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Patient admitted to the intensive care unit for multiple organ failure

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- Variously known as the Multiple Organ Dysfunction Syndrome (MODS),
  - Multi Organ Failure,
  - Multiple Systems Organ Failure,
  - Multiple Organ *Dysfunction*

- **Multiple organ dysfunction syndrome (MODS**) is defined as the **progressive physiological dysfunction of two or more organ systems** where homeostasis cannot be maintained without intervention.

- Although the syndrome involves the ***dysfunction of many organs***, it also affects physiologic systems not classically thought of as organs, (the hematologic system, immune system, or the endocrine system.)

- Although it is described as a ***syndrome***, its clinical course and causes are highly variable, and there is only the most general form of consensus regarding the organs whose dysfunction comprises the syndrome, or the criteria that should be used to describe this dysfunction

- The observation that critically ill patients die, not as a result of the progression of the disorder that precipitated ICU admission, but of a complex series of physiologic derangements that develop following resuscitation and management in the ICU was first made in the 1960's.
- *Baue*, in 1975, published a landmark editorial in which he commented on the striking similarity of the post mortem findings in patients dying in an ICU and suggested that it was not the failure of a single system, but the concomitant failure of multiple interdependent organ systems that was the unsolved problem in critical care.
- Subsequent reports highlighted the important role of occult, uncontrolled infection in the pathogenesis of MODS, although control of infection did not necessarily result in reversal of the physiologic derangements, nor was infection universally present in patients with the syndrome.

Organ dysfunction in a critically ill patient can be described in one of two ways

1. the clinical intervention that was employed to support the failing organ system (mechanical ventilation, hemodialysis, inotropic or vasopressor agents, parenteral nutrition etc),
2. the acute physiologic derangement that made such support necessary.

Each uses the same six organ systems to characterize MODS -the respiratory, cardiovascular, renal, hepatic, neurologic, and hematologic systems.

Organs most commonly affected by MODS include the heart, lungs, liver and kidneys

CAUSE

- The condition results from infection, injury (accident, surgery), hypoperfusion and hypermetabolism.
  - The primary cause triggers an uncontrolled inflammatory response.

  - **Sepsis** is the most common cause of Multiple Organ Dysfunction Syndrome and may result in septic shock.
  - In the absence of infection, asepsis-like disorder is termed systemic inflammatory response syndrome (SIRS).

  - Both SIRS and sepsis could ultimately progress to MODS.

- other causes include:
  - Major trauma;
  - Major surgery;
  - Burns;
  - Pancreatitis;
  - Shock;
  - Aspiration syndromes;
  - Blood transfusions;
  - Autoimmune disease;
  - Acute heart failure;
  - Poisons/toxins
- in one-third of the patients no primary focus can be found.

Systemic inflammatory response syndrome (SIRS) may follow a variety of clinical insults, including infection, pancreatitis, ischemia, multiple trauma, tissue injury, hemorrhagic shock, or immune-mediated organ injury.

SIRS is a nonspecific presentation of these insults and is defined by the presence of 2 or more of the following:

- Temperature > 38.0°C or < 36.0°C
- HR > 90 beats/min
- RR > 20 breaths/min **OR** PaCO2 < 32 mm Hg
- WBC > 12,000/µL, **OR** < 4000/µL, **OR** Including more than10% bands

- Sepsis is a systemic response to infection.
- Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a
  - MAP ≥of 65 mm Hg

