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EUROPEAN CENTRE FOR
DISEASE PREVENTION
AND CONTROL

ECDC **GUIDANCE**

Risk assessment guidelines for diseases transmitted on aircraft

PART 2: Operational guidelines for assisting in
the evaluation of risk for transmission by disease

ECDC GUIDANCE

Risk assessment guidelines for diseases transmitted on aircraft (RAGIDA)

PART 2

Operational guidelines for assisting in the evaluation of risk for transmission by disease

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Contents

Abbreviations

ACI	Airport Council International
AFB	Acid-fast fast bacilli
APU	Auxiliary power unit (in passenger aircraft)
BCG	Bacille Calmette-Guérin
CDC	Centers for Disease Control and Prevention, Atlanta, Georgia, USA
CT	Contact tracing
DZK	German Central Committee against Tuberculosis
ECDC	European Centre for Disease Prevention and Control, Stockholm, Sweden
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
HEPA filter	High-efficiency particulate air filter (in passenger aircraft cabins)
HNIG	Human normal immunoglobulin
HPA	Health Protection Agency, UK
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization
IHR (2005)	International Health Regulations (year of becoming operative)
MDR TB	Multidrug-resistant tuberculosis; defined as resistance to at least isoniazid and rifampin
PEP	Post-exposure prophylaxis
PH	Public health
RKI	Robert-Koch-Institut, Berlin, Germany
SARS	Severe Acute Respiratory Syndrome
TB	Tuberculosis
TST	Tuberculin skin test
VHF	Viral haemorrhagic fever
WHO	World Health Organization
HNIG	Human normal immunoglobulin
MDR	Multidrug resistant
RAGIDA	Risk assessment guidance for diseases transmitted on aircraft
XDR	Extensively drug resistant

Introduction

The founding regulation[i] establishing the European Centre for Disease Prevention and Control (ECDC) gives ECDC a mandate to strengthen the capacity of the EU for the prevention and control of infectious diseases. One of the approaches is to provide independent scientific advice, as well as scientific and technical assistance to assess health threats.

The emergence of severe acute respiratory syndrome (SARS) illustrated the potential for a new disease to suddenly appear, spread and threaten the health, economic and social life of European citizens. The fact that there are more than 800 million passengers carried on national and international flights within the European Union (EU)[ii] alone highlights the potential risk of the introduction and spread of infectious diseases during air travel. Early recognition of disease and appropriate risk assessments are needed in order to initiate the most appropriate public health response when passengers and/or crew members become exposed to an infectious or potentially infectious passenger during a flight without unnecessarily alarming the public or disrupting air traffic.

In order to assist national authorities in the EU Member States in the assessment of risks associated with the transmission of various infectious agents on board airplanes, ECDC commissioned the production of this guidance documents through a call for tender with the Robert Koch Institute, Germany in 2007. Hereafter, this project will be referred to as 'the risk assessment guidance for diseases transmitted on aircraft', or RAGIDA.

The RAGIDA project

The project consisted of two different parts, described below.

Part 1: Systematic literature review and expert interviews

As a first step, a systematic review of over 3700 peer-reviewed articles and grey literature was performed for the following 12 diseases: tuberculosis, influenza, severe acute respiratory syndrome, meningococcal disease, measles, rubella, diphtheria, Ebola haemorrhagic fever, Marburg haemorrhagic fever, Lassa fever, smallpox and anthrax. In addition, general guidelines on risk assessment and risk management from international aviation boards and national or international public health agencies were systematically searched. Standardised questionnaires were used to interview national and international experts to systematically assess case-based information on events.

The results of this first part of the project are available from:
http://ecdc.europa.eu/en/publications/Publications/0906_TER_Risk_Assessment_Guidelines_for_Infectious_Diseases_Transmitted_on_Aircraft.pdf

Part 2: Operational guidance for assisting in the evaluation of risk for transmission by disease

As a second step, the production of a series of operational guidance documents for assisting in the evaluation of risk for transmission of ten diseases prioritised by the Advisory Forum (AF17/2008) was initiated. In June 2009, ECDC convened a technical expert consultation that focused on tuberculosis, new emerging airborne diseases (e.g. SARS) and meningococcal infections. In 2010, other expert consultations will follow covering diseases such as measles, rubella, haemorrhagic fevers, diphtheria, and bioterrorism agents (smallpox, anthrax). Described below are both the methodology and the structure of the guidance documents finalised in part 2 of the project.

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[i] Regulation 851/2004 of the European Parliament and of the Council.
[ii] Total number of passengers carried in 2008 (arrivals and departures for national and international), Europe in figures, Eurostat yearbook 2010.

Methodology

A) Selection of the working group participants

Small, multidisciplinary expert working groups were established for each of the following diseases: tuberculosis, new emerging airborne diseases, meningococcal infections, viral haemorrhagic fevers, measles, and rubella. The participants were selected to include:

- representatives of national public health authorities, including those with experience in the investigation and follow-up of incidents involving infectious diseases in travellers;
- European and international disease experts;
- international experts in microbiology and mathematic modelling;
- representatives of the ECDC disease specific programmes;
- representatives of the European Commission; and
- representatives of the WHO International Health Regulations Coordination Programme, Geneva.

All participants completed a Declaration of Interest form. No conflicts of interest were declared by any of the participants.

B) Base of evidence

Evidence obtained for the three guidance documents included:

- the review of the published literature by disease, related to air travel (see RAGIDA, Part 1);
- the review of data in air travellers obtained from national public health authorities (see RAGIDA, Part 2);
- expert opinions from the working group participants.

The quality of available evidence was assessed by the experts, using elements of the 'Scottish Intercollegiate Guidelines Network' (SIGN) and the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE), by not only taking into consideration the available scientific evidence for transmission but also wider aspects including the following examples: case fatality rate, the potential for public health intervention and availability of treatment.

An illustration of the type of considerations used by the experts in order to assess the evidence can be found in Annex.

C) Development of the final guidance documents

The final recommendations proposed by the three expert groups were shared for comments and suggestions with the members of the ECDC Advisory Forum (AF19/2009 and AF23/2010).

Structure and use of the guidance document

The current document consists of three disease-specific chapters, using the following outline:

- Literature review
- Suggested approach
- Criteria to be considered
- Other considerations
- Draft Q&A for contact tracing

These guidance documents may be adapted to the local situation, national and international regulations or preparedness plans.

These guidance documents represent the views of the experts. If new, relevant evidence becomes available, the RAGIDA documents will be updated accordingly.

1 Tuberculosis

1.1 Literature review

The detailed systematic review of the literature identified a limited number of incidents with evidence for tuberculosis (TB) transmission during air travel; additionally, there was insufficient evidence of the effectiveness of contact tracing [1]. Three studies identified in the review [2–4] presented evidence of tuberculin skin conversion among contacts; however, one was associated with transmission [3] from a crew member to colleagues [2] and another involved passengers from a high incidence country where boosting could not be excluded [4]. A single study provided clear evidence of transmission. This was associated with a long-haul flight following exposure to a sputum smear-positive patient with evidence of transmission to household contacts prior to air travel [4]. No case of TB disease as a consequence of transmission during air travel has been described in the literature so far. The resource implications of the contact tracing processes are high [5,6] and there is no available preventive treatment for multidrug-resistant (MDR) or extensively drug-resistant (XDR) TB. Furthermore, evidence for compliance with isoniazid preventive therapy (IPT) among passengers presenting a positive tuberculin skin test following air travel is also limited.

Using the Scottish Intercollegiate Guidelines Network (SIGN) approach for developing guidelines [7], the working group reviewed the evidence base and concluded that the quality of evidence is weak. Recommendations were formulated for investigating air travel related tuberculosis incidents. These recommendations are all graded D [8].

1.2 Suggested approach

Contact tracing of passengers exposed to tuberculosis during air travel should only be undertaken following a careful risk assessment based on the infectiousness of the index patient, the amount of effective contact/exposure and where possible an assessment of the susceptibility of exposed individuals, as it is done during any routine contact investigation.

An assessment based on the following criteria should follow the outline in Figure 1. Where these conditions are met, exposed passengers in the relevant rows should be contacted using the procedures outlined in the WHO guidelines [9] and investigated and managed for latent tuberculosis infection according to national guidelines.

1.3 Criteria to be considered

The index case

Index case with confirmed infectious pulmonary TB: Defined as culture or molecular probe-confirmed cases with positive sputum smear microscopy (including induced sputum or bronchoalveolar lavage);

The infectiousness of the index case: Evidence of transmission in other settings, such as transmission to household members or other close contacts.

Effective exposure

Duration of flight: Flight duration equal to or exceeding eight hours of flight time including ground delays (www.flightstats.com);

Location on board: Evidence for on-board TB transmission is very low for passengers seated more than two rows ahead or two rows behind the index case; therefore, contact tracing is only recommended for passengers sitting in the same row, two rows ahead and two rows behind the index case.

1.4 Other considerations

Before the flight

Patients with confirmed infectious pulmonary TB should avoid air travel.

If a patient with confirmed infectious pulmonary TB requires unavoidable flight, ask the patient to delay travel until after the patient has received a minimum of two weeks of adequate treatment with clinical improvement. If it is not possible to delay travelling for two weeks, then a travel protocol should be agreed between the patient, the

local public health authority (public health team) and the airline in question. Instruct the patient to cover nose and mouth while coughing to reduce exposure, isolate the patient for the duration of travel and provide a face mask for the patient (educate on how to use it). The risk of infection of passengers with MDR and XDR TB should be assessed using national guidelines.

During the flight

During a flight, if a passenger is suspected of having TB – as with any other respiratory infection – the potentially infectious traveller should be relocated to an isolated seat separate from other travellers (if possible) and be provided with a surgical face mask and a sufficient amount of disposable tissues. Flight attendants should follow IATA guidelines for infection control and, if possible, collect locator cards from travellers to facilitate contact tracing, if needed.

1.5 Template for Q&A sheet: tuberculosis contact tracing

The following lines show a template for public health experts who need to quickly develop a Q&A sheet to complement contact tracing activities. This template should be customised to the current situation and to the decisions made by the public health authorities in charge.

When should contact tracing be considered?

Contact tracing should be considered:

- if the index case is confirmed as having infectious pulmonary TB (sputum smear positive, including induced sputum or bronchoalveolar lavage);

AND

- there is evidence of transmission to other contacts (refers to cases with evidence of transmission in household or other close contacts);

AND

- the duration of the flight is longer than eight hours;

AND

- the time elapsed between the flight and diagnosis of the case is not longer than three months.

When is a patient infectious?

Patients with sputum smear-positive for pulmonary TB are considered infectious.

Who should be considered for contact tracing?

We recommend limiting contact tracing to passengers sitting in the same row, two rows ahead and two rows behind the index case in accordance with the WHO guidelines [9].The exposure of the cabin crew is generally less intensive and should be assessed by the airline's medical service.

