

Fever Pitch: Fever in Children Part II

Rural Rounds

April 3, 2025

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**NOTHING
TO DECLARE**

Objectives

- Present a case-based analysis of fever in children > 90 days of age
 - Definitions
 - Epidemiology
 - Investigations
 - Pitfalls
 - Management

Definitions

- **Fever** is any rectal temperature $\geq 38.0^{\circ}\text{C}$, measured at home or in a clinical setting.
- **Serious bacterial infections (SBIs)** include urinary tract infections (UTIs), bacteremia, and bacterial meningitis.
- **Invasive bacterial infections (IBIs)** include bacteremia and bacterial meningitis.

Definitions

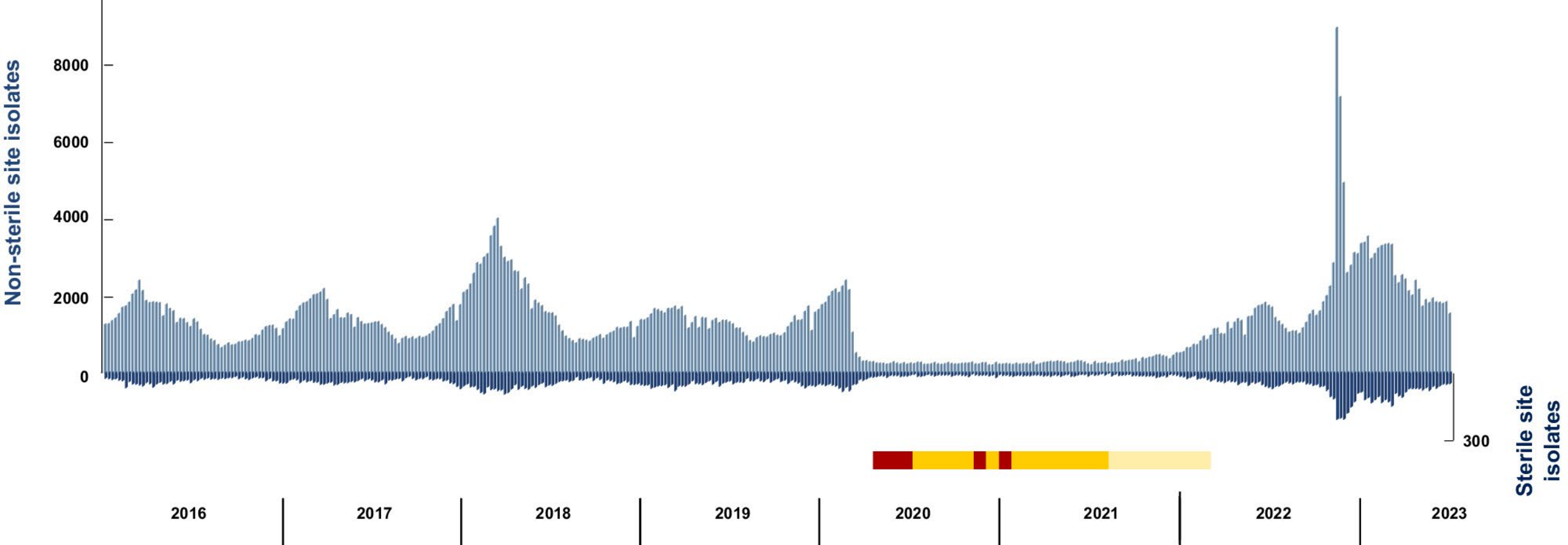
- Axillary, oral, tympanic, temporal are less specific than rectal
- Could be used as a screening method but complemented by rectal or oral routes
- Non-infectious causes of fever include:
 - Vaccine-induced
 - Kawasaki Disease
 - JIA
 - Toxins (anticholinergic or sympathomimetic)
 - Autoinflammatory fever syndromes
 - Cancer
 - Hyperthyroidism

Epidemiology

- Management of fever is an area of significant practice variation and ambiguity, especially in a well-looking child.
- Immunization has reduced the overall incidence of IBI:
 - Pre-immunization: bacteremia 4.3% among healthy well-appearing children
 - Post-immunization: bacteremia in the 1.6% to 1.9% range
- Increased vaccine hesitancy may alter these rates.
- Antibiotic overuse has led to increased antibiotic resistance.

