ADVANCED AND CLINICAL CARE FOR PATIENTS WITH SARI

PATHOPHYSIOLOGY OF SEPSIS AND ARDS

World Health Organization

HEALTH EMERGENCIES programme

Learning objectives

At the end of this lecture, you will be able to:

- Describe the pathophysiology of sepsis.
- Describe the interplay between oxygen delivery, cardiac output and septic shock.
- Describe causes of hypoxaemia, focus on shunt.
- Describe the pathophysiology of ARDS.

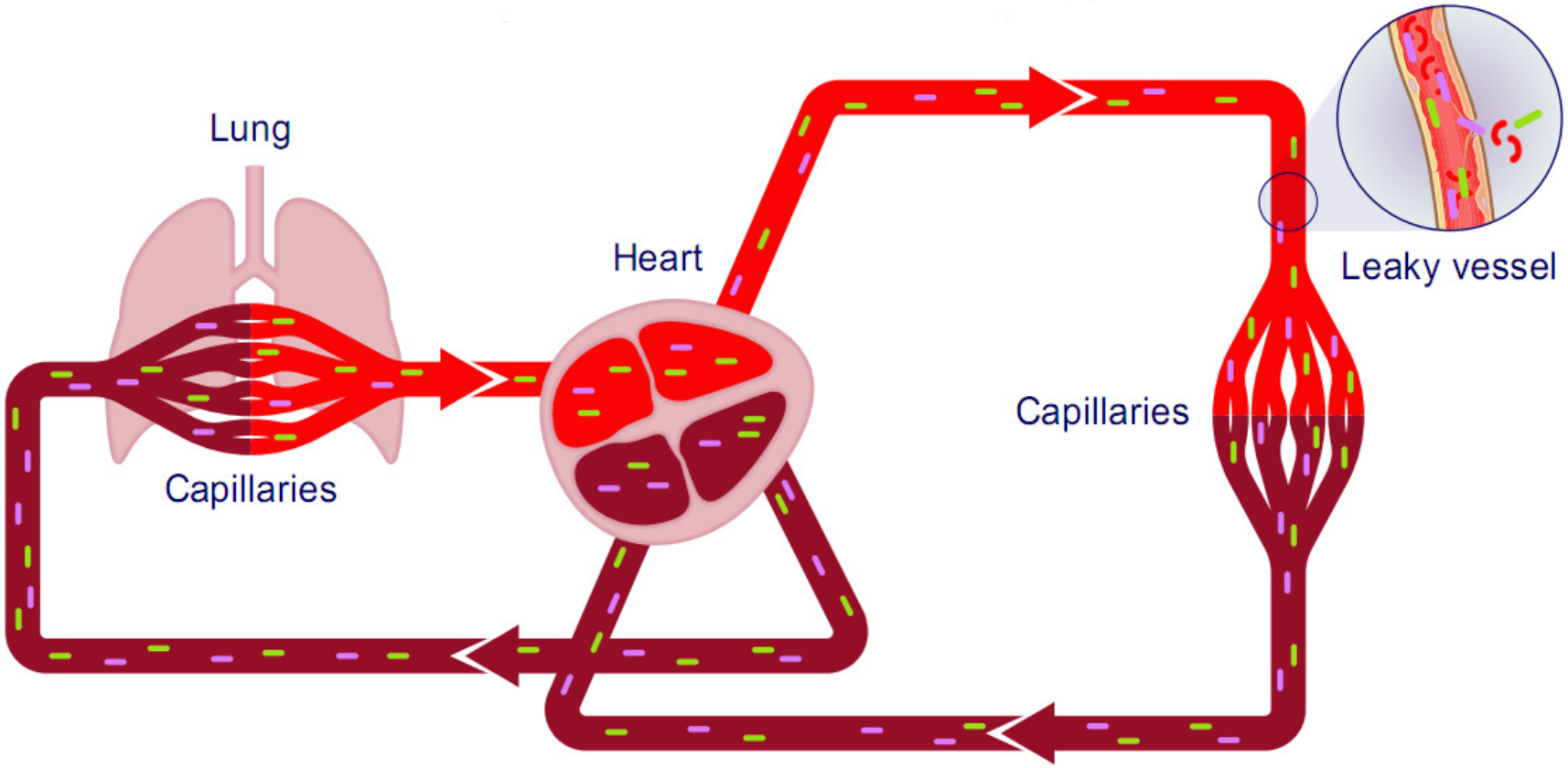
Sepsis

"Sepsis is life-threatening, acute organ dysfunction secondary to a dysregulated host response to infection."

