Therapeutic apheresis (introduction)

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Apheresis

- Removal of blood
- Separation into component parts
- One component is retained and remainder is returned

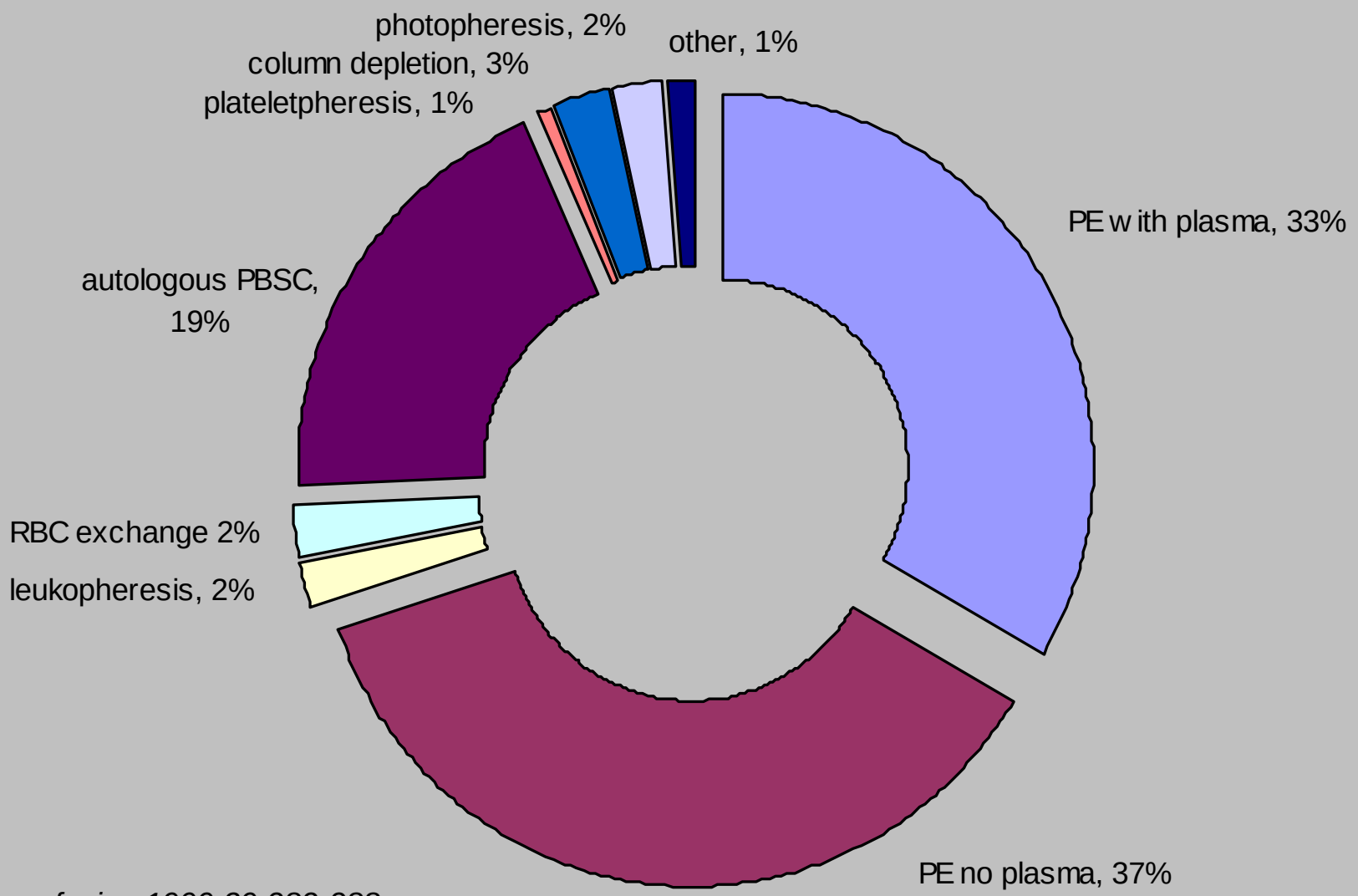
History

- First tried in animals
- In humans it was first performed in patients with hyperviscosity syndrome (1960)
- Increased use following the arrival of automated cell seperators

Goal of Therapeutic Plasma exchange

- remove or reduce levels of pathologic substance
- replace essential substance that is absent
- Modify protein or mediators of inflammation

