Public Health England

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# PHE National Measles Guidelines

# August 2017

## Document information

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|---|---|
| **Title** | PHE national measles guidelines (August 2017) |
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| **Version** | 1 |
| **Date of Issue** | August 2017 |

## Document history

| Date | Reason for change | Issue number |
|---|---|---|
| August 2017 | The 2017 measles guidelines provide updated recommendations for the identification and management of contacts including revised definitions for a significant exposure outside of the household setting and updated indications for post-exposure prophylaxis. Additional information on laboratory testing services including the indications for urgent PCR testing, available through PHE regional laboratories, are summarised. | 1.0 |

## Document review plan

| | |
|---|---|
| Responsibility for review (disease group lead) | Mary Ramsay |
| Next review date | 2020 |
| Next issue date | - |

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## About Public Health England

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Published August 2017
PHE publications
gateway number: 2017249

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# Abbreviations

| | |
|---|---|
| A&E | Accident and Emergency |
| ALL | Acute Lymphoblastic Leukaemia |
| DPH | Director of Public Health |
| EIA | Enzyme Immunoassays |
| HCW | Health care worker |
| HIV | Human Immunodeficiency Virus |
| HNIG | Human Normal Immunoglobulin |
| HPT | Health Protection Team |
| ICT | Infection Control Team |
| LA | Local Authority |
| MMR | Mumps, measles, rubella |
| OF | Oral fluid |
| OH | Occupational Health |
| PEP | Post Exposure Prophylaxis |
| PHE | Public Health England |
| SSPE | Subacute Sclerosing Panencephalitis |
| WHO | World Health Organization |

# Section 1: Background

## 1.1. Introduction

Measles is highly infectious - the most infectious of all diseases transmitted through the respiratory route. Measles can be severe, particularly in immunosuppressed individuals and young infants. It is also more severe in pregnancy, and increases the risk of miscarriage, stillbirth or preterm delivery [1].

The most effective way to control measles is by achieving high uptake of two doses of measles, mumps, rubella (MMR) vaccine. High sustained coverage is key to achieving measles elimination - defined by the World Health Organisation (WHO) as the absence of endemic measles circulation for at least 12 months in a country with a high-quality surveillance system [2]. While recent uptake of MMR in England has been >90% for the first dose and >85% for the preschool booster, overall coverage remains below the ≥95% World Health Organisation (WHO) target.

As a country approaches measles elimination and measles incidence declines, sporadic cases and clusters can continue to occur when infection is imported. Measles surveillance therefore needs to be highly sensitive to detect sporadic cases and to classify cases as endemic or imported/import-related on the basis of complete epidemiology and the viral sequence information. Determining epidemiological and virological links between cases is also vital for detecting outbreaks. Outbreaks pinpoint susceptible communities where vaccination coverage is low, and thus inform targeted vaccination activity. In recent years, several such outbreaks have occurred, particularly amongst Charedi Orthodox Jewish communities, traveller communities and Anthroposophic (Steiner) communities, where vaccine uptake is suboptimal [3-5].

This document provides detailed public health guidance on the risk assessment of suspected measles cases, the management of their contacts and a description of the laboratory testing services available to support this. This is set in the context of a national surveillance system which is required to support and monitor progress towards WHO elimination targets.

Summary recommendations about post-exposure prophylaxis are also provided. However, for more detailed information about post-exposure prophylaxis, please refer to the PHE guidelines on Post-Exposure Prophylaxis for measles.

## 1.2. Rationale for public health action

As the incidence of measles decreases, the reliability of a clinical diagnosis declines and it is therefore important that every suspected case is investigated and excluded using appropriate laboratory methods. Good epidemiological and virological surveillance becomes an increasingly important element of measles control by establishing the source of sporadic cases. Early identification of chains of transmission is critical to ensure effective interventions can be targeted appropriately and initiated promptly to limit further spread. Given the limited effectiveness of most post-exposure interventions, accurate surveillance to inform this more pro-active strategy is a high priority.

Clinicians are required to notify all suspected measles cases as soon as possible to their local Health Protection Team (HPT), both as part of surveillance and so that timely public health management can be undertaken. Vulnerable contacts (such as immunosuppressed individuals, young infants and pregnant women) should be considered for post-exposure prophylaxis (PEP) to reduce the risk of complications. The first priority should be to identify and assess the risk to immunosuppressed individuals,[6] even after limited exposure or where exposed to cases of reinfection (See 1.3.2). For immunocompetent vulnerable individuals, local health protection teams should prioritise contact tracing efforts to those most likely to have had close prolonged exposure. Individuals in this group do not need to be identified and risk assessed if the index case is a presumed measles reinfection (see later section for definition).

Susceptible healthy contacts, including unimmunised children and adults, are unlikely to benefit from post-exposure vaccination, unless offered rapidly following exposure. Healthy contacts who work with vulnerable individuals, in particular health care workers, can be a source of transmission and need urgent assessment and possible exclusion from work. For others, vaccination should confer benefit against future exposures and will also provide protection against mumps and rubella infections. In outbreak settings, such as schools, mass vaccination of susceptible individuals should be considered to prevent tertiary transmission.

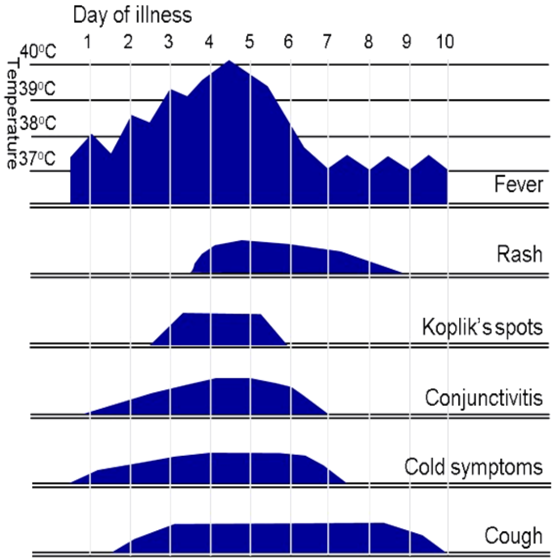
# 1.3. Clinical and epidemiological features of measles, and definitions

Robust measles surveillance and timely public health management rely on clinicians and public health professionals recognising measles based on a combination of clinical and epidemiological features. With increasing progress towards measles elimination, physicians are less likely to have experience of clinically diagnosing measles cases. The risk assessment of any suspected case requires consideration of a range of factors including the age of the case, vaccination history, clinical presentation and epidemiological features such as local outbreaks or an epidemiological link to a confirmed case. Collecting information on possible epidemiological links is essential to making a reliable risk assessment and will contribute towards a better understanding of measles transmission in the population.

## 1.3.1. Clinical presentation of primary measles infection

Figure 1 below shows the clinical course of primary measles infection and its main symptoms.

**Figure 1: Typical clinical course of primary measles infection**




Source: WHO Manual for the laboratory diagnosis of measles and rubella infection [7]

- Measles starts with a 2 – 4 day illness (‘**prodromal phase’**) before the rash appears, which typically includes high **fever, coryzal symptoms, cough and conjunctivitis**. The latter is a more specific symptom that differentiates measles from many other causes of influenza-like illness. Symptoms typically peak on the first day of the rash [6].

