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# **PATHOLOGY** *focus*

*Medical Newsletter*

## **MEASLES:** Vigilance after elimination

*What not to miss this  
respiratory pathogen season*

**By Dr Varsha Sivalingam**

As we enter the winter respiratory season, clinicians appropriately focus on influenza, RSV and SARS-CoV-2. However, recent increases in global measles activity and intermittent local transmission in Australia highlight the importance of maintaining vigilance for this highly infectious disease. Early recognition and testing remain critical, not only for patient care but also for protection of the general public.

Although Australia achieved measles elimination in 2014, measles has not disappeared. Imported cases continue to occur every year, and during the past 12–18 months Australia has experienced an increase in both imported infections and secondary community transmission. During a busy winter season, when patients commonly present with fever, cough and coryza, measles can easily be overlooked unless clinicians actively consider it in the appropriate epidemiological context.

## Why think of measles now?

Measles is caused by a paramyxovirus and remains one of the most contagious human infections, with a basic reproduction number ( $R_0$ ) of 12–18. A single case in a susceptible population can rapidly lead to multiple secondary infections.

**Table 1: Relative contagiousness of common infectious diseases ( $R_0$ ).**

Disease	Approximate $R_0$
Seasonal influenza	1-2
COVID-19 (original strain)	~2-3
Chickenpox	8-10
<b>Measles</b>	<b>12-18</b>

The overlap between early measles symptoms and common winter respiratory illnesses creates a significant diagnostic challenge. The initial prodrome of fever, cough, coryza and conjunctivitis can be indistinguishable from influenza, RSV, adenovirus and other viral respiratory infections. This issue has become more important because the global epidemiology of measles has changed since the COVID-19 pandemic. Interruptions to routine childhood immunisation and catch-up vaccination programs during the pandemic led to a marked fall in global vaccine coverage. Large outbreaks have since occurred in Europe, Southeast Asia and parts of North America. Most Australian cases remain linked to overseas travel or contact with a returned traveller.

Measles vaccine was introduced in Australia in 1968, and widespread vaccination has dramatically reduced the incidence of disease. In 2014, the World Health Organization declared Australia free of endemic measles transmission. However, imported cases have continued to occur, and over the last year there have been several episodes of onward community transmission involving both vaccinated and unvaccinated individuals.

“

*“The overlap between early measles symptoms and common winter respiratory illnesses creates a significant diagnostic challenge.”*

## What does measles look like?

Following exposure, measles typically develops after an incubation period of 10–14 days, although the range may be as short as 7 days or as long as 23 days. Illness begins with a prodromal phase lasting 2–4 days. During this period, patients usually develop a fever together with one or more of the classic “three Cs”: cough, coryza and conjunctivitis. There may also be atypical presentations with gastrointestinal symptoms.

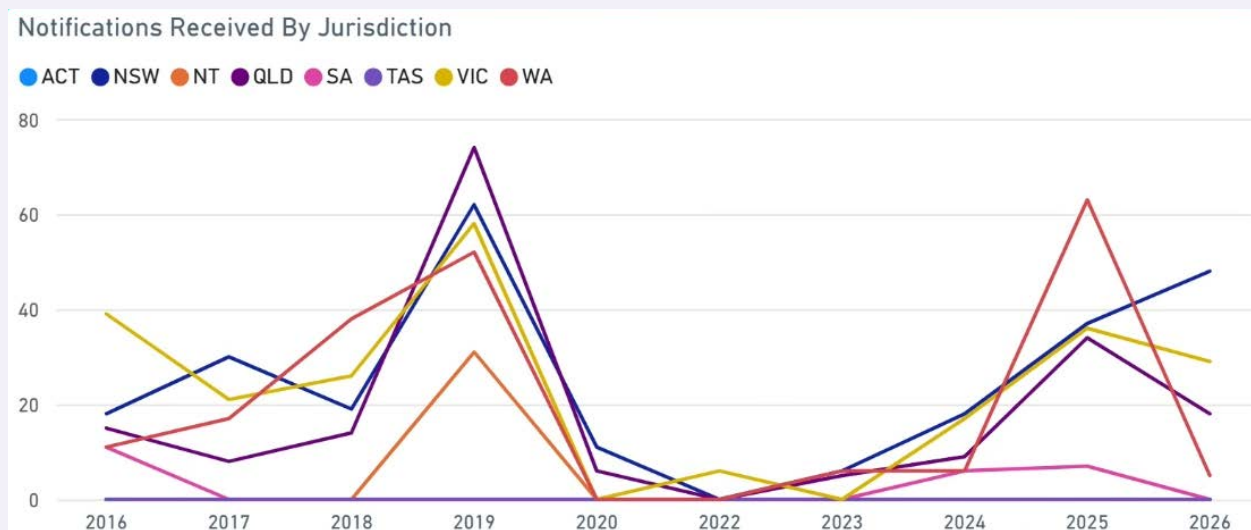
Koplik spots are highly characteristic of measles and, when present, are considered pathognomonic. These are small bluish-white or white lesions on the buccal mucosa. They typically appear 1–2 days before the rash. However, they are not always seen, particularly if patients present late.