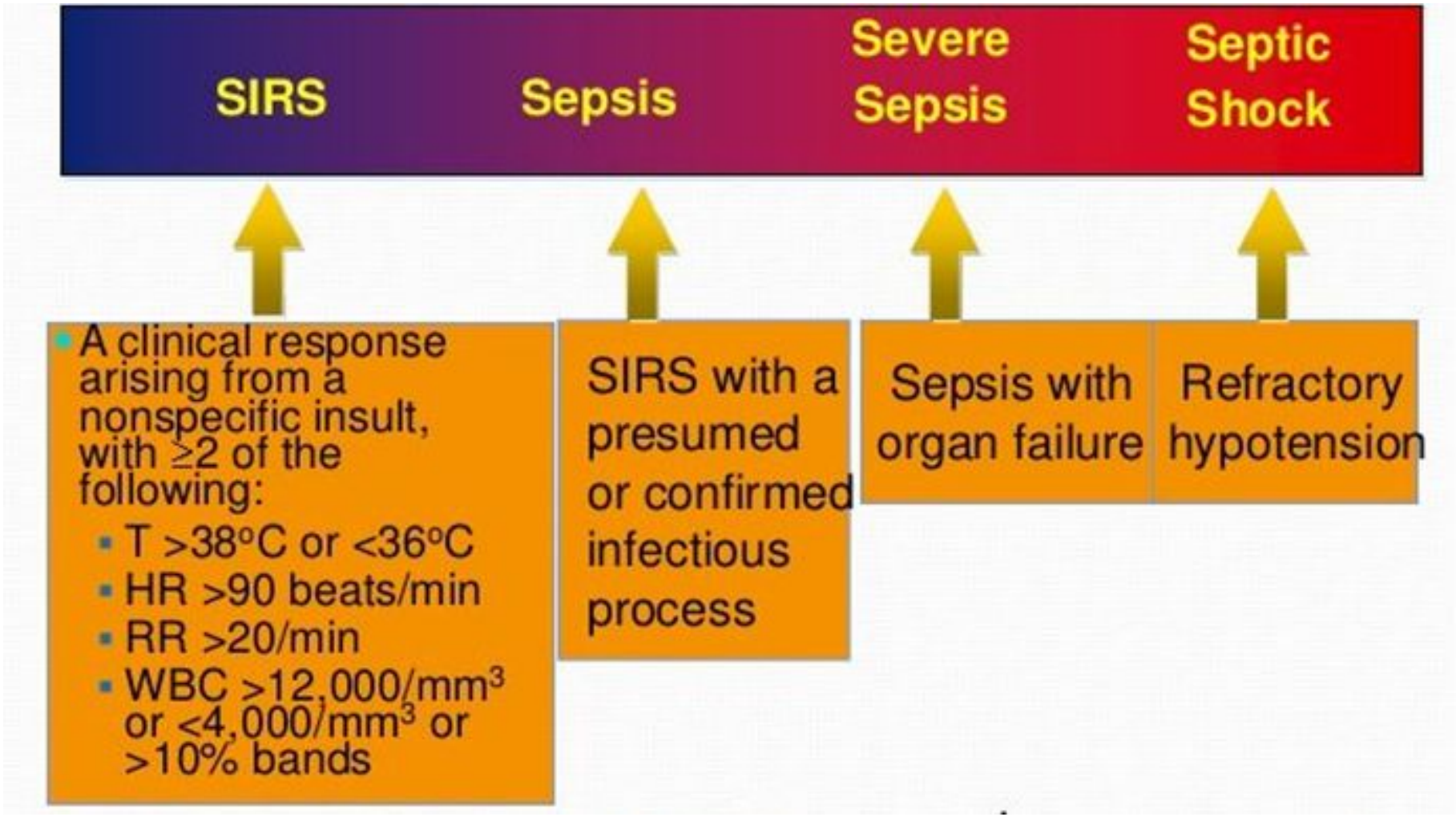
    AND
  - serum lactate level > 2 mmol/L (>18 mg/dL) in the absence of hypovolemia.
- This combination is associated with hospital mortality rates > 40%.

