Don't Forget The Bubbles

NON-BLANCHING RASHES

Facilitators Guide

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Topic: **Non-Blanching Rashes**
Author: **Aoife Fox**
Duration: **1.5 hrs**

OUTLINE

- Pre-reading for learners
- Basics
- Case 1: Meningococcal sepsis (20 min)
- Case 2: Immune thrombocytopenic purpura (ITP) (15 min)
- Case 3: Non-accidental injury (10 min)
- Case 4: Henoch-Schonlein Purpura (20 min)
- Quiz
- 5 take home learning points

PRE-READING/LISTENING FOR LEARNERS

Podcasts

DFTB Podcast – How to use the clinical signs of meningitis

Peds Cases - Meningitis

Two Paeds in a Pod – Managing non-blanching Rashes

Articles

Approach to rashes

EMDocs - What's that Rash? An approach to dangerous rashes based on morphology

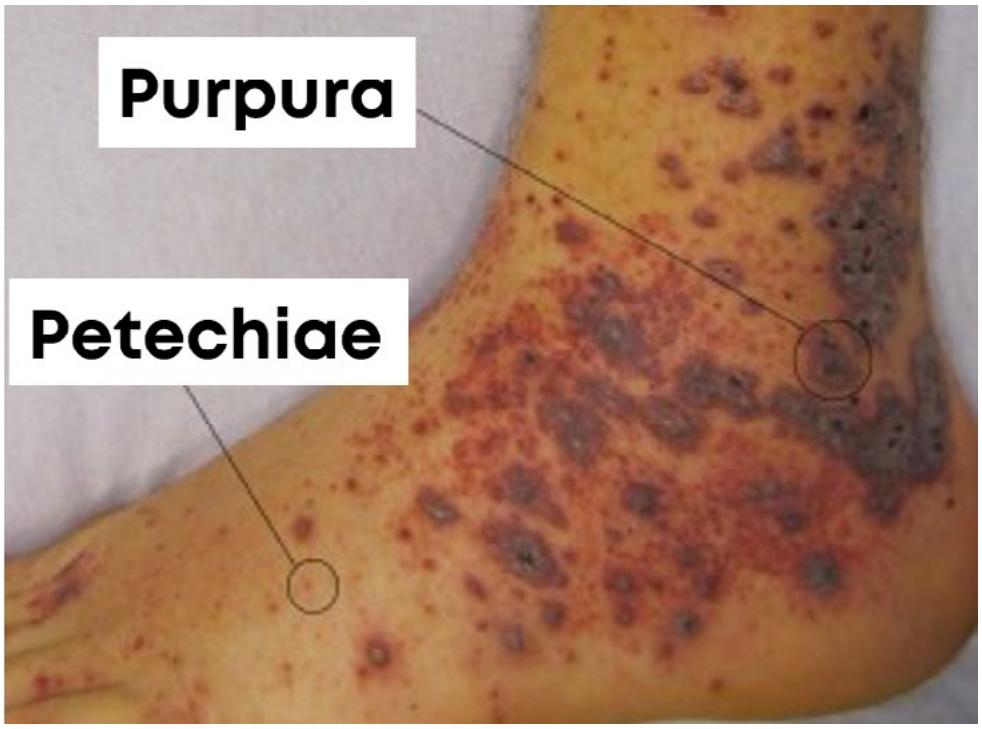
DFTB - Petechiae in Children - the PIC Study

Basics

Key learning points

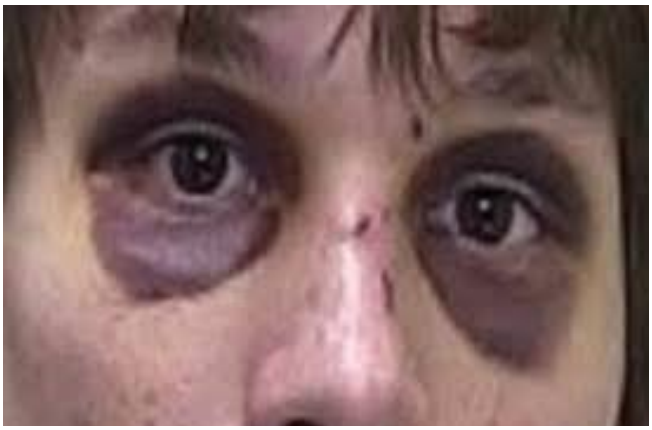
• Petechiae: are pin-point, non-blanching red lesions of the skin or conjunctiva, usually <0.5cm caused by capillaries leaking blood into the skin. Occasionally, they can be raised (palpable). They are caused by physical trauma, infectious, vascular and haematological causes.

• Purpura: a non-blanching area of colour change (red or purple) due to bleeding into the skin secondary to platelet disorders, vascular disorders (e.g. vasculitis), coagulation disorders (e.g. disseminated intravascular coagulation (DIC)) and infection such as meningococcaemia.



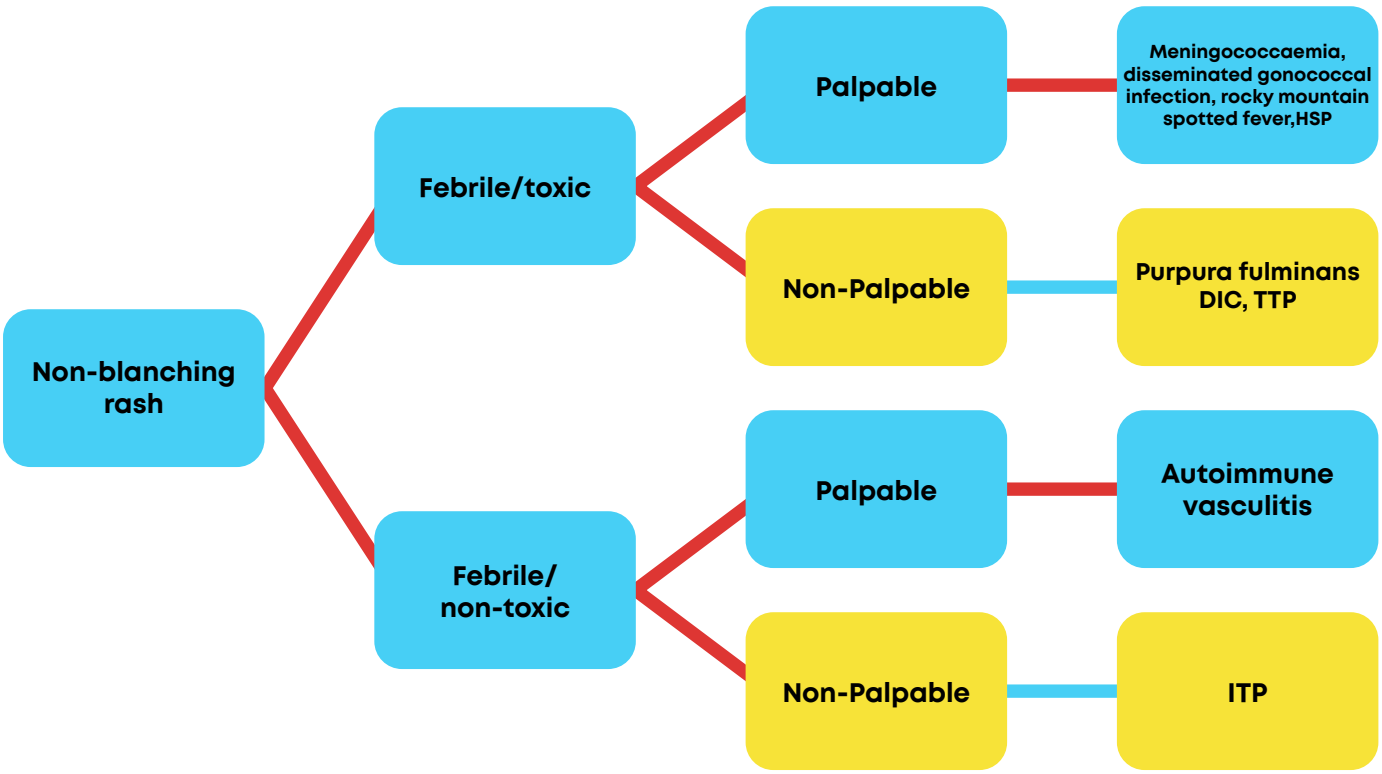
Purpura and petechiae (Image: used with gratitude from Emdocs.net)

• Ecchymosis: a larger area of purpura usually greater than 1cm (e.g., vasculitis, disseminated intravascular coagulation).



