The Cure for Sepsis

Plan
- 2016 Consensus Definitions of Sepsis: Sepsis-3
- Surviving Sepsis Campaign Guidelines 2016
- The Cure for Sepsis

Sepsis
- Common
  - 31 million cases per year
  - 6 million per year
- Mortality rate 60% 3rd world
- Rapid interventions improve outcome
  - Mortality rate falling

What is sepsis?

Old Sepsis Definitions
- Sepsis: SIR's + Infection
  - T >38 C or <36 C
  - P >90/min
  - RR >20/min or PaCO2 <32 mmHg
  - WCC >12 or >10% immature band forms
- Severe Sepsis: sepsis with organ dysfunction
- Septic Shock: hypotensive despite fluid resuscitation

Sepsis-3
- Better define sepsis and septic shock and
- Provide bedside tools to aid risk stratification
- Old sepsis definition picking up too many patients, most of whom weren’t unwell.
- New definitions used to spot the sick ones

Sepsis-3 New Definitions. Why?

Sepsis-3
- Sepsis
- Severe Sepsis
- Septic Shock

Sepsis-3
- Sepsis
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Sepsis-3
- Sepsis
- Severe Sepsis
- Septic Shock
Severe sepsis?

- Old definitions were identifying too many less sick patients (and subjecting them to invasive treatments?) and definition of severe sepsis was interpreted differently across the world

Definition of Sepsis

- Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection

  - Sepsis 2016 = the old severe sepsis

Definition of Septic Shock

- Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

But...

- What exactly is “organ-dysfunction”, “dysregulated host response”?
- Clinicians need something of value at the bedside

Sepsis

- Infection and a raised Sequential (Sepsis–related) Organ Failure Assessment Score (SOFA), with a change in score of 2 or greater from base-line being diagnostic

  - Identifies patients with a mortality of >10%

  - BUT SOFA is complex and not all the information may be immediately available

qSOFA

- Infection and at least 2 of the following criteria
  - Respiratory Rate 22 or greater
  - GCS <15
  - Systolic Bp <100

If qSOFA positive

- Further investigate for organ dysfunction
- Initiate or escalate therapy
- Consider referral to critical care or increase frequency of monitoring
- If negative doesn’t mean you’re not worried (maybe)

qSOFA

- Infection and at least 2 of the following criteria
  - Respiratory Rate 22 or greater
  - GCS <15
  - Systolic Bp <100

Advantages

- Quick: no blood tests
- Mortality risk at that point
- Prompt escalation, investigation

Disadvantages

- Not a diagnostic test
- Needs prospective validation
- Hypo: Oliguria?
- NEWS better?
- Not normally <100, GCS <15
Septic Shock

- Vasopressor requirement required to maintain a MAP of >65mmHg and a serum lactate level >2mmol/L in the absence of hypovolaemia
- Mortality >40%
- Interrogated Surviving Sepsis Campaign database and these criteria associated with increased mortality difference
- Validated in large databases

Risk Stratification

- The new definitions are designed to
- Identify the sickest patients and
- Those who benefit from prompt intervention and in whom empirical broad-spectrum antibiotic therapy is warranted

Recognition

- Often most difficult
- Delays early in course adverse effects
- If patient deteriorating with a raised NEWS, screen for infection and consider sepsis

Initial Clinical Management Goals

- Improve tissue oxygenation and perfusion
- Provide antimicrobial therapy with suitable cover against the causative organism
- Source control

Antibiotics

- Within 1 hour of recognition
- To cover likely pathogens
- Use local guidelines
- MDRs: previous antibiotics, recent hospitalisation, nursing home residents
- Previous results?
- Consider combination of ABs if MDR, immunosuppressed, septic shock
- Micro samples prior to ABs (if possible)
Antibiotics

- "Empiric antimicrobial therapy be narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is noted."
- Daily assessment for de-escalation
- Duration 7-10 days
- Longer courses if slow clinical response, undrained foci, bacteremia with L. aureus, some fungal and viral infections, or neutropenia

IV Fluids

- At least 30 ml/kg of IV crystalloid in first 3 hrs
- Fluids guided by frequent reassessment of haemodynamic status
- Further haemodynamic assessment to determine the type of shock if diagnosis unclear
- Don't use Starches (or colloids?)
- But consider Albumin if large volume of crystalloids infused

Source Control

Within 12 hours
- Least invasive
- Removal of infected lines
- Necrotic pancreatitis is an exception

Monitoring Response

- Previously EGDT recommended
- IRIS, r-norepinephrine, noradrenaline, vasopressin
- Challenged in recent studies: PROMISE, PROCESS, ARISE
- No benefit from EGDT compared to usual care
- Mortality rates low in these trials
- All patients received early fluid boluses and antibiotics
- Early identification and resuscitation, monitoring response to treatment using non-invasive methods remain mainstays of treatment

Lactate

- “We suggest guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion”
- Linear relationship between lactate and mortality
- Lactate clearance associated with improved outcomes
- Easily obtainable, non-invasive
- Trends
- If not improving: escalate, refer, think again
- Not just hypoperfusion: catecholamines, liver failure

Specific Treatments

- Steroids: only if haemodynamic stability unachievle with fluids and vasopressors
- RBC: only if Hb <7 (exceptions bleeding, IHD)
- Bicarbonate: consider only if pH <7.15
- UAMM unless CI
- Stress ulcer prophylaxis
- Glucose control (<10)

Setting Goals of Care

- Goals of care and prognosis be discussed with patients and families
- Goals of care be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate
- Goals of care be addressed as early as feasible, but no later than within 72 h of ICU admission

In Summary

- Early recognition
- Early antibiotics
- IV fluids to restore tissue perfusion
- Source control
- Frequent re-evaluation
• Diagnosis of severe sepsis or septic shock and procalcitonin level >2ng/ml
• Treatment started within 24 hours
• No differences in baseline characteristics or other changes made during study
Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock
A Retrospective Before-After Study

- Vitamin C 1.5g IV qds 4 days or until ICU discharge
- Hydrocortisone 50mg IV qds 7 days or ICU discharge (+ 3 day taper)
- Thiamine 200mg IV bd for 4 days or until ICU discharge

Levels low in sepsis
"Acute scurvy"
Stress hormone in mammals
Antioxidant
Essential to production of catecholamines, cortisol
Endothelial function
Enzyme function (Fe, Cu)
Enhances T cells and macrophages
Safe at high doses but can cause AKI (oxalate deposition)

Synergy
- Sepsis pts thiamine deficient
- Also thiamine decreases risk of oxalate deposition
- Oxidation of glucocorticoid receptor in sepsis
- Cortisol cannot bind (failure steroid trials?)
- Vitamin C restores glucocorticoid receptor function

Criticisms
- Many!
- Not an RCT
- (No blinding)
- Single centre
- Small sample size
- Different time frames for 2 groups
- PCT not readily available (or validated)
- Other things going on here? Restricted fluids

"Metabolic Resuscitation"

- Standard therapy in Eastern Virginia
- Interviews, blogs, testimonials
- Treated >150 patients with only 1 death from sepsis

In Summary
- Use qSOFA or NEWS
- If worried call for help, investigate, treat, reassess
- Take your vitamins

Questions?

References