

15 minute consultation: The child with a non-blanching rash.

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Abstract:

Its 2am and you are called to review a “well looking child” in the emergency department who has presented with a new non-blanching rash. He has been hot at home with some coryzal symptoms. Mum is worried, she thinks the rash has spread in the last hour!

What are you going to do?

In this article, we discuss the aetiology and initial assessment of non-blanching rashes in children.

Introduction

Non-blanching rash (NBR) is a term for any rash in which the colour is unchanged with direct pressure. The presence of a NBR is of concern to both parents and clinicians as it is associated with a wide range of underlying diagnoses, some of which are life threatening. The term is usually used to refer to the presence of petechiae/purpura (figure 1), and in this form it is a relatively common presentation to the emergency department (ED), accounting for around 2% of all attendances(1,2).

In this article, we discuss the aetiology and an initial assessment of NBR in children.

Figure 1.

Petechiae Vs Purpura

Petechiae are non-blanching spots that are <2mm in size and are due to capillary haemorrhage. As more haemorrhages occurs the petechiae coalesce into purpura (>2mm).

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Aetiology

The commonest causes of NBR in children can be broadly classified as infective or mechanical. Other causes are less common and are classified as vasculitic, haematological and “other”. (1–6). (Table 1)

Infectious Causes

Any serious bacterial infection (SBI) can result in a NBR via disseminated intravascular coagulation (DIC). Some infections however, feature a NBR as an early sign. The commonest infections associated with a NBR as an earlier sign are:

- Viral:
 - Enterovirus and Adenovirus are the commonest infectious causes of NBR in children (3).
- Bacterial
 - Streptococcal Infections (1–4)
 - Meningococcal Disease (MD) (6).

Of these infections MD is arguably the one we worry about most in the UK but how commonly is MD responsible for a NBR in a child?

This is surprisingly difficult to answer because studies are difficult to compare due to their heterogeneity. For example one study looking at all presentations of fever (>38°C) and NBR presenting to the ED found that only 1% of children had MD as the cause(2). In contrast, studies of hospitalised children with fever and NBR have reported rates as high as 23%(3).

What about other serious bacterial infections?

Other invasive bacterial infections may also present with a NBR - especially streptococcus infections (1,4,6). Other infectious causes are rare (<1%) of cases (1–3).

Mechanical Causes

A mechanical cause is identified in almost a quarter of NBR in children(3), the most common being straining, coughing or vomiting. This causes raised pressure within the superior vena cava (SVC), with consequent pinpoint petechiae in the distribution of the SVC alone (above the nipple line)(1).

However, the early stages of serious bacterial infections may present with a localised NBR meaning that a mechanical cause is often arrived at through a process of exclusion.

Direct trauma can result in bruising that can appear identical to a true NBR. There is usually a clear history of trauma. In cases where a traumatic cause is likely it is important to consider safeguarding. This is especially important when lesions are localised to the genital area, buttocks, are unusual or linear, or when the history is unclear (7).

Vasculitic Causes

Henoch-Schonlein Purpura (HSP) is the most common vasculitic cause in children, with other less common causes including atypical Kawasaki disease, polyarteritis nodosa, and anti-neutrophil cytoplasmic antibody related vasculitis (13).

HSP typically presents with palpable purpura found in a gravity dependent distribution - classically on the legs and buttocks (8).

Haematological Causes

The main haematological causes likely to present are thrombocytopenia, leukaemia, and coagulopathy.

Thrombocytopenia

Idiopathic thrombocytopenia purpura (ITP) is the most common haematological cause and presents with the sudden development of a NBR. In ITP a Full Blood Count (FBC) should show isolated thrombocytopenia, and a blood film should be normal other than thrombocytopenia(9,10)(10).

Other rare causes of thrombocytopenia include;

- Infection (e.g. EBV(11))
- Drug induced (e.g. Vaccination, Heparin, NSAIDs, Ranitidine(12–15))
- Thrombotic thrombocytopenic purpura
- DIC
- Hypersplenism
- Bone marrow failure

Haematological Malignancy

Children with undiagnosed haematological malignancies can present with a NBR, either as an isolated finding, or in conjunction with other features such as weight loss, fatigue, pallor, and general malaise(16)(12). Clinical features such as lymphadenopathy, hepatomegaly, splenomegaly, jaundice and anaemia should be sought, (12) and any child with an abnormal blood film or deficiencies in multiple cell lines should be discussed with the local haematology service.

