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Concepts

Dialysis

Dialysis is a process by which solutes and water are removed from the vascular space. It is used primarily as an artificial replacement for lost kidney function in people with acute and chronic renal failure.

The main principles by which dialysis works are diffusion of solutes and ultrafiltration of fluid across a semi-permeable membrane. Blood flows on one side of a semi-permeable membrane and dialysis fluid (dialysate) flows on the other side. A concentration gradient exists between the blood compartment and the dialysate compartment. Solute movement is determined by this concentration gradient, with solutes moving from a compartment of high concentration to one of low concentration. Only substances, including fluid, in the vascular space can be dialyzed. Thus, if a patient has significant capillary leak and extravasation of fluid to the extravascular space, methods may be required to promote movement of that fluid into the vascular space so that it is available for removal with dialysis.

There are two types of dialysis - peritoneal dialysis (PD) and hemodialysis (HD). Choosing the mode of dialysis appropriate for a given patient depends on the local resources and expertise, as well as the child’s specific clinical condition. In HD, the membrane is housed in a filter which contains thousands of hollow core fibers through which blood flows. The large number of fibers allows for a greater surface area by which to facilitate diffusion. Dialysate flows in the countercurrent (opposite) direction to blood flow in order to optimize diffusion by maintaining a large gradient between blood and dialysate. Waste and water move from the blood, across the membrane, and into the dialysate.
**Diffusion**

Diffusion refers to the movement of solutes from an area of high concentration to an area of low concentration. Only substances to which the membrane is permeable can diffuse across it, and the diffusion properties are specific for a given substance. Properties of dialyzable molecules include low molecular weight, water soluble (i.e. not lipid-bound), and not protein-bound. However, many toxins that are protein-bound may have metabolites which are not protein-bound. Thus, the characteristics of both the primary toxin and its metabolites should be considered when determining if HD will effectively remove toxic compounds.

In HD, the membrane (thousands of core fibers) is housed in a filter. When choosing a filter, the coefficient of urea ($K_{d\text{ urea}}$) is used to estimate the overall clearance that can be achieved with a particular blood flow. The $K_{d\text{ urea}}$ is documented for filter brand and size, and it varies based on the blood flow rate.

In dialysis, we can take advantage of diffusion by adjusting the concentrations of different substances:

- By having a low concentration of a substance in the dialysate, we promote movement of undesired substances out of the bloodstream and into the dialysate. This is called clearance of solutes. For example, using dialysate with low potassium concentration will promote movement of potassium from the blood into the dialysate.
- By having a high concentration of a substance in the dialysate, we promote movement of desired substances into the bloodstream. For example, using dialysate with a higher calcium concentration will result in minimal losses from the blood.

Sodium, potassium and calcium are the compounds that may be adjusted in dialysate during HD. Whereas, bicarbonate and dextrose are compounds that are not typically adjusted in dialysate during HD.

![Figure 2. Diffusion of potassium from high concentration (blood) to low concentration (dialysate).]
Ultrafiltration

Ultrafiltration (UF) is the term used in dialysis to quantify the net removal of water. Ultrafiltration is the movement of water across a pressure gradient. In HD, ultrafiltration is achieved by inducing a pressure gradient to drive ultrafiltration.

When performing HD, the volume of ultrafiltration desired is programmed into the machine. The machine will often alarm if the pressure needed to achieve the desired ultrafiltration is too great. However, it is possible to remove too much fluid without the alarm signaling. Hence, close monitoring of vital signs during dialysis is critical to ensure delivery of a safe treatment.

The goal for ultrafiltration is patient-dependent. Variables to consider in setting the ultrafiltration goal for a patient include:
- Pre-existing degree of volume overload
- Hemodynamic status
- Respiratory status
- Ongoing urine output
- Changes in daily weight
- Total input and output fluid balance
- Length or duration of the dialysis session

If the desired ultrafiltration cannot be achieved in the same time that is required for the desired clearance, one can continue with ultrafiltration in order to achieve the desired effect. This is done by turning off the dialysate, which limits diffusive clearance, but continues ultrafiltration.

Figure 3. Movement of water across a pressure gradient.
Convection

Convection refers to movement of solute and fluid across a semi-permeable membrane due to a hydrostatic pressure gradient. The hydrostatic pressure gradient causes fluid to flow across the membrane, taking solutes with it by mass transport (also called solvent drag). Both the kidneys and dialysis take advantage of diffusion and convection to achieve solute and fluid removal.

