RENAL REPLACEMENT THERAPY (RRT) PRINCIPLES OF
HAEMODIALYSIS
HAEMOFILTRATION
PERITONEAL DIALYSIS
ASSESSMENT OF GFR

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RENAL PLASMA CLEARANCE

- Clearance: Volume of plasma that is completely cleared of solute by the kidney per minute
- Clearance ratio for a substance: amount of active re-absorption or excretion
  - Ratio <1 = actively reabsorbed
  - Ratio >1 = actively excreted
- Clearance of a substance from plasma
  \[ \text{Clearance} = \frac{U \times V}{P} \text{(mL/min)} \]
  - U (conc of given substance in urine)
  - P (its conc in plasma)
  - V (urine flow rate)
- Clearance ratio = Clearance/GFR
GFR

- Clearance of any substance which is freely filtered, and is neither re-absorbed, secreted, nor metabolized by kidney
  - Substance that is both filtered and secreted by renal tubules (clearance > GFR)
  - Substance that is filtered but reabsorbed by renal tubules (clearance < GFR)

- Normal GFR
  - young men 130mL/min per 1.73m² of BSA
  - young women 120mL/min per 1.73m² of BSA

- Mean GFR declines with age
Factors affecting GFR

- Rate of blood flow through glomerulus
- Permeability of glomerular capillary wall (K)
- Surface area of glomerular capillary bed (S)
- Differences in hydrostatic pressure between glomerular capillary lumen ($P_{gc}$) and Bowmen’s space ($P_t$)
- Differences in oncotic pressure between glomerular capillary ($\pi_{gc}$) and Bowmen’s space ($\pi_t$)

\[ GFR \text{ (single nephron)} = KS([P_{gc} - P_t] - [\pi_{gc} - \pi_t]) \]

- Normally about 1/5 (120mL/min) of plasma that flows through glomerulus is filtered
- Ideal filtration marker is excreted by filtration alone
- Exogenous markers: inulin, iothalamate, EDTA, DTPA, iohexol
  - Complex, expensive, difficult in routine clinical
- Endogenous marker: creatinine
  - Freely filtered at glomerulus
  - A timed urine collection and measurement of serum creatinine conc allows calculation

\[
\text{Clearance (GFR)} = \frac{U \times V}{P} \text{ (mL/min)}
\]
EGFR

- Endogenous production of creatinine depends on muscle mass
- Therefore, serum creatinine will not only vary according to renal function (glomerular filtration), but also according to age, body size, ethnic, and sex.
OVER estimates GFR because of tubular secretion of creatinine, and the value is not adjusted for body surface area

\[ C_{CR} (\text{mL/min}) = \frac{(140 - \text{age}) \times \text{weight}}{(0.84 \times S_{Cr})} \text{ male} \]

\[ = \frac{(140 - \text{age}) \times \text{weight}}{(0.85 \times S_{Cr})} \text{ female} \]

\[ S_{Cr} = \text{serum creatinine (mM/L)} \]
THE MODIFICATION OF DIET IN RENAL DISEASE (MDRD) EQUATION

- Adjusts for body area
  \[
  \text{GFR (mL/min/1.73m}^2) = 30849 \times (S_{\text{Cr}})^{-1.154} \times (\text{age})^{-0.203} \\
  \times 0.742 \text{ if female; } \times 1.212 \text{ if black}
  \]

- The mean difference between eGFR and measured GFR ranging from -5 to 1 mL/min/1.73m\(^2\)
# CKD Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>eGFR (mL/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal / increased GFR</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2</td>
<td>Mild decrease in GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate decrease in GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe decrease GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
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</table>
DIALYSIS

- Greek **dialusis**, "διάλυσις", means **dissolution**, **dia** means *through*, and **lysis** means *loosening or splitting*
- a process for removing waste and excess water from the blood
- principles of the **diffusion** of solutes and **ultrafiltration** of fluid across a **semi-permeable membrane**
- diffusion is a property of substances in water; substances in water tend to move from an area of high concentration to an area of low concentration
Indication for dialysis in ARF

"AEIOU"

- **Acidemia** from metabolic acidosis in situations in which correction with sodium bicarbonate is impractical or may result in fluid overload

- **Electrolyte** abnormality, such as severe hyperkalemia, especially when combined with AKI

- **Intoxication**, that is, acute poisoning with a dialyzable substance. These substances can be represented by the mnemonic **SLIME**: salicylic acid, lithium, isopropanol, Magnesium-containing laxatives, and ethylene glycol

