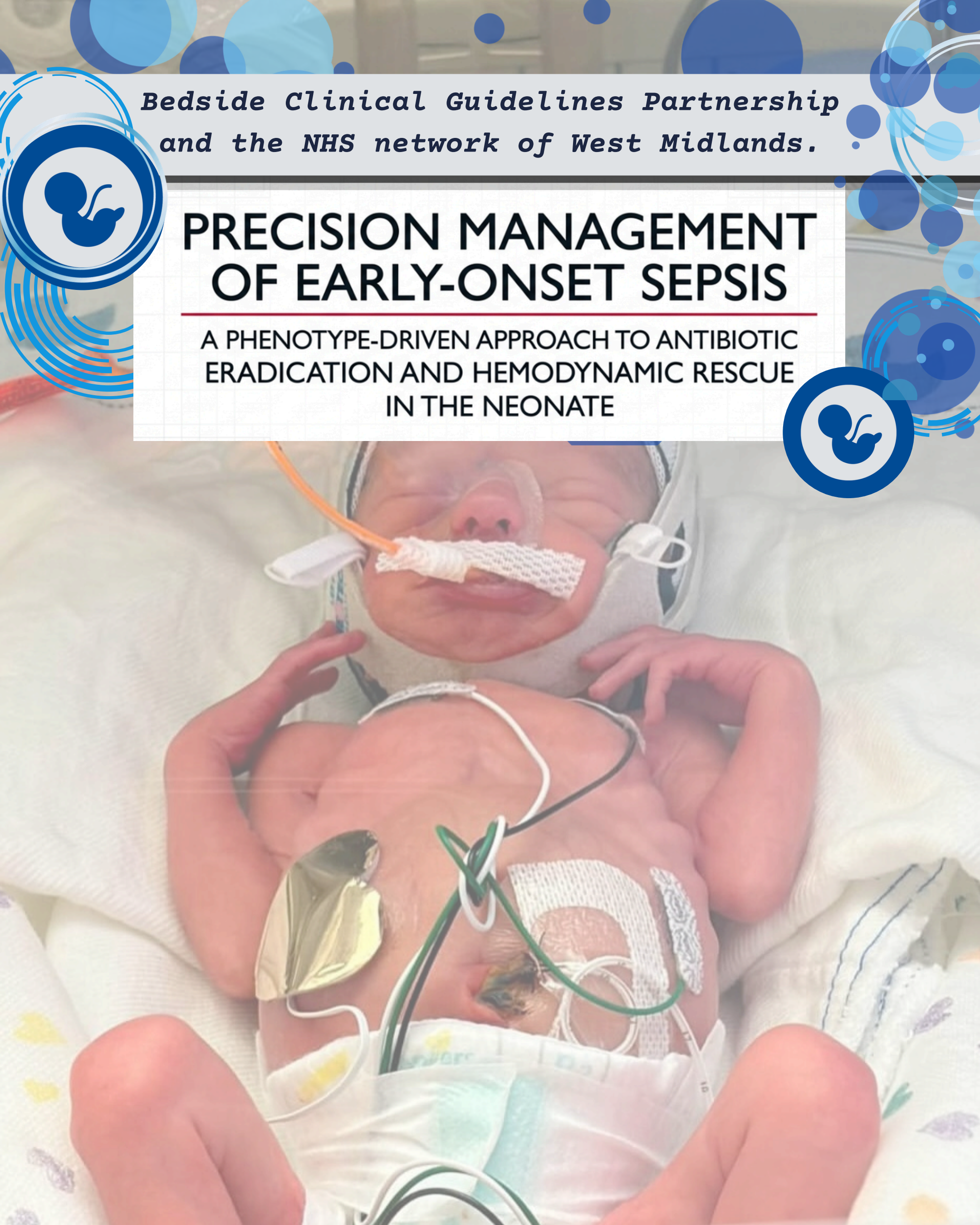


*Bedside Clinical Guidelines Partnership  
and the NHS network of West Midlands.*

