Therapeutic Plasma Exchange: principles and practice in pediatric nephrology

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References

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- Apheresis:Definition & History ;Principles and practice
- TPE: key points
- Pediatric considerations
- TPE in Pediatric Nephrology Diseases

Apheresis:
Definition & History

Definitions

- Apheresis : [in Greek] “to carry away” Cytapheresis;Plateletphresis;Plasmapheresis
- Plasmapheresis: plasma is removed and replaced w/plasma substitute (N.S. and/or 5% albumin)
- Plasma exchange: plasma is removed and exchanged w/allogeneic plasma
- TPE: therapeutic plasma exchange

Use of Apheresis

- **Collection**
  - facilitate collection of a blood component (plt, wbc) from an allogeneic donor
  - collection of hematopoietic progenitor cells
- **Therapy** (therapeutic apheresis):
  - removing undesired substances like antibodies, lipids **from the circulation,which are :**
    - **present in plasma**
    - **tightly bound to plasma proteins**
  - reducing excess wbc/plt in pts w/myeloproliferative disorders
  - automated exchange of sickled rbc

Abnormal Substances Removed From the Circulation by TPE

1)Paraproteins (Waldenstorm's Macroglobulinemia)

2)Autoantibodies (Myasthenia Gravis, Goodpasture's syn.)

3)Lipids (LDL in familial hypercholesterolemia; phynatic acid in refsum's disease

4)Toxins or drugs (that are bound to albumin)

5)Circulating immune complexes (CIC)

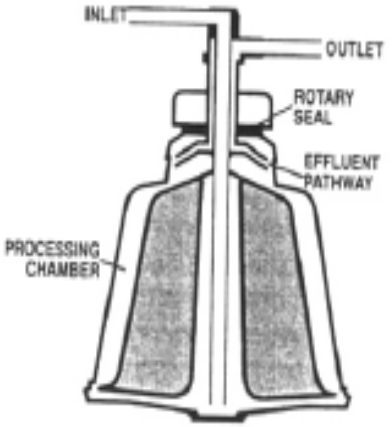
6)Soluble mediators of inflammatory response (activated complement component, vasoactive substances)

History:

- Plasmapheresis (removal of plasma with return of RBC) first performed 1914 John Abel at Johns Hopkins University in a dog in context of artificial kidney research
- 1959 Skoog and Adams used manual plasmapheresis in patient with Waldenstrom's to reduce serum viscosity
- Developed manual plasmapheresis was Major method of collecting source plasma from paid donors until early 1980's

History

- Earliest work in early 1950's by Dr. Edwin Cohn at Harvard
  - Devised fractionation scheme for plasma and important in providing albumin for WWII
  - Blood into conical centrifugal separation chamber