Epidemiology

- Viral and bacterial co-infections are common in children.
- Seasonal variation in bacterial infections usually follows respiratory surge with a nadir in the summer months.
- Post-pandemic increased incidence of invasive bacterial infections
 - iGAS
 - Mycoplasma



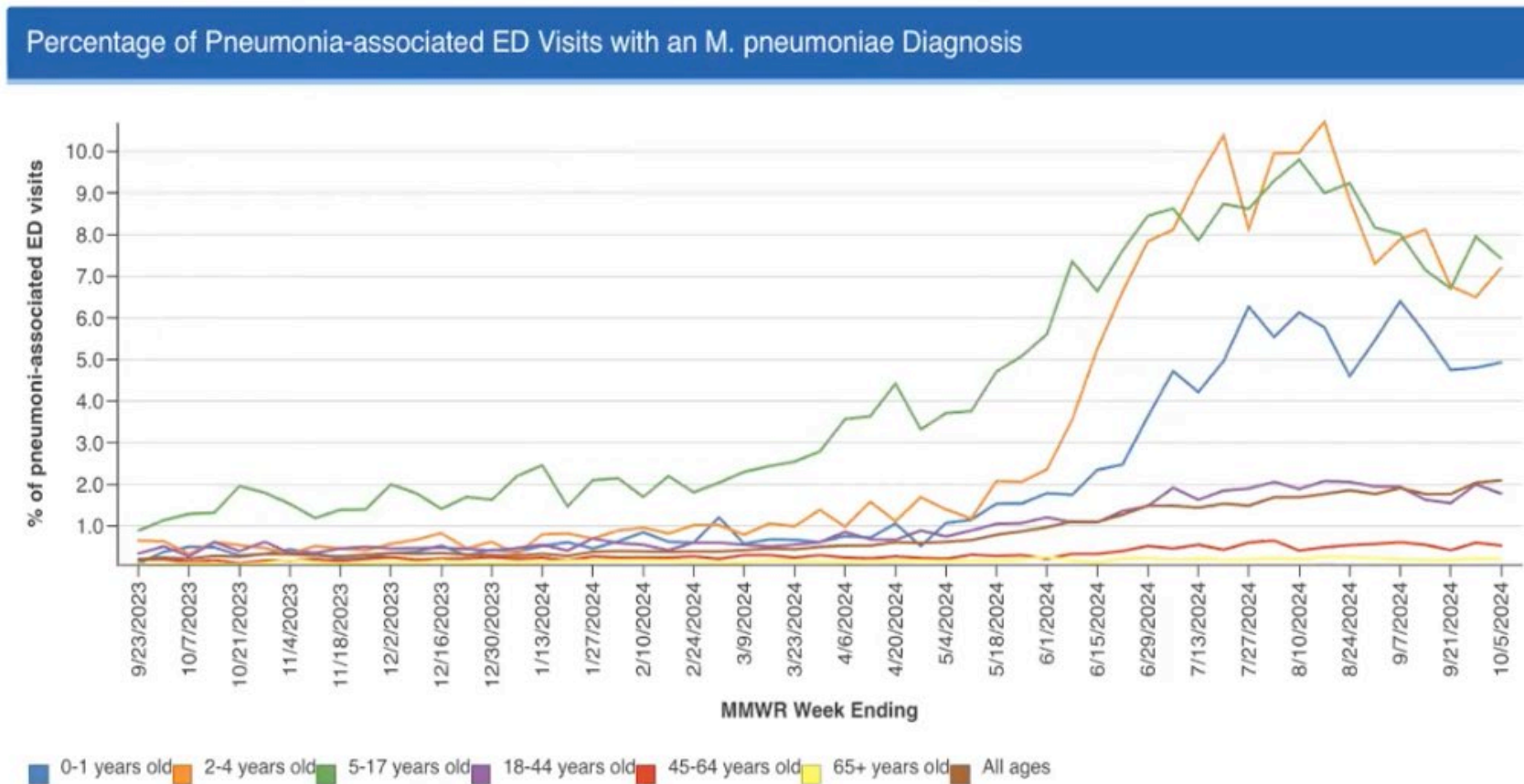
Epidemiology of iGAS

- Cases were rising prior to pandemic
- Sharp decrease during 2020-2021
- Rebound in 2022 with record cases in 2023

Epidemiology of Mycoplasma

Decline in cases in 2020; a re-emergence noted globally since fall of 2023

Increasing *M. pneumoniae* infections – October 2024



Factors affecting the global rise in invasive bacterial infections

- Post-pandemic rebound of respiratory pathogen e.g. influenza and RSV
- Decreased exposure led to less immunity which allowed for spread of these pathogens

Available Diagnostic testing

- **Full Septic Work Up (FSWU)** includes examination of CSF, blood, urine.
- **Partial Septic Work Up (PSWU)** includes examination of blood, urine.
- CXR
- Throat swab
- Respiratory panel:
 - Common viruses
 - Extended respiratory panel
- Newer rapid molecular PCR-based technology
 - CSF Biofire
 - Mycoplasma rapid molecular testing
 - GAS molecular testing
 - Rectal swab PCR testing

Investigations

- Lower threshold in
 - Medically complex
 - Immune compromised
 - Unimmunized
 - Prolonged fever
 - Returned ER visits
 - Returning traveler

Blood Culture

- Limit this test to unwell children or those with risk factors
 - <1% of blood cultures positive for a pathogen
 - Higher chance of growing a contaminant
 - 2:1 false positive to true positive results
 - No increased risk of bacteremia in unvaccinated children aged 2 to 36 months
 - Presence of sufficient herd immunity
 - Need to apply this in context of local vaccine hesitancy rates
 - Febrile children visiting from another area could be at higher risk