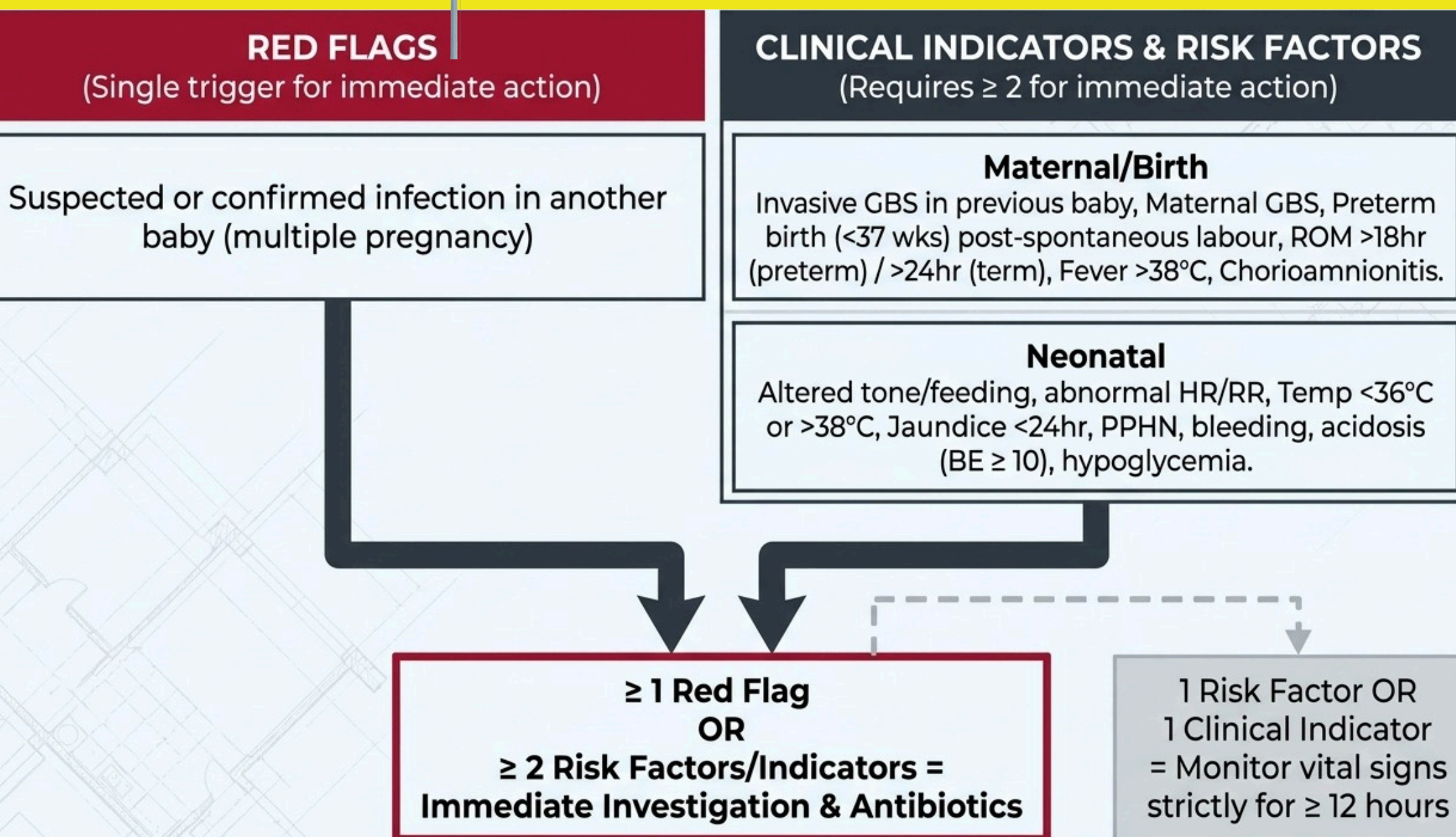
# PRECISION MANAGEMENT OF EARLY-ONSET SEPSIS

A PHENOTYPE-DRIVEN APPROACH TO ANTIBIOTIC  
ERADICATION AND HEMODYNAMIC RESCUE  
IN THE NEONATE





# A UNIFIED PROTOCOL TRANSITIONING FROM RAPID RISK STRATIFICATION TO TARGETED PHYSIOLOGICAL RESCUE.





Identify Candidate: Well baby meeting NICE criteria for possible infection.

