REVISE NEPHROLOGY

A brief overview of Hemodialysis
Sep 2023

Take home points

- Physiology of Hemodialysis (HD)-diffusion and ultrafiltration (UF)
- Fundamental difference between HD and hemofiltration (HF)
- Concept of membrane efficiency and flux
- Vascular access for HD
- Dosing and adequacy
- Complications
- HD usage roughly 4 times that of PD for maintenance dialysis in Australia and New Zealand

Some data on renal replacement therapy on 31st Dec 2020 (HD usage about 4 times of PD)

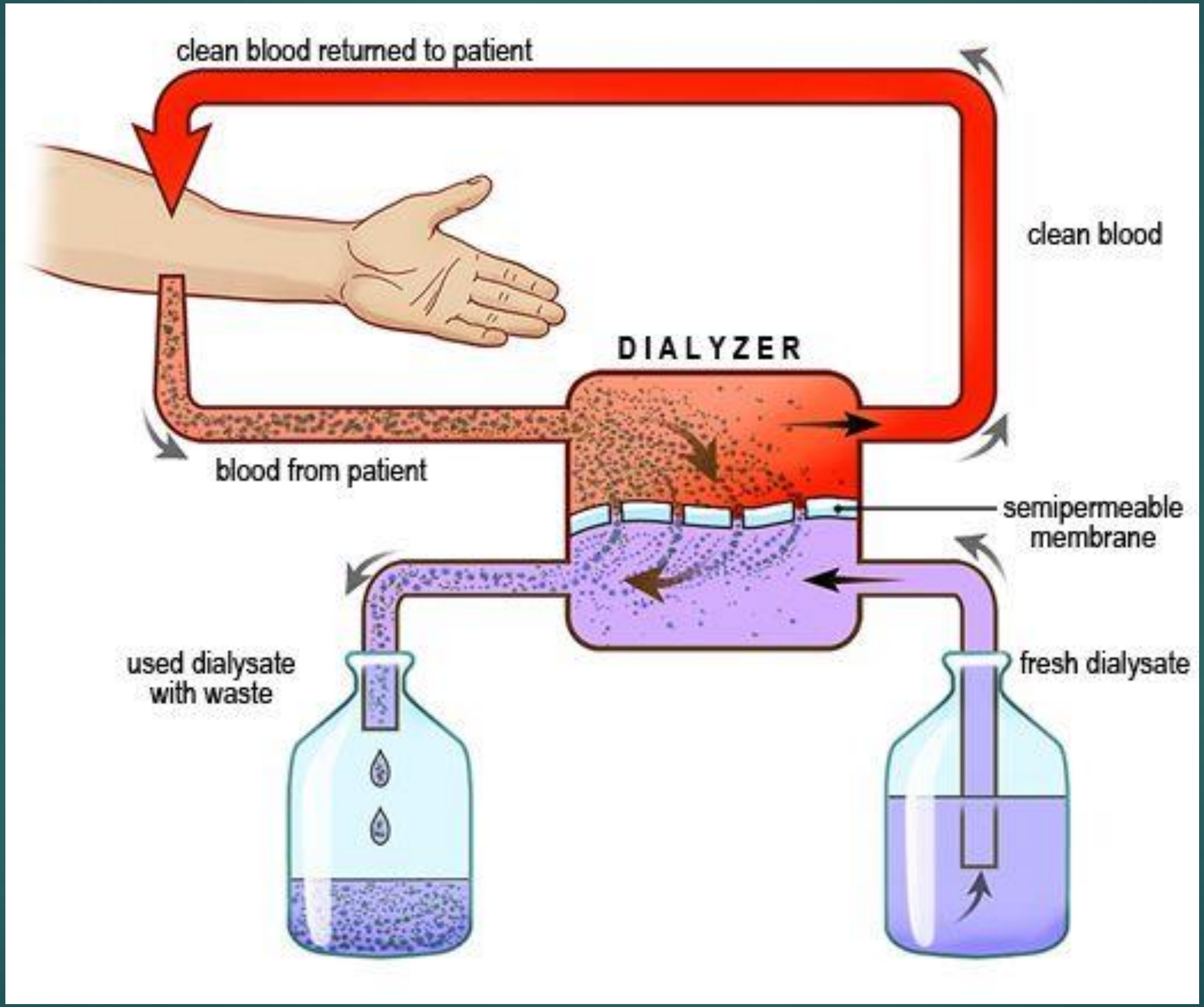
ANZDATA-Australia and New Zealand Dialysis and Transplant Registry

Total new RRT in 2020	Australia	New Zealand
Total new dialysis in 2020	3174	665
Total new transplant in 2020	885	187
Total prevalent dialysis patients	14554	3004
Total prevalent transplant patients	13130	2199

Principles of Hemodialysis (HD)