- Include blood culture if you are ordering biomarkers

Biomarkers

- Include WBC, ANC, CRP, and PCT
- All perform more superiorly than clinical evaluation
- PCT is most specific
- Biomarker more useful when fever has been present at least 12 hours
- Avoid testing in early phases of fever

Urinalysis and Urine Culture

- Risk factors
 - Female or uncircumcised male
 - Age <12 months
 - Temperature $\geq 39^{\circ}\text{C}$
 - Obesity seems to be a risk factor for UTI
- 5-6% of children with febrile UTI's have bacteremia; higher in younger infants
- Sampling
 - Catheter recommended in < 1 yr-old and up to 2 yr-olds
 - In > 6 months of age, bag as screen, cath if +
 - "Clean-catch" technique involves bladder stimulation
 - Higher rates of contamination, especially in female infants (12% vs <2%)
- Definition
 - Pyuria (positive leukocyte esterase or >5 WBC/hpf)
 - At least 10,000 CFU/ml of a single uro-pathogen on culture

CXR

- Used to diagnose C.A.P.
- Limitations:
 - Nonspecific findings
 - High inter-observer variability
 - Not reliable for distinguishing between bacterial and viral pneumonia
 - No evidence for its use in children presenting with bronchiolitis

Rapid Molecular PCR testing

- Panels available:
 - Rapid viral panel
 - RSV/flu/COVID
 - Extended respiratory panel
 - Viral pathogens
 - Atypical bacteria
 - Mycoplasma and Chlamydia
 - Rapid GAS testing
- Advantages:
 - High sensitivity and specificity
 - Bacterial panels not impacted by antibiotics on board
- Limitations:
 - Unable to differentiate between
 - past or current infection
 - carriage state or active infection

Case 1

Jan 30, 2024

- 15-year old boy fever, cough, congestion for 3 days
- Viral swabs and d/c

Virology: Direct, Serological and Molecular

Respiratory Panel; PCR/NAAT

Specimen Description

Nasopharyngeal Swab

Influenza Virus A RNA; PCR/NAAT

Negative

No Influenza A Virus detected by NAT.

