ANNUAL SEPSIS STRIKE FORCE CONFERENCE • HURST, TEXAS

Surviving Sepsis!

2026 Guideline Update | Sepsis Mimics

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Learning Objectives

By the end of this session, participants will be able to:

Summarize what changed

Identify the strongest, upgraded, and downgraded recommendations in the SCCM/ESICM Surviving Sepsis Campaign 2026 guideline.

01

Operationalize the update

Translate 2026 changes — screening tools, fluid strategy, MAP targets, vasopressors, and adjuncts — into concrete order-set and screening-tool actions.

02

Recognize sepsis mimics

Describe the endocrine, toxicologic, vascular/hematologic, and immune conditions that can present identically to sepsis or septic shock.

03

Apply a bedside differential

Use red-flag findings and a structured, parallel-track approach to keep resuscitation and diagnostic reconsideration moving together.

04

Today's Session

Two halves, one goal: get the right treatment to the right patient, fast.

01	**Why the Guidelines Changed** Burden of disease, panel process, and what's new for 2026	0 – 5 min
02	**SSC 2026: Practice Changes** Screening, resuscitation, antimicrobials, vasopressors, adjuncts	5 – 25 min
03	**Pivot: Sepsis Mimics** Why non-infectious mimics matter and how to think about them	25 – 30 min
04	**The Mimic Differential** Endocrine, toxicologic, vascular/heme, and immune look-alikes	30 – 45 min
05	**Strike-Force Takeaways** Red flags, pearls, and a bedside checklist	45 – 50 min

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Sepsis Is Still the Emergency We Miss

166M

estimated sepsis cases worldwide each year globally*

21.4M

sepsis-related deaths annually

129

recommendation statements in the 2026 guideline

46

of them brand-new to this edition

Beyond acute mortality, sepsis drives lasting physical, cognitive, and mental-health impairment in many survivors — early identification and treatment remain the single biggest lever we have.

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026

- Joint initiative of the Society of Critical Care Medicine (SCCM) & European Society of Intensive Care Medicine (ESICM)
- Updates the 2021 edition — published simultaneously in Intensive Care Medicine and Critical Care Medicine, March 2026
- 69-member international panel spanning 23 countries; 38% from low- and middle-income practice settings
- Expanded scope: immediate prehospital and post-hospital care, transitions of care, rehabilitation, and long-term outcomes

*Based on Global Burden of Disease Study (GBD) 2021 analysis

Part 1

SSC 2026 — What Actually Changed

129 statements. 46 are new.

SSC 2026 at a Glance

Four talking points to carry through the rest of Part 1.

BIGGEST UPGRADES

Prolonged β-lactam infusion & de-escalation

Both move from conditional to strong recommendations.

CONTINUED CONCEPTS

Risk-stratified antibiotic timing

Not one clock for all: within 1 hour, within 3 hours, or defer and monitor.

BIGGEST RECALIBRATION

MAP & fluids, individualized

Targets and volumes now flex with age and patient factors.

LONGEST NEW LIST

The “don'ts”

Nearly a dozen adjuncts and therapies now explicitly suggested against.

Two of the Strongest Recommendations Are Organizational

Performance-Improvement Programs

Hospitals and health systems should run a formal sepsis PI program: screening of acutely ill, high-risk patients; standard operating procedures for treatment; and structured QI strategy.

This is the strike force's mandate, written into the guideline itself.

Screen With NEWS / NEWS2 / MEWS / SIRS — Not qSOFA Alone

For acutely ill hospitalized patients, use NEWS, NEWS2, MEWS, or SIRS rather than qSOFA as a single screening tool.

qSOFA remains useful for prognostication, but is no longer favored as the standalone bedside screen.

Choosing a Screening Tool: How They Compare

SSC 2026 favors NEWS, NEWS2, MEWS, or SIRS over qSOFA as a single screen. Thresholds are typical — confirm your EHR's.