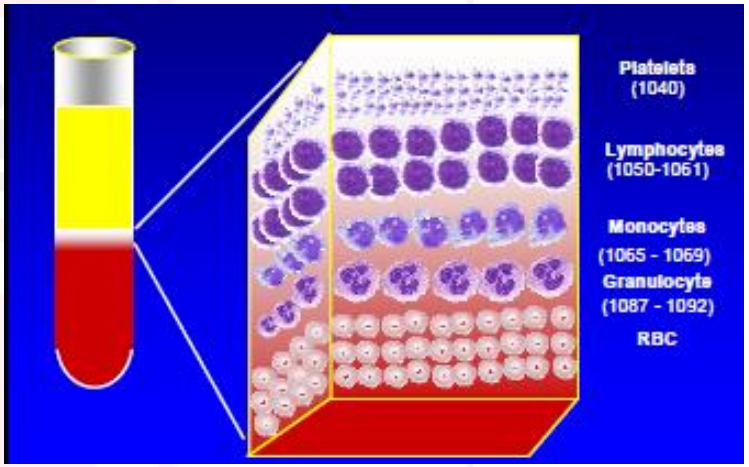


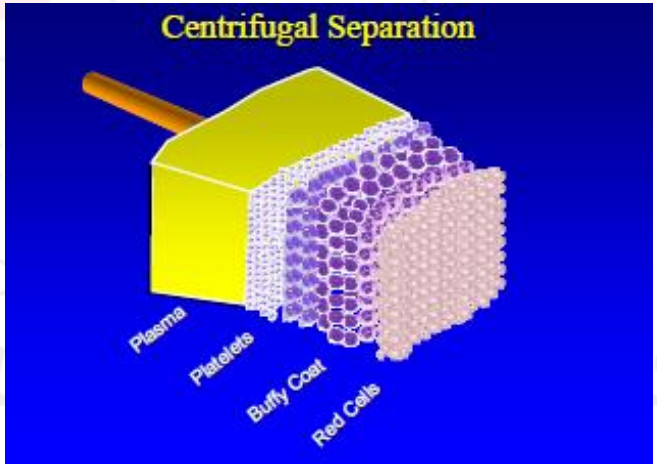
- 1962 IBM engineer son dx with CML
  - Together with Dr. Emil Freireich and IBM developed NCI-IBM (2990) at National Cancer Institute
  - Initially process 11L of blood from CML patients for leukopheresis
- 1964 studies on CLL patient leukopheresis
- 1969 1st automated plasma exchange procedures

Apheresis:
Principles of Separation& Methods

Centrifugal separation based on special gravity

- Plasma (1.025-1.029 specific gravity)
- Platelet (1.040)
- Mononuclear (lymph, mono, PBSC,blast) (1.070)
- Granulocyte (neut, baso, eos) (1.087)
- Neocyte RBC
- RBC (1.093-1.096)





METHODS

1)Centrifugation

A- manual:

B-automatic:

- Intermitent Flow Centrifugation [IFC]
- Continious Flow Centrifugation [CFC]

2)Filtration: based on size ,not gravity

Smaller; less EV

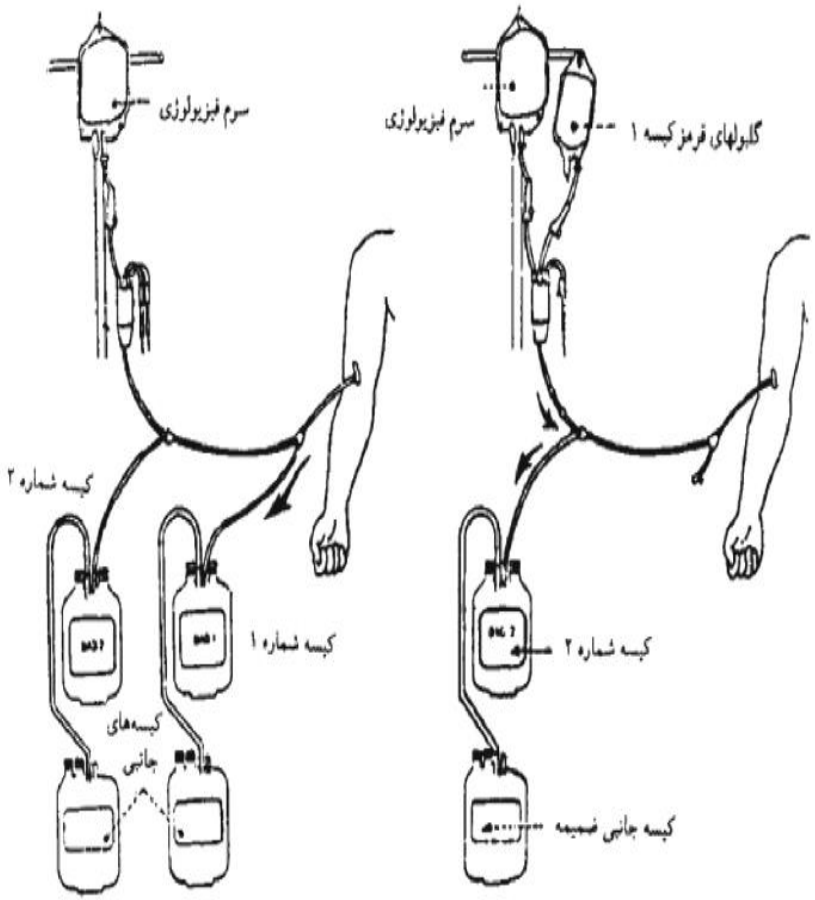
3)Combined Centrifugation &Filtration

4)Afinity Adsorption Apheresis : based on physical,Chemical or Immunological properties