### **INCLUSIONS**

Must be  $\geq 34$  weeks' gestation AND  $\leq 12$  hours old AND clinically well

**ELIGIBLE** -> Apply KP-SRC  
(Incidence baseline: 2/1000).

Observe for  
 $\geq 36$  hours

Blood Culture +  
Empirical Antibiotics

### **EXCLUSIONS**

Clinically unwell, GBS sepsis in previous pregnancy without adequate prophylaxis, or co-twin requires antibiotics

**MEETS EXCLUSIONS** -> Bypass KP-SRC  
-> Immediate antibiotics within 1 hour.



# GOLDEN HOUR TIMELINE



T=0-15 Min

## DIAGNOSTIC SAMPLING

Blood culture via peripheral vein (closed system, non-touch). Avoid cannula hubs to prevent CoNS contamination. Baseline CRP.

T=15-30 Min

## LUMBAR PUNCTURE ASSESSMENT

Perform ONLY if strong clinical suspicion of meningitis AND hemodynamically stable. If LP delays antibiotics, administer ABX first.

T=30-60 Min

## ANTIBIOTIC ADMINISTRATION

**! HARD STOP:** Empirical IV antibiotics must be infusing before the 60-minute mark.

Current WHO guidelines supporting the use of **gentamicin and penicillin for hospital-based** patients OR **gentamicin (IM) and amoxicillin (oral)** when referral to a hospital is not possible are in accordance with currently available evidence and other international guidelines, and there is no strong evidence to change this.

Source:

<https://pmc.ncbi.nlm.nih.gov/articles/PMC6176768/>



# FIRST-LINE EMPIRICAL THERAPY

Drug 1: Benzylpenicillin 25 mg/kg IV



Drug 1: Benzylpenicillin 25 mg/kg IV

(12-hrly; escalate to 8-hrly if clinically severe)

Drug 2: Gentamicin 5 mg/kg IV



(Next dose at 36 hours, pending levels)

## TARGETED ESCALATIONS

Gram-Negative Suspicion



Add Cefotaxime. (Stop Benzylpenicillin if confirmed).

Meningitis Suspicion (Gram Stain Uninformative)



Amoxicillin + Cefotaxime.

**CLINICAL CHECKPOINT:** Review at 36 Hours. **Stop antibiotics if blood culture is negative, baby is well**, and paired CRP levels ( $<15$  mg/L) are reassuring.

The image displays three smartphone screens showing the neofast app interface for Gentamicin dosing. The first screen shows the initial input fields: Gentamicin, Intermittent IV, 10mg/mL Solution, 20mg/mL Solution, 40mg/mL Solution, Weight (kg), Gestational age at birth - WEEKS, Gestational age at birth - DAYS, Postnatal age - DAYS, and Desired dose (mg/kg/dose). The second screen shows the calculated dose and suggested dose: Weight (kg) 2, Gestational age at birth - WEEKS 30, Gestational age at birth - DAYS 6, Postnatal age - DAYS 10, Desired dose (mg/kg/dose) 4, and Suggested dose: 4 mg/kg/dose. The third screen shows the final dilution and infusion rate: Gentamicin Intermittent IV - 10mg/mL Solution, Postmenstrual age 32 weeks and 2 day(s), Dose 8mg, Interval 24/24h, Dose 0.8mL, Dilution (Dilute the dose in mL with NS, D5W or D10W), Final concentration after dilution 8mg/mL, Total volume to be administered 1mL, and Infusion rate 30min. Red arrows indicate the flow from the input fields to the calculated dose and then to the final dilution and infusion rate.

| neofast                          |                  |
|----------------------------------|------------------|
| Medicines                        |                  |
| Gentamicin                       |                  |
| Intermittent IV                  |                  |
| 10mg/mL Solution                 | 20mg/mL Solution |
| 40mg/mL Solution                 |                  |
| Weight (kg)                      |                  |
| Gestational age at birth - WEEKS |                  |
| Gestational age at birth - DAYS  |                  |
| Postnatal age - DAYS             |                  |
| Desired dose (mg/kg/dose)        |                  |

| neofast                                       |                  |
|-----------------------------------------------|------------------|
| Medicines                                     |                  |
| Gentamicin                                    |                  |
| Intermittent IV                               |                  |
| 10mg/mL Solution                              | 20mg/mL Solution |
| 40mg/mL Solution                              |                  |
| Weight (kg)                                   | 2                |
| Gestational age at birth - WEEKS              | 30               |
| Gestational age at birth - DAYS               | 6                |
| Postnatal age - DAYS                          | 10               |
| Desired dose (mg/kg/dose)                     | 4                |
| Suggested dose: 4 mg/kg/dose                  |                  |
| Gentamicin Intermittent IV - 10mg/mL Solution |                  |