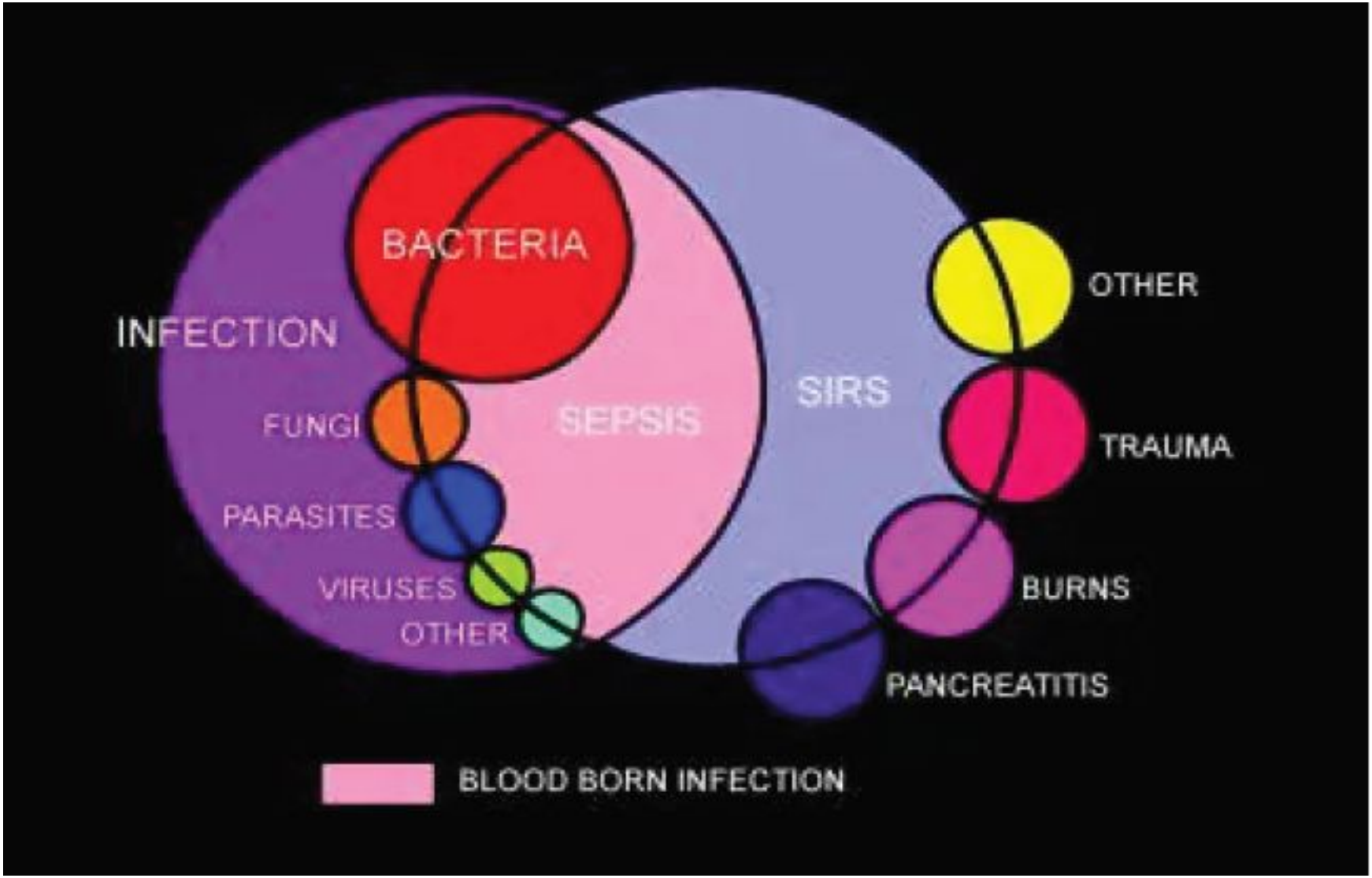
Stages of Sepsis
Consensus Conference Definition

- Systemic Inflammatory Response Syndrome (SIRS)
  Two or more of the following:
  - Temperature of >38°C or <36°C
  - Heart rate of >90
  - Respiratory rate of >20
  - WBC count >12 x 10^3/L or <4 x 10^3/L or 10% immature forms (bands)
- Sepsis
  SIRS plus a culture-documented infection
- Severe Sepsis
  Sepsis plus organ dysfunction, hypotension, or hypoperfusion (including but not limited to lactic acidosis, oliguria, or acute mental status changes)
- Septic Shock
  Hypotension (despite fluid resuscitation) plus hypoperfusion

Multiple organ dysfunction syndrome is well established as the final stage of a continuum:

SIRS + infection → sepsis → severe sepsis → MODS.





Venn diagram showing overlap of infection, bacteremia, sepsis, systemic inflammatory response syndrome (SIRS), and multiorgan dysfunction.

- Primary MODS (Rarely) Is the direct result of a well-defined insult in which organ dysfunction occurs early and can be directly attributable to the insult itself. such as with large-scale physical or chemical injuries or widely disseminated disease.
- Secondary MODS develops as a consequence of a host response and is identified within the context of SIRS. The inflammatory response of the body to toxins and other components of microorganisms causes the clinical manifestations of sepsis.
- Usually MODS is secondary to a combination of SIRS, accumulated effects of various injurious agents (such as drug or oxygen toxicity), episodes of cardiogenic or hypovolemic hypotension, and the effects of failing organ systems on each other.