- Haemodialysis (HD): The solute composition of blood is altered by exposing it to another solution (dialysate) across a semipermeable membrane
- Two main mechanisms involved in solute and water removal:
  - Diffusion: Solutes removed by random molecular motion
  - Ultrafiltration (convective transport): Positive hydrostatic pressure causes solutes to be dragged along with water across the semipermeable membrane
- High-efficiency membrane: A bigger membrane leads to better solute clearance
- High flux membrane: Larger pores allow passage of bigger molecules like B2-macroglobulin as well as more water

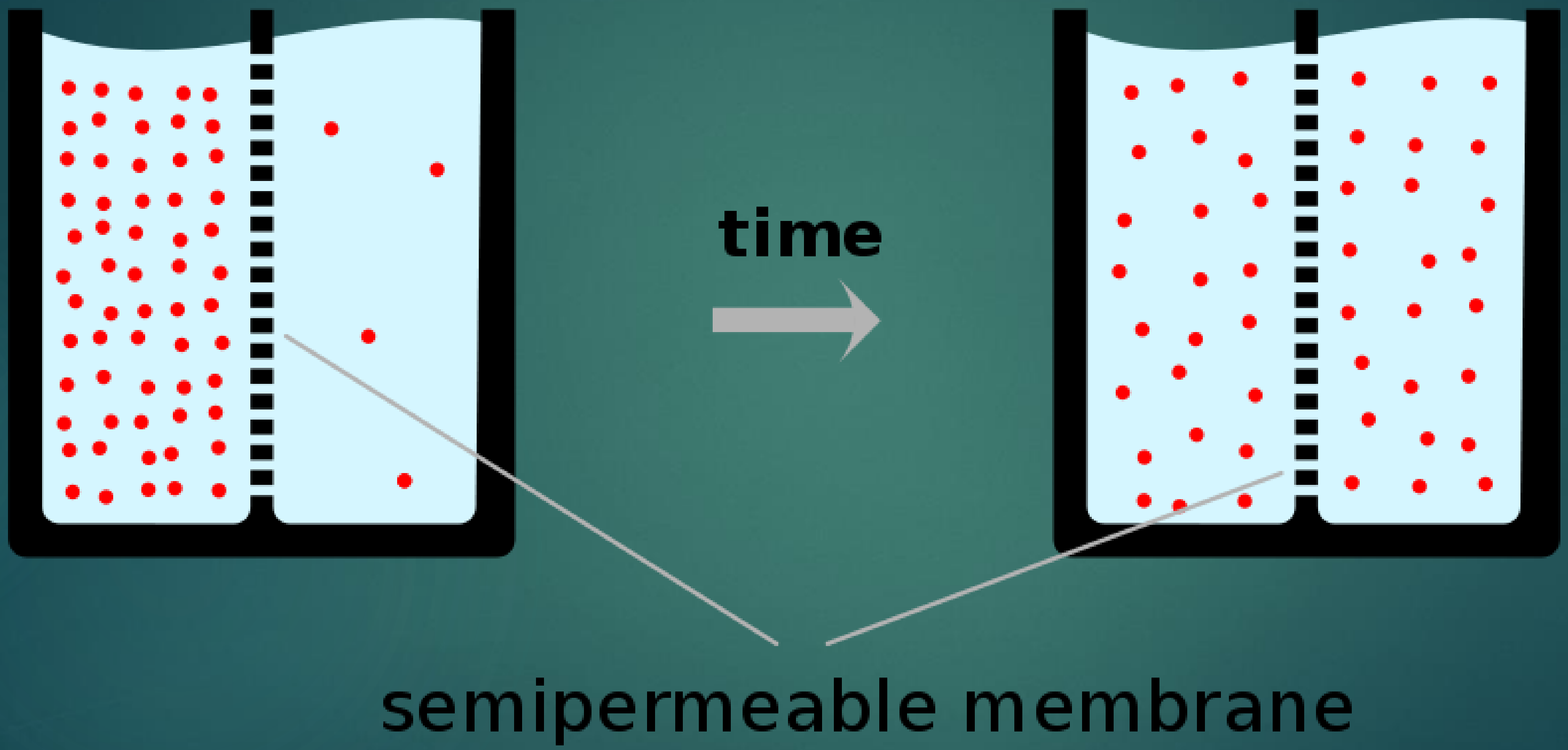
HD simplified diagram



Diffusion in HD

- Diffusion is the net movement of molecules from a region of high concentration to a region of low concentration
  - Smaller molecules more likely to move at higher velocities and cross the membrane
  - Urea (MW 60 Daltons) crosses more easily than creatinine (MW 113 Daltons)
  - Can be bi-directional

