Dialyzers in the 21st Century
The Basics

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An agency of the Provincial Health Services Authority

Overview

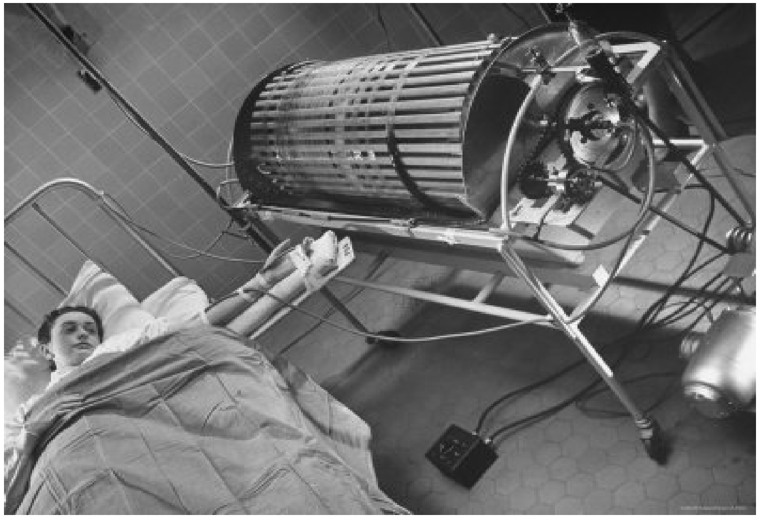
- Evolution of Dialyzers
- Basic Components of Dialyzers
  - Types of membranes
  - Efficiency and Flux
  - Sterilization
- Dialyzer reactions
  - Local Experience of Significant Thrombocytopenia Related to Dialyzer Use

EVOLUTION OF DIALYZERS

History of Dialyzers

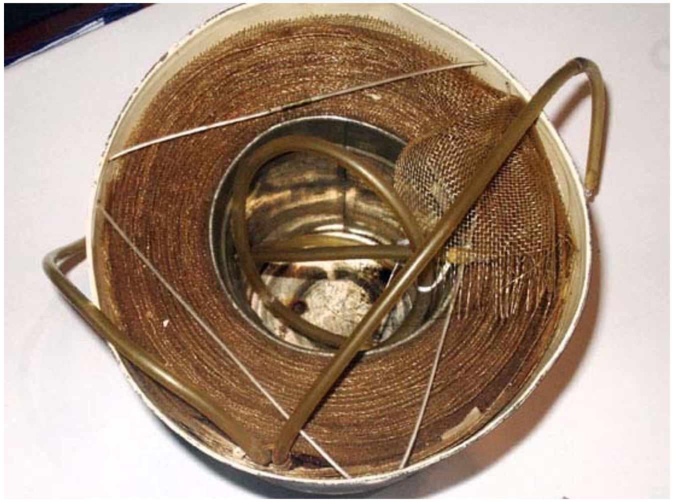
- **1924: Haas Dialyzer**
  - Tubular Device
  - Cellulose trinitrate

- **1944: Kolff Dialyzer**
  - Rotating dialyzer
  - Wooden drum
  - Celluphane tube