The rate of convection depends upon:
- hydrostatic pressure
- porosity of the membrane
- volume or rate of ultrafiltration (With no ultrafiltration, there is little or no convective clearance. With high volume or rates of ultrafiltration, there is more convective clearance.)

Figure 4. Movement of solute and fluid due to a hydrostatic pressure gradient.
Clearance

Clearance is the term used in dialysis to quantify or measure the removal of molecules or solutes, such as urea or creatinine. Both diffusion and convection contribute to clearance of molecules. Thus, adjusting either the concentration gradient and/or the ultrafiltration rate will alter the clearance rate. In intermittent HD, clearance is dependent on the blood flow rate.

Typically in HD, diffusive clearance is much greater than convective clearance. However, during high rates of ultrafiltration, convective clearance may contribute significantly and should be considered when assessing clearance goals.

Indications

HD may be indicated for:

a. Children with acute or chronic kidney injury who require:
   - Ultrafiltration—for volume overload and/or provision of necessary therapies that result in fluid accumulation, such as IV medications or nutrition
   - Solute clearance—for hyperkalemia, hyperammonemia, uremia, metabolic acidosis, and other metabolic by-products
   - Removal of dialyzable toxins or drugs that cannot be cleared sufficiently with other medical maneuvers. Note that for toxin or drug exposures, HD provides much greater clearance per hour than PD, and thus HD should be undertaken if possible.

b. Patients requiring dialysis but who have had recent abdominal surgery, prohibiting the use of PD.

c. Patients requiring dialysis but who have conditions that do not allow for PD, such as gastroschisis, omphalocele, or congenital diaphragmatic hernia.

d. In cases where PD has failed.

Relative Contraindications

- Hemodynamic instability leading to inability to perform HD
- Lack of vascular access options
- Severe bleeding or risk of bleeding in which anticoagulation is prohibited
- Premature infants who are too small
**Access**

**Temporary Catheters**
Temporary catheters are indicated in patients when dialysis is likely to be required for a brief period, are too ill to undergo placement of a permanent catheter, or have limited access options.

Temporary catheters vary in size and are typically uncuffed and untunnelled. They can be inserted at the bedside under sterile technique, preferably with direct ultrasound guidance or fluoroscopy by an experienced practitioner to ensure accurate central placement. They are sutured into place and secured with a sterile occlusive dressing.

**Permanent Catheters**
Permanent catheters are indicated in patients where dialysis is likely to be required for a longer period of time, and are usually placed electively, not emergently.

Permanent (semi-permanent) catheters vary in size, have an internal cuff, and are tunneled under the skin to provide additional anchoring for the catheter, as well as additional protection from infection. They are placed with sterile technique, often by surgeons or interventional radiologists, and sutured into place and secured with an occlusive dressing.

**Catheter Size**
In order to ensure that adequate blood flow can be achieved during HD, select the largest possible catheter size appropriate for the patient. Catheter sizes range from 6 to 14.5 French, and vary between institutions. The length of the catheter also varies and must be selected based on patient size to ensure that the catheter tip is centrally located.

<table>
<thead>
<tr>
<th>Patient's Weight</th>
<th>Catheter Size</th>
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<tbody>
<tr>
<td>&lt;10 kg</td>
<td>6-8 French</td>
</tr>
<tr>
<td>10-25 kg</td>
<td>8-10 French</td>
</tr>
<tr>
<td>25-55 kg</td>
<td>10-12.5 French</td>
</tr>
<tr>
<td>&gt;55 kg</td>
<td>12-14.5 French</td>
</tr>
</tbody>
</table>

Table 1. Typical catheter sizes based on patient’s weight.
Catheter Location

HD catheters are placed in the internal jugular (IJ) vein, subclavian (SC) vein, or femoral vein, typically in that order of preference. The tip of the catheter must be centrally located to allow for adequate blood flow and to limit recirculation. Recirculation is more likely when catheters are non-central. Ideally, catheters placed in the upper body should have the tip located at the superior vena cava/right atrial junction, and placement should be confirmed with a radiograph. Right atrial placement may prevent inlet or outlet hole occlusion by blood vessels and thus allow for the high flow rates needed to provide adequate dialysis. Catheters placed in the lower body should have the tip at the inferior vena cava/right atrial junction. Femoral catheters are associated with an increased risk of infection, and thus should be avoided whenever possible. If femoral catheters are required, they should be changed to another site as soon as possible.