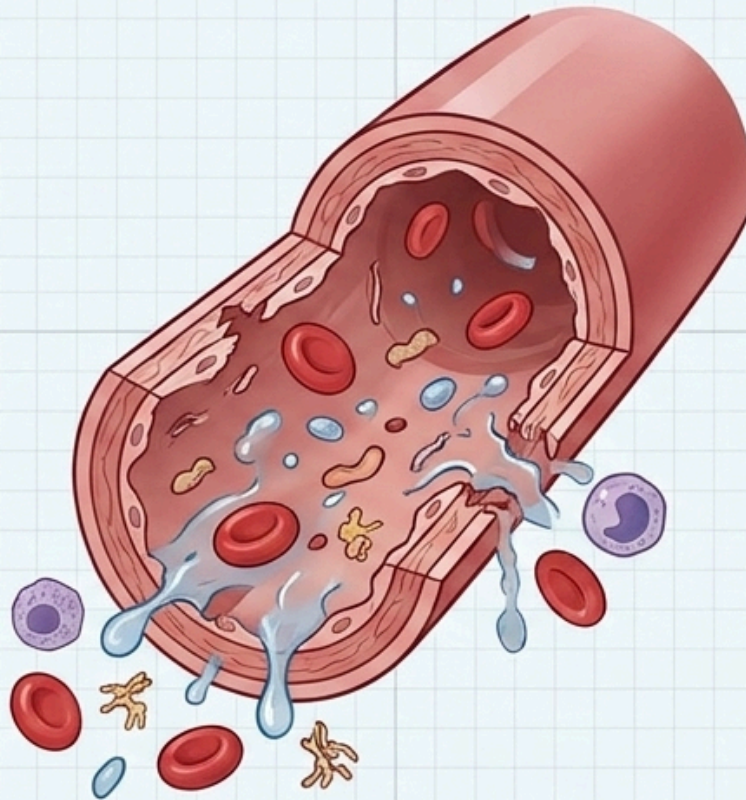
| neofast                                       |                       |
|-----------------------------------------------|-----------------------|
| Medicines                                     |                       |
| Gentamicin Intermittent IV - 10mg/mL Solution |                       |
| Postmenstrual age                             | 32 weeks and 2 day(s) |
| Dose                                          | 8mg                   |
| Interval                                      | 24/24h                |
| Dose                                          | 0.8mL                 |
| Dilution                                      |                       |
| Dilute the dose in mL with NS, D5W or D10W    | 0.2mL                 |
| Final concentration after dilution            | 8mg/mL                |
| Total volume to be administered               | 1mL                   |
| Infusion rate                                 | 30min                 |



**SIRS** → **Endothelial Injury** → **Vasoplegia & Myocardial Depression**

### DIAGNOSTIC REDEFINITION

Do not use Mean Blood Pressure (MAP) as the sole indicator of compromise.



### TARGET METRICS

Use Gestational Age (GA) based systolic and diastolic blood pressure centiles (Target: >3rd centile for GA).

Identify **tissue hypoperfusion**: Raised lactate, metabolic acidosis, oliguria, tachycardia, and altered capillary refill time (CRT).