Risk Factors for Multiple Organ Dysfunction Syndrome

- An individual's genetics may dictate the likelihood and severity of MODS following a trigger.
  - Although uncontrolled, once MODS develops systemic evidence of both pro-inflammatory and anti-inflammatory up-regulation are usually present, suggesting that failure of host defense homeostasis is the final pathway from sepsis to MODS, rather than simple hypotension-induced end-organ injury, as may occur with hemorrhagic shock.
  - Survival from severe sepsis with MODS is usually associated with a generalized reduction in both the pro-inflammatory and anti-inflammatory response.
  - Currently, investigators are looking into genetic targets for possible gene therapy to prevent the progression to MODS.
  - Some authors have conjectured that the inactivation of the transcription factors Nuclear factor κB (**NF-κB**) and activator protein 1 (AP-1) would be appropriate targets in preventing sepsis and SIRS.
- A patient with premorbid organ dysfunction may be prone to further deterioration.
- Medications, therapies and ICU supports may contribute to organ injuries.
- A patient with an infection is at risk of MODS

Pathophysiology-

A definite explanation has not been found. Local and systemic responses are initiated by tissue damage.

- Gut hypothesis
- Endotoxin macrophage hypothesis
- Tissue hypoxia-microvascular hypothesis
- Mitochondrial DNA hypothesis
- Integrated hypothesis

- The histologic features of the organs involved in MODS are less well characterized, but generally include evidence of edema, inflammation, tissue ischemia or necrosis, and variable degrees of fibrosis and repair.
- These alterations, in turn, are responsible for the clinical features of MODS in each of its component systems.

Gut hypothesis

- The most popular hypothesis by Deitch to explain MODS in critically ill patients is the gut hypothesis.
- Due to splanchnic hypoperfusion and the subsequent mucosal ischaemia there are structural changes and alterations in cellular function.
- This results in increased gut permeability, changed immune function of the gut and increased translocation of bacteria.
- Liver dysfunction leads to toxins escaping into the systemic circulation and activating an immune response.. This results in tissue injury and organ dysfunction

Endotoxin macrophage hypothesis

- Gram-negative infections in MODS patients are relatively common, hence endotoxins have been advanced as principal mediator in this disorder.
- It is thought that following the initial event cytokines are produced and released.
- The pro-inflammatory mediators are: tumor necrosis factor-alpha (TNF-α), interleukin-1, interleukin-6, thromboxane A2, prostacyclin, platelet activating factor, and nitric oxide.

Tissue hypoxia-microvascular hypothesis

- As a result of macro- and microvascular changes insufficient supply of oxygen occurs. Hypoxemia causes cell death and organ dysfunction

Mitochondrial DNA hypothesis

- According to findings of Professor Zsolt Balogh and his team at the University of Newcastle(Australia), mitochondrial DNA is the leading cause of severe inflammation due to a massive amount of mitochondrial DNA that leaks into the bloodstream due to cell death of patients who survived major trauma.
- Mitochondrial DNA resembles bacterial DNA. If bacteria triggers leukocytes, mitochondrial DNA may do the same. When confronted with bacteria, white blood cells, or neutrophil granulocytes, behave like predatory spiders. They spit out a web, or net, to trap the invaders, then hit them with a deadly oxidative blast, forming neutrophil extracellular traps (NETs).
- This results in catastrophic immune response leading to multiple organ dysfunction syndrome. McIlroy, Daniel J.; (December 2014). " doi:10.1016/j.jcrc.2014.07.013

- Significant derangement in autoregulation of circulation is typical of sepsis.
- Vasoactive mediators cause vasodilatation and increase microvascular permeability at the site of infection.
- NO plays a central role in the vasodilatation of septic shock.
- Also, impaired secretion of vasopressin may occur, which may permit persistence of vasodilatation.

Diagnosis-

- The European Society of Intensive Care organized a consensus meeting in 1994 to create the "Sepsis-Related Organ Failure Assessment (SOFA)" score to describe and quantitate the degree of organ dysfunction .
- Using similar physiologic variables the Multiple Organ Dysfunction Score was developed. Sequential Organ Failure Assessment score (SOFA score),
- The score is based on six different scores, one each for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems.
- The quick SOFA score (qSOFA) assists health care providers in estimating the risk of morbidity and mortality due to sepsis.
- The SOFA scoring system is useful in predicting the clinical outcomes of critically ill patients.
- According to an observational study at an Intensive Care Unit (ICU) in Belgium, , in the first 96 hours of admission, the mortality rate is
  - at least 50% when the score is increased, regardless of initial score
  - 27% - 35% if the score remains unchanged,
  - less than 27% if the score is reduced.