Bilateral periorbital ecchymosis (Image: used with gratitude from Wikipedia.org)

Diagnostic aide



DIC – Disseminated intravascular coagulopathy, TTP = thrombotic thrombocytopenic purpura

Approach to non-blanching rash

(from LITFL - LITFL - Perilous Pinhead Polka-dots)

Infection	Mechanical	Haematological	Vascular
• Serious bacterial illnesses – (classically meningococcemia, streptococcus, H. influenzae and infective endocarditis) • Viral infections (e.g. influenza, measles, enteroviruses and parvovirus) • Rickettsiae (e.g. Rocky Mountain Spotted Fever in North America, Epidemic typhus and Queensland tick typhus)	• Coughing or vomiting (limited to head and neck regions) • Local pressure or tourniquet application (e.g. petechiae distal to tourniquet) • Strangulation	• Thrombocytopenia (platelets <100 x 10E9/L) e.g. ITP (immune thrombocytopenic purpura), leukaemia and hypersplenism • Platelet dysfunction – e.g. congenital, drugs and renal failure	• Scurvy (classically perifollicular purpura on the lower limbs) • Drugs e.g. steroids • Cushing syndrome • Fat embolism • Dysproteinaemia

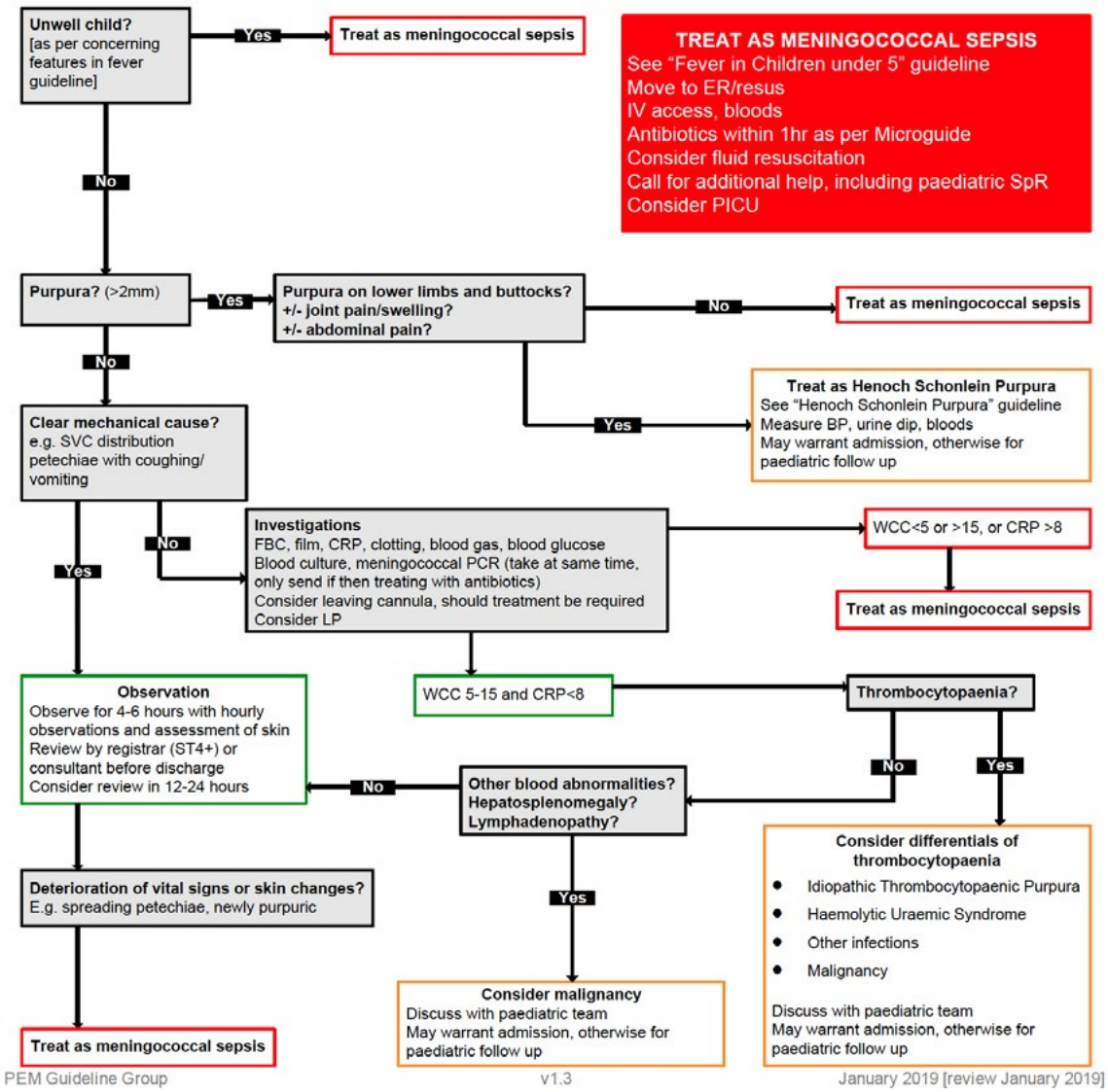
The rash can result from the following **mechanisms:**

- mechanical capillary injury
- impaired haemostasis
- septic emboli or invasion of the capillary walls
- microbial toxin-induced capillary damage
- immune complex deposition

Management

A large study called PIC (Petechiae in Children) was published in 2020. This was a prospective, multicentre cohort study looking at how good existing guidelines were at picking up children with meningococcal disease. Prior to the introduction of meningococcal B and C vaccines the prevalence of meningococcal disease in children presenting with fever and a non-blanching rash was around 10-20%. The PIC study showed that since the introduction of the vaccines, this has fallen to around 1%.

The PIC study looked at regional guidelines and NICE guidelines on investigation and management of a child with fever and a non-blanching rash in terms of their sensitivity and specificity. All the guidelines had 100% sensitivity (i.e. all children with meningococcal disease were detected by following the guidelines) but were not very specific (i.e. many children without meningococcal disease would have received treatment). The best performing guideline in the study was the Barts Health NHS Trust guideline (below).