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

The 3rd International Consensus Definition for Sepsis and Septic Shock. Sepsis-3, JAMA, 2016.

Natural history of sepsis



O_2 delivery (DO_2)

- O_2 is delivered to tissues to maintain normal aerobic metabolism
  - DO_2 ~ 900–1100 mL/min (normal).

- O_2 delivery to tissues is determined by cardiac output × content of O_2 in the arterial blood.

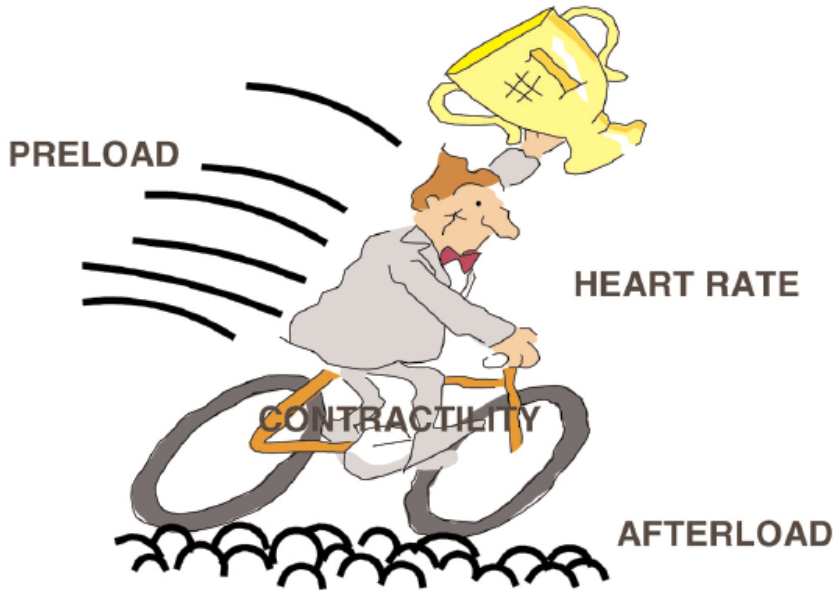
$$DO_2 = CO \times CaO_2$$

Cardiac output (CO)

- **CO is determined by**
  - preload
  - afterload
  - contractility
  - heart rate.

- **CO~5–6 L/min** (normal).

Figure 1 http://ccforum.com/content/12/4/174



Four determinants of cardiac output, using an analogy to the speed of a bicycle.

$$DO_2 = CO \times CaO_2$$

CO determinants	Physiologic adaptations to septic shock and implications for treatment
Preload	• Ventricular underfilling and hypovolaemia are common in sepsis. • **Fluid loading is major intervention to improve preload**.
Heart rate	• HR increases to compensate for septic shock adults and children. • Children have higher basal heart rates and have less HR reserve. • **HR thresholds are targets of resuscitation in children.**
Afterload	• Vascular tone can vary in response to sepsis-from cold mottled peripheries (cold) to vasodilation with wide pulse pressure (warm). • **Vasopressors are used to improve perfusion pressure in adults and children.**
Contractility	• Myocardial function can vary in response to sepsis; from dysfunction to hyperdynamic function. • **Inotropes may improve cardiac dysfunction, when present.**

CaO_2 (oxygen content of arterial blood)

