**Supplemental Digital Content 1.**

**Algorithm for Late-onset Sepsis Workup**

**Risk factors:**

Invasive device, central line, TPN, surgery, invasive mechanical ventilation

**Clinical signs and symptoms:**

1. Temperature instability (fever or hypothermia)
2. Feeding intolerance
3. Abdominal distension
4. New or increased apnea or respiratory distress
5. Increased requirement on respiratory support
6. Lethargy or hypotonia
7. Poor perfusion (mottled skin, prolonged peripheral refill time, reduced urine output)
8. Tachycardia
9. Hypotension
10. Glucose instability (hyperglycemia or hypoglycemia)

**Laboratory tests:**

Whole blood cell count, CRPa, PCT, blood gas, glucose, blood cultureb, urine culture, lumbar puncturec, chest and abdominal X-ray

 **Begin antibiotic therapy**d

**Positive blood culture**

**Negative blood culture**

**Culture-positive sepsis:**

1. Lumbar puncture
2. Adjustment of antibiotics according to culture and sensitivity results

Normal laboratory tests and clinically stable

**Stop antibiotics**

Two or more abnormal laboratory testse and two or more clinical signs or symptoms which could not be explained by non-infectious etiology

**Culture-negative sepsis:**

1. Lumbar puncture
2. Continue antibiotics

This algorithm is recommended for preterm infants with suspicion of late-onset sepsis in the neonatal intensive care unit.

aThere is a delay in the rise of CRP after onset of infection. The sensitivity of CRP increased after 24 hours of infection onset. Repeat CRP 24 hours after the first test.

bBlood and urine culture: Obtain blood and urine samples as soon as possible when infection is suspected. Do culture before antibiotic is given, but do not delay the first dose of antibiotics because of sampling.

cLumber puncture should be considered for all infants with suspicion of late-onset sepsis. Infants with culture-positive or culture-negative late-onset sepsis should have a lumbar puncture done.

dThe first antibiotic should be given within the first hour after diagnosis.

eLaboratory criteria:

* 1. WBC <5＊106/L or >20＊106/L
	2. Platelet count ≤100＊106/L
	3. CRP ≥8mg/L
	4. PCT >0.5ng/ml

Abbreviations: CRP, C-reactive protein; PCT, procalcitonin; TPN, total parenteral nutrition; WBC, white blood cells.