Manual

vs Automatic :

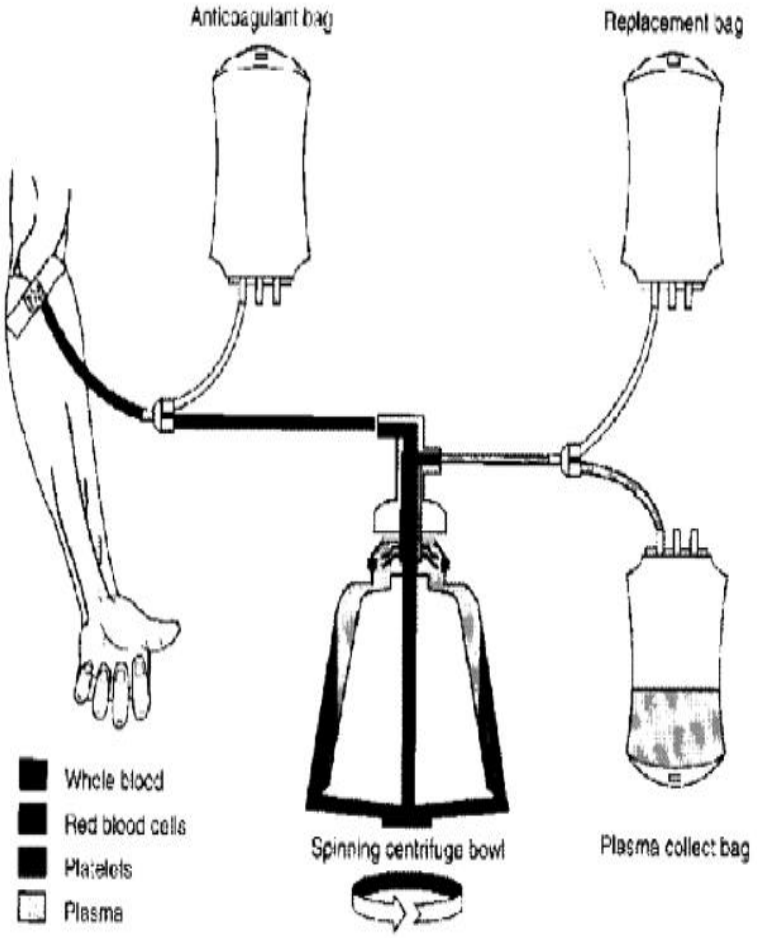
- Cheaper& Simpler
- No machine
- Less dependent to size of IV access
- Less volume/slow
- Error in RBC return
- Alternative to automatic method



Intermitent Flow Centrifugation [IFC]:

- Intermittent flow
  - Blood processed in discrete batches
  - Separation until container filled with dense component (RBC)
  - Needs to empty before next batch