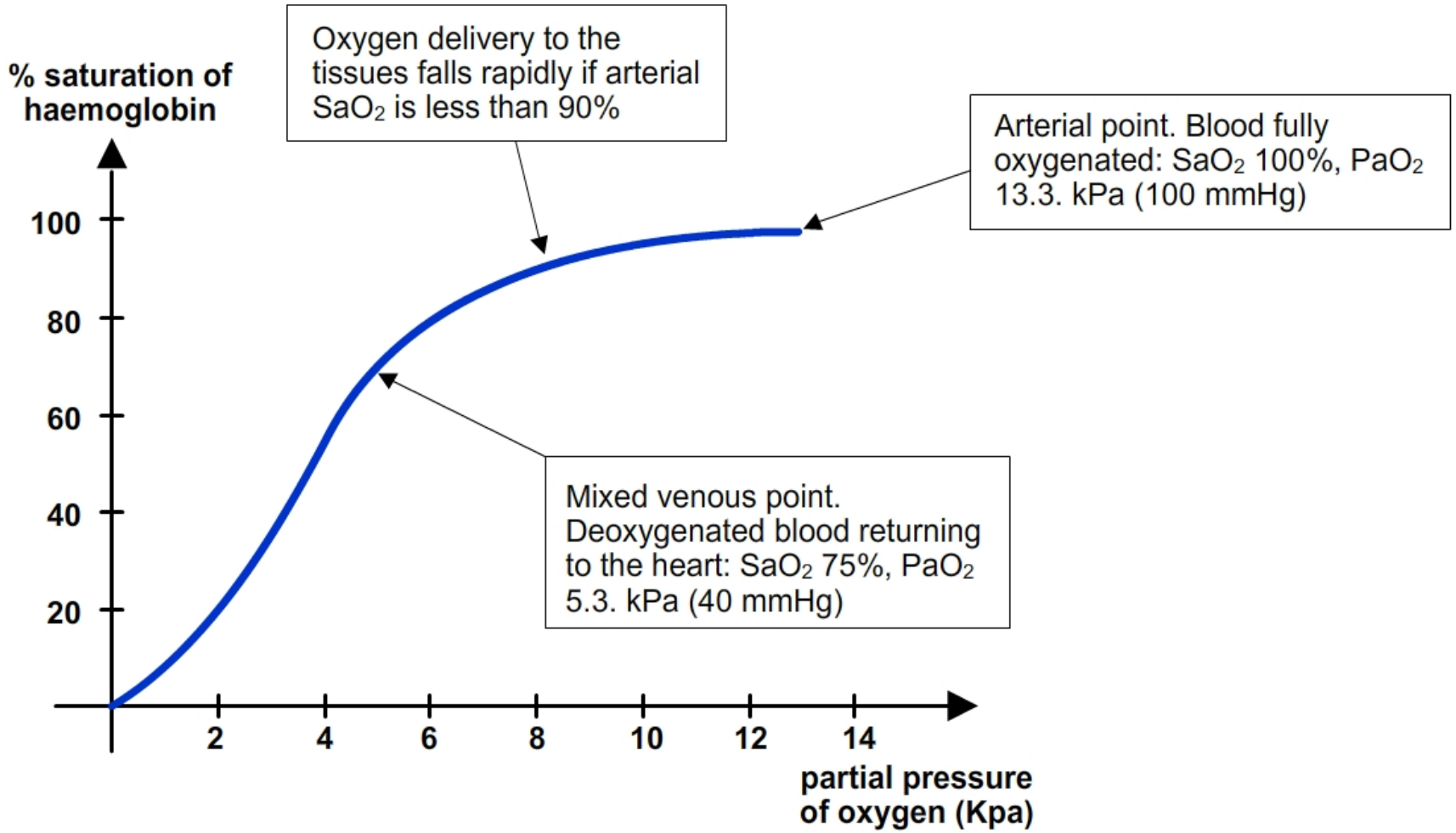
- Determined primarily by saturation of arterial Hb:
  - normal Hb is 120–180 g/L
  - each g Hb carries 1.34 mL O_2 SaO_2
  - normal SaO_2 is 0.98–1.00.

- CaO_2 ~200 mL/L (normal).

$$DO_2 = CO \times CaO_2$$

$$CaO_2 = (Hb \times 1.34 \times SaO_2) + (PaO_2 \times 0.003)$$

Oxyhaemoglobin dissociation curve



(8 kPa = 60 mmHg)

