

Thinking beyond sepsis

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Rani Hospital, Ranchi, Jharkhand
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Clinical signs of bacterial sepsis

Clinical Sign	Percent of Infants with Sign
Hyperthermia	51
Hypothermia	15
Respiratory distress	33
Apnea	
Cyanosis	
Jaundice	
Hepatomegaly	
Lethargy	25
Irritability	16
Anorexia	28
Vomiting	25
Abdominal distention	17
Diarrhea	11

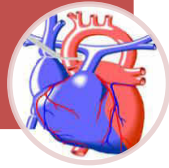
Non-specific

Data from Nyhan WL, Fousek MD: Septicemia of the newborn, *Pediatrics* 22:268, 1958; Gluck L, Wood HF, Fousek MD: Septicemia of the newborn, *Pediatr Clin North Am* 13:1131, 1966; Moorman RS, Sell SH: Neonatal septicemia, *South Med J* 54:137, 1962; and Buetow KC, Klein SW, Lane RB: Septicemia in premature infants, *Am J Dis Child* 110:29, 1965.

Differential diagnosis

- Structural
- PDA
- PPHN

Cardiac



- Pul hypoplasia
- Pul. Hge
- BPD

Respirator
y



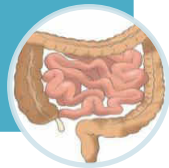
- HIE
- IVH
- ICH
- Seizure

Neurologic



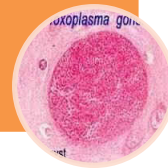
- NEC
- Malrotation
- Obstruction

GIT



- Torch
- Viral

Infections



- Hypoglycemia
- IEM

Metabolic



Need for rapid and reliable tool to diagnose/ exclude sepsis

Need to safely distinguish infected from uninfected newborns, especially in the early phase of the disease.

Infected neonate:

- Need early start of the antibiotic treatment
- Each hour delay matters

Uninfected neonate:

- to avoid the unnecessary use of antibiotics in sepsis-negative infants.

Problem with Broad Spectrum Antibiotics

Previous broad-spectrum antibiotic (third-generation cephalosporin or carbapenem) use was associated with an increased risk of invasive candidiasis (OR 2.2, 95% CI 1.4–3.3). (n=3702, ELBW)

- Cotten CM et al, Pediatrics 2006;118(2):717–22.

Increased risk of death when infants were treated with ampicillin plus cefotaxime versus ampicillin plus gentamicin in the first 3 postnatal days (OR 1.5, 95% CI 1.4–1.7) [n=1,28,914]

- Clark RH et al, Pediatrics 2006;117(1):67–74

Problem with prolonged use of antibiotics

Prolonged antibiotic therapy was associated with increased LOS, NEC (OR 1.12, 6.30). (n=200)

- Kuppala

Unnecessary use of broad spectrum antibiotics and prolonged use of antibiotics should be minimized.

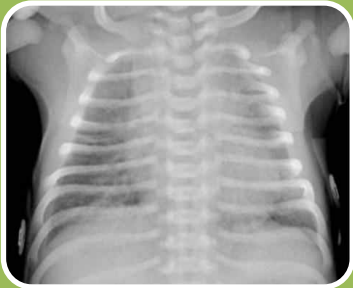
antibiotic therapy was associated with an increase in the odds of NEC or other GI complications (retrospective cohort study, n=5693 ELBW)

- Coates et al, Pediatrics 2009;123(1):58–66.