Coagulopathy

Coagulopathy is a rare cause of a NBR in children (0.4% of cases)(3). A family history of coagulation disorders or a long history of easy bruising and/or a NBR that remains unexplained may suggest an underlying coagulation disorder.

Other causes

It is worth considering whether a well child's rash is in fact a normal variant. A study of infants attending routine health checks found that petechiae were commonly identified in well infants with over ¼ having one or more petechiae (17).

Assessing the child

No guideline or algorithm will ever perform perfectly due to the range of possible causes. The approach discussed here is designed to assist the thought process but isn't a substitute for clinical reasoning or experience.

The steps involved are outlined in figure 2 and include:

- An initial assessment of wellness to identify those requiring immediate treatment
- An attempt to make a positive diagnosis
- If no positive diagnosis can be made then consider if it is appropriate to discharge

Is the child well?

Any child who appears unwell with a NBR should be presumed to have a SBI and be treated accordingly(1–5). In the context of NBR, presenting features of irritability, lethargy or a prolonged capillary refill time confer a significantly increased risk of SBI (1–5) - children with these features should be treated as per national guidance immediately.

- [Meningococcal disease \(Meningitis \(bacterial\) and meningococcal septicaemia in under 16s: recognition, diagnosis and management\)](#)
- [Sepsis: recognition, diagnosis and early management](#)

The presence of fever is a key component of the history and examination, though it should not be relied upon in isolation to make clinical decisions. Whilst not all children with fever and NBR will have SBI, it is also important to note that not all children with SBI and NBR present with a fever - up to 20% of cases of MD have no fever at presentation to ED (1,18). Whilst it may be reasonable to withhold antibiotics from children who appear well it is important to note that children can initially appear well and deteriorate, mandating a period of active observation.

Can I make a positive diagnosis?

If the child appears well it is still important to attempt to make a diagnosis. Whilst undertaking this process it is important to carefully monitor the child for signs of deterioration. As even well appearing children may be harboring an occult SBI.

When searching for a diagnosis a number of tests can be considered (Table 1). NICE Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management guidance includes the assessment of NBR in febrile children and advises (19). These investigations focus on the diagnosis of MD. Whilst this is important (Table 1) below outlines some additional investigations and anticipated results for other causes of a NBR.

- FBC
- C-Reactive Protein
- Coagulation screen
- Blood culture
- Whole-blood polymerase chain reaction (PCR) for N meningitidis
- Blood glucose
- Blood gas

Special considerations are required for children presenting with purpura. These children are at higher risk of MD and other SBI than those with petechiae alone, and some therefore advocate that all children with purpura should be treated for suspected MD/sepsis (1–5). This approach, whilst safe, leads to over-treatment of children with HSP(5). There are no unifying diagnostic criteria for HSP, but the presence of palpable purpura in a characteristic distribution in an otherwise well child suggests HSP as opposed to MD(5). However it is known that even experienced paediatricians may misdiagnose MD as HSP, leading to treatment delays (5).

A list of common causes and possible investigations are outlined below in table 1.

Table 1

Cause	Features	Investigations
Infective	Fever may or may not be present – look for worrying features: <ul style="list-style-type: none"> • Appearing unwell • Irritable/Lethargic • Prolonged CRT • Spread of rash • Purpura • Deterioration 	FBC CRP Meningococcal PCR Viral PCR Blood Culture Blood Gas Glucose
Haematological •ITP •Malignancy •Coagulopathy	Isolated thrombocytopenia in a well child Abnormal film or cell count (Not ITP) Deranged clotting in a well child	FBC Blood Film Coagulation studies
Mechanical	Identification of mechanical cause in an otherwise well child.	Not always needed – when performed they are normal.
HSP	Well child, classical rash, no spread or deterioration. Normal cell counts and film. Where unclear may need to rule out other serious causes.	Urinalysis for evidence of glomerulonephritis Blood Pressure

Can I rule out serious illness?

If a positive diagnosis cannot be made but the child otherwise appears well, then the more difficult question is “Can I rule out SBI and other serious causes?”