- **Fever** typically increases during the prodromal phase, peaks (generally >39$^0$C) around the rash onset, as shown in Figure 1, and will gradually decrease after that.

- **The maculopapular rash** generally starts on the face and behind the ears. The number of lesions/spots generally increase in the first 2 – 3 days, and their distribution expands further to the face, trunk, and can sometimes be generalised. Lesions can become confluent, particularly on the face and the trunk. The rash is red, blotchy, maculopapular (i.e. non-vesicular), not itchy, and generally lasts for 3 - 7 days, fading gradually [6].

- **Koplik spots** may appear around the time of the rash, sometimes one day before, and last for 2 – 3 days after the rash appears. These are small spots with white or bluish- white lesions, of about 2-3mm in diameter, on an erythematous base on the buccal mucosa. These can be confused with other lesions in the mouth and therefore their suspected presence is an unreliable marker for measles.

Several other common rash illnesses present with a similar clinical presentation, including roseola (HHV6 infection), fifth disease (parvovirus B19 infection) and scarlet fever and therefore identification based on clinical features alone, particularly in children, is often unreliable. The timing and nature of symptoms is often helpful in the differential diagnosis. For example, while symptoms, including fever, peak with the onset of rash in measles; in roseola, the onset of rash generally coincides with clinical improvement. A summary of the clinical features of each of these conditions is provided in Appendix A1.

### 1.3.2. Clinical presentation of measles reinfection

Cases of measles reinfection are generally mild, have a shorter duration and may not have the full triad of cough, coryza and conjunctivitis. In some cases the rash may not be typical. Re-infections are usually seen in a patient who has received two doses of measles-containing vaccine, and initial antibody testing may be misleading. The infectivity of these cases is low, and the initial diagnosis is usually made by PCR detection of low levels of measles virus RNA.

### 1.3.3. Complications of primary measles infection

The most frequent complications include viral pneumonitis and otitis media, as well as diarrhoea [6, 8]. Measles infection often leads to a temporary reduction in immune responses in the few weeks following infection, which may increase the risk of severe secondary bacterial and viral infections [1]. Tracheobronchitis (‘measles croup’) and pneumonia due to secondary bacterial infection are frequent complications of measles [6].

Encephalitis occurs more rarely, in about 0.05% to 0.1% of measles cases [9].

Subacute sclerosing panencephalitis (SSPE) is a very rare but very severe complication, occurring in about 0.01% of cases [9]. Cases of SSPE present a few years after measles infection with progressive neuro-cognitive symptoms which in most cases lead to coma and death. The risk of SSPE is increased in children who acquire measles before the age of 1 year.

Immunosuppressed individuals are at higher risk than immunocompetent individuals of developing prolonged and severe measles, and of suffering complications. Viral pneumonitis is the most frequent severe complication, which generally develops within two weeks of symptom onset. It is also the most common cause of death in immunosuppressed individuals [6]. Patients at highest risk include those who have severely impaired cell-mediated immunity, such as patients who have recently undergone bone marrow transplantation, patients with primary T-cell dysfunction, AIDS patients and patients with acute lymphoblastic leukemia (ALL). The risk of severe disease also remains high for patients with other forms of immunosuppression, such as those with other forms of malignancy, and those receiving high doses of steroids or other types of immunosuppressive drugs. Further information about the classification of immunosuppressed individuals is provided in the guidelines on Post-Exposure Prophylaxis for measles.

Measles can be particularly debilitating in very young infants and adults, who are more likely to develop complications and require hospitalisation. Measles can be severe in pregnant women and leads to an increased risk of prematurity and fetal loss, although there is no evidence that it leads to congenital defects [10]. Young infants are at high risk of complications such as pneumonia, otitis media, and SSPE and of a fatal outcome [11].

### 1.3.4. Transmission of primary measles and reinfection

Any patient with suspected measles should be advised to avoid contact with immunosuppressed individuals and other vulnerable people (such as pregnant women and infants). Although most suspected cases will turn out not to be measles it may be important to also avoid exposure to other causes of rash.

Individuals with primary measles infection are infectious from about 4 days before rash onset until 4 full days after the rash appears. Generally, secondary transmission is higher among close contacts, such as household members and non-household members with whom prolonged contact has occurred – such as students in the same classroom [12, 13].

Close prolonged interpersonal contact, such as in household settings, may also lead to a higher infectious dose of virus, which increases both the risk of transmission and the risk of developing more severe disease [6].

Transmission from reinfection is rare, probably due to low and transient infectivity.

Appropriate measures for triage and isolation in health care settings are essential to avoid prolonged exposure to suspected measles cases in waiting areas. In a recent series of cases associated with transmission in health care settings, five of the seven secondary cases were in the same room as the index case for 2.5 - 4 hours [14].

However, whilst most transmission events require face-to-face and/or prolonged contact, transmission through more casual contact has also been documented [15, 16]. For this reason, where a large group of people have been exposed, but the level of contact cannot be defined at an individual basis, it may be appropriate to initiate a mass communication, for example using approaches such as e-mail, text messaging or posters to “warn and inform” those who may have been exposed. This approach aims to encourage rapid self-identification of those who may be vulnerable individuals at high risk, to ensure that any linked cases are identified and diagnosed promptly and to provide reassurance to those who are likely to already be protected.

### 1.3.5. Epidemiological parameters

A good understanding of the transmission parameters of measles is important to undertake an appropriate risk assessment.

Information about the incubation period, period of infectiousness, transmission route and infectivity is summarised here:

- The **incubation period** is typically around 10-12 days from exposure to onset of symptoms, but can vary from 7 to 21 days [8].

- The **period of infectiousness** generally starts from about 4 days before the rash and lasts up to 4 days after the onset of rash [8].

- The **transmission route** of measles is mostly airborne by droplet spread or direct contact with nasal or throat secretions of infected persons. Much less commonly, measles may be transmitted by articles freshly soiled with nose and throat secretions, or through airborne transmission with no known face-to-face contact [15, 16].

- Measles **infectiousness** is one of the highest, with a basic reproduction number (R0) estimated around 15 – 20 (i.e. on average, there will be 15 - 20 individuals infected from a single case in a totally susceptible population).The secondary attack rate is highest among close unimmunised contacts, particularly household contacts [12, 13].

- The **vaccine effectiveness** of a single dose of MMR is around 90% and approximately 95% for two doses [12]. Although vaccine failure is rare, it can occur, particularly after a single dose. In settings with high rates of close interpersonal contacts, such as large households or school settings, controlling measles outbreaks requires a high coverage of 2 doses of MMR [12].

# 1.4. Surveillance of measles

Measles is a notifiable disease under the Health Protection Legislation (England) Guidance 2010. Health Protection Teams should work with local partners to raise awareness of measles among health professionals in order to facilitate early recognition, diagnosis and reporting (see section 3.1). Notification of the local Health Protection Team (HPT) fulfils the physician's responsibility to notify the Local Authority Proper Officer. Physicians managing the case should inform the HPT by phone as soon as is reasonably practical.

