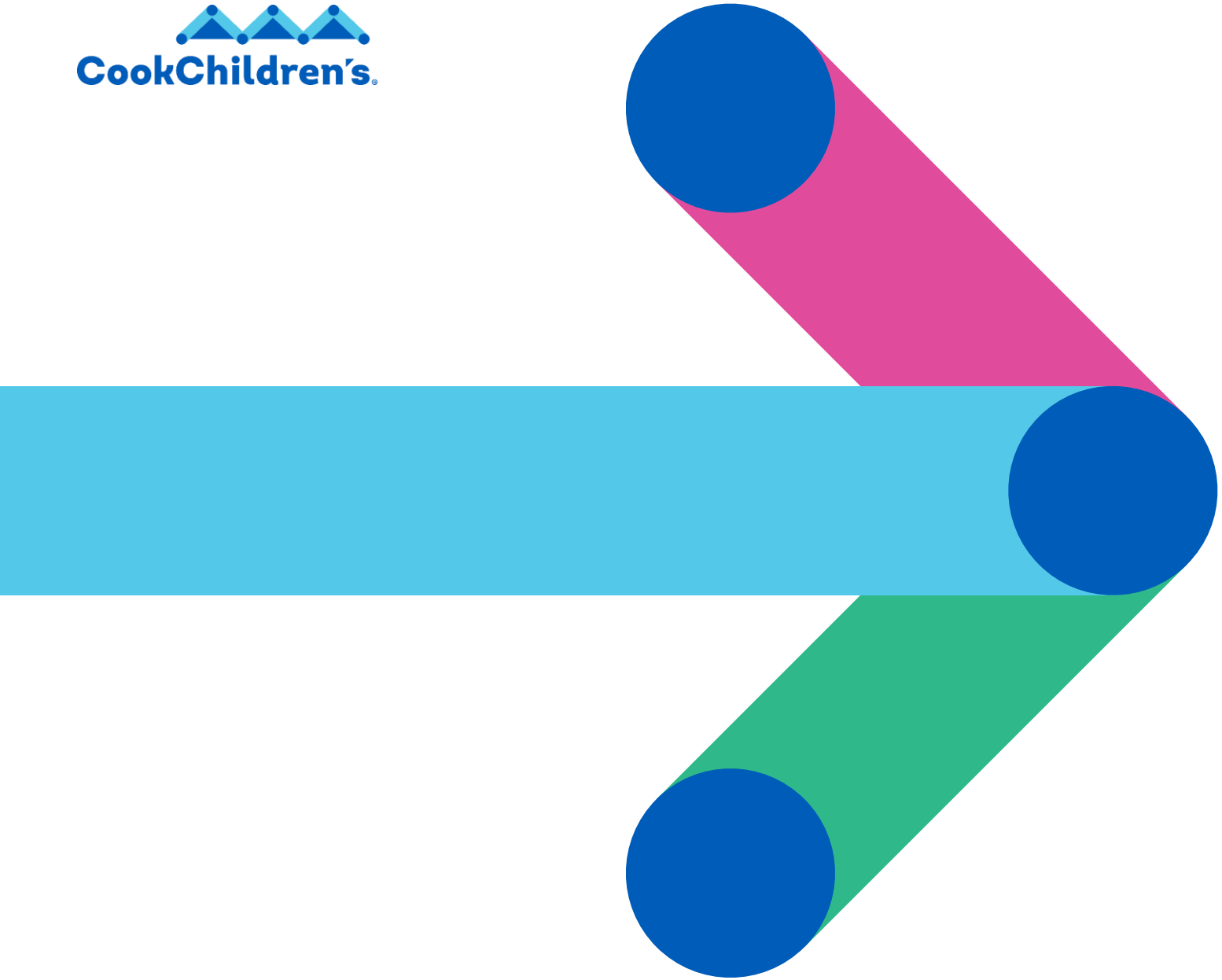


Conquering Pediatric Sepsis: It's a Team Approach

Cook Children's Medical Center
Teddy Bear Transport
Outreach Education

Conflicts of Interest

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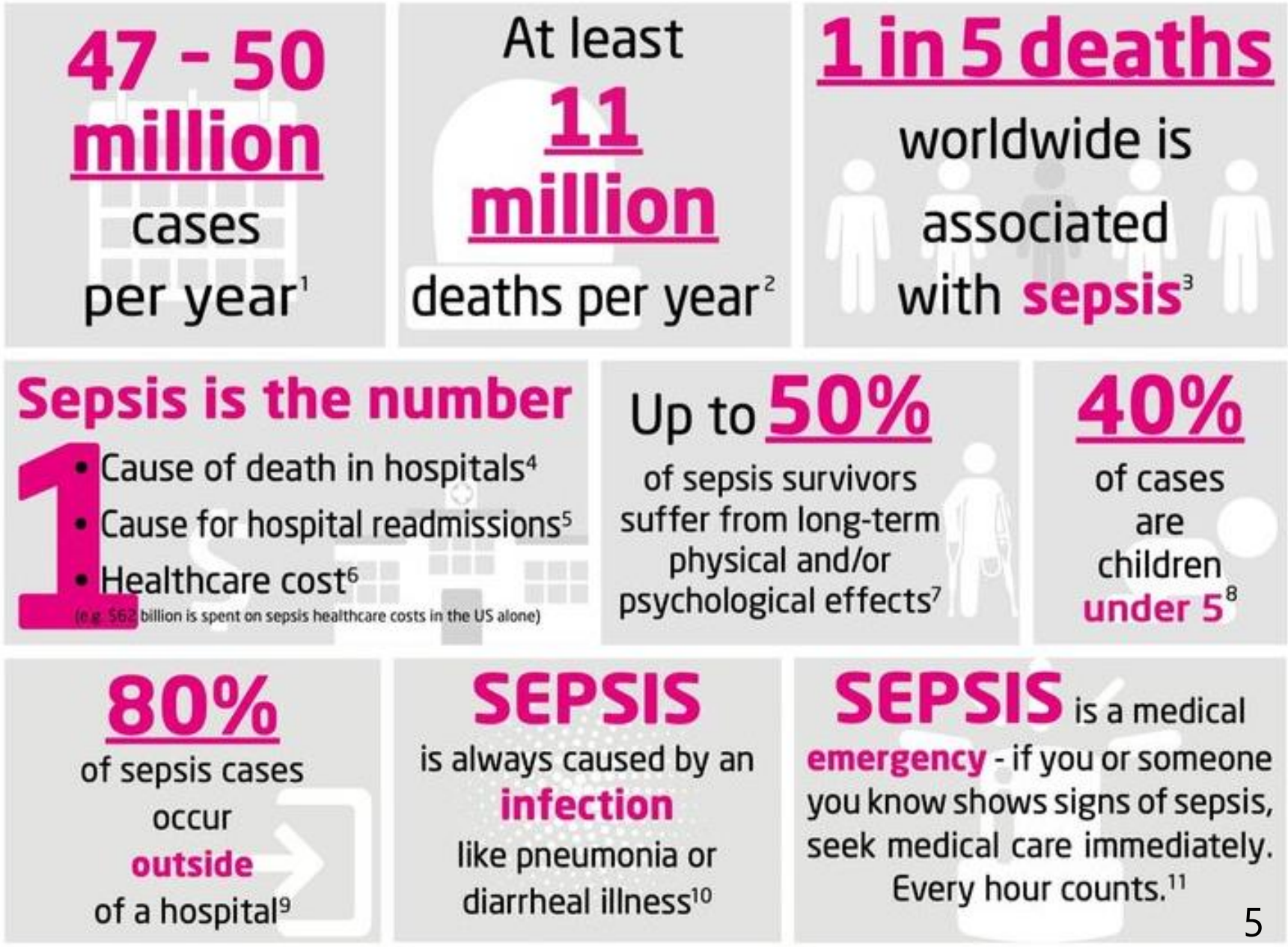
The presenter(s) and the planning committee for this educational event, have no relevant financial relationship(s) with ineligible companies to disclose.

Objectives

- Identify the signs and symptoms of sepsis in the pediatric patient
- Discuss the components of a sepsis scoring tool using the PIRO model
- Examine priority interventions within the sepsis treatment pathway
- Describe specific treatment goals after sepsis protocol is initiated in a pediatric septic patient
- Discuss the importance of a multidisciplinary approach and communication while caring for septic patients in order to decrease mortality rates

Sepsis? In kids?

In fact, there wasn't even a formal definition for pediatric sepsis until 2005!