- **Overload** of fluid not expected to respond to treatment with diuretics

- **Uremia** complications, such as pericarditis, encephalopathy, or gastrointestinal bleeding
INDICATION FOR DIALYSIS IN CRF

- Symptomatic renal failure
- Low GFR (less than 10-15 mls/min/1.73m²). In diabetics, dialysis is started earlier.
- Difficulty in medically controlling fluid overload, serum potassium, and/or serum phosphorus when the GFR is very low
PERITONEAL DIALYSIS

- Uraemic toxins (e.g. urea & creatinine) and solutes (e.g. Na, K) within blood compartment will diffuse freely from the peritoneal microcirculation across the peritoneal membrane into the dialysis fluid (dialysate) within peritoneal cavity

- After a while, the fluid (effluent) is then drained out, to be replaced by fresh dialysate

- By varying the conc of dialysate, different volume of water can be removed (ultrafiltration) with each dialysis exchange, as a result of osmosis
Types of PD

- **Continuous Ambulatory Peritoneal Dialysis (CAPD)**
  - 4 self-administered exchanges of 2L of dialysate in a 24-h period
  - Expected to provide 60-65kg patient with clearance of toxins equivalent to GFR 5-7mL/min

- **Automated Peritoneal Dialysis (APD)**
  - Machine to automatically perform the drain in/out
  - Would provide 5-6 overnight exchanges whilst patient sleep
**Absolute indication** - need for RRT where other methods are contraindicated

**Relative indications** - haemodynamic compromise, clotting problems, bleeding diatheses, difficulty in obtaining vascular access, CCF, children <5, pt preference (eg. living far from dialysis centre)

**Absolute CIs** - recent abdo surgery, VP shunt, faecal or fungal peritonitis

**Relative CIs** - severe malnutrition, IBD, DD, ischaemic bowel, psychotic disorder, poor dexterity, T3 pregnancy
Tenckhoff Catheter

- LA or GA
- Open incision or laparoscopic midline below umbilicus
- Catheter tip (straight or curled) in pelvis
- Proximal catheter is tunneled subcutaneously, to an exit several centimeters from midline
- Cuff to minimise risk of translocation of infecting organisms into peritoneal cavity
Dialysate & Regimes

- Sterile, buffered with bicarbonate
- Available in several glucose concs of different osmotic strengths (1.5-4.25%) to facilitate ultrafiltration
- Some are high transporters of glucose, means that the osmotic effect of the dialysate rapidly dissipates and fluid removal is poor
- In this group, polymer-based dialysates e.g. icodextrin, may be used
Most patients do 4 exchanges per day—after waking, around noon, late afternoon, and before bed.

The dwell time (the time the dialysate stays in the abdomen) should be >4 hours.

Unless a cycler is being used (as in CCPD) no exchanges are done overnight and therefore this dwell time is long.

Since dialysate is always within the abdomen, the patient is being dialysed continuously and this therefore approximately physiology more than HD, with resulting less symptoms of disequilibrium.
PD will only usually be successful for <6 years because:

- Complications of therapy, recurrent peritonitis, encapsulating peritoneal sclerosis (EPS) or peritoneal membrane failure
- Loss of residual renal function – the success of PD relies upon most having some residual renal function (i.e. patients start PD when GFR 7-10mL/min)
Complications

- Catheter malposition or catheter blockage
- Peritonitis
  - rates <1 episode/30 patient months of therapy
  - intra-peritoneal antibiotics for 2/52
  - CONS, Staph aureus, Gram neg bacilli
  - Repeated infections lead to resistance, peritoneal membrane failure, encapsulated peritoneal sclerosis
- Ultrafiltration failure
  - due to repeated peritonitis and exposure to dialysate
Encapsulated peritoneal sclerosis (EPS)
- thickening of peritoneal membrane, reduced function and encasement of intraabdo organs
- Incidence increases with duration of PD (5% of patients after 3 years therapy)
- Symptoms; abdo pain, malnutrition, bowel obstruction, perforation

Hernia
- due to increased abdo P due to the dialysate fluid, needs surgical repair usually

Dextrose absorption can cause weight gain and hypercholaemia so patients need to modify their diets
HAEMODIALYSIS

- Blood is passed through an artificial kidney (dialyser) and returned to the body.
- Within dialyser, solute constituents of the blood are altered by exposing it to dialysis fluid across a semipermeable membrane.
- Dialyser contains hundreds tiny long tubes arranged side by side, made by semipermeable membrane.
- Tubes are bathe with dialysis fluid running in the opposite direction providing a counter current system to maximise the concentration gradient across the membrane.
Schematic diagram of hemodialysis hemodialyzer flow.
H20 molecules and low molecular weight solutes e.g. urea, creatinine and electrolytes can pass through the pores, but high molecular weight solutes e.g. plasma proteins and some drugs can't.