Are there special considerations for MDR/XDR TB?

There is no evidence that patients with MDR or XDR TB are more infectious than patients with sensitive TB; however, the potential clinical implications of these conditions could be more serious [10]. There is also no effective treatment for latent infection caused by MDR or XDR TB [11].

Are there special considerations for individuals of higher susceptibility?

If contact tracing is decided after the risk assessment and there is evidence that passengers with higher susceptibility to TB, such as infants or children, travelled in the same row or two rows ahead or behind the index case, special efforts should be initiated to contact trace them.

Figure 1.1. Risk assessment algorithm tuberculosis

```
┌─────────────────────────────┐
│      Incident reported       │
└─────────────────────────────┘
              │ YES
              ▼
┌─────────────────────────────┐
│        Patient with          │   NO      ╭──────────╮
│   infectious pulmonary TB?*  │ ────────▶ │   No     │
└─────────────────────────────┘           │ contact  │
              │ YES                        │ tracing  │
              ▼                            ╰──────────╯
┌─────────────────────────────┐
│  Evidence of transmission to │   NO      ╭──────────╮
│  close contacts (household   │ ────────▶ │   No     │
│   and other close contacts)? │           │ contact  │
└─────────────────────────────┘           │ tracing  │
              │ YES                        ╰──────────╯
              ▼
┌─────────────────────────────┐
│   Flight duration of 8       │   NO      ╭──────────╮
│     hours or longer?         │ ────────▶ │   No     │
└─────────────────────────────┘           │ contact  │
              │ YES                        │ tracing  │
              ▼                            ╰──────────╯
┌─────────────────────────────┐
│      Flight took place       │   NO      ╭──────────╮
│ less than three months ago?  │ ────────▶ │   No     │
└─────────────────────────────┘           │ contact  │
              │ YES                        │ tracing  │
              ▼                            ╰──────────╯
┌─────────────────────────────┐
│ Contact trace in the same    │
│ row, two rows ahead and two  │
│ rows behind the index case   │
└─────────────────────────────┘
```

Infectious pulmonary TB is defined as culture or molecular probe confirmed cases with a positive microscopy sputum smear (including induced sputum or bronchoalveolar lavage).

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2 Severe acute respiratory syndrome

2.1 Literature review

The detailed systematic review of the literature identified four documented events including 26 passengers with evidence for transmission of severe acute respiratory syndrome (SARS) during air travel [1]. The evidence for on-board transmission was high in 24 of the 26 of the passengers and medium and low for the other two passengers. Seat locations of infected contacts in relation to the index case[i] were available for two events and ranged between the same row and seven rows away. All cases with reported transmission were symptomatic during the flight [2–10].

2.2 Suggested approach

An assessment of possible transmission of SARS on an aircraft should be undertaken on a case-by-case basis. This should occur after careful individual risk assessment, taking into account the index case status, the symptoms of the index case, the epidemiological situation for SARS in country of origin/departure and country of destination/arrival and the purpose of the contact tracing. The undertaken assessment should follow the outline in Figure 2.

2.3 Criteria to be considered

The index case

The index case is a probable or laboratory confirmed case of SARS (see below for ECDC case definitions).

The severity of the symptoms and infectiousness of the index case: There are no reported cases of transmission before onset of symptoms [2]. Transmission is most likely from severely ill patients or those experiencing rapid clinical deterioration, usually during the second week of illness [3].

Epidemiological situation

- **The evidence of transmission in country of departure and country of arrival:** The decision to perform contact tracing for either laboratory confirmed SARS cases with symptoms during a flight or when a probable SARS case had been on a flight should be based on existing evidence for transmission of SARS in the country of departure (see the following three scenarios):
  - **No evidence of transmission in country of departure.** Early phase of a potential outbreak: The diagnosis of SARS cases might be delayed because clinicians do not consider SARS as a differential diagnosis. To ensure that no secondary SARS cases are missed, it is suggested that contact tracing be initiated when a laboratory confirmed SARS case had been symptomatic on a flight that occurred within 20 days (twice the maximum incubation period) after the onset of symptoms;
  - **Evidence of ongoing transmission in country of departure, but no cases in country of arrival.** In this situation, it is suggested that contact tracing be initiated when a probable or laboratory confirmed SARS case had been symptomatic on a flight that occurred within 20 days after onset of symptoms. Comprehensive contact tracing should be considered to prevent potential secondary and tertiary cases;
  - **Evidence of ongoing transmission in country of departure and country of destination**. In this situation, it is suggested that contact tracing be initiated when a laboratory confirmed SARS case had been symptomatic on a flight that occurred within 10 days (the maximum incubation period) after the onset of symptoms.

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[i] Person identified as the initial case.

Effective exposure

Although there is no evidence of on-board SARS transmission beyond seven seating rows, a comprehensive contact tracing of confirmed SARS cases – especially in the inter-epidemic period – should be considered. If all passengers can not be contacted, contact tracing efforts should at least concentrate on the following:

- passengers seated in the same row as the index case;
- passengers seated two rows in front or behind the index case;
- persons providing care for the index case;
- persons having intimate contact with the index case;
- persons having contact with respiratory secretions of the index case;
- passengers living in the same household with the index case; and
- all crew members.

If a crew member is the index case, all passengers seating in the area the crew member was working during the flight should be regarded as contacts, as well as the other members of the crew.

2.4 Other considerations

During the flight

During the flight, if a passenger is suspected of having SARS – as with any other respiratory infection – the potentially infectious passenger should, if possible, be isolated and provided with a surgical face mask. The flight attendant should follow the IATA guidelines for infection control.

Contacts should provide to the health authorities their identification and valid contact addresses for 14 days after the flight (locator cards) in order to facilitate contact tracing, if needed.

Captains should radio ahead to the airport of destination informing it of a suspected SARS case on board (International Health Regulation 2005, Article 28. Available from http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf).

2.5 Template Q&A sheet: SARS contact tracing

The following lines show a template for public health experts who need to quickly develop a Q&A sheet to complement contact tracing activities. This template should be customised to the current situation and to the decisions made by the public health authorities in charge.

When should contact tracing be considered?

After reviewing individual risk assessments considering the global epidemical situation for SARS and susceptibility of passengers, contact tracing should be initiated:

- if there was a probable or confirmed case on board (see case definitions);
AND

- if the patient was possibly infectious;
AND

- if the flight occurred within the last 10 or 20 days (see algorithm).

When is a patient infectious?

There are no reported cases of transmission before the onset of symptoms [2]. Based on the data collected by the World Health Organization (WHO), transmission is most likely from severely ill patients or those experiencing rapid clinical deterioration, usually during the second week of illness [3]. The literature review revealed that, in the four events in which transmission occurred, three index patients were symptomatic during the flight. In another case, the clinical status of the index case during flight was unknown [4–7].

Who should be considered for contact tracing?

In eight out of nine flights with SARS events, comprehensive contact tracing (aiming to identify every passenger) was initiated. In one event, passengers seated in the same row as the index case and the two rows in front or behind the index case were traced 90 days after the flight in order to determine the seroprevalence of SARS antibodies in passengers [8]. Of the 36 out of the 250 (14%) passengers successfully traced, none were infected.

In two of the four events in which transmission occurred, the infected contacts were seated between 0 and seven rows away from the index patient [6,7]. Although evidence for transmission of SARS in a distance beyond seven seating rows does not exist, especially in the inter-epidemic period, a comprehensive contact tracing of probable or confirmed SARS cases should be considered to prevent potential secondary and tertiary transmission.

Does the flight time play a role in contact tracing?

In four out of nine events in which transmission occurred, the flight time exceeded eight hours [4–6]. Nevertheless, in another event with highly plausible evidence of transmission, the flight time was only three hours [7]. Therefore, we suggest not limiting contact tracing to long-haul flights only.

Figure 2.1. Risk assessment algorithm SARS
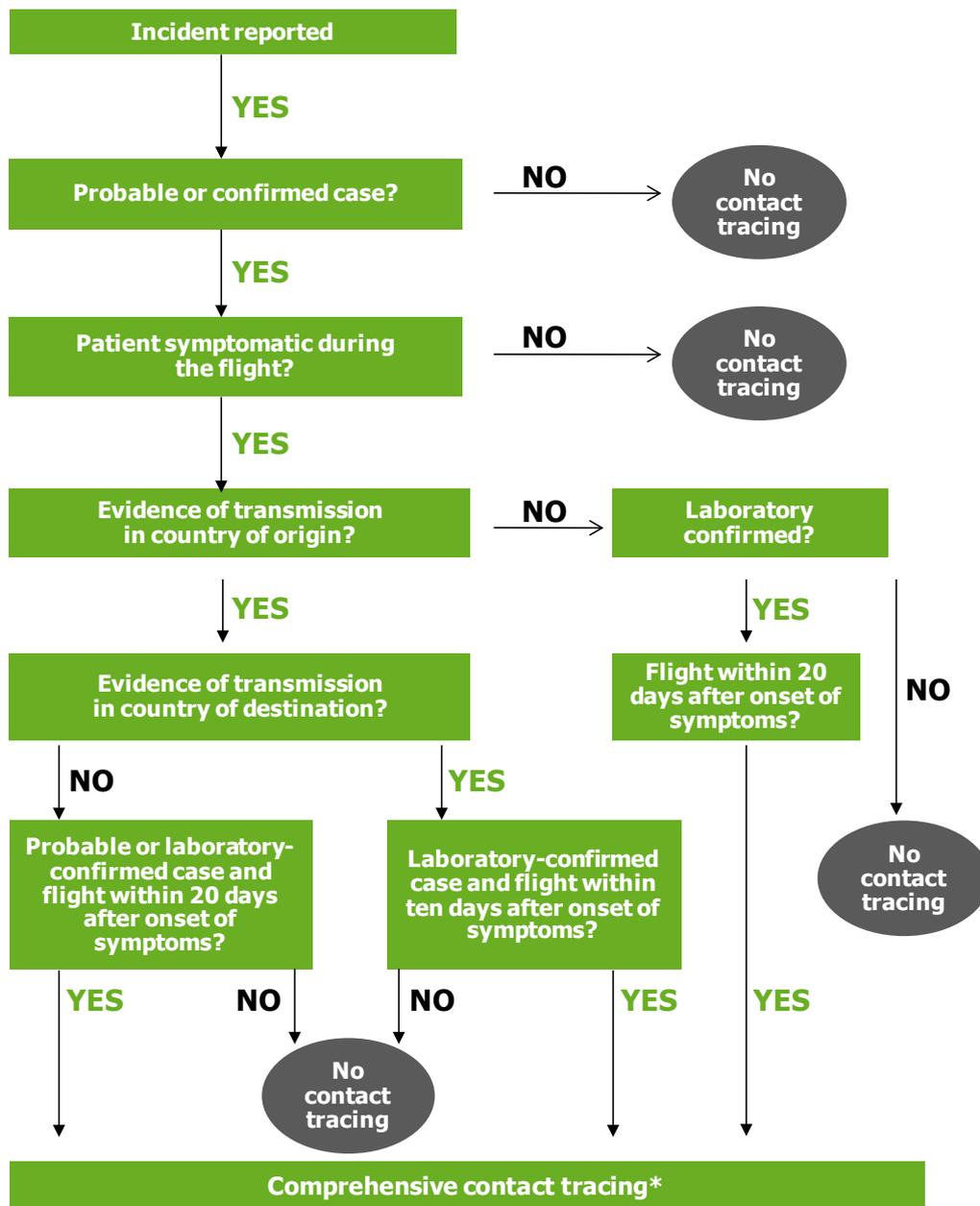
* If all passengers cannot be contacted, contact tracing efforts should at least concentrate on the following: passengers seated in the same row as the index case; passengers seated two rows in front or behind the index case; persons providing care for the index case; persons having intimate contact with the index case; persons having contact with respiratory secretions of the index case; passengers living in the same household with the index case; and all crew members.