### WARM SHOCK (Low SVR State)

**Pathophysiology:** Severe vasoplegia / low systemic vascular resistance.

**Extremities & CRT:** Warm extremities, normal or 'flash' capillary refill.

**Pulses & BP:** Bounding pulses, hypotension with a wide pulse pressure.

### COLD SHOCK (Myocardial Dysfunction)

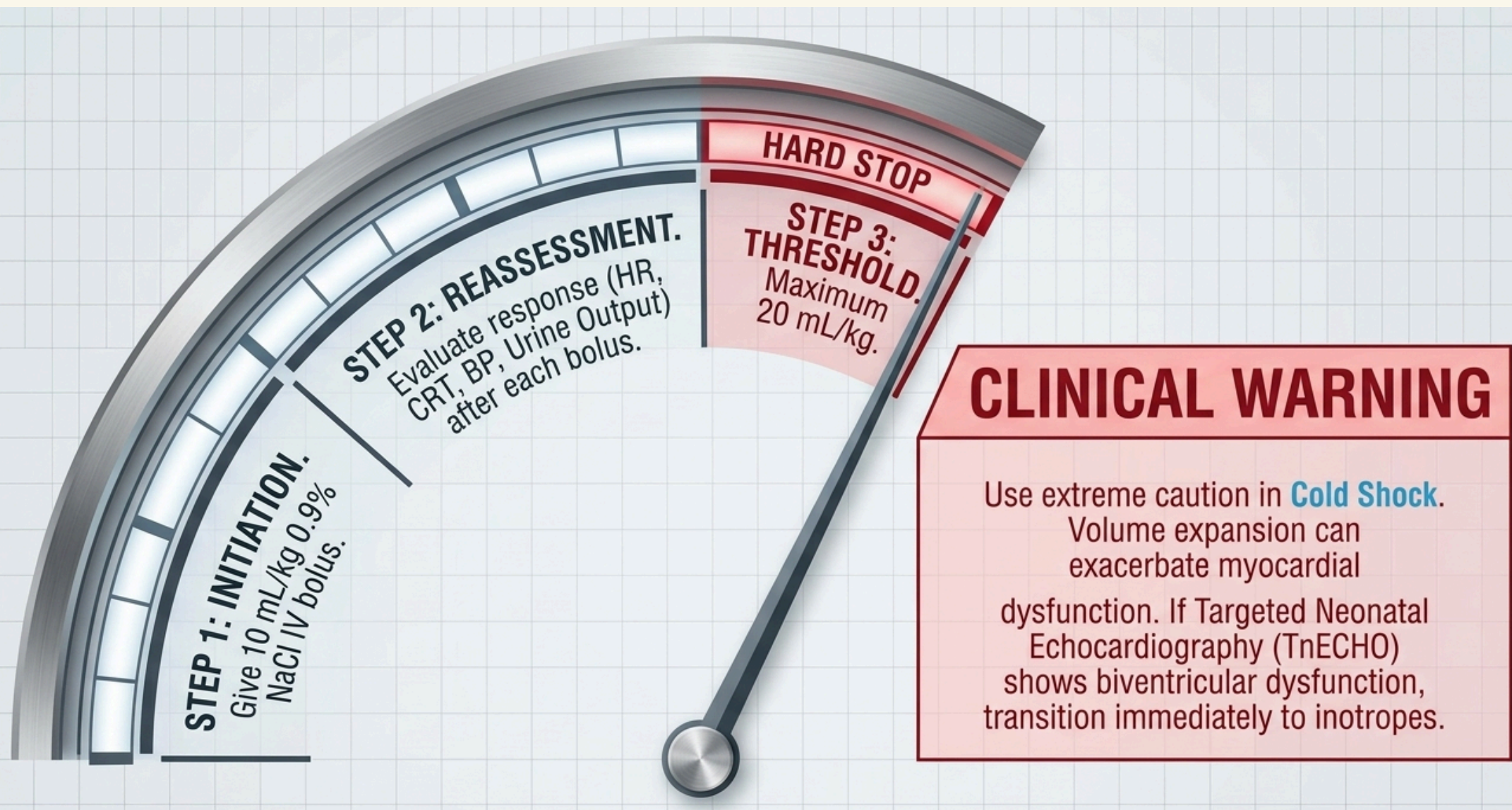
**Pathophysiology:** Reduced contractility / high systemic vascular resistance.