**Ultrafiltration** occurs by increasing the hydrostatic pressure across the dialyzer membrane.

This is done by applying a negative pressure to the dialysate compartment of the dialyzer.

Pressure gradient causes water and dissolved solutes to move from blood to dialysate, and allows the removal of several litres of excess fluid during a typical 4-hour treatment.

Blood flows through dialyser at 300-400mL/min.

Anticoagulated with unfractionated or LMWH to prevent clotting within the circuit.
Dialysis can be altered by changing:
- Electrolytes composition
- Rate of fluid removal (ultrafiltration)
- Duration of treatment

‘Dry weight’
- Body weight without excess fluid

Diet low in K, PO4

Fluid restriction <1L per day
>4hours 3x/week

Studies have demonstrated the clinical benefits of dialyzing 5 to 7 times a week, for 6 to 8 hours
- called "nocturnal daily hemodialysis"
- significant improvement in both small and large molecular weight clearance

INITIATION OF HEMODIALYSIS

- Needs sBP > 100mmHg
- In chronic setting, HD usually initiated when eGFR is between 8 and 10mL/min
- If dietary and medical therapies have failed to control fluid overload and K level
**Haemofiltration**

- has certain advantages over haemodialysis, primarily that fluid removal can be achieved gradually over a period of time
- solute movement with hemofiltration is governed by convection rather than by diffusion
- dialysate is not used
- a positive hydrostatic pressure drives water and solutes across the filter membrane from the blood compartment to the filtrate compartment
- solutes, both small and large, get dragged through the membrane at a similar rate by the flow of water
an isotonic replacement fluid is added to the blood to replace fluid volume and electrolytes

replacement fluid must be of high purity, because it is infused directly into the blood line

usually contains lactate or acetate as a bicarbonate-generating base, or bicarbonate itself

use of lactate can occasionally be troublesome in patients with lactic acidosis or with severe liver disease, because in such cases the conversion of lactate to bicarbonate can be impaired

in such patients, bicarbonate as a base is preferred
also remove accumulated extracellular fluid in a short time
highly efficient, gives good extracellular fluid volume control and can be used in the hypotensive patient
in patients with a robust circulation, intermittent haemodialysis can correct biochemical abnormalities, but is usually associated with a degree of hypovolaemia and hypokalaemia
haemodialysis may lead to gross hypotension and cardiac arrhythmias due to rapid removal of volume
with continuous veno-venous haemofiltration almost any quantity of fluid can be removed over a 24-hour period, thus allowing for administration of other fluid, e.g. parenteral nutrition
Venous blood from patient

Pump

Heparin

Ultrafilter (permeable hollow fibres)

Replacement fluid

To patient’s vein

Ultrafiltrate

Haemofiltration circuit
HAEMODIAFILTRATION

- combination of haemodialysis and haemofiltration
- can be achieved if the space surrounding the highly permeable membranes of the machine is perfused with a dialysate solution, so that diffusion down a concentration gradient can occur across the membrane
- Haemodiafiltration results in:
  - improved solute clearance
  - slower rates of ultrafiltration
  - easier management of fluid balance
Haemodiafiltration circuit

Venous blood from patient

Pump

Heparin

Ultrafilter (permeable hollow fibres)

Replacement fluid

To patient's vein

Dialysate

Dialysis fluid

Out

In
**TERMS**

- **SLEF** (slow extended hemofiltration) =
- **CHF** (continuous hemofiltration) =
- **CVVH** (continuous veno-venous hemofiltration) =
- Continuous Renal Replacement Therapy (CRRT)

- *(SLED-F or CHDF or CVVHDF)*
  - =haemodiafiltration

Native access for hemodialysis (e.g. AVF or grafts) are unsuitable for CHF because the prolonged residence of the access needles required might damage such accesses.
**Complications**

- Early complications of subclavian or internal jugular placement include pneumothorax, arterial injury, thoracic duct injury, air embolus, inability to pass the catheter, bleeding, nerve injury, and great vessel injury.
- Thrombotic complications occur in 4% to 10% of patients.
- Infection (3 to 5 days) or late in the life of the catheter and may be at the exit site or the cause of catheter-related sepsis.
- Rate of infection between 0.5 and 3.9 episodes per 1000 catheter-days.
- Catheter thrombosis increases the incidence of catheter sepsis.