Is there evidence as to whether the on-board HEPA-filter makes a difference?

None of the retrieved and analysed publications mention the functionality of the on-board HEPA-filter systems. In consequence, evidence for a possibly increased risk of SARS transmission on board in case of non-functioning HEPA filters is inconclusive.

2.6 Case definitions (ECDC, 2008)

The Commission of the European Communities; Commission decision of 28/IV/2008 amending decision 2002/253/EC laying down case definition for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and the Council, 2008.

Clinical criteria

Any person with fever or history of fever and at least one of the following three:

Cough, difficulty breathing, or shortness of breath
AND
at least one of the following four:
- radiographic evidence of pneumonia,
- radiographic evidence of acute respiratory distress syndrome,
- autopsy findings of pneumonia,
- autopsy findings of acute respiratory distress syndrome;
AND
no alternative diagnosis can fully explain the illness.

Laboratory criteria

Confirmed case

A laboratory confirmed case includes at least one of the following three:

- isolation of the virus in cell culture from any clinical specimen and identification of SARS coronavirus (SARS-CoV) using methods such as reverse transcription polymerase chain reaction (RT-PCR);
- detection of SARS-CoV nucleic acid in at least one of the following three: at least two different clinical specimens; the same clinical specimen collected on two or more occasions during the course of the illness or; two different assays or repeat RT-PCR using a new RNA extract from the original clinical sample on each occasion of testing;
- SARS-CoV specific antibody response by one of the following two: seroconversion by enzyme linked immunosorbent assay (ELISA) or immunoflourescent assay (IFA) in acute and convalescent phase serum tested in parallel or; fourfold or greater rise in antibody titre in between acute and convalescent phase sera tested in parallel.

Probable case

A probable case, based on laboratory findings, includes at least one of the following two:

- a single positive antibody test for SARS-CoV;
- a positive PCR result for SARS-CoV on a single clinical specimen and assay.

Epidemiological criteria

Epidemiological criteria include at least one of the following three:

- any person with at least one of the following three: employed in an occupation associated with an increased risk of SARS-CoV exposure (e.g. lab, handling animals); close contact of one or more persons with confirmed SARS or under investigation for SARS or; history of travel to or residence in an area experiencing an outbreak of SARS;
- two or more healthcare workers with clinical evidence of SARS in the same healthcare unit and with onset of illness in the same 10 day period or;
- three or more persons with clinical evidence of SARS with onset of illness in the same 10 day period and epidemiologically linked to a healthcare facility.

Case definition for inter-epidemic period

Possible case

Any person meeting the clinical criteria and with an epidemiological link.

Probable case

Any person meeting the clinical criteria,
AND
an epidemiological link,
AND
that meets the laboratory criteria for a probable case.

Confirmed case, nationally confirmed:

Any person meeting the clinical criteria and the laboratory criteria for case confirmation where the testing has been performed at a **national reference laboratory**.

Confirmed case:

Any person meeting the clinical criteria and the laboratory criteria for case confirmation where the testing has been performed at a **WHO SARS Verification** and **Reference Laboratory**.

Case definition during an outbreak[i]

Possible case

Any person meeting the clinical criteria.

Probable case

Any person meeting the clinical criteria
AND
who has an epidemiological link to a nationally confirmed or a confirmed case.

Confirmed case, nationally confirmed:

Any person meeting the clinical criteria
AND
the laboratory criteria for confirmed case where the testing has been performed at a national reference laboratory.

Confirmed case:

One of the following three:

- any person meeting the clinical criteria and the laboratory criteria for case confirmation where the testing has been performed at a WHO SARS verification and reference laboratory;
- any nationally confirmed case with an epidemiological link to a chain of transmission where at least one case has been independently confirmed by a WHO SARS reference and verification laboratory;
- any person meeting the clinical criteria and with laboratory criteria for probable case with an epidemiological link to a chain of transmission where at least one case has been independently confirmed by a WHO SARS reference and verification.

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[i] Applies during an outbreak in a country/area where at least one person has been laboratory confirmed by a WHO SARS verification and reference laboratory.

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3 Invasive meningococcal disease

3.1 Literature review

The detailed systematic review of the literature [1] identified one documented incident with strong evidence for transmission of invasive meningococcal disease (IMD) during air travel, probably from an asymptomatic carrier to two persons sitting 12 rows apart and without contact with each other [2]. In at least 25 events[i] with symptomatic index cases, no transmission was observed [3–5].
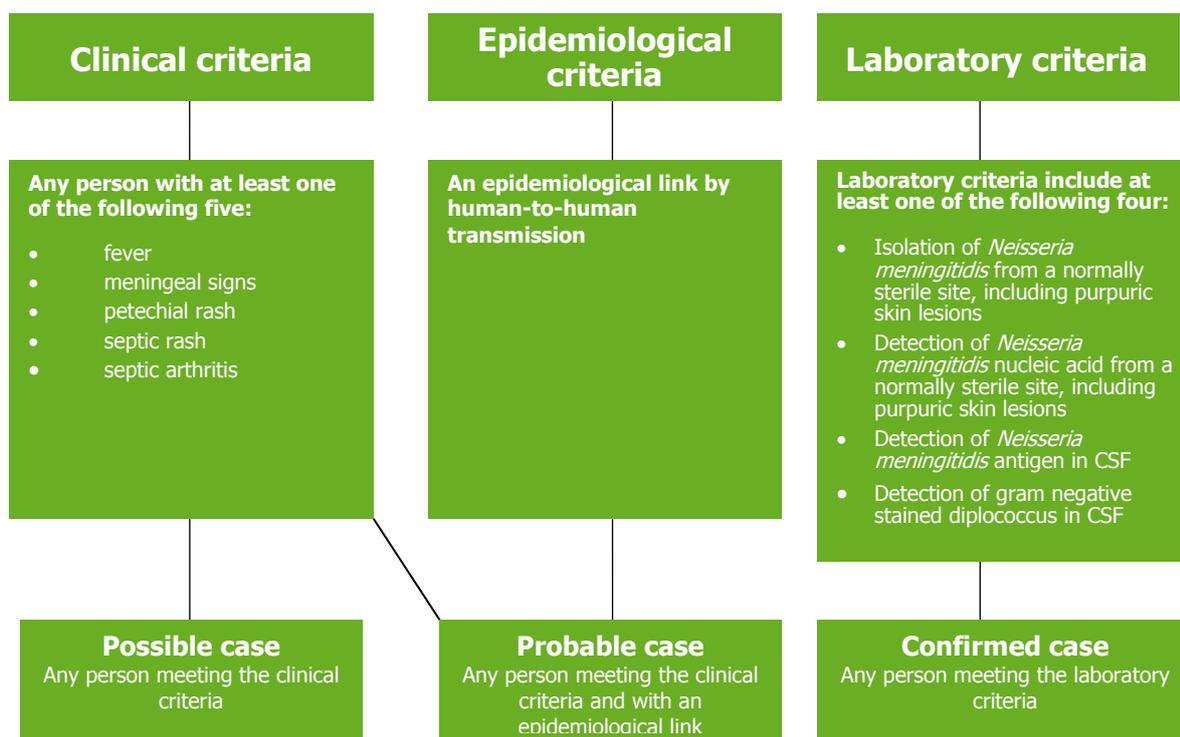
The available evidence base is poor, but the paucity of published events suggests that the risk of meningococcal disease transmission on board aircraft is low. There is a lack of evidence to indicate that passengers merely sitting beside an index case in airplanes are subject to an increased risk of acquiring meningococcal disease, unless the passenger is already identified as a close contact (e.g. household contact).

3.2 Suggested approach

The assessment of possible transmission of meningococcal disease on an aircraft should be undertaken on a case-by-case basis. This should occur after careful individual risk assessment, taking into account the symptoms of the patient and the duration and closeness/type of contact to fellow travellers and crew. The undertaken assessment should follow the outline in Figure 3.2.

3.3 Criteria to be considered

Figure 3.1. EU case definition for invasive meningococcal disease, 2008 [6]

Clinical criteria	Epidemiological criteria	Laboratory criteria
Any person with at least one of the following five: • fever • meningeal signs • petechial rash • septic rash • septic arthritis	**An epidemiological link by human-to-human transmission**	**Laboratory criteria include at least one of the following four:** • Isolation of *Neisseria meningitidis* from a normally sterile site, including purpuric skin lesions • Detection of *Neisseria meningitidis* nucleic acid from a normally sterile site, including purpuric skin lesions • Detection of *Neisseria meningitidis* antigen in CSF • Detection of gram negative stained diplococcus in CSF
Possible case Any person meeting the clinical criteria	**Probable case** Any person meeting the clinical criteria and with an epidemiological link	**Confirmed case** Any person meeting the laboratory criteria

[i] An event is described as an incident during which the possible transmission of invasive meningococcal disease from one or more index cases through contact with other travellers during air travel can be suspected, proven or ruled out.

The index case

The index case is a probable or confirmed case of meningococcal disease (Figure 3.1).

The symptoms and infectiousness of the index case: Cases are often considered as potentially infectious from seven days before onset of symptoms to 24 hours after onset of effective treatment [7]. However, the infectious period is not known and it is quite possible that cases of meningococcal disease are not infectious before the onset of symptoms [8].

Timing of flight

Flight occurrence within past 10 days: Published guidelines recommend chemoprophylaxis for contacts within 10–14 days of symptom onset in the index case: The incubation period is 3–4 days and ranges between 2–10 days [9–11]. Thus, even if the assessment reveals that either the passengers or crew had unprotected contact to nasopharyngeal secretions from the patient, consideration of contact tracing (contact tracing) is only warranted if administration of chemoprophylaxis is possible within 10 days of exposure.