Tool	Parameters	Labs?	Typical trigger	Strengths / limits	SSC 2026
SIRS	Temp > 38 or < 36 °C; HR > 90; RR > 20 or $PaCO_2$ < 32; WBC > 12k, < 4k, or > 10% bands	Yes (WBC)	≥ 2 criteria	Highly sensitive, poorly specific — fires in many non-infectious states	**Use over qSOFA**
NEWS	RR, SpO_2, supplemental O_2, temp, SBP, HR, consciousness (AVPU)	No	Aggregate ≥ 5 (or 3 in one parameter) → urgent review; ≥ 7 → emergency	Continuous ward track-and-trigger; strong for deterioration	**Use over qSOFA**
NEWS2	NEWS + new confusion (ACVPU) + a separate SpO_2 scale for hypercapnic failure	No	Same as NEWS; ≥ 5 → consider sepsis	UK NHS standard; same strengths as NEWS	**Use over qSOFA**
MEWS	RR, HR, SBP, temp, consciousness (AVPU)	No	Usually ≥ 4–5; varies by institution	Simple; least standardized across sites	**Use over qSOFA**
qSOFA	RR ≥ 22; altered mentation; SBP ≤ 100	No	≥ 2 criteria	Predicts mortality, but misses many septic patients early	**Not as a single screen**

Upgraded: Stronger Evidence, Firmer Recommendations

Two antimicrobial statements moved from "suggest" to "recommend" — plus one fluid point that is often overstated.

Prolonged (extended or continuous) β-lactam infusion after a loading dose, over bolus administration (stmt 33)

2026: strong (was conditional) — 18-RCT meta-analysis incl. BLING III (9,108 pts): mortality RR 0.91 (95% CI 0.85–0.97), high certainty

Pearl: *BLING III alone was not significant (90-day mortality 24.9% vs 26.8%). Load first. NEW: β-lactam TDM case by case (stmt 34)*

De-escalation once a confirmed organism and susceptibility profile is available (statement 36)

2026: strong recommendation (was conditional / suggested)

Note: *de-escalation when no pathogen is identified on final cultures remains conditional (statement 37)*

Crystalloids as first-line resuscitation fluid, over colloids and starches

2026: strong recommendation — unchanged

Note: *"balanced crystalloids over 0.9% saline" is a separate, still conditional suggestion; 0.9% saline is suggested in sepsis with TBI*

Fluid Strategy: From Bolus to De-Resuscitation

The 2026 update reframes fluids as a full arc, not just an opening bolus.

Initial Resuscitation

Crystalloids first-line (strong). 30 mL/kg retained but individualized (stmt 10; conditional, low certainty) — dose by ideal/adjusted weight if BMI > 30. Balanced over 0.9% saline is conditional.

MAP 65 + Early Pressors

MAP 65 is strong for adults generally; 60–65 suggested if age ≥ 65 (next). NEW: in unstable shock, vasopressors may start concurrently with initial fluid, case by case (stmt 11).

After the Initial Bolus

Either a liberal or a restrictive strategy is acceptable, guided by dynamic measures (stmt 49) — individualize to patient and health-system factors.

Active Fluid Removal

NEW: once initial resuscitation is complete, consider active fluid removal (conditional, very low certainty; sepsis-subgroup effect uncertain, RR 1.33, 95% CI 0.75–2.34).

Resuscitate to Perfusion, Not Just Pressure

After the initial bolus, SSC 2026 adds bedside perfusion targets to guide ongoing fluids and pressors.

Capillary Refill Time

≤ 3 seconds

Suggest CRT to guide resuscitation as an adjunct to other measures of perfusion.

Conditional • Low certainty

Serial Lactate

Trend it — don't chase it

Suggest serial lactate to guide resuscitation when lactate is elevated or in shock; individualize fluids after the initial fall rather than continuing until it normalizes.

Conditional • Low certainty

The evidence: the ANDROMEDA-SHOCK trials

- ANDROMEDA-SHOCK (2019, n = 424): CRT- vs. lactate-targeted resuscitation — 28-day mortality 34.9% vs. 43.4% (not significant, P = 0.06); less organ dysfunction at 72 h.
- ANDROMEDA-SHOCK-2 (2025, n = 1,501): CRT-targeted personalized resuscitation improved a composite of death, organ support and LOS (win ratio 1.16) — 28-day mortality unchanged.
- Bedside: firm pressure on the distal phalanx for 10 s, time the color return; reassess every 30 min during early resuscitation.

One MAP Target Isn't Enough Anymore

2026 splits the MAP recommendation by age — and adds a practical remark on how to read "65 mmHg" at the bedside.

Adults, General Population

65 mmHg

Initial MAP target over higher targets in septic shock.

Strong recommendation • Moderate certainty

Adults, Age ≥ 65

60–65 mmHg

"Permissive hypotension" range over higher ranges.