## 1.4.1. Laboratory surveillance

Since November 1994, enhanced surveillance including oral fluid (OF) testing of all notified and suspected cases has been provided through the Virus Reference Department (VRD) at Colindale. PHE Colindale supplies each HPT with OF testing kits.

When a suspected case of measles is reported and/or notified to the local HPT, an OF kit should be sent to the case (or their parent/guardian), or their general practitioner (GP). Samples should be taken as soon as possible after measles is suspected, and posted or couriered back to the Virus Reference Department, PHE Colindale, where it is tested for anti-measles IgM, measles IgG and/or measles RNA. Results are reported back to the patient's GP and to the local HPT.

Staff from the national immunisation team at PHE Colindale will follow up both cases confirmed by the VRD and cases which have tested positive at local diagnostic laboratories to obtain further epidemiological and clinical information and to document vaccination history.

Accurate national data is essential to understanding chains of transmission and identifying susceptible populations where the vaccination strategy may require modification.

## 1.4.2. International surveillance

To monitor progress towards measles elimination in England, the surveillance system should be able to identify and test all suspected cases of measles and reliably exclude cases based on appropriate laboratory testing in a WHO accredited laboratory [2]. To support the national surveillance system, laboratory testing of suspected measles cases is undertaken at VRD Colindale. This enables systematic testing, using reference methods which are both highly sensitive and specific.

Confirmatory testing, genotyping and further characterization are undertaken at the WHO Global Specialised Reference Laboratory based in VRD, Colindale. Measles virus sequences are entered on the WHO global Measles Nucleotide Sequence (MeaNS) database hosted by the VRD. VRD also report monthly data on the number of samples tested for measles to the WHO laboratory network.

PHE Colindale holds the central repository of all confirmed cases in England, and conducts systematic follow up of all confirmed cases. When combined with genotyping, this enables classification of imported cases and the identification and disentangling of local clusters. This process is critical to assessing progress towards elimination, to identify pockets of susceptibility and inform appropriate public health interventions.

PHE Colindale is responsible for reporting case-based information on confirmed cases to The European Surveillance System (TESSy), a database hosted at the European Centre for Disease Control and Prevention (ECDC), on monthly basis. Information is also reported independently to WHO Europe.

# 1.5. Laboratory investigation

### 1.5.1. Types of sample

Measles is a single-stranded RNA virus (*genus Morbillivirus, family paramyxoviridae*). There are 24 described genotypes, many of which have been eliminated as part of the global control of measles. Less than 10 genotypes are currently found globally, the distribution of which varies across geographic areas. Genotyping on confirmed samples is an integral part of laboratory surveillance for measles, to identify imported cases and monitor progress towards elimination.

Oral fluid (OF) is the optimal sample for measles surveillance. These samples are minimally invasive and are more acceptable than serum for confirming cases in infants and children. Importantly, OF can be tested for IgM, IgG and measles RNA, and can therefore: i) reliably **exclude** measles diagnosis, as well as confirm it; ii) indicate whether the case is a primary or reinfection; and iii) genotype confirmed cases. In the absence of OF, serum AND a mouth swab should be sent to VRD instead.

It is important to note that oral fluid samples cannot be used to assess the immune status of vulnerable contacts and serum should be used instead.

Figure 2 provides an overview of the timing of laboratory tests and biological parameters for measles diagnosis.

## Oral Fluid (OF)

- OF is the optimal sample for measles surveillance and should be taken from all suspected cases regardless of any other samples that may have already been taken, including when other laboratory methods have not confirmed measles.
- OF can be tested for both measles IgM/IgG using specific enzyme immunoassays (EIA), and viral RNA using specifically designed assays.
- Testing for IgM on OF is more sensitive and more specific than serum, particularly in the first few days after the rash, as IgM antibodies are positive in >50% of samples on day 1 of the rash, and in over 90% by day 3 of the rash (Figure 2). For oral fluid samples taken within 7 days of onset of disease, the VRD also performs PCR analysis for RNA detection.
- Oral fluid can be tested for measles IgG, and although measles IgG avidity is not done on OF samples, the relative level of measles IgG can be used to predict whether the case is a primary or re-infection with measles
- Measles viral RNA can be detected from before the onset of the rash and for at least 2 weeks after the onset of symptoms
- Genotyping for molecular epidemiology can be performed on PCR positive samples, which allows the characterisation of the virus into one of the 24 known genotypes, and help identify clusters and imported cases
- Measles genotyping also allows the distinction between wild-type virus and vaccine in those developing a measles-like rash following vaccination.
- OF is not appropriate to assess the immune status of contacts, for which serum should be tested instead (see below)

## Serum

- Serum samples can be used for IgM/IgG detection through enzyme immunoassays (EIA).

- Serum is the most appropriate sample to assess the immune status of contacts
- Serum samples may still be IgM negative within 3 days of onset of rash (Figure 2). This may be longer with IgM assays used in laboratories other than VRD, so documenting the timing of the sample in relation to rash onset is therefore essential to properly interpret results.
- Serum can be used to confirm reinfection by detection of high avidity measles IgG
- Serum is **not suitable** for PCR detection and viral typing
- Serum **cannot** be used to distinguish wild-type measles from vaccine-derived measles following recent vaccination

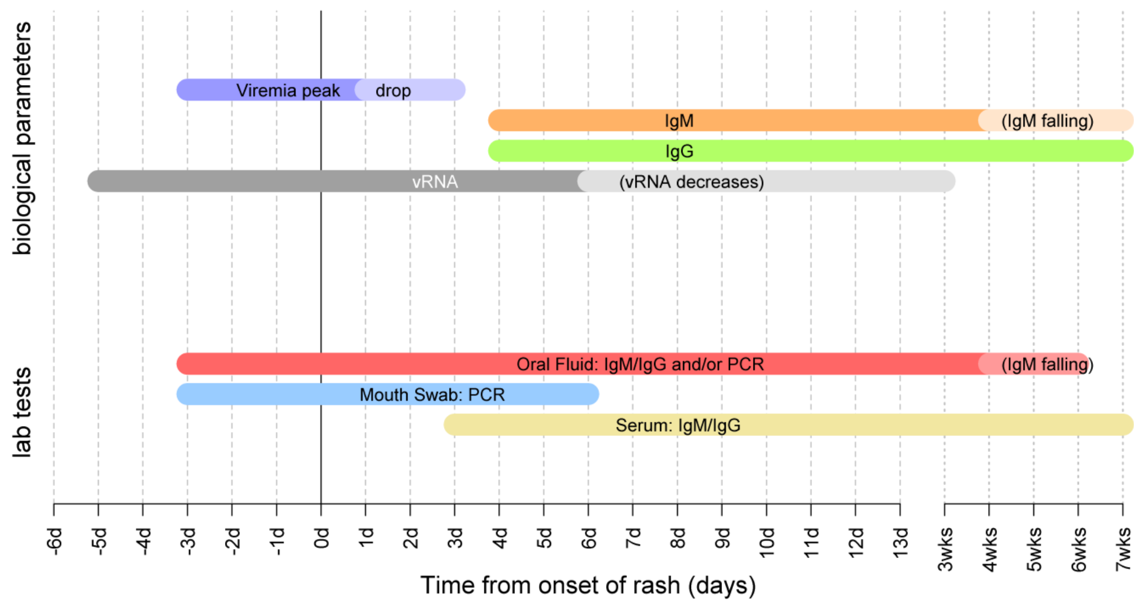
### Mouth swabs

- Can be used for PCR if collected within 6 days of the onset of rash. However a negative PCR result does not exclude a diagnosis of measles.
- Can be used to distinguish between wild-type virus and vaccine in someone who has recently been vaccinated
- Cannot be used to distinguish between a primary infection and a reinfection

### Throat swabs/Nasopharyngeal Aspirate/Urine/EDTA blood

- Such samples can be used for PCR if collected within 6 days of the onset of rash (see Figure 2)
- However, such samples **are less suitable and generally not advisable** for measles testing than the others mentioned above

**Figure 2: Dynamics of biological/viral indicators and timings of laboratory tests during primary measles infection**




## 1.5.2. Collection of samples

Kits for collecting oral fluid samples are available through the local PHE HPT. It is important that the sample is collected according to the instructions.

