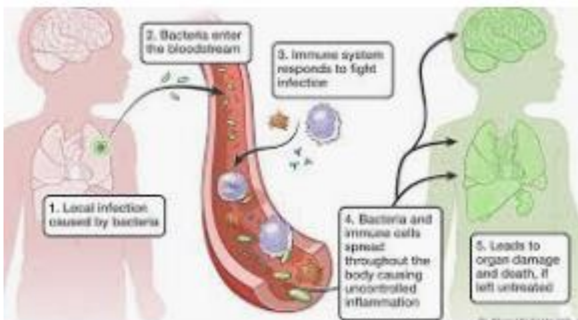
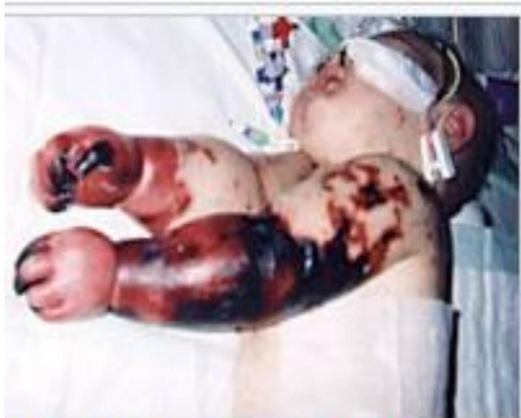


SEPSIS

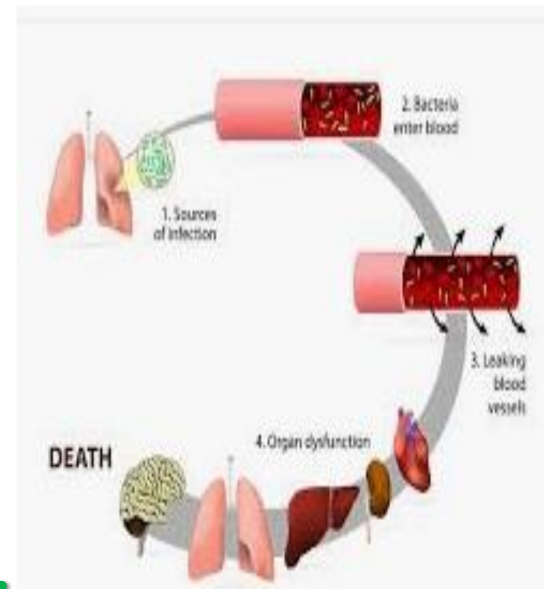
SYMPTOMS OF SEPSIS

- **S** Shivering, fever, or very cold
- **E** Extreme pain or general discomfort ("worst ever")
- **P** Pale or discolored skin
- **S** Sleepy, difficult to rouse, confused
- **I** "I feel like I might die"
- **S** Short of breath

SEPSIS IS A MEDICAL EMERGENCY



Charlotte Cleverley-Bisman, with sepsis from a meningococcal bloodstream infection



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OVERVIEW

- most common cause of mortality in ICU & 10th leading cause of death overall, with incidence still rising, mostly due to:
  - Aging population
  - ↑ invasive procedures
  - ↑↑Life support implements (prosthetics)
  - ↑↑↑ immunocompromised patients

OVERVIEW……

- Sepsis is a syndrome that occurs when the body loses its ability to favourably alter an initial provocation
- The ass overwhelming IR to infection results in a spectrum of clinical conditions characterised by systemic cascades of inflamm & coagulation at endothelium level →MOD syndrome being a continuum of host injury response to microbial infection
- Coagulation cascade (if unchecked) may move down the continuum even with adequate antibiotics

WHAT IS SEPSIS

- Prev used to describe process yielding foul-smelling pus >> septic wound OR abortion
- Microbiology changed this notion
- Confined infected wound means healing.....but even better if not infection at all
- Microbial spread →lymphatics →b/stream (septic blood) → → septicaemia and pyemia →leucocytosis