Effective exposure

Type and length of exposure: Passengers at risk are those who have been directly exposed to the index case's nasopharyngeal secretions. For close contacts, defined as household-like contacts of a case or individuals with intense unprotected contact to the nasopharyngeal secretions of an infected person (e.g. exposed to cough secretions, intubating, resuscitating or examining the oropharynx without wearing a mask), chemoprophylaxis is ideally administered within the first 24 hours and at the latest within 10 days after exposure. There is a lack of evidence to indicate that passengers merely sitting beside an index case in airplanes are subject to an increased risk of meningococcal disease, unless the passenger has already been identified as a close contact. Thus, routine follow up of passengers sitting beside the index case is not recommended by the expert group. Contact tracing should only be considered if there is evidence that other passengers or crew members were exposed to nasopharyngeal secretions of the patient during contact that occurred either while the patient was symptomatic or in the seven days prior to the onset of symptoms.

3.4 Other considerations

Purpose of contact tracing (e.g. administration of post-exposure prophylaxis (PEP), interruption of infection chains, scientific research): There is no evidence to support the provision of widespread chemoprophylaxis for persons who are not close contacts. Widespread use may result in eradication of benign strains of *Neisseria* that provide protective antibodies, the generation of drug-resistant strains and an increase in the prevalence of drug-related adverse events [12]. Gathering scientific data may be justification for contact tracing.

Status of air ventilation – HEPA filter: In view of the vertical air circulation in airplanes with little horizontal flow in combination with the HEPA filters, prolonged close contact is likely required for transmission to occur on board aircraft [13,14]. In one event, no transmission occurred even though the HEPA-filter was not functioning [1].

3.5 Template Q&A sheet: meningococcal disease contact tracing

The following lines show a template for public health experts who need to quickly develop a Q&A sheet to complement contact tracing activities. This template should be customised to the current situation and to the decisions made by the public health authorities in charge.

When should contact tracing be considered?

Contact tracing should be considered:

- if the index case is a probable or confirmed case of IMD (see EU case definition, 2008, Figure 1);
AND

- the flight occurred within the previous 10 days;
AND

- the case travelled within seven days prior to symptom onset;
AND

- there is evidence that crew members or fellow travellers had intense exposure to nasopharyngeal secretions of the case.

When is a patient infectious?

Cases are often considered as potentially infectious from seven days before the onset of symptoms to 24 hours after the onset of effective treatment [2]. However, the infectious period is not known and it is quite possible that cases of meningococcal disease are not infectious before the onset of symptoms [2].

Who should be considered for contact tracing?

Passengers and crew with close contact to nasopharyngeal secretions should be considered for contact tracing. The expert group defines close contact as:

- household-like contacts of a case *or*;
- individuals with intense, unprotected contact to the nasopharyngeal secretions of an infected case (e.g. exposed to cough secretions, intubating, resuscitating or examining the oropharynx without wearing a mask).
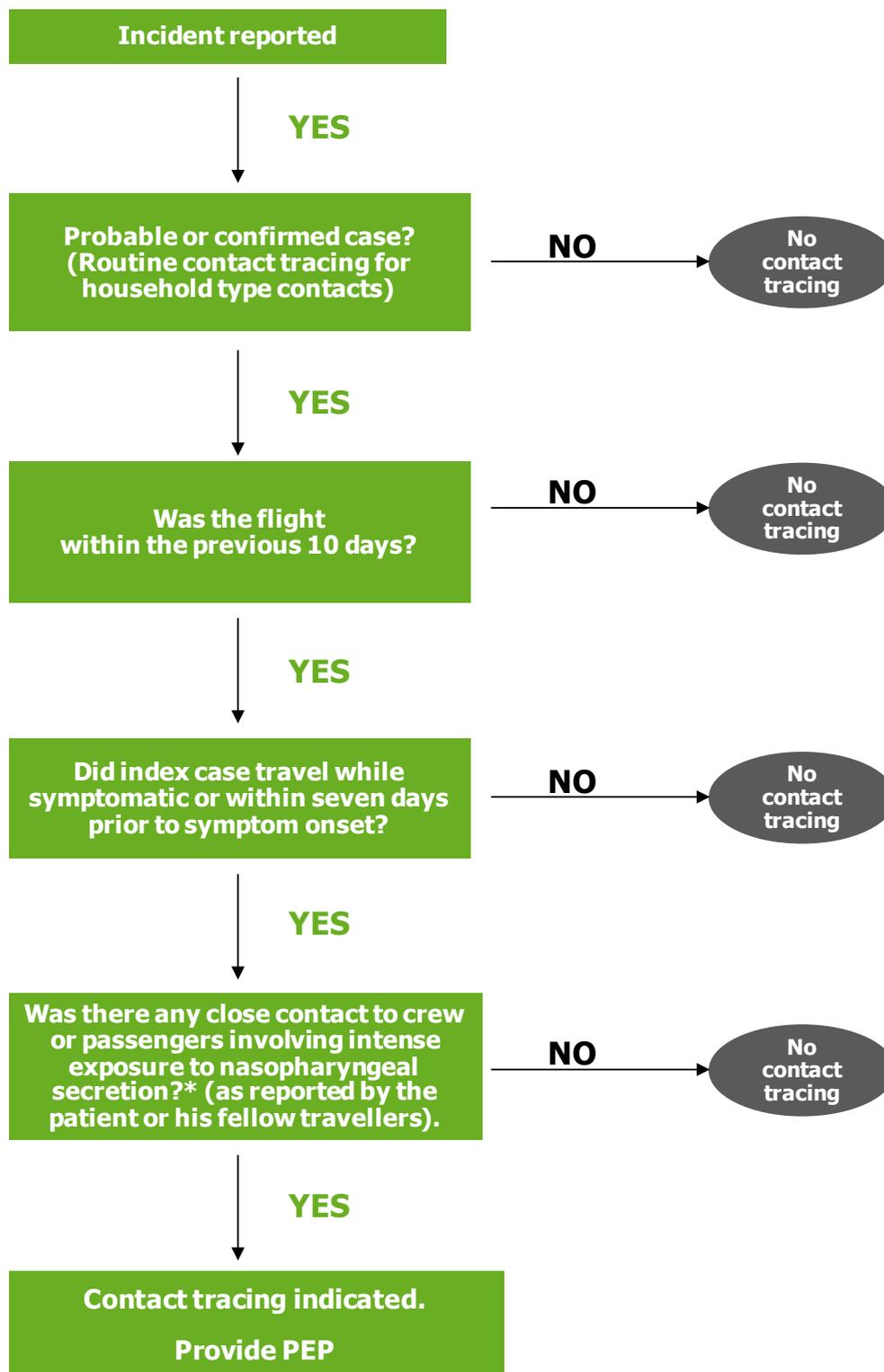
Are there special considerations for certain serogroups?

Serogroup B (currently not vaccine preventable) is the most common serogroup in Europe. Therefore, waiting for the results of serogrouping is of little use; the timely administration of PEP to passengers who have been identified as close contacts should be given first priority.

Are there special considerations for individuals of higher susceptibility?

As so few cases of IMD have been described in association with air travel, it is not known whether fellow passengers with a higher susceptibility for IMD (e.g. infants younger than one month old and persons with congenital or acquired immune deficiency, terminal complement defects) would be at a higher risk of contracting the disease. In many cases, predisposing factors will not be known to those affected; even if they were, they could only be identified by exhaustive contact tracing, which would only be indicated if the conditions under section 3.5.1 are met.

Figure 3.2. Risk assessment algorithm invasive meningococcal disease

```
                    ┌──────────────────────────┐
                    │   Incident reported      │
                    └──────────────────────────┘
                               │
                             YES
                               │
                               ▼
     ┌──────────────────────────────────┐                  ╭──────────╮
     │   Probable or confirmed case?    │      NO           │   No     │
     │   (Routine contact tracing for   │  ──────────▶      │ contact  │
     │   household type contacts)       │                   │ tracing  │
     └──────────────────────────────────┘                  ╰──────────╯
                               │
                             YES
                               │
                               ▼
     ┌──────────────────────────────────┐                  ╭──────────╮
     │         Was the flight           │      NO           │   No     │
     │   within the previous 10 days?   │  ──────────▶      │ contact  │
     │                                  │                   │ tracing  │
     └──────────────────────────────────┘                  ╰──────────╯
                               │
                             YES
                               │
                               ▼
     ┌──────────────────────────────────┐                  ╭──────────╮
     │   Did index case travel while    │      NO           │   No     │
     │   symptomatic or within seven    │  ──────────▶      │ contact  │
     │   days prior to symptom onset?   │                   │ tracing  │
     └──────────────────────────────────┘                  ╰──────────╯
                               │
                             YES
                               │
                               ▼
     ┌──────────────────────────────────┐                  ╭──────────╮
     │  Was there any close contact to  │      NO           │   No     │
     │  crew or passengers involving    │  ──────────▶      │ contact  │
     │  intense exposure to             │                   │ tracing  │
     │  nasopharyngeal secretion?* (as  │                   ╰──────────╯
     │  reported by the patient or his  │
     │  fellow travellers).             │
     └──────────────────────────────────┘
                               │
                             YES
                               │
                               ▼
     ┌──────────────────────────────────┐
     │   Contact tracing indicated.     │
     │                                  │
     │          Provide PEP             │
     └──────────────────────────────────┘
```

* Unprotected contact with patient, e.g. exposure to cough secretions, intubating, resuscitating or examining the oropharynx without wearing a mask.

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4 Viral haemorrhagic fevers

4.1 Lassa fever

Literature review

A detailed systematic literature review identified nine incidents of Lassa fever cases imported into Europe, (including one case which was in transit in London while en route to the US) between 2000 and 2010 (1–10).

Details about contact tracing were included for seven of the events in the literature review. Contact tracing was initiated in all seven events because the index cases were symptomatic while on board, and the incubation period still allowed for preventive measures to be taken. A comprehensive search was initiated for two events: passengers could be traced because their seat location in relation to the index case's seat was known. Contact categories according to risk exposure were applied in two events. Contact tracing was done by actively contacting passengers with the help of manifests provided by the airlines. 179/293 contacts were successfully traced, none were infected (11).

The literature review showed that while the existing evidence suggests a low risk of transmission of Lassa during air travel, it also suggests that the risk remains low even if a high-risk exposure occurred (2, 5).

Suggested approach

The risk assessment of possible transmission of Lassa fever on an aircraft should be undertaken on a case-by-case basis and should take into account the status of the index case, presence of symptoms during the flight, any potential exposures during the flight, and the goals of contact tracing. The assessment should follow the outline in Figure 4.2.

Criteria to be considered

Index case
The index case is a probable or laboratory-confirmed case of Lassa fever.