The swab needs to be rubbed along the gum line for two minutes.

If young children chew on the swab whilst the sample is being collected it should not compromise the sample collection. Sputum samples are not suitable for testing.

Oral fluid samples sent for measles IgM testing are also tested for total IgG as an indication of whether the sample is suitable for testing. If the total IgG is less than 1 mg/L then this indicates a poor quality sample and the test may need to be repeated. If oral fluid collection kits are not available then a serum sample PLUS mouth swab can be taken instead (and sent to VRD). A serum or oral fluid sample is required for distinguishing a primary infection from reinfection.

### 1.5.3. Laboratory definitions

- **Laboratory confirmed case of measles**: a suspected case with evidence of laboratory confirmation of acute measles infection (i.e. measles IgM in blood or oral fluid (OF) in the absence of recent vaccination, or confirmed wild-type measles RNA in any clinical specimen)

- **Presumed primary infection**: a laboratory confirmed case with no evidence of two doses of measles containing vaccine.

  - **Presumed reinfection:** detection of measles virus RNA in a suspected case of measles who has received two doses of measles containing vaccine. Reinfection can be confirmed by detection of high avidity measles IgG in serum or high levels of measles specific IgG in oral fluid. Measles IgM in serum may be negative.

### 1.5.4. Measles IgG testing of contacts

Assays can be either qualitative, where results are reported as positive, negative, or equivocal, or quantitative, where a defined measure of antibody level is provided. Enzyme immunoassays (EIA) are commonly used to test for measles IgG antibody, and various different assays are available. A positive test is useful to avoid unnecessary use of Human Normal Immunoglobulin (HNIG) or Intravenous Immunoglobulin (IVIG). However, although the specificity of most qualitative EIAs is high, their sensitivity remains low, and recommendations about post-exposure prophylaxis for equivocal results will differ by age and type of vulnerability (see specific guidelines).

# Section 2:

# Public Health Management

The management of the index case and their contacts, based on the initial assessment, is summarised in Figure 3. For accurate exclusion of measles **an oral fluid (OF) sample should always be requested, an OF kit sent to the patient or their GP, and a sample sent back to VRD** regardless of any local test results. The specimen should be taken as soon as possible and up to 6 weeks after the onset of rash (Appendix 3). All samples from cases testing positive at a local laboratory should be forwarded to VRD for confirmation and further characterisation.

## 2.1. Assessment of the Index case

When measles is not endemic, the positive predictive value of a clinical diagnosis is generally poor. In the absence of laboratory results, the likelihood of measles will therefore depend upon an assessment of the epidemiological features.

Case management should commence on the basis of this assessment, without waiting for the results of laboratory testing (even when requested urgently). Public health professionals should advise, as needed, on the use of appropriate laboratory samples for testing, at the right time, to reduce the likelihood of false negative results (Section 1.5).

### 2.1.1. Management definitions

For deciding on management, any patient in whom a clinician suspects measles requires an assessment to be undertaken by the HPT. For cases that are reported from sources other than a clinician, if the source is considered reliable and the history of the illness is compatible, the case should be managed as a suspected case whilst seeking further information. Box 1 summarises the information to collect. All suspected cases should be entered onto HPZone by the HPT.

Each case should be promptly investigated and classified in one of four categories: laboratory confirmed, epidemiologically confirmed, likely, or unlikely. For each reported case the classification may change as more information (e.g. on the epidemiology or laboratory results) becomes available. The distinction between likely and unlikely is a qualitative judgement based on the overall picture, rather than presence or absence of a specific number of criteria.

Categories are defined as follows:

- **Laboratory confirmed case of measles**: A suspected case with laboratory confirmation of acute infection (See section 1.5).

- **Epidemiologically confirmed case of measles**: A suspected case of measles who has a direct epidemiological link to a confirmed case of measles (i.e. where the onset of symptoms occurred within 7 – 21 days of exposure), or related to another epidemiologically confirmed case (e.g. in an outbreak setting).

- **Likely case of measles**: A **clinically typical*** case of measles **with epidemiological features** that either increase the likelihood of the patient having been exposed and/or favour the diagnosis of measles relative to other causes of rash illness. Epidemiological factors for risk assessment are summarised in Box 2.

  ***Clinically typical measles** is defined as measles presenting with classical symptoms, at the minimum:

  - Cough AND
  - Coryzal symptoms AND
  - Conjunctivitis AND
  - Fever ≥39$^{0}$C in the absence of antipyretics AND
  - Maculopapular rash

- **Unlikely case of measles:** A suspected case of measles which does not meet the definition of a likely case, either because it is clinically atypical or because the epidemiological context is not suggestive of measles.

Epidemiologically confirmed and likely cases of measles will require active contact tracing and management of vulnerable contacts without waiting for laboratory results (Section 3).

**Box 1: Patient information required for assessment of suspected measles cases**

**Demographic details**

- Name
- Sex
- Date of birth
- Address
- NHS number
- Contact details

**Clinical and laboratory features**

- **Signs and symptoms:** collect information on signs and symptoms, and importantly the onset dates of rash
- **Laboratory results:** document the type of tests conducted and results

**Individual epidemiological features**

- **Travel:** any travel within and outside the UK during the incubation period, with an assessment of whether travel was in an area where measles is known to be circulating.
- **Ethnic and cultural/religious background:** obtain details on the patient's ethnicity, and importantly, **assess whether the patient is a member of an under-vaccinated population group** (e.g. Charedi Orthodox Jewish community, Steiner community)
- **Immunisation history:** any known vaccination history or history of measles. If not known, ask where the patient was born and grew up to help assess the likelihood of vaccination and/or natural exposure.
- **Epidemiological link:** assess if there has been a known epidemiological link with another laboratory or epidemiologically confirmed case.

Generally, epidemiological information is a better predictor of measles than the clinical features. Given the implications of an incorrect classification, it is recommended that classification for management should be undertaken by or discussed with an experienced member of the Health Protection Team.