>>> a local process that becomes systemic<<<

- Sepsis is mostly caused by bacteria BUT it may result from fungi (candida), parasites (f. malaria), and even viruses (adenovirus); bacterial sepsis may not yield bacteria at all

- Host's molecules are the proximate cause of sepsis via host IR with release of cytokines (microbial toxins may contribute)

"the final common path of host response to a variety of microbial molecules"

MANIFESTATIONS

- **Sepsis** = Systemic Inflammatory Response Syndrome (SIRS) + Infection

- SIRS = 2/4 of
  - Temp >38 or <36
  - HR >90
  - Respiratory Rate >20 or P_aCO_2 <32 (4.3kPa)
  - WCC >12 or <4 or >10% bands
- Infection = either
  - Bacteraemia (or viraemia/fungaemia /protozoan)
  - Septic focus (abscess / cavity / tissue mass)

Thus:

- It is a severe systemic illness marked by characteristic hemodynamic derangements and organ malfunction, brought about by the interaction of certain microbial products with host reticoloendothelial cells.

- All organs/systems may be affected – one organ after another may fail >>> multi-organ dysfunction syndrome (MODS)

  ......affected organs incl:

BRAIN:

- confusion, delirious, stuporous, or comatose

HEART:

- depression of myocardial contractility
- heart compensates by dilation and faster beating
  ↑↑cardiac output
- in some pts compensation may fail

VASCULATURE:

- BP falls due to peripheral vasodilatation

"warm shock" (v ↓BP and ↑ cardiac output) pt has warm/flushed skin!!

CLOATING SYSTEM:

- endothelial damage may lead to microvascular thrombosis → disseminated intravascular coagulation (DIC)
- consumes platelets and clotting factors
  - ↑tendency to bleed
- thrombosis and bleeding may both be present
- activation of fibrinolytic system counteracts thrombosis, but adds to coagulopathy (since fibrin degradation products inhibit clotting)

LUNGS:

- Lung capillaries gen become leaky

› activated neutros adhere and damage pulm endothelium by spewing oxygen radicals

› fluid exudes into interstitium and alveolar spaces

› lung becomes soggy, stiff, denied adequate gas exchange →→acute respiratory distress syndrome (ARDS)

KIDNEY:

- acute renal failure due to acute tubular necrosis may occur ("the lungs leak, the kidneys don't")

LIVER:

- stasis of bile; focal necrosis and jaundice

GASTROINTESTINAL TRACT:

- loss of mucosal integrity can lead to hemorrhagic necrosis of mucosa …? Ischemia

ENDOCRINE & METABOLIC EFFECTS:

- sepsis is a catabolic state ► proteolysis, lipolysis, glycogenolysis
- ↑ stress hormones circulating (cortisol, catecholamines, glucagon)
- O2 metabolism deranged, high levels returned to heart unused (cell impairment/no perfusion)
- Impaired Kreb's cycle, ↑rate of glycolysis, more lactic acid ››› lactic acidosis

SOURCES OF INFECTION

1) Endogenous bacteria

- Gp A streps., *Staph aureus* (wounds, puerperal fever, abortions)
- pyelonephritis infection (enteric G –ve bacilli)
- Ruptured appendicitis (enterics & anaerobes), *N meningitidis* cause fulminant sepsis in healthy people

2) Nosocomial source:

commonly seen now and caused by:

- *E.coli, Klebsiella, Enterobacter, Proteus, Pseud aeruginosa*

all associated with antibiotic therapy and burn wounds; with v high mortality rate.