Influenza Virus A H1 RNA; PCR/NAAT

Negative

No Influenza A Virus subtype H1 detected by NAT.

Influenza Virus A H3 RNA; PCR/NAAT

Negative

No Influenza A Virus subtype H3 detected by NAT.

Influenza Virus B RNA; PCR/NAAT

Positive

AA

Influenza B Virus DETECTED by NAT.

Reported to Public Health

Feb 1, 2024

Bacteriology: Culture

Throat; Culture

Source : Strep

- Returned with fever and sore throat

Throat; Culture

- Throat C/S done

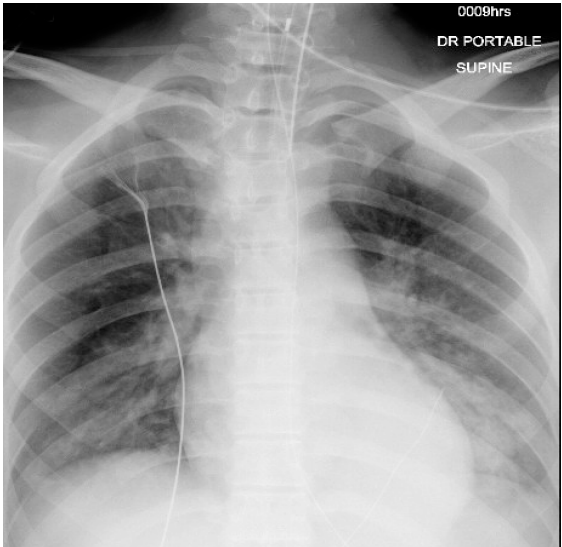
ISOLATE 1 Group A streptococcus
Isolated

- Dex given

- Abx Rx given; was asked to wait for swabs

Feb 2, 2024

- Diffuse erythematous rash evolved
- Presented again to ER with lethargy
- Toxic and hypotensive
- Blood work done; IV Abx started
- Hematemesis and pink frothy sputum noted
- Started on EPI infusion
- Intubated
- Transferred to PICU



CBC & Differential

	List of add on tests:
	Requested by: NG,B
WBC	5.0
RBC	5.17
Hemoglobin	142
Hematocrit	0.43
MCV	84
RDW	13.1
Platelets	167
Neutrophils	4.6
Lymphocytes	0.2
Monocytes	0.1
Eosinophils	< 0.1
Basophils	< 0.1
Granulocytes Immature	< 0.1
C Reactive Protein; High Sensitivity	
27.9	

Chemistry Panel

	List of add on tests:
	Requested by: NG,B
Sodium	138
Potassium	3.7
Chloride	101
Bicarbonate	23
Anion Gap	14
Glucose Random	6.0
Urea	5
Creatinine	82

Chemistry Panel

	List of add on tests: TROP	
	Requested by: NG,B	
Protein	69	
Alanine Aminotransferase	115	H
Aspartate Aminotransferase	99	H
Alkaline Phosphatase	64	L
Gamma Glutamyl Transferase	24	H
Bilirubin, Total	4	
Albumin	34	L



Bacteriology: Culture

Bacteria; Isolate

Setup Date/Time	05/Feb/2024 1556
Special Requests	Streptococcus pyogenes (Group A Streptococcus)