## Local transmission

If there have been no confirmed recent cases, despite adequate surveillance, in the area and the index case has not visited an area where cases are occurring, (either in the UK or internationally) during the incubation period, most cases can be assumed to be unlikely. To ensure that true cases are not missed however, there should be a very low threshold for OF testing and all suspected measles cases, whether or not they meet the clinically compatible criteria, should be tested (see algorithm Figure 3). [17]

**Box 2: Factors to consider in the risk assessment**

**Factors increasing the risk of exposure**

- Membership of a community known to be more susceptible e.g. traveller community, Charedi Orthodox Jewish community, anthroposophic (Steiner) communities, local community with low MMR vaccination coverage [2,3]
- Visited an area (local or international) where measles is known to be circulating, during the incubation period
- Attendance at large international mass gathering events, where substantial mixing occurs between individuals potentially travelling from areas where measles is circulating. This would include events such as music festivals etc. [17]

**Factors favouring the diagnosis of primary measles infection**

- Age: the likelihood of a suspected case being confirmed as measles is higher among adolescent and young adults. In infants and toddlers, measles-like clinical presentations due to other illnesses, such as roseola or scarlet fever, are common (see Appendix A1).

- A lack of immunity or incomplete vaccination: The diagnosis is more likely if cases are unvaccinated or partially vaccinated, and have no prior history of measles infection.

**Regardless of any other testing performed, all cases should have OF samples taken and sent to VRD for exclusion / confirmation of the diagnosis.**

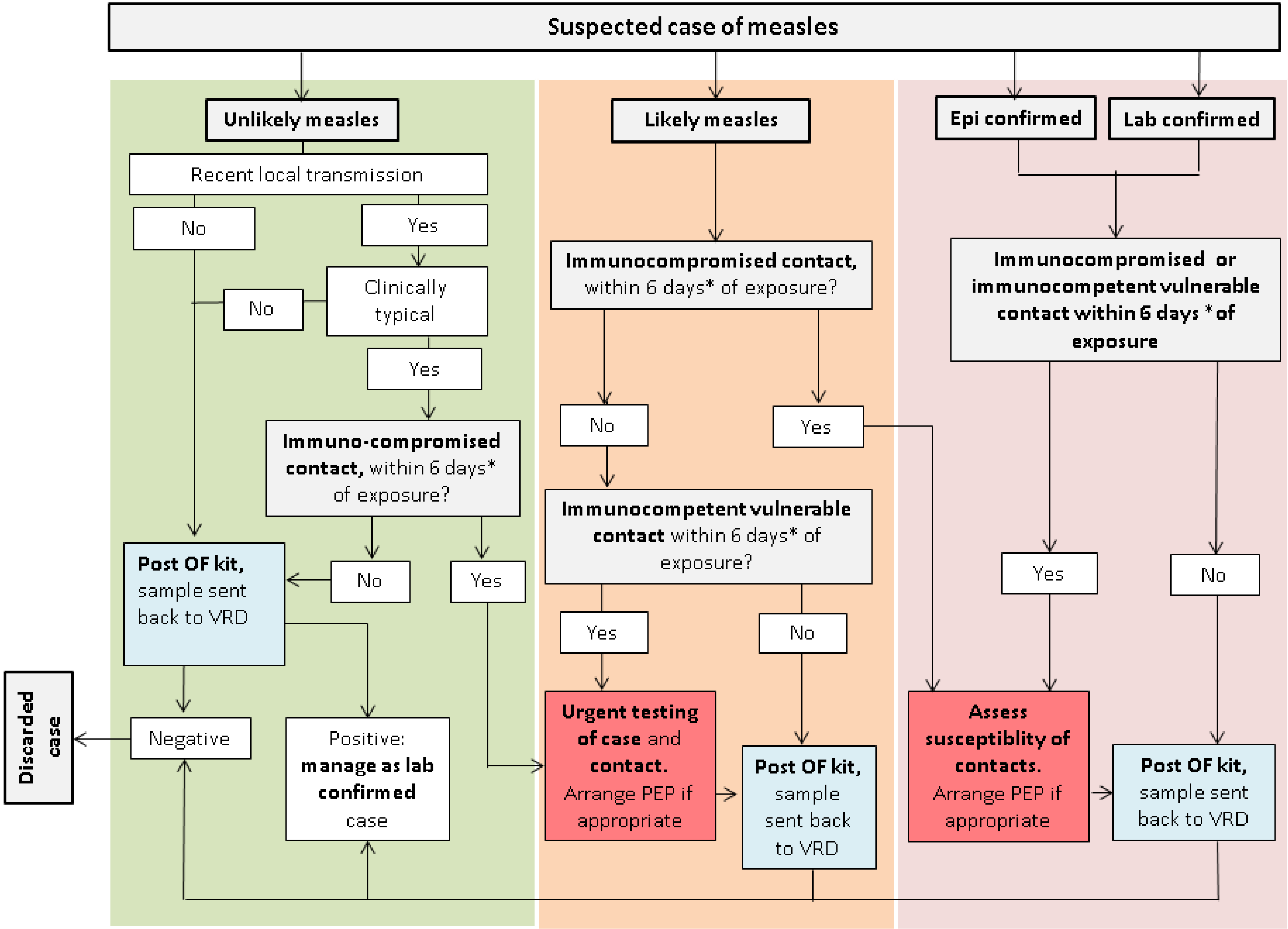
**HPZone case classification**

Using current HPZone classification terminology, likely and epidemiologically confirmed cases should be categorised as **probable** and unlikely cases as **possible.**

### 2.1.2. Urgent testing of the index case

In cases where rapid confirmation of the clinical diagnosis is required (e.g. when the clinical and epidemiological features do not strongly support measles but where vulnerable contacts have been exposed), PCR testing is available through the lead public health laboratories. The date of onset of symptoms including date of onset of rash and history/dates of MMR should be documented on the request form, which must be included with the sample. Local laboratory testing does NOT preclude the requirement of obtaining an oral fluid sample and sending it to Colindale for testing. In addition, a negative local result does not necessarily exclude measles, as it will depend upon the timing and adequacy of the sample and the test undertaken. Regardless of other testing, all locally-tested measles IgM and/or measles PCR positive samples should also be forwarded on to Colindale for further testing and characterisation.

**Figure 3: Risk assessment algorithm**



# 2.2. Management of contacts

### 2.2.1. Identification of contacts

The best way to protect individuals and to achieve measles elimination is with high vaccination coverage with two doses of MMR vaccine (≥95%). There is a duty of care to follow up each reported case of measles with the aim of identifying others who may have been exposed, both to a common source of infection and to the reported case. This will help to ensure early identification of chains of transmission and inform the need for pro-active interventions. Where practicable, **all contacts should be provided with information to ensure early detection of symptoms and exclusion from schools or other settings.**

Although post exposure prophylaxis is of limited effectiveness, there may be an opportunity to offer some protection to exposed vulnerable contacts. This requires identification of contacts in the following order of priority:

1. **Immunosuppressed contacts**
2. **Pregnant women and infants <12 months**
3. Health care workers
4. Healthy contacts

The management of each identified contact will depend on their exposure risk (including whether the index case is presumed to be primary or reinfection) and their vaccination status or susceptibility to measles. For immunosuppressed contacts, an appropriate assessment of the nature and level of immune suppression is essential to assess the requirement for post-exposure prophylaxis.