**Extremities & CRT:** Cold extremities, pale/mottled skin, prolonged CRT (>3s).

**Pulses & BP:** Weak pulses, hypotension with a narrow pulse pressure.

**Late-onset sepsis/NEC predominantly presents with Warm Shock physiology.**





## WARM SHOCK TREATMENT PATHWAY



### FIRST LINE: Noradrenaline Base

**Action:** Reverses vasoplegia and low SVR.

**Dose:** Start 0.05 µg/kg/min. Titrate up by 0.05 every 30 mins to achieve goal BP.

### REFRACTORY: Hydrocortisone

**Action:** Addresses relative adrenal insufficiency/HPA axis dysfunction common in severe sepsis.

**Dose:** 2.5 mg/kg IV every 6 hours. (Obtain serum cortisol prior if possible).

### RESCUE: Vasopressin

**Action:** Severe vasoplegia refractory to Noradrenaline (Max 0.4 µg/kg/min).

**Requirement:** ONLY if no LV dysfunction is present.

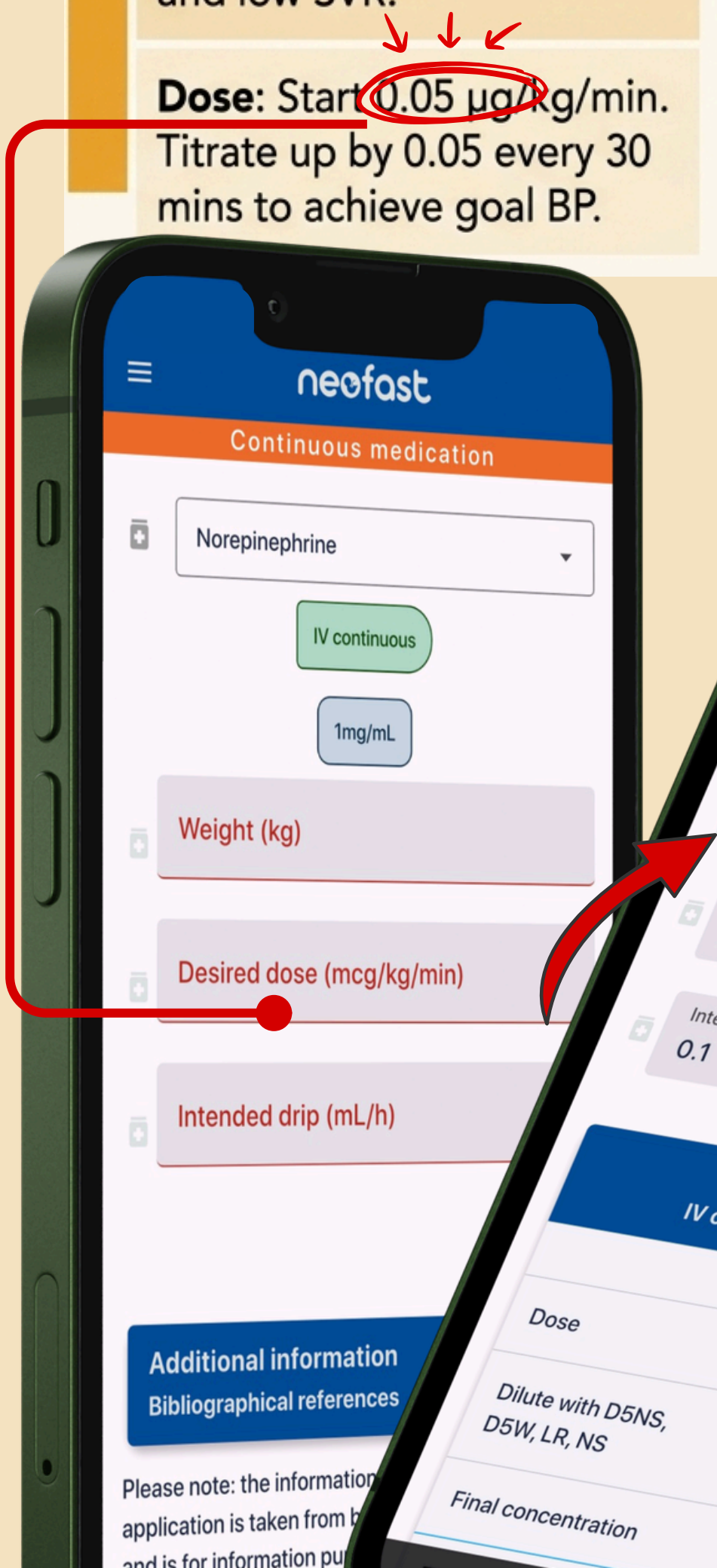




## FIRST LINE: Noradrenaline Base

**Action:** Reverses vasoplegia and low SVR.

**Dose:** Start 0.05  $\mu\text{g}/\text{kg}/\text{min}$ .  
Titrate up by 0.05 every 30 mins to achieve goal BP.



| Continuous medication                    |          |
|------------------------------------------|----------|
| Norepinephrine<br>IV continuous - 1mg/mL |          |
| Dose                                     | 0.14mL   |
| Dilute with D5NS, D5W, LR, NS            | 2.26mL   |
| Final concentration                      | 60mcg/mL |
| Total in 24 hours                        | 2.4mL    |