When should we think beyond sepsis



Clinical signs/symptoms suggestive of other diagnosis



Symptomatic neonate with no risk factors for sepsis



Investigations not suggestive of sepsis

Risk factors for early neonatal sepsis

Mother

- maternal fever, UTI
- other systemic infections

Baby

- Prematurity
- Birth asphyxia

Labour

- spontaneous preterm onset of labor

Membrane

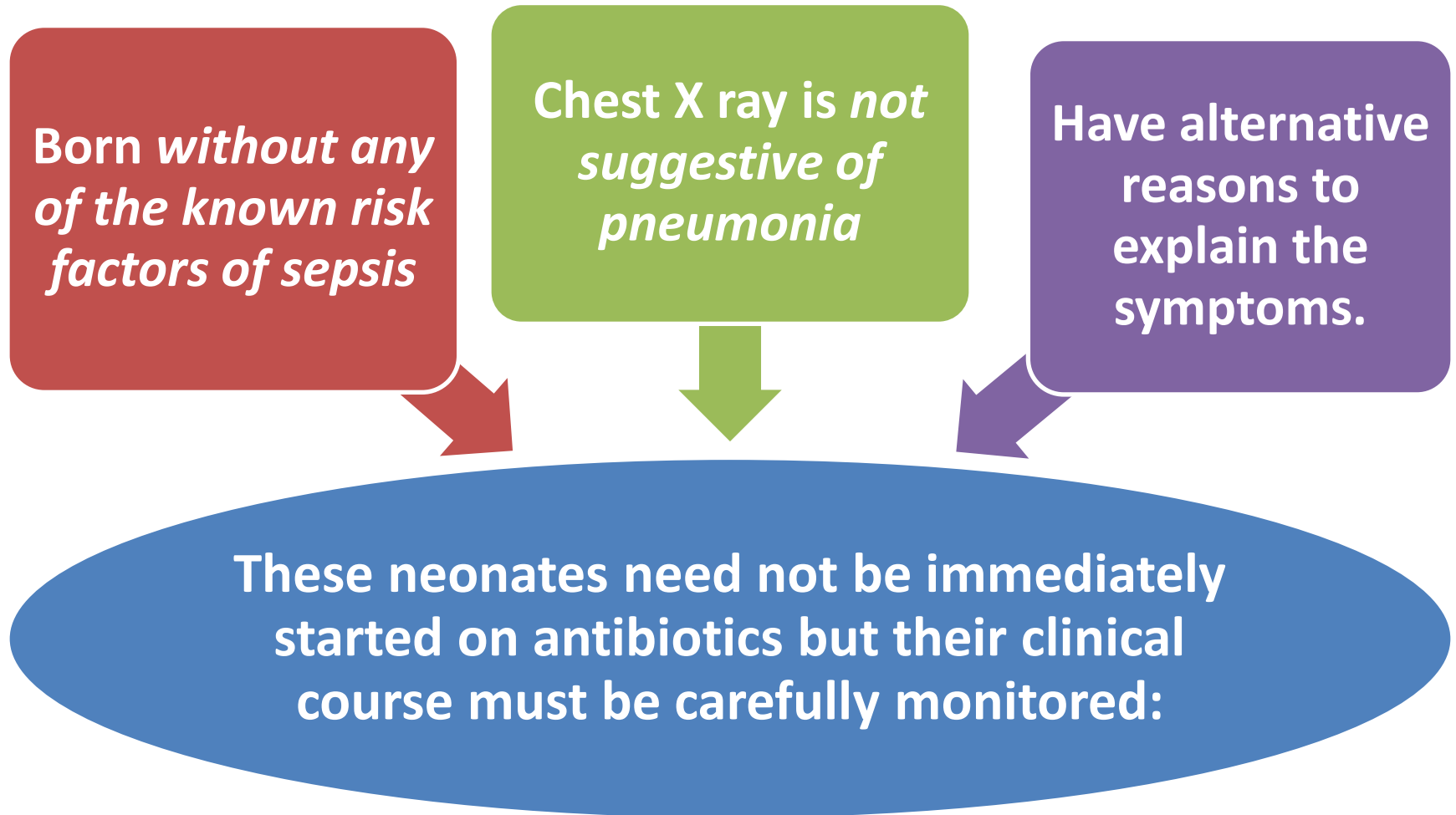
- Premature Rupture of membrane
- Prolonged rupture of membrane (>18 hrs),

Infection related

- clinical chorioamnionitis, FSL
- unclean vaginal exam, >3 PV exam in labor

Symptomatic neonate at birth:

No antibiotics



When do we think beyond sepsis (LOS)

Symptomatic Neonate

Clinically low probability of sepsis
Do Septic screen

Clinically high probability of sepsis

if positive
send blood culture
and start on
antibiotics

If negative
repeat septic
screen after 24 hrs

Send blood
culture, do septic
screen and start
on antibiotics

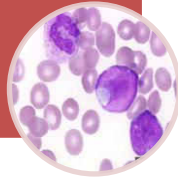
If again negative
Think beyond sepsis

Diagnostic Markers in neonatal sepsis

- Neutrophil indices:

I/T ratio, ANC,
mESR

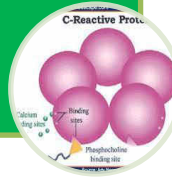
early 80's:



- Acute phase proteins:

CRP,
Procalcitonin

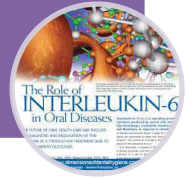
mid 80's -
early 90's :



- Cytokines

(IL-6)

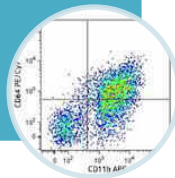
1990's :



- Cell surface antigens

(CD64)

2000's :



- Molecular diagnosis:
PCR,
Genomics,
Proteomics

2010s

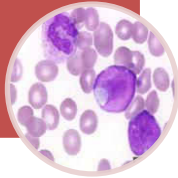


Diagnostic Markers in neonatal sepsis

- Neutrophil indices:

I/T ratio, ANC,
mESR

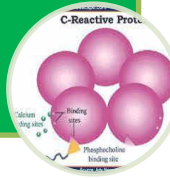
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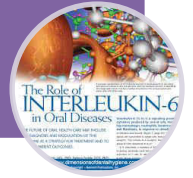
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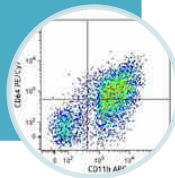
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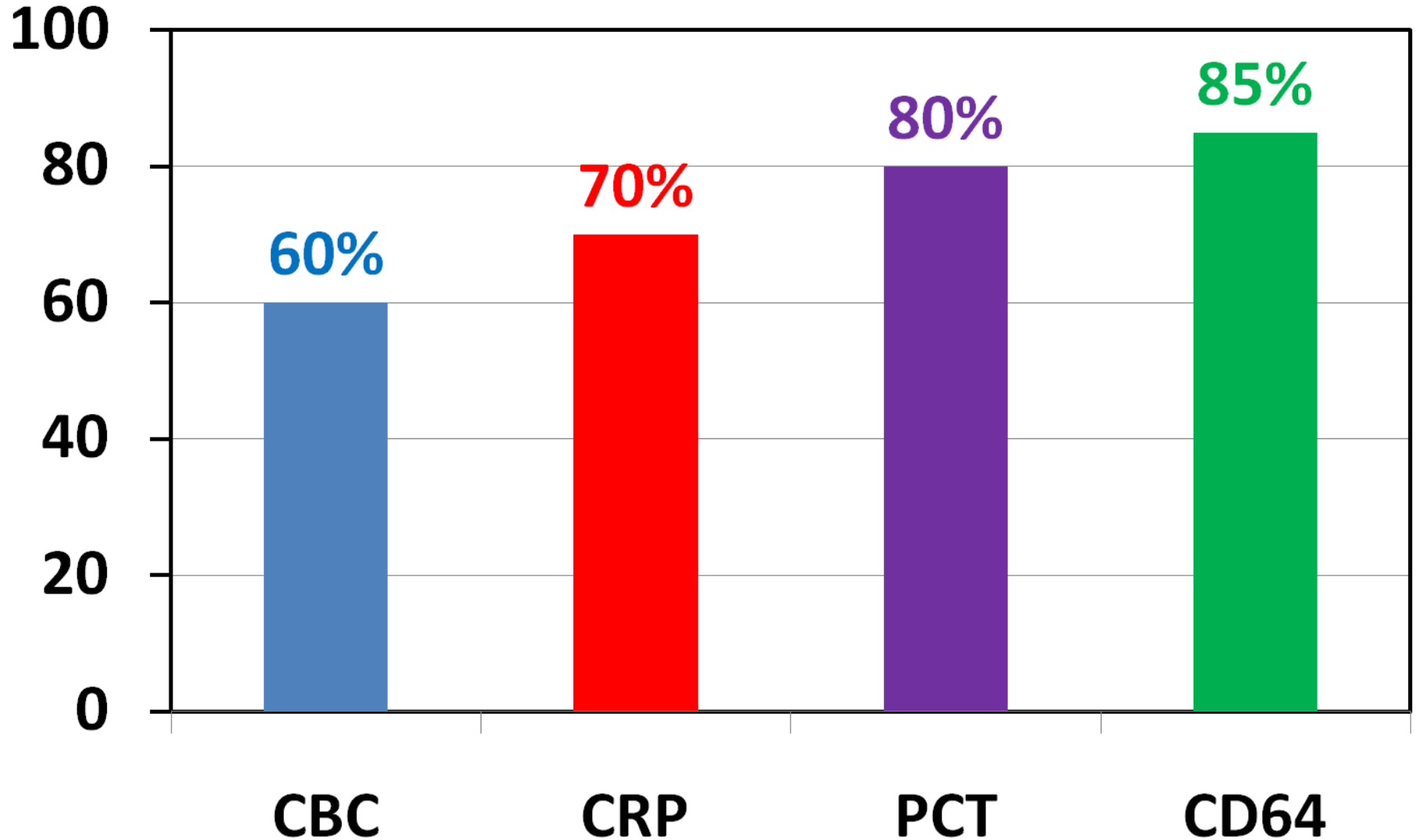


