MANAGEMENT OF FEVER WITH PETECHIAE

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INTRODUCTION

Every child presenting with a fever and petechial rash poses a substantial challenge – could this be a case of meningococcal disease (MD)?

Meningococcal disease (MD) remains a major cause of death and disability in childhood[1] with an incidence of 2.5-3 cases/100,000/year in the UK. The disease has an overall mortality of 10%[2] which can go up to 50% in those who develop shock[3]. Case fatality rates have not fallen since the late 1960s in population-based studies[4] though specialist paediatric units describe a decline more recently[3].

Neisseria meningitidis is present in 10% of the population in the nasopharyngeal mucosa. Invasion occurs on contact with a virulent strain, which colonizes and then penetrates the mucosa. The survival and multiplication of the meningococcus in the bloodstream is dependent on the individual's immunity at that time. Some will resolve spontaneously and others progress to a fulminant septicaemia.

In fatal cases the time from onset to death is often short. Early recognition and prompt treatment may therefore save lives. Whilst one patient presenting with fulminant purpura and circulatory collapse and/or nuchal rigidity leaves little doubt about appropriate therapeutic procedures, another in relatively good general condition with only small skin haemorrhages represents a real diagnostic challenge.

Not all children with fever and petechiae have invasive bacteraemia – in fact only the minority do. In three published studies of children with fever and petechiae the frequency of MD varied from 0.5% to 10%. In the majority the aetiology remained unknown.

SYSTEMIC INFECTIONS ASSOCIATED WITH PETECHIAE

Virus	Bacteria
Echovirus	Staph. aureus
Coxsackie	Neisseria meningitidis
Atypical measles	Neisseria gonorrhoea
Adenovirus	
Rubella	
Congenital CMV	

Protozoa	Non infective
Plasmodium falciparum (malaria)	Henoch Schonlein purpura (HSP)
	Idiopathic thrombocytopenic purpura (ITP)
	Kawasaki disease
	Trauma
	Superior vena cava congestion (secondary to vomiting, cough, eczema)

A new clinical guideline for the management of children presenting with fever and petechiae, the ILL criteria (Irritability, Lethargy, Low capillary refill) was suggested by Brogan et al in December 2000[5]. It was followed by another study[6] aimed at developing an algorithm for the prediction of MD in children with fever and skin haemorrhages. This came up with five clinical variables:

1 Characteristic appearance of skin haemorrhages
2 Universal distribution of skin haemorrhages
3 Maximum diameter of one or more skin haemorrhages of more than 2mm
4 Poor general health (using a standardised observation scheme)
5 Nuchal rigidity.

Where any two or more of these clinical variables were present, the probability of identifying a patient with MD was 97% and the false positive rate was only 12%. More importantly, simple clinical observations were noted to have high discriminatory power.

A separate study[7] confirmed that most children with MD are ill, have a purpuric rash, fever and delayed capillary refill time. It demonstrated good specificity for the ILL criteria (81%), purpura (88%), low capillary refill (85%) and 100% negative predictive value for a C reactive protein (CRP) value of < 5 mg/L. Also, where the purpura was confined to the distribution of the superior vena cava, MD was very unlikely. Lack of fever did not exclude MD.

STUDY

Aims

Utilising this information a study was performed at the Royal Lancaster Infirmary (RLI) with the aims of:

1 Identifying risk factors predictive of MD in children with fever and petechiae
2 Establishing a set of clinical guidelines to aid management – a simple algorithm for identification of early meningococcal disease.

STANDARDS

Proposed risk factors for the prediction of Meningococcal disease[5]:

- Irritability – inconsolable crying, distressed
- Lethargy – subjectively determined by carer/staff (weary, quiet, not feeding)
- Low capillary refill – capillary refill time more than two seconds

- Elevated C Reactive Protein (CRP) – above 5mg/L
- Abnormal white cell count (WCC) – outside normal range of 5-15 x 10^9/L.

Methodology
A retrospective and prospective audit of referrals to the paediatric department at the RLI was performed. The time period was 18 months from November 2000 to April 2002. November 2000-February 2001 was retrospective and February 2001-April 2002 prospective.

All patients presenting with fever (peripheral temperature above 37.4°C) and petechial rash were included. Data was collected on a set proforma, designed with the help of the audit department at the RLI.

RESULTS

Eighty-four (n=84) patients satisfied the entry criteria, of which fifteen were diagnosed with meningococcal disease (MD=15). See table 1. The remainder (others=69) comprised mainly of viral illnesses, two cases of SVC congestion (cough/vomiting induced), two HSP, one ITP and one streptococcal tonsillitis.

Irritability
Seven of the fifteen MD (47%) were irritable on presentation. Specificity 97%, (95% confidence interval-CI 90-100%); positive predictive value (PPV) 78% (CI 40-97%) and negative predictive value (NPV) 89% (CI 80-95%).
Only two of the sixty-nine negative cases (3%) presented with irritability.