Diffusion



Ultrafiltration

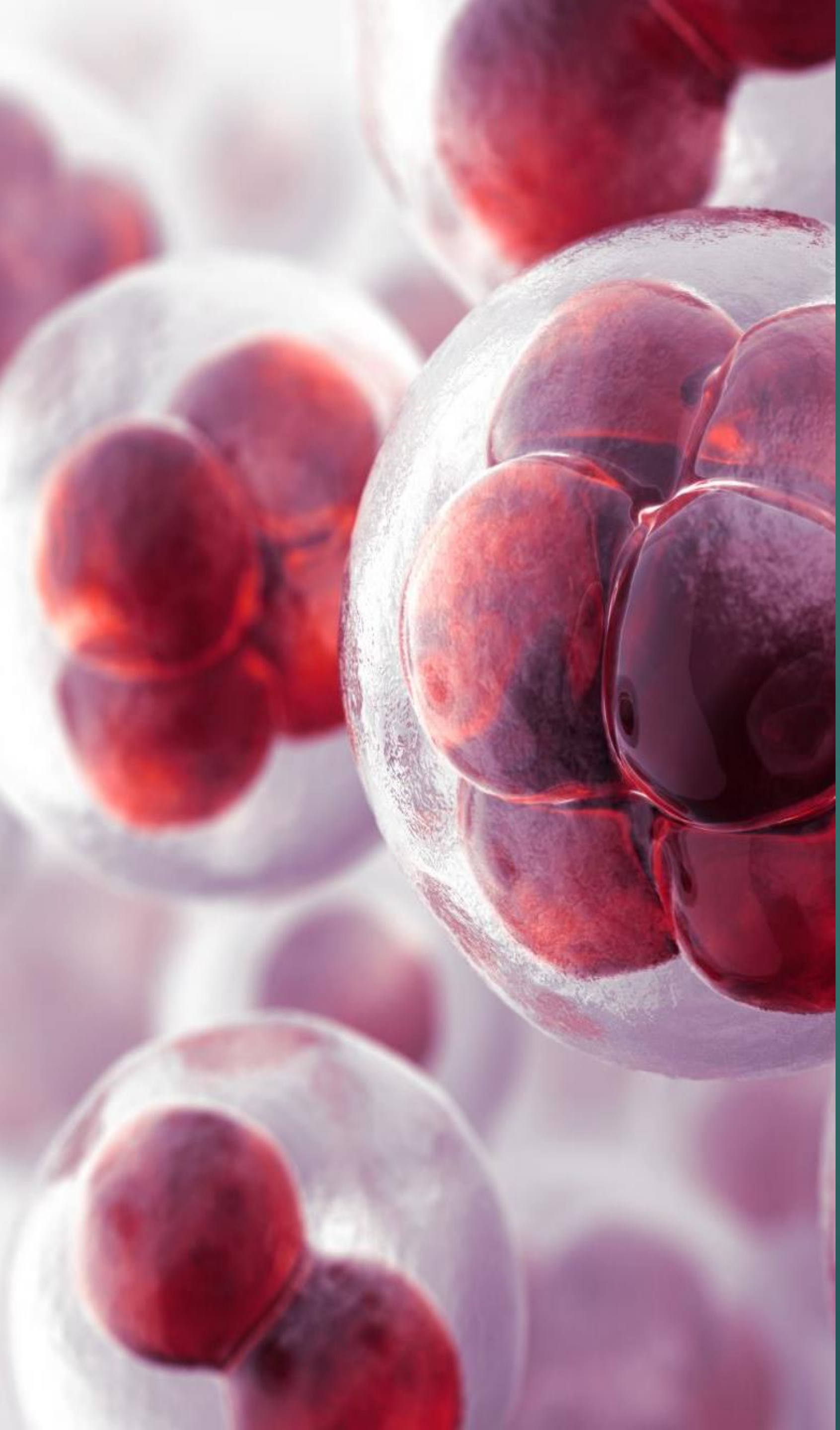
- Ultrafiltration (UF): Positive pressure across the membrane drives water across the membrane (convective transport)
  - Solutes are dragged across the membrane with water (solvent drag)
  - Molecules smaller than the pore size of the membrane dragged equally i.e., urea and creatinine cleared equally
  - Unidirectional movement
  - Not affected by blood and dialysate flow rates (depends on the transmembrane pressure-TMP)
  - Typically, is a hydrostatic process and not osmosis driven in contrast to UF in peritoneal dialysis

Convection

HD versus PD- some facts

- PD modality lasts for 2 – 3 years on average with loss of efficacy and residual renal function over time
- Less cardiovascular instability
- Performed at home everyday
- Can't go swimming ☹

- HD can be continued indefinitely
- Higher dialysis dose achievable
- Dialysis free days
- Can be done at home
  - If you can drive a car you can do home haemodialysis
  - If you do home haemodialysis you can do 2nd daily dialysis and avoid the 2-day gap