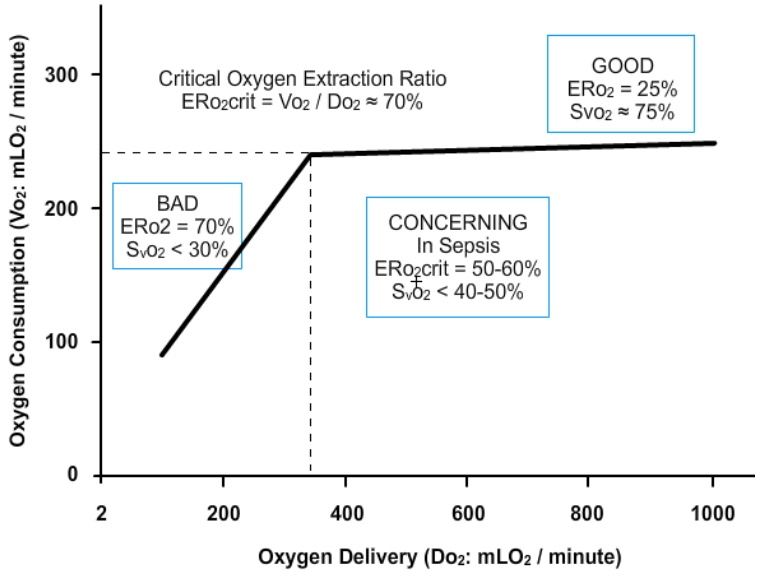
Oxygen consumption (VO_2)

- VO_2, tissue oxygen consumption:
  - ~ 200–270 mL/min(normal)
  - determined by:
    - metabolic demand (most important)
      - **e.g. increased in sepsis**
    - tissue ability to extract oxygen from arterial blood
    - oxygen delivery, especially when this is very low.

Oxygen extraction (ERO_2) (1/2)

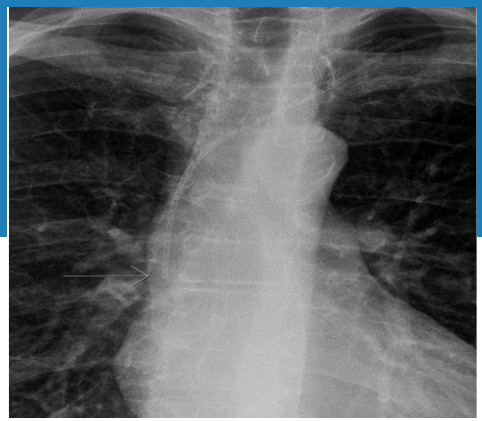
- Relationship between O_2 consumption and O_2 delivery is the O_2 extraction ratio (ERO_2)
  - Normally, the body extracts 25% of the oxygen that is delivered
  - The rest goes back to the heart
  - $ERO_2 = VO_2/DO_2 \sim 25\%$
  - If $SaO_2 > 0.9$, then $ERO_2 \approx 1\text{-}SvO_2$.