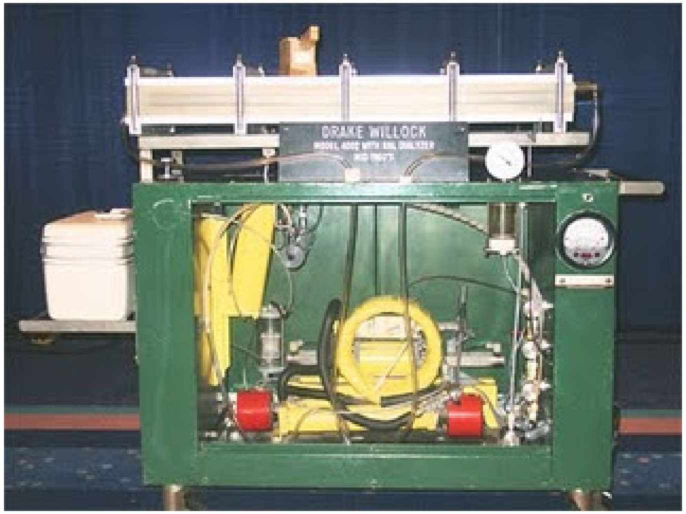


History of Dialyzers

- **1956: Kolff Dialyzer**
  - Coil dialyzer



- **1960: Kiil Dialyzer**
  - Plate dialyzer
  - Cellulosic flat sheet

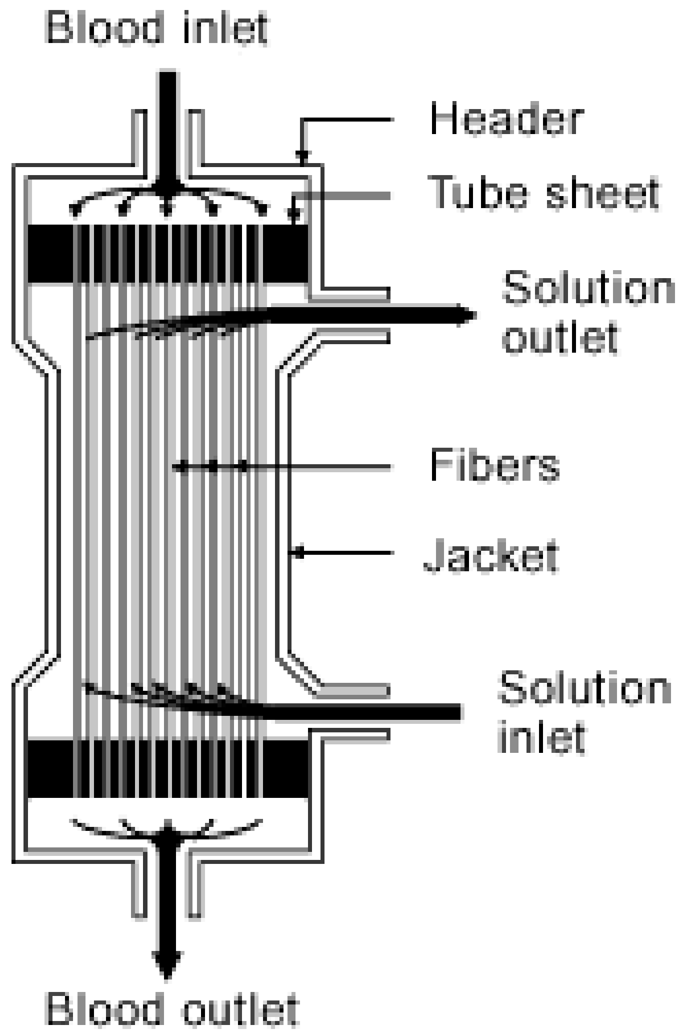


History of Dialyzers

- **1966: Hollow Fiber Dialyzer**
  - Cellulose Acetate
- **1969: First Synthetic Membrane**
  - Polyacrylonitrile (AN-69)

The Hollow Fiber Dialyzer

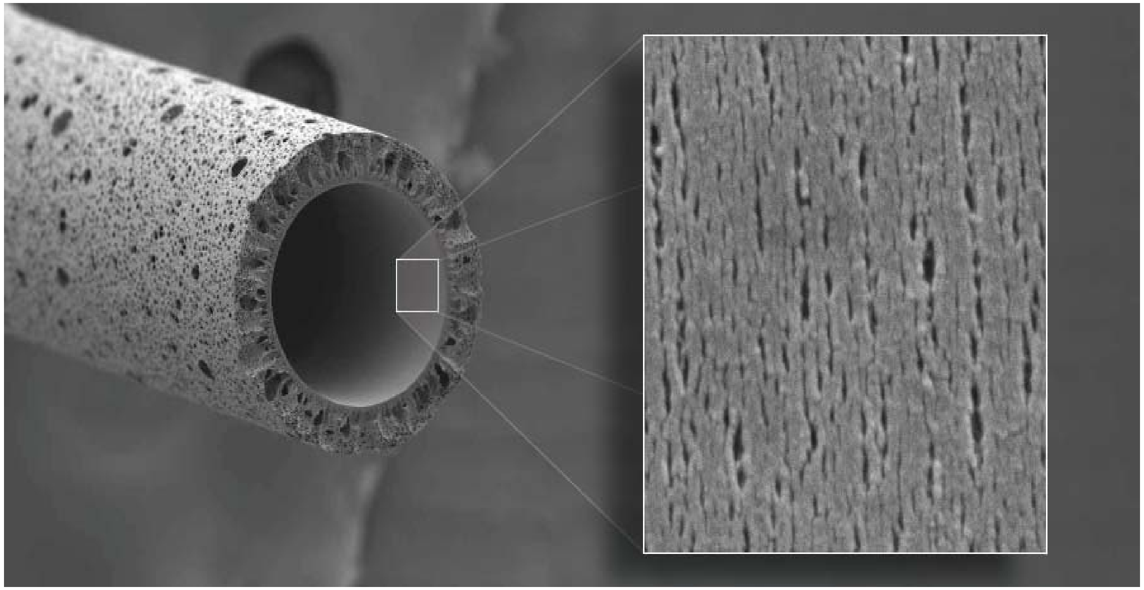
- **Components**
  - Membrane
    - Hollow fibers
  - Potting compound
  - Header
  - Housing



