ENT 318/3
Artificial Organ

Artificial Lung

Lecturer
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Outline

- Classification and principle operation of artificial lung
- The membrane unit of artificial lung, plasma wetting
- The membrane permeance, gas transfer rate
- Blood oxygenator and flow rate of blood
- Natural lung vs artificial lung
- *In vitro* evaluation of artificial lung
Artificial Lung

- Medical device to take over or supplement the respiratory function of the lungs.

- Used in cardiopulmonary bypass (CPB) (up to 10 hours) for open-heart surgery
  - valve replacement, coronary artery bypass and transplants, congenital abnormality
  - bloodless operating field
  - blood flow through an extracorporeal circuit
  - take over the functions of heart and lung

- Extracorporeal Membrane Oxygenation (ECMO) to treat respiratory insufficiency (25-30 days).
Classification

CURRENT

EXTRACORPOREAL
External Blood Circuit
CPB and ECMO
Temporary Support

INTRACORPOREAL

PARACORPOREAL
Integrated Pump/Oxygenator
Wearable
Temporary to Semi-Permanent

INTRATHORACIC INTRAVENOUS

Surgical Implant
Semi-Permanent
Percutaneous Insertion
Temporary Support
Artificial Lung

Total Artificial Lung

- Treating chronic respiratory failure as bridge-to-transplant.
Blood Oxygenator

- A type of artificial lung which is widely used.
- **Direct contact** – Bubble oxygenator (easy to prepare and operate, low cost, cause red blood cell damage with extended operation)
- **Indirect contact** – membrane oxygenator (minimal blood trauma, higher transfer efficiencies)
  - Either **microporous polypropylene hollow fiber membranes** or one design, **silicone sheets**

How it works?
- Blood enters the oxygenator through an **inlet port** and flows either along the outside of the hollow fibers.
- Blood is then collected in a manifolded region, flows through a heat exchanger, and then exits the device through an outlet port.
- Gas can be pure oxygen or a mixture of oxygen and room air.
- Gas enters the oxygenator through a gas inlet port and flows through the inside of the hollow fibers.
- Then it exits the device via an **outlet port**.
Hollow fiber

A modern artificial lung - Capiox1 SX from Terumo Cardiovascular Systems
Principle Operation

Hollow Fiber
- Hollow of fiber membranes form basic gas exchange unit.
- Small polymer tubes, microporous walls 20 to 50 um, outer diameters 200 to 400 um.
- Made of hydrophobic polymers, often polypropylene, so that membrane wall pores remain gas-filled and respiratory gases can diffuse readily across it.

Principle Operation
- Oxygen (O$_2$) “sweep gas” flows through the inside lumens of the hollow fibers.
- Blood flows outside the hollow fibers through spaces in the hollow fiber bundle.

Figure 1.3: A schematic of CO$_2$ removal in a single fiber within an artificial lung. CO$_2$ diffuses along its gradient into the fiber where it is swept away.
Blood Oxygenator

• Characterized by rated flow as a measure of gas exchange capacity of the device.

• Rated flow is flow rate through the oxygenator at which an inlet blood saturation of 70% can be oxygenated to outlet blood saturation of 95%.
Silicone Membrane Oxygenator

- Often used in extracorporeal membrane oxygenation for respiratory support.
- Plasma leakage does not occur.
- Silicone sheet is nonporous.
- Thus thickness of sheet reduced.
- Gas exchange efficiency below that of hollow membrane.
- Resistance to blood flow also higher.

*Fig. 1 - Diagram of oxygen diffusion through a porous membrane*
Blood Oxygenator

• Fiber membranes with outer diameters of 200–400 mm
• Wall thickness of 20–50 mm
• Total membrane surface area of 2–4 m²,
• Blood priming volume of 135–340 ml.
• The arrangement of the fiber bundle and blood flow patterns differ between devices.