Feb 6, 2024

- Left sided opacity evolved

Feb 7

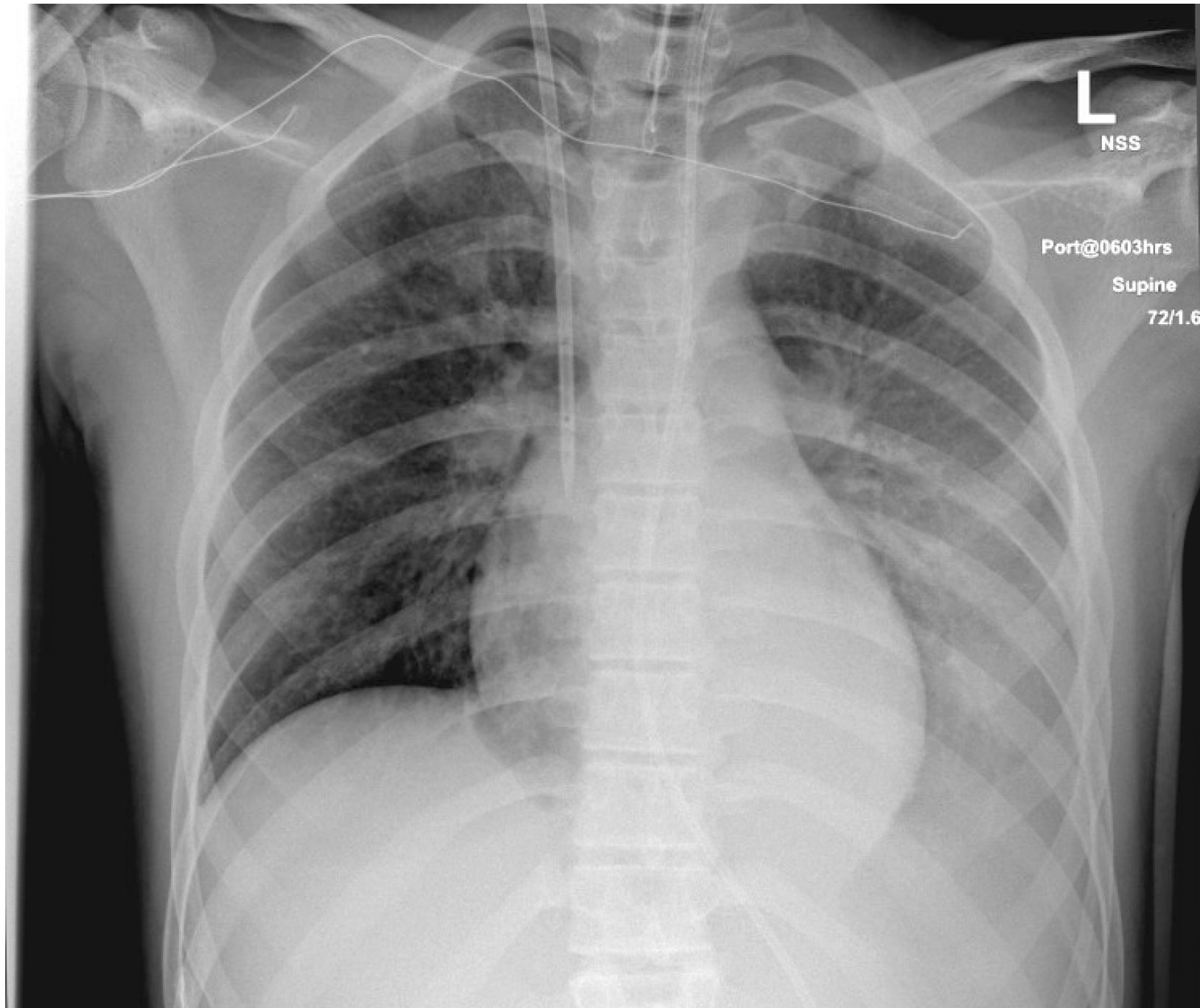
- extubated

Feb 14

- Pleural effusion drained
 - C/S negative
 - GAS PCR positive

Feb 23

- discharged



Learning Pearls

- Beware of a child presenting with fever on multiple occasions:
 - Viral infections are often a risk factor for bacterial infections
- IBI can mimic ILI in early stages
- Measure BP in all febrile children on repeat occasions during your observation