BASIC DIALYZER COMPONENTS

The Dialyzer Membrane

- Membrane material
- Efficiency
- Pore size (Ultrafiltration coefficient = Flux)
- Sterilization



Dialyzer Membrane Material

- **Unmodified Cellulose (Cuprophane)**
  - Polysaccharide based obtained from pressed cotton
  - Chains of glucosan rings with abundant free hyroxyl groups
- **Substituted cellulose**
  - Cellulose Acetate: acetate binds to the hydroxyl groups
  - Diacetate, triacetate

Dialyzer Membrane Material

- **Cellulosynthetic**
  - Addition of a synthetic material such as diethylaminoethyl = Hemophane
- **Synthetic membranes**
  - Polysulfone
  - Polyacrylonitrile (PAN)
  - Polycarbonate
  - Polyamide
  - Polymethylmethacrylate (PMMA)

Membrane Biocompatibility

- **Biocompatible membranes**
  - Less activation of the immune system and inflammatory response
  - Substituted cellulose and the synthetic membranes essentially similar in biocompatibility
    - Some patients can have sensitivity to certain membrane material

Polysulfone membranes

- High physical strength & chemical resistance
- Heat and radiation sterilization possible
- Often combined with PVP to increase hydrophylicity
- Ability to retain endotoxins

Polyethersulfone membranes

- Advanced fiber spinning process
- Creates larger, uniformly sized and densely distributed pores
- Achieve better middle molecule clearance with minimal albumin loss

PAN derived membranes

- **AN-69 membranes**:
  - Polymer of PAN and methanllylsulfonate
  - Negatively charged surface can activate bradykinins and cause dialyzer reactions
    - May be aggravated by use of ACEI
- **AN-69 ST membranes:**
  - Coated with polycationic polymer to decrease reactions
  - Heparin (negatively charged) can bind to the membrane

Efficiency

- Efficiency related to:
  - Membrane size (Surface Area)
  - Porosity
  - Thickness
  - Internal diameter of the fibers
    - Reduces the resistance of the more static blood layers
  - Design
    - Wavelike or crimped vs straight fibers

Flux

- **Flux**: related to Kuf (Coefficient of ultrafiltration)
  - volume of fluid (ml/hr) transferred across the membrane per mmHg of pressure gradient
  - High flux dialyzers
    - Kuf > 15 ml/mmhg or B_2M clearance > 20 ml/min
- **Advantages of high flux**:
  - Improve middle molecule clearance
- **Disadvantages of high flux:**
  - Errors in TMP can cause large UF
  - Backfiltration

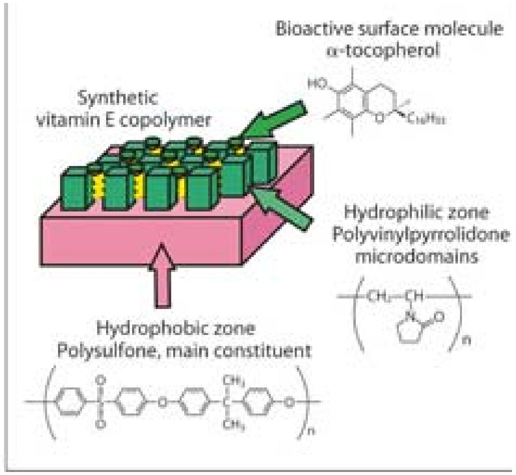
Evidence for Flux

- Cochrane review of RCT’s could not determine overall efficacy of high flux dialysis
  - Concluded may reduce CV mortality
- HEMO study
  - Decreased CV mortality in pts on HD > 3.7 yrs
- MPO study
  - Increased survival in pts with albumin < 40 and in diabetics

High Cut-Off Membranes

- Higher molecular weight cut-off ~ 65KDa
- Better B2M clearance compared to high flux dialyzers
- Increase clearance of free serum light chains:
  - Potential use in treatment of patients with multiple myeloma
- Increase Albumin clearance

Vitamin E coated dialyzers



- Cellulose or PS backbone
- Coated with vitamin E (α - tocopherol)
  - Reduce reactive oxygen species
- Decrease inflammatory markers
- No survival benefit yet