- Molecular diagnosis:
PCR,
Genomics,
Proteomics

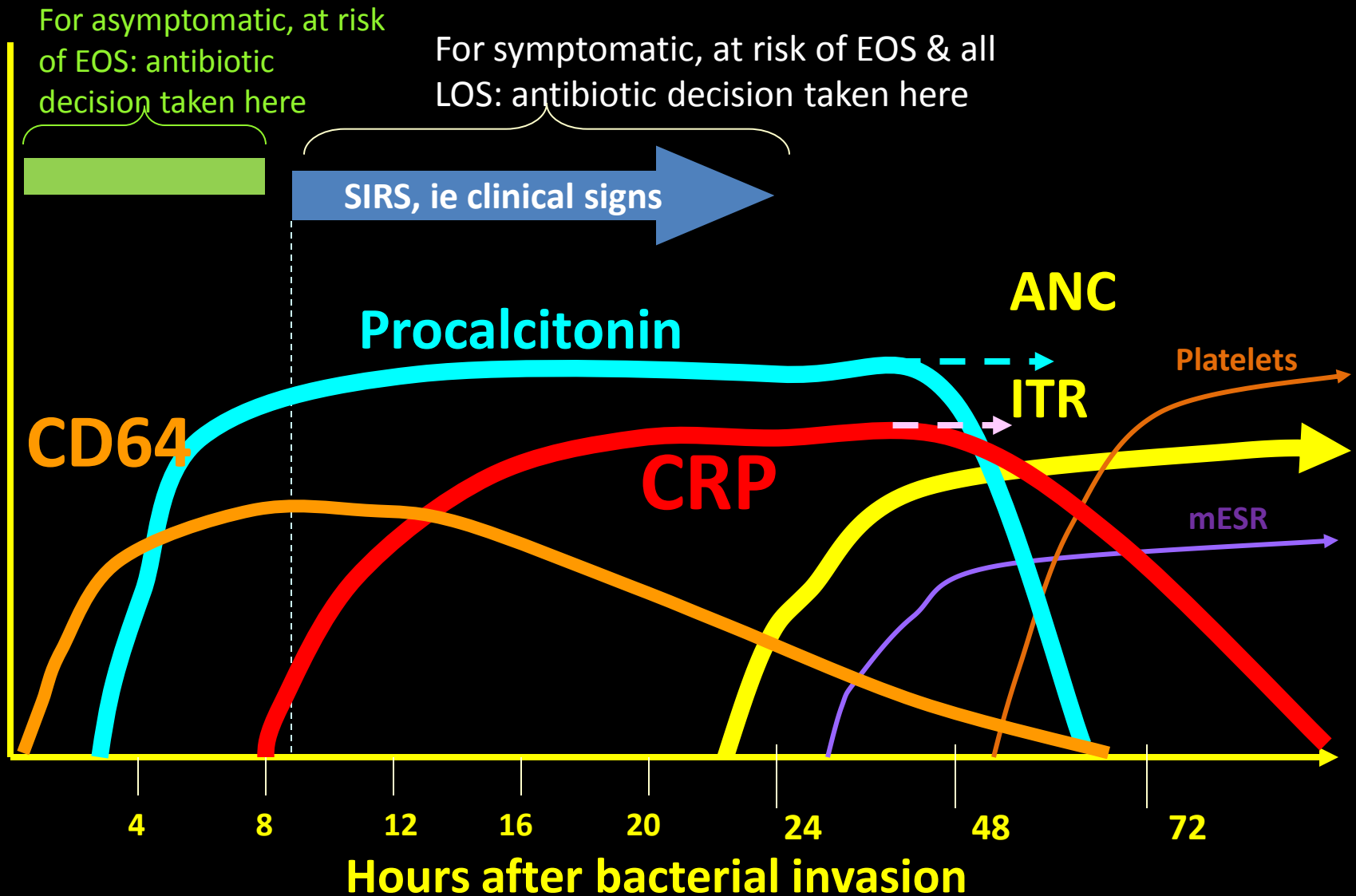
2010s



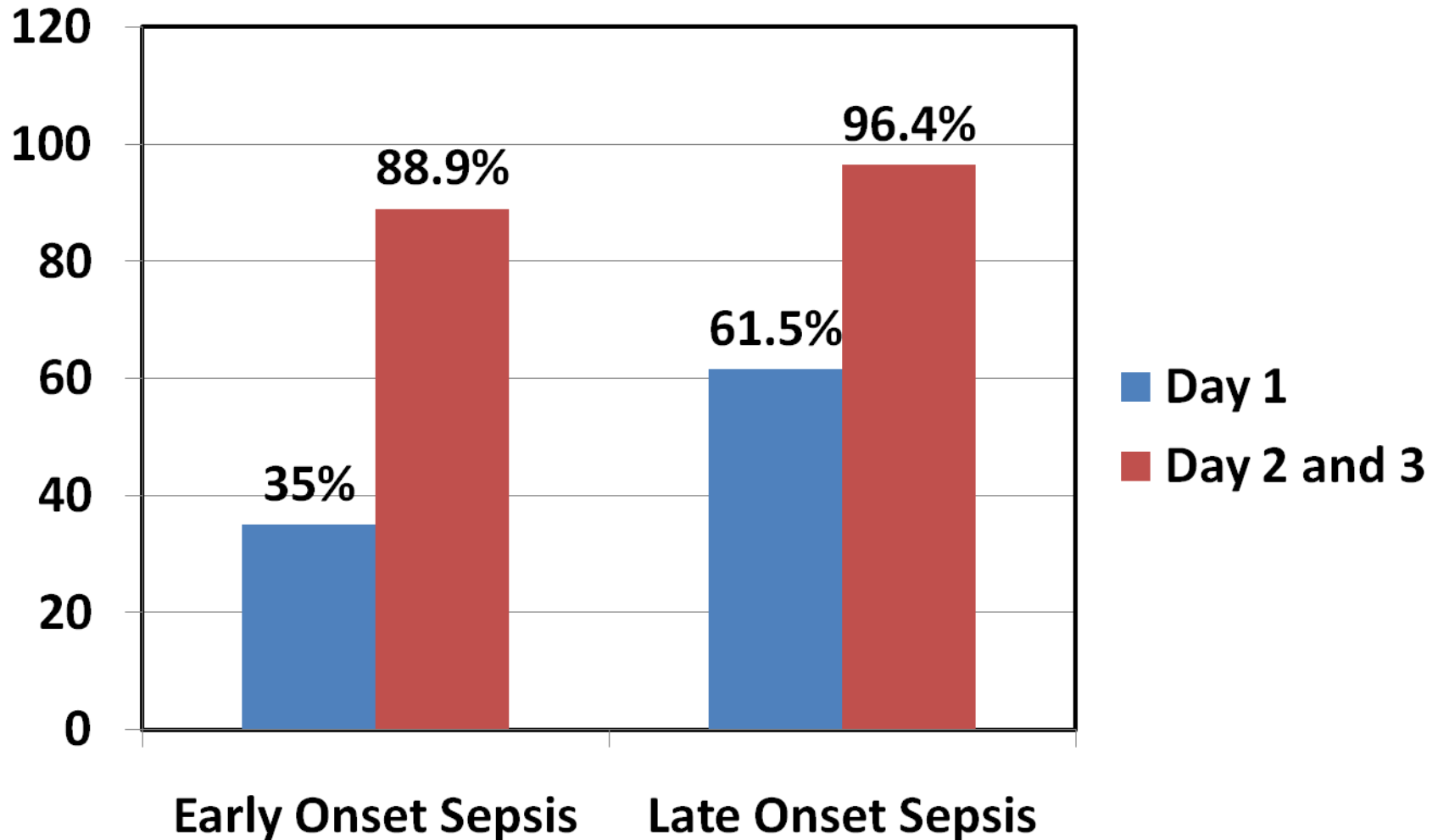
Sensitivity of sepsis markers



Time line for sepsis markers