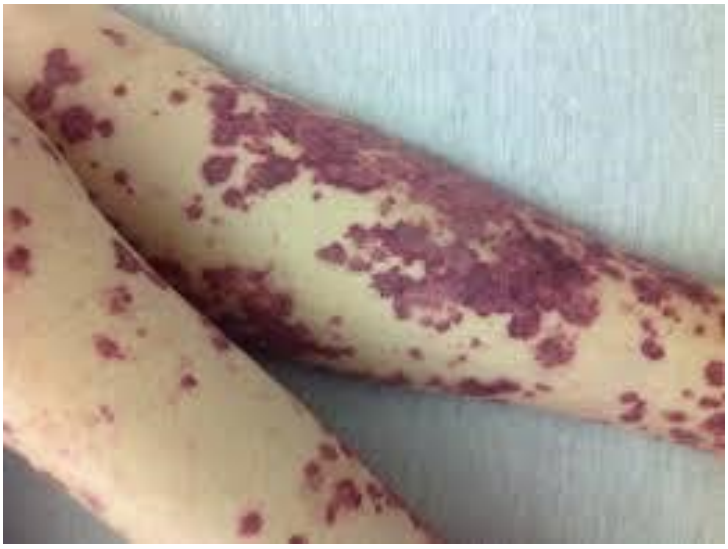


CASE 1: MENINGOCOCCAL SEPSIS

(based on a case from EMDocs - **EMDocs -The Sick Meningitis Patient – From Bad to Worse)**

James, a 13-year old boy, presents to the ED with his father. His father reports that before leaving for class the patient was complaining of slight headache and body aches. James went to school, but his teacher phoned his parents at 11am to come and collect him as he was unwell. She said he looked sweaty, was warm to touch, was complaining of neck pain and was saying things that didn't make sense.

On examination you notice he has extensive purpura over both thighs and abdomen. He is hypotensive with a BP of 80/40 and tachycardic with a HR of 130 bpm.



(Image used with gratitude from Wikipedia.org)

What is the most likely diagnosis?
What is the most likely organism causing this?
What percentage of these patients present with the classic petechial/purpuric rash?
What investigations would you like to do?
What treatment would you like to commence?
What is an extensive rash an indicator of?
James, over develops the following rash. What is it? How does this influence his prognosis? How would you like to treat it?
What other complications of bacterial meningitis might occur?
One of the nursing staff ask you to review James as his eye "looks funny". On exam you diagnose a unilateral 6th neve palsy. What has happened?

Apart from the dexamethasone which you have already given, what other strategies could you employ to reduce intracranial pressure (ICP)?
In terms of the safety of yourself and your colleagues is there anything you need to consider?
James' mum is tearful and tells you she is sure James is up to date with all his vaccinations. **What can you tell her about the meningococcal vaccine?**

What is the most likely diagnosis?
Sepsis in the setting of bacterial meningitis secondary to meningococcemia complicated by shock and raised ICP

What is the most likely organism causing this?
Neisseria meningitidis

In meningococcal infection, what percentage of patients present with the classic petechial/purpuric rash?
The rash may be absent in up to 50% of cases (in meningitis and the early stages of septicaemia). Be mindful of non-specific clinical features such as limb pain in the alert child which is present in 30 - 60% in the early stages of sepsis.

What investigations would you like to do?
James is unstable, so do not do any investigations that would delay treatment. Do bloods (VBG, FBC, U+E, CRP, coagulation study), take two EDTA tubes for meningococcal DNA PCR and blood culture. Microbiological confirmation is important for disease identification and institution of public health measures. Blood cultures are positive in 50-80% of cases, and CSF cultures are positive in 80-90% of cases of meningitis. Meningococcal PCR is both sensitive (97%) and specific (99.6%) and will remain positive for several days after the start of antibiotics.

What treatment would you like to commence?
UpToDate - Bacterial meningitis in children: Dexamethasone and other measures to prevent neurologic complications

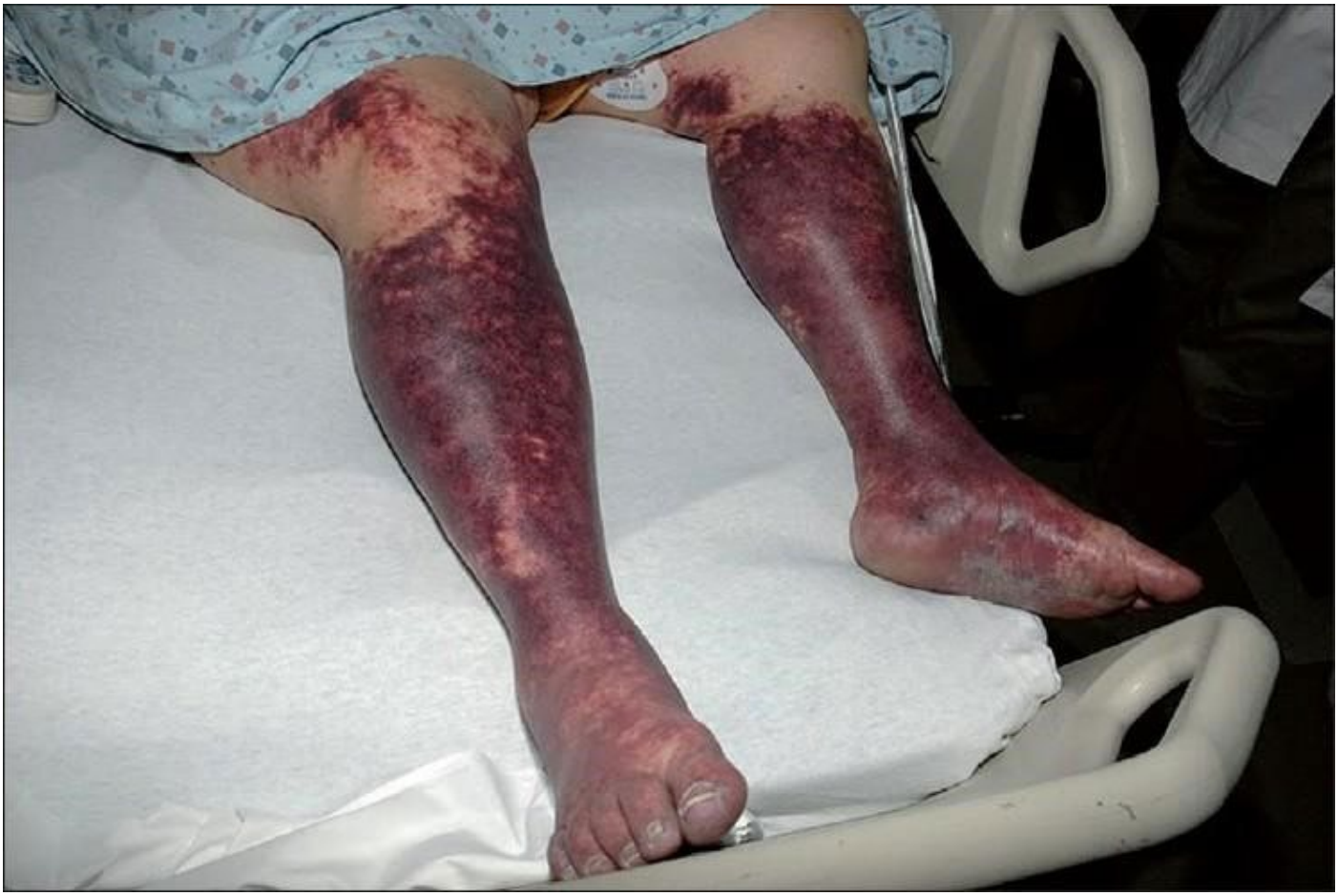
Firstly, attend to ABCDEFG (don't ever forget glucose!) H (and get help…). High flow oxygen should be delivered routinely from the outset. If no major airway or breathing problem is present, priority is given to the assessment and treatment of the circulation. Give fluid resuscitation as required. Treat with a third generation cephalosporin (Ceftriaxone or Cefotaxime). Add Vancomycin if Gram positive

cocci on Gram-stain. Add acyclovir if signs of encephalitis (fluctuating consciousness, motor or sensory deficits, altered behaviour and personality changes, speech or movement disorders).