Sterilization Techniques

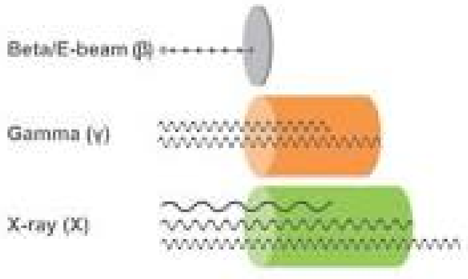
- Advances in Sterilization
  - Chemical
  - Heat
  - Radiation
    - Gamma-radiation
    - Beta-radiation (electron-beam)

Overview of Sterilization Techniques

	Microbiological Efficacy	Effect on Dialyzer Material	Release of sterilization byproduct	Cost
Chemical (ETO)	High	Very low mechanical stress No thermal stress	Residual ETO from potting compound	Low
Heat	High	High thermal stress. Not suitable for all membranes	None	High
Radiation	High	Intermediate material stress	Cytotoxic compounds from some dialyzers & from some potting compunds	High

Radiation Sterilization

- **Gamma Radiation**
  - Use radioactive isotope
  - Usually cobalt 60
  - Very penetrating



- **Beta Radiation (electron-beam)**
  - Stream of high energy electrons accelerated by means of a linear accelerator
  - Limited depth of penetration
  - More focused and precisely delivered
  - Exposure time is shorter

Dialyzer Reactions

- **Type A**
  - IgE mediated, hypersensitivity reactions
  - Often severe and usually associated with exposure to an antigen (most common ETO)

- **Type B**
  - Complement mediated, less severe
  - Can result in changes in count or function of the blood cell lines
  - Can result in neutropenia followed by rebound leukocytosis