Sensitivity of repeat CRP as sepsis marker

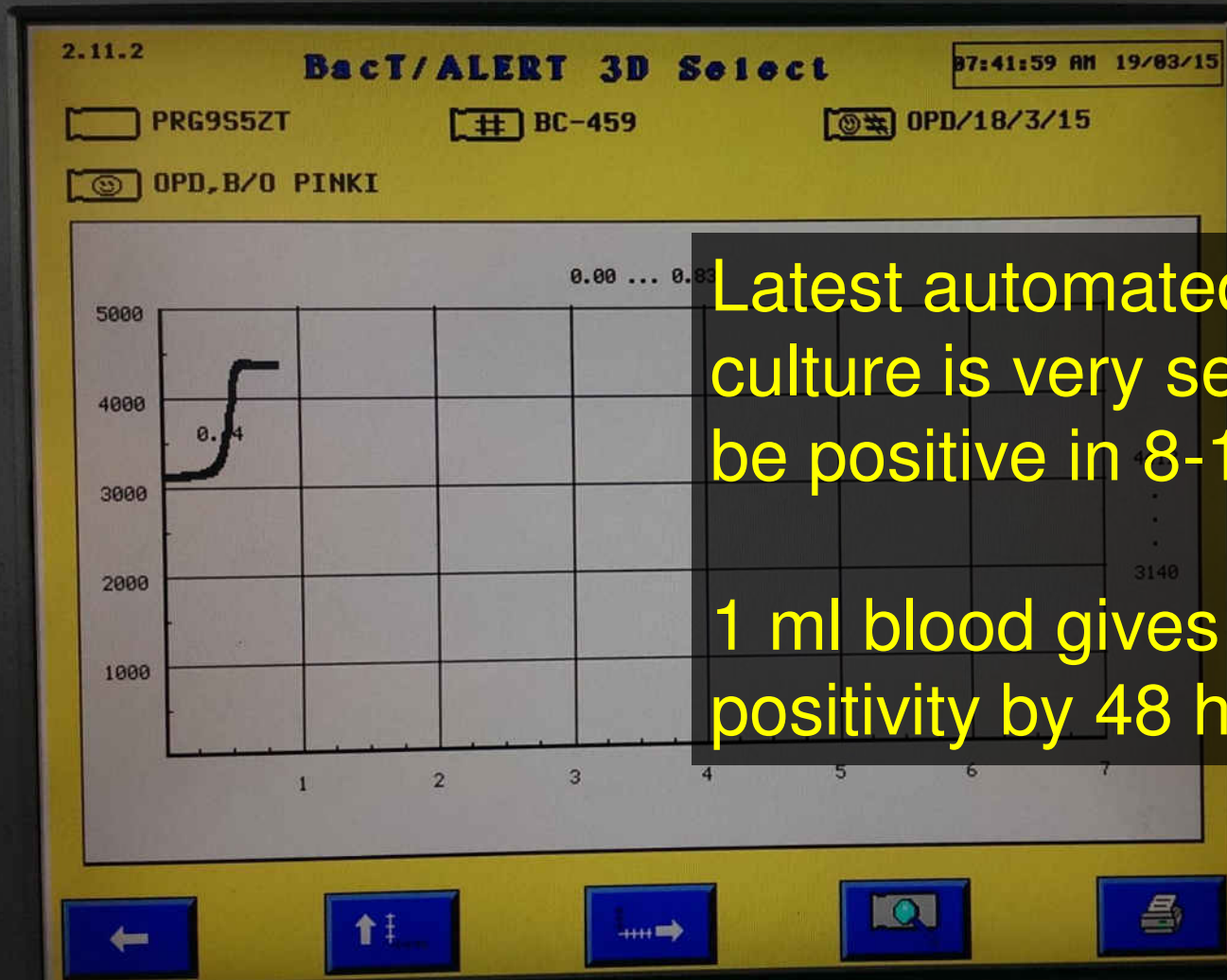


Serial Serum C-Reactive Protein Levels in the Diagnosis of Neonatal Infection

William E. Benitz, Michael Y. Han, Ashima