**Results  
in  
seconds!**





## REFRACTORY: Hydrocortisone

**Action:** Addresses relative adrenal insufficiency/HPA axis dysfunction common in severe sepsis.

**Dose:** 2.5 mg/kg IV every 6 hours. (Obtain serum cortisol prior if possible).

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Medicines

Hydrocortisone

IV bolus or IM Intermittent IV

100mg Powder 250mg Powder 500mg Powder

Without BSA BSA (height) BSA (without height)

Weight (kg)

Desired dose (mg/kg/dose)

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Medicines

Hydrocortisone  
IV bolus or IM - 100mg Powder

|                                       |         |
|---------------------------------------|---------|
| Dose                                  | 5mg     |
| Interval                              | 12/12h  |
| Reconstitution                        |         |
| Reconstitute with SWFI or own diluent | 2mL     |
| Concentration after reconstitution    | 50mg/mL |
| Dose after reconstitution             | 0.1mL   |
| Infusion rate                         | 30s     |

Note: reconstitute the 100 mg powder with 2 mL of the appropriate diluent, obtaining a concentration of 50 mg/mL.

Additional information  
Bibliographical reference

Please note: the information presented in this application is taken from bibliographical references

Weight (kg)  
2

Desired dose (mg/kg/dose)  
2.5

Suggested dose: 0.25 to 0.5 mg/kg/dose

Hydrocortisone  
IV bolus or IM - 100mg Powder





## RESCUE: Vasopressin

**Action:** Severe vasoplegia refractory to Noradrenaline (Max 0.4  $\mu\text{g/kg/min}$ ).

**Requirement:** ONLY if no LV dysfunction is present.

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Continuous medication

0.001 to 0.01 UI/kg/min

| Vasopressin<br>IV continuous - 0.2UI/mL |          |
|-----------------------------------------|----------|
| Dose                                    | 14.4mL   |
| Final concentration                     | 0.2UI/mL |
| Total in 24 hours                       | 14.4mL   |
| Drip                                    | 0.6mL/h  |

Volumes for equipment  
IV continuous - 0.2UI/mL

Additional information  
Bibliographical references

Please note: the information presented in this application is taken from bibliographical references and is for information purposes only. The doctor is solely responsible for prescribing, administering and making the necessary adjustments. This app does not replace medical guidelines or clinical judgment.

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Continuous medication

Vasopressin

IV continuous

0.2UI/mL 0.4UI/mL 0.6UI/mL 1UI/mL 20UI/mL

UI/kg/min UI/kg/h

Weight (kg)  
2

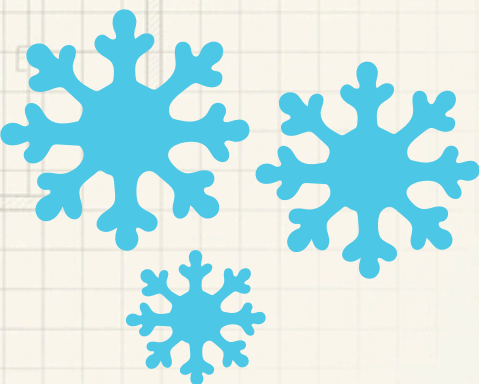
Desired dose (UI/kg/min)  
0.001

0.001 to 0.01 UI/kg/min

Vasopressin  
IV continuous - 0.2UI/mL



# COLD SHOCK TREATMENT PATHWAY



## FIRST LINE: Adrenaline

**Action:** Augments myocardial contractility and SVR.

**Dose:** Start 0.05 µg/kg/min. Titrate by 0.01-0.02 every 30-60 mins.

## REFRACTORY: Hydrocortisone

**Action:** Reverses glucocorticoid resistance at the receptor level.

**Dose:** 2.5 mg/kg IV every 6 hours.

## RESCUE: Dual Therapy

**Action:** Severe refractory shock.

**Detail:** Combine Adrenaline (up to max 0.2 µg/kg/min) with Noradrenaline to balance contractility and vascular tone.

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Continuous medication

Adrenaline (Epinephrine)

IV continuous

1mg/mL

Weight (kg)

Desired dose (mcg/kg/min)