Infection Control

HD is a sterile process. In order to prevent infection, sterile technique must be followed for insertion of the HD catheter, and with any entry into the catheter or circuit. HD catheters should not be used for infusions or procedures unrelated to HD to reduce the risk of infection. Exceptions may be made in arrest situations when access is otherwise limited.

Infection prevention centers on patient and staff precautions and hygiene. Routine access to a HD catheter for dialysis involves institution-specific protocols for cleaning the hubs and placing locks on the caps, to reduce the risk of central line-associated blood stream infections. A mask should be worn and sterile technique always utilized when accessing catheters or de-accessing catheters or changing dressings. Routine application of topical antibiotic ointment is associated with significant reduction in rates of infection.

Catheter-related infections are a significant cause of morbidity and mortality with HD. Catheter-related infections include exit site infections, tunnel infections, and bacteremia. Risk factors include immunocompromised status, history of previous infection, recent hospitalization, longer duration of catheter use, inadequate dialysis, and poor patient hygiene.
Catheter Complications

Catheters may become dislodged, or crack due to exposure to chemicals or trauma. If a catheter is dislodged or partially pulled out of the body, one must confirm that the tip remains central. If the tip is no longer central, the catheter must be replaced, as the portion pulled outside the patient is no longer sterile, and thus cannot be advanced back into the patient. Cracked catheters usually require replacement; however, some catheters may be repaired, although this increases the risk of infection.

Arteriovenous Fistula

Patients who require long-term dialysis may be candidates for placement of an arteriovenous fistula or graft. Arteriovenous fistulae or grafts create a permanent high blood flow arteriovenous connection which can be accessed using large-bore needles to perform dialysis. Fistulae and grafts are never appropriate in the acute dialysis setting, as they take time to mature and provide adequate blood flow for dialysis. Such access should be placed by an experienced surgeon. In adults requiring long-term dialysis, such access is preferable over catheters as there is a lower risk of infection.

Figure 8. Arteriovenous fistula.
Circuit Set-Up

Overview
There are many steps to correctly set up the HD machine and circuit. An appropriate size filter and blood lines/tubing must be attached. Water and dialysate (selection based upon patient's laboratory values) should be connected to the machine. The circuit must be primed with an appropriate solution.

The patient is evaluated clinically to determine the HD session goals. The patient's degree of volume overload, metabolic derangements and the cardiopulmonary status influence the amount of clearance and ultrafiltration desired for the treatment. Once goals are established, they must be programmed into the HD Machine. Next, the machine must complete a self-test. Once the prescription has been programmed into the machine, the patient is connected to the HD circuit via the HD catheter and the machine is then started.

Once the machine has started, blood will flow from the arterial catheter limb, through the port that allows for blood sampling and medication administration, to the roller pump. A pre-membrane pressure sensor is located before the blood enters the filter. The blood then enters the HD filter where clearance and ultrafiltration occur. The filter receives dialysate from the HD machine, which has mixed the water and dialysate to the appropriate concentration. After flowing through the filter, the blood goes through the post-membrane pressure sensor, and then an air detector; and if air is detected in the circuit, the machine will alarm and shut down. If no air is detected, the blood flows back to the patient via the venous catheter limb.

Figure 9. Components of the Hemodialysis machine and patient set-up.
Filter Size

The choice of filter size is dependent on the patient’s body surface area (m²). Exact filter sizes vary between manufacturers, but in this simulator, the filter sizes are classified as either small, medium, or large. Selection is based on body surface area as noted to the right:

<table>
<thead>
<tr>
<th>Patient’s Body Surface Area</th>
<th>Filter Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5 m²</td>
<td>Small</td>
</tr>
<tr>
<td>0.5-1 m²</td>
<td>Medium</td>
</tr>
<tr>
<td>&gt;1 m²</td>
<td>Large</td>
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The filter is connected to the water and dialysate supply to generate the gradients necessary for clearance and ultrafiltration.

Blood Lines

Blood lines are single-use sets of tubing which connect to both the venous and arterial access ports of the catheter. Although the entire catheter is inserted into a vein, venous and arterial designation is used to describe the function of the catheter lumens. The arterial line removes blood from the body, while the venous line returns the blood from the dialysis machine to the body.

The volume of the blood lines varies between infant, pediatric, and adult tubing sets, and is documented on the package. On average, a pediatric patient’s blood volume can be estimated as 75-80 mL/kg of dry weight. If the volume of the blood lines and the filter (extracorporeal volume) will exceed 10% of the patient’s total blood volume, then a blood prime should be used to prevent hemodilution and hemodynamic instability.