47 - 50 million cases per year[1]
At least 11 million deaths per year[2]
1 in 5 deaths worldwide is associated with sepsis[3]
Sepsis is the number 1
• Cause of death in hospitals[4]
• Cause for hospital readmissions[5]
• Healthcare cost[6]
(e.g. $62 billion is spent on sepsis healthcare costs in the US alone)
Up to 50% of sepsis survivors suffer from long-term physical and/or psychological effects[7]
40% of cases are children under 5[8]
80% of sepsis cases occur outside of a hospital[9]
SEPSIS is always caused by an infection like pneumonia or diarrheal illness[10]
SEPSIS is a medical emergency - if you or someone you know shows signs of sepsis, seek medical care immediately. Every hour counts.[11]

5

The sepsis epidemic by the numbers:

48.9 million cases of sepsis worldwide

~25 million of these cases were in the pediatric population

11 million sepsis related deaths

3.4 million of these deaths were pediatric patients

18+ pediatric deaths from sepsis in the U.S. every day

Difficulty Identifying Patients with Sepsis

❑ Rory Staunton 2012

- **12 years old**
- **He cut his arm in gym class**
- **Developed fever, vomiting, and pain in legs**

❑ Following morning

- **Pediatrician sent him to ED and was diagnosed with dehydration**
- **New York ER: Took blood samples, gave him fluids, and sent him home**

❑ Following day

- **The pain and fever continued**
- **His leg was mottled and his nose turned blue. They took him to the Emergency Room again**



4 days after his accident this boy dies of septic shock.

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THE RORY STAUNTON FOUNDATION FOR SEPSIS PREVENTION

The High Cost of Pediatric Severe Sepsis

72,000 Pediatric Severe Sepsis Hospitalizations



2016 Nationwide Readmissions Database
Age 0-19 years

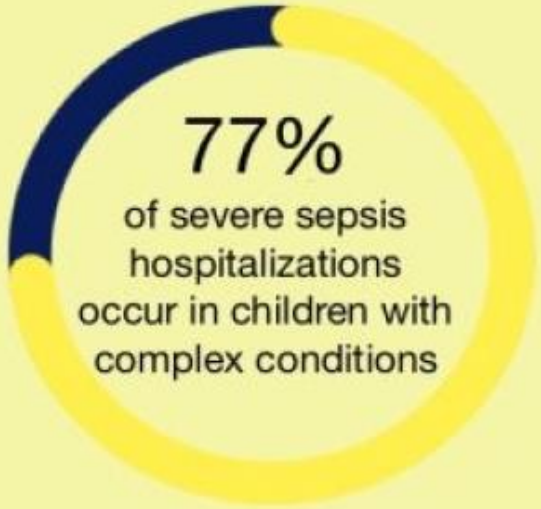
$7.31 Billion
Total Nationwide Estimate



18% of all hospitalization costs

An average severe sepsis hospitalization is 12x costlier than a non-sepsis hospitalization

Children with Chronic Conditions Impacted Disproportionately



M | C.S. MOTT CHILDREN'S HOSPITAL

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Number one key is prevention of infection!



Kids are still dying from Sepsis….How is this still possible?

~ 50% of pediatric deaths from sepsis happen in the first 24 hours

Around 8% of pediatric sepsis cases are missed during initial ED visits

Age-specific vital signs and response to illness can mask serious symptoms, causing delays in recognition, interventions, or transfer to appropriate unit or hospital

What exactly is sepsis?

Infection SIRS Sepsis ~~Severe Sepsis~~ Septic Shock

Old term



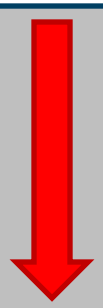
Clinical response non-specific that includes at least 2 of the following
•Temperature >38° C or
•<36° C
HR>90 /min
• Respirations >20/min
• WBC's >12,000/mm^3 or
• <4,000/mm^3 or >10% ANC



Infection presumed or confirmed; life threatening organ dysfunction



Sepsis w/ greater than 1 sign of organ failure:
• Cardiovascular **Hypotension**
• Renal
• Respiratory
• Hepatic
• Hematologic
• CNS
• Metabolic acidosis



Subset of sepsis with cardiovascular dysfunction (elevated lactate, hypotension, vasopressors)



Sepsis is subtle..

Pediatric patients don't suddenly deteriorate.

Healthcare professionals just suddenly notice!

What am I looking for?

Signs and Symptoms



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Signs and symptoms

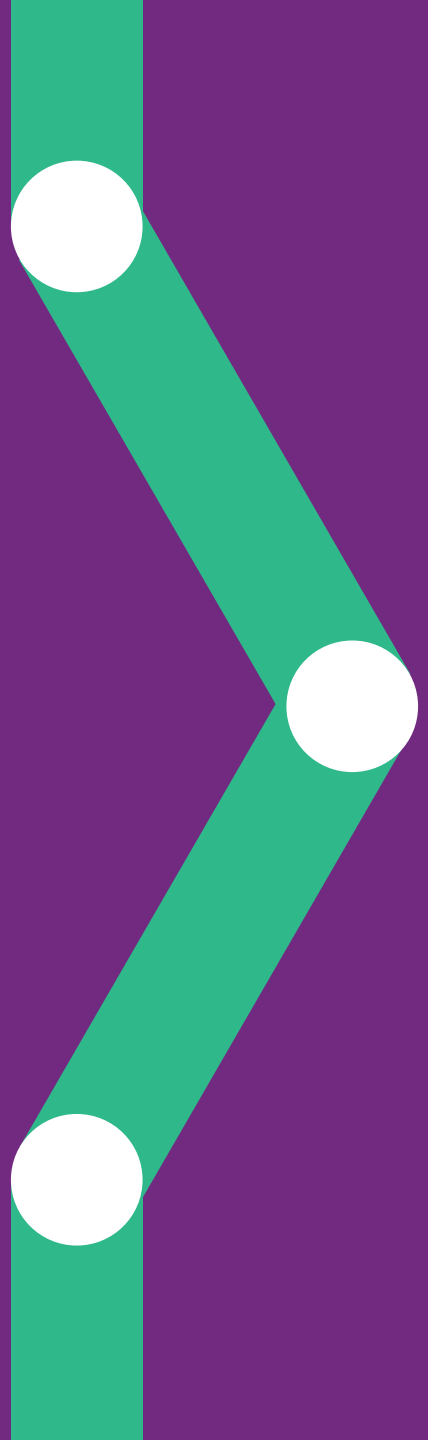
If the caregiver of the patient is concerned, we should be too.



Early detection saves lives







What do we do now?

Sepsis Scoring

The scoring tool:

- Is based on the PIRO model of sepsis
- Uses goal-directed therapy for treatment

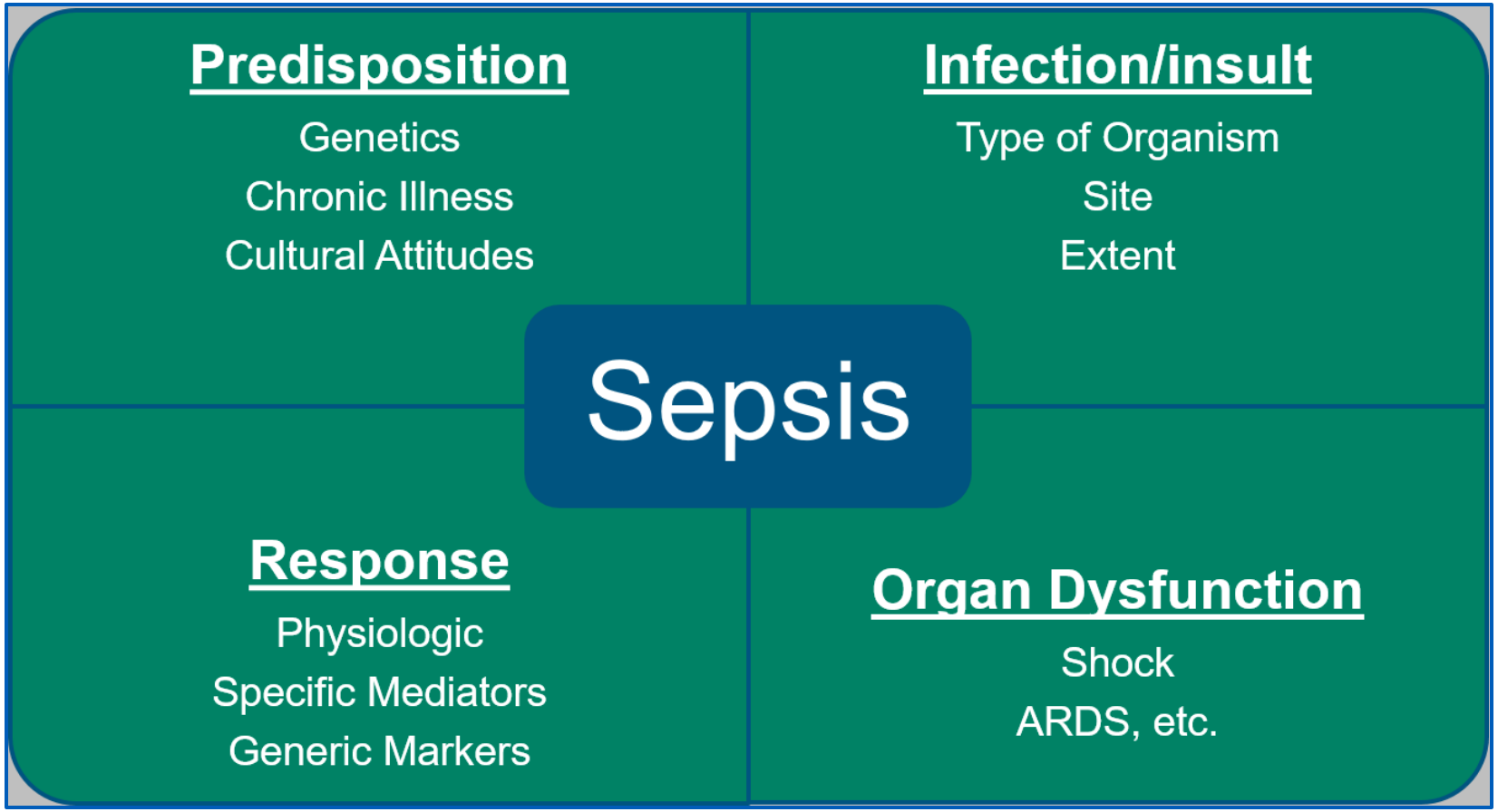


Table. The Phoenix Sepsis Score[a]

