. In addition, an unvaccinated Danish teenager (B4) developed rash 19 September. Even though he was not on the same flight as the index case, he was at the airport in Stockholm on 02 September at the same time as the index case. One tertiary case was observed (B5), who was a household contact of B2 with two documented doses of MCV. Genotype D8 with WHO unique sequence ID 4742 was detected in the index case and in cases B1–B4. In Sweden, a case of measles (B6) with the same strain was reported during the same time period as cases B1–B5. Contact investigations could not establish a direct epidemiological relationship to any of the other cases, but the absence of travel history in the case and of other measles cases in the area, the matching strain, timing of the onset of disease and geographical proximity of the case (in the south of Sweden, close to Denmark), suggests that the case could be linked to the outbreak.

In summary, two male Berlin residents, both unvaccinated, above 30 years of age and who flew within Europe in their infectious period prior to developing rash, were index cases to which we could epidemiologically link eight cases; six secondary and two tertiary cases. All but one were adults older than 25 years (median age: 32 years) and resided in three countries; four had a documented history of measles vaccination, three of them twice. Five secondary cases shared a flight with one of the index cases. All three of those cases, where the LHA was able to obtain contact information in a timely manner, had been informed before the onset of disease through LHA. The remaining two cases were retrospectively identified through enhanced case investigations. Two further epidemiological links were identified through contacting national authorities and one case was a household contact of one of the secondary cases.

3. Discussion

The two clusters are noteworthy for at least four things. Firstly, transmission was related to flights of rather short duration (< 2 h) and involved, at least in one cluster, a seat distance of nine rows between the index case and the secondary case. Both characteristics (i.e., a short flight and seat distances > 2) have been described before, albeit rarely. This reinforces RAGIDA, which recommend to not restrict contact tracing based on seating proximity or flight duration. It also takes into account that transmission in connection with air travel is not occurring solely in-flight, but can occur also during boarding, disembarking or elsewhere at the airport [7,8].

Secondly, both index cases travelled in their prodromal phase, i.e. before the rash appeared (2 and 3 days, respectively). In a review of measles transmission among airplane travelers in the US, most cases travelled during their prodromal phase [5]. Diagnosis of measles, however, occurs mostly after patients have begun to develop a rash. When reviewing data on measles cases notified in Berlin since 2017, the median time between rash and diagnosis or notification was 2 days and 5 days, respectively (Table 1). This indicates that for most flight-related transmission events involving index cases travelling prior to their rash, the time window for prevention, i.e. administering PEP, is very small or has already passed. If the window is still open, competent authorities must rapidly obtain (sufficient) passenger details in order to be able to prevent further transmission. In our experience, three currently present obstacles must be overcome: i) Identifying contact persons at (multinationally) operating airlines, who are competent in deciding about releasing personal data. ii) Airline concerns, legally or otherwise, regarding personal data transfer. iii) Obtaining contact information of all passengers allowing for timely contact and, if necessary, prioritization of passengers. Taken together - timing of measles notification and challenges in timely obtaining (complete and sufficient) passenger information - contact tracing of airline passengers will rarely lead to the prevention of secondary cases. Rather, timely identification and information of potential secondary cases will be the result in most tracing efforts to limit further spread to tertiary cases [9].

Table 1
Time from onset to notification in measles cases notified in Berlin between 01/01/2016 and 12/31/2018 (data as of 04.04.2019).

	Diagnosis		Notification	
	N	Median days (IQR)	N	Median days (IQR)
After disease onset	100	5 (3–7)	175	7 (5–10)
After rash[a]	69	2 (1–4)	93	5 (3–7)

[a] rash onset is only included in the electronic case report since 2017.

Thirdly, all cases but one were adults with a median age of 32 years. Since October 2016, measles are resurging in the EU/EAA region [10]. The median age in reported measles cases increased from 10 years in 2009 to 17 in 2018/2019 (24 years in Berlin) [11]. This highlights immunity gaps that extend far beyond those in children where the MCV2-coverage target of 95% still has not been achieved at European level. This is concerning as MCVs are not systematically provided to susceptible adults through immunization services in most countries.

Lastly, apart from contact tracing, enhanced cross-border case investigations, such as ours, can identify international transmission chains, thereby reducing the number of cases with unknown infection source. This is important to convincingly document measles elimination to the WHO.

Notwithstanding the resurgence of measles, more than 80% of the EU Member States had interrupted endemic measles transmission in 2017 [12]. Air travel, which has steadily increased in Europe over the last decades [13], is an effective means for introducing measles into a country. For those that are close to or already have eliminated measles, measles importation by air-travel can have substantial consequences both for the use of public health resources and for persons who are still susceptible [5,14,15]. Thus, early detection is pivotal to limit further spread in the community. This legitimates tracing of individuals exposed to measles, a public health measure that requires considerable time and effort. For this to be effective, passenger information must be obtained in a very short time frame, a condition often not met today. It is debatable in this context whether contact investigations should be conducted by LHA, like in Germany, which have to request passenger information from international airlines whose competent organizational unit is often located outside their jurisdiction, sometimes even outside their country, to then trying to inform passengers who, for the most part, do not reside in their jurisdiction. In several incidences in Europe, airlines have been doubtful of the legal basis for providing personal data to LHA, i.e., the International Health regulations (IHR), and concerns about data protection led to a delayed or no release of passenger manifests [9]. Support at national or international level could be of great help to address air lines and facilitate cooperation with health authorities (as e.g. practiced in the United States by the CDC with the help of Customs and Border Protection [16]). A list with relevant contact persons from airlines operating European airports could be managed and maintained centrally in Europe (e.g. at the ECDC) and local health authorities should be able to access this information rapidly through secure channels. Knowing these relevant contact persons could be furthermore an opportunity to generally inform and update airlines about their responsibilities and rights concerning such public health incidences.

The above described impediments principally also apply to many

other infectious diseases that can be transmitted via the respiratory route. Diseases like Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), hemorrhagic fever like Ebola or new pandemic influenza strains have even shorter incubation periods than measles [17] and effective vaccines are not available in most cases, which makes the timeliness of the response even more important to prevent further spread.

4. Conclusion

Current guidance on public health measures in relation to air travel related measles put a strong emphasis on preventing secondary cases, which is, albeit desirable, seldom achievable. We believe, in keeping with others [9,18], there is a need not only to revisit current guidelines but also the methods for the public health response to exposure to measles virus during air travel. It is difficult to comprehend that today passengers can be quickly informed about flight delays through e-mails or push-up messages on their mobile phones, but not about the possibility of having acquired a severe infectious disease and the appropriate precautionary measures.

The ultimate goal should be for all regions to be able to encounter measles exposure during air travel with the same composure as Canadian public health authorities, who simply rely on the high vaccination rates of the Canadian population [19]. Meanwhile, increasing vaccine coverage rates in children to meet the 95% target and Supplementary Immunization Activities in the adult population are apparently needed in at least some countries of the EU.

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Declaration of competing interest

None.

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