The aim of this section is to provide guidance on the risk assessment and need for post-exposure prophylaxis. More detailed information including recommended dosage and immunoglobulin products can be found in the PHE Post Exposure Prophylaxis for Measles.

### 2.2.2. Defining exposure risk

#### 2.2.2.1. Defined contacts

Generally, secondary transmission is higher among close contacts, such as members of a household or individuals who have close contact with each other over a long period of time, or students in the same classroom [12, 13].

### Immunosuppressed individuals

Whilst most transmission events require face-to-face contact, transmission through more casual contact does occur [15, 16]. For immunosuppressed individuals, who are more likely to develop severe measles disease[6], it is particularly important to consider even limited exposure. Any level of contact should trigger an assessment of an immunosuppressed individual, even if the index case is presumed to be a reinfection. If immunosuppressed contacts are identified, assessment of their susceptibility and post-exposure prophylaxis should be considered without waiting for, or in parallel with, laboratory testing of the index case.

### Vulnerable immunocompetent individuals (infants, pregnant women)

For immunocompetent vulnerable individuals (infants, pregnant women), local HPTs should prioritise contact tracing efforts to those most likely to have had close or prolonged exposure to a primary measles infection. If the index case is a presumed measles reinfection, individuals in this group do not need to be identified and assessed.

Contact tracing should focus primarily on:

- close contacts including household contact
- face to face contact of any length
- more than 15 minutes in a small confined area e.g. room in a house.

### 2.2.2.2. Poorly defined contacts

There will often be situations where a number of individuals may have been exposed in a shared setting e.g. hospital A&E or GP waiting area, where the level of contact is unclear.

- When the information provided cannot clearly define the level of contact but there are known immunosuppressed individuals involved, these should be managed as close contacts and rapidly assessed for post-exposure prophylaxis.
- Where there is a defined list of contacts, but it is not clear if the group contains immunosuppressed individuals, an individual risk assessment is not practicable. In this situation, 'warn and inform' letters / messaging should be issued to all potential contacts (see Appendix A2).
- If there is no identifiable list of contacts at all, then other means of case-finding should be considered, such as writing to local healthcare providers, information leaflets /posters in public areas and so on.

### 2.2.3. Assess susceptibility

In determining the need for post-exposure prophylaxis, it is important to assess the susceptibility of any vulnerable contacts identified.
**Immunosuppressed individuals** who are likely to have retained immunological memory from previous vaccination or measles infection (conditions listed in **Group A** of the Post-Exposure Prophylaxis Guidelines) should be managed on the basis of evidence of protection obtained at any time (prior to or since the diagnosis or treatment end).

Immunosuppressed individuals who may lose or not adequately maintain antibody levels from past infection or vaccination (conditions listed in **Group B** of the Post-Exposure Prophylaxis Guidelines) should be managed on the basis of (i) an IgG test following diagnosis / treatment end or (ii) an urgent IgG test at the time of exposure. In some severely immunosuppressed individuals, IVIG should be administered without an IgG test. For patients already on IVIG replacement therapy, testing and post exposure prophylaxis is not required.

**Immunocompetent vulnerable contacts (pregnant women, infants)**
The assessment of the susceptibility of pregnant women should be based on the person's age, vaccination history and/or past measles exposure, with urgent IgG testing as necessary (see Post-Exposure Prophylaxis Guidelines).

All infants should be considered susceptible before their first dose of MMR. Measles IgG testing is not indicated and post-exposure treatment should be based on age and level of exposure.

### 2.2.4. Urgent IgG testing of contacts

Where susceptibility cannot be adequately assessed on the basis of history, management may be based on testing for measles IgG. Doctors caring for vulnerable groups should be encouraged to perform IgG testing as part of routine care, so that patients understand the risk and can be managed appropriately after exposure.

IgG testing (on serum) of vulnerable contacts (immunosuppressed and pregnant women) is available in all regional public health laboratories, as well as many NHS laboratories. Most testing can be done the same day or out of hours. Further details are provided in the PHE Guidelines on Post-Exposure Prophylaxis. Urgent testing of any vulnerable contacts should not await testing of the index case.

### 2.2.5. Defining the time window for receiving Post-Exposure Prophylaxis

Cases are considered infectious from 4 days before to 4 days after the onset of rash with peak infectiousness occurring during the prodromal phase.

**For household contacts**, or any contact with ongoing exposure during the episode of illness, the time window for receiving post exposure prophylaxis should be calculated <u>from the date of onset of rash in the index case</u>.
**For other contacts**, the time window for receiving post exposure prophylaxis should be calculated <u>from the last day of exposure</u>. In most instances, susceptible contacts will have been exposed on a single day. However, if exposure has occurred over several days (e.g. a child attending nursery in the early prodromal phase) the time for receiving post exposure prophylaxis should be calculated from the last day of exposure to the infectious source.

## 2.3. Post-Exposure Prophylaxis

**Immunosuppressed, Pregnant and Infant contacts:** Detailed recommendations for Post-Exposure Prophylaxis of vulnerable contacts with immunoglobulin or MMR can be found in the PHE Post-Exposure Prophylaxis Guidelines.

**Other healthy contacts**: MMR can be offered to any healthy contact who is unvaccinated or incompletely vaccinated and not likely to be immune. In circumstances where measles is circulating in the local community or where there has been contact with a confirmed case, the second dose of MMR can be given at an earlier age, as long as there is at least one month from the first dose. Where a second dose is given to child who is under the age of 18 months and within three months of the first dose, the child will still require the pre-school booster dose of MMR.

**Individuals who develop symptoms within 10 days of receiving post-exposure vaccination should be assumed to have true measles unless the index case has been discarded. OF samples should be sent to VRD for confirmation and genotyping.**

# Section 3:

# Specific settings and situations

All staff working in health care settings with any contact with patients (including ambulance drivers, receptionists etc.), should have their immune status assessed and, if non-immune or unclear, offered MMR vaccination.

## 3.1. Primary care settings

Whenever possible, signs should be placed in GP surgery waiting areas advising patients with any rash illness to report to reception. Receptionists should know that any patients with fever and rash are potentially infectious and, ideally, should attend at the end of surgery to minimise the risk of transmission. Where patients with a fever and rash attend when other patients are in the waiting room, they should be directed to a side room.

When a GP refers a suspected measles case to A&E/hospital they should inform the hospital staff ahead of time, so that the case can be appropriately isolated on arrival.

When a likely case of measles is reported from a primary care setting, the HPT staff should advise about infection control measures and conduct a risk assessment. If the patient was not isolated, and for example, exposed other patients in the waiting room, then HPT staff should conduct a risk assessment as per current guidelines.

## 3.2. Acute hospital settings

### 3.2.1. General control measures

Suspected measles cases that are hospitalised (wards or A&E) need to be appropriately isolated. The hospital Infection Control Team (ICT) should be informed of all suspected measles cases in their Hospital Trust so that they can undertake a risk assessment and provide appropriate advice. They ICT will help to assess the exposure of patients, with particular attention to identifying and managing immunosuppressed and vulnerable contacts. They should also liaise with occupational health to assess the status of any exposed health care staff (including ambulance staff). Hospital ICTs should have the main responsibility for identifying contacts exposed in the hospital setting, and will need to work with HPTs on the follow up and management of those contacts who are now in the community.