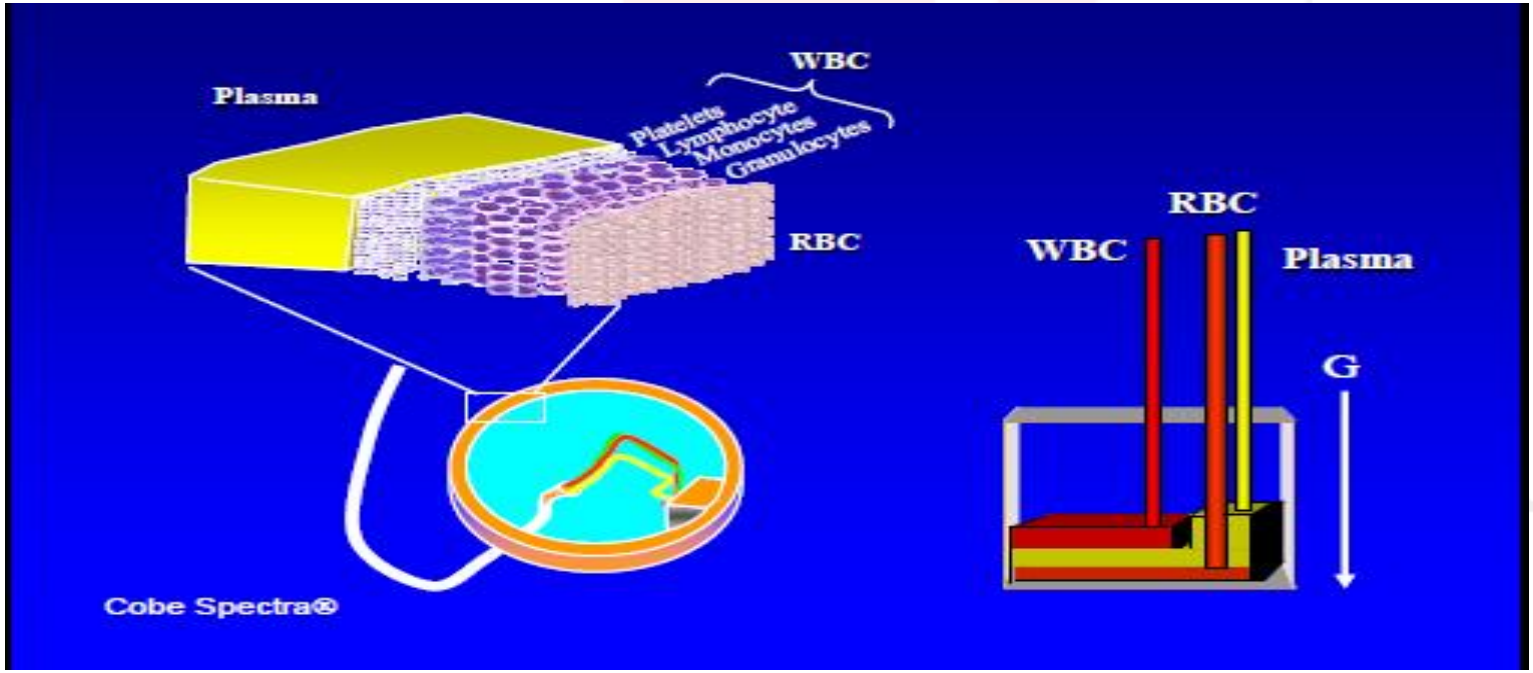
Haemonetics MSC plus, V50,V30



Continious Flow Centrifugation [CFC]

- All fractions can be removed in ongoing manner
  - Do not need to empty container until end of procedure