Madan and Pramela Ramachandra

Pediatrics 1998;102:e41

Blood Culture

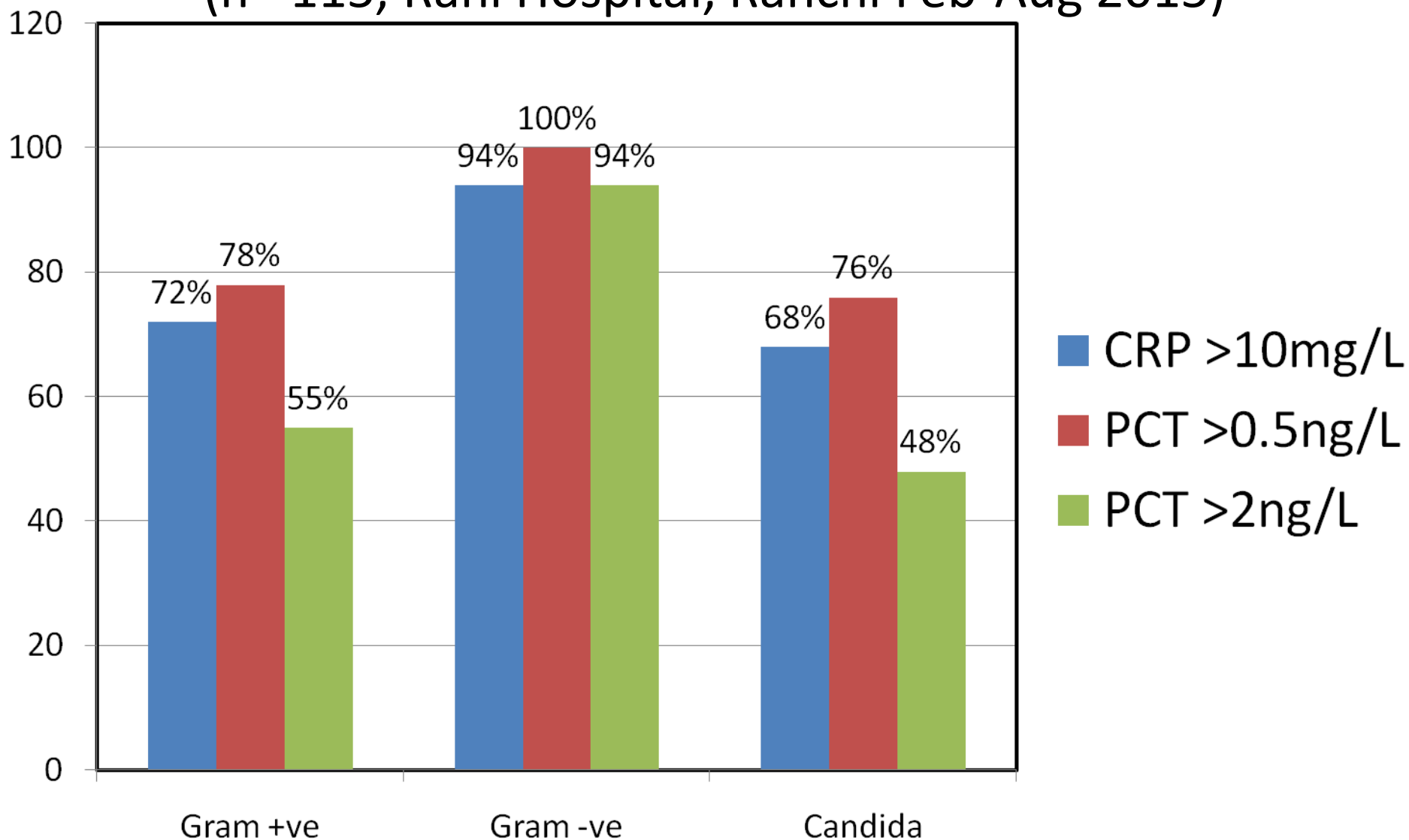


Latest automated blood culture is very sensitive, can be positive in 8-12 hrs also.