Dexamethasone therapy should be administered to all patients early in disease course with or before the initial IV antibiotics. In children with bacterial meningitis, dexamethasone appears to reduce the risk of hearing loss (particularly in those with Haemophilus influenzae type b [Hib] meningitis). However, it does not appear to reduce the risk of other neurologic sequelae or mortality.

What is an extensive rash an indicator of?
Larger and more extensive rashes are an indicator of a greater degree of thrombocytopenia and coagulopathy (DIC) secondary to septicaemia.

James develops the following rash. What is it? How does this influence his prognosis? How would you like to treat it?
UpToDate - Clinical manifestations of meningococcal infection
UpToDate - Disseminated intravascular coagulation in infants and children



(Image used with gratitude from Journal of Postgraduate Medicine (**jpgmonline.com**))

This is purpura fulminans; it occurs in 15 to 25% of those with meningococcemia. It is the deadliest form of skin involvement secondary to meningococcal infection. It is characterized by the acute onset of cutaneous haemorrhage and necrosis due to vascular thrombosis and disseminated intravascular coagulopathy. Initially, there is cutaneous pain followed by erythema and petechiae. Ecchymoses develop and these lesions, if the course is not altered with therapy, evolve into painful indurated, well-demarcated purple papules with erythematous borders. These areas progress to necrosis with formation of bullae and vesicles. Gangrenous necrosis can follow with extension into the subcutaneous tissue and occasionally involves muscle and bone.

These patients will benefit from fresh frozen plasma (FFP) and/or protein C concentrate. There have been no randomized controlled trials to study the efficacy of platelet, FFP, or cryoprecipitate transfusions in children or adults with DIC. Nevertheless, the use of these agents seems rational in patients with

significant bleeding due to thrombocytopenia and clotting factor consumption. If soft tissue/skin necrosis is found, consultation with general surgery is recommended as debridement, fasciotomy, and/or amputation may be indicated based on progression of illness. Multi-disciplinary input from orthopaedic, vascular and plastic surgeons may be needed for limb salvage.

What other complications of bacterial meningitis might occur?

Systemic	Neurologic
• Septic arthritis • Immune-mediated arthritis • Pericardial effusion	• Impaired mental status • Cerebral oedema and increased intracranial pressure • Seizures • Focal deficits (eg, hearing loss, cranial nerve palsies, hemiparesis, or quadriparesis) • Ataxia • Cerebrovascular abnormalities • Neuropsychologic impairment, developmental disability • Subdural effusion or empyema • Hydrocephalus • Hypothalamic dysfunction

One of the nursing staff asks you to review James as his eye "looks funny". On exam you diagnose a unilateral 6th neve palsy.
What has happened? Apart from the dexamethasone which you have already given, what other strategies could you employ to reduce intracranial pressure (ICP)?

Once elevated ICP is identified or suspected, time is of the essence, as it can progress to herniation and/or death.

Dexamethasone may reduce ICP through reducing inflammation as well as increase vascular perfusion. Other strategies include head of bed elevation to 30 degrees, pain control, adequate sedation, fever control, hypertonic saline (2.7% in 3-5mls/kg boluses over 20minutes) to aim for serum sodium levels of >140 or mannitol infusion and/or craniotomy.

Should intubation be required for airway protection, it should be performed by the most experienced physician, as you want to avoid hypoxia and recurrent attempts will potentially increase ICP. Once intubated, the patient should be adequately sedated with a fast acting, easily titratable sedative such as propofol that allows for frequent repeat neuro exams such as checking pupil size and reactivity every 15 minutes. Ventilate to a lower limit of between 30-38mmHg (4-5kPa) with continuous capnography.

James is clearly unstable so organising a CT head is not appropriate until he is stabilised.

Symptoms of raised ICP are:
- Headache
- Vomiting
- Diplopia

Signs of raised ICP are:
- Decreased level of consciousness
- Tense cranial fontanelle
- Pupillary asymmetry
- Seizures

Signs of brain herniation are:
- Pupillary dilatation

- Hypertension
- Bradycardia
- Respiratory depression

Urgent CT head is indicated in patients with these signs and symptoms once they are stabilised.

In terms of the safety of yourself and your colleagues is there anything you need to consider?

Prophylaxis (Ciprofloxacin, Rifampicin, Azithromycin as an alternative in pregnancy) should be given to those who had prolonged close contact with the patient during the seven-day incubation period, intimate contacts and those exposed transiently to large droplets from the upper respiratory tract of the patients during their admission to hospital e.g. those intubating or suctioning the airway without wearing appropriate PPE.

	Ciprofloxacin	**Rifampicin**
Adults and children ≥ 12 years	500mg po as a single dose	600mg bd for 2 days
5 – 11 years	250mg po as a single dose	10mg/kg for 2 days (max. dose 600mg)
	Full term neonates – 4 years: 300mg/kg po as a single dose up to a maximum of 125mg	1 – 5 years: 10mg/kg for 2 days (max. dose 600mg) < 12 months: 5mg/kg for 2 days

James' mum is tearful and tells you she is sure James is up to date with all his vaccinations. What can you tell her about the meningococcal vaccine?
DFTB - Quadrivalent Meningococcal Vaccination What's The Fuss About

The quadrivalent meningococcal vaccination (MenACWY) is effective against A, C, W135 and Y serotypes. The aim of this vaccination is to stop transmission from asymptomatic colonised people and those who are susceptible and non-colonised. Vaccination is recommended for those most at risk of invasive meningococcal disease:
- Immunocompromised patients (e.g. those with complement disorders, functional or anatomical asplenia)
- Children <2 years and adolescents (age groups where there are high carriage rates of meningitidis)
- Those living in close quarters (e.g. boarding school or college accommodation)
- Travellers to endemic areas

The meningitis B vaccination (4C-MenB) was approved for use in Europe in 2013. It was introduced onto the UK and Irish vaccination schedule in 2015 and 2016 respectively. The current Australian National Immunisation Program (NIP) funds the MenACWY vaccine, whilst the 4C-MenB vaccine can be purchased separately for $250 – $500.

Preliminary results have been positive - in the UK, there was a 50% reduction in the incidence rate ratio of serogroup B IMD cases in the vaccine- eligible cohort compared with the pre-vaccine period. Cases in vaccine-eligible infants halved in the first 10 months of the programme. However, at this stage, the effect of 4CMenB vaccination on meningococcal carriage is not known. Data on the effect on carriage will be important for vaccination scheduling. Adolescents have the highest carriage, and if the 4CMenB vaccination is found to disrupt it, vaccinating adolescents may be an effective vaccination strategy. Many countries are waiting for post-licensure studies from those countries that have universally introduced the vaccine, such as the UK, before continuing or starting an assessment of the vaccine. These studies will be vital to filling the existing data gaps, especially around vaccine impact.

CASE 2: IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

(Case from DFTB - **DFTB - ITP**; treatment from UpToDate - **UpToDate - ITP in Children)**

Maddie, a 4-year-old girl presents with bruising over her legs, trunk and face. Mum has noticed them appear over the last week. She has been completely well with no other symptoms. There is no history of trauma. After an anxious 1 hour wait, the bloods are back-Hb 113, WCC 7.3, Plt 8 x 109/L.

What is the most likely diagnosis?

ITP – because of an isolated thrombocytopaenia with no evidence of abnormal cells on the peripheral smear.

Could it be anything else?

Yes it could. Confirmation of ITP is based on excluding other differentials such as acute leukaemia, aplastic anaemia, HUS. A full blood count and film is usually adequate to make the diagnosis.