Cobe spectra, CS 3000, Fresnius AS 104

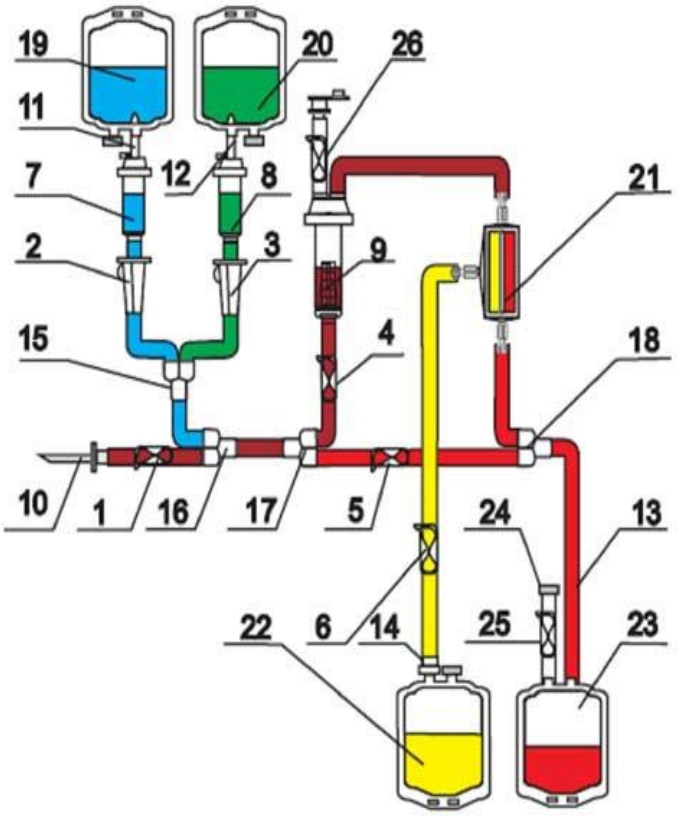


Intermittent vs. Continuous Flow

- Intermittent flow: procedure performed in cycles (withdrawal, separate, re-infuse).
  - Pro: Smaller machine; one needle access for peripheral access
  - Con: extracorporeal volume (ECV) can be high (bad in kids and the elderly with low total blood volume or TBV), fluctuations in hemodynamics
  - E.g: Haemonetic V50
- Continuous flow: blood withdrawn, processed and reinfused simultaneously
  - Pro: smaller ECV, hemodynamic stability, faster
  - Con: 2 venipuncture sites for peripheral access
  - Examples: **COBE Spectra,** Fenwal C3000 Plus, Fresenius AS 104

Membrane Filtration

- Conceptually similar to hemodialysis
- Use limited to plasma exchange
- Blood is pumped to the filter membrane
- Membranes with pore sizes that can trap high MW proteins, exclude cellular elements
- Cellular components combined with replacement fluid, returned to patient



Membrane Filtration (MF) vs. Centrifugation

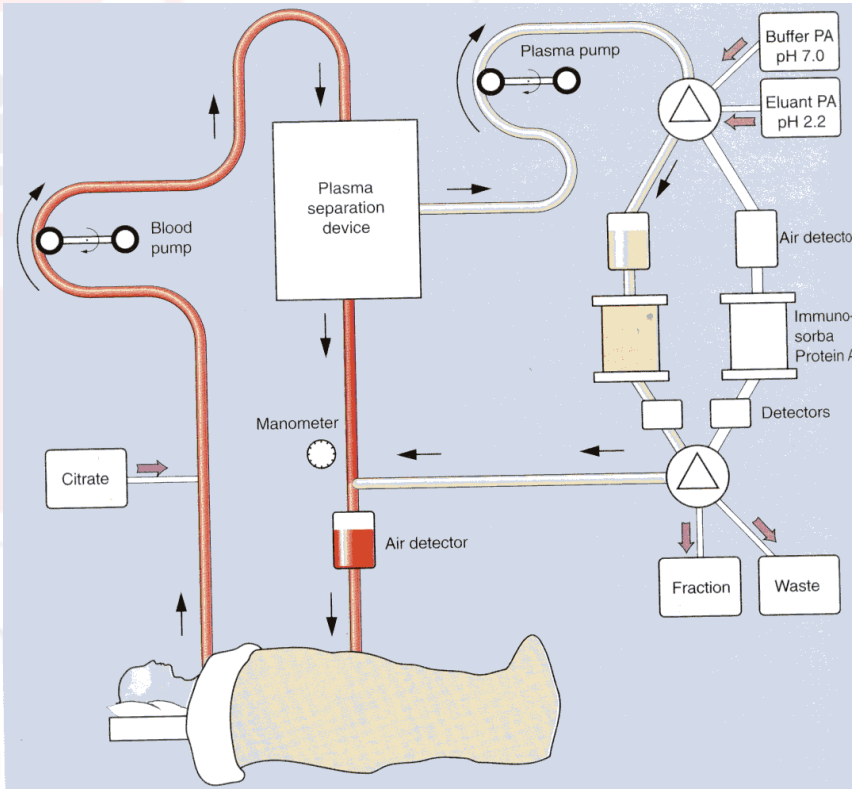
- Similar efficiency and safety
- Membrane filtration (MF) is faster: because time is required to set up a centrifugal interface
- Different anticoagulants:
- Membrane filtration: heparin
- Centrifugation: usually citrate
- MF cannot remove cellular elements, therefore use is limited to plasma exchange
- MF widely used in other areas of the world: Japan, Europe. Uncommon in the US