Intended drip (mL/h)

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Continuous medication

Adrenaline (Epinephrine)

IV continuous

1mg/mL

Weight (kg)

2

Desired dose (mcg/kg/min)

0.05

Suggested dose: 0.05 to 1 mcg/kg/min

Intended drip (mL/h)

0.1

Adrenaline (Epinephrine)

IV continuous - 1mg/mL

|                     |           |
|---------------------|-----------|
| Dose                | 0.14mL    |
| Dilute with NS      | 2.26mL    |
| Final concentration | 0.06mg/mL |
| Total in 24 hours   | 2.4mL     |



## RESCUE: Dual Therapy

**Action:** Severe refractory shock.

**Detail:** Combine Adrenaline (up to max  $0.2 \mu\text{g/kg/min}$ ) with Noradrenaline to balance contractility and vascular tone.

17:12 50

neofast

Continuous medication

Adrenaline (Epinephrine)

IV continuous

1mg/mL

Weight (kg)

Desired dose (mcg/kg/min)

Intended drip (mL/h)

Additional information

17:23 48

neofast

Continuous medication

Norepinephrine

IV continuous

1mg/mL

Weight (kg)

Desired dose (mcg/kg/min)

Intended drip (mL/h)

Additional information  
Bibliographical references



# NEONATAL VASOACTIVE MEDICATION REFERENCE

| DRUG                      | STARTING DOSE          | TITRATION                      | MAXIMUM / CLINICAL NOTES                                      |
|---------------------------|------------------------|--------------------------------|---------------------------------------------------------------|
| <b>Noradrenaline Base</b> | 0.05<br>µg/kg/min      | +0.05<br>every 30 min          | 0.4 (up to 1.0 in extremis)<br>µg/kg/min                      |
| <b>Adrenaline</b>         | 0.05<br>µg/kg/min      | +0.01-0.02<br>every 30-60 min  | 0.2 µg/kg/min                                                 |
| <b>Vasopressin</b>        | 0.0003<br>units/kg/min | +0.0001-0.0003<br>every 30 min | 0.002 units/kg/min<br>(Monitor U&Es/urine output<br>4-6 hrly) |
| <b>Hydrocortisone</b>     | 2.5<br>mg/kg/dose IV   | <b>Every 6 hours</b>           | <b>Indication:</b><br>Inotrope-unresponsive shock             |

## NEONATAL SHOCK: OPTIMAL PHYSIOLOGICAL STABILIZATION TARGETS



### MACRO-CIRCULATION

BP > 3rd centile for Gestational Age.  
Normalization of pulse pressure.



### MICRO-CIRCULATION

Capillary refill time < 3 seconds.  
Resolution of metabolic acidosis (pH > 7.2) and clearing of serum lactate.



### RENAL PERFUSION

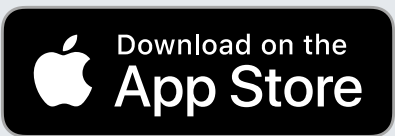
Urine output > 1 mL/kg/hr.  
(Strict monitoring required if on Vasopressin due to hyponatremia risk).



### CARDIAC FUNCTION

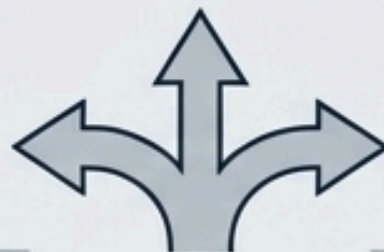
TnECHO showing normalized biventricular function and resolved pulmonary hypertension (aPHN).





## PHENOTYPE IDENTIFICATION

Limit fluids to 20 mL/kg max

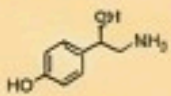


Diverge based on pulse pressure and CRT (Warm vs. Cold)

## PRECISION RESCUE

Warm:

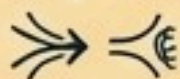
Noradrenaline



Hydrocortisone



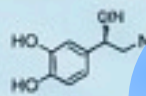
Vasopressin



Vasodilation

Cold:

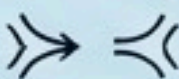
Adrenaline



Hydrocortisone



Dual Inotropes



Vasoconstriction

## STRATIFY & ERADICATE

Action threshold met

60-minute window

Blood Culture

Benzympenicillin + Gentamicin

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