Red flags that may be present in leukaemia but not ITP include hepatomegaly, lymphadenopathy, fever, weight loss and musculoskeletal pain; pancytopenia is a sign of aplastic anaemia, while the diagnosis of HUS is clinically based on the classical triad of microangiopathic haemolytic anaemia, thrombocytopenia, and acute kidney injury. It is important to rule out conditions such as these before making a diagnosis of ITP.

Ok, great, we have decided it's ITP – what is it? How did she get it?

ITP is a reduction in platelet count in the absence of any other cause (<100 × 109/L). Whilst normal platelets last eight to ten days, in ITP there are autoantibodies that destroy them in the first few hours.
The incidence in children is approximately 4 in 100,000 in the UK. It has a peak incidence of two to five years of age (chronic ITP peaks in adolescence).
There is often a recent history (one to six weeks) of a viral illness or immunisation.

What other symptoms and signs would you like to know about?

The most common sign is petechiae on the skin or mucosa – these indicate capillary haemorrhages. Some mucocutaneous bleeding is often seen, but it is rare for this to be severe (<5%).
Other symptoms of autoimmune disorders should NOT be present in ITP – e.g. no weight loss, rashes, alopecia, joint swelling. The examination should be normal with no hepatosplenomegaly or lymphadenopathy.
Presence of systemic symptoms such as fever, anorexia, bone or joint pain and weight loss warrant a work up for malignancy and are not typical of ITP.

Physical exam findings of ITP		
Cutaneous bleeding	**Mucous membrane**	**Internal**
• Petechiae • Purpura	• Epistaxis • Wet Purpura – Buccal mucosa, Gingiva, palate, tonsillar pillar purpura or petechiae • Melena / GIB • Haematuria • Menorrhagia	• CNS haemorrhage (fortunately, rare (<1%)) • Abdomen • Pulmonary • Joint / Muscle

Are there any scoring systems you could use to rate the severity?

Pediatric EM Morsel - Wet Purpura and ITP

• There is proposed scoring system to help determine management (Buchanan 2002), which is also solely based on clinical findings.
• Skin (degree of petechiae and bruises)
• Epistaxis (mild to active bleeding)
• Oral (petechiae on the palate to mucosal bleeding)
• Overall (mild skin findings without mucosal involvement to internal haemorrhage)

What investigations would you like to do as part of your workup? In what situation would you like to do a bone marrow aspirate?
It is diagnosed by having a low platelet count with a normal haemoglobin (unlike in leukaemia, TTP, HUS and DIC). If there is a history of previous bleeding then consider other diagnoses. Bone marrow aspirate is only recommended if there is persistent bleeding in spite of a platelet count >20 × 109/L.

What treatment should we use?

The answer is simple: treat the patient not the platelet count.

Assess if the patient has haematuria, melaena, menorrhagia, epistaxis, mucosal bleeding or tonsillar purpura/petechiae.
Although there is variation between specialists, they will all be more concerned with the signs of wet purpura or haematuria rather than just the petechiae on the skin. Majority of children do improve spontaneously in 6-12 weeks irrespective of treatment. Hence if there is no significant bleeding in the first week watchful wait

is sufficient. Parents are advised to avoid medications such as ibuprofen, aspirin as they increase the risk of further bleeding.

• **Tranexamic acid**
Can be tried for 5-7 days to improve clot formation if there is a history of gum bleeds, epistaxis or heavy periods
Contraindicated in haematuria

• **Steroids**
For mucocutaneous and severe visceral bleeds
- Prednisolone 1-2mg/kg OD for 7-21 days, followed by tapering
OR
- Methylprednisolone 30mg/kg/day (up to 1g) IV for 3-4 days (no need to taper for this short course)

• **IVIG (intravenous immunoglobin)**
- Consider where there is life threatening severe bleeding (0.8-1g/kg) – halt autoimmune destruction of platelets and can rapidly raise the platelet count. Effect takes place in one to five days and lasts for two to four weeks

• **Platelets**
- Only give platelets if there is an intracranial hemorrhage or significant bleeding. Can be effective after IVIG administration and this can prolong platelet survival (otherwise transfused platelets are quickly destroyed).

• **Anti-D immune globulin**
- Can be used as a reasonable alternative to IVIG for appropriately selected children. Anti-D is ineffective when used in patients with Rhesus (Rh)-negative blood type or those who have had splenectomy. Anti-D should also be avoided in patients with underlying comorbidities such as renal abnormalities, cirrhosis, or acute febrile illness.

When should Maddie be admitted to hospital?
Admit if there is significant bleeding: epistaxis>1 hour; haematemesis; haemoptysis, intracranial haemorrhage (ICH), melaena. Or if there is an unclear diagnosis or problematic social circumstances.

Her parents are asking when the rash/bruising will resolve. What will you tell them?
Most ITP self resolves. 80% will have resolved by six months (with or without treatment). 5% of ITP patients will have a recurrence. Although it seems

counterintuitive, the lower the platelet count at the beginning, the better. Uncomplicated ITP normally has a platelet count of <20 × 109/L. Chronic ITP does not resolve within six months and accounts for 10% of ITP.

What do you need to advise the parents to look out for?

While the platelets are low, the patient is at risk of bleeding. ICH is a serious but rare (1%) side effect. Parents should watch out for any signs of ICH, urinary bleeding, GI bleeding, excessive mucosal bleeding and menorrhagia (in older patients).

They should avoid NSAIDs while the platelet count is low.

Older children should avoid contact sports. This is completely impractical for young children so is not helpful advice – will only stress out the parents!

When should follow up for Maddie be arranged for?

She should be reviewed within two weeks of initial presentation and have a repeat FBC. Aim for weekly GP follow up initially and then PRN until resolution.

Paediatric outpatient review at six weeks three months and six months. Refer to haematology if unclear diagnosis, unresolved after six months or a haematological malignancy is suggested by the blood count.

Her parents are very concerned that Maddie will develop chronic ITP and wonders if she receives treatment now can this be prevented. What will you tell them?

Blood - Intravenous immunoglobulin vs observation in childhood immune thrombocytopenia: a randomized controlled trial

DFTB - Childhood Immune Thrombocytopenia: To treat or not to treat?

This is not currently recommended. Many children can be safely managed with observation, advice about safety precautions and carer education.

Let's delve a little deeper...

Katja et al. published a prospective randomised controlled trial (RCT) in 2018 which examined if IVIG treatment of ITP reduces the likelihood of developing chronic ITP.

Patients were between three months and 16 years with a diagnosis of ITP, platelets ≤ 20 × 109/L and grade 1-3 bleeding on the Buchanan Bleeding Score.
Exclusion criteria were: severe bleeding, receiving immunomodulatory drugs in the past month or contraindications to IVIg such as renal failure or IgA deficiency.

Between 2009-15, 206 patients from 48 centres were randomly allocated within 72 hours of diagnosis to receive either a single dose of IVIg (at 0.8g/kg, 102 patients) or no treatment and observation (104 patients). Primary outcome was development of chronic ITP. Secondary outcomes were rate of recovery, safety, and efficacy of treatment choices.

Initial study design used a platelet count ≤ 150 × 109/L for chronic ITP; the study was modified to reflect current consensus since 2009 guidelines of ≤ 100 × 109/L platelets where possible.

Essentially, platelet recovery was significantly higher in the IVIG group at 1 week, 1 and 3 month intervals. However, there was no significant difference in presence of chronic ITP at 6 and 12 months (10% in IVIG group vs 12% without at 12 months)

Image used with gratitude from Katja et al.. 2018

Lightning Learning: Immune Thrombocytopenia

em3.org.uk @EM3FOAMed

STOP!