immunoadsorption

- In contrast to conventional plasma-exchange therapy, immunoadsorption removes harmful agents while retaining natural plasma components, enabling the patient's own modified plasma to be used as a replacement solution.
- Perfuse plasma through a selective removal column/filter
  - Dextran sulfate column: removes LDL
  - Staphylococcal protein A: removes IgG by binding to the Fc portion

immunoadsorption

- Maximum rate of 50ml/min
- 2.5 -3 plasma volume are proccessed in each session
- Treatment period#2 days , allowing overnight equilibrium
- The same columns can be kept refrigerated (in0.1% Thiomersal) and used again for same patient



TPE :
key points

Main Questions about TPE

- **Characteristics of pathogen for uptake**
- **Expectation for success**
- **Plasma Volume for Exchange in each session**
- **TPE intervals**
- **Fluid substitutions**
- **TPE and interactions**
- **Lab tests needed before and during TPE**
- **Where and by Whom it should be done**

Characteristics of pathogen for the most efficient uptake

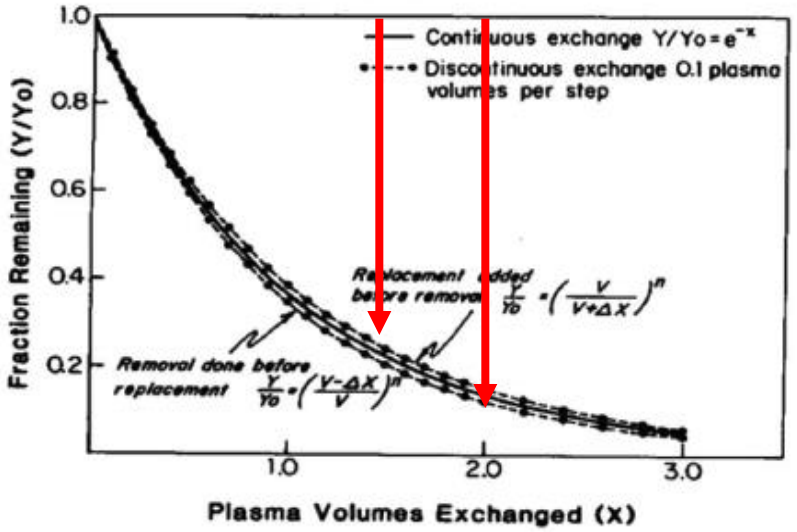
- Macromolecules(>15000 D)
- Long half life : IgG with21 days hl
- Slow synthesis rate
- Intravascular compartment
- Toxic OR refractory to conventional less complicated treatments

Expectation for success

- The correlation will be correct If pathogen is:
  - **totally intravascular ;**
  - **not produced ;**
  - **not consumped**.

- Accordingly the success rate could be sorted descendingly:

1. Fibrinogen ,C3
2. IgM,Cholestrol,ALP
3. IgA,IgG,LDH,CK
4. Small molecules & minerals



- **Little advantage beyond 1.0-1.5 volumes:**
  - Decrease efficiency:
    - **1pv= 63%,**
    - **2 pv=86% ,**
    - **3 pv=95%**
  - More time (2Hr for each PV)
  - More cost

Removal of IgG and IgM by plasma exchange:

	IgG	IgM
Intravascular amount	45%	76%
"total body"removal		
1 PV Ex.	28%	48%
1.5 PV Ex.	35%	59%
2 PV Ex.	39%	65%