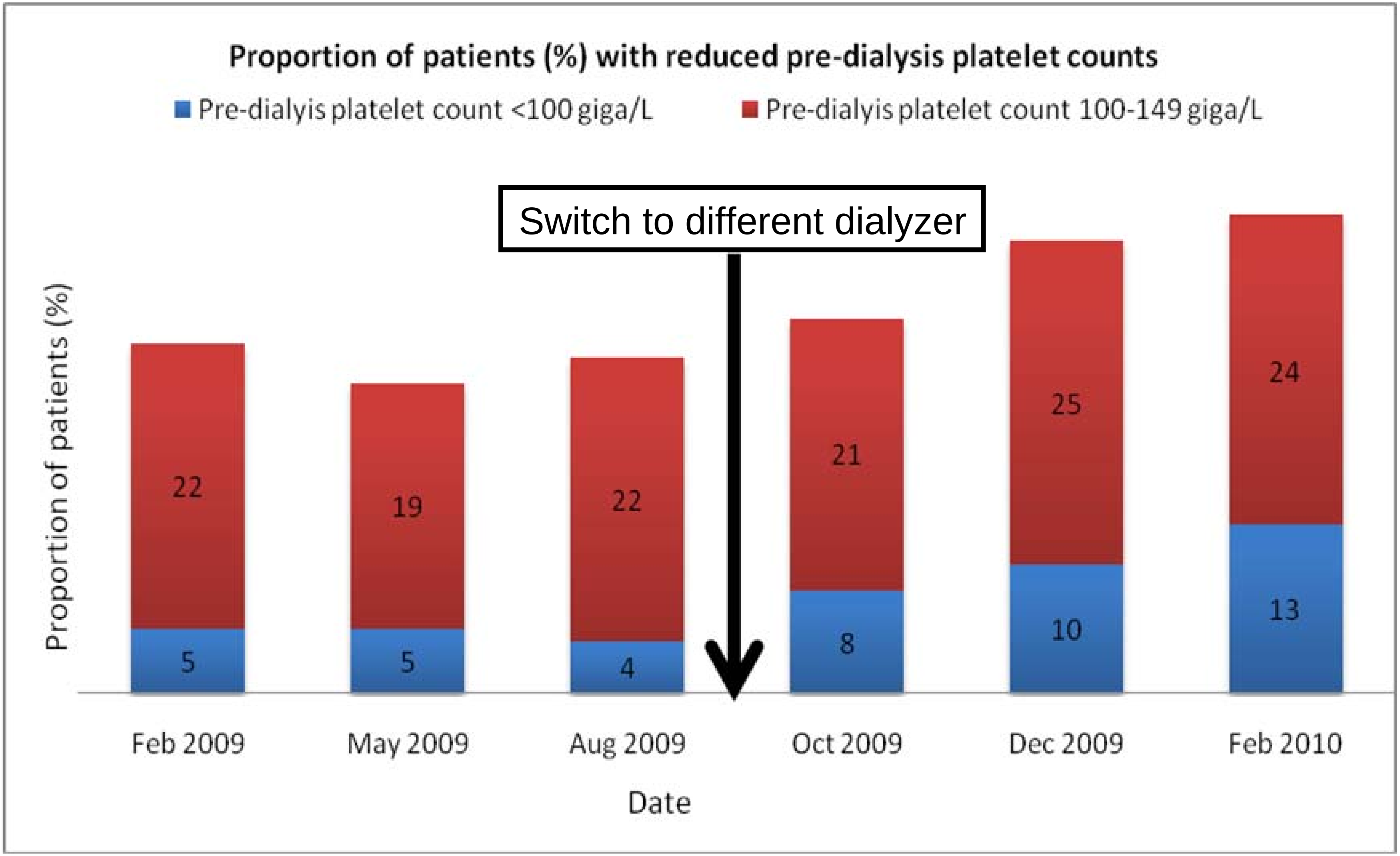
Dialyzer Reactions

- **Protein-Membrane Interactions:**
  - Dialysis membrane and the coagulation proteins which can result in binding of fibrinogen, platelet adhesion and thrombocytopenia
  - Platelet count can drop during initial part of dialysis but usually rebound to pre-dialysis levels at the end of the session
  - Overall drop of greater than 7-9% is unusual with biocompatible membranes