A patient could be considered a probable case,
if he or she has symptoms compatible with Lassa (malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhoea, myalgia, chest pain, hearing loss) (12);
AND
if he or she, within 21 days of symptom onset,
- had risk exposure to rats or their droppings in rural areas of West Africa (13);
  OR
- had contact with a case of Lassa fever (e.g. healthcare worker, caregiver, etc.).

WHO recommends a case definition for surveillance standards, which would also be helpful for contact tracing (14).

Epidemiological situation
Travel to West Africa: Certain West African countries are considered endemic areas for transmission of Lassa fever (13)[i].

Effective exposure
Direct contact to body fluids: Human-to-human transmission of Lassa virus occurs through direct contact with infectious body fluids such as blood, urine, faeces, or vomit. Therefore, contact tracing of a Lassa case should only be considered if exposure to blood, urine, faeces, or vomit occurred during the flight. Otherwise the likelihood of a transmission is considered negligible.

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[i] However, non-endemic countries may also be taken into consideration if the passenger has certain risk exposures. A new member of the arenavirus family, Lujo, which is similar to Lassa virus, was identified in a case from Zambia with secondary transmission in South Africa (15). Its exact epidemiology remains to be determined.

Time factor
Detection of the event within 21 days after the flight: The incubation period of Lassa is usually seven to 12 days but may range between three and 21 days (16–19). In order to find potential cases, passenger tracing should only be considered if the flight took place within the previous 21 days. After this time, a message to raise awareness among doctors and public health professionals should be considered.

Symptomaticity during flight
Symptomatic index case: No evidence exists that Lassa cases are infectious before the onset of symptoms. Therefore a trace-back should only be considered if the index patient was already symptomatic during the flight.

Other considerations

Purpose of contact tracing: Treatment for Lassa fever is available, and most effective if initiated early in the disease (20). Other reasons for contact tracing are to raise awareness for early detection and to prevent onward transmission.

The severity of the symptoms and infectiousness of the index case: Patients with more severe symptoms are more infectious, but as it is difficult to judge when the symptoms indicate infectiousness, severity was not a criterion for trace-backs. Instead, the presence of symptoms during the flight is used as the only criterion.

Route of transmission: The main route of transmission for the Lassa fever virus is direct contact with body fluids. Transmission through aerosols was considered negligible. Therefore, contact tracing is only considered if spilled body fluids are detected during the flight. In the absence of specific incidents, the use of the lavatory by the index case is not considered a risk for others and therefore not relevant when considering contact tracing.

Duration of flight: Since the transmission of Lassa fever virus is by direct contact to the index case and exposure to their body fluids, duration of flight is not relevant when considering a trace-back.

Starting to collect event and passenger information: We recommend a trace-back as soon as the diagnosis is laboratory confirmed. While waiting for laboratory results, the airline should be contacted and asked whether crew members remember (or even recorded) any incidents on board which resulted in potential exposures to crew or passengers. In addition, the availability of the passenger manifest should be ascertained. This will facilitate prompt action should Lassa fever be confirmed. If a diagnosis cannot be laboratory confirmed in a timely manner, contact tracing should be considered if the evidence strongly suggests a viral haemorrhagic fever as the likely cause of the index case's disease.

Scale of contact tracing

Passengers and crew with reported direct contact: Co-travellers and crew members who report direct contact **with body fluids** of the index case should be traced back. To gather this information, any records of significant events on the flight should be obtained from the airline.

Passengers +/-1 seat: As direct contact is the main route of transmission for Lassa, only the passengers who sat in direct proximity to the index passenger should be included in the trace-back, i.e. only passengers who were one seat away from the index case (+/- 1 seat in all directions) should be traced back. If the index case occupied an aisle seat, the three passengers seated directly across the aisle from the index case should also be traced back (see Figure 4.1).

Crew members of plane section: Crew members who provided in-flight service in the section of the aircraft where the index case was seated should be included in the trace-back, as well as other crew members who had direct contact with the patient.

Cleaning staff of plane section: The cleaning staff that cleaned the section and seat where the index case was seated should be traced back.

Template for Q&A sheet: Lassa fever contact tracing

The following is a template for public health experts who need to quickly develop a Q&A sheet to complement contact tracing activities. This template should be adapted according to the individual situation and to the decisions made by the public health authorities in charge.

When should contact tracing be considered?
Contact tracing should be considered:

- if the index case is a laboratory-confirmed Lassa case;

AND

- the index case was symptomatic during the flight;

AND

- the detection of the event took place within 21 days after the flight;

AND

- there was exposure to body fluids of the index case on board (blood, faeces, urine, vomit).

When is a patient infectious?

A symptomatic patient is considered potentially infectious.

Who should be considered for contact tracing?

The contact tracing should only include passengers who were one seat away from the index case (+/- 1 seat in all directions). Additionally, all persons who reported direct contact with body fluids of the index case should be traced back. Crew members who provided in-flight service for the section of the aircraft where the index case was seated as well as the cleaning staff for this section should be included in the trace-back.

Are there special considerations for individuals of higher susceptibility?

Specific risk groups with higher susceptibility to VHFs have not been identified. Consequently, trace-back criteria should only refer to exposure.

Although not associated with higher susceptibility, pregnant women have high rates of maternal death and fatal neonatal loss if infected with the Lassa virus (21), therefore the trace-back of pregnant women with potential exposure should be given a high priority.

4.2 Ebola fever

Literature review

The literature review did not find any event articles in the peer-reviewed literature related to Ebola virus on flights. Interviewed experts reported no events related to Ebola virus. One event article, retrieved from the grey literature, reported about a patient who took a commercial flight from Gabon to Johannesburg in 1996 for hospital treatment (22). During the time of flight, the diagnosis (Ebola haemorrhagic fever, later laboratory confirmed) was not known. He presented with fever and jaundice, both not severe. He was only traced back after a nurse caring for him died and Ebola was diagnosed. This happened some time after the flight, so no passenger trace-back was initiated (personal communication).

In the absence of flight-related Ebola events, we looked at other studies describing the risk of Ebola virus transmission: the reviewed studies show a low risk of transmission in the early phase of symptomatic patients, even with high-risk exposure. Risk of transmission may increase with transition to later stages of the disease with increasing viral titres (23). In a household study, secondary transmission only took place if direct contact occurred. No transmission was reported without direct physical contact (24). In an outbreak in 2000 in Uganda, the most important risk factor was direct repeated contact with a sick person's body fluids during the provision of care. The risk was higher when exposure took place during the late stages of the disease. Simple physical contact with a sick person appeared to be neither necessary nor sufficient for contracting Ebola infection: one person who developed the disease was probably infected by contact with heavily contaminated fomites, and many persons who had simple physical contact with a sick person did not become infected. Transmission through heavily contaminated fomites is apparently possible (25). In summary, physical contact with body fluids seems necessary for transmission, especially in the early stages of disease (as is likely in passengers still able to travel on a plane), while in the later stages contact with heavily contaminated fomites might also be a risk for transmission.

Suggested approach

An assessment of possible transmission of Ebola on an aircraft should be undertaken on a case-by-case basis. This should occur after careful risk assessment, taking into account the index case status, the presence of symptoms during the flight, any potential exposures during the flight, and the goals of the contact tracing. The assessment should follow the outline in Figure 4.2.

Criteria to be considered

The index case

The index case is a probable or laboratory-confirmed case of Ebola fever.

A patient could be considered as a probable case:

if he or she has symptoms compatible with Ebola fever (sudden onset of fever, intense weakness, muscle pain, headache, sore throat, vomiting, diarrhoea, rash, impaired kidney and liver function, internal and external bleeding) (26);
AND
if he or she, within 21 days of symptom onset,

- had risk exposure in sub-Saharan Africa (medical treatment, contact to body fluids of ill persons, contact with primates or bats in areas with suspected or known Ebola activity) (27);
  OR
- had contact with a case of Ebola fever.

WHO recommends a case definition for surveillance standards, which would also be helpful for contact tracing (14).

Epidemiological situation

Travel to sub-Saharan Africa: Certain sub-Saharan African countries are considered risk areas for transmission (27). However, it is important to also take into consideration other countries than those where cases have already been reported, as the index patient could be the first case in a country.

Risk exposure: Evidence points to bats as one of the reservoirs of Ebola fever (28). Also, contact with primates has been reported in Ebola cases (29,30). Human-to-human transmission has taken place during medical treatment, through direct contact with body fluids of ill or dead persons. Big outbreaks have been reported in hospital settings. This should be taken into consideration when assessing the risk exposure of a probable case.

Effective exposure

Direct contact with body fluids: Human-to-human transmission of Ebola virus occurs through direct contact with infectious body fluids. However, Ebola virus has also been detected in sweat (31,32) and, although the risk of infection is very low, passengers who may have had direct contact with the case should be contacted and followed-up, even if exposure to body fluids was not reported.

Time factor

Detection of the event within 21 days after the flight: The incubation period of Ebola usually ranges between two and 21 days (33). In order to find potential cases, tracing passengers should only be considered if the flight took place within the previous 21 days. After this time, a message to raise awareness among doctors and public health professionals should be considered.

Symptomaticity during flight

Symptomatic index case: Ebola cases are not considered to be infectious before they are symptomatic. Therefore a trace-back should only be considered if the index patient was already symptomatic during the flight.

Other considerations

Purpose of contact tracing: No treatment is available for Ebola, which limits contact tracing to the prevention of onward transmission and awareness-raising for early detection.

The severity of the symptoms and infectiousness of the index case: Patients with more severe symptoms are more likely to be infectious, but for practical reasons the severity of symptoms is not considered a suitable criterion for trace-backs; instead, the presence of any symptoms displayed during the flight that are compatible with Ebola should be used as criteria.

Route of transmission: The main route of transmission for a VHF infection is by direct contact with infectious body fluids. The transmission of VHF through aerosol spread was considered negligible. In the absence of specific incidents, the use of the lavatory by the index case is not considered a risk for others and therefore not relevant when considering contact tracing.

Duration of flight: Since direct contact is necessary for the transmission of Ebola, the duration of flight is not taken into consideration when considering a trace-back.

Starting to collect event and passenger information: We recommend a trace-back as soon as the diagnosis is laboratory confirmed. While waiting for laboratory results, the airline should be contacted and asked whether crew members remember (or even recorded) any incidents on board which resulted in potential exposures to crew

or passengers. In addition, the availability of the passenger manifest should be ascertained. This will facilitate prompt action should Ebola be confirmed. If a diagnosis cannot be laboratory confirmed in a timely manner, contact tracing should be considered if the evidence strongly suggests a viral haemorrhagic fever as the likely cause of the index case's disease.

Scale of contact tracing

Passengers and crew with reported direct contact: Co-travellers and crew members who had reported direct body contact with the index case should be traced back. To gather this information, any records of significant events on the flight should be obtained from the airline.