Variables	0 Points	1 Point	2 Points	3 Points
Respiratory, 0-3 points				
	Pao_2:FIo_2 ≥400 or Spo_2:FIo_2 ≥292[b]	Pao_2:FIo_2 <400 on any respiratory support or Spo_2:FIo_2 <292 on any respiratory support[b,c]	Pao_2:FIo_2 100-200 and IMV or Spo_2:FIo_2 148-220 and IMV[b]	Pao_2:FIo_2<100 and IMV or Spo_2:FIo_2 <148 and IMV[b]
Cardiovascular, 0-6 points				
		1 Point each (up to 3)	2 Points each (up to 6)	
	No vasoactive medications[d]	1 Vasoactive medication[d]	≥2 Vasoactive medications[d]	
	Lactate <5 mmol/L[e]	Lactate 5-10.9 mmol/L[e]	Lactate ≥11 mmol/L[e]	
Age based[f]				
	Mean arterial pressure, mm Hg[g]			
<1 mo	>30	17-30	<17	
1 to 11 mo	>38	25-38	<25	
1 to <2 y	>43	31-43	<31	
2 to <5 y	>44	32-44	<32	
5 to <12 y	>48	36-48	<36	
12 to 17 y	>51	38-51	<38	
Coagulation (0-2 points)[h]				
		1 Point each (maximum 2 points)		
	Platelets ≥100 × 10^3/μL	Platelets <100 × 10^3/μL		
	International normalized ratio ≤1.3	International normalized ratio >1.3		
	D-dimer ≤2 mg/L FEU	D-dimer >2 mg/L FEU		
	Fibrinogen ≥100 mg/dL	Fibrinogen <100 mg/dL		
Neurological (0-2 points)[i]				
	Glasgow Coma Scale score >10; pupils reactive[j]	Glasgow Coma Scale score ≤10[j]	Fixed pupils bilaterally	
Phoenix sepsis criteria				
Sepsis	Suspected infection and Phoenix Sepsis Score ≥2 points			
Septic shock	Sepsis with ≥1 cardiovascular point(s)			

Cook Children's Sepsis Scoring Tool

Predisposition:		
Predisposition includes (not limited to): Transfer from any healthcare facility for a diagnosis of sepsis, rule out sepsis, or bacterial infection; 2 or more recent visits to healthcare facility for same complaint during the last 7 days; History of confirmed flu with new fever after 5 days or symptoms lasting more than 5 days; Age less than 60 days; use of tampons during current menses; indwelling catheters; **two previous hospitalizations during the patient's lifetime for serious bacterial infection including pneumonia, bacteremia, meningitis, bone or joint infection;** Acute or chronic immunocompromised status; Chronic medical problems (i.e. Status Post Bone Marrow Transplant, Chronic respiratory failure, Sickle Cell Disease, Complex Congenital Heart Disease, Chronic Liver failure, Chronic Renal Failure, Profound Neurological Impairment).		
If yes, circle applicable predisposition	**Primary Screen:** Yes 2 No 0	**Secondary Screen:** Yes 2 No 0

Cook Children's Sepsis Scoring Tool

Infectious symptoms: **In the last week, is there history or physical exam suggesting infection such as:** fever or hypothermia, rash, reddened draining area of skin, joint pain, dysuria, productive cough *If yes, circle applicable symptoms*	Primary Screen:				Secondary Screen:			
	Yes	2	No	0	Yes	2	No	0

Response (vital signs):

If abnormal heart rate **AND** tachypnea choose yes:

0 - < 2 months:	< 100 or > 180 HR	and	> 50 RR
2 months - < 1 y.o.:	< 90 or > 180 HR	and	> 40 RR
1 - < 2 y.o.:	< 90 or > 180 HR	and	> 35 RR
2 - < 6 y.o.:	> 140 HR	and	> 25 RR
6 - < 13 y.o.:	> 130 HR	and	> 20 RR
13 – 18+ y.o.:	>110 HR	and	> 14 RR

Tachycardia AND Tachypnea

Primary Screen:

Yes 2 No 0

Organ Dysfunction: Organ dysfunction can include **any of these categories.**

		Primary Screen:				Secondary Screen:			
Respiratory dysfunction If hypoxemia or O2 sats <91% on RA, OR O2 sats <97% on 1 L OR O2 sats <95% on 2 L O2 or more OR Need for ventilatory support (HFNC, BVM or ETT) Check "no" if patient has chronic respiratory failure AND is at baseline home oxygen and or ventilator settings		Yes	1	No	0	Yes	1	No	0
Neurological dysfunction GCS <11 or decreased by 3 OR Acute change in mental status OR Inconsolable or confused		Yes	1	No	0	Yes	1	No	0
Circulatory dysfunction: hypotension Use SBP mmHg/ Percentile SBP by age chart to left. **Patient on vaso-active agents for hemodynamic stability**		Yes	2	No	0	Yes	2	No	0
ANY positive organ dysfunction (If answered yes for respiratory OR neurological OR circulatory, answer yes here.)		Yes	2	No	0	Yes	2	No	0
TOTAL for organ dysfunction (Add respiratory, neurological, circulatory plus row above, if applicable.)									
Count these points *IF* patient has any *TWO* of the following:		Primary Screen:				Secondary Screen:			

Circulatory Dysfunction

Age	SBP mm/HG	Percentile SBP
0-2 months	< 56	n/a
2 months - < 6 months	<65	n/a
6 months - < 12 months	<70	n/a
12 months - 13 years	n/a	Trigger based on percentile (< 10%)
> 13 years	< 100	n/a

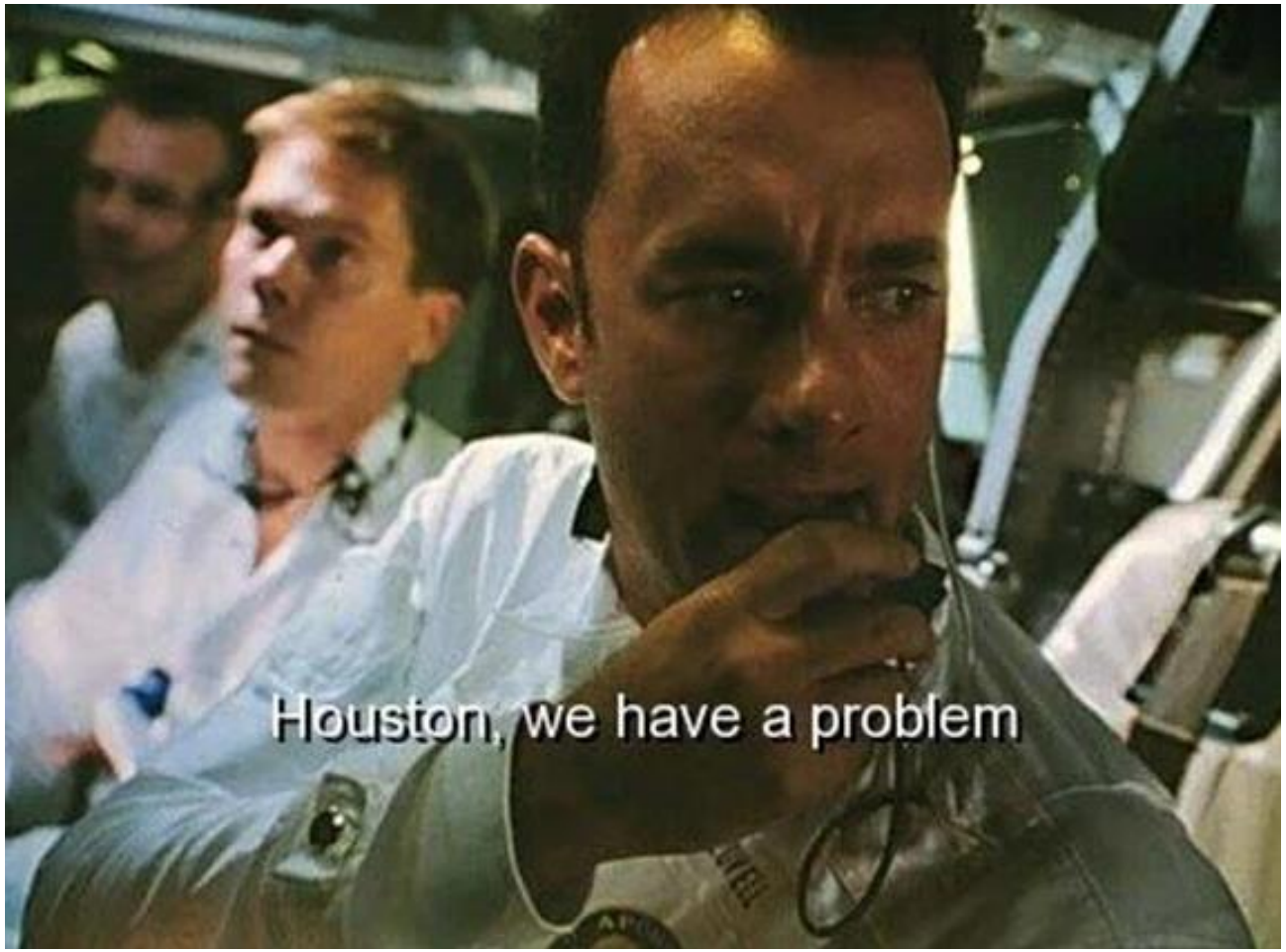
Count these points *IF* patient has any *TWO* of the following:	Primary Screen:			
Decreased urine output OR elevated creatinine (w/in 24 hr) by age (see chart to left) *EXCLUDE Chronic Renal Failure Patients*	Yes	1	No	0
Capillary refill: > 3 seconds	Yes	1	No	0
Decreased OR bounding pulses	Yes	1	No	0
Skin cool, mottled, red, pale, cyanotic OR gray	Yes	1	No	0
Lactate >2	Yes	1	No	0
Platelet count <150,000 *Exclude H/O, HUS and TTP Patients*	Yes	1	No	0