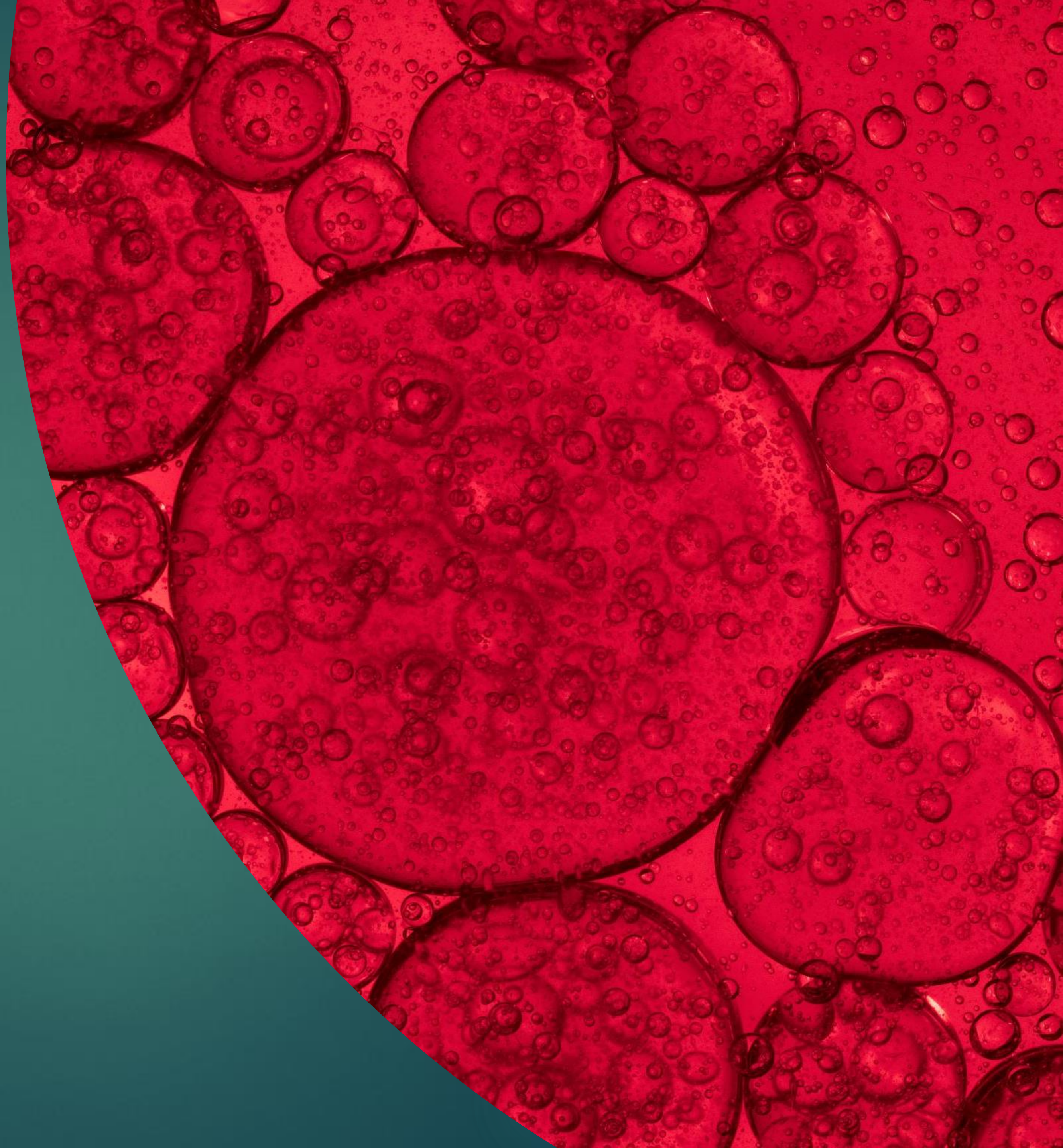
Hemofiltration and hemodiafiltration

- Hemofiltration (HF) uses only convection and no diffusion
  - large volume of replacement fluid (25 to 50 L per day) infused into either the inflow or outflow blood line and both this replacement fluid and excess fluid in the patient are removed by UF
  - Larger sized molecules cleared better by HF in comparison to HD
  - Used in the slow, continuous renal replacement therapies (CRRT) for the sick and hypotensive patient in ICU
  - No dialysis fluid (dialysate) needed