The characteristic measles rash is an erythematous maculopapular eruption that generally appears a few days after the onset of fever. The rash usually begins on the face before spreading downwards to involve the trunk, arms and legs. As the rash progresses, it may become confluent, particularly over the face and upper body.

## Community transmission: why early detection matters

Measles is so contagious that even brief exposure can be sufficient for transmission. Recent Australian outbreaks have demonstrated that imported cases can rapidly lead to local transmission, particularly when diagnosis is delayed. Early recognition, immediate isolation and prompt notification to Public Health remain critical.

**Figure 1: Annual notified measles cases by state and territory, Australia (past 10 years).**



National Communicable Diseases Surveillance Dashboard, Assessed 10 June 2026.

Although measles most commonly occurs in unvaccinated individuals, infection can occasionally occur in people who have previously received measles-containing vaccine, including those who have had two documented doses. These “breakthrough” cases may occur due to either primary or secondary vaccine failure. A single dose of a measles-containing vaccine is more than 95% effective, while two doses provide up to 99% protection against measles.

**Primary vaccine failure** is rare. Primary vaccine failure may occur due to failure to produce any humoral response to viral antigen (non-seroconversion) or problems with vaccine storage, cold-chain maintenance or administration. Patients with primary vaccine failure generally present with typical measles, including fever, cough, coryza, conjunctivitis and a classic rash.

**Secondary vaccine failure** occurs when a patient initially develops immunity after vaccination, but protection declines over time as antibody levels wane. Measles occurring in this setting is often termed “modified measles syndrome”. Some patients may present only with a febrile rash illness or mild respiratory symptoms. As a result, modified measles can easily be overlooked during influenza season. Patients with secondary vaccine failure generally have lower viral loads and are less infectious than unvaccinated patients with measles; however, transmission can still occur, and these cases remain important to identify.

### Which patients should be tested?

Clinicians should maintain a low threshold for testing in patients with a compatible illness and relevant epidemiological risk factors. Testing should be strongly considered in patients with fever and a descending maculopapular rash, particularly when accompanied by



Image 1: Confluent maculopapular measles rash on the torso.

cough, coryza or conjunctivitis, especially in the context of the following risk factors:

- Recent overseas travel, particularly to areas with known outbreaks or endemic transmission
- Contact with a suspected or confirmed measles case
- Infants too young to be vaccinated

Clinicians should also remember that measles does not always present classically. Increasingly, Australian cases are being recognised in partially immune individuals, who may present with mild or atypical symptoms.

An important point to note is that after receiving a measles-containing vaccine, people may develop a fever lasting two to three days, with associated malaise and a mild, non-infectious rash. The fever usually develops 7–10 days after vaccination (typically within 5–12 days). Approximately 15% of young children who receive the MMR vaccine experience a high fever (>39.4°C). Laboratory testing can distinguish wild-type (circulating infectious) measles from non-wild-type (vaccine strain) virus.

### Recommended specimens for suspected measles cases

A combination of molecular and serological testing can be performed for suspected cases; however, **polymerase chain reaction (PCR) testing is critical to confirm acute infection**. PCR is the diagnostic modality of choice early in illness and is most useful within the first few days after symptom onset, including during the prodromal phase before the rash develops.

Ideally, **both a respiratory specimen and urine** should be collected, as this increases diagnostic sensitivity.

#### Specimens to collect:

- **Respiratory specimens:** 2 x nasopharyngeal swabs in viral transport medium (VTM)
  - o 1 swab specifically labelled for **measles PCR** (sent to the Public Health laboratory)
  - o 1 swab for routine respiratory multiplex PCR (sent to the local laboratory)\*
- **Urine:** Standard yellow-top container for measles PCR

It is important to **notify the local Public Health unit** of suspected cases so they can contact the lab to expedite testing.