- Bact fragilis – anaerobic septicaemia
- Staph aureus – Tpxic Shock syndrome (TSS)
- Strep pneumoniae
- Strep pyogenes – Strep Toxic Shock Syndrome

WAY IN ……

- Often start with localized infection
- Also can result from damaged heavily colonized surfaces (colonic mucosa)

3 things necessitates sepsis:

(1) Large pop of infecting/colonizing organisms, strong microbial resistance + defects in host's containment and clearing mechanisms

(2) Presence of bacterial products to stimulate release of cytokines

(3) W/spread dissemination of microbial products to host RES

Host defense defects also predispose to sepsis, these may include:

(a) Disruption/penetration of anatomic barriers

- wounds, catheters, IV drugs/medication
- ischemic necrosis, tumours
- cytotoxic chemo

(b) Devitalised tissue

- necrotic tissue ….no blood supply, no phagocytes, complement, or Ab protection; creates rich culture media

(c) Granulocytopenia and defective granulocyte function

- lack of neutros predisposes to bacterial and fungal infection
- diabetics v prone to bacterial infs (adherence, chemotaxis, ingestion, oxidative burst and killing are all impaired)

(d) Complement defects

- Homozygous C/pathway components and C3
- Propedin def in A/pathway predisposes to fulminant sepsis with

N meningitidis

- def in late components (C5 – C9) mild susceptibility to neisserial infection
- Cirrhosis and severe burns – comp – deficient states may easily tip into sepsis

(e) Immune Defects

- humoral defects (loss of opsonic, bactericidal Ab)
- cellular defects (loss of ability to activate specific ag stimuli)
- B-cell malignancies, burns, AIDS

(f) Splenic Malfunction or Absence

- loss of spleen creates humoral imm def
- impairment of clearance of encapsulated bacteria from blood
- sickle-cell pts at high risk with *S pneumoniae, H influenzae, N meningitidis*
- May require long term prophylaxis antibiotics.

DAMAGE

- Interaction of microbial molecules with host Φphages initiate the cascade leading to sepsis syndrome
  - In G +ves - teichoic/lipoteichoic acids, peptidoglycan
  - In G –ves - endotoxin (LPS) → Lipid A moiety
    - → LPS binds to CD14 on macrophages
    - → Triggers production of TNF-α
    - → TNF-α able to induce sepsis
    - → TNF-α stimulates macros to produce IL-1β

Why does the body self-destruct? Can the process be stopped?

- Body is self-protective and response to injury ought to be damage control and repair
- In sepsis, this is not so….host seems to be bent on self-destruction….WHY? Or

Is sepsis, however deadly, a protective mechanism …. Would the host die faster without it??

- What good are IL-1, TNF, & other mediators in acute response!!!
- More learning needed to understand sepsis!!

DIAGNOSIS

- ❑ Signs of sepsis may be obvious or subtle
- ❑ Absence of fever may delay diagnosis

  ↘ signs may be misinterpreted

- BP may not fall much initially
- Blood culture often +ve
- Hemodynamic changes may be apparent
- Only sepsis is assoc with rise in cardiac output, and a fall in systemic vascular resistance

TREATMENT

Mainstays are:

» optimisation of O2 delivery to tissues

» drainage of pus

» devitalised tissue debridement

» antibiotics

- Sepsis is a state of O2 starvation
- V low O2 is extracted from arterial supply
- Ventilators often used for more O2 supply and to keep airways under pressure

›› Iv fluids to maintain blood volume – xfusion?

›› adrenergic drugs to maintain tissue perfusion pressure, ↑ myocardial contractility

To Conclude…..

?? Could antibiotics be deleterious….

?? If microbes are killed, don't they release mediators such as LPS

- Ordinarily, not so obvious, tho common to see pts get worse before they get better!!
- Antibiotics must be properly prescribed
- In future, maybe a poss of a cocktail of anticytokine /antibiotics to be useful??

SUMMARY

- Sepsis may be obvious or subtle – alertness
- Carries high mortality and morbidity
- Have a high index of suspicion
- Know local organisms / susceptibilities
- Take appropriate cultures
- Treat early and aggressively
- Investigate early and aggressively
- Refer early and aggressively
- Be aware of new developments

End