### 3.2.2. Considerations for contact tracing through 'warn and inform' messages

When detailed information on the health and immune status of contacts is difficult to obtain (e.g. patients exposed in an emergency department waiting rooms), attempting to obtain detailed medical information on a large number of individuals at low risk could lead to unnecessary delay. In these situations, contact tracing through mass messaging (e.g. by email, text or letter) should be considered. This would involve the hospital Infection Control Team contacting all individuals who were in the same area as the index case and providing information (e.g. by using a link to a webpage) about measles, and advising individuals who may be vulnerable to contact their HPT of residence for further risk assessment (or local HPT for the hospital for non-UK residents). A template text/email and information letter are provided in Appendix A2.

Similarly, this approach can be used by HPTs to contact large groups of individuals who may all have been exposed in the community, and for whom contact details exist (e.g. passengers on a coach).

### 3.2.3. Considerations for health care workers

All healthcare workers (including receptionists, ambulance workers etc.) should have satisfactory evidence of protection against measles to protect both themselves and their patients. Satisfactory evidence of protection includes documentation of having received two or more doses of measles containing vaccine and/or a positive measles IgG antibody test.[8].

Health care workers (HCWs) who are **exposed to a confirmed or likely case** and do not have satisfactory evidence of protection should be excluded from work from the 5th day after the first exposure to 21 days after the final exposure. If HCWs are tested rapidly after exposure, they can continue to work if found to be measles IgG positive within seven days of exposure (as this is too early to be due to infection from the recent exposure). Where MMR vaccine is given post-exposure, it is unlikely to prevent the development of measles but if the HCW remains symptom-free for at least 14 days after MMR was given, they can return at that stage. Health care workers with satisfactory evidence of protection can continue to work normally but should be advised to report to Occupational Health (OH) if they develop prodromal symptoms or a fever between 7 days after the first exposure and 21 days after the last exposure.

Exposed HCWs that develop fever or rash should be excluded from all work until 4 full days after onset of the rash. Those HCW should be treated as an epidemiologically confirmed case and laboratory confirmation and notification should be sought in the usual way.

## 3.3. Educational settings

Confirmed and likely cases should be excluded from nursery or school for at least four full days after onset of rash. Given the high risk of secondary infection following measles, it is advisable to return to nursery or school only after full recovery. Susceptible contacts of cases (e.g. unvaccinated siblings) are at high risk of developing measles and should be advised to self-exclude from school for the incubation period.

Cases considered unlikely may be suffering from other infections, some of which may have public health implications (e.g. scarlet fever, roseola (HHV6 infection) – see differential diagnosis in Appendix A1) and therefore, general advice about staying away from school during the acute illness should be provided.

A health care staff member or appropriate senior staff at the institution (e.g. the school nurse and/or welfare officer, head teacher, health and safety officer or student health advisor) should be informed of all cases that are likely or confirmed. Schools should be asked whether they are aware of any vulnerable students or teachers, even if not yet exposed, so that their status can be assessed and steps taken to reduce the risk of future exposure. Head teachers may wish to consider excluding unvaccinated pupils who have been exposed, because of the risk to other students. An appropriate letter/fact sheet should be sent to the school/nursery for dissemination to parents (nursery/school) or students (higher education setting). The immunisation coordinator and/or Director of Public Health (DPH) for the local authority (LA) should also be informed.

More detailed information about infection control in school settings can be found in the PHE guidance on infection control in schools and other childcare settings as well as in the PHE measles frequently asked questions for schools.

## 3.4. International Travel

All likely or confirmed cases linked to international travel, or who have travelled on aircrafts (including domestic travel) should be notified by email to the UK International Health Regulations (IHR) Focal Point (IHRNFP@phe.gov.uk) at PHE Colindale, and the national immunisation team (via Immunisation.Lead@phe.gov.uk).

For likely or confirmed cases who were infectious whilst abroad in a non-endemic country, or who are likely to have acquired their infection in a non-endemic country, contact with the relevant National Focal Point should be made through the IHR Focal Point and the national immunisation team at PHE Colindale. Further information can be found in the International Health Regulations 2005: UK National Focal Point Communication Protocol.
Reporting of cases linked to international travel is an essential part of international surveillance and reporting should not be limited only to cases where immediate post-exposure interventions can be conducted. Classification of imported cases, and identifying international links between cases is an important component of regional and global elimination and would be expected by most other countries.

### 3.4.1. Air travel

For a **likely or confirmed** case of measles who has travelled internationally during the infectious period, a risk assessment should be undertaken. The flight details should be collected and added as a context on HPZone, so that colleagues across PHE can access the details if other linked cases are reported later.

In most instances, HPTs should make contact with the airline, and ask the airline to circulate a “warn and inform” message to all passengers via text or email, with a link to further information about measles prevention and control, information about when and how passengers should contact their local HPT, and about what to do if they develop symptoms. The details can be found in the ‘Measles: public health response to cases who have travelled by air whilst infectious’ guidelines. The need for more active follow up will depend on the plane’s country of departure and the time since exposure.

- **Country of departure**: For direct flights from endemic countries, there is limited benefit of contact tracing as passengers should have been aware of the risk of acquiring measles during their stay in that country. If the flight is indirect through or direct from, a country of low measles incidence however, there is added benefit in informing passengers as soon as possible, so that vulnerable people can be urged to seek public health advice.
- **Time since exposure**: If exposure on the flight occurred **more than five days** before, active contact tracing is not required as it is unlikely that this will allow the provision of post-exposure prophylaxis (PEP) to vulnerable patients, if required, within six days post exposure.

Full details about the assessment and public health action following a case of measles on aircrafts are provided in the ‘Measles: public health response to cases who have travelled by air whilst infectious’ guidelines.

### 3.4.2. Other modes of transport

For **likely or confirmed cases** of measles linked to travel other than by air during the infectious period, sending a “warn and inform message” through the transport provider should be considered. If the transport provider does not have contact details of passengers, no further action is required, unless a defined group is known from the index case and can be contacted through other means (e.g. children on a school trip).

## 3.5. Outbreaks

An outbreak is defined as two or more epidemiologically linked cases that occur within one incubation period of each other (i.e. the second case occurs between 7 and 21 days of the first case).[2]

While most outbreaks will occur within the household setting, an outbreak control team may need to be convened when transmission has occurred in other settings where a large number of people been exposed (e.g. school outbreak) or where the population exposed may be more vulnerable (e.g. hospital outbreak). If the reported number of measles cases across a local area or community is above the expected level, an outbreak control team should be considered to identify common factors and implement control measures.

### 3.5.1. Outbreak Control Team

An appropriate outbreak control team is likely to include, if appropriate:

- Health Protection specialist from the local HPT
- Screening and Immunisation team representative
- Education representative from Local Authority
- School nurse/Team Leader
- GPs (if identifiable practices within community)
- Local DPH or appropriate representatives
- Local Clinical Commissioning Groups (CCGs)
- Communications leads (PHE, LA to liaise as necessary)
- Acute Trust representative (microbiologist, Director of Infection Prevention & Control; microbiologist (if different); Infection Control Team /paediatric consultant/medical director, Occupational health)

Hospital outbreaks/clusters will require close liaison with the Director of Infection Prevention & Control; microbiologist (if different), Infection Control Team, Clinical Directors or Service Managers, Occupational Health Manager, as well as the local Director of Public Health.