- **Lethargy**

Ten of the fifteen MD (67%) were lethargic.
Specificity 86% (CI 75-93%) and NPV 92% (CI 83-97%).
Ten of the sixty-nine negative cases (14.5%) were lethargic.

- **Irritability and lethargy together**

Five cases in all presented with both irritability and lethargy of which four were MD and the fifth a viral meningitis.
Specificity 99% (CI 92-100%), PPV 80% (CI 28-99%) and NPV 86% (CI 76-93%).

- **Low Capillary Refill Time (CRT > 2 seconds)**

There were five cases with prolonged CRT including three MD, one HSP and one viral illness.
Specificity 97% (CI 90-100%), PPV 60% (CI 15-95%) and NPV 87% (CI 77-94%).

- **Elevated CRP (CRP> 5mg/L)**

Fourteen of the MD (93%) and twenty-three of the negatives (33%) had an elevated CRP. It was not done in the 15th.
Sensitivity 100% (CI 77-100%), specificity 43% (CI 27-59%), PPV 38% (CI 22-55%) and NPV 100 % .

- **Abnormal White Cell Count (WCC outside range of 5-15 x 10^9/L)**

Eight of the MD (53%) had an abnormal WCC. In six, it was

ID	Age	Sex	Month	Symptoms	Signs	Rash
1	11.92	F	December	Fever, rash vomit, lethargy, headache	GCS 14/15 CRT 4	Petechial
2	12.5	M	January	Fever, rash, vomit, lethargy, headache, stiff neck	Lethargic	Petechial
3	13	M	January	Fever, rash, vomit, lethargy, headache, stiff neck, photophobia	Lethargic (unwell)	Petechial
4	1.58	F	November	Fever, rash, sore throat, runny nose	Lethargic	Petechial
5	3.45	M	January	Fever, rash, vomit, cough, lethargy, irritable	Irritable, lethargic CRT <2 inc to 3	Blanching
6	2.83	M	April	Fever, rash, cough, lethargy, irritable	Lethargic	Petechial and Purpuric
7	10	F	March	Fever, rash, vomit, lethargy, headache, stiff neck, photophobia	Irritable, lethargic, GCS 14/15	Petechial
8	4.92	F	August	Fever, vomit, headache, stiff neck, sore throat, sore ankle	Lethargic	Purpuric (rash developed on ward)
9	1.08	F	January	Fever, rash, lethargy, irritable, ptosis	Irritable	Petechial (new spots appeared 2 days later)
10	16	F	May	Fever, rash, headache, stiff neck, chest pain	Felt and looked unwell grey and cold	Petechial and purpuric
11	0.58	F	December	Fever, vomit, cough, lethargy, coryza	Irritable (distressed), lethargic (tired)	No rash
12	16.33	F	December	Fever, irritable (agitated)	Irritable, lethargic	Petechial (in A&E)
13	3.67	M	January	Fever, rash		Petechial
14	0.75	M	February	Rash, stiff neck, staring episodes	Lethargic, shut down and unwell – staring, GCS 14/15, CRT 4	Petechial
15	1.67	F	January	Fever, rash, irritable	Irritable	Petechial

Table 1 Signs and symptoms Meningococcal cases n = 15

ID	Temp °C	WCC	CRP	Organism	Method of detection
1	38	39.9	171	Clinical	
2	37.9	2.9	5.2	N Meningitidis	+ve PCR; –ve BC
3	38.5	21.3	167	Clinical	
4	37.9	5.8	231	N Meningitidis Gp B	+ve PCR; –ve BC
5	38.7	16.5	5.9	N Meningitidis	+ve BC
6	39.5	11.6	20	N Meningitidis GP B	+ve PCR; +ve BC
7	39.5	16.9	16.5	N Meningitidis	+ve PCR
8	39	8.3	25.8	N Meningitidis	+ve PCR; +ve BC
9	37	35	286	Clinical	–ve PCR; –ve blood culture
10	37	1.2	89.3	N Meningitidis	+ve PCR; –ve BC
11	39.8		24.7	N Meningitidis Gp B	+ve BC
12	38.1	26.1		N Meningitidis Gp B	+ve PCR; +ve BC
13	36.5	9.8	7.1	Clinical	
14	37.8	13.9	372.9	N meningitidis Gp B	+ve PCR; –ve BC
15	38.5	6.1	15.2	Clinical	

Table 2 Investigations Meningococcal cases n = 15

above 15 x 10^9/L and in two below 5 x 10^9/L . Fifteen of the negative group (22%) had an abnormal WCC.
Sensitivity 57% (CI 29-82%), specificity 63% (CI 46-77%) , PPV 35% (CI 16-57%) and NPV 81% (CI 63-93%) for MD.

Antibiotic Treatment
All fifteen cases of MD were given antibiotics from admission. In the negative group, nineteen had antibiotics for forty-eight hours (27%), twenty-three had blood investigations only and no antibiotics (33%) and twenty-seven cases were observed only (39%).