Frequency of therapeutic procedures by type

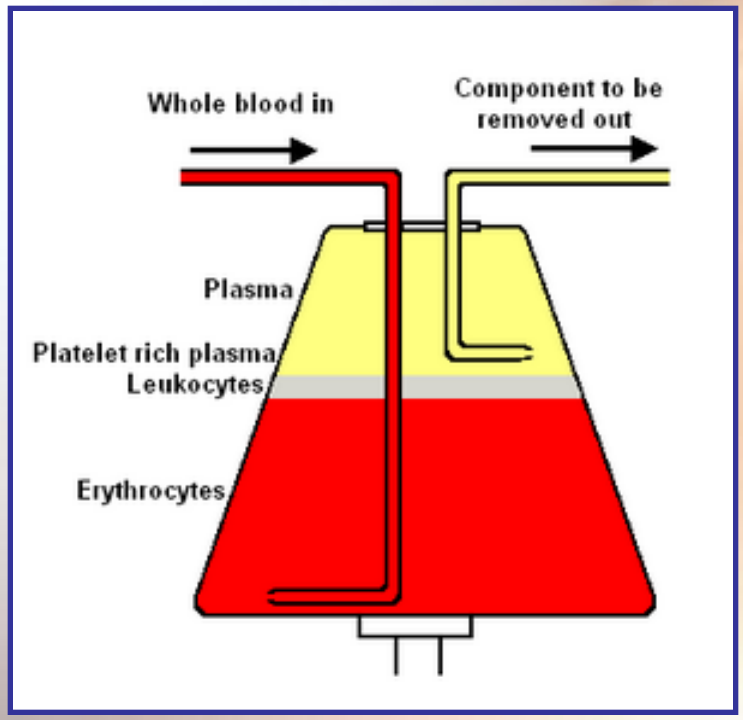


Transfusion 1999;39:282-288

Instrumentation

cell separation device

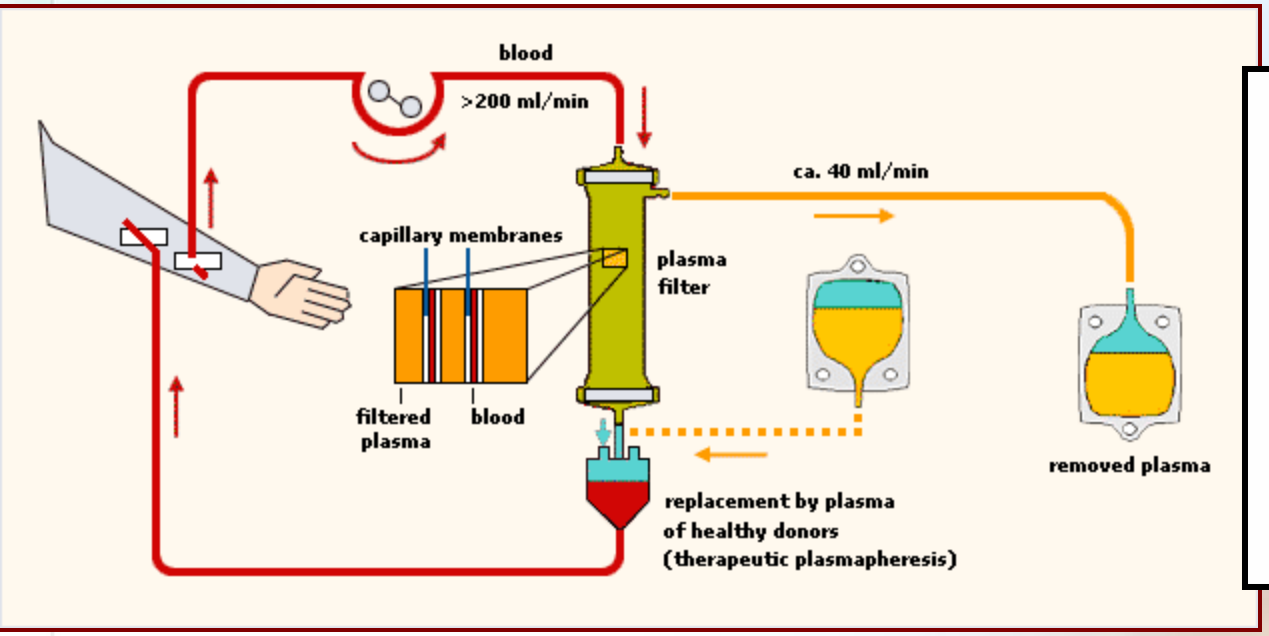
- -Centrifugation
  - Continuous or intermittent flow
- -Retrieve one component and return the rest

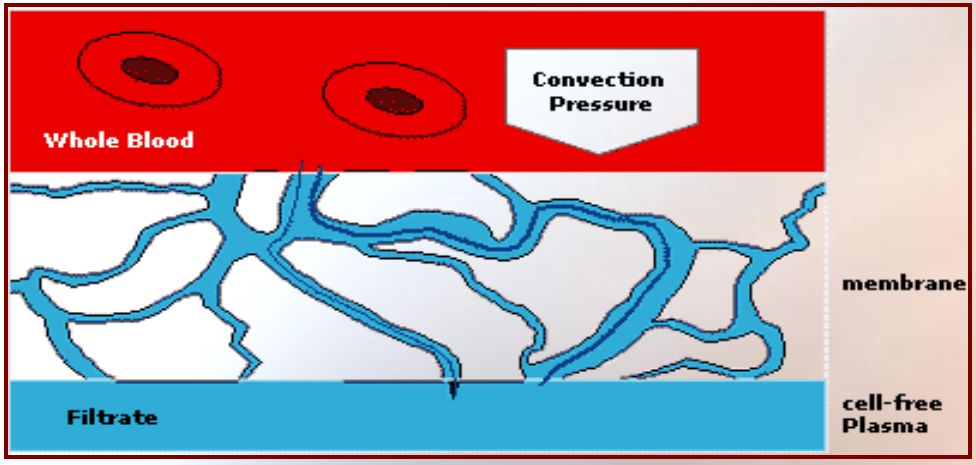


Centrifugation

- Blood is drawn from patient
- Anticoagulant solution is added
- Pumped to rotator bowl, chamber or tubular rotor
- Layering of components occurs based on density