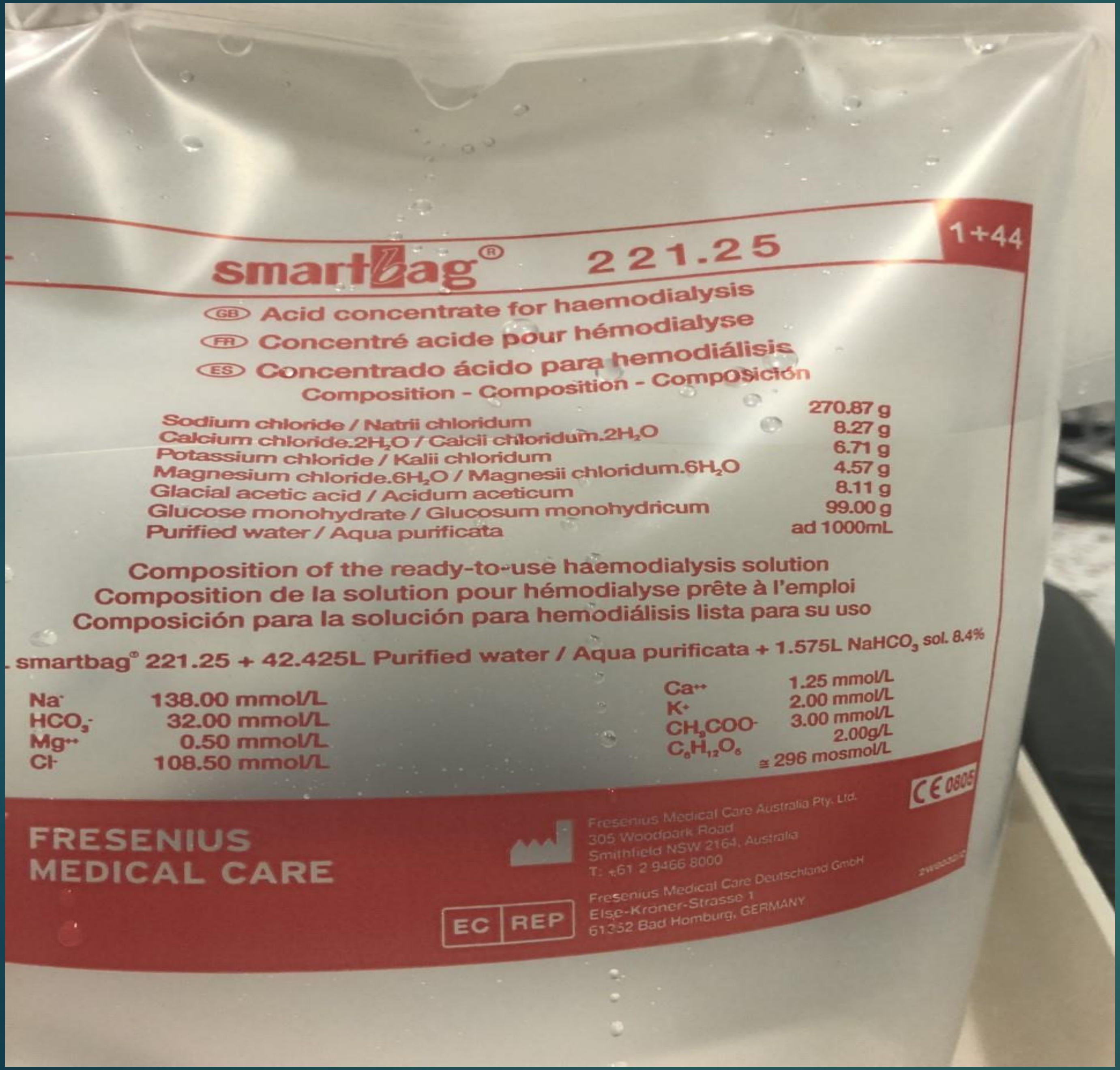
- HDF utilizes convective in combination with diffusive clearance i.e., combination of HD and HF (More expensive than HD)
  - HDF allows increased clearance of larger-molecular-weight molecules compared to HD
  - HDF requires the infusion of significant amounts (usually 15 to 30L per session) of infusate to replace the ultrafiltrate
  - Better tolerated in those with lowish BP

Hemodialysis Circuit

- The dialyzer contains two solutions blood and dialysis fluid(dialysate) separated by a semipermeable membrane
- Dialysis fluid contains sodium, potassium, calcium, magnesium, chloride, bicarbonate and dextrose
- If blood and dialysate were left in static contact with each other via a membrane, the concentrations of urea and creatinine would equalise and no more transfer would happen
- Above prevented by continuously refilling both the compartments and running the fluids countercurrent to each other



Fresenius bag



Kuf and KoA: high flux VS high efficiency membranes

- Ultrafiltration coefficient (Kuf): Number of mls of water transferred per hour across the membrane per mm Hg pressure gradient
  - Is a function of the membrane thickness and pore size
  - *High flux membranes* (larger pores) *have Kuf> 10 (usually >20) mL per hour per mm Hg*
- KoA is the maximum possible clearance of a toxin (usually urea) in mL/min by a dialyzer at infinitely large blood and dialysate flow rates
  - KoA helps us to compare the efficiency of dialyzers
  - Usual efficiency dialyzers have KoA values for urea between 500-700mL/min while *high efficiency dialyzers (bigger membranes) have KoA>700 mL/min*

Efficiency versus flux of membranes

- High efficiency dialyzer is basically a big dialyzer that by virtue of large size can remove more urea (MW 60)
  - KoA > 700 mL/min and urea clearance >210mL/min @ blood flow rate 300mL/min
  - **High efficiency dialysers needs good blood flow> 200 ml/min to be actually efficient**
- High flux dialyzer has bigger pores that can pass larger molecules
  - High flux dialyzers also have high water permeability and therefore Kuf >10 mL/min/mm Hg (usually>20 mL/min/mm Hg)
  - Remove molecules with MW up to 20 kDa (beta2-microglobulin has MW 11.8 kDa)
  - Flux also defined by its clearance of beta2-microglobulin, with rates of <10, 10 to 20, and >20 mL/min denoting a low-, mid-, and high-flux membrane, respectively
- **High cut off dialysis membrane used in myeloma can remove molecules with up to 65 kDa size (albumin sized 55-60 kDa, Ig light chain-25 kda)**

