Alternate Dialysis Platforms:

Sorbents

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Sorbents in a Nutshell

• Potential benefits of sorbents  Why?

• Mechanisms for improved solute transport  How?

• Examples of currently available sorbents and sorbents in development  What?
Why sorbents?

- Ability to be used orally
  - for CKD patients not yet on dialysis

- Ability to purify dialysate (reduce water required)
  - e.g. original REDY system and its descendants today

- Ability to target and remove specific toxins or classes of toxins
  - e.g. \(\beta_2\) microglobulin, cytokines (sepsis), viruses

- Ability to overcome transport limitations for hard-to-remove toxins
  - e.g. protein-bound substances
How do sorbents work?

• **Adsorption—Adhesion of a Molecule to a Surface**
  – Binding occurs as a result of random collisions
  – Generally a reversible, equilibrium process
  – Higher concentration in solution => more solute bound

• **High Internal and External Surface Area**
  – Typically porous beads offer extremely large internal surface area (e.g. 300-800 m²/g) for binding.
  – Smaller particles offer better transport due to higher external surface area, but higher pressure drop.

• **Mechanism of Binding**
  – Van der Waals forces, including hydrogen bonds
  – Electrostatic forces
  – Covalent (not typically used)
The Evolution of a Sorbent Particle
Benefits of Sorbents

• Enhancing removal of one solute while avoiding loss of other solutes
  – A high specificity sorbent preferentially binds one solute.
  – Such sorbents allow removal one solute independent of other similarly-sized molecules, enabling increased removal of large MW toxins.

• Removing unknown solutes
  – A low specificity sorbent (such as activated charcoal) can remove many different solutes.
  – Used in treatment of liver failure and accidental poisoning
  – Also used in sorbent dialysis cartridges that purify tap water

• Removing hard-to-dialyze toxins
  – Solute adsorption drives diffusion into blood compartment, and drives release of protein-bound toxins.
  – A high affinity sorbent is one in which adsorption is thermodynamically favorable compared to desorption, so that bound molecules tend to stick.
  – Such sorbents improve removal from low concentration solutions.
Mechanism for Improved Clearance from Intracellular Compartment
Mechanism for Improved Clearance of Protein-Bound Toxins

- Low Solute Concentration in Plasma Compartment
- Protein-Bound Solute
- Improved clearance

Dialysate ↔ Sorbent

Dialysis Membrane
Examples of Sorbents in CKD

• Currently available sorbents by mode of use
  – Oral
  – For dialysate regeneration
  – Adsorption from plasma
  – Adsorption from blood

• Sorbents in development
  – For dialysate regeneration
  – Targeting middle molecular size
  – Targeting large molecular size

Thanks to Amanda Stennett for assembling the following examples.
Oral sorbent use

• Example: AST-120 (Kureha Corp.)

  Carbon microspheres remove low molecular weight toxins (ammonia, indoles, etc.) but not proteins in the large intestine

• Application: Chronic Kidney Disease Stage 4

Pros:
  Engineered to have size specificity not seen in most activated charcoal

Cons:
  Can only remove what is available in the intestines

Image: Ocera Therapeutics
For dialysate regeneration

• Example: SORB cartridge (SORB Technology)
  Removes toxins in dialysate (urea, phosphate, etc.) and replaces dialysate components (bicarbonate)

• Application: Stage 5 Chronic Kidney Disease

Pros:
  Eliminates need for water purification system

Cons:
  Column can saturate and require unplanned end of treatment
Adsorption from plasma

- **Example:** TheraSorb Ig (Miltenyi Biotec)
  - Selectively removes immunoglobulins using polyclonal sheep anti-human Ig on sepharose support

- **Application:** Treat humoral rejection of transplant

**Pros:**
Column can be regenerated for multiple treatments

**Cons:**
Requires plasma separation

Image: Miltenyi Biotec
Adsorption from blood

- **Example: DALI (Fresenius Medical Care)**
  Polyacrylate coated polyacrylamide beads remove LDL-cholesterol, lipoprotein A, triglycerides, and some HDL-cholesterol

- **Application: Familial hypercholesterolemia**

**Pros:**
- Does not require plasma separation
- Retains more “good” cholesterol than plasma exchange

**Cons:**
- Possible hypocalcemia due to citrate anticoagulant use

Image: Fresenius Medical Care SE
Sorbents in development
For dialysate regeneration

• Example: WAK (Fresenius Medical Care)
  Combination membrane and sorbents for portable and wearable dialysis

• Application: Stage 5 Chronic Kidney Disease

Pros:
- Ion-rejecting membrane increases the sorbent capacity by excluding ions competing for ammonia binding sites
- Increases patient autonomy

Cons:
- Requires patients comfortable with self-care
Sorbents in development
Targeting middle molecular size – cytokines

- **Example: CytoSorb (CytoSorbents)**
  - Removes cytokines directly from blood using polymeric beads with size-specific pores
- **Application: Adjunctive therapy for sepsis**

**Pros:**
- Binds species that are normally retained by dialysis membrane

**Cons:**
- No chemical specificity

Image: CytoSorbents Investor presentation
Sorbents in development
Targeting large molecular size – Virus

- **Example: Hemopurifier (Aethlon Medical)**
  Removes pathogens with high mannose content using lectin
- **Application: Hepatitis C, HIV**

**Pros:**
Can remove mutated viruses that are drug/vaccine resistant

**Cons:**
Can require use in combination with pharmacological agents
Summary

• Use of sorbents in CKD is growing.

• Currently-available sorbents enable removal of a wide spectrum of solutes.

• Sorbents in development provide hope for improving the adequacy of dialysis in the broadest sense of the term.