Primary **Immune Thrombocytopenia (ITP)** is an acquired immune mediated disorder characterised by isolated thrombocytopenia.

Defined as a peripheral blood platelet count of *less than* $100x10^9$/L in the absence of any obvious initiating or underlying cause.

ITP typically presents with...

- sudden appearance of a petechial rash
- and/or spontaneous bruising
- and/or bleeding in an otherwise well child.

Secondary ITP refers to immune-mediated thrombocytopenia with an underlying cause, including drug-induced, or associated with systemic illness.

LOOK

The incidence in children is approximately *4 in 100,000 in the UK.* Whilst most cases are minor and require no treatment, the **primary cause of mortality and morbidity is haemorrhage (including ICH).**

History should be focused on assessing the risk or extent of bleeding and excluding other causes:

- ➔ Type, severity and duration of bleeding
- ➔ Presence of systemic symptoms such as fever, anorexia, bone or joint pain and weight loss *(malignancy)*
- ➔ History of recent viral infection is common
- ➔ Exposure to relevant drugs *(e.g. Phenytoin, Valproate, Carbamazepine, Vancomycin, Septrin)*

LEARN

Acute Immune Thrombocytopenia Purpura (ITP) *(UHL Local Guidance)* http://bit.ly/2NwOU32

Immune Thrombocytopenia (ITP) in Children: Initial Management *(UpToDate)* http://bit.ly/2C1knsR

Wet Purpura and ITP *(Pediatric EM Morsels)* http://bit.ly/2MC2AqS

Author: Paul Hydes *Date: 17.09.2018* *Version: 1.0*

CASE 3: NON-ACCIDENTAL INJURY

(based on case from St. Emlyn's Blog - **Don't Be Rash – Petechiae in Well Kids at St Emlyn's)**

Daisy, a 6-month-old girl, is brought by mum to the ED with a cluster of non-blanching spots to her right lower leg noticed while bathing her. She has a mild cough and snotty nose but is otherwise well – there is no history of fever and she is feeding well without diarrhoea or vomiting and with normal urine output. There is no history of trauma, no family history of coagulopathy, and an uncomplicated birth history. She is up-to-date with his immunisations and has never needed to attend ED before.

Examining her, you find a cluster of non-blanching spots, around five discrete lesions, approximately 2mm in diameter which do not disappear under pressure to the capillary bed. The rest of the examination is normal, apart from a runny nose. No other petechiae could be identified on top-to-toe examination. Her obs are normal.

Do you want to do blood tests on Daisy?

Petechiae in well babies occur commonly; a **study published in 2002** found a prevalence of 27.6% of a cohort of 116 babies less than twelve months of age at child health surveillance clinics, predominantly to the trunk and lower limbs. Observation is the mainstay of ruling out early septicaemia, in addition to blood tests if there is demonstrable or historical pyrexia.

What are the causes of petechiae in children?

Infection	Mechanical	Haematological	Vascular
• Serious bacterial illnesses – (classically menococcemia, streptococcus, H. influenzae and infective endocarditis) • Viral infections (e.g. influenza, measles, enteroviruses and parvovirus) • Rickettsiae (e.g. Rocky Mountain Spotted Fever in North America, Epidemic typhus and Queensland tick typhus)	• Coughing or vomiting (limited to head and neck regions) • Local pressure or tourniquet application (e.g. petechiae distal to tourniquet) • Strangulation	• Thrombocytopenia (platelets <100 x 10E9/L) e.g. ITP (immune thrombocytopenic purpura), leukaemia and hypersplenism • Platelet dysfunction – e.g. congenital, drugs and renal failure	• Scurvy (classically perifollicular purpura on the lower limbs) • Drugs e.g. steroids • Cushing syndrome • Fat embolism • Dysproteinaemia

The rash can results from the following **mechanisms:**

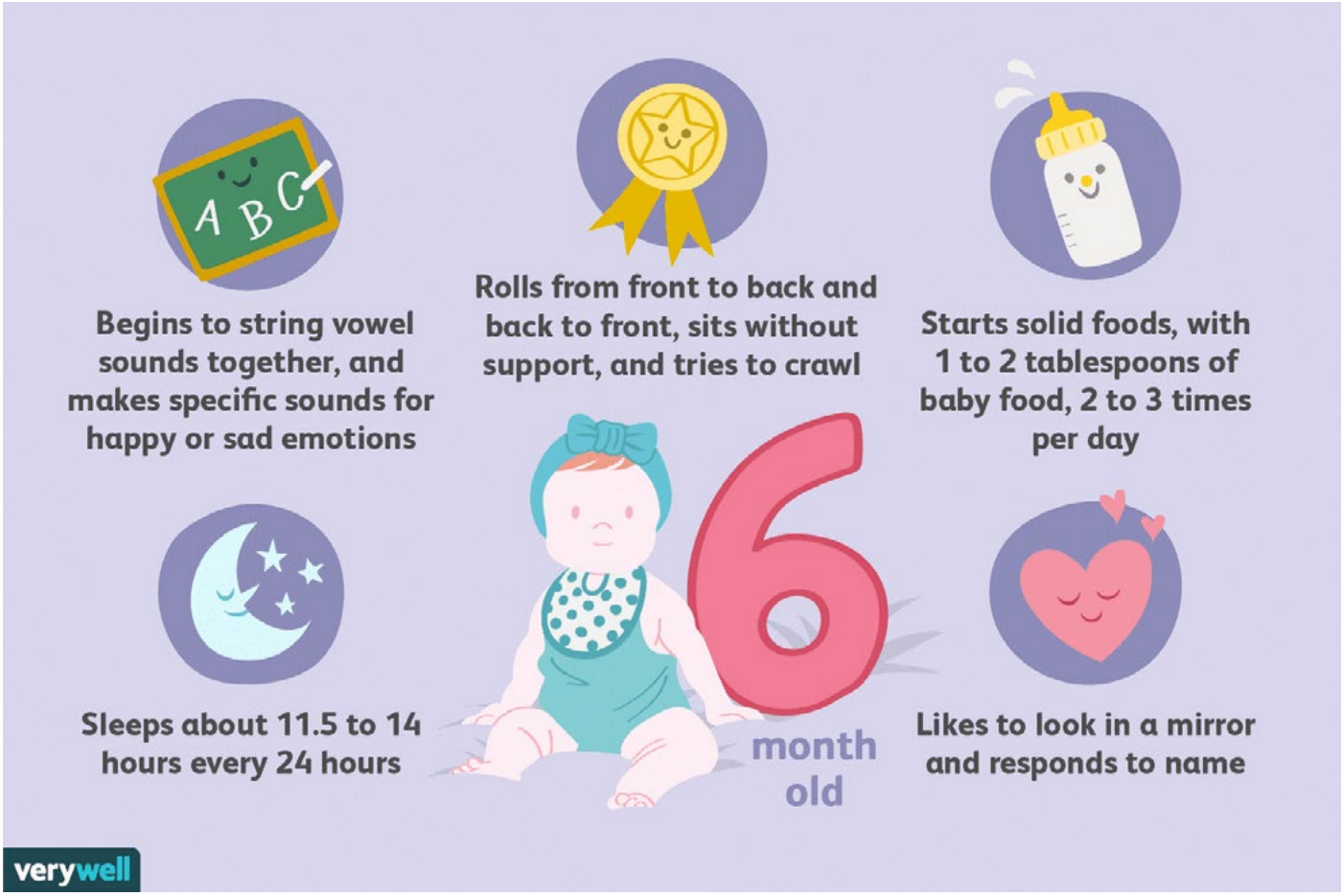
- mechanical capillary injury
- impaired haemostasis
- septic emboli or invasion of the capillary walls
- microbial toxin-induced capillary damage
- immune complex deposition

What factors in the history and presentation might make you suspicious of NAI? **One study** found a high proportion of children with non-accidental injury were brought by a third party (extended family member or teacher, for example). There are well documented prompts to consider non-accidental injury in event of;

- Delay in presentation of the injury
- Discrepant or absent history
- History incompatible with the injury
- Pattern of injury more suggestive of abuse
- Repetitive injuries
- Unusual parental behaviour or mood
- Child's demeanour, behaviour, or interaction with the parent/caregiver unusual
- Disclosure by child or witness

It is always important to consider the child's age and their developmental milestones. In Daisy's case what are they?