Molecular size in Daltons- a comparison

- Small
  - Sodium (23)
  - Phosphate (31)
  - Potassium (35)
  - Urea (60)
  - Creatinine (113)
- Medium
  - Vitamin B12 (1355)
- Large
  - Inulin (5200 or 5 kDa)
  - B2 microglobulin (11800 OR 11.8 kDa))
  - Immunoglobulin light chain (25000 OR 25 kDa)
  - Albumin (55000-60000 OR 55 to 60 kDa)

Vascular Access in HD

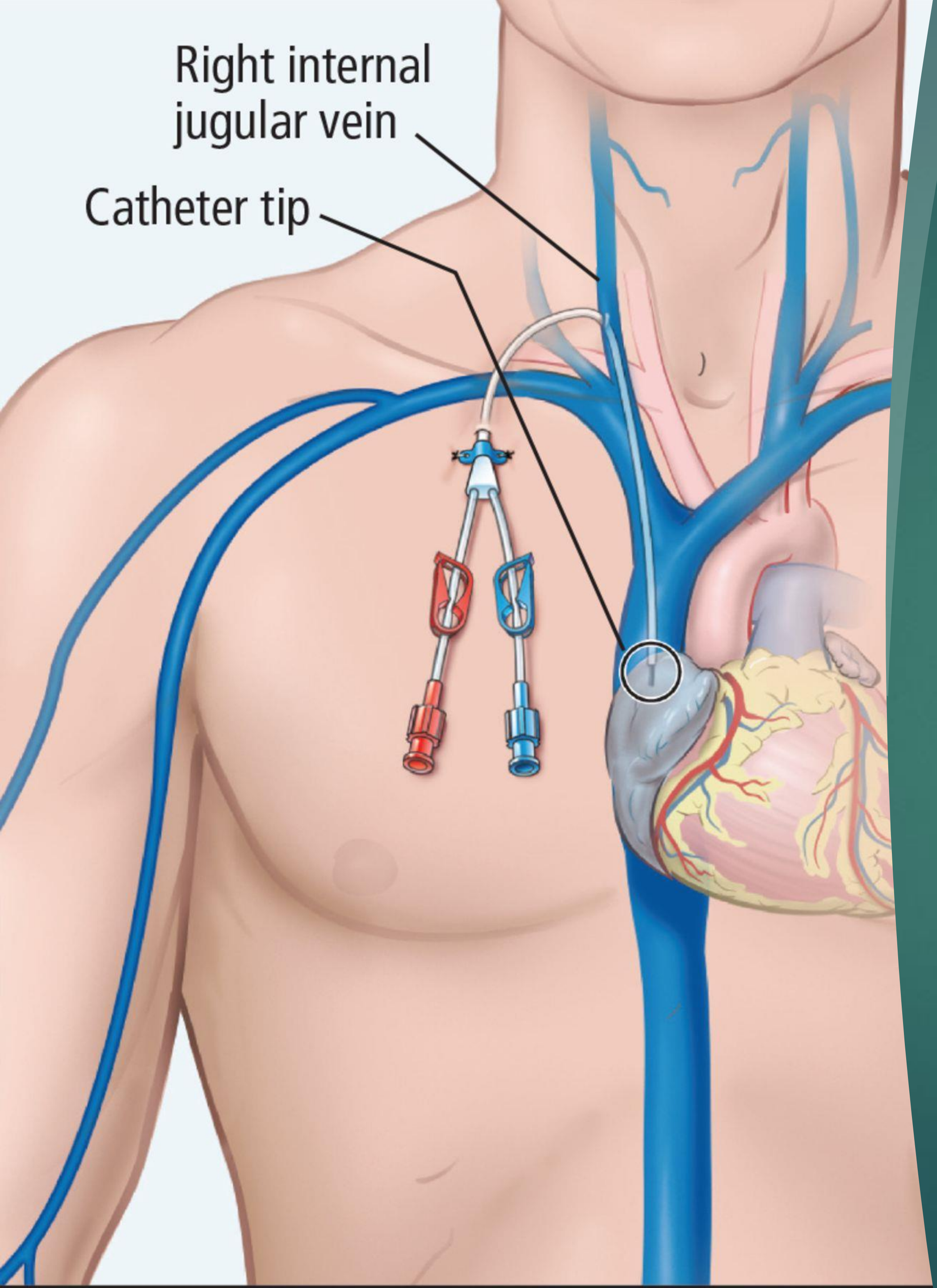
- Needs to be able to support a dialysis circuit flow of 300mL/minute
- Preference serially
  - AV fistula: An AV fistula is a deliberate connection between a native artery and vein and is typically constructed with an end-to-side, vein-to-artery anastomosis
  - AV grafts: Constructed by interposing graft material between an artery and vein.
  - Tunnelled dialysis catheters: Tunnelled, cuffed central venous access dual-lumen catheters
- <u>**AV fistulas associated with the lowest complication rates**</u>
- Guidelines recommend limiting use of non tunnelled catheters to one week only