Passengers +/-1 seat: As direct contact is the main route of transmission for Ebola, only the passengers who were seated in direct proximity to the index passenger should be included in the trace-back, i.e. only passengers who were one seat away from the index case (+/- 1 seat in all directions) should be traced back. If the index case occupied an aisle seat, the three passengers seated directly across the aisle from the index case should also be traced back (see Figure 4.1).

Crew members of plane section: Crew members who provided in-flight service in the section of the aircraft where the index case was seated should be included in the trace-back, as well as other crew members who had direct contact with the patient.

Cleaning staff of plane section: The cleaning staff that cleaned the section and seat where the index case was seated should be traced back.

Template for Q&A sheet: Ebola fever contact tracing

The following is a template for public health experts who need to quickly develop a Q&A sheet to complement contact tracing activities. This template should be adapted according to the individual situation and the decisions made by the public health authorities in charge.

When should contact tracing be considered?
Contact tracing should be considered:

- if the index case is a laboratory-confirmed Ebola case;
AND

- the index case was symptomatic during the flight;
AND

- the flight took place less than 21 days before the detection of the event.

When is a patient infectious?
A symptomatic patient is considered as potentially infectious.

Studies show a low risk of transmission in the early phase of symptomatic patients, even if high risk exposure is experienced. Risk of transmission may increase with transition to later stages of the disease with viral titres increasing (23,24).

Who should be considered for contact tracing?
The contact tracing should only include passengers who were seated in direct proximity to the index case, i.e. only passengers who were one seat away from the index case (+/- 1 seat in all directions). Additionally, all persons who reported direct contact with the index case should be traced back. Crew members who provided in-flight service in the section of the aircraft where the index case was seated should be included in the trace-back, as well as cleaning staff that cleaned the section and seat where the index case was seated.

Are there special considerations for individuals of higher susceptibility?
Specific risk groups with higher susceptibility to VHFs have not been identified. Consequently, criteria for inclusion in a trace-back should only depend on the exposure.

4.3 Marburg fever

Literature review

The literature review only showed few peer-reviewed reports. One was an event where a Marburg patient travelled on a plane to the Netherlands in 2008 (34). No transmission occurred in this event. A US tourist who had

visited the same bat cave in Uganda as the Dutch case in January 2008, developed symptoms after returning to the US and was retrospectively diagnosed in January 2009 (35).

Literature information about risk of transmission is very sparse. The WHO fact sheet on Marburg fever states that transmission of the virus from person to person requires extremely close contact with a patient. Infection results from contact with blood or other body fluids (faeces, vomit, urine, saliva, and respiratory secretions) with high virus concentration, especially when these fluids contain blood. Infection through casual contact is thought to be exceedingly rare (36). The largest Marburg outbreak recorded was in Angola in 2005, with 374 reported cases (158 laboratory confirmed) and 329 deaths (37). The disease spread particularly among people exposed to the Marburg virus during home care or at funerals, via contact with body fluids of those who died from the disease. The dangerous use of home-based injections was also identified as a major cause of the outbreak's spread (38, 39).

However, in a study in the Democratic Republic of Congo in 1998, no antibodies were found in HCW despite frequent high-risk procedures and without stringent barrier nursing. In the original outbreak in 1967, the 32 cases reported produced only six secondary infections in close family members (31). In another study, only one of 207 close contacts of a case patient with Marburg contracted the virus (18).

Suggested approach

An assessment of possible transmission of Marburg on an aircraft should be undertaken on a case-by-case basis. This should occur after careful individual risk assessment, taking into account the index case status, the presence of symptoms during the flight and the purpose of the contact tracing. The undertaken assessment should follow the outline in Figure 4.2.

Criteria to be considered

The index case
The index case is a probable or laboratory-confirmed case of Marburg.

A patient could be considered as a probable case:

if he or she has symptoms compatible with Marburg (abrupt onset, severe headache, severe malaise, muscle aches and pains, high fever, severe watery diarrhoea, abdominal pain and cramping, nausea, vomiting) (36); *AND*
- if he or she, within 21 days of symptom onset, had risk exposure in sub-Saharan Africa (medical treatment, contact with body fluids of ill persons, contact with primates or bats – all of the above in areas with suspected or known Marburg activity) (27);

OR
- had contact with a case of Marburg haemorrhagic fever.

WHO recommends a case definition for surveillance standards, which would also be helpful for contact tracing (14).

Epidemiological situation
Travel to sub-Saharan Africa: Certain sub-Saharan African countries are considered risk areas for transmission (27). However, it is important to also take into consideration other countries than those where cases have already been reported, as the index patient could be the first case in a country.

Risk exposure: The reservoir of Marburg is not known, nonhuman primates and bats are recognised sources of infection (34,35,40). Human-to-human transmission route is through direct contact with blood or other infected body fluids. This should be taken into consideration when assessing the risk exposure to a probable case.

Effective exposure
Direct contact with body fluids: Human-to-human transmission of Marburg virus occurs through direct contact with infected body fluids. As the transmission of Marburg virus through sweat cannot be excluded, and although the risk is very low, passengers who may have had direct contact with the case should be contacted and followed-up, even if exposure to body fluids was not reported.

Time factor
Detection of the event within 21 days after the flight: Incubation period for Marburg fever ranges between two and 14 days (41). In order to find potential cases within the possible longest incubation period, tracing passengers should only be considered if the flight took place within the previous 21 days. To keep in line with the other VHFs we decided to keep the 21-day period for Marburg fever. After this time, a message to raise awareness among doctors and public health professionals should be considered.

Symptomaticity during flight

Symptomatic index case: Marburg cases are not considered to be infectious until they become symptomatic (42). Therefore a trace-back should only be initiated if the index patient was symptomatic during the flight.

Other considerations

Purpose of contact tracing: No treatment is available for Marburg, which limits contact tracing to the prevention of onward transmission and awareness-raising for early detection.

The severity of the symptoms and infectiousness of the index case: Patients with more severe symptoms are more infectious. As it is difficult to judge when the symptoms indicate infectiousness, severity of symptoms is not considered a suitable criterion for trace-backs; instead, the presence of any symptoms displayed during the flight that are compatible with Marburg should be used as criteria.

Route of transmission: The main route of transmission for a VHF infection is by direct contact with infectious body fluids. The transmission of VHF through aerosol spread was considered negligible. In the absence of specific incidents involving body fluids, the use of the lavatory by the index case is not considered a risk for others and therefore not relevant when considering contact tracing.

Duration of flight: Since direct contact is necessary for the transmission of Marburg, the duration of flight is not taken into consideration when considering a trace-back.

Starting to collect event and passenger information: We recommend a trace-back as soon as the diagnosis is laboratory confirmed. While waiting for laboratory results, the airline should be contacted and asked whether crew members remember (or even recorded) any incidents on board which resulted in potential exposures to crew or passengers. In addition, the availability of the passenger manifest should be ascertained. This will facilitate prompt action should Marburg be confirmed. If a diagnosis cannot be laboratory confirmed in a timely manner, contact tracing should be considered if the evidence strongly suggests a viral haemorrhagic fever as the likely cause of the index case's disease.

Scale of contact tracing

Passengers and crew with reported direct contact: Co-travellers and crew members who had reported direct body contact to the index case should be traced back. To gather this information, any records of significant events on the flight should be obtained from the airline

Passengers +/-1 seat: As direct contact is the main route of transmission for Marburg, only the passengers who were seated in direct proximity to the index passenger should be included in the trace-back, i.e. only passengers who were one seat away from the index case (+/- 1 seat in all directions) should be traced back. If the index case occupied an aisle seat, the three passengers seated directly across the aisle from the index case should also be traced back (see Figure 4.1).

Crew members of plane section: Crew members who provided in-flight service in the section of the aircraft where the index case was seated should be included in the trace-back, as well as other crew members who had direct contact with the patient.

Cleaning staff of plane section: The cleaning staff that cleaned the section and seat where the index case was seated should be traced back.

Template for Q&A sheet: Marburg fever contact tracing

The following lines show a template for public health experts who need to quickly develop a Q&A sheet to complement contact tracing activities. This template should be customised to the current situation and to the decisions made by the public health authorities in charge.

When should contact tracing be considered?

Contact tracing should be considered:

- if the index case is a laboratory-confirmed Marburg case;

AND

- the index case was symptomatic during the flight;

AND

- the flight was less than 21 days before the detection of the event.

When is a patient infectious?

A symptomatic patient is considered potentially infectious.

Who should be considered for contact tracing?

The contact tracing should only include passengers who were seated in direct proximity to the index case, i.e. only passengers who were one seat away from the index case (+/- 1 seat in all directions). Additionally, all persons who reported direct contact with the index case should be traced back. Crew members who provided in-flight service in the section of the aircraft where the index case was seated should be included in the trace-back, as well as cleaning staff that cleaned the section and seat where the index case was seated.

Are there special considerations for individuals of higher susceptibility?

Specific risk groups with higher susceptibility to VHFs have not been identified. Consequently, inclusion criteria for trace-back should only depend on the exposure.

Figure 4.1. **Relevant area for trace-backs, viral haemorrhagic fevers (Lassa, Marburg, Ebola)**