Fig. currently used oxygenators. From left to right: Capiox1 SX from Terumo Cardiovascular Systems, Quadrox1 from Jostra, and Affinity1 from Medtronic.
Blood Oxygenator

Diagram showing the components of a Blood Oxygenator system, including Blood Drainage, Blood Return, Drug Infusions, Roller Pump, Oxygenator & Heat Exchanger, Servo-Regulator, Oxygen Supply, and Water Heater. Additionally, images of ECMO Oxygenator Prototypes are shown, categorized as Neonatal (0.6 m²), Pediatric (1.12 m²), and Adult (2.8 m²).
Gas Exchange

- Oxygen diffuses down its concentration gradient across the fiber wall into blood.
- Carbon dioxide (CO$_2$) diffuses down its concentration gradient from the blood into the sweep gas.
- CO$_2$ removed when the sweep gas exits the device.
- O$_2$ exchange rate is:
  \[
  \dot{V}_{O_2} = K_{O_2} A (P_{O_2g} - P_{O_2b})
  \]
  where $K$ is gas exchange permeance.
- PO$_{2g}$ and PO$_{2b}$ are the average O$_2$ partial pressures in the sweep gas and blood phases.
- $A$ is the total membrane area of the hollow fiber bundle.
- CO$_2$ gas exchange rate is:
  \[
  \dot{V}_{CO_2} = K_{CO_2} A (P_{CO_2b} - P_{CO_2g})
  \]
Membrane Permeance

- Overall transfer resistance in artificial lung device:

\[ \frac{1}{K} = \frac{1}{K_m} + \frac{1}{K_b} \]

- where \( K_m \) and \( K_b \) are the membrane and blood-side permeances for each gas.
- \( 1/K_m \) represents a diffusional resistance for the membrane.
- \( 1/K_b \) represents a resistance for gas diffusing between the membrane and the flowing blood stream.

Figure: Determinants of gas exchange in artificial lungs
PCO2w represents the partial pressure of CO2 at the membrane wall.
Membrane Permeance

- Microporous hollow fibers used as membrane.
- Fixed submicron pores within the membrane wall.
- Gas exchange occurs by **diffusion** through these gas-filled pores.
- Nature of hydrophobic polymers (polypropylene) prevent blood plasma from entering fiber pores under normal condition.
Diagram of a hollow fiber membrane oxygenator and heat exchanger unit. Blood enters the heat exchanger first and flows over water-cooled or warmed coils and then enters the oxygenator to pass between woven strands of hollow fibers. Oxygen enters one end of the bundles of hollow fibers and exits at the opposite end. Oxygen and carbon dioxide diffuse in opposite directions across the aggregate large surface of the hollow fibers.
Plasma Wetting

- A process - blood plasma infiltrates the microporous walls of hollow fibers.
- A common problem when extracorporeal oxygenators are used in extended respiratory support.
- Allowing for wetting of the pores either partial /complete plasma infiltration.
- Can lead to device failure within days. Diminishes membrane permeance, Km.
- Gas phase diffusion is replaced by diffusion through stagnant plasma within fiber pores.
- Even partial plasma infiltration into fiber membranes can reduce membrane permeance and degrade artificial lung performance.

Composite Hollow Fiber Membrane

- To prevent plasma wetting.
- Incorporate a thin nonporous polymer layer as a true membrane or “skin” on the microporous fiber surface.
- True membrane blocks infiltration of plasma into pores.
Plasma Wetting

Uncoated microporous fiber

Siloxane coated microporous fiber

Composite microporous fiber
Membrane Permeance

- But, nonporous polymer skin diminishes membrane permeance because it can present an impediment to gas diffusion.
- Membrane permeance of a composite hollow fiber is dominated by the nonporous polymer layer.

\[ K_m = \frac{\alpha_p D_p}{\delta} = \frac{P_m}{\delta} \]

- \( \alpha_p \) and \( D_p \) are the solubility and diffusivity of the gas within the nonporous polymer.
- \( \delta \) is polymer layer thickness.
- \( P_m \) is the polymer permeability to specific gases.
Membrane Permeance

- The design of composite hollow fiber membranes for artificial lungs requires a Km that does not significantly reduce overall gas exchange.
  - no more than a 5% reduction in overall gas exchange
  - Km needs to be greater than 20 times Kb.

- Blood-side permeance:
  \[ K_b = \frac{\alpha_b D_b}{\delta_{bl}} \]

- where \( \alpha_b \) and \( D_b \) are the effective solubility and diffusion coefficient of the diffusing gas in blood.

- \( \delta_{bl} \) is an average boundary layer thickness.