Normal Creatinine (mg/dL) by age		
	MALE	FEMALE
0-14 days	1.06	1.06
15 days – <1 year	0.64	0.64
1-<4 years	0.74	0.74
4-<7 years	0.84	0.84
7-<12 years	1.04	1.04
12-<15 years	1.24	1.24
15-<17 years	1.24	1.14
17-<19 years	1.33	1.14
>19 years	1.43	1.33

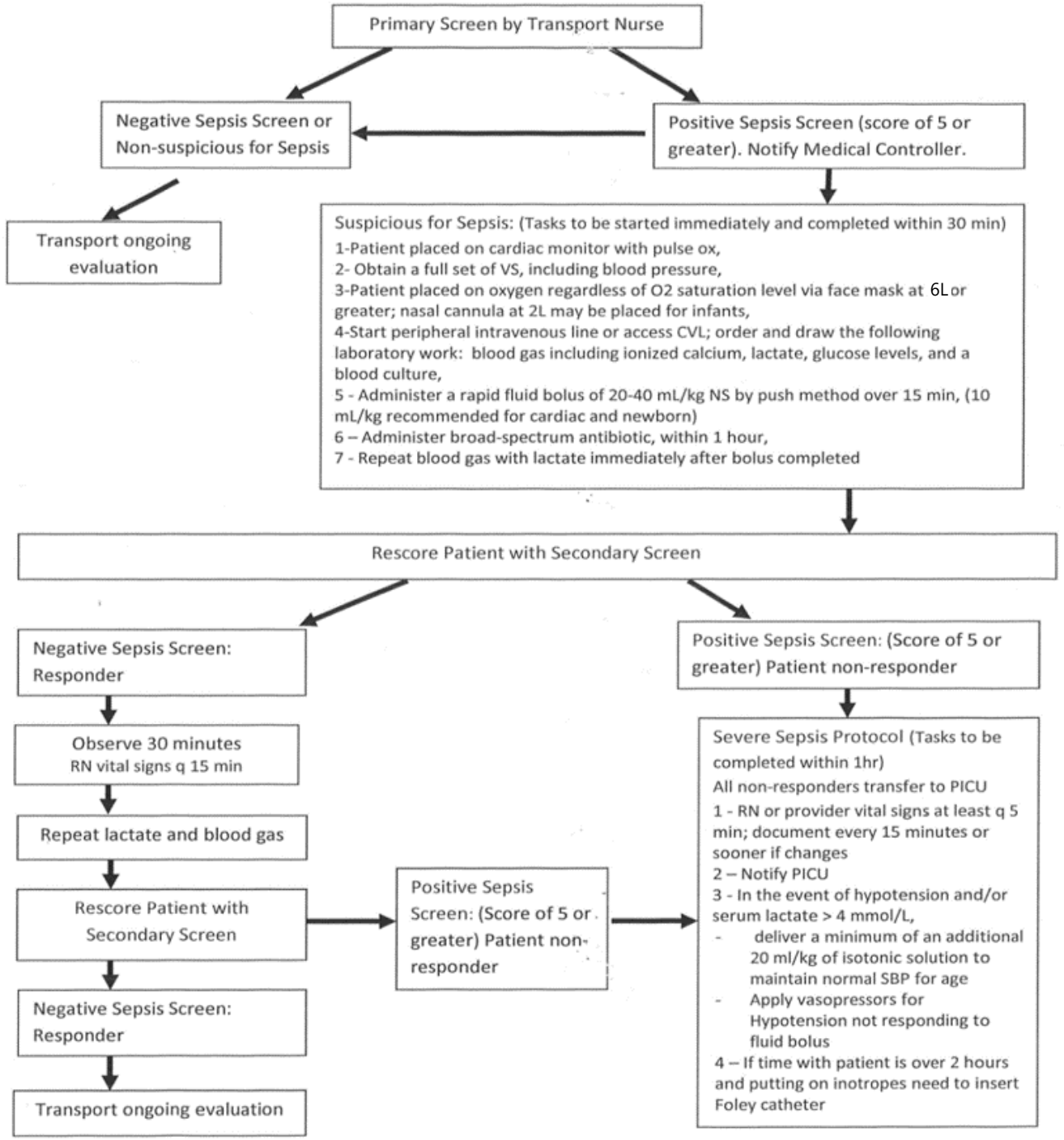
TOTAL PRIMARY SCREEN POINTS: *If ≥ 5, screen for organ dysfunction (next page) and start Sepsis Protocol*		
TOTAL SECONDARY SCREEN POINTS: *If ≥ 5, initiate Severe Sepsis Protocol*		
DATE and TIME	/ / @	/ / @

The sepsis treatment pathway

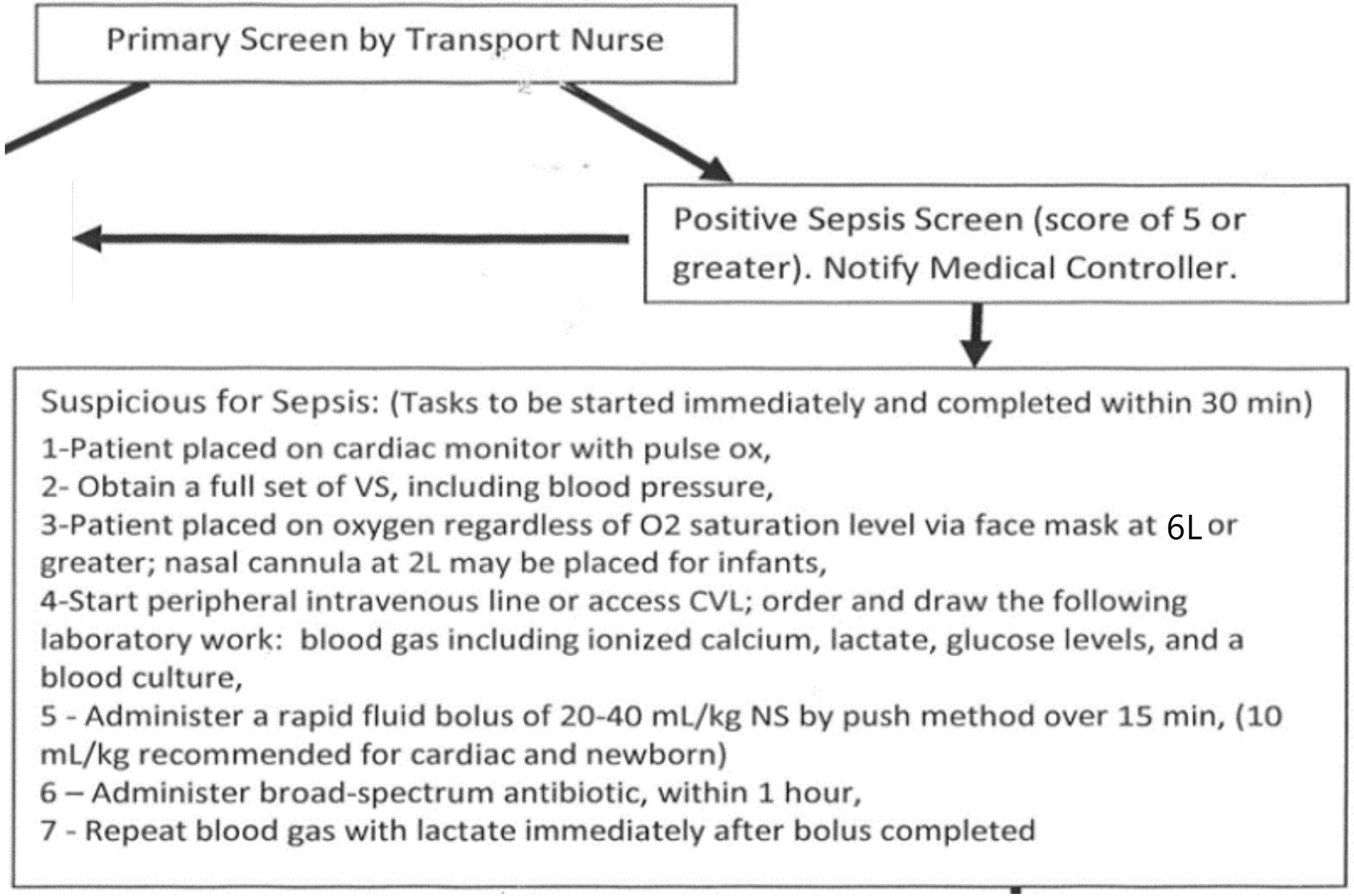
Now that we have identified the problem, what's next?