- Desired fraction is diverted
- Other components are returned to the patient

Membrane filtration





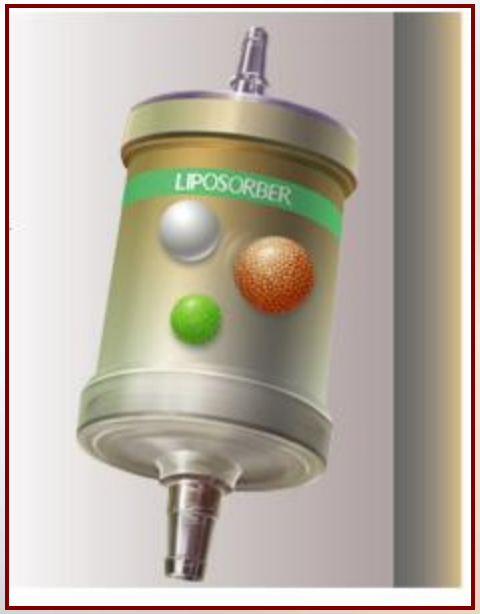
Blood flows across a membrane containing pores of a defined size

http://www.membrana.com/oxygenation/plasma/plasmasep.htm

Separation by adsorption

Can modify centrifugal or membrane devices to absorb specific pathologic materials

http://www.freseniushc.com



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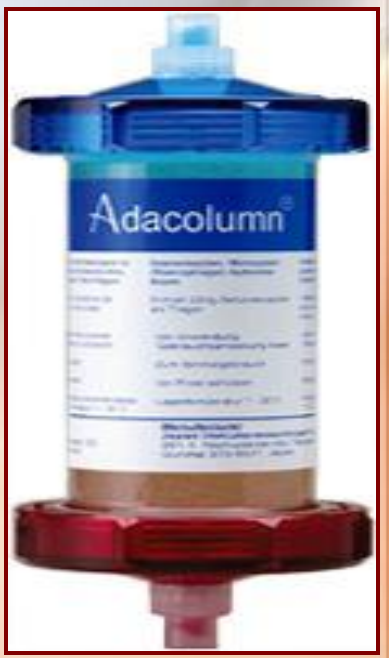
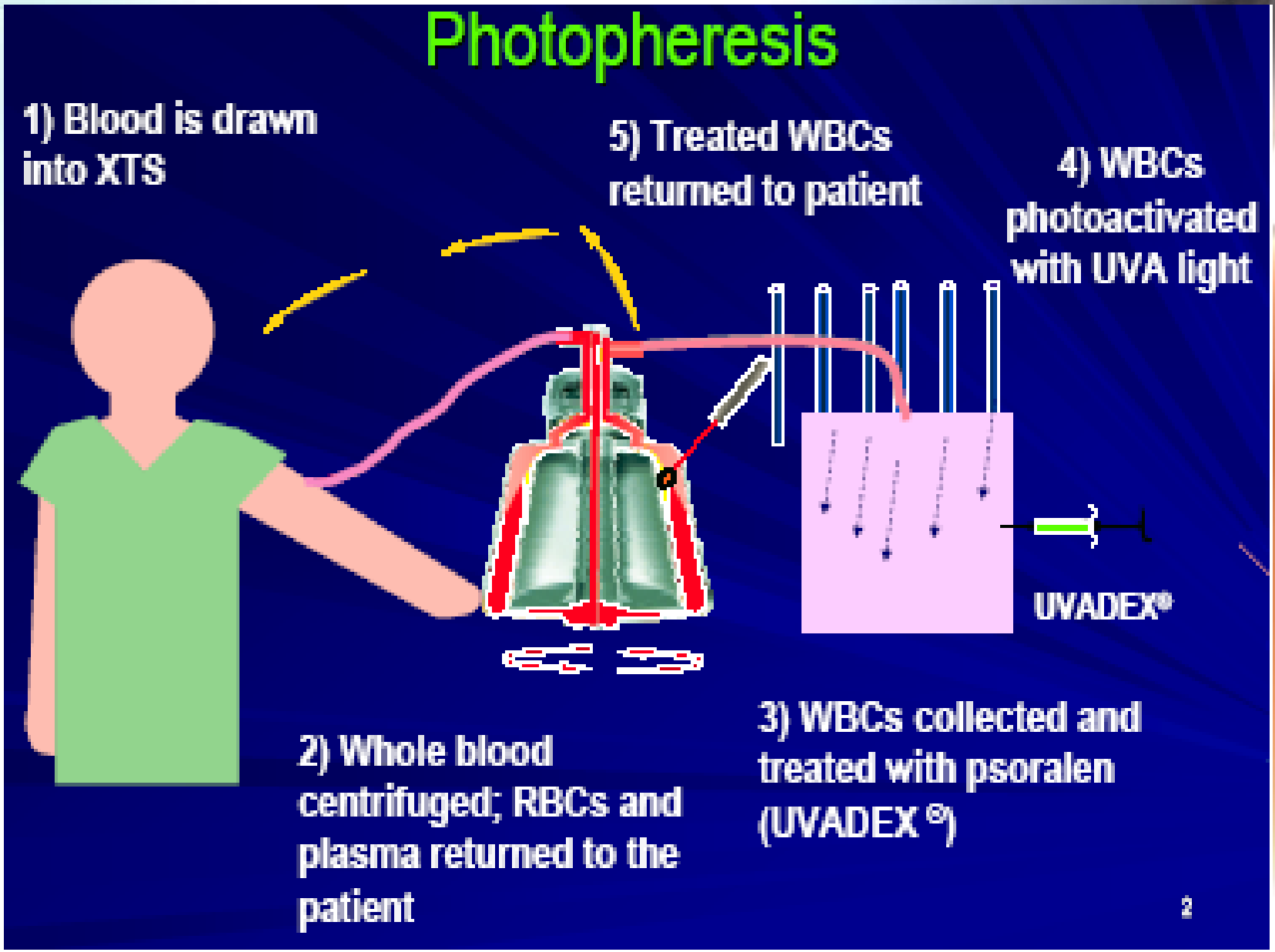