The boundary layer thickness, \( \delta_{bl} \), depends on the local interaction between diffusional and velocity fields in the flowing blood phase subjacent to the fiber surfaces of the artificial lung.
Fig. 7  Classical diffusional boundary layer on a flat surface. $P_w$ represents the species partial pressure at the membrane wall.
Design considerations:

- **Gas exchange** – to maintain physiological O₂ and CO₂ levels in arterial blood. Gas transfer rate depend on blood flow rate and venous conditions (i.e. temperature, PCO₂, PO₂ and saturation)
  - For adult CPB, blood flow rates up to 7.0l/min
- **Priming volume** – reservoir contain a minimum blood volume 0.75-2 litres.
- minimizing the resistance to blood flow,
- easy debubbling at setup
- minimizing blood activation and thrombogenicity.
  - anticoagulant therapy
Natural Lungs vs Artificial Lung

Natural Lungs:
- Alveolar-capillary area: 100-150 m².
- Surface to blood volume ratio: 300 cm⁻¹.
- Diffusion distance: 1-2 um.
- Gas exchange rate: 200-250 ml/min at rest and 10-20 times under exercise.

Artificial Lung:
- Membrane area: 1-4 m².
- Surface to blood volume ratio: 10 times less than natural lungs.
- Diffusion distance: 10-30 um.
- Gas exchange rate: 200-400 ml/min.
- Typical flow rate: 5 l/min.
Cardiopulmonary Bypass (CPB)

- Used in open heart procedures.
- Take over function of heart and lungs.
- Blood is drained by gravity from the inferior/superior vena cava or the right atrium into a **venous reservoir**.
- Blood then pumped through the oxygenator by either a **roller** or **centrifugal pump** back into the ascending aorta.
- Blood flow during CPB is kept low (2–2.4 l/m²/min) to minimize bleeding.
- **Heat exchanger** is required to cool and rewarm the patient.
- Mixture of oxygen and carbon dioxide, is fed through flow meters and blenders into the oxygenator at flow rates of 5–10 l/min.
Cardiopulmonary Bypass (CPB)

- The oxygenator must be capable of transferring up to 250 ml/min of oxygen and 200 ml/min of carbon dioxide.
- This is to meet the metabolic needs of the patient.
- The bypass circuit also includes suction devices that are used to maintain a blood-free surgical field.
- The suctioned blood is collected and filtered in a cardiotomy reservoir and is then pumped into the venous reservoir.
- Other components include pressure and temperature monitors, sampling ports, filters, tubing, and cannulae.
Components of CPB

- Venous reservoir.
- Membrane oxygenator.
- Heat exchanger.
- Centrifugal pump.
- A microfilter-bubble trap.
Cardiopulmonary Bypass (CPB)
Extracorporeal Membrane Oxygenation (ECMO)

- Uses blood oxygenator.
- Pump-driven external circuit.
- Respiratory support, lung rest.
- Recovery for prolonged periods of time (1-30 days).
- For patients with severe lung failure.
- Adult respiratory distress syndrome (ARDS), Pneumonia, Trauma, Primary graft failure following lung transplantation.
- Similar to CPB: pump, heat exchanger, oxygenator.
- No suction equipment.
- Patient continuously anti-coagulated with heparin.
- Required blood flow: 50 ml/kg/min for adults, 120 ml/kg/min for neonates, 75 ml/kg/min for pediatric.

ECMO is essentially a modification of the cardiopulmonary bypass circuit which is used routinely in cardiac surgery.
Clinical situations initiate the ECMO

- Hypoxemic respiratory failure: (PaO2/FiO2) of <100 mmHg
- Hypercapnic respiratory failure with an arterial pH <7.20
- Refractory cardiogenic shock
- Cardiac arrest
- Failure to wean from cardiopulmonary bypass after cardiac surgery
- As a bridge to either cardiac transplantation or placement of a ventricular assist device
How ECMO Works:
The oxygenator in venovenous ECMO. The ECMO pump delivers venous blood to the oxygenator. This device is divided into two separate chambers by a semipermeable membrane. The venous blood enters the oxygenator and travels along one side of the membrane (the blood side), while fresh gas, known as sweep gas, is delivered to the other side (the gas side). Gas exchange (oxygen uptake and CO₂ elimination) take place across the membrane. The oxygenated blood is then reinfused into the patient's venous system. The composition of the gas on the gas side of the oxygenator membrane is determined by adjustment of a blender that mixes room air with oxygen for delivery into the oxygenator.
Extracorporeal Membrane Oxygenation (ECMO)

