Laboratory Investigation of Measles Infection in NVRL
Date: 12/03/2024, Version 1.3

Clinicians should immediately notify suspect measles cases to Public Health. Do not wait for test results.
This document summarises testing options for the diagnosis of measles. **Testing is currently done in the NVRL**. The possibility of regional testing is also under review and this document will be updated.

Testing of suspect measles is recommended for individuals with symptoms compatible with measles (cough, runny nose/coryza, conjunctivitis, fever and rash). A risk assessment should be undertaken including: history of travel to country/region where measles cases reported, contact with a measles case, age, absence of previous measles infection, absence of age-appropriate MMR vaccination.

Highly suspect measles case in the circumstances below. This will aid preliminary local action or decision to arrange a courier if urgent testing is required or if routine lab transport is unavailable.

- Prodromal-like symptoms (no rash) with epi-link to confirmed or highly clinically suspect case or travel to high-risk area with measles transmission + not age appropriately vaccinated – consider age risk*
  - Or
- 'Possible case' classification + not age appropriately vaccinated – consider age risk*
  - Or
- 'Probable case' classification (with epi-link to confirmed or highly clinically suspect case or travel to high-risk area), regardless of vaccination status

Case classification
A. **Possible case**
Any person meeting the clinical criteria
B. **Probable case**
Any person meeting the clinical criteria and with an epidemiological link
C. **Confirmed case**
Any person not recently vaccinated and meeting the clinical and the laboratory criteria

Clinical criteria
Any person with fever AND maculo-papular rash AND at least one of the following three:
- Cough
- Coryza
- Conjunctivitis

**For Irish born individuals, those born before 1978 are considered likely to be immune; for non-Irish born individuals assumption of immunity is less certain*

Testing (please also see *Measles: Indications for testing and which tests to use* Algorithm – Appendix A)

- Collect oral fluid using the OraCol collection device **OR** Swab using a mouth-throat VTM/UTM swab
- **PLUS** collect a serum sample where possible (recognising that phlebotomy may not be feasible on younger patients or if it is not possible to safely bring a patient into the practice due to IPC limitations)
- The following information should be provided on the request form: date of rash onset; date of prodromal symptoms onset; date of sample collection; MMR vaccine history (1 or 2 doses, including dates) if possible; epi linked to (close contact with) a confirmed or highly clinically suspect case; travel to high-risk area; pregnant or immunocompromised; referring clinician contact number (ideally mobile number and out of hours number) and address.

This document outlines the following:

I. Information to be provided on samples.
II. Description of the sample types and testing, transport of specimens to NVRL.
III. Diagram describing test results and temporal correlation with symptoms.
IV. Summary table of samples/tests/and testing scheduling in NVRL

NB For more information on criteria for testing please see ***Measles: Indications for testing and which tests to use Algorithm* – Appendix A**.

I. Information to be provided with samples sent to laboratory.

The sample should be labelled with patient name, date of birth- this should be accompanied on the laboratory request form as per NVRL guidance https://nvrl.ucd.ie/info

A laboratory investigation form for the Oracol investigation can be downloaded from NVRL https://nvrl.ucd.ie/sites/default/files/uploads/pdfs/LF_UM_001m_rev_10_Oral_Fluid_Investigation_Request_Form.pdf.

It is recommended that this form is also used for serum investigations but the sample type changed to serum

It is **essential that the following information** accompanies the sample to determine the significance of the results and appropriate investigations and rapid communication of results.

- Date of rash onset and date of prodromal symptoms onset
- Date of sample collection
- Measles containing vaccine history (1 or 2 doses, and dates) if possible
- Referring clinician contact number (ideally mobile number and out of hours number) and address- NVRL will phone positive results

Other **useful information**

- Epi link to (close contact with) a laboratory confirmed or highly clinically suspect case
- Travel history to high-risk area
- Pregnant or immunocompromised

II. Description of sample types and testing (See Section III for further information on timing of tests)

1. Oral fluid (OraCol)

As of 21/02/2024 - Oracol swabs can be obtained from NVRL on the website. From 28/02/2024 the HSE plans to have stock to supply hospitals and GPs and will provide updated information to clinicians on how to order.