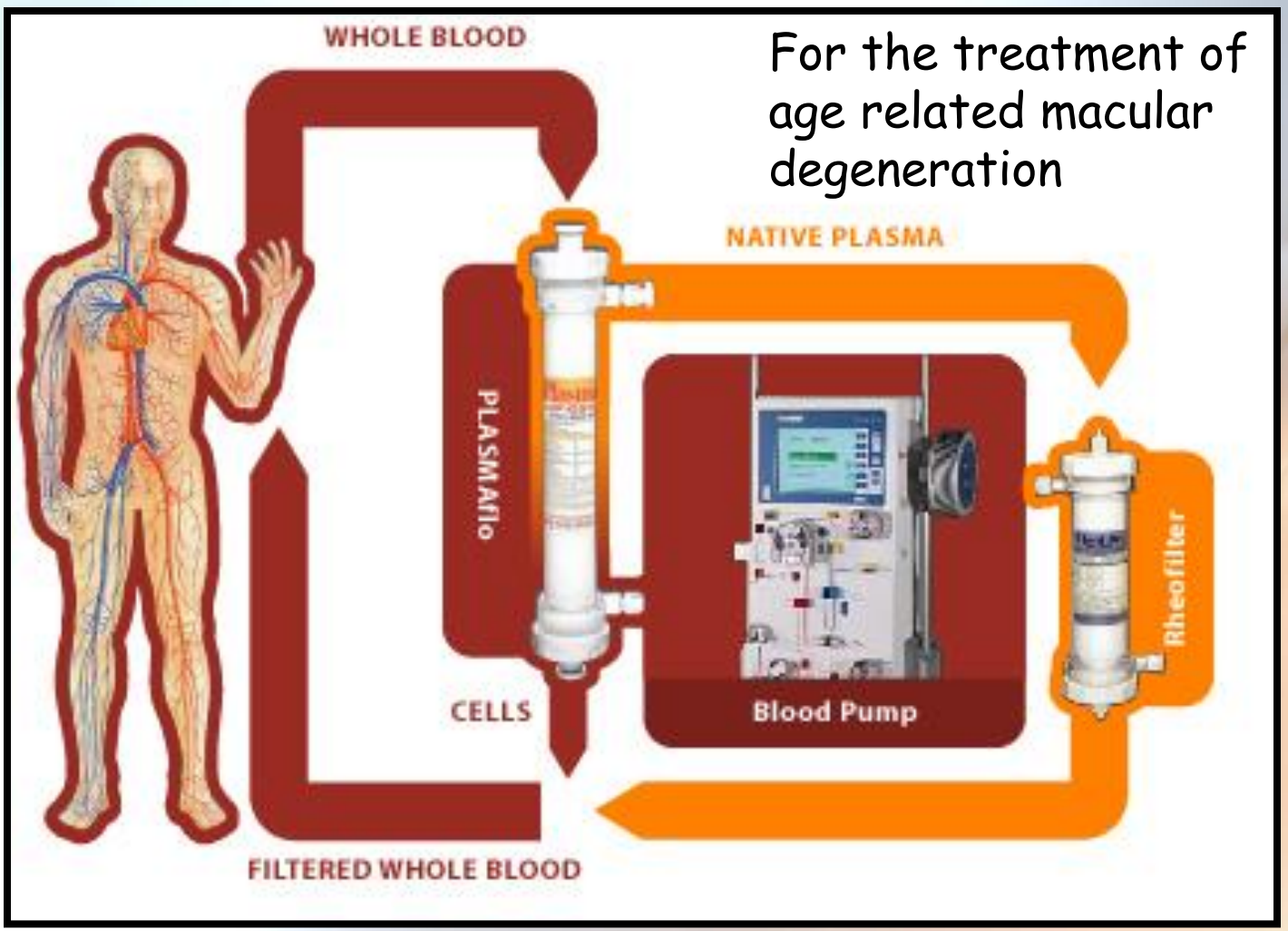
http://www.adacolumn.com

Photopheresis



http://www.apheresis.org/~documents/Marques.pdf

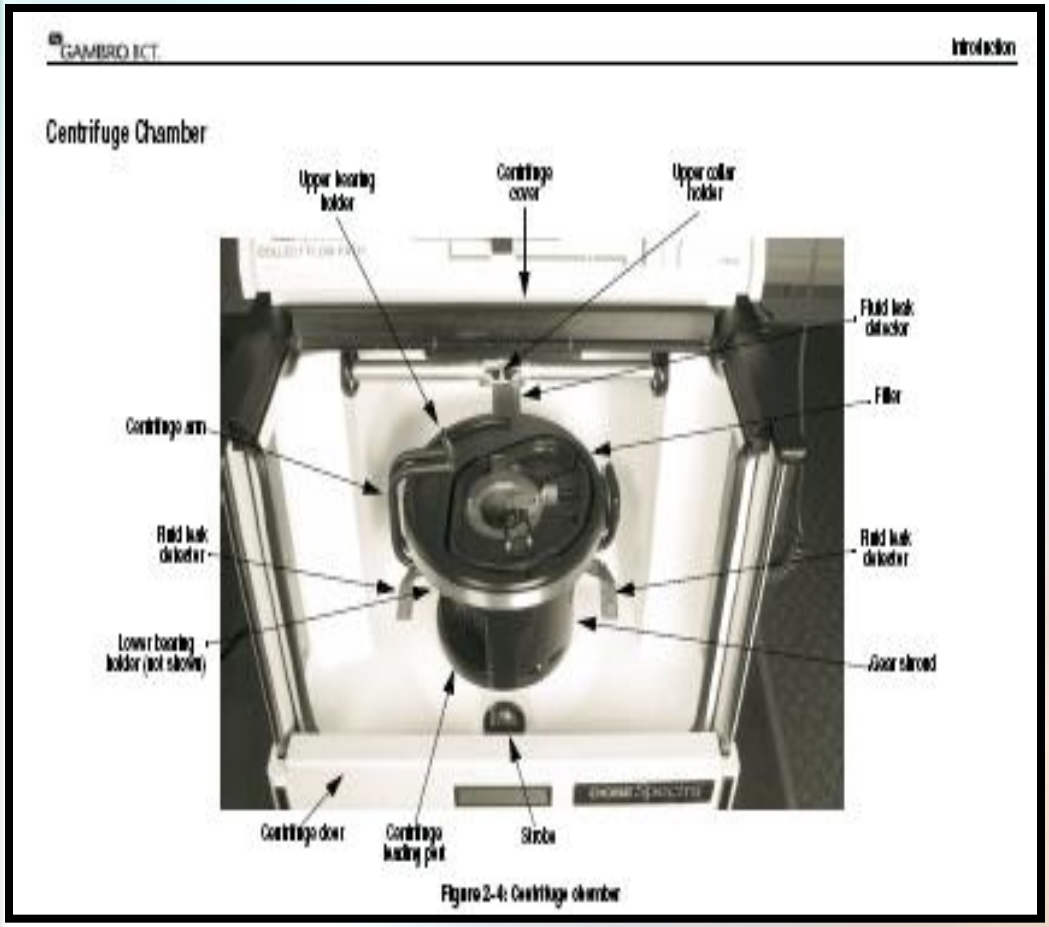
Rheopheresis

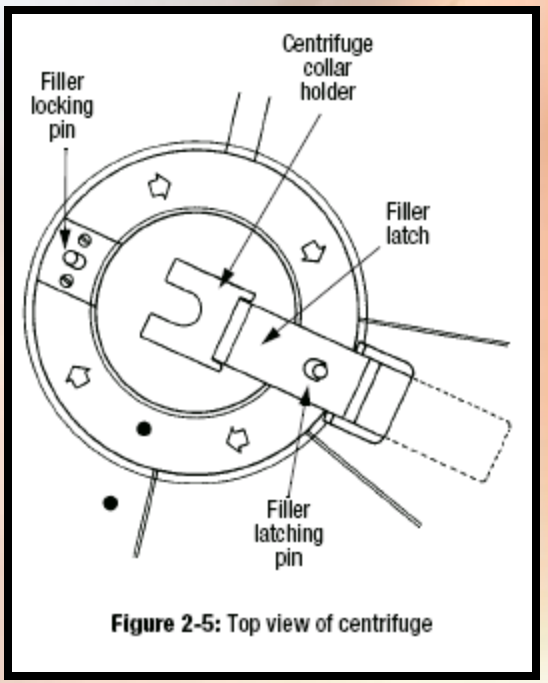


www.amdstudy.com

Mr. Cobe Spectra

Cobe's body parts





COBE Spectra System

- Uses six parameters to determine flow rates and exchange parameters in TPE
  - Sex
  - Height
  - Weight
  - Hematocrit
  - Type of fluid replacement
  - Fluid balance

Pump flow rates

- AC infusion rate – based on TBV and replacement fluid
  - Takes into account citrate content of replacement fluid
  - Initial AC infusion rate : 0.8ml/min/Liter TBV (upper limit of 1.2ml/min/L TBV
  - Inlet: AC ratio is about 10: 1
  - Plasma pump flow rate : based on patient hematocrit
  - Replace pump flow rate: based on fluid balance chosen

Types of therapeutic apheresis or exchange procedures

- Plasma exchange
- Red cell exchange
- Plateletpheresis
- Leukopheresis
- Immunoadsorbtion
- Photopheresis
- LDL extraction

Physiology of apheresis

- Anticoagulation
  - Citrate anticoagulant of choice
    - Chelates calcium and blocks calcium dependent clotting factor reactions
    - Minimizes activation of circulating cellular and plasma components
    - Citrate content varies depending on the anticoagulant used

