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Event Cluster of neonatal myocarditis reported in Wales and South West England (June 2022 – current)

Notified by Shamez Ladhani, Paediatric Infectious Diseases Consultant, Immunisation and Vaccine Preventable Diseases Division

Authorised by Mary Ramsay, Director Public Health Programmes
William Welfare, Director of Regions

Contact shamez.ladhani@ukhsa.gov.uk; phe.neonatalmyocarditis@nhs.net

NIRP Level National routine incident response

Incident Lead Shamez Ladhani

Instructions for Cascade

- **UKHSA Private Office Groups** to cascade within Groups
 - **Devolved Administrations** to cascade to Medical Directors and other DA teams as appropriate to their local arrangements
 - **Regional Deputy Directors** to cascade to Directors of Public Health
 - **UKHSA microbiologists** to cascade to non-UKHSA labs (NHS labs and private)
 - **UKHSA microbiologists** to cascade to NHS Trust infection leads
 - **NHS labs/NHS infection leads/NHS microbiologist/NHS infectious disease specialists** to cascade to neonatologists, paediatricians, paediatric emergency departments, paediatric intensivists and paediatric infectious disease specialists.
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Issue: a cluster of severe neonatal myocarditis associated with enterovirus infection has been noted in South Wales and South West England. This briefing note provides information on this cluster to raise awareness amongst clinicians and laboratories. Cases of neonatal enteroviral myocarditis should be reported by email to UKHSA, with local testing for enterovirus, and referral of positive samples to UKHSA Enteric Virus Unit for typing.

Current issue

Public Health Wales is investigating a cluster of severe enterovirus infections with myocarditis in very young babies from the South Wales region ([Written Statement: Ongoing investigation into neonatal myocarditis cluster in South Wales \(3 May 2023\) | GOV.WALES](#)). The investigation to date has identified a total of 10 severe neonatal enteroviral myocarditis (NEM) cases (age under 28 days) between June 2022 and April 2023 in South Wales. Eight neonates have been discharged home, one remains in hospital, and one died before referral to tertiary care.



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The neonates presented to hospital severely unwell, with cardiogenic shock, requiring ventilatory and circulatory support in the paediatric intensive care unit (PICU), often for prolonged periods. All 10 neonates had confirmed enterovirus infection and, of the five strains that were typed, all were identified as coxsackie B3 or B4 viruses. Retrospective case finding identified only two other cases of NEM in the previous 6 years prior to June 2022 in the same region. A further five cases have been identified over the same period in the South West of England – of the four strains that were typed, all were identified as coxsackie B3.

PICUs in the South West of England (3 cases) and South Wales (5 cases) have published a case series on 8 of the 15 known NEM cases diagnosed during September-December 2022 (1). Seven of the 8 infants had been born at term and their median age at presentation was 10 days (range 9-16 days). All eight neonates, including two who initially had enteroviral meningitis, were very unwell at presentation, with reduced feeding, tachypnoea, cardiogenic shock and severe left ventricular dysfunction on initial echocardiography.

This recent NEM cluster in South Wales and the South West of England represents an unusual increase in case numbers compared to previous years in the same region. The peak of the cluster occurred during September-December 2022, in keeping with peak seasonal enterovirus activity. The underlying factors driving this increase are unclear. Routine laboratory surveillance data for enteroviruses shows that, after a very quiet period during the COVID-19 pandemic, enterovirus activity was high in the 2021/2022 and the 2022/2023 epidemiological years. Most of the increase in laboratory reported infections was seen in children under 5 years, especially infants with under 1 year during 2022/2023. This surveillance is based on voluntary reporting of enterovirus testing results by hospital laboratories, which is not consistent across the UK.

UKHSA have established a national routine incident to coordinate prospective and retrospective NEM case finding across the UK. Early investigations have not identified any other NEM clusters in any other UK region so far. Clinicians and laboratory colleagues are asked to report NEM cases diagnosed since 01 June 2022 to UKHSA by email to phe.neonatalmyocarditis@nhs.net.

Background

Enteroviruses are a common cause of seasonal childhood infections and typically cause respiratory disease, hand-foot-and-mouth and viral meningitis. The vast majority of infections are mild and self-limiting. Neonates can, however, rarely develop severe enterovirus infection, which may present as a sepsis-like syndrome or viral meningitis. Myocarditis (inflammation of the heart muscle) is a very rare complication of enterovirus infection, and typically associated with coxsackie B viruses.