Box 13-1 Common Clinical Laboratory Tests in Patients with SIRS

ETIOLOGIC

Blood cultures
Sputum and urine: Gram stain and cultures
Microbial products: Stool toxins; blood fungal polysaccharides
Blood serology for organisms
Blood polymerase chain reaction for organisms
Lipase or amylase (to rule out pancreatitis)
Troponin I (to rule out ischemic cardiogenic)
Imaging for potential infectious sources, pulmonary emboli

INFLAMMATORY VARIABLES

C-reactive protein
Procalcitonin
White blood cell count
White blood cell differential

ASSESSMENT OF ORGAN PATHOLOGY

Bilirubin (liver)
Creatinine (kidney)
Platelet count (thrombocytopenia)
D-dimer (coagulopathy)
Lactate (general organ hypoperfusion and metabolic imbalance)

Respiratory system

PaO_2/FiO_2 [mmHg (kPa)]	SOFA score
≥ 400 (53.3)	0
< 400 (53.3)	+1
< 300 (40)	+2
< 200 (26.7) **and** mechanically ventilated	+3
< 100 (13.3) **and** mechanically ventilated	+4

Nervous system

Glasgow coma scale	SOFA score
15	0
13–14	+1
10–12	+2
6–9	+3
< 6	+4

Cardiovascular system

Mean arterial pressure OR administration of vasopressors required	SOFA score
MAP ≥ 70 mmHg	0
MAP < 70 mmHg	+1
dopamine ≤ 5 µg/kg/min or dobutamine (any dose)	+2
dopamine > 5 µg/kg/min OR epinephrine ≤ 0.1 µg/kg/min OR norepinephrine ≤ 0.1 µg/kg/min	+3
dopamine > 15 µg/kg/min OR epinephrine > 0.1 µg/kg/min OR norepinephrine > 0.1 µg/kg/min	+4

Liver

Bilirubin (mg/dl) [µmol/L]	SOFA score
< 1.2 [< 20.53]	0
1.2–1.9 [20-32]	+1
2.0–5.9 [33-101]	+2
6.0–11.9 [102-204]	+3
> 12.0 [> 204]	+4

Coagulation

Platelets×10^3/µl	SOFA score
≥ 150	0
< 150	+1
< 100	+2
< 50	+3
< 20	+4

Kidneys

Creatinine (mg/dl) [µmol/L] (or urine output)	SOFA score
< 1.2 [< 110]	0
1.2–1.9 [110-170]	+1
2.0–3.4 [171-299]	+2
3.5–4.9 [300-440] (or < 500 ml/d)	+3
> 5.0 [> 440] (or < 200 ml/d)	+4

SOFA Score	Mortality if initial score
0-1	0.0%
2-3	6.4%
4-5	20.2%
6-7	21.5%
8-9	33.3%
10-11	50.0%
12-14	95.2%
>14	95.2%

Table II Prognosis in multiple organ failure

Number of failing systems	Mortality (%)
0	< 10
1	0–30
2	20–50
3	40–80
4	60–100
5 or more	> 80

In out-of-hospital, emergency department, or general hospital ward settings, adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes typical of sepsis if they have at least two of the following clinical criteria that together constitute a new bedside clinical score termed quick SOFA (qSOFA) :

Assessment	qSOFA score
Low blood pressure (SBP ≤ 100 mmHg)	1
High respiratory rate (≥ 22 breaths/min)	1
Altered mentation (GCS ≤ 14)	1

Prognosis

- Mortality from MODS remains high.
- Mortality from ARDS alone is 40-50%; once additional organ system dysfunction occurs, mortality increases as much as 90%.
- mortality ranging from 40% to 75% in patients with MODS arising from sepsis.
- The poor prognostic factors are
  - advanced age, infection with a resistant organism, impaired host immune status, and poor prior functional status.
  - Development of sequential organ failure despite adequate supportive measures and antimicrobial therapy is a harbinger of a poor outcome.