The OraCol collection device provides a non-invasive oral fluid sample which is rich in gingival crevicular fluid (GCV), which is a plasma transudate, which emerges at the margin of the tooth and gum. This transudate contains IgM and IgG derived from plasma but diluted. This sample can be used for the determination of measles IgM. Testing for IgM is more sensitive than using serum in the first few days after rash development and over 50% may be positive on day 1.

In addition, the oral fluid can be used for the detection of measles RNA (PCR methods) and subsequently sequenced to discriminate between wild type measles genotype and vaccine strain. The oral fluid can be tested for measles RNA during the prodrome of suspected measles infection and up to 7 days post rash onset.

The laboratory results generated are heavily dependent upon the quality of the sample. Therefore, great care is needed to follow the instructions (see Measles Swab Infogram linked below) for collecting the oral fluid, to ensure that there are sufficient cells for measles RNA investigation and antibodies for measles IgM detection.

Measles Swab Infogram [English] [Ukrainian] [Russian] [Turkish] [Georgian] [Arabic] [Pashto] [Somali] [Urdu]

Optimal sample collection

RNA DETECTION: few days before rash develops to seven days post rash. **PCR testing is done Monday-Saturday in NVRL** (Saturday service commencing 24th February 2024, maximum of 22 samples case be tested on Saturday)**.** If the sample is received by the NVRL by 9.30 am, the measles RNA result will be available the same day providing the sample is suitable (i.e. sufficient cells). If the result is inconclusive, the sample may be investigated again the next day.

IgM DETECTION: The day the rash develops up to 4 to 5 weeks.

2. Serum samples

Serum (Blood) samples can be used to detect measles IgM and measles IgG.

Measles IgM can be detected 4 days after rash onset. In situations when the rash has developed greater than 4 days, diagnosis can be confirmed on a serum sample within hours of arrival at the NVRL and **this is available 7 days a week** (Saturday and Sunday by specific request). Therefore, this approach could provide a more rapid diagnosis of acute measles infection. If possible, an OraCol sample, or a throat swab, should be collected in parallel to serum sample for measles RNA determination and genotyping.

The added value of the serum sample is that measles IgG can also be detected, and this provides information regarding the immune status of an individual following exposure for patient management and also to determine if the infection is a primary infection or breakthrough (reinfection) infection.

It is recognised that phlebotomy on younger patients may not be feasible and that IPC limitations may preclude serology samples being taken within a GP practice.

Note: Out of hours contact details are available here NVRL out- of- hours service

Optimal sample collection

Measles IgM and IgG: For patients with rash onset greater than 4 days -results available within 2 hours of receipt at the NVRL

Measles IgG: For immune status and breakthrough infection investigation.

Please note that the measles IgG assay was not designed to determine the measles vaccine response. Therefore, whilst the test is useful to guide immediate patient management following exposure to determine susceptibility, the assay should not be used to determine previous vaccine response.

Measles IgM detection using either the OraCol or serum is important to out-rule measles infection and to discard possible cases.

3. Throat swabs or mouth swabs

Throat swabs (VTM or UTM) and mouth swabs (VTM or UTM) can be used to detect **Measles RNA** within 6 days of rash onset. It is recommended that these samples are collected by a health professional. These sample types are not suitable for IgM investigations**.**

Optimal sample collection

Throat swabs and mouth swabs: **Measles RNA DETECTION ONLY** within 6 days of rash onset**.**