Conditional / suggested • Low certainty

Why: the "65 trial" and a guideline-specific meta-analysis

- The 65 trial: adults ≥65 with vasodilatory shock, MAP 60–65 vs. usual care (achieved MAP 67 vs. 73 mmHg).
- Less vasopressor exposure in the permissive arm; 90-day mortality 41.0% vs. 43.8%.
- Guideline meta-analysis limited to patients ≥65: lower targets associated with reduced mortality (RR 0.89, 95% CI 0.81–0.98).
- Bedside remark: treat MAP as a range (e.g., ±5 mmHg), not a single hard number.

Recalibrated: Softer Language, More Individualization

Several 2021 “recommend” statements moved to conditional “suggest” as new comparator evidence emerged.

Norepinephrine remains first-line — but the recommendation is now split by comparator

2026: strong over dopamine, epinephrine, selepressin • conditional (“suggest”) over vasopressin or angiotensin II

was: *"we recommend" norepinephrine over other vasopressors*

Escalation: add vasopressin, then epinephrine if MAP goals aren't met; dobutamine or epinephrine for cardiac dysfunction

2026: conditional, individualized escalation

was: *previously framed with firmer language*

IV corticosteroids in septic shock, and blood purification therapies

2026: steroids: conditional, for vasopressor-requiring shock (~200 mg/day hydrocortisone; no added benefit above ~260 mg/day) • blood purification: suggested against as a class (stmts 83–84)

was: *steroids likewise for ongoing vasopressor requirement; only polymyxin B hemoperfusion was addressed*

Antimicrobials: Timing Is Now Risk-Stratified

Risk-stratified antimicrobial timing *replaces a single threshold (statements 16–20)*

Within 1 hour

Possible, probable, or definite septic shock — and probable/definite sepsis without shock (stmts 16–17)

Within 3 hours

Possible sepsis without shock: time-limited rapid investigation, then treat (stmt 18)

Defer & monitor

Low likelihood of infection and no shock: withhold antimicrobials with close monitoring (stmt 20)

Anaerobic coverage

Suggest against empiric anaerobic coverage without anaerobic risk factors — a notable reversal from 2021.

Empiric antifungals

Suggest against routinely (stmt 27); reserve for risk factors — immunosuppression, prolonged antibiotics or hospitalization, intra-abdominal source.

SDD

NEW: selective digestive decontamination in ventilated patients where resistance prevalence is low (stmt 41; conditional, moderate certainty).