- Cannulation techniques that is used:
  - venovenous (VV)
  - venoarterial (VA)
  - arteriovenous (AV) – opposite to venoarterial.
- These terms refers to blood drainage and returns site.
- Complication: plasma wetting due to long-term exposure of oxygenator to blood.
Veno-arterial (VA) configuration

- Blood being drained from the venous system and returned to the arterial system.
- Provides both **cardiac and respiratory support**.
- Achieved by either peripheral or central cannulation

![Diagram of VA configuration]

**AV Bypass**
- Ascending Aorta – Arterial
- Right Atrium

Central ECMO Cannulation
Veno-Venous (VV) configuration

- Provides oxygenation
- Blood being drained from venous system and returned to venous system.
- Only provides **respiratory support**
- Achieved by both central and peripheral cannulation, usually of both femoral veins.

**Single Catheter in the Right Atrium**

**Peripheral ECMO Cannulation**
Central vs. Peripheral Cannulation

- Advantages

  - Flow from Central ECMO is directly from the outflow cannula into the aorta provides intergrades flow to the arch vessels, coronaries and the rest of the body.

  - In contrast, the retrograde aortic flow provided by peripheral leads to mixing in the arch.
Central vs. Peripheral Cannulation

- Disadvantages

  - Previously insertion of central ECMO required leaving chest open to allow the cannulae to exit.
    - Increased the risk of bleeding and infection
    - Newer cannulae are designed to be tunneled through the subcostal (below a rib) abdominal wall allowing the chest to be completely closed.

  - Central cannula are costly (approximately 4 times as much as peripheral)
Complications of ECMO

- **Bleeding/Hemolysis**
  - Bleeding occurs in 30 to 40 percent of patients receiving ECMO and can be life-threatening

- **Non-pulsatile perfusion to end organs**
  - Kidneys
  - ulceration and perforation, Liver impairment

- **Mechanical Complications**
  - Tubing rupture, Pump malfunction, Cannula problems (complications are rare; <5 percent)

- **Local complications: Leg ischemia**
  - Particularly at peripheral insertion site of VA

- **Air embolism/Thromboembolism**
  - Impact is greater with VA ECMO than VV ECMO because infusion is into the systemic circulation
Future of ECMO

- Include percutaneous temporary left ventricular assistance
- Low flow ECMO for CO₂ removal (ECOOR)
- Improve the simplicity and safety of ECMO, including new oxygenators, pumps, and surface coatings.
Arteriovenous Carbon Dioxide Removal (AVCO$_2$R)

- Extracorporeal type respiratory support.
- Involves blood oxygenator.
- Provide lung rest to Acute Respiratory Distress Syndrome (ADRS) patient.
- Reduce tidal volume, minute ventilation and pressure.
- Divert blood flow through femoral arterial cannula to blood oxygenator and back to femoral venous cannula.
- Removes CO$_2$ before blood returns to patient.
- No blood pump needed.
- Blood flow rate lower than ECMO.
- Dictated by arterial-to-venous pressure difference and hydraulic resistance of oxygenator.
- Oxygenator must have low hydraulic resistance.
- Adequate blood flow from arterio-venous pressure difference to remove sufficient amount of CO$_2$. 
Artificial Lung

Femoral Insertion Site

Artery to artificial lung

Artificial lung to vein
Intravascular Artificial Lung

- Gas exchange via intravenous hollow fiber membrane.
- Insertion through a peripheral vein (femoral or jugular).
- Placement in the vena cava, the largest blood vessel in the body through which blood returns to the heart.
- Intravascular artificial lungs must be compact for insertion, yet possess sufficient membrane area to achieve adequate respiratory support.
- Uses a centrally positioned pulsating balloon within a fiber bundle made from fiber fabric wrapped around the central balloon.
- Balloon pulsation pumps blood around the hollow fiber surfaces at greater blood flow velocities than would otherwise flow in the vena cava.
- Enhances gas exchange by decreasing diffusional boundary layers.
Artificial Lung

**Specification**

<table>
<thead>
<tr>
<th>Specification</th>
<th>Design target</th>
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<tbody>
<tr>
<td>O$_2$ transfer rate</td>
<td>&gt;200 ml/min</td>
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<tr>
<td>Blood-side pressure drop</td>
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<td>Blood flowrate</td>
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<td>Surface area</td>
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<td>Priming volume</td>
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Mobilization ECMO