Let's get this ball rolling.



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Primary Screen by Transport Nurse
Positive Sepsis Screen (score of 5 or greater). Notify Medical Controller.
Suspicious for Sepsis: (Tasks to be started immediately and completed within 30 min)
1-Patient placed on cardiac monitor with pulse ox,
2- Obtain a full set of VS, including blood pressure,
3-Patient placed on oxygen regardless of O2 saturation level via face mask at 6L or greater; nasal cannula at 2L may be placed for infants,
4-Start peripheral intravenous line or access CVL; order and draw the following laboratory work: blood gas including ionized calcium, lactate, glucose levels, and a blood culture,
5 - Administer a rapid fluid bolus of 20-40 mL/kg NS by push method over 15 min, (10 mL/kg recommended for cardiac and newborn)
6 – Administer broad-spectrum antibiotic, within 1 hour,
7 - Repeat blood gas with lactate immediately after bolus completed

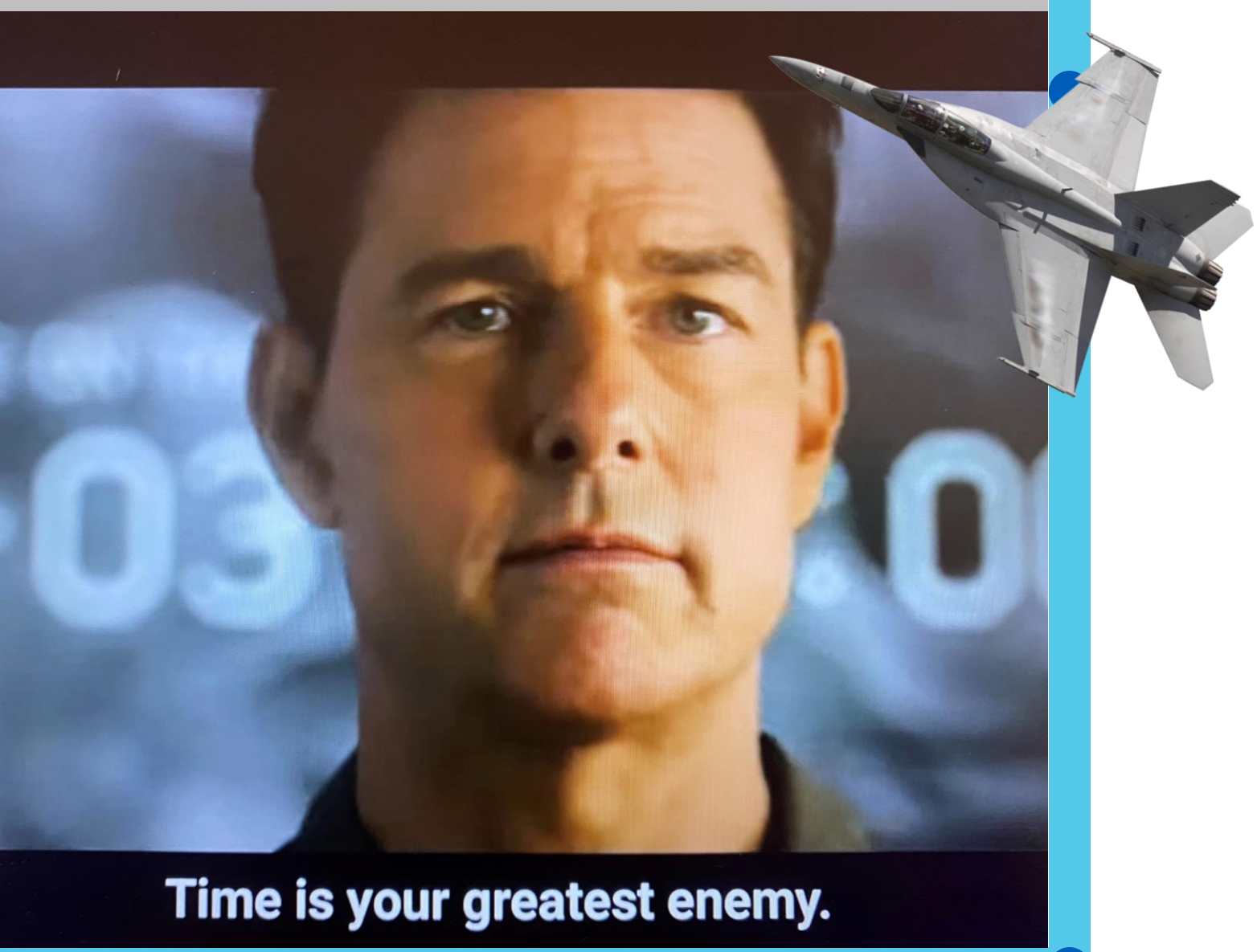
We approach the problem as a team.

Sepsis protocols should involve:

- Clinics
- Transport
- Emergency Department
- Inpatient units
- ICU

Protocols should be initiated when patient meets criteria in any location





Time is organ function.

Time starts at time of triage!

Bundles are how we organize and save time!

We have STEMI alerts, Stroke alerts.. All with bundles of evidence based care that must be completed within a certain TIME.

…Sepsis should be no different!

Data from 50 hospitals in the Improving Pediatric Sepsis Outcome collaborative showed that bundle compliance decreased morbidity and mortality by 50%!

At Cook Children's we follow our Sepsis Pathway/Bundle.

What is our goal?



What happens if we treat a patient with a positive score that isn't septic?

Better to treat some that may not need it than to miss some of these…

- Bacteremia
- Group A Streptococcal Infection
- Necrotizing Enterocolitis
- Adrenal Insufficiency (Addison Disease)
- Aseptic Meningitis
- Bacterial Meningitis
- Candidiasis
- Enterococcal Infection
- Escherichia Coli Infections
- Fungal Endocarditis
- Herpes Simplex Virus Infection
- Infective Pericarditis
- Influenza
- Meningococcal Infections
- Pneumococcal Infections
- Salmonella Infection
- Urinary Tract Infection
- Shigella Infection
- Staphylococcus Aureus Infection
- Haemophilus Influenzae Infection