Proving a negative is always more difficult in medicine and this is where the real challenge in managing childhood NBR occurs, given that so few have a serious underlying cause. Where determining a cause is not possible the challenge is deciding who is safe to be discharged and who should be treated(3)? If a decision is

taken to discharge a child it is important to provide clear advice to return if there is any; deterioration in the child's health, spread of the or change of the rash.

The current best evidence for the management of this group comes from the Newcastle-Birmingham-Liverpool algorithm (NBL)(5). This algorithm has been validated with a reported sensitivity of 100%, and a specificity of 82% for the diagnosis of MD(5). In the NBL algorithm a child can be discharged if the child remains well, has no purpura, no spread of the rash over 4-6 hours of observation and a CRP <6 and WBC 5-15(5). This approach out-performed current NICE guidance in a comparative validation exercise, with NICE guidance displaying a sensitivity of 97% and specificity of 50% (5). The difference in the performance of the two algorithms was statistically significant ($p < 0.001$)(5). Both NICE and NBL algorithms are designed as "rule out" algorithms and as such both are highly sensitive but poorly specific. This means that very few cases of MD will be missed but that many children will receive unnecessary treatment.

Summary

Non-blanching rashes are a common reason for children presenting to healthcare, often with non-specific findings. Whilst SBI is rare it is important to promptly identify and treat those at greatest risk. For well-appearing children, a structured approach can lead to a positive diagnosis in many, coupled with safe discharge decision making.

Figure 2

Questions

1. A 3-year-old child presents with a petechial rash seen on the trunk. He is otherwise well apart from being a bit tired over the last few weeks. He is afebrile and examination is otherwise unremarkable.

FBC: Hb 64 WCC 33 Plts 23 Neut 7

Which of the following is the best next step?

- A) IV ceftriaxone and send blood cultures
 - B) Reassure and discharge
 - C) Discuss with haematology
 - D) Blood transfusion
 - E) Oral Steroids
- (C)

2. An 8-month-old girl presents with a purpuric rash over her extremities with a temperature of 39.6. She has a capillary refill time of 5 seconds and is lethargic. Heart rate is 160 and blood pressure is 83/56.

What is the most appropriate initial management?

- A) CT head
 - B) LP and blood cultures
 - C) Contact the transport team
 - D) Immediate intubation
 - E) Fluid Bolus & IV Antibiotics
- (E)

3. In an 8-year-old child with palpable purpura for 3 days on the legs and buttocks with normal observations, the most likely diagnosis is?

A) ANCA related vasculitis

B) HSP

C) Meningococcal sepsis

D) Adenovirus

E) Enterovirus

(B)

4. A 6-month-old with 3 petechial spots is brought to A&E by his parents as they noted that the spots didn't disappear with the "cold glass test". They have been there for 1 day and have not spread. He had normal observations and appeared well. At 6 hours, his observations remained within the normal limits. His CRP was <6, white cell count 10 and no further petechiae have appeared.

What is the next most appropriate step in management?

A) Contact social services

B) Discharge with safety netting advice

C) Discharge with oral antibiotics

D) IV ceftriaxone

E) LP and blood cultures

(B)

5. A 9-month-old child comes in with a 5-day history of cough and coryza. You diagnose bronchiolitis and they are medically fit to be discharged. As Mum is changing the nappy you notice a linear bruise on one buttock.

What would be the next appropriate action(s)?

A) IV ceftriaxone

B) LP and blood cultures

C) Top to toe examination and consider safeguarding background checks

D) Discharge home with safety netting advice

E) Topical emollient and discharge

(C)