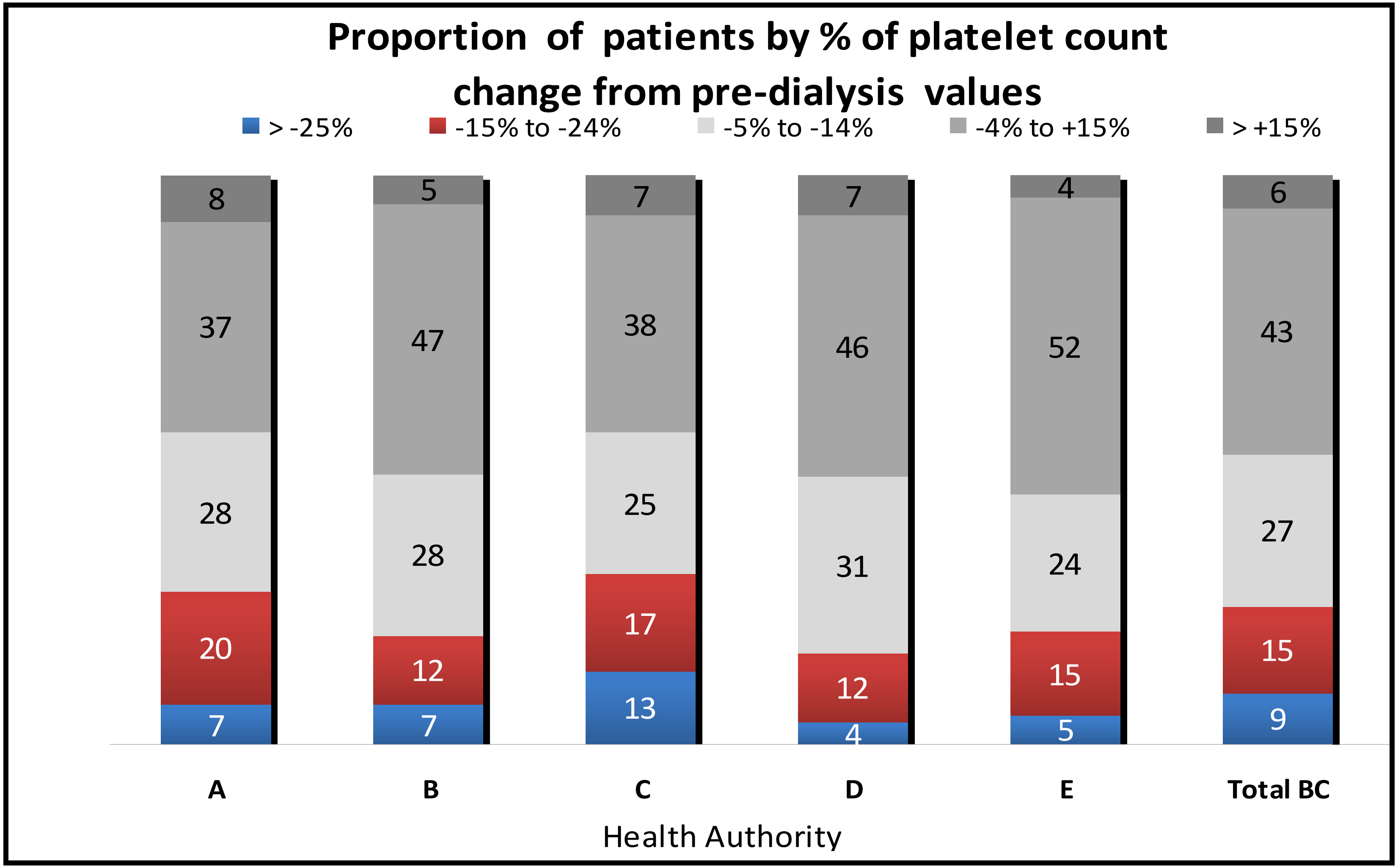
LOCAL CANADIAN EXPERIENCE

BRITISH COLUMBIA AND CALGARY, CANADA

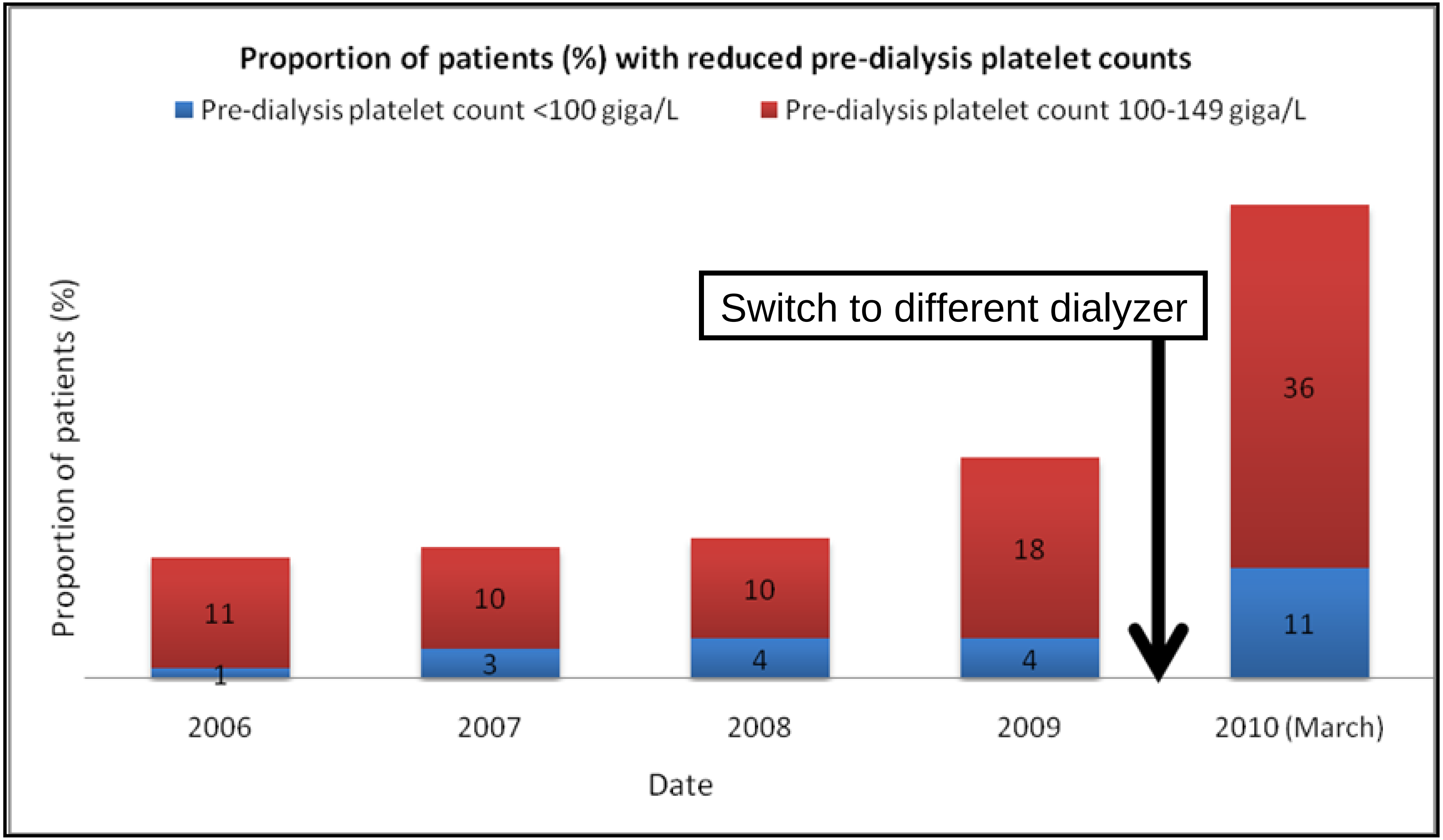