Expert advice can also be sought from the Virus Reference Department or the national immunisation team at PHE Colindale.

### 3.5.2. Planning and response

Health Protection Teams should work with their local NHS England Screening and Immunisation teams to ensure that the necessary resources are available within their area to manage outbreaks. HPTs should know where to access urgent laboratory testing services (particularly measles IgG) and HNIG supplies. Access to a small stock of MMR vaccine should be available by the next day, including at weekends, and HPTs should ensure they know which walk-in clinics or out of hours GP services are available at the weekend to enable prompt administration of MMR or HNIG if required.

When outbreaks occur in school settings, all students who are susceptible or incompletely vaccinated should be offered MMR promptly, even if direct contact with the index case has not occurred.

If a school with an outbreak is planning a school trip, all students who are not vaccinated or incompletely vaccinated should be vaccinated at least two weeks prior to departure. Similar considerations apply to students about to go on work placements, particularly in health care or with vulnerable patients.

Further information containing advice around school trips and international travel can be found in the PHE measles frequently asked questions for schools.

If an outbreak occurs in a school where vaccination coverage is known to be low, an urgent campaign should be considered. **Vaccination of all susceptible students will limit the risk of tertiary transmission within the school setting.** Commissioners should have contracts in place to provide support for a vaccination campaigns in defined settings, such as a schools, and providers should have arrangements in place to source MMR promptly for outbreak control.

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# Appendix

## A1. Differential diagnosis

### Roseola (exanthema subitum, sixth disease)

Pathogen: Human herpesvirus 6 (HHV6), occasionally HHV7

Clinical presentation: Generally mild, often asymptomatic. When symptomatic, illness starts with 3 – 5 days of fever, which might be followed by a maculopapular rash, although most children have a viral illness without rash. Unlike measles, the onset of rash occurs when patients improve clinically and the fever recedes.

Epidemiology and transmission: Most infections occur in children aged 6 – 24 months. Transmission occurs through the respiratory route/droplet transmission. Seroprevalence studies have shown that by two years of age 90% of children are immune against HHV6 [18]. Cases in older children may be due to HHV7, which tends to be acquired later in life, with seroprevalence studies showing that about 65% of children in the UK are immune by the age of three years [19]. As HHV6 and HHV7 remain latent after infection, they can therefore reactivate among immunosuppressed individuals later on in life

Incubation period: around 5 – 15 days.

### Scarlet Fever

Pathogen: Group A streptococcus

Clinical presentation: Sore throat, pharyngeal exudate, high fever. Cough is generally absent. The maculopapular rash typically appears about 12 – 48 hours after the start of symptoms. It generally starts on the abdomen, spreading to neck, back and limbs. A white coating of the tongue may be present (‘strawberry tongue’).

Epidemiology and transmission: Transmission occurs through the respiratory route/droplet transmission. It is most common during winter months or in early spring. Scarlet fever affects mostly children of school and pre-school age.

Incubation period: around 2 days, ranging from 1 – 5 days [20]

More information on scarlet fever and its management can be found in the PHE 'Scarlet fever: managing outbreaks in schools and nurseries' guidelines.

## Fifth disease ('slapped cheek' syndrome)

Pathogen: Parvovirus B19

Clinical presentation: The infection generally presents with typical features of 'slapped cheeks', followed by a rash which is most visible on the extremities. There may be prodromal symptoms leading to the rash, such as coryza, fever or headache. Arthralgia and arthritis may be present- these are more common among adults.

Epidemiology and transmission: Transmission occurs through the respiratory route/droplet transmission. It is most common during winter months or in early spring. Children of all ages can be affected, and an infection among adults is not uncommon. Secondary attack rates among households and schools is high [21]. Transmission occurs in the week preceding the rash and individuals are considered non-infectious when the rash appears.
Incubation period: around 13 – 18 days[22]

## Rubella (German measles)

Pathogen: rubella virus

Clinical presentation: Generally mild, asymptomatic in up to 50% of the cases (particularly in children). A prodromal phase of 1 – 5 days may precede the rash, with symptoms of malaise and coryza, with or without fever. Post-auricular and sub-occipital lymphadenopathy may be present. The rash is non-specific, generally mild and is most often seen on the face and behind the ears, where it starts before spreading.

Epidemiology and transmission: Rubella is prevented by MMR vaccination and few cases of rubella are now being reported. Most reported cases are imported.

Incubation period: 14 days (range 12 – 21 days) [23].

## Infectious Mononucleosis (Glandular fever)

Pathogen: mostly Epstein-Barr virus (EBV). Rarely CMV, HHV6, HSV

Clinical presentation: It mainly presents with a sore throat (pharyngitis/tonsillitis). Malaise and fever are common presentations. A rash only occurs in only about 10% of infected individuals and may not always be maculopapular. A more typical

maculopapular rash frequently occurs after starting antibiotic treatment for pharyngitis.
Epidemiology and transmission: EBV is transmitted mostly through direct contact with saliva. About half of infections are asymptomatic, but more so in young children than in adolescents and adults.

Incubation period: thought to be about 30 – 50 days

## Other differential diagnoses to consider: Zika, Dengue, Chikungunya

# A2: Warn and Inform Letter

**LETTER**

This information sheet is only intended for people who attended ______________ [SETTING]

Public Health England has been informed that a person who attended _______________ [SETTING] at the same time as you/your child had measles.

## What is measles?

Measles is a disease which spreads very easily. People with measles can get a cough, runny nose, rash and fever. Measles can be serious, particularly for people whose immune, system is not working normally. The best way to prevent measles is through vaccination.

## What is the risk of catching measles?

Most older children and adults are immune to measles – either because they had measles as a child or because they have been vaccinated – and so are very unlikely to catch measles.

## Who needs medical advice?

- **People with a weakened immunity**: You should contact your doctor straight away if you have weakened immunity (due to illness or medication). The doctor will then assess whether you are immune (i.e. have antibodies) against measles; and if the exposure was within the past few days, your doctor may be able to organise treatment to prevent you becoming seriously ill.

- **Pregnant women**: If you are **pregnant** and not sure of your immunity it may also be worth seeking your doctor's advice.

- **Children under one year:** If you attended _____________ with an infant aged under one year, please also contact your doctor for advice.

**If you are well and not in the groups listed above** you do not need to take urgent action. However if you are unsure if you are protected from measles, check with your doctor. If you would like more information on measles visit [http://www.nhs.uk/conditions/measles/Pages/Introduction.aspx](http://www.nhs.uk/conditions/measles/Pages/Introduction.aspx)

### What if you become unwell?

**If you become unwell and think it could be measles** (within three weeks of attending_________ [SETTING]), you should see a doctor. You should ring the doctor or clinic beforehand so they can make sure you do not pass the disease to others in the waiting room.

Take this information sheet with you and tell your doctor that you have been in the same room as someone with infectious measles. Your doctor should seek advice from the local Health Protection Team (postcode search for local unit and phone number at https://www.gov.uk/contacts-phe-regions-and-local-centres).