*\*An important practical point is that **routine respiratory viral PCR testing does not include measles**. Given the overlap in symptoms between measles and other viral infections, it is good practice to also collect a sample for respiratory multiplex PCR.*

Measles serology can be used to assess immunity and as an adjunctive diagnostic test in suspected acute infection. Suggestive features of an acute infection include identification of measles-specific IgM antibodies or demonstration of a rising titre of IgG antibodies in the absence of recent vaccination. In acute infection, serology (serum tube) should be collected at the time of illness, with convalescent serology performed two weeks later. A negative IgM result early in illness does not exclude measles. If clinical suspicion remains high, repeat serology and PCR testing.

#### Serum specimen required:

- **Serum tube**
  - o Acute infection: IgM and IgG
  - o Immunity assessment only: IgG

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## How to Order Respiratory Multiplex PCR Testing (SA/NT)

What to request:	Respiratory Multiplex PCR
<b>Tests included</b>	<ul style="list-style-type: none"> <li>Influenza A</li> <li>Influenza B</li> <li>RSV (A &amp; B)</li> <li>Parainfluenza 1 2 3 &amp; 4</li> <li>Human metapneumovirus</li> <li>Human adenovirus</li> <li>Human rhinovirus</li> <li>SARS-CoV-2 (COVID-19) If specified</li> <li><i>Bordetella pertussis/Bordetella parapertussis</i></li> <li><i>Mycoplasma pneumoniae</i></li> <li>Human enterovirus</li> </ul>

### Test ordering

For the following pathogens, please specify if required on the request form: *Bordetella pertussis*, *Mycoplasma pneumoniae*, and/or Human Enterovirus.

### Specimens required

- Nose/throat or nasopharyngeal swab(s)

### Additional tests

If you suspect a lower respiratory infection, the appropriate sample is sputum for MCS. If the patient presents with symptoms of pharyngitis, obtain a throat swab for culture.

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# TB or Not TB?

## Making Sense of QuantiFERON Conundrums

By Dr Linda Dreyer



Interferon-gamma release assays (IGRAs) are *in vitro* blood tests that measure cell-mediated immune responses to antigens specific to the *Mycobacterium tuberculosis* complex. In Australia, QuantiFERON-TB Gold Plus (QFT-Plus) is the most widely used IGRA for the diagnosis of latent tuberculosis infection (LTBI).

LTBI represents persistent immune sensitisation to *M. tuberculosis* without clinical or radiological evidence of active disease. Individuals with LTBI are asymptomatic and not infectious, but carry a lifetime risk of progression to active tuberculosis (TB), estimated at approximately 5–10%, with the highest risk occurring within the first two years following infection.

IGRAs are not diagnostic of active TB and must always be interpreted in conjunction with clinical assessment, exposure history, and, where indicated, imaging and microbiology.



### Understanding QuantiFERON results

QuantiFERON-TB Gold Plus measures interferon-gamma (IFN- $\gamma$ ) released by sensitised T lymphocytes following stimulation with *M. tuberculosis*-specific antigens.

The assay consists of four blood collection tubes:

- **Nil control** – measures background IFN- $\gamma$
- **Mitogen control** – positive control assessing immune competence
- **TB1 antigen tube** – primarily stimulates CD4<sup>+</sup> T-helper lymphocytes (ESAT-6 and CFP-10 peptides)
- **TB2 antigen tube** – includes additional peptides designed to stimulate CD8<sup>+</sup> cytotoxic T lymphocytes

After incubation, IFN- $\gamma$  concentration is measured using enzyme-linked immunoassay (ELISA).

### Sensitivity and specificity

Because there is no gold standard for LTBI, assay performance is inferred from surrogate populations. Sensitivity is estimated in patients with microbiologically confirmed active TB and specificity is estimated in low-risk populations in low-incidence settings. In low-risk populations, current published data suggest sensitivity and specificity are 85–90% and >95%, respectively.

QFT-Plus is not affected by prior BCG vaccination, and when compared with tuberculin skin testing (TST), it has less cross-reactivity with most non-tuberculous mycobacteria.

### Interpretation of results

According to the manufacturer:

- **Positive:** If either TB1 or TB2, after subtracting Nil, is  $\geq 0.35$  IU/mL
- **Negative:** No antigen response with adequate mitogen control
- **Indeterminate:**
  - High Nil value (excess background IFN- $\gamma$ )
  - Inadequate mitogen response (suggesting immunosuppression or technical failure)

### What to make of low-positive results?

In low TB-prevalence settings, results between 0.35 and 0.99 IU/mL are associated with a higher likelihood of false positivity.

These results should be:

- Interpreted in the context of clinical and epidemiological risk
- Correlated with exposure risk
- Not used in isolation to make treatment decisions

In these low-risk individuals, repeat testing or discussion with a specialist is advised.