- Rebound effect & Neg Feedback:
  - less IgG level leads to more synthesis
  - Immunosuppresive treatment has agonistic effect on TPE
- IVIG blocks FcRn :more free Intravascular pathogen IgG ;more pathogen IgG catabolism and more pathogen IgG available for TPE
- TPE is more efficient for natural IgG than Paraprotein IgG(due to more plasma volume)

TPE intervals & sessions

- Depends on:
  - Type of pathogen particle
  - Severity of disease & clinical status
  - Regeneration of pathogen
  - Redistribution of pathogen
  - Adjuvant Rx: Immunosuppresive Rx ; IVIG

TPE intervals & sessions

- GBS: continue 1-2 times/W untill clinical improvement
- TTP: daily untill clinical improvement: normalization of LDH and Platelet level for at least 2-3 days
- GPS: daily for at least 2 weeks
- Combination with immune suppresives:continue for 5-10 times untill drug response expectation

Substance to Remove	Treatment Volume (ml/kg)	Treatment Interval (in hours)	Treatment Endpoint
Autoantibodies	40-60	24-48	Four to six treatments
Immune complexes	40-60	24-48	Treat for response
Paraproteins	40-60	24	Treat for response
Cryoproteins	40-60	24-48	Treat for response
Toxins	40-60	24-72	Treat for response
Thrombotic thrombocytopenic purpura/ Hemolytic uremic syndrome	40	24	Treat to establish remission
Immunologic rebound	40-60	24-48	Two to three treatment followed by immunosuppressive medication

Fluid substitutions

Replacement solutions	Advantages	Disadvantages	Indication
Crystalloids	• Low cost • Hypoallergic • No viral risk	• Rapid exit to EVC: 2-3 volumes required • No Coaglation • No Immunoglobulins	• <500-1000 cc TPE • Hyper viscosity
Albumin 5%	• Iso/mild hyper-oncotic • No inflammatory mediators • No viral risk	• High cost • No Coaglation • No Immunoglobulins • Dilutional anemia • **Drug cross reaction: ACEI**	• Rare reactions due to pre-kalicrein and pyrogens

Plasma:
FFP
CPP
SDT-plasma
QR-Plasma
	• Low cost
	• Maintain levels of:
	  • Immunoglobulins
	  • Complements
	  • Antithrombin
	  • proteins
		• Viral transmission risk
		• ABO compatibility test
		• Allergic reaction
		• TRALI
		• Sensitization
		• Citrate load
			• First choice in:
			  •TTP
			  •Repeated TPE
			  •Bleeding tendency
			  •Liver failure
			•Cryo-poor plasma is indicated for TTP refractory to TPE with plasma

Hydroxyethyl starch	• Moderate cost • Isotonic • No inflammatory mediators	• No Coaglation • No Immunoglobulins • Long-term residual of HES • **Contraindicated in renal failure**	• Indicated in patients with sever reactions to albumin and plasma

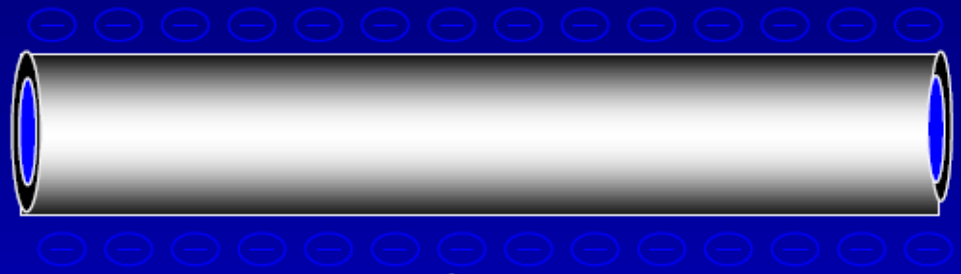
Recommended method

- Due to Hypo-oncotic characteristic of crystalloids which may lead to intravascular fluid deficit,usually used in combination with albumin: start procedure with NS replacement, then finish with albumin repalcemen
- Albumin 4-4.5% (Albumin5% 60-70% + N/S 30-40%)
- TTP: FFP or CPP 60-70% +20-30% N/S
- Repeated TPE(prevention of coagulopathies): last cycle of each session 10-15 cc/kg FFP