Figure 1. UTM swab

4. Urine and EDTA blood

These sample types are not recommended for measles investigation**.**

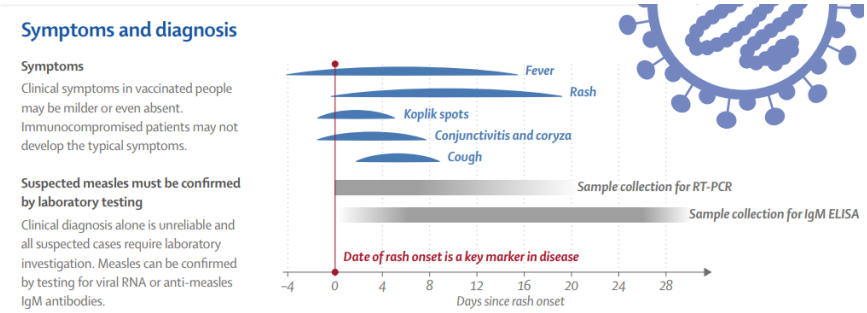
5. Transport of samples to NVRL

- Please transport samples for measles investigation in a biohazard bag and clearly labelled for measles investigation when sending to the local laboratory for easy identification by the laboratory when arranging courier transport to NVRL
- There are scheduled courier services that routinely link hospital labs to NVRL, link hospitals to hospitals, and may also be used by primary care practices to send to hospital labs.
- Patients seen Monday-Thursday in primary care
    - GPs can send samples to the regional/local hospital laboratory- this will allow transport to NVRL the following day as part of routine transport of samples from the local laboratory.
- Patients seen on Friday or Saturday
    - GPs can send samples to the local laboratory for routine courier service to the NVRL
    - HSE is looking at alternative options for courier services for urgent measles samples and will inform GPs – rapid turn-around-time in testing and results plays a key role in measles control
- For GPs –if sending by post, Express Post is the only postal option recommended to allow rapid testing

CLINICIANS should not delay notification to Public Health while waiting for a result.

III. Diagram describing test results and temporal correlation with symptoms

Figure 2. Timeline of measles symptoms and laboratory testing



Source: https://www.thelancet.com/pb/assets/raw/Lancet/infographics/measles/image.pdf

Test	Timeline of Symptoms												
OraCol	Measles RNA PCR (Mon-Sat; must be received by 9:30am)*												
					Measles IgM								
Throat					Measles RNA only								
Serum	IgG – useful for immune status/breakthrough infection investigation												
									IgM (Mon-Sun; results in 2 hours)				
Days	-4	-3	-2	-1	0 Rash	1	2	3	4	5	6	7	Up to weeks

*** Noting that an OraCol swab taken during the prodromal phase that is RNA negative may have to be repeated if there is still a strong suspicion of measles.**

IV. Summary table of samples/tests/and testing scheduling in NVRL (as of 09/02/2024)

Table 1 Summary of Sample type, test and availability

Sample type	IgM	IgG	Measles RNA (PCR)	Useful for	NVRL testing available
Oral fluid (OraCol swab)	✓ (day of rash onset up to 4-5 weeks post rash onset)	✘	✓ (prodrome and up to 7 days post rash onset)	• Early (pre-rash) measles infection • Acute measles infection • Outrule measles infection (discard possible cases based upon IgM result) • Measles genotyping	• Monday-Saturday‡ • Same day result if sample received at NVRL pre-09:30h*
Serum sample	✓ (4 days post rash onset)	✓	✘	• Acute measles infection • Outrule measles infection (discard possible cases) • Immune status • Primary infection vs breakthrough infection	• Daily • Saturday and Sunday by triggering the out of hours service – see https://nvrl.ucd.ie/
Throat/ mouth swab (VTM or UTM)	✘	✘	✓ (within 6 days of rash onset)	• Acute measles infection • Measles genotyping	• Monday-Friday • Same day result if sample received at NVRL pre-09:30h*
EDTA blood	Not recommended				
Urine	Not recommended				