Enterovirus myocarditis is associated with high morbidity and mortality, especially in neonates, and can lead to severe complications, including heart failure, arrhythmias and haemophagocytic lymphohistiocytosis (HLH).



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In a poorly feeding neonate presenting with respiratory distress, sepsis or shock, especially in the presence of inappropriate persistent tachycardia, an underlying myocarditis should be considered. Myocardial dysfunction can be identified by measuring cardiac enzymes, electrocardiography and echocardiography.

Aetiology can be confirmed by identification of enterovirus in a respiratory sample, blood, stool or cerebrospinal fluid. Enterovirus infection is not notifiable in the UK. Consequently, laboratory surveillance for enteroviruses is dependent on voluntary laboratory reporting of positive samples to SGSS and referral of samples to the UKHSA Enteric Virus Unit in Colindale for further characterisation (2).

There is no specific antiviral therapy for enteroviruses. Treatment relies primarily on management of complications, including fluid management, usually in PICU settings. In very severe cases, intravenous immunoglobulin (IVIG), intravenous steroids, investigational antivirals (e.g. pocapavir (V-073), an investigational enterovirus capsid inhibitor) and immunomodulation (e.g. anakinra) have been used (1).

Implications & Recommendations for NHS

Awareness, testing and reporting

Front line clinicians, including neonatologists, paediatricians, paediatric emergency departments, paediatric intensivists and paediatric infectious disease specialists, are reminded to consider the possibility of an underlying myocarditis and myocardial dysfunction in neonates presenting with features of respiratory distress, sepsis-like syndrome, shock, or meningitis

In such cases, clinicians should consider testing for enteroviruses. **The minimum sample set for enterovirus testing includes EDTA blood, an upper respiratory tract sample (throat swab, nasopharyngeal swab and/or nasopharyngeal aspirate), stool sample and, if clinically indicated, cerebrospinal fluid (3).**

Paediatricians, neonatologists and intensivists should strongly consider contacting their local paediatric/neonatal cardiologists and infectious diseases specialists early for further investigation and management of suspected NEM.

NHS laboratories are reminded that all enterovirus positive samples should be referred to the Enteric Virus Unit (EVU) using the E1 form which can be found [here](#), for further characterisation to monitor the diversity of current strains and aid detection of novel strains which may be linked to severe clinical syndromes. If all samples cannot be referred to EVU, then enterovirus positive samples from NEM cases and other severe enterovirus presentations such as sepsis and meningitis should be prioritised for referral to EVU.

Clinicians and laboratory colleagues are asked to report NEM cases diagnosed since 01 June 2022 to UKHSA by email to phe.neonatalmyocarditis@nhs.net.



Implications & Recommendations for UKHSA Regions

Enterovirus (non-polio) infections and clinical myocarditis are not notifiable, so HPTs are unlikely to become aware of individual cases. Clinicians and laboratory colleagues are asked to report NEM cases diagnosed since 01 June 2022 to UKHSA by email to phe.neonatalmyocarditis@nhs.net. If cases are reported to HPTs, then please direct to this email address. Suspected cases should have appropriate cardiac investigations and testing for enterovirus (see below).

Implications & Recommendations for UKHSA sites and services

Consultants in Public Health Infection (CPHI) should be aware of the recent NEM cluster.

Local and Regional laboratories are reminded of the request to refer all enterovirus positive samples to the UKHSA Enteric Virus Unit (EVU) to monitor the diversity of current strains and aid detection of novel strains which may be linked to severe clinical syndromes.

UKHSA Public Health Laboratories should work with NHS laboratories to ensure that enterovirus positive samples, especially from NEM cases and other severe enterovirus presentations such as sepsis and meningitis, are prioritised for referral to EVU.

Implications and recommendations for Local Authorities

Nil

References/ Sources of information

1. Ng KF et al. Arch Dis Child Feb 2023;108:417-419
<http://dx.doi.org/10.1136/archdischild-2023-325316>
 2. [Enterovirus: summary of strain characterisation - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/publications/enterovirus-summary-of-strain-characterisation)
 3. [PHE National Polio Guidelines - Local and regional services \(publishing.service.gov.uk\)](https://publishing.service.gov.uk/government/publications/phe-national-polio-guidelines-local-and-regional-services)
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