1 ml blood gives up-to 90% positivity by 48 hrs.

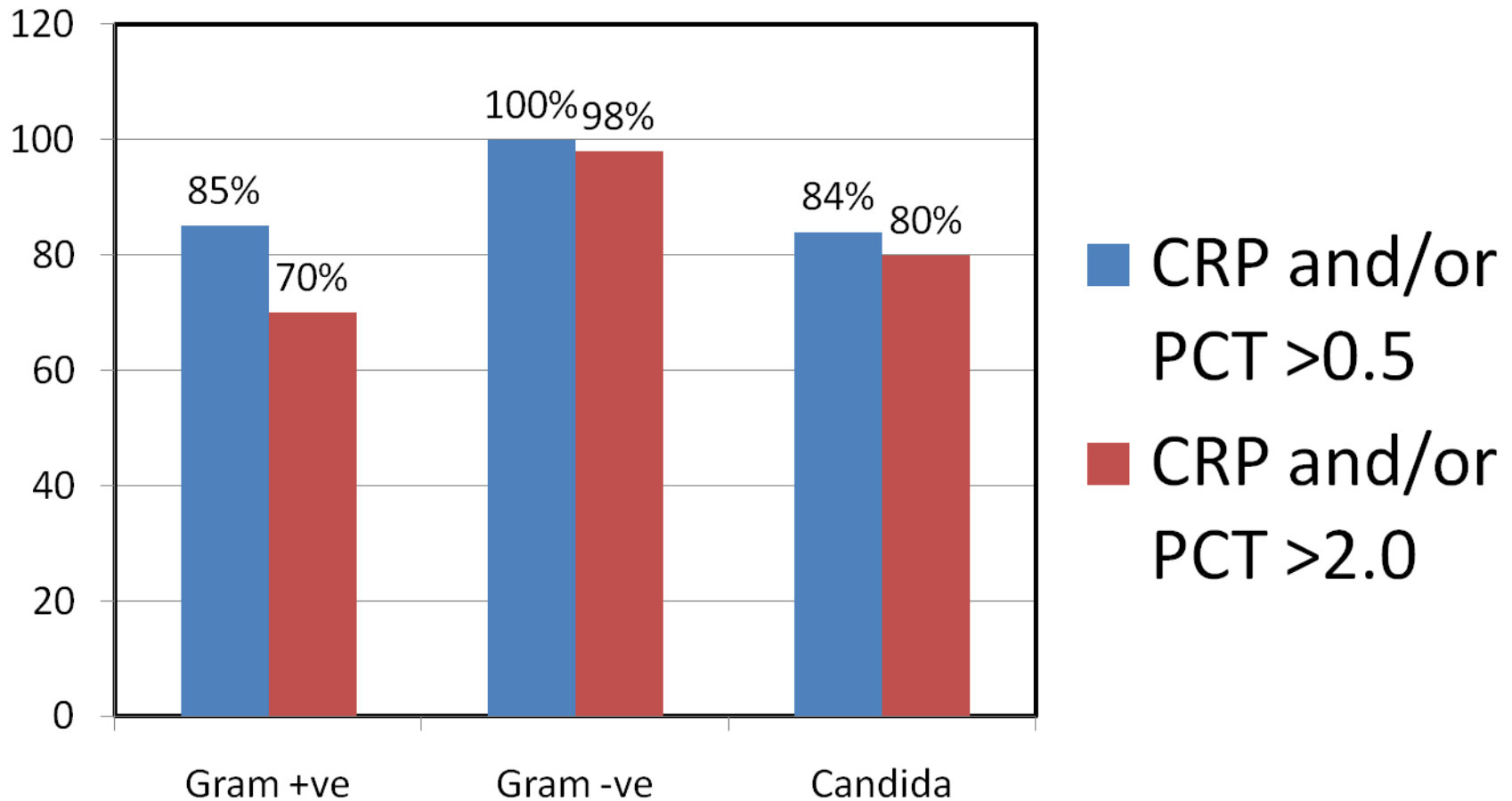
Sensitivity of CRP and PCT in different types of sepsis

Referred cases on antibiotics after 72 hrs of life
(n= 115, Rani Hospital, Ranchi Feb-Aug 2015)



Sensitivity of CRP and PCT in different types of sepsis

Referred cases on antibiotics after 72 hrs of life
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What we do (Baby in emergency dept.)