Oxygen extraction (ERO_2) 2/2



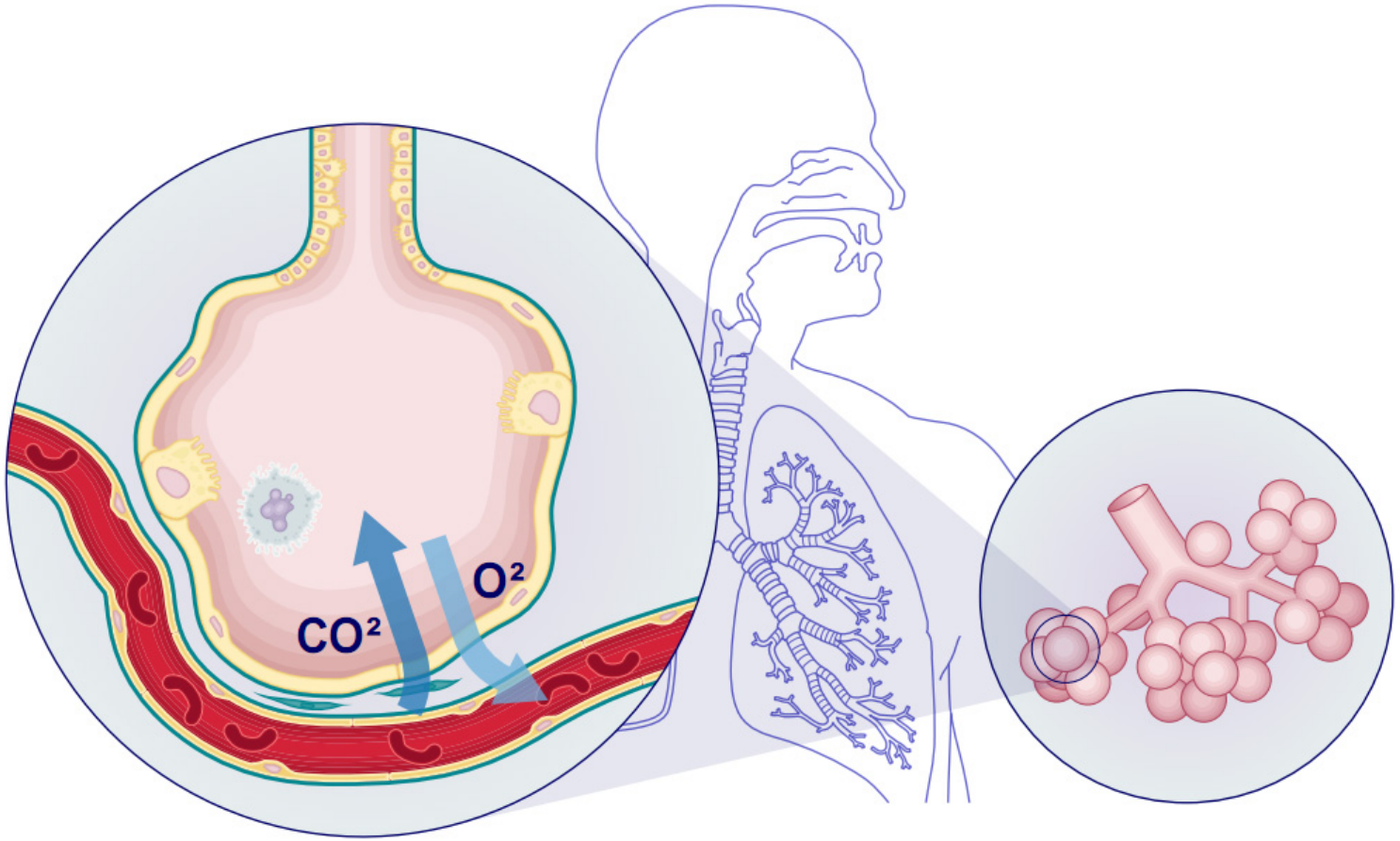
- $ERO_2 = VO_2/DO_2$ (normal 25%).
- As DO_2 ↓, ERO_2 ↑ to preserve VO_2.
- ERO_2 crit is the maximum possible ERO_2
  - in sepsis, the body is less able to extract O_2.
- If DO_2 ↓ to the point that ERO_2 crit is reached, then VO_2 falls and tissues become ischemic.

Central venous saturation ($ScvO_2$)



- $ScvO_2$, saturation of central venous blood (right atrium):
  - Determined by oxygen consumption relative to oxygen delivery.
  - Measured by blood sample from distal tip of internal jugular or subclavian central line at the junction of the superior vena cava and right atrium.
  - > 70% (normal).