SPH Dialysis Unit Review



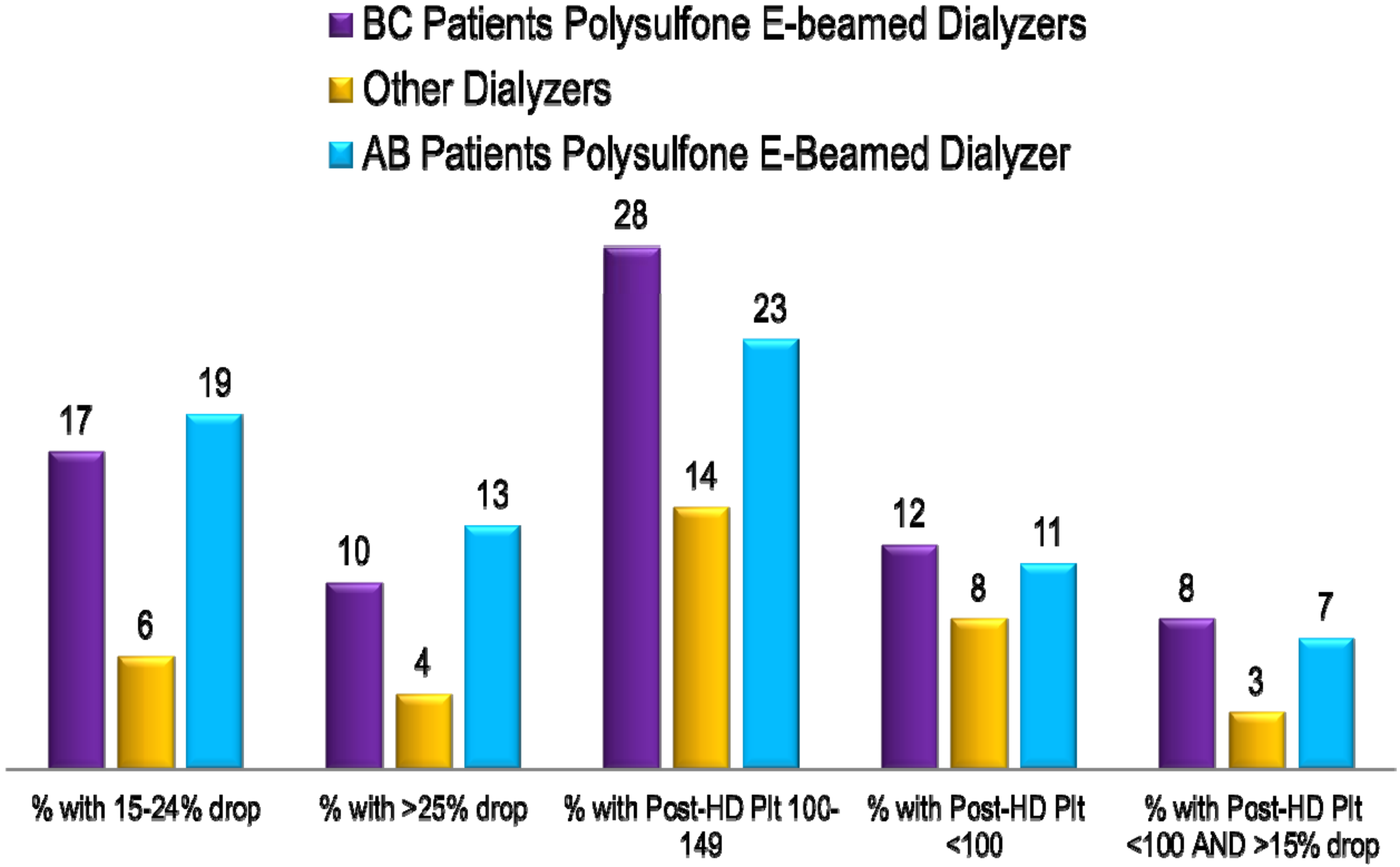
BC-Wide Provincial Investigation (broken down by health authority)