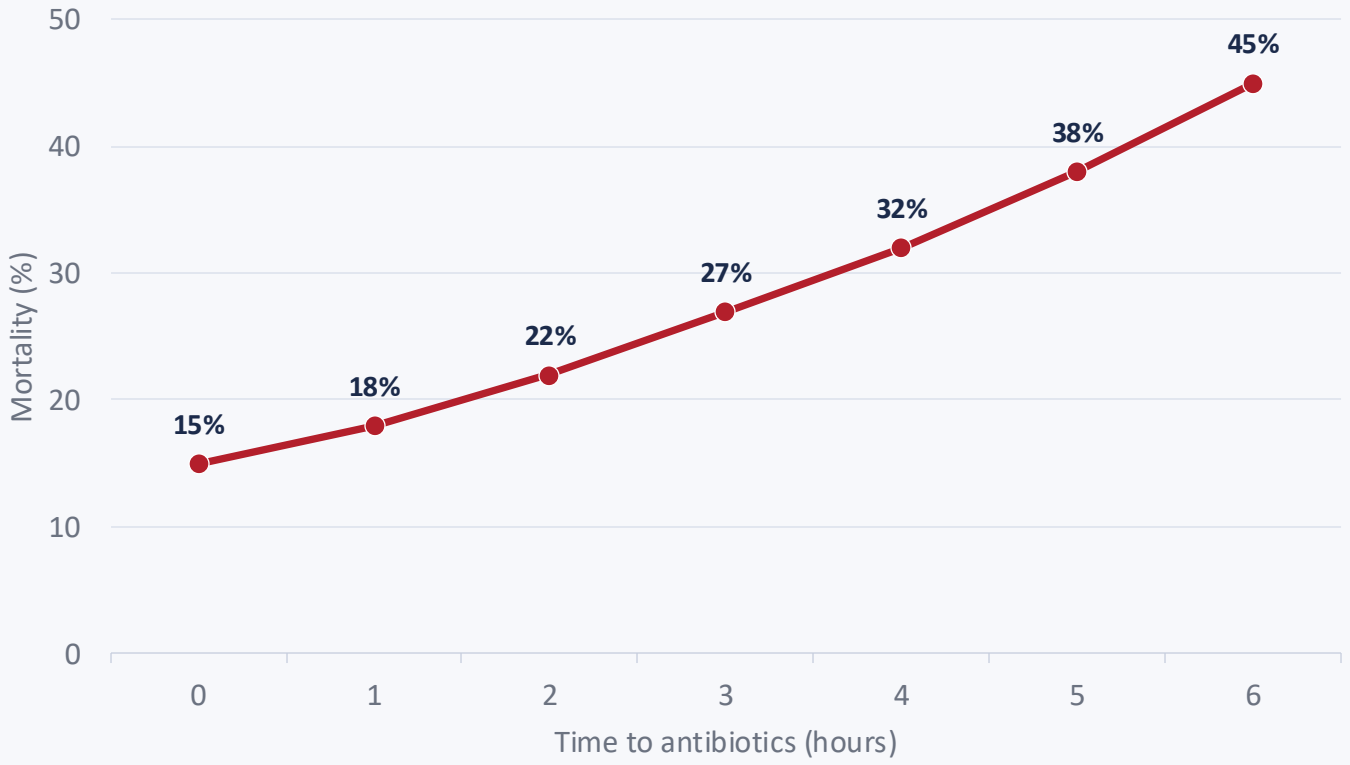
β-lactam TDM

NEW: therapeutic drug monitoring for β-lactams, case by case — the companion to prolonged infusion.

Every Hour Counts in Septic Shock

Why the shock tier gets the 1-hour clock: mortality climbs with each hour antimicrobials are delayed.

Mortality vs. time to antibiotics in sepsis



Illustrative trend of the time–mortality relationship.

↓ 7.6%

average decrease in survival for each hour of delay in septic shock with hypotension

Kumar A, et al. Crit Care Med. 2006

Strongest in septic shock

Early antibiotics lower mortality most when shock is present — the rationale for the ≤ 1-hour tier and for the time-limited workup in possible sepsis without shock.

Then Stop Smart: Duration & Discontinuation

The other half of stewardship — reassess daily and stop as soon as it is safe.

Reassess daily

Stop empiric therapy if an alternative cause is demonstrated or strongly suspected (stmt 35).

Good practice statement

De-escalate

Recommend de-escalation once a microbiologic diagnosis is confirmed (stmt 36); suggest it even when no pathogen is identified (stmt 37).

Strong (36) • Conditional (37)

Shorter courses

Suggest shorter over longer duration with an initial diagnosis of sepsis or septic shock and adequate source control (stmt 39).

Conditional • Very low certainty

Procalcitonin to stop — not to start

Suggest PCT plus clinical evaluation to decide when to stop, where optimal duration is unclear (stmt 40). To start therapy, clinical evaluation alone (stmt 22).

Conditional • Low certainty

Respiratory Support: New Ground in 2026

Oxygenation and ventilation recommendations for sepsis-associated respiratory failure.

High-flow nasal cannula first

HFNC (30–60 L/min) suggested over conventional oxygen and over NIPPV when $PaO_2/FiO_2 < 200$ or $SpO_2/FiO_2 < 235$ (conditional; low to very-low certainty).

Individualized oxygen targets

Individualized oxygen targets rather than a fixed, universal SpO_2 goal.

Awake proning

Consider awake proning in appropriately selected patients.

Tidal volume without lung injury

Higher tidal volumes (6–8 mL/kg over 4–6 mL/kg) are acceptable in the absence of lung injury; goal plateau pressure < 30 cm H_2O.

New “Don'ts”: The Longest List in 2026

Suggested against for treating sepsis or septic shock — nearly a dozen adjuncts and therapies.

Empiric anaerobic coverage
Without anaerobic risk factors — a reversal from 2021

Blood purification as a class
Hemoperfusion, high-dose hemofiltration, plasma exchange, polymyxin B

IV vitamin C
Monotherapy or in combination

Vitamin D

Sodium bicarbonate
To improve hemodynamics or reduce vasopressor needs

KRT without a definitive indication
Hyperkalemia, acidosis, fluid overload, or uremic complications

Antipyretics to improve outcomes
Stmt 80; comfort, neuro and post-arrest use exempted

Short-acting IV beta-blockers
Esmolol, landiolol (conditional, very low certainty)

IV immunoglobulins

Probiotics

XueBiJing injection
Outside jurisdictions with regulatory approval

Most are conditional — several very low certainty. Present them as “suggest against,” not firm prohibitions.