Case 2

- 11 mo girl; unimmunized
- May 10th: Presented with fever and rash involving mouth, and areas of hands and feet
- HFM disease suspected but a 'sepsis panel' is done due to unvaccinated status
- Discussed with PEDS
- Will be seen in 2-3 days

Hematology Profile, Differential and Blood Film Review

CBC & Differential

WBC	22.0
RBC	3.71
Hemoglobin	82
Hematocrit	0.26
MCV	71
RDW	14.3
Platelets	447
Neutrophils	15.5
Lymphocytes	5.1
Monocytes	1.1
Eosinophils	0.1
Basophils	< 0.1
Granulocytes Immature	0.1

Routine Chemistry

Chemistry Panel

Sodium	135
Potassium	4.3
Chloride	98
Bicarbonate	23
Anion Gap	14
Glucose Random	5.6
Urea	2
Creatinine	< 27

Consult with Medical Biochemist

C Reactive Protein; High Sensitivity

61.7

H

- Presented May 11th with fever
- Unwell; is seen by PEDS and admitted for urosepsis

Urinalysis

Urinalysis Panel				
Colour; Urine	Yellow			
Appearance; Urine	Clear			
pH; Urine	5.0		5-7	
Leukocyte Esterase; Urine	100	H	Negative	/uL
Nitrite; Urine	Positive	H	Negative	
Protein; Urine	0.25	H	Negative	g/L
Glucose; Urine	Negative		Negative	mmol/L
Ketones; Urine	Small	H	Negative	
Hemoglobin; Urine	Trace	H	Negative	

Comment; Urinalysis

If physician requires a urine microscopic after Urinalysis results have been reported then enter an 'Add on' request for urine microscopic as per physician orders.

Urinalysis Microscopic Panel				
Leukocytes; Urine	15-25	H	0-5	/ [HPF]
Erythrocytes; Urine	2-5		0-5	/ [HPF]
Epithelial Cells; Urine	Few			/ [HPF]
Specimen Volume; Urine	10			mL

ISOLATE 1 Escherichia coli
 >100 10*6 [CFU]/L

ANTIMICROBIAL AGENT	ISOLATE 1
Amoxicillin+Clavulanate	S
Ampicillin	R
Cefixime	S
Ceftriaxone	S
Cephalexin	S
Fosfomycin	S
Gentamicin	S
Nitrofurantoin	S
Piperacillin+Tazobactam	S
Trimethoprim+Sulfamethoxazole	R

Hematology Profile, Differential and Blood Film Review

CBC & Differential

WBC	32.6
RBC	3.75
Hemoglobin	82
Hematocrit	0.26
MCV	69
RDW	14.6
Platelets	562
Neutrophils	28.4
Lymphocytes	3.9
Monocytes	0.3
Eosinophils	< 0.1
Basophils	< 0.1
Granulocytes Immature	< 0.1

Routine Chemistry

Chemistry Panel		
Sodium	136	
Potassium	4.9	
Chloride	99	
Bicarbonate	20	
Anion Gap	17	H
Consider ketoacidosis (DKA, also acidosis, renal failure, dehydration, salicylates, or toxic alcohols, glycol.		
Glucose Random	7.4	
Urea	4	
Creatinine	< 27	
Consult with Medical Biochemist		

C Reactive Protein; High Sensitivity	92.1	H
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Learning Pearls

- UTI is a common bacterial co-infection in infants with viral infections.
- UA should be considered in workup of all children who receive a 'septic panel.'