References

1. L.C. W, J.C. S, V.C. W, J. C, Wells LC, Smith JC, et al. The child with a non-blanching rash: How likely is meningococcal disease? *Arch Dis Child* [Internet]. 2001;85(3):218–22. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=11517104>
2. Mandl KD, Stack AM, Fleisher GR. Incidence of bacteremia in infants and children with fever and petechiae. *J Pediatr* [Internet]. 1997;131(3):398–404. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=9329416>
3. Nielsen HE, Andersen EA, Andersen J, Bottiger B, Christiansen KM, Daugbjerg P, et al. Diagnostic assessment of haemorrhagic rash and fever. *Arch Dis Child* [Internet]. 2001;85(2):160–5. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=11466193>
4. Brogan PA, Raffles A. The management of fever and petechiae: making sense of rash decisions. *Arch Dis Child* [Internet]. 2000;83(6):506–7. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=11087287>
5. Riordan FAI, Jones L, Clark J. Validation of two algorithms for managing children with a non-blanching rash. *Arch Dis Child*. 2016;709–13.
6. Bourke TW, McKenna JP, Coyle P V, Shields MD, Fairley DJ. Diagnostic accuracy of loop-mediated isothermal amplification as a near-patient test for meningococcal disease in children: an observational cohort study. *Lancet Infect Dis* [Internet]. 2015;15(5):552–8. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=25728843>
7. Burrows NP. Purpura in infants and children. *J Am Acad Dermatol* [Internet]. 1998 Oct [cited 2017 Sep 5];39(4 Pt 1):661–2. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9777785>
8. Barut K, Şahin S, Adroviç A, Kasapçopur Ö. Diagnostic approach and current treatment options in childhood vasculitis. *Turk Pediatr Ars* [Internet]. 2015 Dec 30 [cited 2017 Sep 5];50(4):194–205. Available from: <http://www.turkpediatriarsivi.com/sayilar/298/buyuk/194-205y.pdf>
9. Buchanan GR. Immune thrombocytopenia during childhood: new approaches to classification and management. *J Pediatr* [Internet]. 2014 Sep [cited 2017 Sep 5];165(3):437–9. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0022347614004570>
10. Provan D, Stasi R, Newland AC, Blanchette VS, Bolton-Maggs P, Bussel JB, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood* [Internet]. 2010 Jan 14 [cited 2017 Sep 5];115(2):168–86. Available from: <http://www.bloodjournal.org/cgi/doi/10.1182/blood-2009-06-225565>
11. Tilden W, Valliani S. Severe thrombocytopenia and recurrent epistaxis associated with primary Epstein-Barr virus infection. *Case Reports* [Internet]. 2015 Apr 9 [cited 2017 Nov 7];2015(apr09 1):bcr2014208018–bcr2014208018. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25858924>
12. Chaudhry R, Wegner R, Zaki JF, Pednekar G, Tse A, Kukreja N, et al. Incidence and Outcomes of Heparin-Induced Thrombocytopenia in Patients Undergoing Vascular Surgery. *J Cardiothorac Vasc Anesth* [Internet]. 2017 Oct [cited 2017 Nov 7];31(5):1751–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28864160>
13. Bangia A, Kamath N, Mohan V. Ranitidine-induced thrombocytopenia: A rare drug reaction. *Indian J Pharmacol* [Internet]. 2011 Feb [cited 2017 Nov 7];43(1):76. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21455428>
14. V. U, A. E, Urbonas V, Eidukaite A, Tamuliene I. The predictive value of soluble biomarkers (CD14 subtype, interleukin-2 receptor, human leucocyte antigen-G) and procalcitonin in the detection of bacteremia and sepsis in pediatric oncology patients with chemotherapy-induced febrile neutropenia. *Cytokine* [Internet]. 2013;62(1):34–7. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=23510625>
15. Moulis G, Sommet A, Sailler L, Lapeyre-Mestre M, Montastruc J-L, the French Association of Regional. Drug-induced immune thrombocytopenia: A descriptive survey in the French Pharmacovigilance database. *Platelets* [Internet]. 2012 Sep 18 [cited 2017 Nov 7];23(6):490–4. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22098130>
16. Clarke RT, Van den Bruel A, Bankhead C, Mitchell CD, Phillips B, Thompson MJ. Clinical presentation of childhood leukaemia: a systematic review and meta-analysis. *Arch Dis Child* [Internet]. 2016;101(10):894–901. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=27647842>
17. Downes AJ, Crossland DS, Mellon AF. Prevalence and distribution of petechiae in well babies. *Arch Dis Child* [Internet]. 2002 Apr 1 [cited 2017 Sep 4];86(4):291–2. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11919110>
18. Hart CA, Thomson APJ. Meningococcal disease and its management in children. *BMJ* [Internet]. 2006;333(7570):685–90. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1584345&tool=pmcentrez&rendertype=abstract>
19. NICE. Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management | Guidance and guidelines | NICE. 2015 [cited 2017 Oct 10]; Available from: <https://www.nice.org.uk/guidance/cg102>