Strike Force Action List: SSC 2026

What to build into order sets, screening tools, and audit criteria this quarter.

Screening tool	Confirm NEWS/NEWS2/MEWS/SIRS is embedded in EHR alerts — retire qSOFA as sole trigger
Antimicrobial order sets	Risk-stratified timing (≤1 h / ≤3 h / defer); prolonged β-lactam infusion after a loading dose; TDM case by case
Source control	Prompt evaluation for an emergent source; intervene early, ideally within 6 h of diagnosis (stmt 24)
Stewardship	De-escalation prompts at 48–72 h; default to shorter courses; procalcitonin + clinical evaluation to support stopping
Fluids	Crystalloids first-line; individualize 30 mL/kg; guide with CRT and serial lactate; add a de-resuscitation phase
Vasopressors	Norepinephrine first-line; concurrent start with initial fluid if unstable; clarify escalation to vasopressin / epinephrine / dobutamine
Respiratory	HFNC as first device on sepsis-associated respiratory failure order sets
Remove from bundles	Routine antipyretics, anaerobic/antifungal coverage without risk factors, vitamin C/D, IVIG, bicarbonate, probiotics, beta-blockers, blood purification

Part 2

The Pivot: When It Isn't Sepsis

Guideline-concordant care starts with asking the right diagnostic question at the bedside.

SIRS and Sepsis Sit on a Continuum

Many non-infectious conditions trigger the same physiologic alarm bells — and our screening tools can't tell the difference.



Shared Physiology

Fever or hypothermia, tachycardia, tachypnea, leukocytosis, and hypotension are the final common pathway of many disease processes, not proof of infection.



Labs Alone Don't Settle It

Lactate, procalcitonin, and white count abnormalities occur in numerous non-infectious mimics — no single value rules infection in or out.



Resuscitate While You Differentiate

For the patient in extremis, resuscitation takes precedence — but continued non-response to standard therapy should trigger active reconsideration.

A Practical Approach at the Bedside

1. **Resuscitate first** — Don't delay fluids, source control, or antimicrobials while working the differential in an unstable patient.
2. **Re-examine the history** — Medication list, recent procedures/transfusions, endocrine or psychiatric history, toxin/withdrawal exposure, travel, and trauma.
3. **Targeted exam findings** — Rash pattern, joint findings, thyroid exam, clonus/rigidity, JVD, abdominal exam — mimics often leave a specific fingerprint.
4. **Adjunct studies, not gestalt alone** — Bedside echo, ECG, cortisol, TSH, ammonia, lipase, LDH/haptoglobin/smear, drug levels — chosen by pretest probability, not reflex panels.
5. **Reassess non-responders** — Failure to improve with source control and resuscitation is itself a diagnostic clue — pause and reconsider.

Endocrine & Metabolic Mimics

The great imitators — often missed because the trigger is a stressor, not a pathogen.

Adrenal (Addisonian) crisis	Refractory hypotension despite fluids/pressors + hyponatremia, hyperkalemia, hypoglycemia; recent steroid withdrawal or pituitary/adrenal disease. Empiric hydrocortisone can be lifesaving and diagnostic. (Dexamethasone will also work here and is preferred if planning cosyntropin stimulation test).
Thyroid storm	Fever, tachycardia out of proportion, agitation/delirium, GI symptoms; history of Graves' disease or recent iodine load, thyroid surgery, or medication non-adherence.
Myxedema coma	Hypothermia (not fever), bradycardia, altered mental status, hyponatremia — the mirror image of storm; consider in unexplained hypothermic shock.
DKA / HHS and severe pancreatitis	Tachycardia, tachypnea (Kussmaul), leukocytosis, and abdominal pain can all mimic septic shock; anion gap, lipase, and glucose quickly redirect the workup.

Toxicologic & Drug-Related Mimics

Look at the med list and the vitals pattern before you anchor on infection.