It is generally accepted that non-mobile children are unlikely to have bruises. Babies **"do not injure themselves"**, and blame attributed to siblings is rarely appropriate. **A study of 973 well children** under the age of 36 months found only 2.2% of non-mobile children had bruises, compared to 17.8% of cruisers and 51.9% who were walking. **This systematic review** of patterns of bruising found from pooled data that bruising in non-mobile babies was rare, occurring in <1%. 'Can't cruise, can't bruise'.



(Image used with gratitude from verywellfamily.com)

What is a normal pattern of bruising in children?

In mobile children, bruises on bony prominences (particularly the anterior tibia and knee) and the forehead are common, reflecting frequent falls in those beginning to walk. Bruises in those aged 9 months to 4 years of age are more suspicious of non-accidental injury when found on other parts of the face, the head, neck, trunk or buttocks.

"Normal" bruises are not associated with petechiae in a child without an underlying medical or haematological problem. Petechiae which coexist with bruises **are considered to have a high positive predictive value for non-accidental injury** (80%: 95% confidence interval 64.1%-90.0%)

Linear petechiae may suggest the shape of a hand, having been formed by capillary rupture at the edge of injury from a high velocity slap. They may also represent specific mechanisms such as suction, squeezing, slapping, strangulation or suffocation. Blunt trauma may generate a negative impact of the offending

object, outlined by petechiae, or deep to a constricting ligature . Petechiae to the earlobe commonly represents non-accidental injury, and linear petechiae may be associated with cultural practices such as cupping or coining.

A word of warning...

Beware, though: The consensus of medical opinion is that bruises cannot be accurately aged by clinical assessment either in vivo or by photograph, with **one study** finding that aging to within 24 hours of occurrence is accurate less than 50% of the time, with poor interobserver reliability. There are no studies which discuss the changes in colour or appearance of petechiae over time.

CASE 4 – HENOCH-SCHOENLEIN PURPURA

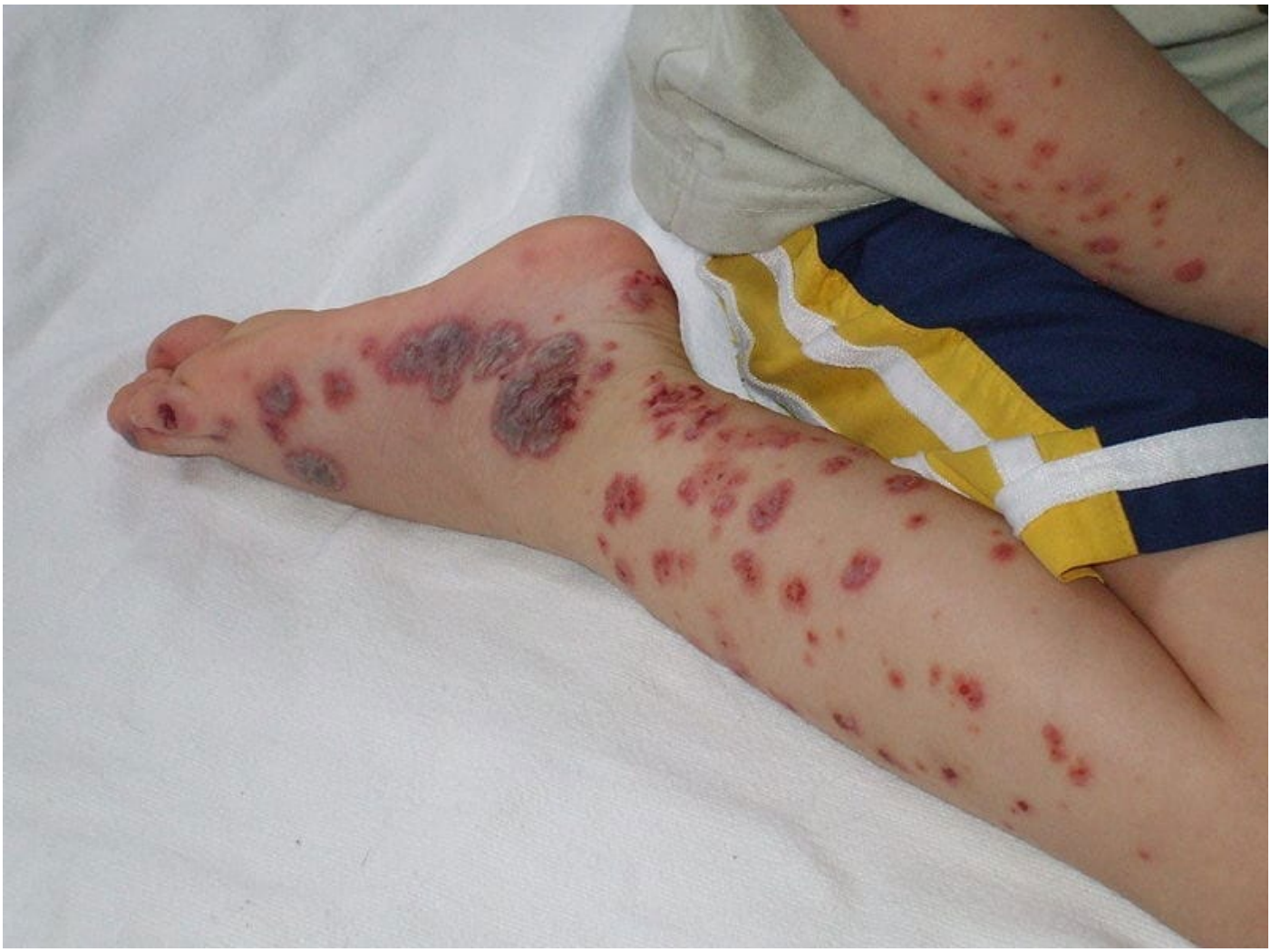
(based on case from LITFL - **LIFTL - Horrible Spots and Pain**)

A 4 year-old boy is brought to the emergency department by his parents with a history of increasing numbers of red spots on his legs over the past 6 days. They took him to two different family doctors and have tried various creams. The spots have spread to his buttocks and his arms, and now his legs are sore and look swollen. He has also had abdominal pains.

On examination he looks well with age-appropriate vital signs, but he is reluctant to move his lower limbs.

A urine dipstick shows 2+ RBCs.

His rash looks like this:



What is the diagnosis?
What other symptoms not already mentioned would you look for?
What are the differentials?
What investigations would you like to do?
In what circumstances would you like to admit Jack to hospital?
When would you speak to a nephrologist?
What complications can occur?
Jack's mum is wondering what the usual time course of the illness is. Can you counsel her on what to expect?
What is your management?
What is the role of steroids?

What is the diagnosis?