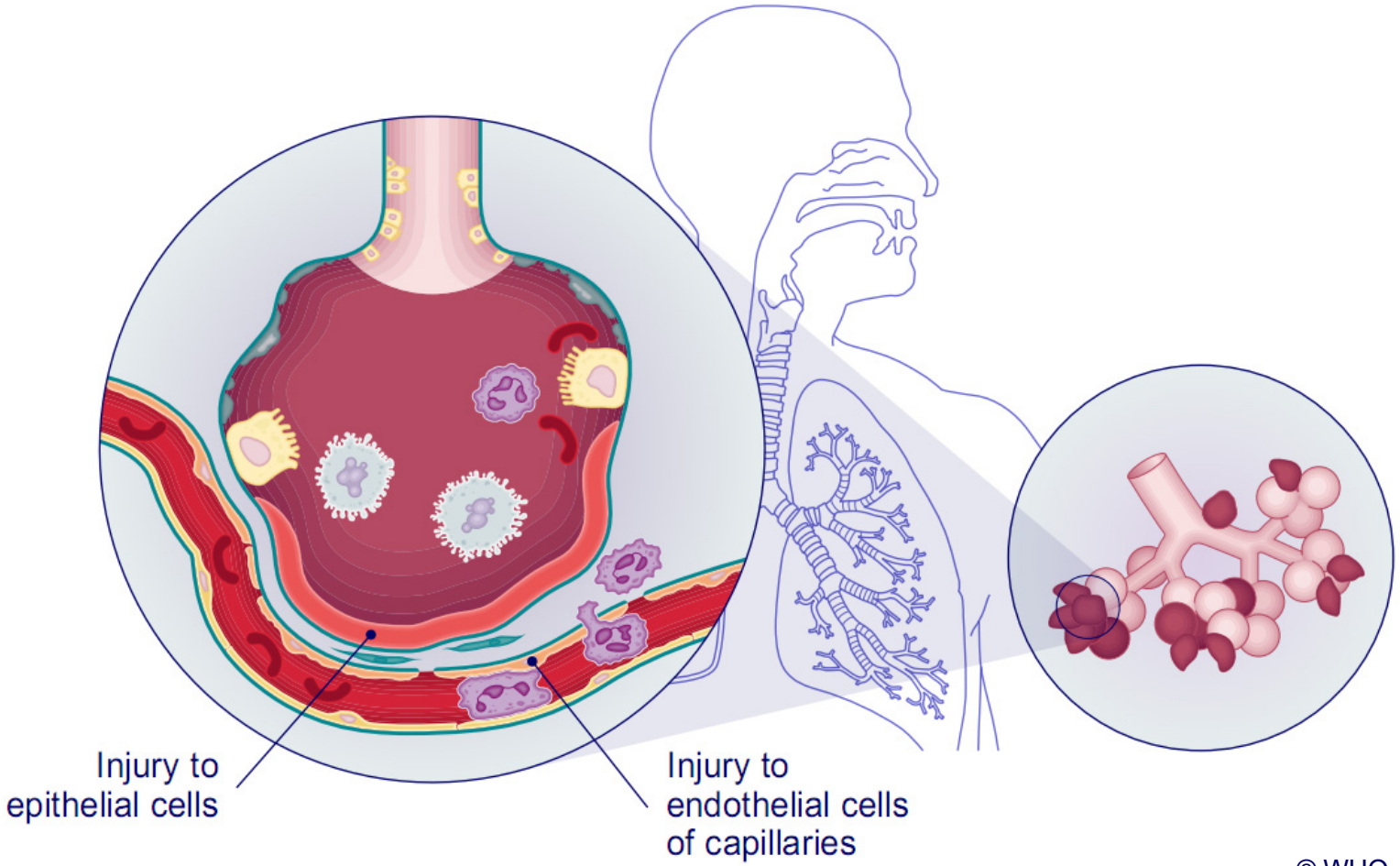
Oxygen uptake and delivery



World Health Organization

HEALTH EMERGENCIES programme

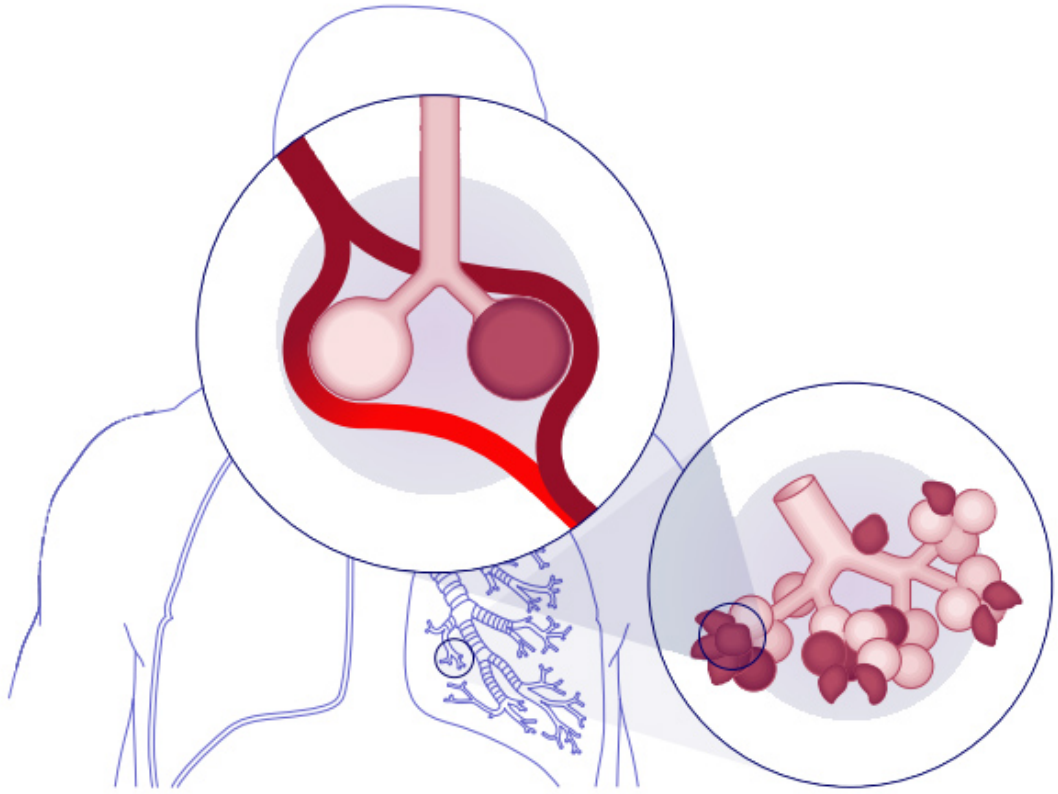
Natural history of ARDS



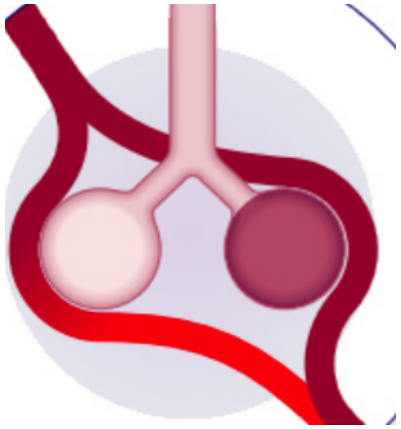
World Health Organization

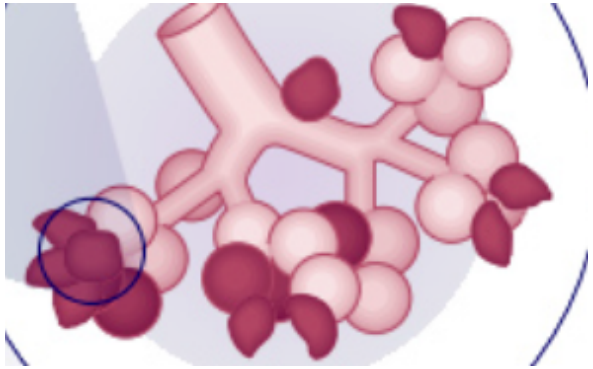
HEALTH EMERGENCIES programme

Cause of hypoxaemia in ARDS



Intrapulmonary shunt





- Severe form of ventilation perfusion (V/Q) mismatch:
  - areas of lung perfused but not ventilated (V/Q < 1).

- Increasing FiO_2 does not readily improve hypoxaemia:
  - PEEP may recruit collapsed alveoli and improve shunt.

Wasted ventilation (dead space ventilation)

- Areas of lung that are ventilated but not perfused
  - due to vascular obstruction from thrombosis or destruction associated with inflammation
  - $Vd/Vt = (PaCO_2 - P \text{ expired } CO_2)/PaCO_2$.
- If present, associated with worse prognosis in ARDS.
- Can lead to severe respiratory acidosis.

Recognize ARDS by S/F or P/F ratio

- Traditional diagnosis with arterial blood gas
  - $PaO_2 \div FiO_2$ ratio < 300
    - Partial pressure of arterial O_2 ÷ by fraction of O_2 in inspired gas.

- More easy bedside diagnosis with pulse oximeter

$SpO_2/FiO_2 < 315$

$SpO_2/FiO_2 \leq 264$

  - O_2 saturation ÷ by fraction of O_2 in inspired gas.

Summary

- **In sepsis**, infection causes a dysregulated host response leading to widespread inflammation and altered coagulation which injures the microvasculature, leading to vasodilation, increased capillary permeability, hypovolaemia, hypoperfusion, life-threatening organ dysfunction and shock (in most severe form).

- **In ARDS** there is an overwhelming inflammatory process that injures alveoli, which become flooded with protein-rich oedema fluid. Alveolar collapse creates widespread ventilation perfusion mismatch; clinically, patients present with severe and refractory hypoxaemia.

Acknowledgements

Contributors

Dr Neill Adhikari, Sunnybrook Health Sciences Centre, Toronto, Canada

Dr Janet V Diaz, WHO consultant, San Francisco CA

Dr Shevin Jacob, University of Washington, Seattle, USA

Dr Paula Lister, Great Ormond Street Hospital, London, UK