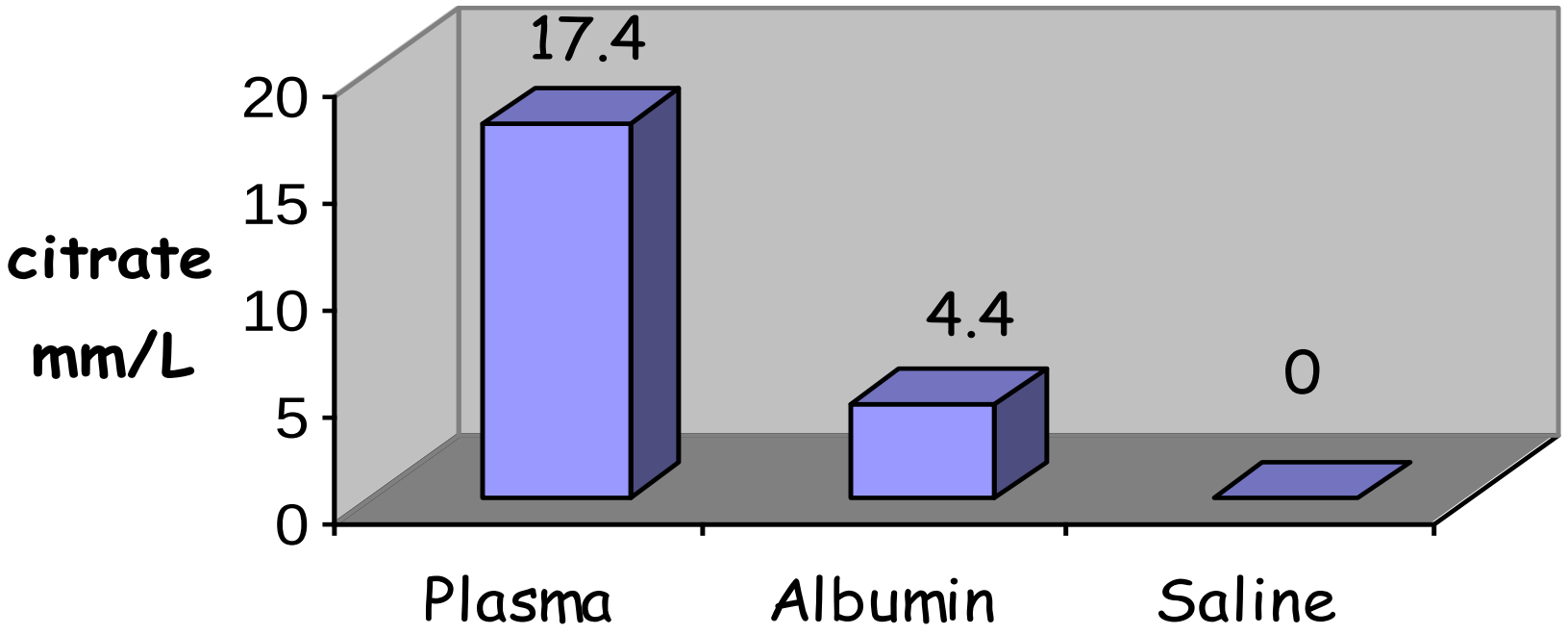
Calcium homeostasis during apheresis

- A lot of work done on platelet donors
- Citrate levels range between 17mg/dL to over 30mg/dL
  - 23 – 33% reduction in ionized calcium especially in the first 15 minutes
    - Increases renal excretion of calcium, magnesium, potassium, sodium
  - Parathormone rises rapidly in the first 15 minutes then levels off
- Citrate returns to baseline levels 4 hrs after infusion ceases

In TPE…

- Similar effects, more citrate infusion in TPE
  - FFP contains citrate
  - Albumin can bind ionized calcium
    - Usually do not become symptomatic
  - Some citrate is discarded with plasma
  - Poor citrate metabolism in liver failure, alkalosis in renal disease
- Current apheresis equipment limit citrate dose and rate, reactions less with continuous flow instrument

Amount of citrate in replacement fluids



Heparin

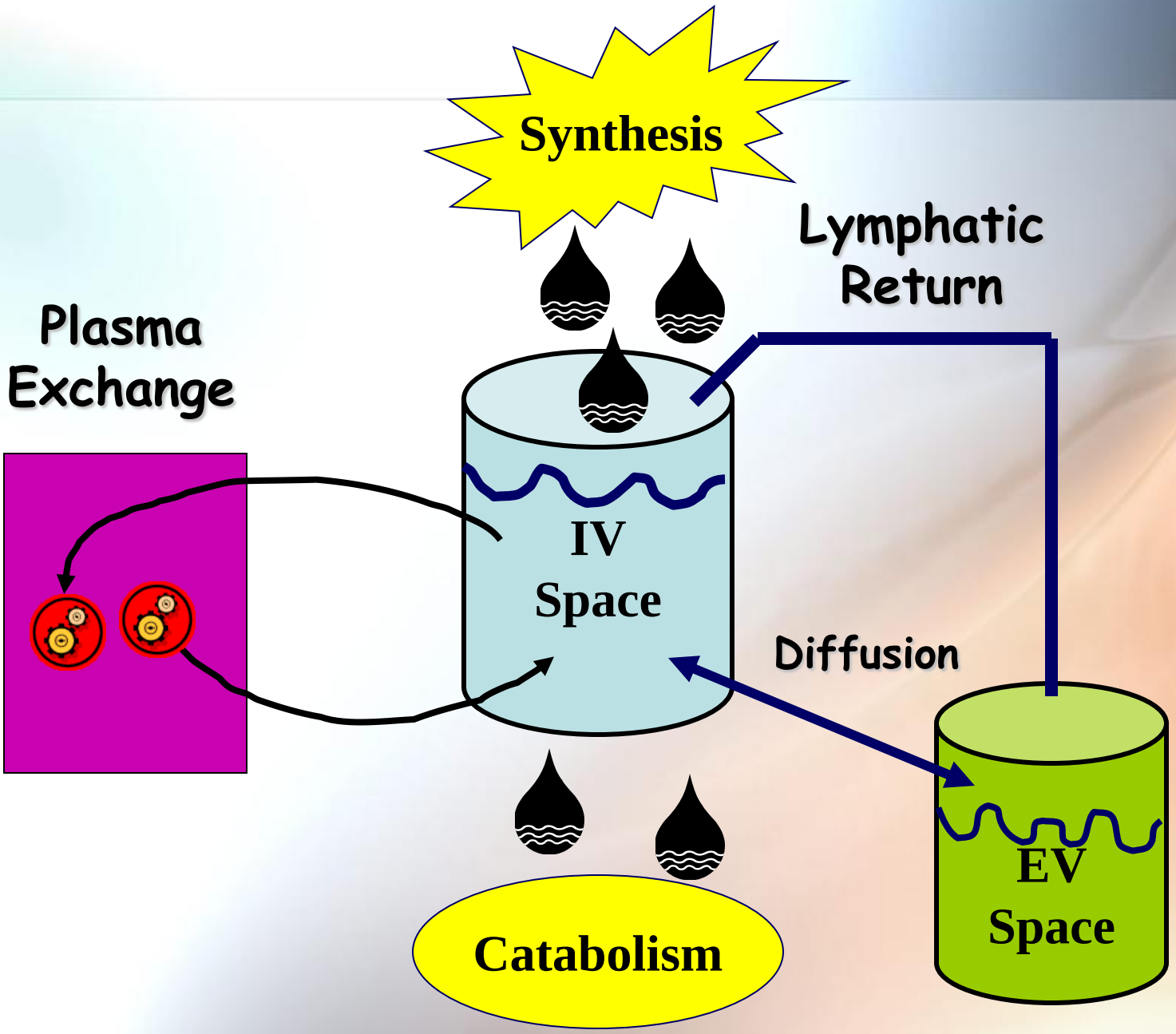
- Can theoretically be used
  - Need about the same dose for heparinization of hospitalized patients
- Low toxicity
- However not used
  - Anticoagulant properties neutralized by normal plasma
  - Risk of Heparin induced thrombocytopenia
  - Used for LDL separation

Other changes

- hemodynamic changes
  - Hypo or hypervolemia
- dilutional effects
  - From replacement fluid
  - Requilibration

Effect on proteins

- Depends on whether they are in the intra or extravascular compartment
- Requilibration
- Rate of protein catabolism
- Synthesis by the liver



Courtesy of Beth Hartwell, MD

Alterations in blood constituents by a single volume exchange

Constituent	% decrease from baseline	% recovery after 48 hrs
Clotting factors	25-50	80-100
Fibrinogen	63	65
Immunoglobulins	63	45
Paraproteins	30-60	Variable
Liver enzymes	55-60	100
Bilirubin	45	100
C3	63	60-100
platelets	25-30	75-100