Dialysate and Water

The choice of dialysate is dependent on many patient clinical factors and is covered in the next section. A source of deionized water is connected to the HD machine. This source may be a reverse osmosis machine or a sterile water line, both of which provide the volume of water needed to perform dialysis.

Prime

The blood lines and filter must be primed with fluid. The volume of the prime must be documented at the start of dialysis. All prescriptions must include instructions about removal of prime volume. Options for priming include saline, 5% albumin, and blood.

1. **Saline** is typically used in patients with stable blood pressures, an adequate hematocrit, and those who weigh more than 8kg. If a saline or albumin prime is used, the volume of blood in the tubing at the end of dialysis should be re-infused into the patient to prevent blood loss, and the volume of the saline prime should be
removed by ultrafiltration during the treatment. This should result in no significant change to the patient's hematocrit.

2. **Albumin** is typically used in patients with hypotension or hypoalbuminemia (typically less than 2.5 g/dL). Albumin may help maintain blood pressure and promote movement of fluid into the vascular space from the extravascular space, allowing for better ultrafiltration.

3. **Blood** is used when the patient weighs less than 8 kg or the volume of the circuit (extracorporeal volume) is greater than 10% of the patient’s estimated total blood volume (75-80 ml/kg). Priming with non-blood fluids could lead to a precipitous drop in hematocrit (hemodilution) and hemodynamic instability. Blood prime is also used for patients who are in need of a packed red blood cell transfusion.

When using blood for priming the circuit, one unit of packed cells is diluted with 5% albumin to achieve a circuit hematocrit between 35-45%. The volume of the blood lines and dialyzer is not typically infused into the patient at the end of the session, unless the patient requires a blood transfusion. In the case of a blood transfusion, the circuit volume and volume of additional blood provided should be removed by ultrafiltration.

Repeated use of blood primes leads to significant exposure to blood products and can lead to the patient developing antibodies against blood components, also called “sensitization.” For the patient with end-stage renal disease, this may lead to difficulty obtaining a renal transplant, and so effort should be made to move away from blood primes as soon as the patient is large and stable enough to tolerate an albumin prime.

**Selecting a Prescription and Machine Self-Test**

Once you have determined your goals for your HD session (to be covered in the next section), you will program these goals into the HD machine. A self-test must be performed prior to connecting the HD machine to the patient to ensure that all lines are connected properly to the machine and that the system is adequately prepared for a safe treatment. The self-test includes the machine testing the pH and tonicity of the dialysate.

**Connecting the Patient**

Once the self-test has been completed, the patient is connected to the circuit. Strict attention to sterile technique is required. Vital sign monitoring must begin immediately.
Monitoring and Sensors

The extracorporeal blood in the circuit is monitored continuously during the dialysis session.

1. **Pressure sensors** monitor the pre- and post-filter pressures. Adequate pressures must be maintained in the circuit to promote ultrafiltration and prevent clotting. The system will alarm if the pressures are too low or too high. **Low or high pressures can indicate complications such as a clot in the filter or an occlusion in the catheter.**

2. **Air sensors** monitor the extracorporeal blood for air that may be introduced into the circuit during HD. Bubbles may enter the system either through a break in the circuit, or while infusing medications or sampling blood from the access port. If air is detected, the machine will alarm and the circuit will stop automatically to prevent air from being infused into the patient.

3. **Temperature sensors** monitor the extracorporeal blood, ensuring that the temperature remains stable during the session. Blood may cool down as it flows extravascularly, and if the machine gets too cold some HD machines may be programmed to warm the blood, or warmers may be placed around the tubing to prevent hypothermia, especially for small infants. Cooling the blood lines also can be employed for those with fever or malignant hyperthermia.
Prescription

Overview
The HD prescription includes selection of the following:
   a. Dialysate
   b. Anticoagulation (if required)
   c. Blood Flow Rate (Qb)
   d. Dialysate Flow Rate (Qd)
   e. Treatment Time
   f. Ultrafiltration Goal

Sodium
The sodium concentration in the dialysate may be fixed or variable during the treatment. The sodium concentration is typically between 135-145 mEq/L* to avoid inducing hypo- or hypernatremia in the patient. However, it is critical to remember that fluid removed by ultrafiltration is isotonic. Thus, removal of large volumes may result in total body sodium depletion.

*Conversion of sodium from mEq/L to mmol/L is 1:1 (Na 135 mEq/L=135 mmol/L).