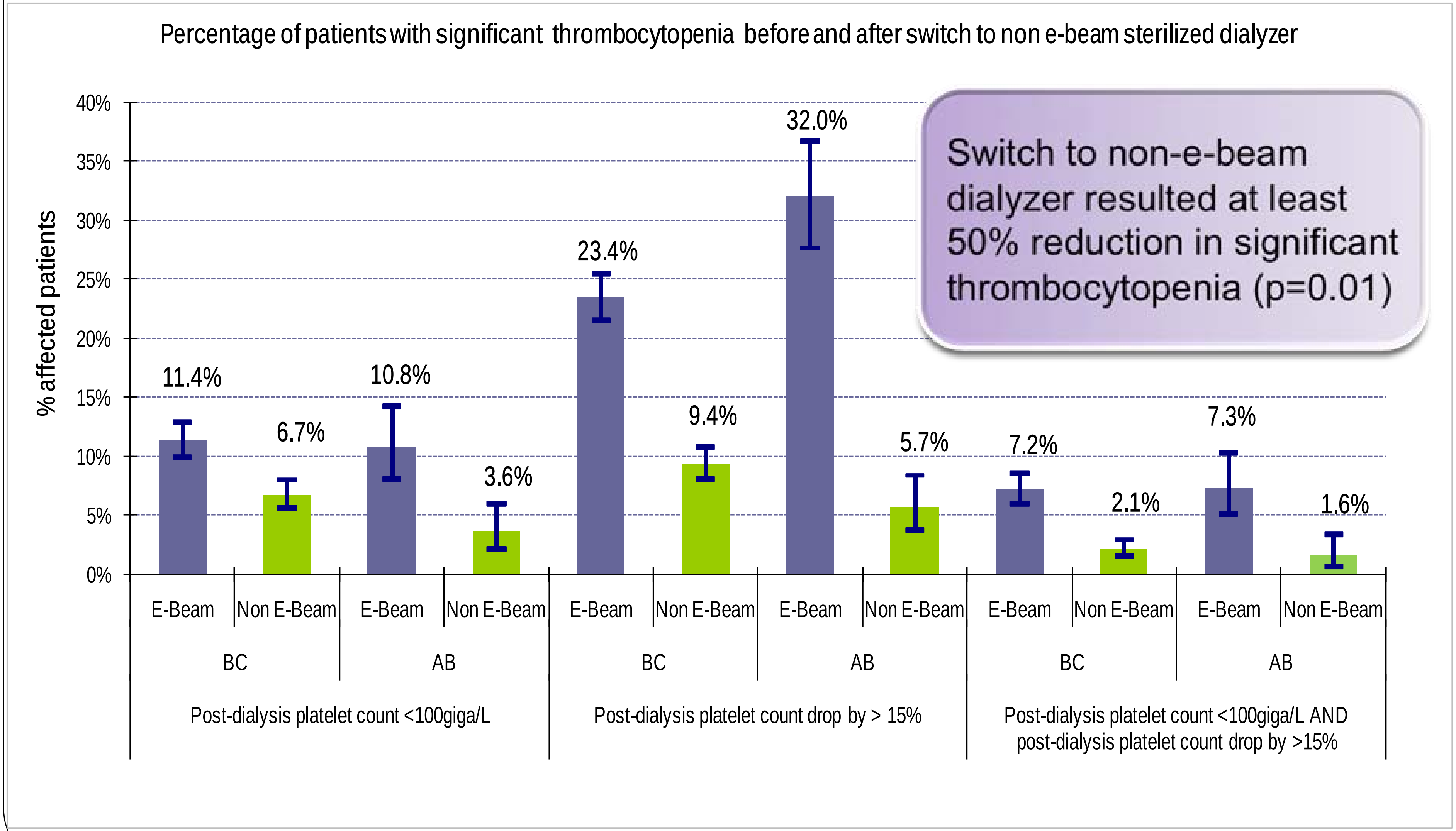
Calgary Experience



Prevalence of Significant Thrombocytopenia in HD Population



Impact of Intervention



CHOOSING A DIALYZER

Dialyzer Specifications

- **Membrane material**
  - Polysulfone: Fresenius, Asahi
  - Poly(aryl)ethersulfone: Gambro (Revaclear), Baxter (Xenium)
  - AN-69-ST: Gambro (Nephral ST)
  - Cellulose Triacetate: Baxter (Exeltra)
- **Clearance** (Qb: 200-400 ml/min and Qd: 500 ml/min)
  - Urea, creatinine, vitamin B12, B2M

Dialyzer Specifications

- **Kuf (Flux)**: High flux standard, required for HDF
- **Sterilization:**
  - Steam and Gamma radiation preferred
- **Other:**
  - Heparin requirement
  - Coating of dialyzer
    - Vitamin E, Heparin grafted (Evodial)
  - Wet vs Dry
  - Cost

Summary

- Most dialyzers currently available are high efficiency & have similar clearance performance
- High flux dialyzers have some advantages and required for delivering hemodiafiltration
- Every unit must have options for patients with possible sensitivity to certain dialyzer membrane
  - Have choice of two different membrane materialf
- Current preferred modes of sterilization are steam and gamma radiation

QUESTIONS / DISCUSSION