Sepsis Data at Cook Children's

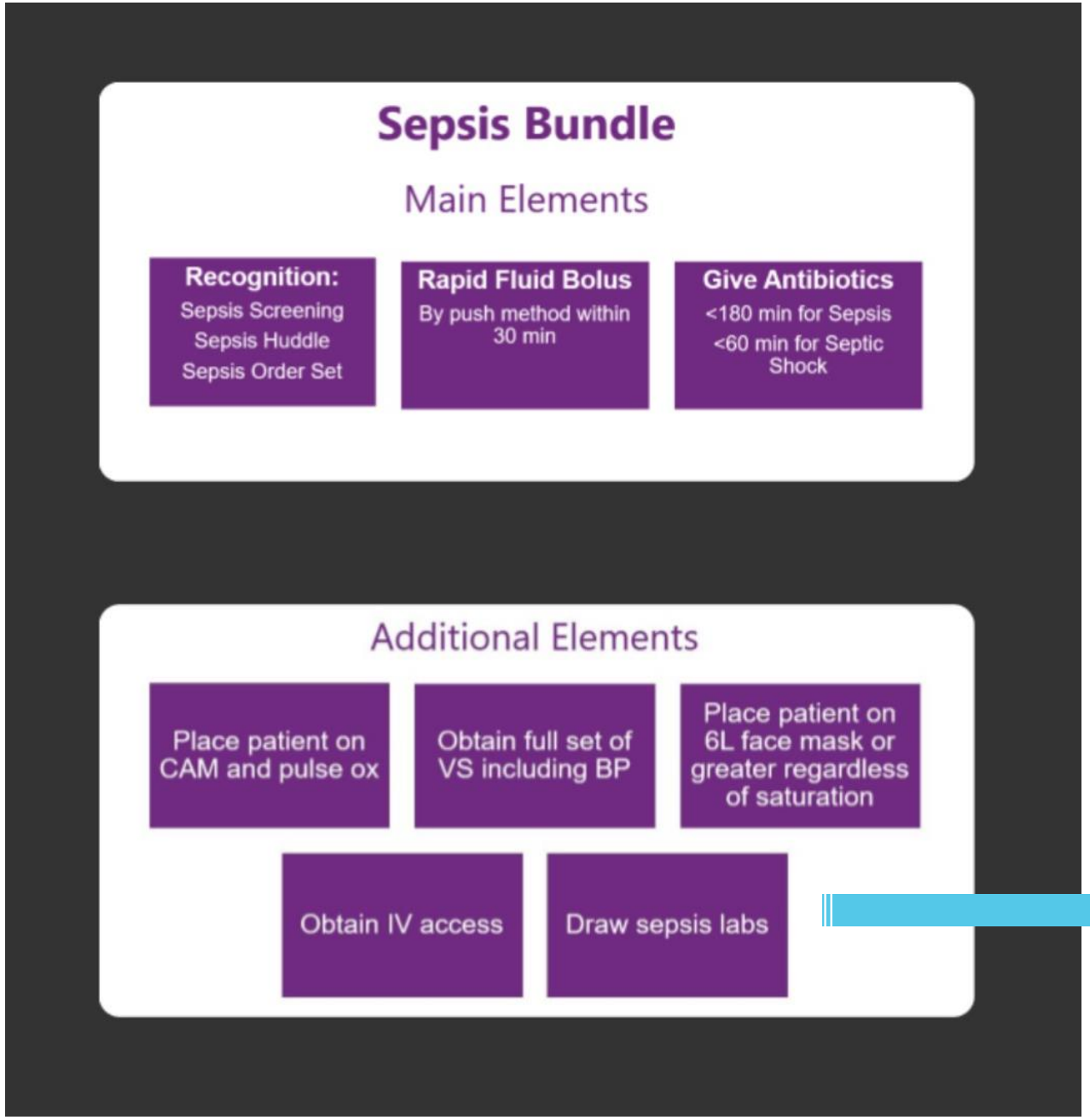
Consistently for the past ten years:

- 47% of patients that come into the ED are screened for sepsis
- 5% of patients that are screened screen positive

In September of 2026:

- 11,939 patients visited the ED
- 4,848 patients screened
- 122 patients screened positive

- **Average time to bolus: 28 minutes**
- **Average time to antibiotics: 49 minutes**
- **Average number of sepsis alerts per day: 4**



Key sepsis labs we look at are:

- WBC
- Platelets
- Lactic Acid
- Procalcitonin
- CRP
- Creatinine
- Blood Gas
- Blood/urine culture
- LP for neonates or those thought to have meningitis



Within the first hour:

- Measure blood gas with Lactate level
- Obtain blood cultures
- Administer broad-spectrum antibiotics
- Aggressive IV fluid resuscitation

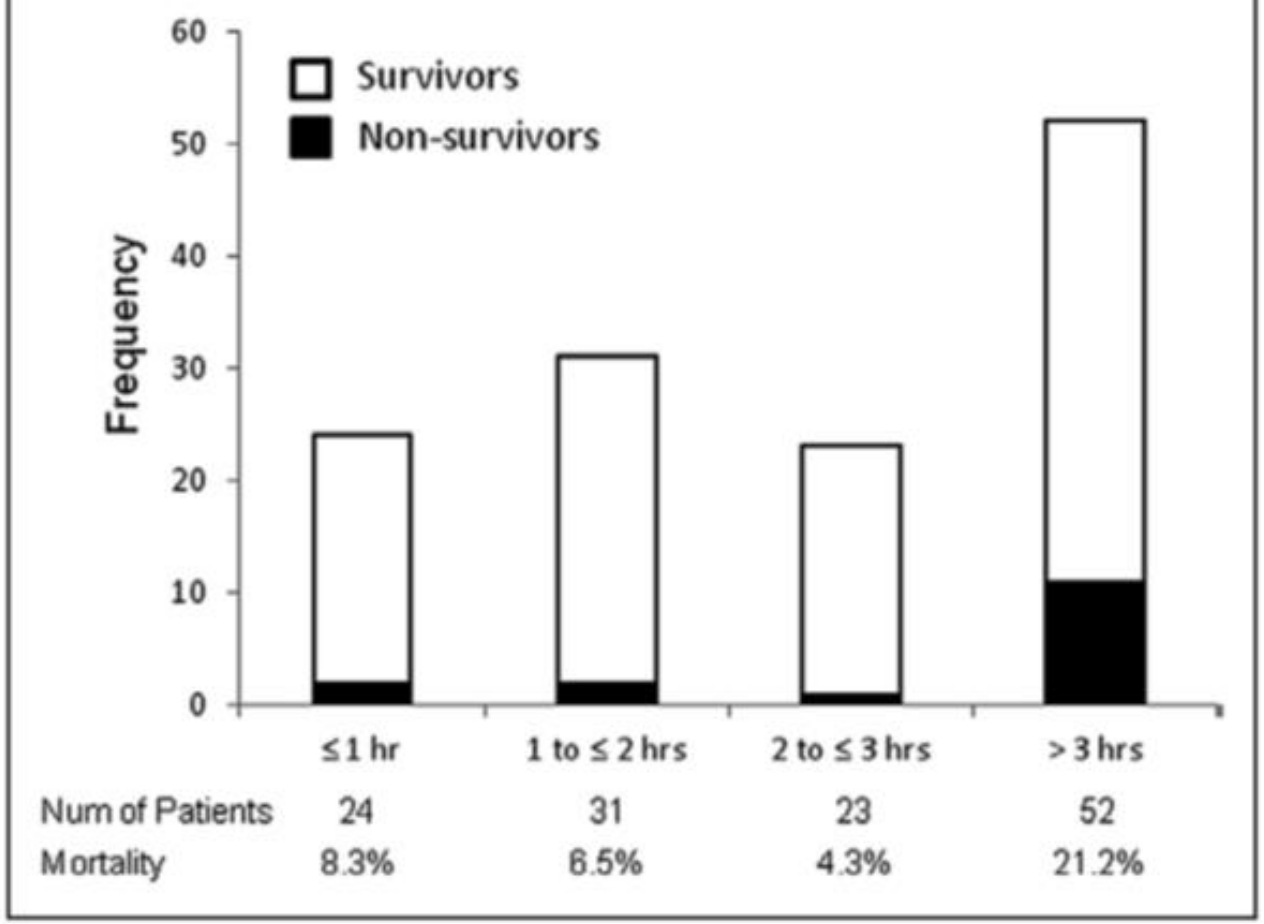


Figure 1. Time from sepsis recognition to initial antimicrobial administration with survival fraction. Total number of patients at hourly intervals from sepsis recognition to administration of initial antimicrobial therapy. The shaded portion of each bar indicates the number of nonsurvivors in each time interval.

8

Why the time crunch?

In this study of pediatric ICU patients with sepsis, mortality increased to over 20% when time to antibiotics was greater than three hours

But time isn't the only factor to consider!

In this study, survival rates decreased 5 fold when inappropriate antibiotics were given

	Appropriate (N=4579)	Inappropriate (N=1136)	OR (95% CI
Survived	52%	10.3%	9.45 (7.74-11.54)
Immuno-Suppressed*	15%	19.8%	<0.05
COPD	13.6%	14.1%	<0.05
Dialysis	7.3%	10.7%	<0.05

*Immunosuppression = chemotherapy or chronic steroids (>10 mg prednisone daily)

Chest 2009;136:1237-1248

So how do we choose?

most patients receive Rocephin; oncology patients receive cefepime

Risk Group	Antibiotics	Rationale
Previously Healthy (Non-neonate)	Ceftriaxone + Vancomycin	Broad coverage for community acquired infections for gram-negatives and gram-positives including MRSA
Neonate	Ampicillin + Gentamicin OR Cefepime	Broad coverage for gram-negatives and gram-positives including *Listeria*
Sickle Cell	Ceftriaxone +/- Azithromycin	Asplenia increases risk for encapsulated bacteria such as *S. pneumoniae* or *H. influenzae* (Azithromycin for possible atypical pneumonia)
Intraabdominal	Piperacillin-tazobactam	Enteric gram-negatives, gram-positives, and anaerobes often co-pathogens
Immunocompromised	Cefepime + Vancomycin	Higher risk for resistant gram-negatives (eg, *Pseudomonas*) and MRSA

Which one do I give first?