Potassium
The potassium concentration in the dialysate is usually fixed during the treatment. In commercially available dialysate, the potassium concentration is typically between 0 and 3 mEq/L*.

For patients with hyperkalemia, dialysate containing little or no potassium should be used. For those who are normokalemic or hypokalemic, dialysate using 3 mEq/L potassium should be used.

Remember that solutes will move down a concentration gradient and the greater the clearance, the greater the patient's potassium losses. Thus if the patient's potassium concentration is 3 mEq/L and there is lower potassium in the dialysate, the patient's potassium will decrease. Of note, the use of dialysate containing no potassium has fallen out of favor.

*Conversion of potassium from mEq/L to mmol/L is 1:1 (K 2 mEq/L=2 mmol/L).

Dextrose
The dextrose concentration in the dialysate is usually fixed at 100 mg/dL during the treatment. This concentration is chosen to avoid inducing hypoglycemia in the patient.
Calcium
The calcium concentration in the dialysate is usually fixed during the treatment. In commercially available dialysate, calcium concentration is typically between 2.5 and 3.5 mEq/L*. For patients with hypocalcemia, dialysate containing the higher calcium concentration should be used.

*Ca 2.5 mEq/L = Ca 1.25 mmol/L; Ca 3.5 mEq/L = Ca 1.75 mmol/L

Anticoagulation
Anticoagulation may be required to prevent blood from clotting as it circulates through the circuit. Each center has its own protocol for anticoagulation, but the most important factors to prevent circuit clotting are to have a clear and well-established anticoagulation protocol for administration and monitoring of the patient, and an experienced staff to follow this protocol. Heparin is the most common anticoagulant utilized globally for both acute and chronic HD.

Patients who require acute HD may be coagulopathic and not require any anticoagulation, or may have a contraindication to anticoagulation, such as those with recent hemorrhage. HD can be performed either with low-dose heparin, saline flushes without heparin, or regional anticoagulation with citrate, prostacyclin, or heparin-protamine. If saline flushes are used, the volume of flushes is removed through ultrafiltration during the treatment.

Blood Flow Rate
Clearance is limited by the blood flow rate (Qb). Thus, to optimize clearance, the highest blood flow rate one can safely achieve should be used during HD.

The typical blood flow rate for children receiving HD is 6-8 mL/kg/min.

Most machines have a minimum blood flow rate of 35-50 mL/minute and maximum of 400 mL/min. Thus for small infants, the blood flow rate may be greater than 8 mL/kg/minute.

Dialysate Flow Rate
Dialysate flow rate (Qd) is typically set at a minimum of twice the blood flow rate in order to maintain the high concentration gradient along the length of the hollow core fibers in the filter. This allows for maximum clearance.

Dialysate flow rate is generally 400-800 mL/min.
Treatment Time (t)

The length of the treatment depends on the desired clearance and the prescribed blood flow rate. Rapidly lowering the BUN with hemodialysis can result in disequilibrium syndrome. Thus, a stepwise approach should be used in those with significant uremia by providing increasing clearance each day to allow for gradual equilibrium. Initial clearance for a child with significant uremia should be limited to provide 30% urea reduction rate on the first day, followed by sequential increases in urea reduction (30%, 50%, 70%) to avoid disequilibrium syndrome. If the child's BUN is very high and clearance for removal of other solutes is required, one can administer mannitol to avoid rapid osmotic changes, and thus prevent disequilibrium and cerebral edema.

Dialysis initiated for removal of other substances, such as ammonia or toxins, should focus on removal of that particular substance. In that case, maximal clearance should be attempted with each treatment, including the initial treatment. The treatment may continue longer than the time calculated initially for 100% clearance, as there may be ongoing generation of the substance, such as ammonia, or release into the bloodstream, such as with toxic ingestions.

The following equation is used to determine treatment time based on the desired clearance.

\[ e^{\frac{C_t}{C_0}} = \frac{kt}{V} \text{ or } \frac{kt}{V} = -\ln \frac{C_t}{C_0} \]

- \( k \) = clearance of urea at a set blood flow. This number is based on filter properties, related to blood flow, and provided with each filter. \( k \) has no units as it is a constant.
- \( t \) = treatment time (minutes)
- \( V_d \) = volume of distribution (mL). In general, it is estimated as 60% of the patient's dry weight. For example, a patient weighing 10kg has a volume of distribution of 6kg or 6 L.
- \( C_t/C_0 \) = the percentage of what is remaining of a solute at the end of dialysis. The goal for clearance depends on whether dialysis is being initiated for uremia (stepwise gradual reduction) or toxin/ammonia (maximum clearance). For example, if your initial treatment goal is to provide 30% clearance, then 70% or 0.7 will remain.
Let’s try an example:

A 30kg child has a goal clearance of 50% and blood flow of 200 mL/min:

\[ \text{kt/v} = -\ln \frac{C_t}{C_o} \]

\[ k = 180 \text{ (from filter)} \]

\[ V_d = 18,000 \text{mL (30kg x 0.6 = 18kg = 18,000mL)} \]

\[ \frac{C_t}{C_o} = -0.69 \text{ (ln 0.5 = -0.69)} \]

\[ (180)(t)/18000 = 0.69 \]

\[ t = 69 \text{ minutes} \]

Ultrafiltration Goal

The desired fluid removal or ultrafiltration (UF) goal for each dialysis session is chosen based on the patient’s volume status and hemodynamic stability. For children, ultrafiltration should not exceed 5% of the patient’s dry weight in each dialysis session. The initial UF rate is typically up to 10 mL/kg/hour, and net UF should not exceed 100 mL/hour for infants and small children.

In all patients, the UF goal needs to consider the degree of volume overload, and that reducing volume overload may take many sessions. For patients who are euvolemic, the UF goal should be equal to the total fluid input between HD sessions to maintain euvolemia. For patients who are volume-overloaded, the UF goal should be greater than the total fluid input between HD sessions to reduce fluid volume over time.

More aggressive UF may result in hemodynamic instability. The UF goal must also be considered in the context of the desired clearance of solutes. If the UF goal is larger than what can be safely removed during the calculated treatment time (which is based on clearance goal and limited to avoid disequilibrium or excessive removal of solutes), the session can be extended to include a period of ultrafiltration only.
Complications

**Hypokalemia**

Because solutes move down a concentration gradient, patients may develop hypokalemia during HD. In patients with hypokalemia, potassium concentration in the dialysate should be maximized (3 mEq/L or 3 mmol/L). Potassium should not exceed greater than physiologic concentrations in the dialysate. If the serum potassium is dangerously low, potassium can be administered either orally or intravenously.

**Hyperkalemia**

Many patients requiring acute HD have hyperkalemia. In this circumstance, the dialysate should contain the lowest possible potassium concentration. If hyperkalemia persists despite the lowest possible potassium concentration, you can increase potassium clearance by increasing the blood flow rate or extending the treatment time to decrease the potassium level.

In cases of symptomatic or severe hyperkalemia, when potassium levels exceed 6.5 mEq/L (6.5 mmol/L) or ECG changes are noted, one should consider administration of:
1. calcium to stabilize the myocardium
2. kayexalate to bind excess potassium
3. beta-agonist therapy, insulin and glucose, and/or sodium bicarbonate to shift potassium intracellularly

**Hypotension**

Dialysis-induced hypotension is a serious complication of HD. The main mechanism is ultrafiltration in the setting of a decreased intravascular volume. Remember that ultrafiltration only removes fluid from the intravascular space. Intravascular volume depletion may occur when the rate of fluid removal by ultrafiltration is significantly faster than the rate of refill of fluid from the interstitial space into the intravascular space. Many patients requiring acute HD are edematous, but have a low intravascular volume because of significant capillary leak and third spacing of fluid.

The acute management of hypotension includes:
- Reducing or stopping ultrafiltration
- Reducing blood flow rate
- Placing patients in the Trendelenburg position
- Replacing intravascular volume with intravenous fluids, albumin, or mannitol
- Ensuring serum albumin is adequate to provide oncotic pressure to maintain intravascular volume
- Supporting blood pressure during ultrafiltration with vasopressors

*Note that only one parameter should be adjusted at a time.*
Bleeding

Patients on HD may have an increased bleeding risk related to renal failure and uremia, resulting in platelet dysfunction. Thus, HD requires the addition of an anticoagulant to prevent blood clots in the circuit and catheter.

For the patient who is bleeding while on HD, the source of blood loss should be identified immediately and the HD session may need to be stopped, especially if the patient develops significant bleeding and/or hypotension. Local bleeding at the catheter site can occur as a patient becomes less edematous or in patients with poor wound healing. Local pressure on the catheter can be helpful to stop bleeding in many cases. If the bleeding persists, it may be necessary to remove the anticoagulation in the circuit.