Changes in PT, PTT, fibrinogen

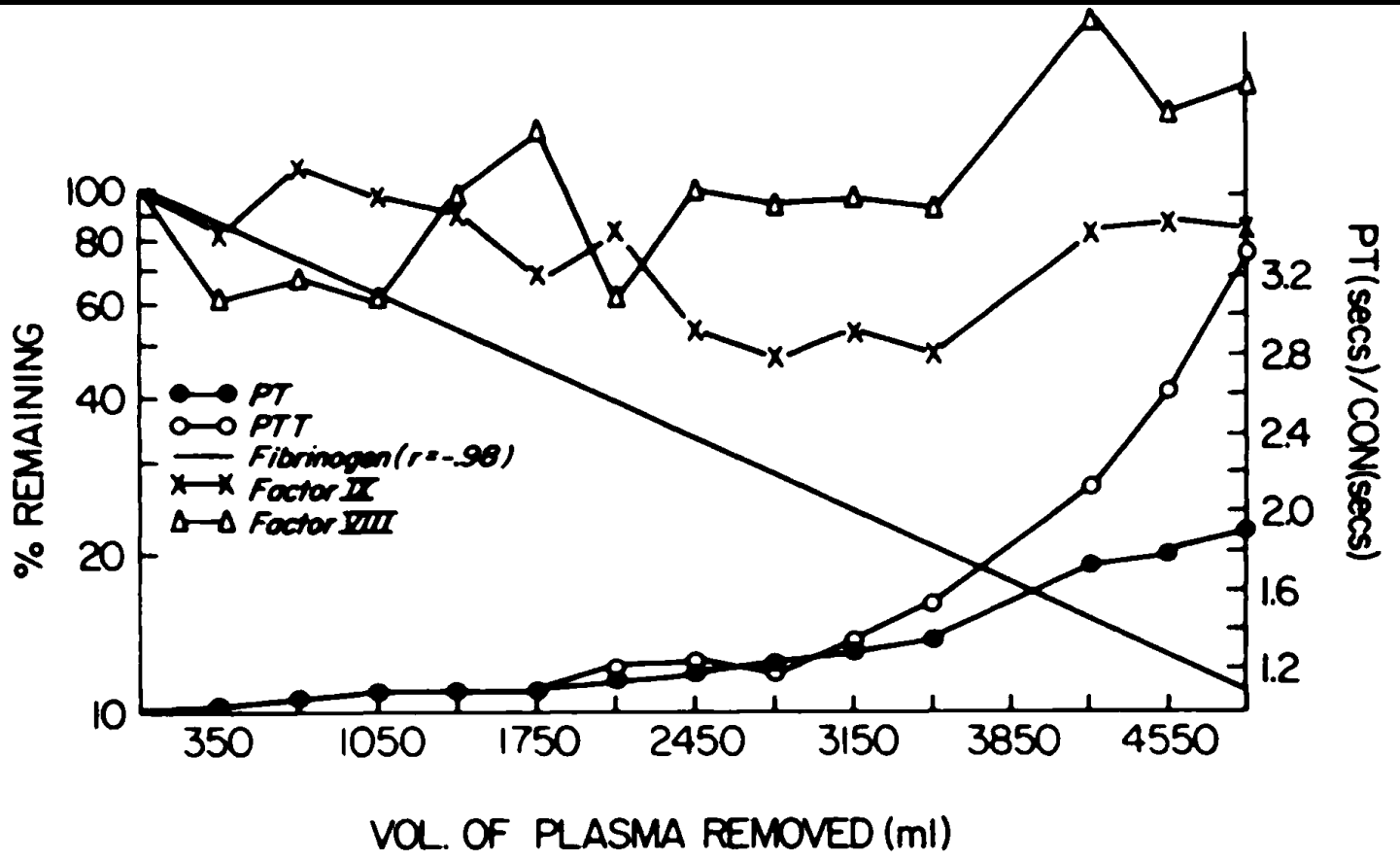


Fig. 1. Changes in the PT, PTT and concentrations of factors VIII and IX during a single partial plasma exchange with albumin replacement. Individual points represent actual measurements. The Fibrinogen curve is based upon a least squares regression analysis of 13 data points.

Effect on electrolytes

- Potassium
  - Observed decrease of 0.25mEq/L after 1.3-2 plasma volume exchanges with albumin and 0.7mEq/L with FFP
- Bicarbonate
  - Decreased
- Chloride
  - Decreased
- Sodium
  - No significant change

Cellular loss

- Red Blood Cells
  - Decreased Hb by about 12% when albumin is used, recovery within 24hrs
- White blood cells
  - Transient increase in WBC count
- Platelets
  - 30% decline, recovery in 48hrs

Drugs

Some drugs especially if protein bound can be removed during plasma exchange

- Antibiotics
- Antiseizure medications

The patient

- Is TPE indicated?
  - History and physical, lab data
  - Co existing health problems
  - Medications
  - Likelihood of response
  - Published experience
  - AABB and ASFA guidelines

Categories

- Category I
  - Primary or standard acceptable therapy
- Category II
  - Accepted in a supportive role to other primary therapies
- Category III
  - Insufficient data to determine therapy
- Category IV
  - No response to apheresis therapy

Current medications

- Can they cause adverse effects?
  - ACE inhibitors
- Will they be removed by apheresis?
  - IV antibiotics
- Needed to treat disease?

Management plan

- Urgency
  - TTP
  - Hyperviscosity syndrome
  - Guillain- Barre syndrome
  - Myasthenia gravis (crises)
  - Sickle cell disease (acute chest, priapism, stroke)
  - Acute liver failure

Management Plan

Extracorporeal blood volume assessment

- Assess patients ability to tolerate the procedure
- Total extracorporeal volume is the amount of cells and plasma needed to displace the saline used to prime the lines
- RBC Extracorporeal volume is the RBC volume required to fill the bowl or channel or all the tubing
  - Proportional to the hematocrit

Management of Extracorporeal volume

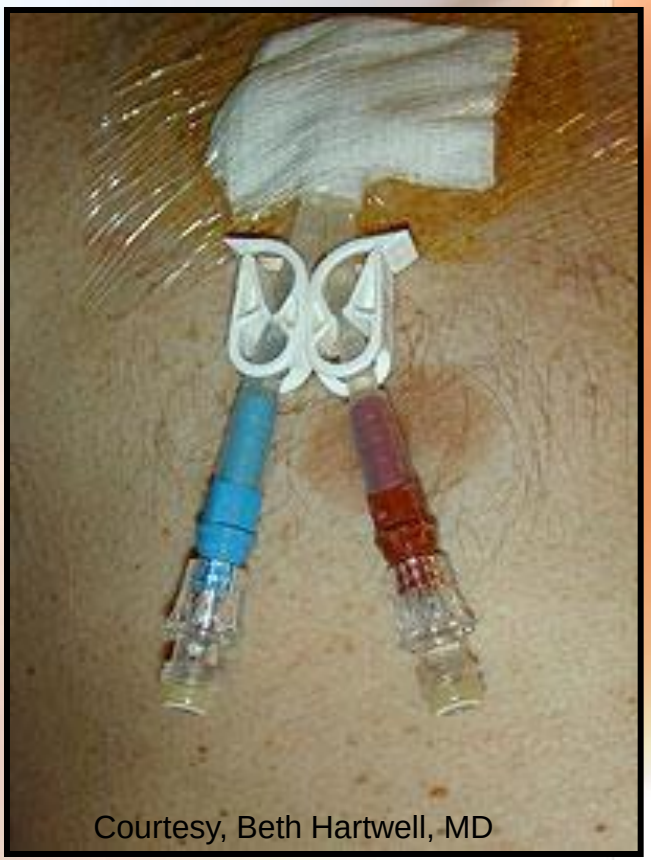
- Total or RBC ECV should not exceed 15%
- If total ECV >15% but RBC ECV < 15%
  - Give saline bolus or colloid prime
- If total ECV < 15% but RBC ECV > 15%
  - Transfuse RBC
  - Prime with RBC

Management Plan

- Vascular access
  - Peripheral or central? Need to consider risks of central catheters, frequency of procedures

What is the ideal catheter?