Figure 4.2. **Risk assessment algorithm, viral haemorrhagic fevers (Lassa, Marburg, Ebola)**
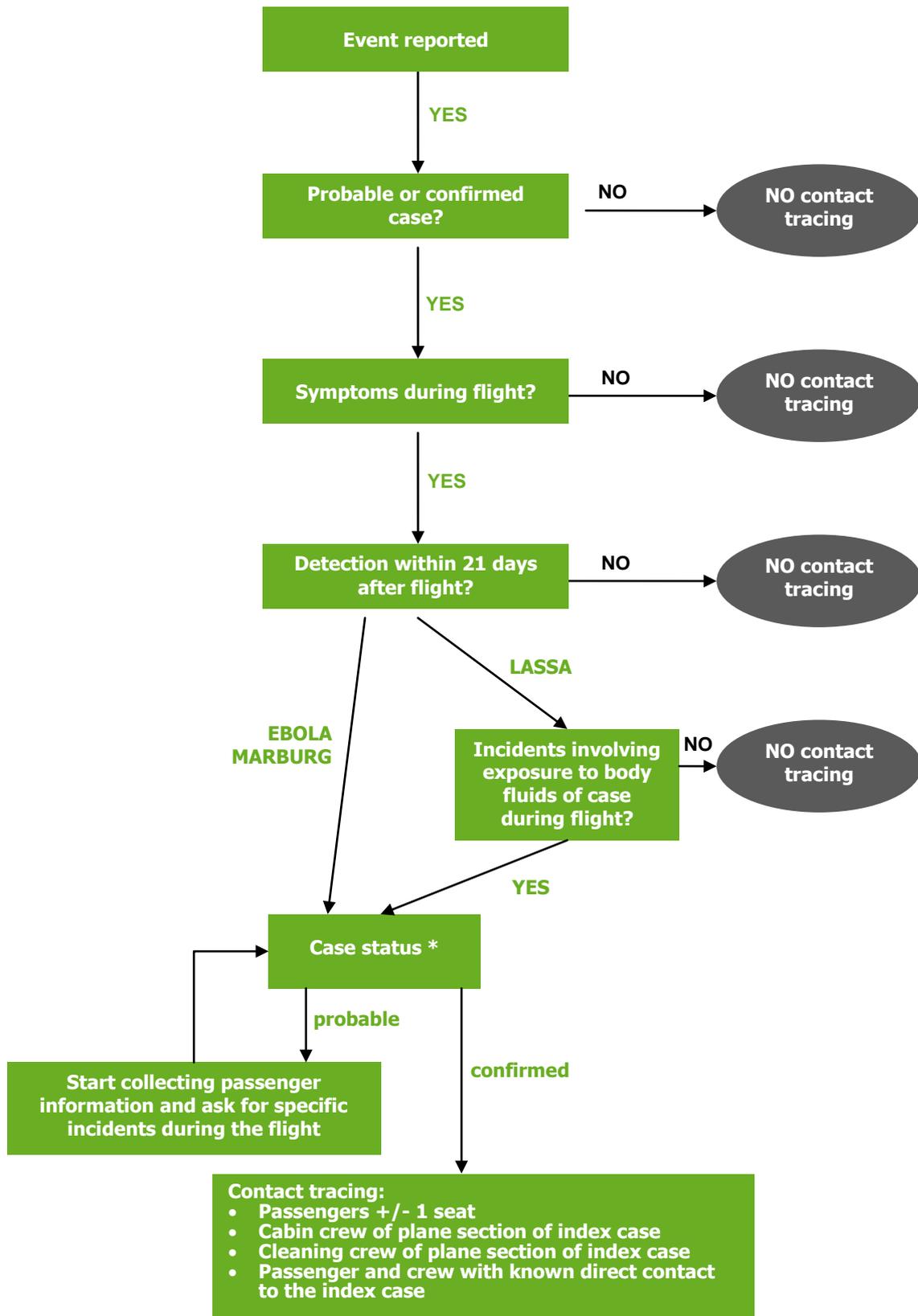
* If the diagnosis cannot be laboratory confirmed (e.g. if clinical samples are unavailable), contact tracing should be considered if the clinical and epidemiological picture is strongly suggestive of a VHF as the likely diagnosis

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5 Measles

5.1 Literature review

The detailed systematic review of the literature identified eight events (including an instance with a possibly infectious measles case on board an aircraft, with evidence of transmission during flight [1–4,6,7,9,10,17]. Further events were reported, but in these instances measles transmission during the flight could not be detected [5,8] or determined [11]. Contact tracing of passengers was initiated in five events. Evidence of further transmission to other passengers was found four times [6,7,10,17], and in one event no transmission occurred [5]. In two events post-exposure prophylaxis (PEP) was offered to susceptible passengers [6,10]. There is evidence that restricting contact tracing to passengers seated in rows close to the index case is inadequate [10], as secondary cases were identified seated as far as eight rows from the index case. No evidence was published that the risk of measles transmission was related to the duration of air travel or seating distance from the index case in the airplane.

Overall, these eight events provide substantial evidence that measles transmission on board airplanes may occur ([2–4,6,7,9,10,17]. This is in line with the very high infectiousness of the disease and observations of transmission during travel by other means of transportation such as busses [12,13]. The risk of transmission depends on the likelihood of being both exposed and susceptible (neither being fully vaccinated nor having had measles previously).

5.2 Suggested approach

Contact tracing of flight passengers and attendants is strongly recommended if PEP can still protect susceptible persons, prevent complications, and limit further transmission – provided that risk assessment, available resources, and the feasibility of measles control allow that effort. PEP includes post-exposure vaccination and administration of human normal immunoglobulin (HNIG).

The time frame during which an infectious case is identified is of utmost importance for the decision on appropriate measures, including contact tracing: intervention approach and goals differ depending on whether a symptomatic case was already identified on board or later, after disembarking the aircraft.

An assessment of the likelihood of measles transmission on an aircraft should only be done after careful individual risk assessment on a case-by-case basis, taking into account the index case status according to the case definition (see Figures 5.3 and 5.1), the symptoms of the index case, the epidemiological situation for measles in the country of departure and arrival, and the options for intervention.

The assessment based on the following criteria should follow the outline in Figure 5.2.

5.3 Criteria to be considered

The index case

Symptoms and infectiousness of the index case
Almost all infected persons will present with symptoms. The incubation period for measles usually ranges from seven to 18 days from exposure to onset of fever; in exceptional cases 19 to 21 days have been observed [15]. The median incubation period from infection to the onset of rash is 13 days [16].

The infectious period starts four days prior to the onset of rash and lasts until four days after onset of rash [15]. Typical symptoms in the prodromal period, which usually starts three days prior to the onset of rash, include cough, runny nose, red eyes, and fever. Measles is an airborne disease spread by droplets. Paroxysmal cough is likely to be associated with increased infectiousness [18].

Categories of the index case
Considering the fact that the EU case definition of a possible measles case is overly sensitive for contact tracing and the case definition of a probable case is too specific, we propose the use of an additional category ('likely case') for the operational purpose of contact tracing.
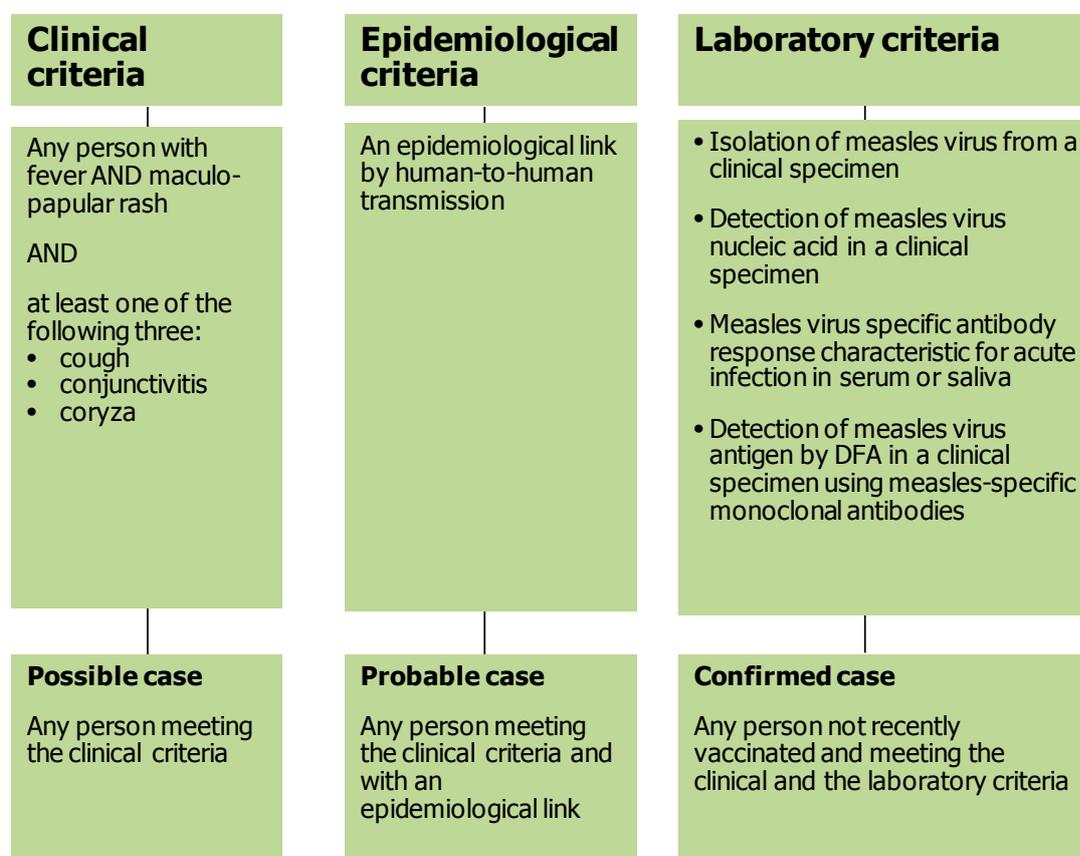
An index case is assessed as 'likely', based on:

- epidemiological considerations, such as immunisation history, travel history to an endemic area or an area where measles cases are reported or belong to a population group with high risk of being susceptible; and

- presenting with symptoms indicating measles, e.g. cough, runny nose, red eyes, fever, and rash.

The index case is a probable or laboratory-confirmed measles case according to the EC measles case definition (Figure 5.1 [14]).

Figure 5.1. EU case definition for measles [14]

Clinical criteria	**Epidemiological criteria**	**Laboratory criteria**
Any person with fever AND maculo-papular rash AND at least one of the following three: • cough • conjunctivitis • coryza	An epidemiological link by human-to-human transmission	• Isolation of measles virus from a clinical specimen • Detection of measles virus nucleic acid in a clinical specimen • Measles virus specific antibody response characteristic for acute infection in serum or saliva • Detection of measles virus antigen by DFA in a clinical specimen using measles-specific monoclonal antibodies
Possible case Any person meeting the clinical criteria	**Probable case** Any person meeting the clinical criteria and with an epidemiological link	**Confirmed case** Any person not recently vaccinated and meeting the clinical and the laboratory criteria

Epidemiological situation

Evidence of ongoing measles transmission in country of departure
Based on clinical symptoms alone, a symptomatic passenger is more likely to have measles if originating from a country were measles is still endemic or measles outbreaks occur. In a country with ongoing transmission, vaccination coverage is considered sub-optimal, increasing the likelihood of susceptible passengers on board.

However the likelihood of being susceptible is not only related to vaccination coverage alone but also depends on individual aspects such as eligibility to vaccination (as determined by age or health status) or belonging to certain groups with lower coverage (e.g. hard-to-reach populations, objectors to vaccination).

Evidence of no transmission in country of arrival
In a country were measles elimination is achieved or within reach, usually strong efforts are made to prevent measles importation and next-generation cases due to imported cases. Thus, in these countries contact tracing is recommended to prevent re-introduction and further spread of measles.

Effective exposure

Passengers who are susceptible (i.e. individuals who are not fully vaccinated or have not had measles previously, e.g. infants who are too young for vaccination) have a high risk of contracting measles, regardless of flight duration and seating distance from the index case, due to the high infectiousness of the virus.