Serious, life-threatening causes of bleeding include blood leak (caused by membrane rupture, allowing red blood cells to cross over the membrane into the dialysate, and diagnosed by detecting blood in the dialysate), blood line separation, loose circuit caps/connections, needles dislodging from fistula, or rupture of fistula. If any of these occur, stop the treatment immediately to prevent excessive blood loss from the patient.

Disequilibrium Syndrome

Disequilibrium syndrome is defined as neurologic symptoms (mental status changes, headaches, nausea, vomiting, dizziness, blurred vision, or confusion) that occur during hemodialysis due to rapid solute clearance, particularly urea. Disequilibrium syndrome is generally benign and self-limited; however, severe cases may progress to seizures, coma, and/or death. The etiology is postulated to be due to a rapid shift in solute and fluid movement resulting in central nervous system (CNS) symptoms and cerebral edema. The rapid reduction in blood urea (BUN) results in lower plasma osmolality, and thus, rapid movement of water into the brain cells and the development of cerebral edema. This process is called reverse osmotic shift. Intracerebral acidosis also occurs during reverse osmotic shift. The drop in cerebral intracellular pH also increases intracellular osmolality by stimulating production of organic acids and attracting more sodium and potassium to bind to the hydrogen ions located in the brain cells.

Factors contributing to disequilibrium syndrome include:
- First dialysis treatment
- Uremia: BUN >175 mg/dL or >60 mmol/L
- Pediatric patients or elderly patients
- Concomitant neurological condition – epilepsy, thrombi, trauma
- Hyponatremia
- Hepatic encephalopathy
- Malignant hypertension
- Increased permeability of blood brain barrier: sepsis, vasculitis, meningitis,
- Severe metabolic acidosis
Disequilibrium syndrome is a diagnosis of exclusion; there is no specific test for it. Organic etiologies, particularly CNS conditions, must be evaluated first. Electrolytes should be monitored. Imaging studies should be considered.

**Prevention of disequilibrium syndrome involves the slow removal of urea during hemodialysis.** Methods to provide safe removal of urea include the following:

- Target initial urea reduction rate of ≤30%
- Target lower hemodialysis blood flow rates
- Use a filter that has a smaller surface area (0.9 to 1.2 m²)
- Consider ultrafiltration without dialysis (hemofiltration) for patients who are severely fluid overloaded
- Administer a mannitol infusion during hemodialysis
- Correct hyponatremia
- Monitor blood pressure closely to prevent hypotension

Treatment of disequilibrium syndrome includes:

- Supportive care of symptoms (headaches, nausea, vomiting) and optimize oxygenation
- Decrease blood flow rates
- Stop hemodialysis immediately if symptoms worsen or progress to seizures, coma, or obtundation
- Administer a bolus of mannitol or hypertonic saline

**Circuit Clotting**

The hemodialysis circuit may clot for many reasons. Contact of blood with dialysis tubing material and filter activates platelets adhesion and the intrinsic coagulation pathway, resulting in thrombin production and formation of fibrin clots.

Risk factors for circuit clotting include:

- Intravascular hypovolemia
- Aggressive ultrafiltration
- Small-sized dialysis catheter
- Slow blood flow rates
- Venous thrombosis at site of HD catheter
- Frequent stopping of the blood pump
- No heparin or insufficient heparin dose
- Transfusion of blood products during no-heparin dialysis session
- Thrombocytosis
- Polycythemia
- High arterial or venous pressures
- Low dialysate pH
- Reusing filter
Circuit clotting is managed by:
- Limiting the above risk factors
- Adequate dosing of heparin

**Catheter Malfunction**

Proper catheter management is important to preserve patency and reduce risk of infection. Catheter dysfunction can result in inadequate dialysis dose delivery, which increases the morbidity and mortality of patients on HD. Catheter occlusion is a major cause of catheter dysfunction and can be due to thrombosis, kinking or malpositioning of the catheter. Replacing or repositioning of the catheter may be necessary.

Thrombotic occlusions can occur early or after prolonged usage. Management includes anticoagulation, thrombolysis or catheter replacement. If thrombosis is present or suspected, thrombolytics can be administered into the catheter and left to dwell per institutional protocol. This is often successful, but may require repeated attempts. Thromboses must be identified early on as they can provide a substrate for bacterial growth. Between HD treatments, dialysis catheters are filled with a highly concentrated heparin solution to prevent thrombus formation. The catheter volume must be known to the provider, and prior to each treatment, the appropriate volume of heparin must be removed from the catheter to avoid administering this heparin dose to the patient.