- Should allow adequate flow rates
- Double lumen for input and return lines
- Staggered ports
- Minimal length
- Sufficient firmness
- Infection resistance

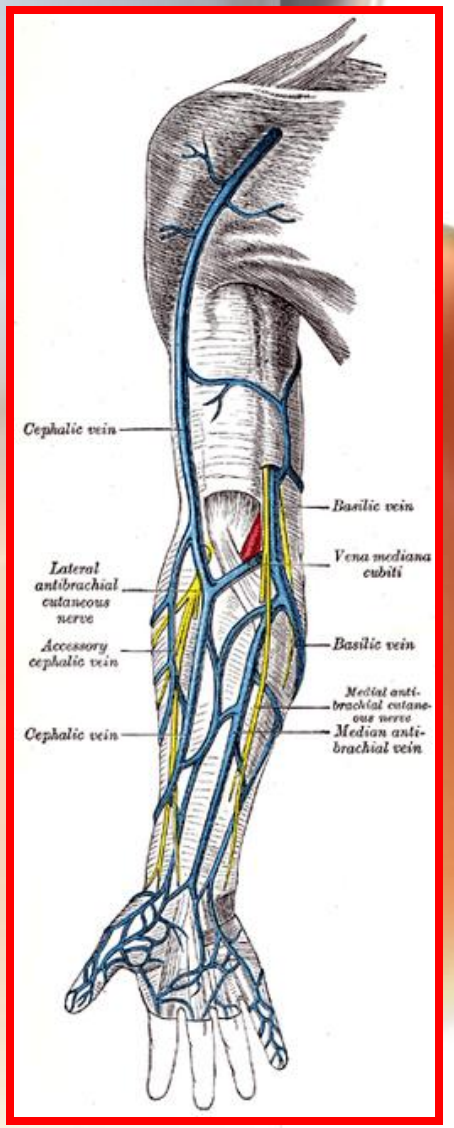


Courtesy, Beth Hartwell, MD

Peripheral access

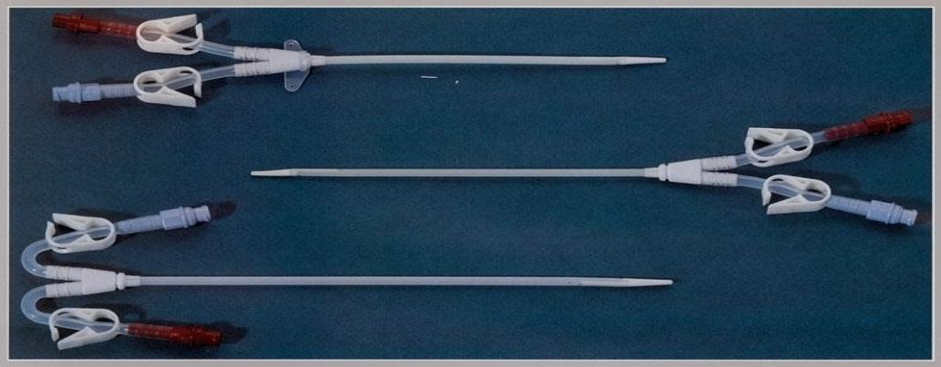
http://www.terumomedical.com

- Preferred
- Fewer side effects
- Use medial cubital, cephalic and basilic veins in the antecubital fossa of the arms
- Use thin walled steel needles (16 or 18 gauge)
- Appropriate skin preparation



Hemodialysis

Quinton® Mahurkar Dual Lumen Hemodialysis Catheters



"...the [Quinton-Mahurkar] catheter appears to have significant clinical and practical advantages over other available forms of acute dialysis access...one can greatly reduce the incidence of problems and provide patients and staff with a comfortable, easily used, temporary access."[1]

1. Graber DA, Dinerstein C: The Quinton-Mahurkar dual lumen subclavian catheter—preliminary clinical evaluation. *Dial Transplant* 12:847-850, 1983.

Catheter Advantages

Quinton® Mahurkar Dual Lumen Catheters:

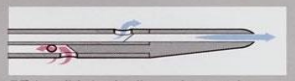
- Preserve peripheral vessels and allow dialysis while chronic accesses mature
- Provide maximum patient comfort by softening when exposed to body heat
- Are made of highly kink-resistant, radiopaque polyurethane and have a special soft tip to reduce trauma to the vein
- Can be inserted in the ICU and other bedside situations
- Can be used with all standard dialysis machines
- Eliminate expensive single-needle equipment and high recirculation values

Choice of Sizes and Lengths

You have a choice of 10 or 11.5 French sizes (O.D.) and a variety of catheter lengths—one just right for each patient.

10 French Mahurkar Catheters:

- Choice of 12, 15, or 19.5 cm implantable length
- ≤ 100 mm Hg venous pressure at 200 cc/min blood flow rate



Efficient dialysis—the distance between the arterial intake and the venous return lumina typically provides recirculation rates of 5% or less.

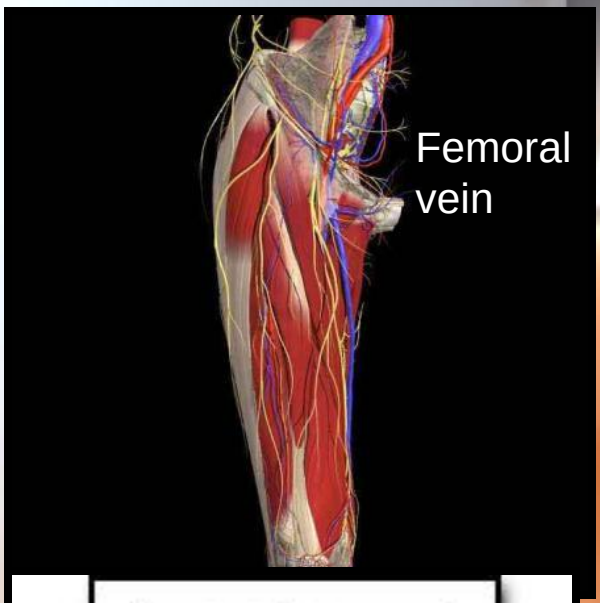
11.5 French Mahurkar Catheters:

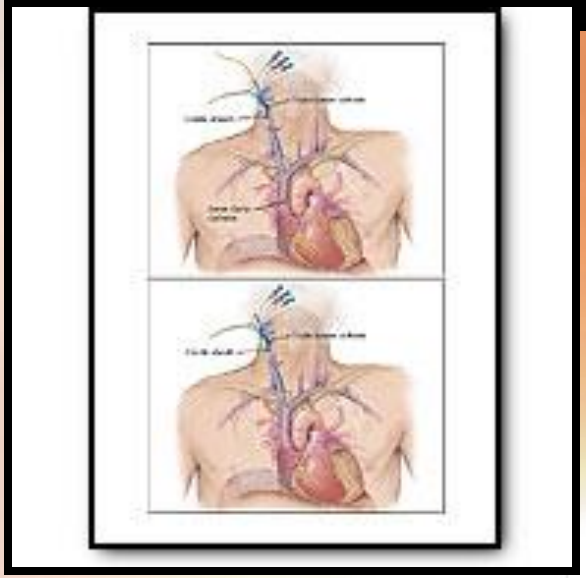
- Choice of 13.5 or 19.5 cm implantable length
- ≤ 150 mm Hg venous pressure at 300 cc/min blood flow rate

Curved Extensions Option

Our 19.5 cm (11.5 Fr) catheter with curved extensions is especially useful for jugular insertions. The catheter extensions bend away from the neck, improving patient comfort. Also, the adapters are positioned caudad, simplifying access for dialysis and catheter care.