Arterio-venous fistula (AVF)

- A surgical connection between an artery (high pressure) and a vein (low pressure)
- Creates a vein with continuous pulsatile high-volume flow (typically more than 500mL/minute)
- Two needles are then inserted to remove and return blood from the fistula/patient

Arterio-venous grafts

- A loop of synthetic material is connected between the artery and vein
- Needles are inserted directly into the graft to remove and return blood for dialysis
- Prosthetic material is prone to clotting and infection
- Uncommon in Australia (< 20% of total)



Hemodialysis Catheters

- Inserted into a large volume central vein
- Two lumens-one for removal and blood and one for return
- Each lumen is separated to minimise mixing of blood
- Highest infection rate, infections are often serious
- Used in 10-20% of Australian patients

Catheter related bacteremia (CRB)

- Average rate is 1 episodes per 1000 catheter days (2-3 years) for a tunnelled line (AV fistula rate of infection is 1 per 30-40 years)
- 40-80% gram positive for Coagulase-negative staphylococci and S. aureus
- S aureus CRB associated with ***20-30% mortality***
- ‘Around catheter’ contamination more common than ‘inside catheter’
- Higher in
  - Patients with diabetes
  - Non tunnelled lines
  - Femoral>internal jugular>subclavian

Treatment of CRB

- Always assume the catheter is source of infection in a febrile dialysis patient until proven otherwise
- Cultures from catheter and peripheries
- Mandatory removal (send tip for culture) if
  - Non tunnelled line
  - Severe sepsis in tunnelled line
- Broad spectrum antibiotics
  - Empiric Cephazolin or vancomycin/linezolid if MRSA/ VRE colonised
  - Include gram negative cover with gentamicin 80 mg
  - 14 days treatment for S aureus
- Evaluate for metastatic infection (endocarditis, osteomyelitis, epidural abscess) if persistent fevers or bacteraemia

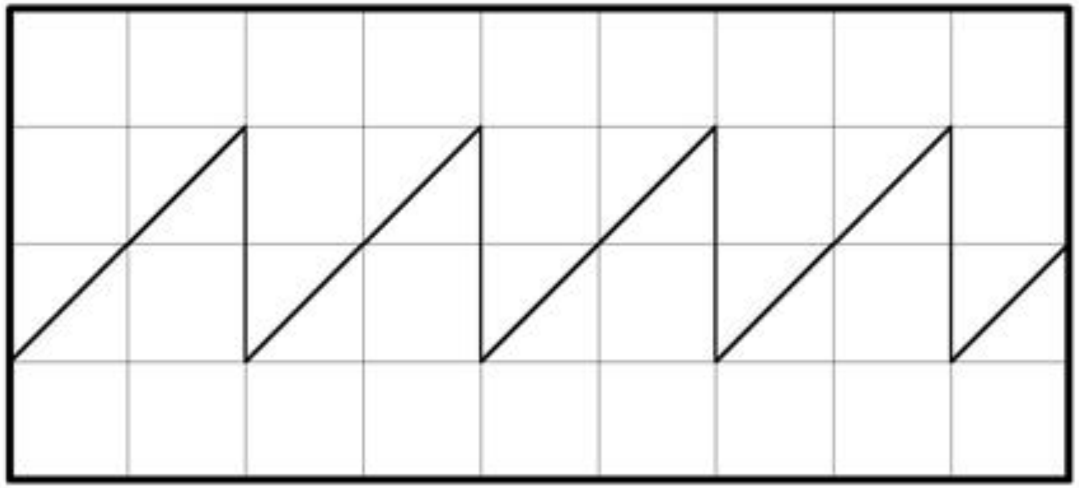
HD in Australia

Conventional HD in Australia

- Typically given 3 times weekly, 4-5 hours per treatment, 2-4L of fluid removed each treatment
- Centre based in 90%, no membrane re-use
  - Hospital centre
    - Resource intensive
    - 77Kper year per patient
  - Satellite or community centre
    - Lower infrastructure costs
    - 67K per year per patient
  - Home
    - More flexible, costs 48K per year per patient

Sawtoothing- Consequence of intermittent HD

- Solutes and fluid removed during HD and gradually accumulate between dialysis sessions
- More pronounced in Mon/Wed/Fri HD patient with no HD over weekend
- All cause mortality higher in HD patients after long interval