If a catheter was previously functioning appropriately and malpositioning is suspected, placing the patient in a recumbent position or adjusting the patient’s neck position may improve flow. Sedation may be helpful for patients that are intubated, under-sedated and moving causing catheter kinking during a dialysis session.

For a catheter that is not functioning or achieving the prescribed blood flow, the following steps should be taken:
1. Assess patient and catheter position.
2. Consider a chest X-ray to assess the catheter location.
3. Attempt to flush the catheter.
4. Consider administration of thrombolytics (typically tissue plasminogen activator) to lyse a catheter thrombus.
5. If the above are unsuccessful, consider line replacement.

**Infection**

Each center should have an institutional protocol for the assessment and management of catheter-associated infections. Patients with a fever and central venous access should have a blood culture obtained, and empiric IV antibiotics considered while cultures are pending. If cultures are positive, an appropriate course of intravenous antibiotics should be administered and the likelihood of overcoming the infection must
be assessed depending on the offending organism. Certain organisms, especially yeast, often require removal of the catheter for the infection to be adequately cleared from the bloodstream. In some cases, antibiotics are instilled into the catheter to dwell in between treatments. This is called an antibiotic “lock.”
Special Considerations

Medication Clearance

Just as many harmful molecules are cleared with HD, many therapeutic medications may also be cleared during HD, such as antimicrobials and sedatives. Consultation with a pharmacist is recommended whenever a patient is initiated on HD, and with any medication changes. Some medications, such as vancomycin, have levels that can be checked to assist with dosing.

Special Indications

1. **Tumor lysis syndrome**

   Approximately 3-5% of patients with cancer develop laboratory and/or clinical evidence of tumor lysis syndrome (hyperkalemia, hypocalcemia, hyperuricemia and hyperphosphatemia). Management involves treatment of electrolyte abnormalities, uric-acid lowering agents, fluids, diuretics, and in severe cases, the use of hemodialysis.

   Indications for dialysis in this setting include severe oliguria or anuria, hyperkalemia and/or hyperuricemia refractory to medical management, and/or hyperphosphatemia-induced symptomatic hypocalcemia. Hemodialysis is more effective than peritoneal dialysis for rapidly removing solutes released in tumor lysis syndrome. In patients with tumor lysis syndrome, close collaboration with the oncology team is required to ensure adequate dosing of chemotherapy around dialysis while balancing the metabolic abnormalities of the patient.

2. **Hyperammonemia**

   Patients with urea cycle disorders or liver failure can develop hyperammonemia. HD is the quickest and most effective method to remove excess ammonia. HD should be started immediately for patients with severe hyperammonemia, particularly if ammonia is above 350 to 400 micromol/L, increasing rapidly, or resistant to initial drug therapy.

   Maximal clearance should be attempted to remove ammonia, including during the initial treatment. HD should continue for patients with hyperammonemia until the ammonia is decreased to an agreed-upon safe level, and therapeutic interventions to decrease the generation rate of ammonia are in place. The treatment may have to continue longer than the time required for the initially calculated clearance, as there may be ongoing generation and continued release of ammonia from tissues into the bloodstream. Reversal of a catabolic process driving the hyperammonemia may take 24-48 hours or longer if infection is present. Due to the ongoing catabolism producing nitrogen waste, ammonia levels may rise again. Individual centers have different protocols for starting...
and stopping dialysis and the user should become familiar with these to determine the appropriate practice.

3. Intoxications

Not all drugs or toxins can be effectively removed by HD. Drugs removable with HD must have certain properties:

- Low degree of protein-binding
- Low volume of distribution (<1 L/kg)
- Low molecular weight or size (<500 daltons)
- High water solubility (drugs that are not lipid-soluble)
- Dialysis clearance is greater than endogenous clearance

The following drugs/toxins are easily removed by HD:

- Acetaminophen
- Alcohols (ethanol, isopropanol, acetone, methanol, ethylene glycol)
- Ampicillin
- Atenolol
- Barbiturates
- Chloral hydrate
- Lithium
- Procainamide
- Salicylates
- Theophylline
- Vancomycin

Urea Reduction Ratio

After a hemodialysis session, the urea reduction ratio (URR) is often calculated by comparing the pre- and post-dialysis urea measurements. Once the URR is calculated, one can determine a more accurate volume of distribution for future calculations.

For example:
If the pre-dialysis urea level was 50 mg/dL and the post-dialysis urea level was 28 mg/dL, the amount of urea removed was 50-28 = 22 mg/dL. The amount of urea removed is expressed as a percentage of the pre-dialysis urea level: 22/50 = 44%.