Serotonin syndrome	Fever, clonus, hyperreflexia, agitation, tremor; recent serotonergic agent or interaction (SSRIs, MAOIs, tramadol, linezolid).
Neuroleptic malignant syndrome	Fever, “lead-pipe” rigidity, altered mental status, autonomic instability; recent antipsychotic initiation/dose change or dopaminergic withdrawal.
Malignant hyperthermia	Rapid hyperthermia, muscle rigidity, rhabdomyolysis intraoperatively or shortly after volatile anesthetics/succinylcholine.
Drug fever & withdrawal states	Isolated fever without another source on a new drug; alcohol/benzodiazepine withdrawal producing tachycardia, hypertension, agitation, and fever.

Vascular, Hematologic & GI Mimics

Shock without infection — the differential the resuscitation itself should prompt.

Massive pulmonary embolism	Hypotension, tachycardia, hypoxia, and even fever; look for RV strain on echo/ECG, sudden onset, and a provoking risk factor.
Occult GI hemorrhage / hypovolemic shock	Tachycardia and hypotension with a normal or rising lactate; melena, hematemesis, or a falling hemoglobin reframe the picture quickly.
TTP / HUS and other thrombotic microangiopathies	Fever, altered mental status, thrombocytopenia, and organ dysfunction can mimic septic shock with DIC; check smear for schistocytes, LDH, and haptoglobin.
HLH / macrophage activation syndrome	Persistent fever, cytopenias, hyperferritinemia, hepatosplenomegaly, and coagulopathy in a patient not responding to broad-spectrum therapy.

Immune, Cardiac & Dermatologic Mimics

Rounding out the differential — and a reminder that skin findings matter.

Anaphylaxis	Rapid-onset hypotension, tachycardia, flushing, and bronchospasm after a trigger exposure; treat with epinephrine, not just fluids.
Cardiogenic shock / tamponade / myocarditis	Hypotension with poor forward flow rather than vasoplegia; bedside echo distinguishes a pump problem from a vasodilated one quickly.
Transfusion reactions & cytokine release syndrome	Fever, rigors, hypotension temporally linked to a transfusion or cellular/immunotherapy product.
Generalized pustular psoriasis (von Zumbusch) & vasculitis flares	Fever and systemic inflammation with a distinctive pustular or purpuric rash; procalcitonin is often unhelpfully low, not high.

Red Flags: “Pause and Reconsider”

None of these rule out sepsis — but each should widen the differential before you close the chart.

Fever with a normal or low procalcitonin	*Consider pustular psoriasis, gout/pseudogout flare, drug fever, or malignancy*
No source found after a thorough infectious work-up	*Revisit endocrine, toxicologic, and hematologic mimics*
Refractory shock despite adequate fluids and escalating pressors	*Consider adrenal crisis, tamponade/PE, or cardiogenic shock*
Rigidity, clonus, or a clear temporal drug link	*Think serotonin syndrome, NMS, or malignant hyperthermia*
Hypothermia instead of fever, with bradycardia	*Consider myxedema coma or an overwhelmed/immunosuppressed host*
Cytopenias, coagulopathy, or a falling hemoglobin	*Consider TTP/HUS, HLH, or occult hemorrhage*

Bringing It Together: One Patient, Two Lenses

Guideline-driven resuscitation and mimic-awareness are not competing priorities — they run in parallel.

Minute 0–60: Treat the Bundle

- Screen with NEWS/NEWS2/MEWS/SIRS
- Cultures, then antimicrobials on a risk-stratified clock (≤1 h shock or probable sepsis; ≤3 h possible sepsis)
- Find and control the source — ideally within 6 h of diagnosis
- Crystalloids, individualized; MAP 65 (60–65 if age ≥ 65); follow CRT and lactate
- Norepinephrine first-line — concurrent with fluids if unstable

In Parallel: Keep the Differential Open

- Medication & endocrine history at triage
- Targeted exam: skin, thyroid, tone/reflexes, JVD
- Bedside echo if response to fluids/pressors is poor
- Escalate the mimic work-up if not improving by the 3–6 hour mark

Take Back to Your Strike Force

Update screening & order sets

Embed NEWS/NEWS2/MEWS/SIRS, risk-stratified antimicrobial timing, source-control targets, prolonged β-lactam infusions, and stop-date and de-escalation prompts.

Individualize after the first 30 mL/kg

Liberal vs. restrictive fluids and steroid use are now conditional, patient-specific decisions — not one-size-fits-all.

Build mimic-awareness into non-responder pathways

Any patient not improving with source control and resuscitation should trigger a structured mimic differential.

Protect against anchoring bias

A normal/low procalcitonin, a clean infectious work-up, or refractory shock are each a cue to widen the lens.

Selected Sources

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