Time factor

Flight occurrence within the past five days (the limit of five days was chosen considering the window of opportunity for providing HNIG (six days), minus at least one day needed for organising the intervention): According to international protocols, PEP using vaccination with a measles-containing vaccine is recommended

within three days after exposure for unvaccinated persons without contraindications. Children too young to be vaccinated, susceptible persons (i.e. individuals who are not fully vaccinated or have not had measles previously) with increased risk for complications, pregnant women, and immunocompromised patients should receive HNIG within six days after exposure, if available and possible. Alternatively, HNIG should be given according to national recommendations on PEP for measles.

Even if the assessment reveals that exposure on board might have led to infection, consideration of contact tracing is only warranted if administration of PEP is still possible or containment measures are still an option. This depends on the time of exposure and the time necessary to prepare the intervention.

5.4 Other considerations

Any identified measles case on a plane (regardless of the level of infectiousness, the time elapsed, and the epidemiological situation as described above) should be reported to the country of destination so that surveillance activities can be enhanced if necessary.

Before the flight

Patients who suspect they may have contracted measles due to recent exposure and recent onset of symptoms should seek medical/public health advice prior to embarkation.

Patients with laboratory-confirmed measles should avoid air travel. If patients with laboratory-confirmed measles are unable to cancel their flight, patients should be asked to delay their flight by a minimum of five days after onset of rash. If it is not possible to put off or delay travel plans, a travel protocol should be agreed between the patient, the local public health authority (public health team), and the airline in question. Instruct the patient to cover nose and mouth when coughing to reduce the spread of infections, apply distancing measures during the flight, and provide a face mask with instructions for proper use for the patient.

During the flight

Any likely, probable or confirmed measles case travelling during his infectious period should be relocated to an isolated seat separate from other travellers (if possible) and provided with a surgical face mask and a sufficient amount of disposable tissues. Flight attendants should follow IATA guidelines for infection control and, if possible, collect locator cards from travellers to facilitate contact tracing, if necessary. It is recommended to inform the ground staff and health authorities at the airport of arrival.

5.5 Template for Q&A sheet: measles contact tracing

The following is a template for public health authorities who need to quickly develop a Q&A sheet to complement contact tracing activities. This template is indicative only and should be adapted according to the specific situation and to the decisions taken by the public health authorities in charge.

When should contact tracing be considered?

Contract tracing should primarily be considered when interventions are likely to be effective (e.g. timely identification of cases allowing PEP for contacts) or will contribute to maintain measles elimination/control in a Member State (low-endemic areas).

More specifically, contact tracing should be considered:

- if the index case is a probable or laboratory-confirmed measles case according to EU case definition or can be assessed as likely to have measles based on symptoms, immunisation status, travel history, or belonging to a high-risk population;

AND

- if the index case travelled during his/her infectious period;

AND

- if the flight occurred within the previous five days.

The limit of five days was chosen considering the window of opportunity to provide HNIG (six days), minus at least one day needed for organising the intervention.

After five days, contact tracing might still be an option if:

- there was an infectious case on board as described above;

AND

- the incubation period has not elapsed;

AND

- information of the fellow passengers is still available (by passenger manifests or locator cards);

AND

- there is evidence of transmission in the country of origin/departure;

AND

- measles elimination is achieved or within reach in country of arrival;

AND

- resources are available.

Therefore, countries close to measles elimination may consider contact tracing of all passengers if a probable or confirmed case of measles arrives who has been travelling while being infectious, even after the time for effective PEP has elapsed. The rationale is to identify secondary cases and ensure appropriate interventions to limit further spread.

When is a patient infectious?

Measles cases are considered infectious within four days before and four days after onset of rash.

Who should be considered for contact tracing?

Generally, all passengers and crew should be considered for contact tracing, but priority should be given to children below two years of age as they are likely to be unvaccinated (or not fully vaccinated) and have a higher risk of complications. Further prioritisation should be considered as the effective time window for contact tracing is short, particularly when aiming at PEP.

Contact tracing should also aim at identifying pregnant women and immunocompromised patients who might benefit from HNIG (see national recommendations).

For organisational reasons (provided that resources are available), the expert group recommends that contact tracing should commence with children below two years of age and passengers that were seated in the same row as the index case. Contract tracing should then proceed row by row in each direction, for as long as it is possible to carry out PEP or effective containment measures.

Figure 5.2. Risk assessment algorithm for contact tracing
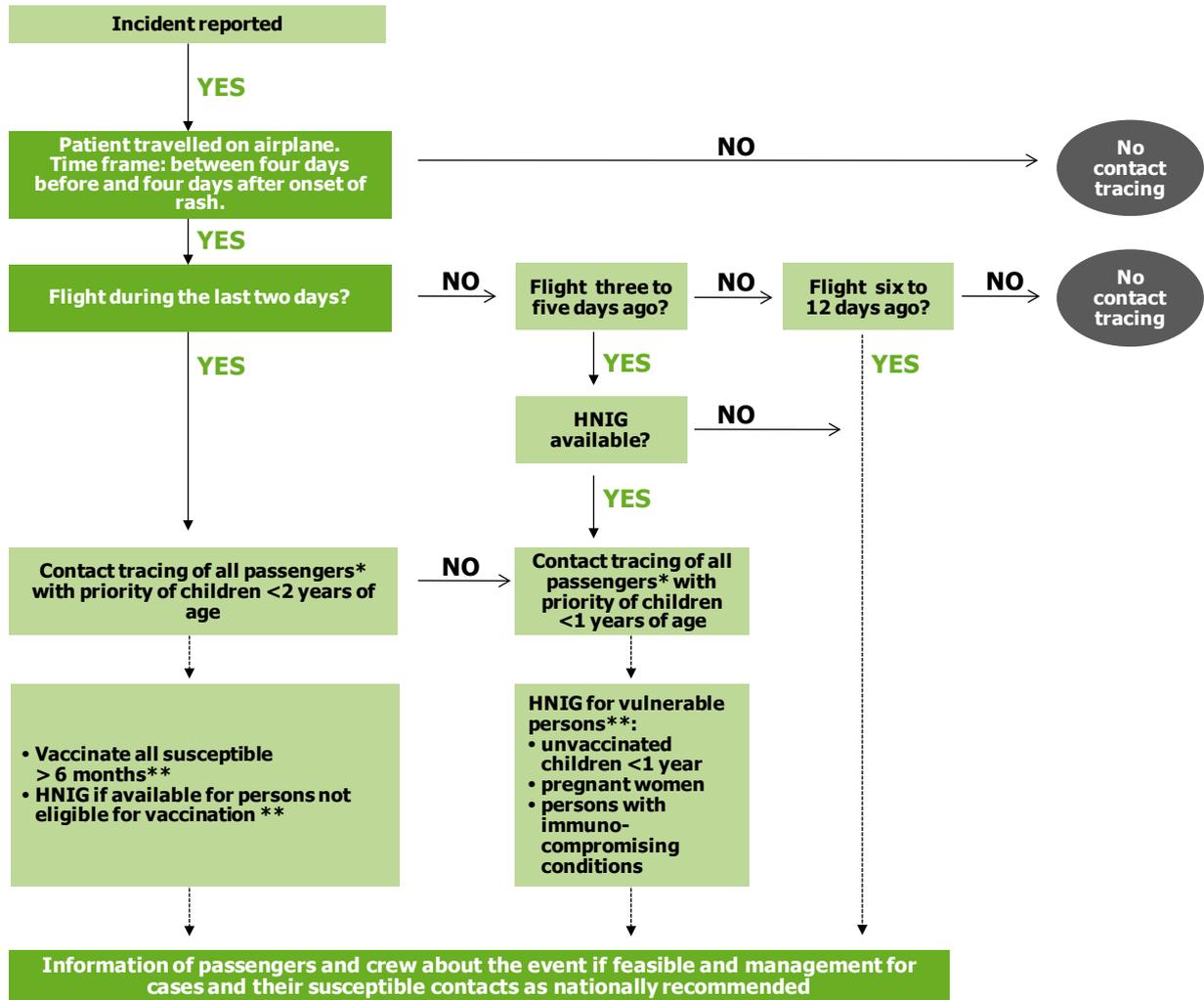
* For practical reasons, contract tracing should start with the seating row of the index case and then proceed row by row in both directions, for as long as time allows.

** As defined by national guidelines

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6 Rubella

6.1 Literature review

A systematic review of literature did not reveal any peer-reviewed event articles, grey literature event articles, or experts that could provide information on rubella transmission during air travel.

Therefore, there is no evidence available on the transmission of rubella during air travel.

6.2 Suggested approach

Public health intervention to prevent rubella in possibly exposed persons during air travel is generally not considered relevant, although unimmunised pregnant women with no previous history of rubella are at risk when exposed to rubella. Rubella infection during pregnancy, especially during the first trimester, can lead to congenital rubella syndrome and foetal death.

The absence of evidence for rubella transmission on board aircraft and the fact that rubella is usually a mild disease (up to 50% of cases are asymptomatic, rubella is three to four times less contagious than measles, and no effective post-exposure prophylaxis is available) does not justify extensive public health measures. In addition, the communication of a possible exposure could lead to undue anxiety in pregnant women and possibly to unnecessary interruption of pregnancies.

Annex. Examples of considerations for assessing evidence

The quality of available evidence was assessed by the experts, using elements of the Grading of Recommendations Assessment, Development and Evaluation (GRADE), by not only taking into consideration the available scientific evidence for transmission but also wider aspects. The following list includes examples of the considerations used by the experts in order to assess the evidence.

- Contact tracing requires significant resources (human, money, time) and should be implemented wisely.

- Aircraft manifests lack uniform standards across airlines and passenger manifests are rarely kept after 48 hours, which limits the possibility to trace and detect events.

- Multiple factors need to be taken into account for decision making on contact tracing, such as the following:
    - the epidemiological situation in the country of departure and arrival of a flight, the distribution of the disease by geographic region;
    - infectivity of the index case during the flight amidst symptomatic or pre-symptomatic stage;
    - evidence on potential transmission of disease during flight;
    - susceptibility of the population for the disease;
    - the maximum incubation period, as this reflects the time period during which it is possible to intervene with public health measures. Beyond this, contact tracing could be initiated for scientific purposes;
    - mode of transmission (airborne, droplet, contact);
    - ethical aspects (e.g. is treatment available, are containment and/or mitigation measures acceptable?);
    - actions that follow contact tracing should be a part of the decision making (e.g. what are the public health actions taken after identification of infected individuals? What can be offered to the infected individuals identified by contact tracing?);
    - possible alternatives for contact tracing (e.g. leaflets for passengers of the flight; information on airports?);
    - the susceptibility of the affected passengers;
    - level of vaccine coverage;
    - pathogen type/subtype, antibiotic resistance; and
    - the quality of the cabin air (e.g. influenced by length of ground delay).

- Purpose of identifying potential infected flight passengers by contact tracing, for example:
    - to initiate disease containment measures;
    - to initiate disease mitigation measures;
    - to delay spread of the disease;
    - to eradicate the disease.