*** If the sample requires retesting the result will be available the next day**

‡ as of 24th February 2024 and based on assessment of need

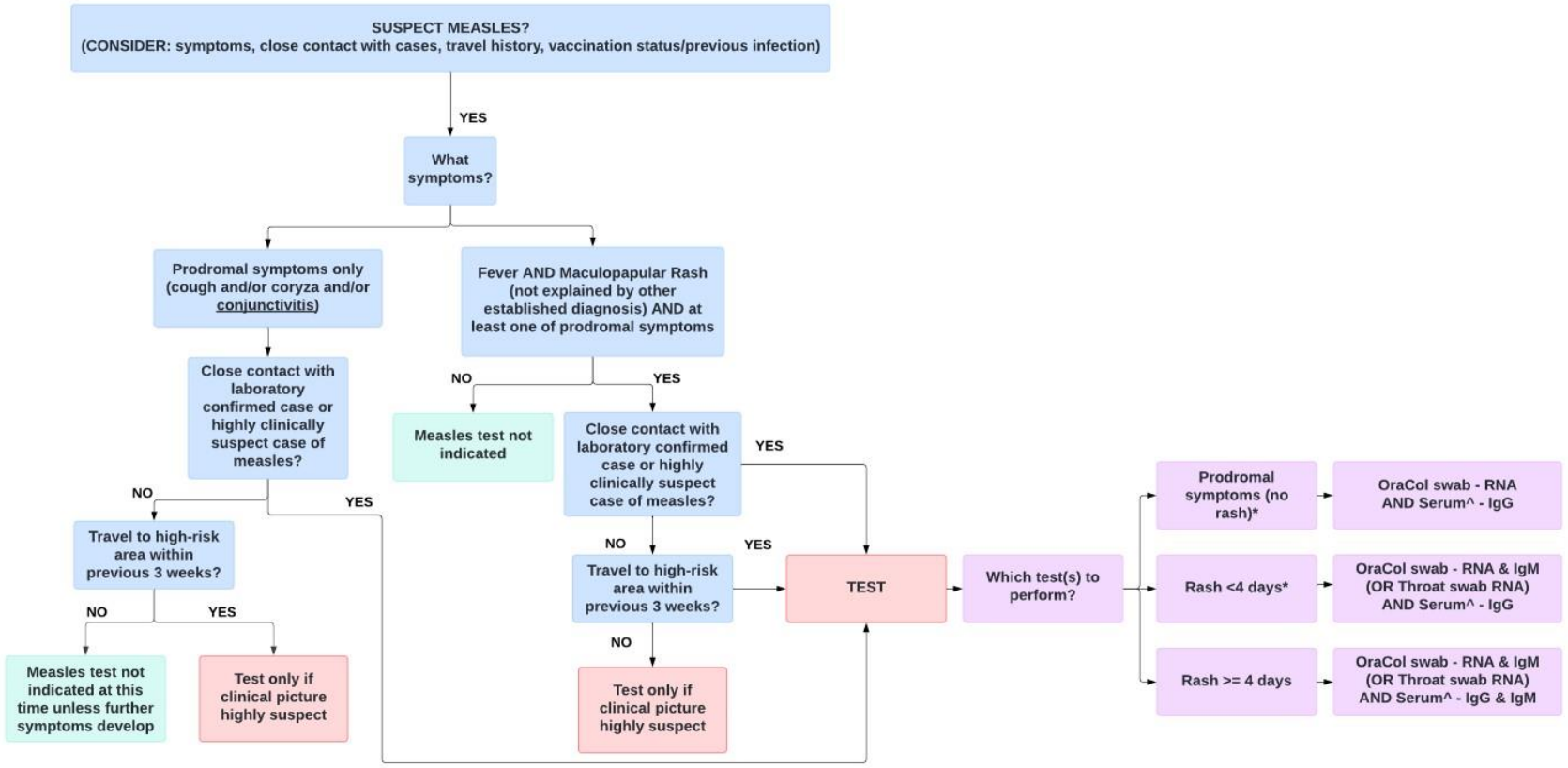
Appendix A

Measles: Indications for testing and which tests to use (Version 1.2)

For use when community transmission is low [document correct as of11/03/2024]

NB If testing for measles, report immediately to Regional Department of Public Health (contact details here) & advise patient to isolate until results available

This should be read in conjunction with *Laboratory Investigation of Measles Infection in NVRL* (available on HPSC website)



Data that should be included on the test request form(s):

- date of rash onset;
- date of prodromal symptoms onset;
- date of sample collection;
- MMR vaccine history (1 or 2 doses +/- dates) if possible;
- referring clinician contact number (ideally mobile number) / address

Extra data that is useful for NVRL:

- pregnant or immunocompromised;
- close contact with a laboratory confirmed case or highly clinically suspect case;
- travel to high-risk area in the previous 3 weeks

Notes:

- This flowchart is accurate as of 11/03/2024 – should the epidemiological situation in Ireland change, this flowchart will need to be updated.
- **NB Conjunctivitis is often the dominant symptom of the prodrome**
- For high-risk areas see latest WHO updates: Europe and Global

* An OraCol swab taken during the prodromal phase (or early in the infection) that is RNA negative may have to be repeated if there is still a strong clinical suspicion of measles.

^ Recognising that phlebotomy may not be feasible on younger patients or if it is not possible to safely bring a patient into the practice due to IPC limitations.