Oct 7, 2024

Case 3

- 2 year-old child presented to SMH with a limp following a injury a few days ago

REASON FOR VISIT: RT ANKLE INJURY
CHIEF COMPLAINT: Lower Extremity Injury
COMMENT:

TRI. DATE/TIME: 07 Oct 2024 1535		CTAS: 3	ALERTS		
Temp	HR	BP	RR	02 Sat	GC8
38.0	152	133/75	30	99	15
PHYSICIAN NOTES					
Allergies:					

Miscellaneous Sample Differential

Differential; Synovial Fld
Neutrophils/100 Leukocytes; Synovial Fld
88 H <25 %
Other Cells/100 Leukocytes; Synovial Fld
12 %
Fluid Other Cells include Monocytes, Macrophages,
Lymphocytes, Lining cells, etc.

Miscellaneous Sample Cell Count and Differential

Cell Count & Differential; Fld
Appearance; Fld Cloudy
Cell Count & Differential; Synovial Fld
Nucleated Cells; Synovial Fld
257600 H < 150 10*6/L
Comment; Fld See Comment
Fluid sample is > 4 hrs old. Differential and cell count may
be compromised due to cellular degeneration.
RBC noted on Diff.



Synovial Fluid; Culture

ISOLATE 1 Group A streptococcus
4+

As required by regulations for the control of communicable disease, this case will be reported to the Medical Health Officer.

A copy of the result has been sent to Infection Control.

Report faxed to: SM.ERTPEDS
Date: 08/10/24 Time: 1512

ANTIMICROBIAL AGENT	ISOLATE 1
Ampicillin	S
Cefazolin	S
Ceftriaxone	S
Cephalexin	S
Clindamycin	S
Penicillin	S
Vancomycin	S

Blood; Culture

ISOLATE 1 Group A streptococcus
Sets positive:
One out of one.
Isolated after:
Less than 12 hours of incubation.

As required by regulations for the control of communicable disease, this case will be reported to the Medical Health Officer.

A copy of the result has been sent to Infection Control.

****CRITICAL VALUE****
Nursing unit/office to notify physician immediately.
Phoned to nursing unit/office: SM.ERTPEDS
Date: 08/10/24 Time: 0614

ANTIMICROBIAL AGENT	ISOLATE 1
Ampicillin	S
Cefazolin	S
Ceftriaxone	S
Clindamycin	S
Penicillin	S
Vancomycin	S

Throat; Culture

Source : Strep Screen Routine

Throat; Culture

ISOLATE 1 Group A streptococcus
Isolated

This beta-hemolytic group A Streptococcus is predictably susceptible to all beta-lactam antibiotics such as penicillins and cephalosporins. Susceptibility to clindamycin is variable. If this patient is penicillin allergic, please contact the Fraser Health Microbiology Laboratory as soon as possible to perform susceptibility testing.

- Despite isolation at multiple sites, he did well on IV antibiotics.
- He never developed shock.
- He was switched to PO antibiotics and discharged within one week.

Learning Pearls

- IBI can present with subtle signs.
 - Can fool clinicians and parents
- Beware of a child with fever and extremity pain.
 - These children always require investigation.
- iGAS can present with TSS (hypotension and end-organ failure +/- rash) or without TSS.

Case 4

- 5 year-old immunized girl
- Presented on Dec 1 and Dec 2 with vomiting
- Was "playful" on first presentation
- Both times received Ondansetron and discharged with diagnosis of viral illness
- Presented on Dec 3 with lethargy and stiff neck

Hematology Profile, Differential and Blood Film Review

CBC & Differential		
WBC	20.0	
RBC	4.42	
Hemoglobin	111	
Hematocrit	0.34	
MCV	77	
RDW	14.6	
Platelets	405	
Neutrophils	17.4	
Lymphocytes	1.5	
Monocytes	0.8	
Eosinophils	< 0.1	
Basophils	0.1	
Granulocytes Immature	0.2	

C Reactive Protein; High Sensitivity
372.3

Bacteriology: Culture

Blood; Culture
Source : Blood
Spec Desc : Peripheral

Blood; Culture

ISOLATE 1 Streptococcus pneumoniae
Sets positive:
One out of one.
Isolated after:
Less than 12 hours of incubation.