Quinton instrument co.





Management Plan

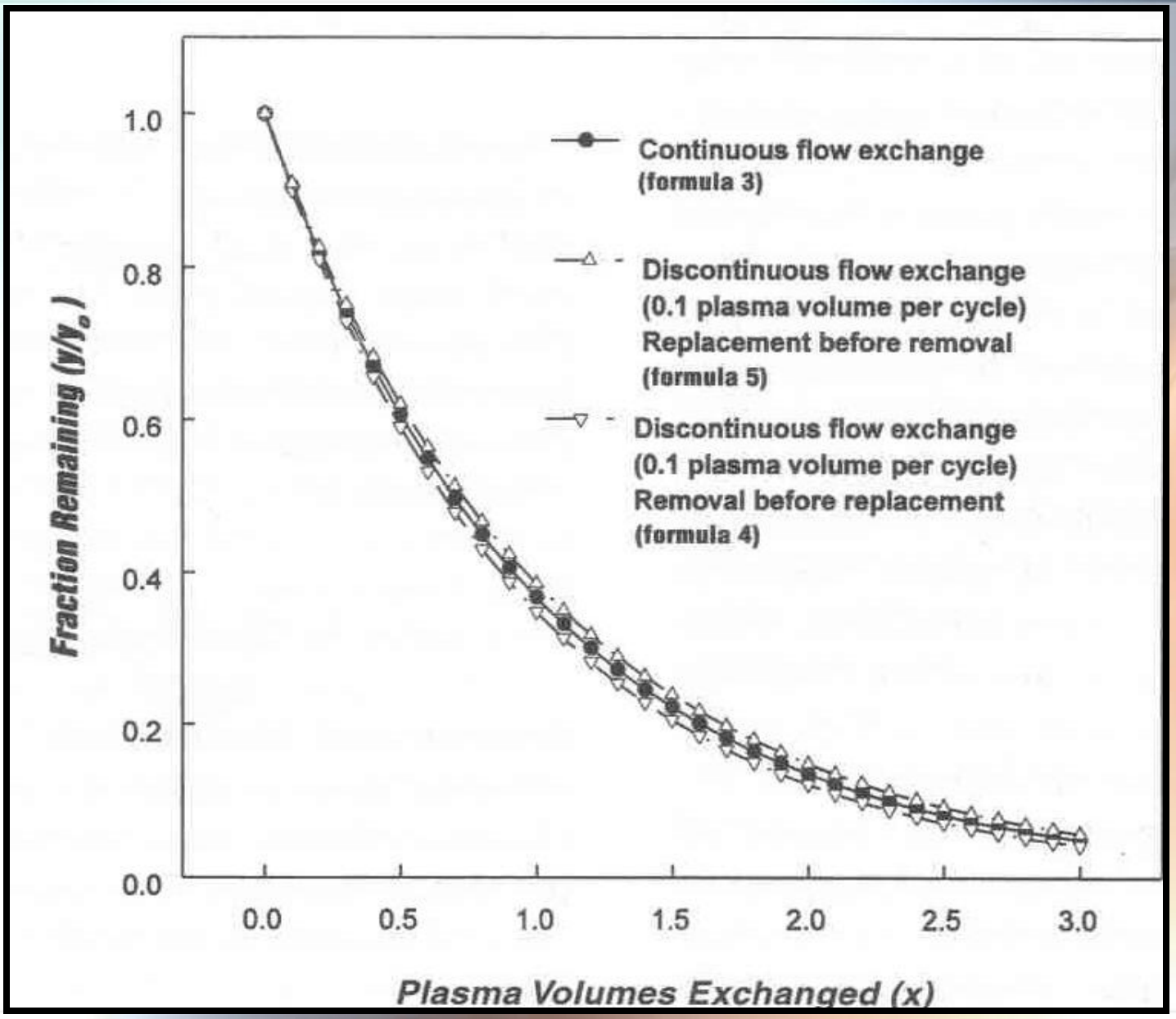
- Laboratory data
  - CBC, electrolyte panel including ionized calcium
  - Related to disease
    - LDH, ADAMTS13, coagulation profile
    - Antibody assays
- Hemoglobin should be ~8.0g/dL,
- Normal K, Ca^{2+}

Intensity of exchange

How many plasma or red blood cell volumes?

- Calculation of TBV, PV, RCV
  - TBV= 70 x (weight kg)
  - PV = TBV x (1-hct)
  - RCV = TBV x hct
  - There are established formula that take into account the weight and BSA
- 1 or 1.5 plasma volumes usually exchanged
- 1 to 2.5X red cell volume

Efficacy of plasma exchange



Replacement fluid

Replacement solution	Advantages	Disadvantages
Crystalloids	Low cost Hypoallergenic No viral risk	2-3 volumes required Hypooncotic No coag factors,immunoglobulins
Albumin	Iso-oncotic No viral risk	High cost No coag factors
Hydroxyethyl starch	Moderate cost Iso-oncotic	Urticarial and pruritic reactions Long term residual levels of HES Contraindicated in renal failure Possible coagulopathy
Plasma	Normal levels of immunoglobulin, coag factors, other plasma proteins	Viral transmission risk Citrate load Allergic reactions sensitization

Frequency

Depends on the disease you are treating

- Removing something?
  - Characteristics of that something?
    - autoantibody, LDL
- Replacing something?
  - TTP
- Is the patient on something?
  - Need to deal with rebound phenomenon?

Targets and goals

Substance	Treatment volume (mL/kg)	Treatment interval	Treatment endpoint
Autoantibodies	40-60	24-48	4-6 treatments
Immune complexes	40-60	24-48	Response
Paraproteins	40-60	24	Response
Cryoproteins	40-60	24-48	Response
Toxins	40-60	24-72	Response
TTP	40	24	Remission
Immunologic rebound	40-60	24-48	2-3 followed by immunosuppressives

Other things you need to do

- Obtain Informed consent
- Write a consult note
- Premedication if needed
- Order blood components

Complications of TPE

- Relatively safe procedure
- Adverse events occur in 4 – 17% procedures
- Most adverse reactions are mild
- Rare deaths, most cardiac

Complications of TPE

- Vaso vagal reactions
- Vascular access complications
- Citrate reactions
- Bleeding
- Hypotension (vasovagal, hypovolemia, Bradykinin, neurologic)
- Allergic reaction
- Volume overload
- Coagulopathy
- Arrhythmia
- Infection (blood products, catheter related)

TPE in pediatric patients

Problems

- Extracorporeal fluid volume
- Vascular access
- Lack of universally acceptable indications
- Experienced personnel

- Need to sedate?
- heparin may be preferred
- May need to prime the circuit with RBC

In case you have a few $$ to spare