HD associated complications

- **Intradialytic Complications**
  - Hypotension – 25 to 55 percent of treatments
  - Cramps – 5 to 20 percent
  - Nausea and vomiting – 5 to 15 percent
  - Headache – 5 percent
  - Chest pain – 2 to 5 percent
  - Back pain – 2 to 5 percent
  - Itching – 5 percent
  - Fever and chills – <1 percent
- **Interdialytic Complications**
  - Fluid overload
  - Hyperkalaemia
  - Thrombosis of a haemodialysis catheter or arteriovenous access

Intradialytic hypotension

- Target or dry weight set too low: extent of ultrafiltration is too high
- Rate of ultrafiltration is too fast
- Rate of plasma refilling is too slow
- Underlying cardiac insuffiency
- Excessive anti-HTN therapy
- Impaired plasma refill due to low serum albumin
- ‘Reverse plasma refill’ occurs: more likely when the pre-dialysis urea, glucose or sodium (contributors of plasma osmolality) are excessively high
- Mechanisms to maintain blood pressure during dialysis are impaired (usually due to diminished cardiac reserve or autonomic neuropathy)
- Diversion of blood to GIT due to meal during dialysis

Management of intradialytic hypotension

- Lie patient flat or in the Trendelenburg position, where the body is laid flat on the back with the feet higher than the head by 15 to 30 degrees; administer oxygen if unconscious
- Turn off machine ultrafiltration
- Infuse 200-500mL of normal saline via venous line (or fluid replacement bolus in patients on hemodiafiltration)
- Consider whether the hypotension is unrelated to the dialysis treatment itself e.g. due to sepsis, blood loss, myocardial infarction, or pulmonary embolus
- Avoid meals during dialysis

Muscle cramps

- Thought to be due to hypotension, hypovolemia (excess fluid removal), need for high UF (due to excess water intake in inter-dialytic period)
- Pre dialysis quinine sometimes helpful
- Carnitine supplementation
- BEWARE of hypocalcaemia, hypokalaemia or hypomagnesemia causing cramps

Intradialytic haemolysis

- Usually presents with chest pain or tightness, backpain, and dyspnoea
- Signs include port-wine appearance of the blood in the venous line, pink discolouration of plasma in centrifuged specimens, rapidly falling haematocrit and sometimes a dramatic deepening of skin colouration
- Causes include:
  - Overheated dialysis solution
  - Hypotonic dialysis solution
  - Dialysis solution contamination with formaldehyde, bleach, chloramine, fluoride or nitrates from the water supply and copper from copper tubing or piping
  - Blood line obstruction or narrowing due to kinks

Intradialytic haemolysis management

- If not detected early, haemolysis can lead to severe hyperkalaemia due to release of potassium from the damaged erythrocytes
- Stop dialysis immediately, clamp the blood lines (to prevent return of blood to avoid increasing the risk of hyperkalaemia)
- Treat hyperkalaemia and the potentially severe anaemia

Why is HD never truly adequate

- Small proportion of ‘renal function’ is replaced
  - 10-15% for ‘standard’ therapies-i.e., three treatments per week
  - 20% for extended or daily treatments
  - Residual renal function is critical to total amount of ‘renal replacement’ provided
- Poor removal of some toxins (e.g., phosphate, beta-2 microglobulin)
- Wide swings in fluid state occur
- Does not correct endocrine functions of kidney
  - Supplemental treatments are needed for anemia and bone disease
- Heightened cardiovascular risk remains
- Treatment itself introduces further risk of complications (e.g., infection complicating access) and problems (e.g., inconvenience, cost, travel)

Dialysis initiation

- Average GFR at initiation is 5-10mL/minute
- Conventional indicators are (my rule of 4Ps)
  - High potassium- not responding to medical management
  - Low pH (metabolic acidosis)- not responding to medical management
  - Pulmonary oedema
  - Pericarditis

- And uremic symptoms including encephalopathy and intractable itching

HD dosing and prescription

- More dialysis is better but is a trade-off
- Dialysis is never truly ‘adequate’
- The most effective way of providing more dialysis is by longer duration treatments
- Urea removal markers (kT/V)
  - Loom large in dialysis literature
  - Actually unrelated to dialysis survival
  - Easy to manipulate
- Basic HD prescription incorporates
  - Frequency and duration
  - Anticoagulation
  - Targeted dry weight (enables calculation of fluid removal)

Prognosis

- According to the United States Renal Data System (USRDS) 2018 report, for patients starting dialysis in 2011, the adjusted five-year survival from day 1 was 52 percent for patients on peritoneal dialysis and 42 percent for those on haemodialysis (worse in diabetics)
- Observed survival is best in patients treated with home hemodialysis:
  - 89 percent at 5 years
  - 74 percent at 15 years in nondiabetics
  - 50 percent at 15 years overall
- While the leading cause of death is cardiovascular , the 2nd commonest is withdrawal
- Australian data:

  https://www.anzdata.org.au/wp-content/uploads/2019/09/c03_mortality_2018_ar_2019_v1.0_20191202.pdf

Thank you

I don't care what day it is.
Four hours is four hours.