Clinical diagnosis
of sepsis.

Send sepsis
profile

(CBC, CRP, PCT,
Blood Culture, ABG
with lactate and urea)

lab is
supportive
of sepsis

continue
treatment

lab is not
supportive
of sepsis

Do bedside
screening
USG-ECHO
and X-ray

Cardio-
respiratory

Neurological

Surgical

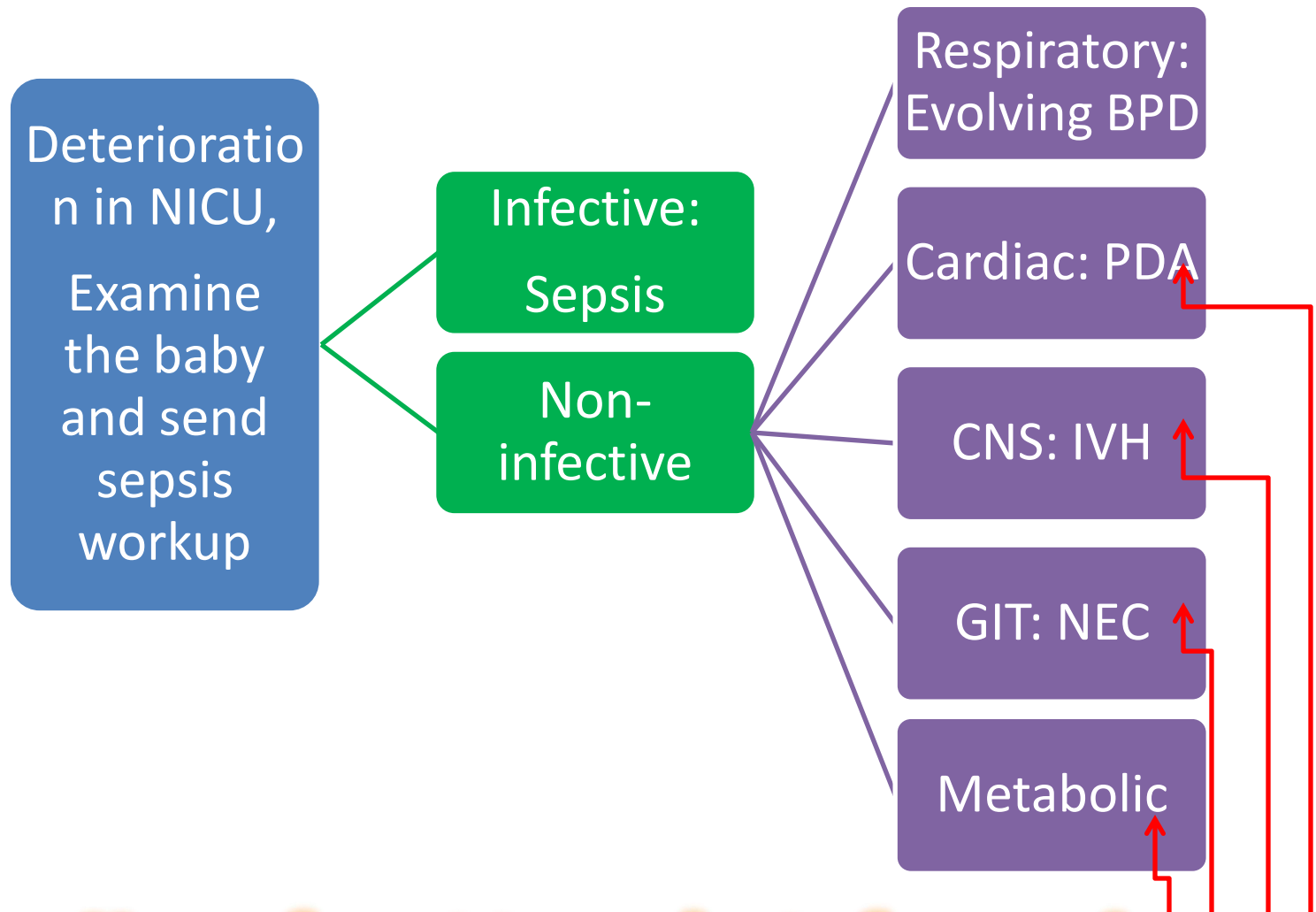
Others:
metabolic

Admission

1 hr

2hrs

Deterioration in premature baby



Never forget to evaluate for sepsis if there is no simple explanation

Symptomatic neonate with no definite pointers for diagnosis

No risk factors for sepsis

Sepsis screen is negative

Think beyond sepsis when

Repeat sepsis screen after 24 hrs is negative

Blood culture is sterile



Thank you

07/01/2015