These antibiotics can be given over 30 minutes or less, so we give these first!

- Cefepime (Maxipime)
- Ceftriaxone (Rocephin)
- Ampicillin
- Meropenem
- Piperacillin-tazobactam (Zosyn)

This antibiotic runs over an hour or more, so we give this second!

- Vancomycin

If you have enough access, you can give them at the same time!

When we get blood culture results, we must narrow our antibiotic choices.

The best way to decrease time to positivity of blood cultures is to use an adequate blood sample volume!

Table 1. Clinical Characteristics and Time to Positivity

Description	No. (%)	Time to Positivity, Mean (SD), h	*P* Value
Total No.	392 (100)	15.4 (8.3)	
Sex			
Male	201 (51)	15.4 (7.7)	.90
Female	191 (49)	15.5 (8.8)	
Age at blood drawn, d			
0-30	155 (40)	13.9 (4.9)	<.001
31-60	154 (39)	15.6 (9.0)	.01
61-90	83 (21)	17.9 (10.8)	1 [Reference]
Highest temperature recorded within 1 h, C°[a]			
<38.0	107 (27)	17.0 (9.9)	.006
≥38.0	210 (54)	14.9 (7.8)	
Infant risk stratification			
Low	99 (25)	15.7 (9.1)	.56
Nonlow	293 (75)	15.3 (8.0)	
Site			
1	87 (22)	14.9 (5.4)	1 [Reference]
2	53 (14)	17.0 (8.6)	.06
3	44 (11)	19.3 (13.5)	<.001
4	36 (9)	13.7 (4.3)	.24
5	31 (8)	14.1 (8.9)	.45
6	27 (7)	14.5 (6.8)	.74
7	23 (6)	12.9 (6.4)	.13
8	17 (4)	16.6 (11.8)	.30
9	14 (4)	14.3 (3.2)	.69
10-17	60 (15)	14.9 (7.9)	NA

Abbreviation: NA, not applicable.

[a] Seventy-five (19%) had no temperature recorded within 1 hour of the blood culture.

1

How do we decide which antibiotics to use?

Suspected source of infection

- What organisms to target

Antibiogram

- Local resistance patterns

Age

- Common pathogens are different among neonates and differ by age group in children

Patient condition

- Previously healthy
- Immunocompromised, chronic illness
- Presence of invasive devices (i.e., central line, trach)

How long do we continue antibiotics?

Treatment duration of 7-10 days is adequate for most infections causing sepsis

Longer courses may be needed in certain cases

- Slow clinical response
- Cannot achieve source control of the infection
- Bacteremia caused by *S. aureus*
- Infections in patients with neutropenia

Procalcitonin levels may be used to support shortening the duration or discontinue antibiotics but not routinely done; look at trends of all labs, vital signs, and clinical picture

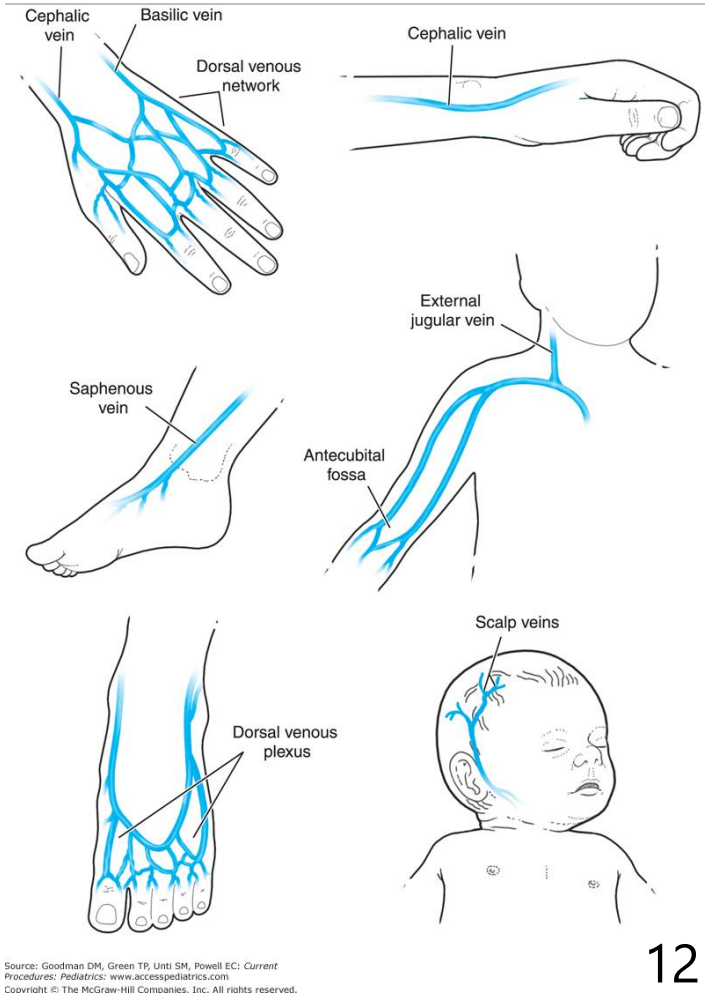
- Consider discontinuing antibiotics when PCT levels <0.5 ng/mL or drop by >80% from baseline

What else should we do?

Volume Resuscitation!

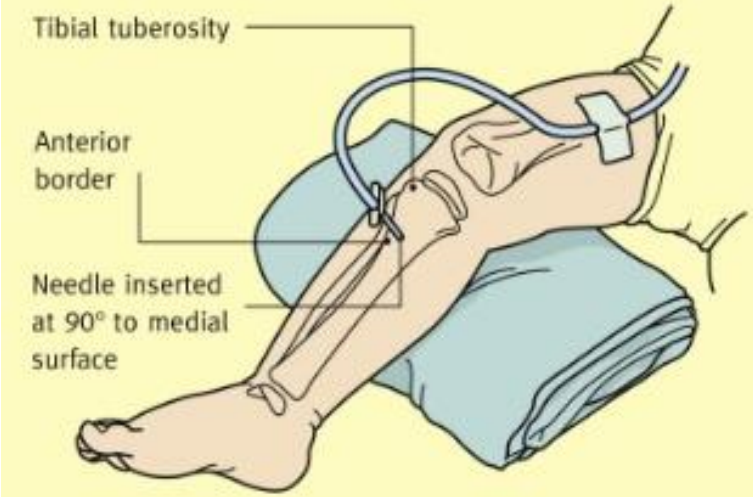
Large fluid deficits typically exist

Initial volume resuscitation usually requires 40–60 mL/kg, but can be much higher!



Source: Goodman DM, Green TP, Unti SM, Powell EC: *Current Procedures: Pediatrics*: www.accesspediatrics.com
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The site of needle insertion is 1–3 cm (children) or 0.5–1 cm (babies) below and just medial to the tibial tuberosity on the flat, medial aspect of the tibia where the bone lies subcutaneously. Support the leg on a firm surface, grasping the thigh and knee above and lateral to the site of insertion. Insert the needle at right angles to the coronal plane, directing the needle tip slightly caudally and away from the tibial growth plate. To prevent dislodgement, carefully immobilize the cannula and splint the limb