### Who to test?

The primary purpose of LTBI testing is to identify individuals who would benefit from preventive treatment; therefore, testing should be targeted.

### Common indications include:

- Close contacts of a patient with infectious pulmonary TB (after the appropriate window period)
- Migrants, refugees and expatriates from countries with high TB prevalence

Article continues over page



- Healthcare workers and others with occupational TB exposure
- Immunocompromised patients, including:
  - HIV infection
  - Planned or current treatment with TNF- $\alpha$  inhibitors or other biologic agents
  - Solid organ or stem cell transplantation candidates
  - Chronic renal failure, haematological malignancy or chemotherapy
- Pre-immunosuppression screening, including corticosteroids  $\geq 15$  mg prednisolone daily for  $>1$  month.

### Can QuantiFERON be used in children?

In young children, immune immaturity significantly affects the performance of IGRAs. In those under 5 years of age, QFT-Plus is considered unreliable, and the tuberculin skin test remains the preferred method of testing. For children aged 5 years and older, QFT-Plus may be used, particularly in those who have received previous BCG vaccination.

False-negative results are more common in younger children, and because the risk of progression to severe tuberculosis is higher in this group, a negative IGRA does not exclude infection.

### Use in immunocompromised populations

Immunocompromised patients are at increased risk of LTBI progressing to active disease. Risk varies according to the patient's immunosuppressive state, including underlying conditions (such as HIV infection, malignancy, transplant or renal failure requiring dialysis) and the type and intensity of immunosuppressive therapies used.

It is important to remember that QFT-Plus may produce:

- **False negative results**, due to impaired T-cell function
- **Indeterminate results**, reflected by a failed mitogen control

In these groups:

- A negative result does not exclude LTBI
- Repeat testing or alternative strategies (e.g. TST, specialist review) may be required
- Clinical risk assessment is critical

### Indications for treatment of latent TB

The decision to treat LTBI must be carefully assessed and depends on the following:

#### 1. Pre-test probability

- Recent exposure
- Origin from or prolonged residence in high-burden countries
- Occupational exposure

#### 2. Risk of progression to active disease

- Approximately 50% of lifetime risk occurs within 2 years of infection
- Highest-risk groups include:
  - Infants and young children
  - HIV infection
  - TNF- $\alpha$  inhibitor therapy
  - Transplant recipients
  - Chronic kidney disease, silicosis, haematological malignancy
  - Untreated or inadequately treated prior TB

#### 3. Risks of treatment

- Hepatotoxicity (risk increases with age, alcohol use and pre-existing liver disease)
- Peripheral neuropathy
- Drug interactions and adherence challenges

## How to Order QuantiFERON-TB Gold Plus

### Request Form Instructions:

- Complete the Clinical Labs general pathology request form, requesting Quantiferon Gold (TB).
- Blood samples can be collected at any Clinical Labs collection centre.

### Clinical Notes:

- Provide the reason for testing (e.g., exposure to active case, immunosuppressed, dialysis etc.).

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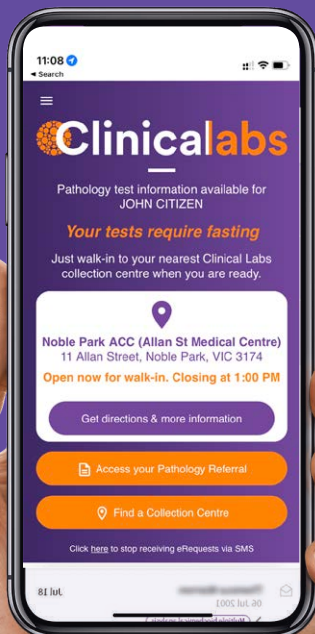
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# Needle Pain in Children:

## Why it matters and what we can do

By Professor Jane Munro

*Paediatric Rheumatologist, Director,  
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*Professor Jane Munro is a paediatric rheumatologist at the Royal Children's Hospital Melbourne and Director of Victorian Children's Clinic, a private paediatric practice in Malvern, Victoria, with special interests in pain medicine and musculoskeletal health.*

### The problem we've been ignoring

For most adults, a blood test is a minor inconvenience. For a child, it can be one of the most distressing experiences of their healthcare journey. Needle pain, including venepuncture, cannulation and capillary sampling, is the most common source of iatrogenic pain in children and is largely preventable.

Yet despite decades of evidence, needle pain in paediatric patients remains undertreated. Children frequently undergo procedures with no analgesic preparation, no distraction support and no recognition that their fear and pain are a clinical problem worth solving. The consequences extend beyond the moment. Poorly managed procedural pain in childhood is a well-documented driver of healthcare avoidance, needle phobia, and anxiety in adolescence and adult life.