Henoch-Schoenlein purpura (HSP)

HSP is an autoimmune, self-limiting, immunoglobulin A-mediated, small-vessel vasculitis. It typically affects children aged 2-8 years and is the most common vasculitis affecting children. It is often preceded by upper respiratory tract symptoms (occurring 1-3 weeks earlier).

The diagnosis is likely in the presence of the triad of:

- purpuric rash (commonly palpable) on the limbs (mainly lower) and buttocks (especially the dependent surfaces). This is the main diagnostic feature.
- joint pain/ swelling
- abdominal pain – diffuse, colicky, acute onset

What other signs and symptoms not already mentioned would you look for?

Haematuria is present in 90% of cases, but only 5% are persistent or recurrent. Less common renal manifestations include proteinuria, nephrotic syndrome, isolated hypertension, renal insufficiency and renal failure. Subcutaneous oedema of the scrotum, hands, feet and sacrum may be present and can be very painful.

What are the differentials?

If atypical distribution or the child is unwell, consider meningococcaemia, thrombocytopenia (ITP), or other rare vasculitides. Other differentials include causes of an acute abdomen (e.g. bowel infarction or perforation), drug reactions and systemic lupus erythematosus.

What investigations would you like to do?

Suggested investigations for a child presenting with palpable purpura, suspected of having HSP include

- Blood Pressure
- Urine analysis
- Full blood count
- Serum creatinine
- Urine protein: creatinine ratio

These are carried out in an attempt to exclude other diagnoses and to identify the presence of renal impairment. The FBC allows detection of thrombocytopaenia. Renal involvement is common but usually limited to haematuria and/or mild proteinuria. More severe nephritis produces greater levels of proteinuria, but it is unusual for the serum creatinine to be raised at presentation.

In what circumstances would you like to admit Jack to hospital?
Jack may require admission if symptoms of joint pain or abdominal pain are very severe caused by gastrointestinal bleeding or more rarely intussusception.
If a surgical review is needed to rule out a testicular torsion or if there is evidence of severe renal disease.

When should you speak to a nephrologist?

Children with haematuria and/or proteinuria should be kept under review and those with significant proteinuria (early morning urine protein:- creatinine ratio persistently greater than 50 mg/mmol), hypertension or impaired renal function should be discussed with a paediatric nephrologist, because of the risk of long-term renal problems.

What complications can occur?

HSP is a multi-system disease involving all organs:

- Renal – Haematuria (persistent or recurrent in 5%) is common and usually self-limiting; significant proteinuria (less commonly), acute nephritis (very rarely but can lead to renal impairment); nephrotic syndrome, isolated hypertension, renal insufficiency and renal failure (<1%). May not be present acutely but become apparent during the convalescent period.

• Gastrointestinal – caused by inflammation of the intestinal mucosa include intussusception (rare), bloody stools, haematemesis, spontaneous bowel perforation, and pancreatitis.
• Subcutaneous oedema – particularly affects the scrotum, hands, feet, and sacrum can be very painful and may present as an acute scrotum in boys
• Rare CNS and pulmonary complications can also occur.
• Liver – cholecystitis
• Heart – rheumatic fever with complete atrioventricular block, pericarditis
• Recurrence rate is between 25-50%

Jack's mum is wondering what the usual time course of the illness is.
Can you counsel her on what to expect?
Typically, a URTI may precede the onset of symptoms by 1-3 weeks. Joint pain has a short course and lasts <48 hours, abdominal pain last < 72 hours. The purpuric rash should resolve in 4-6 weeks.
In a large paediatric study by Allen et al, children older than 2 years had a recurrence rate of 50%, whereas those younger than 2 years had a recurrence rate of less than 25%.

Allen DM, Diamond LK, Howell DA. Anaphylactoid Purpura in Children (Sch□nlein-Henoch Syndrome): Review with a Follow-Up of the Renal Complications. AMA Am J Dis Child. 1960;99(6):833–854. doi:10.1001/archpedi.1960.02070030835021Available online:
https://jamanetwork.com/journals/jamapediatrics/article-abstract/499525

What is your management?

Management is typically supportive. Analgesia, education and observation for complications. Most cases can be managed in the outpatient setting by the GP and general paediatrics. Concern about the possible development of renal complications is the main driver for the follow up of children after an episode of HSP. Patients need to be followed for a minimum of 6 months.

What is the role of steroids?

DFTB - HSP –Are Steroids helpful in preventing neuropathy?

The role of corticosteroids in HSP to reduce the risk of developing nephropathy has always been controversial because there have never been good quality studies.

The best study to date has just been published in Arch Dis Child and effectively demonstrates that steroids are either of no help or of sufficiently small effect not to justify treating large numbers of patients with HSP to prevent a small difference in the risk of developing renal complications in a small proportion of patients.

RCH Clinical practice guidelines outline: "The use of prednisolone has not been shown to make clinically important improvements in the rate of long-term renal complications. It has been shown to reduce the duration of abdominal and joint pain and may reduce the risk of abdominal complications. It may be considered for use in patients with more than mild joint or abdominal pain. Consider prednisolone 1mg/kg while symptoms persist.

Dudley J, Smith G, Llewelyn-Edwards A, Bayliss K, Pike K, Tizard J. Randomised, double-blind, placebo-controlled trial to determine whether steroids reduce the incidence and severity of nephropathy in Henoch-Schönlein Purpura (HSP). Archives of disease in childhood. 2013 Oct 1;98(10):756-63. Available online: **http://europepmc.org/article/med/23845696**

Weiss PF, Klink AJ, Localio R, Hall M, Hexem K, Burnham JM, Keren R, Feudtner C. Corticosteroids may improve clinical outcomes during hospitalization for Henoch-Schönlein purpura. Pediatrics. 2010 Oct 1;126(4):674-81 Available online: **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3518383/**

Question 1

Which of these is a sign of raised ICP?

A - Diarrhoea

B - Vomiting

C - Non-blanching rash

D - Thrombocytopenia

Question 2

Which of the following can be an appropriate treatment for ITP?

A - Tranexamic acid

B - Steroids

C - Platelet infusion

D - All of the above

Question 3

Which of the following is not a side-effect of HSP?

A - Intussusception

B - Cholecystitis

C - Hearing loss

D - Rheumatic fever

Question 4

Which of the following would make you suspicious of NAI?

A - Bruising on the knees of a 5-year-old

B - Delay in presentation of the injury

C - Petechiae on the lower limb of a 6-month-old

D - Both B and C

Question 5

Which of the following investigations is sensitive for diagnosis of invasive meningococcal disease?

A - Blood cultures

B - DNA PCR

C - CT head

D - Skin scrapings

5 practical take home tips

1. Recognising if a child is toxic or non-toxic is one of the most important steps in managing a child with a non-blanching rash
2. Meningococcal sepsis is a condition with high mortality which should not be missed – have a high index of suspicion!
3. A period of observation may be an appropriate course of action in itself
4. Always check the urine for haematuria
5. Do not forget to consider non-accidental injury in a child with a non-blanching rash

REFERENCES

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Peds Cases - Meningitis

Two Peads in a Pod – Managing non-blanching Rashes

EMDocs - What's that Rash? An approach to dangerous rashes based on morphology

LITFL - Perilous Pinhead Polka-dots

The Royal Children's Hospital Melbourne – Fever and Petechiae Flowchart

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The Royal Children's Hospital Melbourne – Fever and Petechiae Flowchart

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DFTB - Childhood Immune Thrombocytopenia: To treat or not to treat?

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DFTB - HSP –Are Steroids helpful in preventing neuropathy?

St. Emlyns – Petechiae in the well child

DFTB - Petechiae in Children - the PIC Study

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