COMMENTS

An immediate injection of benzyl penicillin is recommended for any case presenting in primary care with the slightest suspicion of MD, ie any child presenting with fever and petechiae. Nine of the fifteen MD cases (60%) and twenty-eight of the sixty-nine negatives (40%) received benzyl penicillin prior to admission, ie a total of only 44%. Of the six MD cases who had not received benzyl penicillin prior to admission one was allegedly allergic to it (the only fatality in the study). Two were admitted via A&E (1 WGH and 1 RLI). Of the remaining three, one was referred as a 'possible' meningococcal disease, one had no rash and the third developed a rash on admission only.

Observation Fulminant meningococcal septicaemia can develop very quickly, where there is no doubt about the diagnosis at presentation. However, at the opposite end of the spectrum there is another group of patients who, despite having meningococcus in the bloodstream, will remain well, and in whom clinical and haematological features may not be abnormal. In such situations simple clinical observation has a high discriminatory power. Therefore if a patient remains well after four hours' observation in a controlled setting it is very unlikely that fulminant sepsis will subsequently develop.

ALGORITHM

As a result of our study, a simple diagnostic algorithm was proposed for the management of children presenting to the assessment unit with fever and a non-blanching rash.

(i) **Well child – observe**
If the child is well, with a mild fever of less than 38.5°C and micropetechiae ≤ 2mm in SVC distribution only – observe on unit for six hours. Discharge home if condition remains unchanged, with information to parents and 24-hour direct access if concerns.

(ii) **Criteria for bloods**
Blood count, culture (BC), profile, CRP, clotting studies and PCR are done if any of the following are present:

- Temperature > 38.5° C
- Petechiae (< 2mm diameter) below SVC distribution with no explanation
- Purpura (> 2mm diameter) with no explanation
- Recent contact with MD (< 7days)
- History of low immunity (neutropenia, oral steroids, immunosuppressants)
- ILL-irritability/unwell/lethargy/low capillary refill.

(iii) **Criteria for antibiotics**
Systemic antibiotics are commenced in the following cases:

- One or more of the ILL criteria present (irritable, lethargic, low capillary refill)
- One or more of the criteria in (ii) above plus abnormal WCC or CRP. The antibiotic may be stopped after 48 hours, dependent on culture results and clinical status.

Pending results of investigations, the case is initially designated as probable, possible or unlikely. The 'probables' are immediately reported to Public Health, and intimate and household contacts commenced on antibiotic prophylaxis with either rifampicin or ciprofloxacin.

DISCUSSION

Any febrile child with petechiae (and even some without) may have a bacteraemia caused by Neisseria meningitidis. Untreated, some of these will progress to purpura fulminans and others will resolve spontaneously. The combined risk factors of irritability, lethargy and low capillary refill have a high specificity and negative predictive value and can be used for identifying MD. An elevated CRP level adds to the

sensitivity of the screening as a whole but reliance in isolation for detection of early MD is not recommended. An abnormal WCC is unreliable on its own but may help in conjunction with the diagnostic algorithm.

In the case of the apparently well-looking patient presenting with fever and non-blanching rash, a period of clinical observation is of utmost importance.

There was referral bias as only the 'sicker' population was considered as compared to those in the primary care setting. However, as many GPs do refer any child with a petechial rash, there is no reason to believe that the results would be any different.

It is hoped that this algorithm may be helpful in the management of apparently well-looking children presenting with fever and a non-blanching rash in the community.

A note of caution

1 The guidelines are useful only for suspected meningococcal disease and re-evaluation in a larger cohort is required.

2 The presence of micropetechiae in the superior vena cava distribution consequent on vomiting or coughing is a familiar picture. However, vomiting is also common in MD.

3 Lack of fever at the time of assessment does not exclude MD.

4 Whenever a suspicion of MD is raised, however remote it may seem initially, parenteral benzyl penicillin should be given immediately as it can prove life-saving. Even in suspected penicillin allergy it should still be given, but with the precaution of adrenaline drawn up. Penicillin should only be withheld if there is a clear history of anaphylaxis in which case Cefotaxime must be given as an alternative.

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Small Talk

Compiled by Nanette Newman

I nearly know how to have babies but we don't do it till next term.
Frances aged 7

If you don't want babies you should practice contradiction.
Lynn aged 9

If you don't want to have a baby you have to wear a safety belt.
Alison aged 5

A baby comes out of the mummy's tummy and bites the doctor and the doctor smacks it.
Edward aged 6

If you don't love your baby it won't come and visit you when you are old.
Noura aged 7

My auntie's baby jumped out of her tummy when she wasn't looking and she hadn't bought the cot yet.
Isabelle aged 6

We are going to Windsor Castle to see the Queen's private parts.
Becky aged 7

Bananas are the best fruit because you can undress them.
Yasmin aged 5

My mummy cried on my first day at school so I had to take her home.
Penny aged 5

Joseph's wife Mary had an immaculate contraption.
Cathy aged 7