- There is a graded severity from SIRS to sepsis, severe sepsis, and septic shock, with associated 28-day mortality rates of approximately 10%, 20%, 20-40%, and 40-60%, respectively .
- Of all deaths, 27% occurred within 2 days of the onset of severe sepsis, and 77% of all deaths occurred within the first 14 days.
- The risk factors for early mortality were a higher severity of illness score, the presence of 2 or more acute organ failures at the time of sepsis, shock, and a low blood pH (< 7.3).

- While MODS itself is the complication of an underlying condition, it represents a spectrum of dysfunction and can rapidly increase in severity.
- In the later stages of MODS, the affected organs may completely lose function (multiple organ failure). This carries a mortality risk of up to 80 to 96% and may not be reversible. Preventing MODS from progressing into organ failure is therefore crucial .
- If the patient becomes increasingly unwell, they may require intensive care admission and aggressive treatment to maximize organ function.

What is Multiple Organ Dysfunction Syndrome?

- **Multiple organ dysfunction syndrome (MODS**) is defined as the **progressive physiological dysfunction of two or more organ systems** where homeostasis cannot be maintained without intervention .

- MODS is generally initiated by illness, injury or infection, causing a state of immuno-depression and hypo-metabolism .

- Rather than a single event, MODS is considered a continuum where the extent of dysfunction can vary greatly from mild impairment to irreversible failure.

- Organs most commonly affected by MODS include the heart, lungs, liver and kidneys (Gu et al. 2018).

- It is estimated to affect around 15% of ICU patients and contributing to about 50% of deaths in ICU (Nickson 2019; Osterbur et al. 2014).

Causes of MODS

- MODS is induced by illness, injury or infection that triggers an unregulated systemic inflammatory response (**systemic inflammatory response syndrome**),resulting in tissue injury.

The most common trigger is SEPSIS , but other causes include:

- Major trauma;
- Major surgery;
- Burns;
- Pancreatitis;
- Shock;
- Aspiration syndromes;
- Blood transfusions;
- Autoimmune disease;
- Acute heart failure; and
- Poisons/toxins

Presentation and Symptoms of MODS

- In order to be diagnosed with MODS, the patient should be experiencing dysfunction of at least two organs (this may be mild or severe) in addition to systemic inflammatory response syndrome .
- Organ dysfunction may present as:
  - ✔ Acute kidney injury (AKI) and uremic acidosis;
  - ✔ Acute respiratory distress syndrome (ARDS);
  - ✔ Cardiomyopathy;
  - ✔ Encephalopathy;
  - ✔ Gastrointestinal dysfunction;
  - ✔ Hepatic dysfunction;
  - ✔ Coagulopathy and bone marrow suppression;
  - ✔ Acute neurological dysfunction.

Presentation and Symptoms of MODS

- The patient may display some of the following symptoms depending on which organs are affected:
  - An altered mental state;
  - A decrease in renal perfusion (decrease in urine output);
  - Respiratory deterioration;
  - A decrease in cardiac function;
  - Deranged metabolic status;
  - A compromised fluid balance;
  - Pale, clammy, peripherally cool skin and faint pedal pulses; and
  - A decrease in cardiac output (e.g. low blood pressure, arrhythmia).

Treatment and Management of MODS

MODS is difficult to treat, escalates quickly and is often fatal. Therefore, early detection is crucial in preventing its progression.

Positive patient outcomes rely on immediate recognition, ICU admission and invasive organ support

Therapy, is usually mostly limited to supportive care

Management and treatment may include:

- Identifying and treating the underlying causes, comorbidities or complications
- Maintaining adequate tissue oxygenation is a principal target.
- Starting enteral nutrition within 36 hours of admission to an ICU (↓infectious complications.)
- Fluid resuscitation to increase perfusion;
- Support care and monitoring:
  - Multi-organ support;
  - Mechanical or non-invasive ventilation;
  - Maintaining fluid homeostasis; and
  - Renal replacement therapy.

Preventing Multiple Organ Dysfunction Syndrome

- As a complication of an illness, injury or infection, MODS is difficult to prevent. Early recognition improves patient outcomes - this is the only way to prevent damage.
- It is important to monitor patients closely and administer appropriate therapies to facilitate organ function.
- Maintain an accurate fluid balance chart;
- Support the hemodynamic needs of the patient (identify low blood pressure, analyze trends, escalate to the medical team and treat early);
- Identify any potential triggers of MODS;
- Ensure regular blood tests are performed;

Referrences

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- wikipedia
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