3

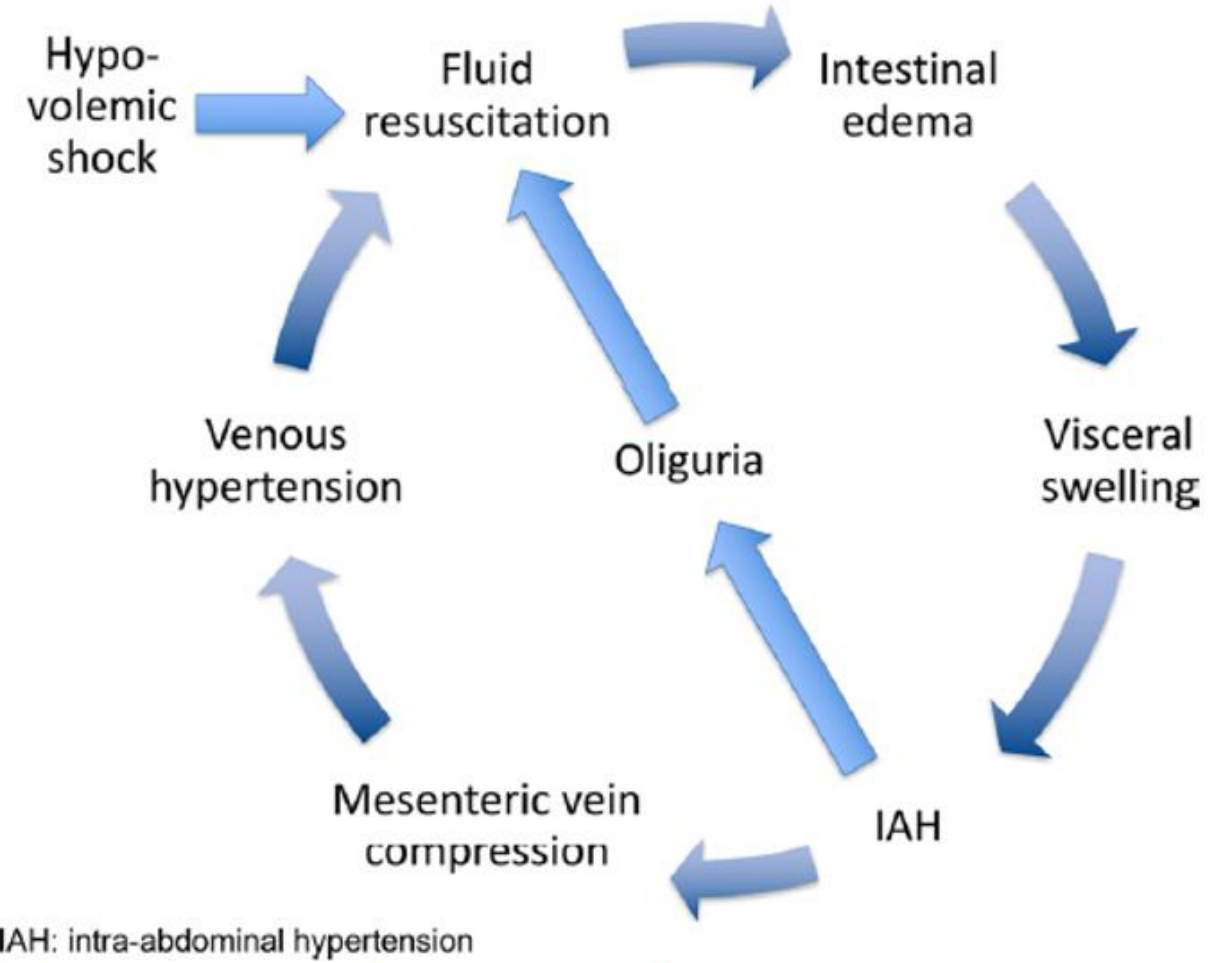


Fig. 1 The vicious cycle of septic shock resuscitation. Adapted from Peeters et al. with permission [96]. IAH: intra-abdominal hypertension

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Volume Resuscitation

Plasmalyte or LR is preferred

20 mL/kg bolus over 15 minutes

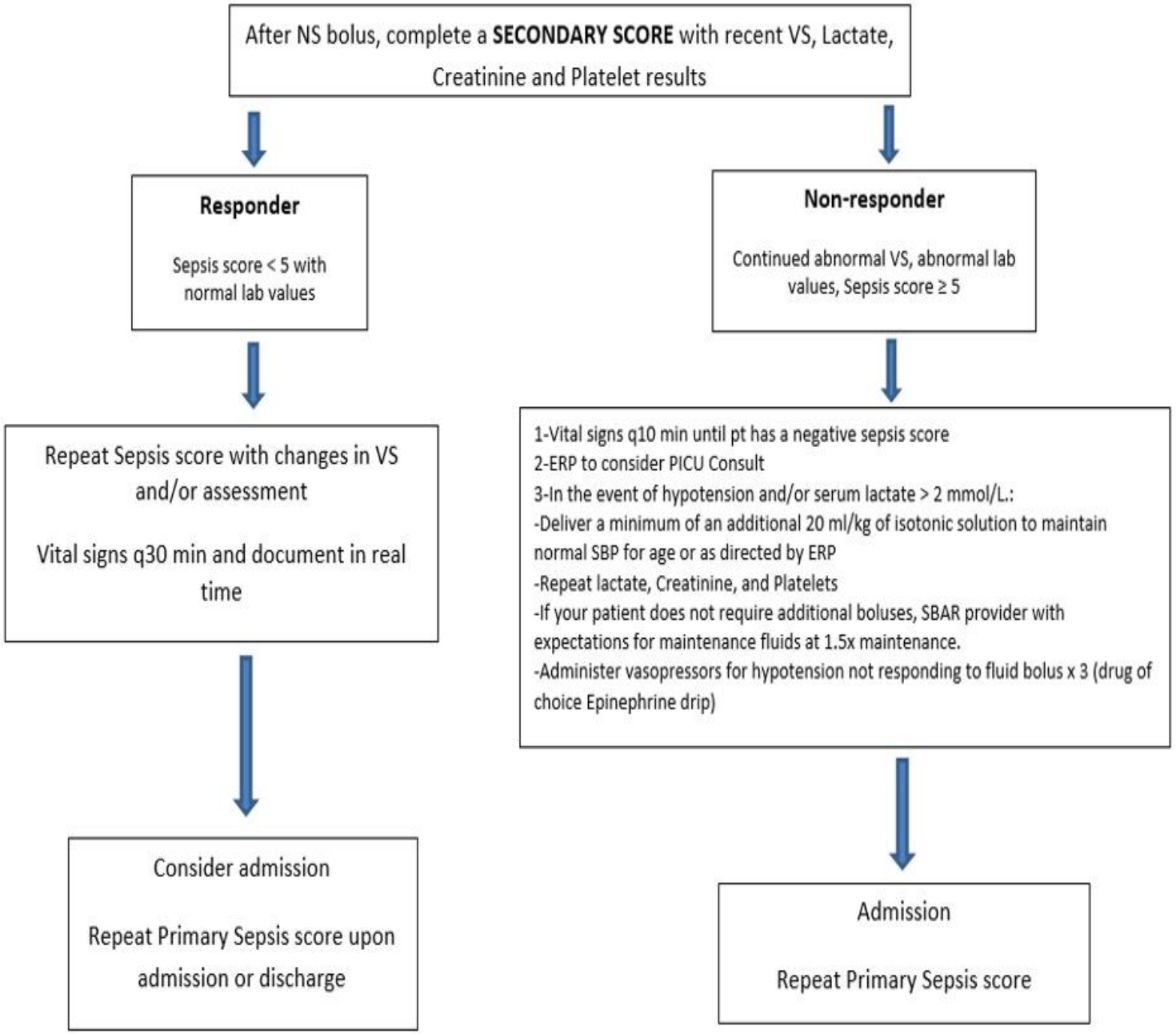
If cardiac history, 10 mL/kg over 30 minutes

Now we do it all again!

Now that we have assessed and intervened… we reassess!

Repeat a secondary assessment and look for changes!




After NS bolus, complete a **SECONDARY SCORE** with recent VS, Lactate, Creatinine and Platelet results
Responder
Sepsis score < 5 with normal lab values
Non-responder
Continued abnormal VS, abnormal lab values, Sepsis score ≥ 5
Repeat Sepsis score with changes in VS and/or assessment
Vital signs q30 min and document in real time
1-Vital signs q10 min until pt has a negative sepsis score
2-ERP to consider PICU Consult
3-In the event of hypotension and/or serum lactate > 2 mmol/L.:
-Deliver a minimum of an additional 20 ml/kg of isotonic solution to maintain normal SBP for age or as directed by ERP
-Repeat lactate, Creatinine, and Platelets
-If your patient does not require additional boluses, SBAR provider with expectations for maintenance fluids at 1.5x maintenance.
-Administer vasopressors for hypotension not responding to fluid bolus x 3 (drug of choice Epinephrine drip)
Consider admission
Repeat Primary Sepsis score upon admission or discharge
Admission
Repeat Primary Sepsis score

Treatment goals

Maintain effective hemodynamics!

Which looks like..

- Normalized heart rate
- Normalized capillary refill, pulses, and temperature
- Urine output of 1 mL/kg/hr.
- Appropriate mental status for patient's baseline
- Decreased lactate levels and improved base deficit

- If able to calculate: CVP of 8-12 and CPP normal

On the horizon….

- Individualized, tailor-made medicine coming from EMR data available such as genetic determinations (proteomic, transcriptomic, or metabolomics) to aid in customized treatment to each patient's unique physiology
- Studies in progress looking at specific genomic markers that can identify which patients will benefit from corticosteroid therapies
- AI used to pull data from EHRs and detect signs of sepsis up to 6 hours earlier than traditional methods (Machine learning-based clinical decision support tools)

Key Points

- Complex baselines shift the threshold
  - Same vital signs in a healthy child may mean something different in a complex medical patient; look at the entire picture
- Re-examine, do not reassure- the "well-appearing" child who comes back is the one we miss
  - A 24-48 hour return with worsening symptoms should be considered a "new encounter", not a follow-up; approach it with open eyes and new perspective. Re-score with Phoenix scoring tool
- Antibiotic coverage MUST cover the pathogens the patient is most likely to get
  - Patients that are medically complex and immunocompromised, empiric coverage must include Pseudomonas and other GNR's (not only Staph & Strep)
- First hour: balanced crystalloid, empiric antibiotics, early pressors
  - 10-20 mL/kg boluses up to 40-60 mL/kg, reassess after every bolus, peripheral epi/norepi is acceptable short-term
- Steroids: not routine



we are just a phone call away… 1-800-KID-HURT

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