CSF Differential

Cell Count & Differential; CSF				
Specimen Volume; CSF	1.0			mL
Volume; CSF Tube 2	1.0			mL
Volume; CSF Tube 3	1.0			mL
Volume; CSF Tube 4	1.0			mL
Appearance; CSF	Cloudy/Yellow	H		
Appearance; CSF Tube 2	cloudy/Yellow	H		
Appearance; CSF Tube 3	cloudy/Yellow	H		
Appearance; CSF Tube 4	cloudy/Yellow	H		
Colour; CSF spun	Colourless			
Erythrocytes; CSF	150	H	0-5	10*6/L
Erythrocytes 4th Tube; CSF	Tube #1 RBC count was done to rule out traumatic tap			
Leukocytes 4th Tube; CSF	175	H	0-5	10*6/L
	1674	HH	0-7	10*6/L
	* CRITICAL VALUE			
Neutrophils/100 Leukocytes; CSF	90	H	0-2	%
Monocytes/100 Leukocytes; CSF	10		3-37	%
Comment; CSF	Findings resembling bacteria are seen; suggest microbiology testing.			

CSF Chemistry

Glucose; CSF	< 0.6	L	2.0-4.0	mmol/L
Protein; CSF	3250	H	150-450	mg/L

Bacteriology: Direct, Serological and Molecular

Meningitis+Encephalitis Pathogens DNA & RNA Panel; CSF; PCR/NAAT
Source : Lumbar puncture - Drip
Meningitis+Encephalitis Pathogens DNA & RNA Panel; CSF; PCR/NAAT
ISOLATE 1 Strep. pneumoniae detected

Learning Pearls

- Beware of a repeat visitor with fever
- Not all cases of vomiting are gastro.
- Vomiting could be a sign of CNS disease.

Management strategies - sepsis

- Sepsis
- ABC, IV, oxygen, monitor, sepsis panel
- Fluid resuscitation
- Antibiotics within 60 minutes:
 - Ceftriaxone 100 mg/kg/dose q24h
 - Vancomycin 20mg/kg/dose q6h
- OR
 - Piperacillin-tazobactam 75 mg/kg/dose q6h

Management strategies – antibiotic stewardship principles

- Narrow spectrum antibiotics
 - Amoxicillin
 - Cephalexin
- Avoid broad spectrum antibiotics
 - Azithromycin for pneumonia
 - Amoxicillin-Clavulanate for pneumonia

Antibiotic Stewardship

- Diagnosis-specific dosages and intervals and duration
 - Amoxicillin
 - Pneumonia: 15-30 mg/kg TID 5 days
 - Otitis Media:
 - 40-45 mg/kg BID for 10 days < 2 yrs
 - 40-45 mg/kg BID for 5 days > 2 yrs
 - GAS pharyngitis: 25 mg/kg BID for 10 days (max 500 mg/dose)
 - Cephalexin is the second most common antibiotics
 - UTI: 10-25 mg/kg QID 5-7 days
 - Cellulitis: 10-25 mg/kg QID 5 days
 - Adenitis: 10-25 mg/kg QID for 7 days
- Preprinted Rx project

Delabeling Amoxicillin Allergy

- > 90% of 'penicillin allergy' patients do not have true IgE-mediated allergic reaction
- Delabeling:
 - Attenuated dose: 15 mg/kg PO
 - Observe for 1 hour
 - Delabel if no reaction in 1 hour
 - Complete the dose as necessary based on diagnosis
 - Fax a note to pharmanet formally delabeling the patient

Conclusions

- Post-pandemic rise in invasive bacterial infections
- Consider investigations in select patients; be mindful of limitations
- Consider missed diagnoses in repeat visits of febrile children to the ER
- Sepsis mimics influenza-like illness and non-specific complaints
- Beware of intercurrent viral and bacterial infections
- Consider basic principles of antibiotic stewardship
 - Single agent with diagnosis-specific narrow spectrum coverage
 - Amoxicillin delabeling

References

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