### Why children are different

Pain is not simply a sensory experience. In children, the emotional and contextual components of pain—anticipatory anxiety, loss of control, unfamiliar environments and parental distress—are amplified. Young children lack the cognitive tools to rationalise what is happening to them. Even older children and adolescents may display significant distress disproportionate to what adults expect. Effective pain management must be age-appropriate, not one-size-fits-all.

Fear and pain also interact in a self-reinforcing cycle. A child who has had a traumatic blood collection experience arrives at their next appointment already in a state of heightened distress - making procedural success harder

and pain perception worse. Breaking this cycle early is far more effective than managing an entrenched needle phobia later.

### What the evidence tells us

The good news is that we know how to manage needle pain effectively. A strong and growing evidence base, including systematic reviews, the international gold standard in this space, identifies a cluster of interventions that, used in combination, dramatically reduce pain and distress in children undergoing needle procedures.

These fall into three categories:

#### 1. Topical anaesthesia

Topical local anaesthetic creams (such as EMLA or AnGEL) applied 30–60 minutes before a procedure significantly reduce pain at the needle site. They are safe, effective and underused. Incorporation into standard pre-procedure preparation, including providing families with a prescription or take-home cream for elective blood tests, is a straightforward systems change with immediate impact.

#### 2. Positioning and physical comfort

Supine restraint, the traditional approach of lying a child flat and holding them still, is associated with greater distress, poorer outcomes and lasting psychological harm. Current best practice favours upright positioning (seated on a parent's lap for young children, sitting independently for older children) and avoidance of forceful restraint. This simple change requires no equipment and can be implemented immediately.

#### 3. Psychological strategies

Distraction is the most evidence-supported non-pharmacological intervention for procedural pain in children - actively engaging the brain's attentional systems and competing with pain processing. Coaching parents to lead distraction, rather than offering reassurance ("it'll be okay, it won't hurt"), is a nuanced but important distinction. Reassurance-focused parental behaviour is associated with *increased* child distress.

Sucrose solution (for infants under 12 months) and breastfeeding during procedures are also well-supported and easily implemented.

## The role of pathology services

Pathology collection centres occupy a critical position in this story.

They are often the point of care for elective blood tests, a setting where preparation time exists, where the environment can be designed to support children and where staff training can be systematically implemented.

## What referring clinicians can do

When ordering blood tests for children, consider:

- Bundling tests where clinically appropriate to minimise the number of collections.
- Prescribing or recommending topical anaesthetic for elective procedures, particularly for younger children or those with known needle anxiety.
- Flagging children with significant needle phobia on referral, so collection staff can prepare appropriately.
- Discussing the collection experience with families before the appointment - what to bring, how to position their child and how to use distraction.

For children with chronic conditions requiring frequent blood tests - including those with juvenile idiopathic arthritis, inflammatory bowel disease, renal disease or oncological conditions - a proactive pain management plan is part of good clinical care.

## A word on consent and restraint

Forceful restraint of a child for a non-emergency procedure is ethically problematic and, in most cases, clinically unnecessary when proper preparation has occurred.

Where a child is extremely distressed, deferral and rescheduling with enhanced preparation, or referral to a service with specialised paediatric care and/or procedural analgesia and sedation, is almost always preferable to proceeding under duress.

## Conclusion

Needle pain is not a trivial side effect of paediatric healthcare; it is a clinical problem with documented short- and long-term consequences. The evidence base for prevention is strong, the interventions are accessible, and the opportunity for pathology services and referring clinicians to lead meaningful change is real.

## Useful clinical resources

- The Meg Foundation for Pain: procedural pain resources for providers and families. [www.megfoundationforpain.org](http://www.megfoundationforpain.org)
- Comfort Kids: Toolkit and other resources for kids and families [rch.org.au/comfortkids](http://rch.org.au/comfortkids)
- ChildKind International: [childkindinternational.org](http://childkindinternational.org)
- HELPinKids & Adults / It Doesn't Have to Hurt: <https://phm.utoronto.ca/helpinkids/index.html>
- Canadian Paediatric Society (CPS), updated March 2025: <https://cps.ca/en/documents/position/managing-pain-and-distress>

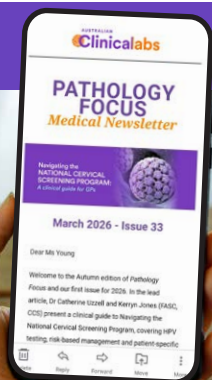
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