Patient History and Medications

- Does patient have a disease which is amenable to treatment by the requested apheresis procedure
- Does the patient/donor capable of sustaining the fluid shifts associated with apheresis
- Certain medications, most notably antibiotics and anticoagulant can be removed by apheresis -should be given *immediately after* the procedure
- Angiotensin-converting enzymes (ACE) inhibitors

ACE inhibitors and Apheresis



ACE Inhibitor

Kinase I & II

X

Breaks down Bradykinin

XII

XII a

Prekalikrein

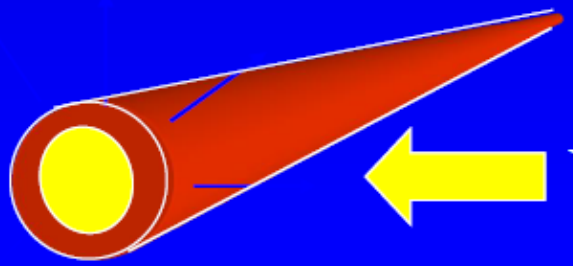
Kallikrein

H.M.W.K

Bradykinin

1- Activation of XII

2- Inhibition of Kinase II



Vasodilatation

TPE and interactions: Drug clearance

- No change needed:

  Digixin;prednisolone;propranolol;valporic acid; phenobarbital;cyclosporine;ceftriaxone;ceftazidim
- Added dose needed:

  Salycilates;aminoglycosides;phenytoin(?)
- Should be omitted immediately after TPE(partial enzyme deficiency)
  - Choline esterase: neuromuscular blocking drugs (succinylcholine)
  - Catabolic Enzymes for bradykinins :ACEI(captopril,enalapril)

Normal Constituents Removed

- **Coagulation factors:**
  - **Most coagulation factors are lost at the same rate**
  - **Rapidly synthesized;replacement usually is 2-3 days following exchange (**VIII;X; VWF:RCO after4 h)
  - **Practical: measure PT/PTT/Fibrinogen every 2-3 days (rather then daily)**
- **Platelets:**
  - **25-30% per procedure**
  - **Endogenous synthesis replaces lost platelets within 2-4 days (except hypoplastic/aplastic marrow)**
- **Lab work(esp. chemistry): not immediate post-procedure; allow equilibrium intra/ extravascular space**

Alteration in Blood Constituents by a 1- PV Exchange

Constituent	% decrease	% recovery 48 hrs post exchange
Clotting factors	25 – 50	80 – 100
Fibrinogen	63	65
Immuneglobulins	63	45
Paraproteins	20 – 30	Variable
Liver Enzymes	55 – 60	100
Bilirubin	45	100
C3	63	60 – 100
Platelets	25 – 30	75 – 100

Modified from : Weinstein, in McLeod, Apheresis, Principles and Practice, 3rd edition, AABB press, 2010

- Routine supplementation with FFP not necessary for most patients
- Fibrinogen replaced most slowly (but this is variable depending on patient –Fg is an acute phase reactant, elevated in many patients
- If consecutive TPE's with albumin replacement are performed, check fibrinogen. If falls <100mg/dL, consider increasing interval between exchanges, or supplement with FFP/cryoprecipitate

Lab tests needed before and during TPE

- Pathogen particle or element
- CBC:Hct; Platelet
- PT;PTT
- Electrolyte
- Serum Albumin & Globulin

Some hours after session or just before the next session

Site & persones

- Expert persons: Nurse and physician
- CPR and Cardiac monitoring and assist set
- In sever cases, and frequent,high volume TPE :in hospitals with ICU

Pediatric Apheresis - Considerations

- How Small Is Too Small?
- Vascular Access
- TBV Calculation
- Blood Prime
- Anticoagulation
- Pump Flow Rates
- Collect Flow Rates
- Volumes Processed
- Adverse Effects

Background

The use of therapeutic apheresis in paediatric patients is still very limited:

- technical difficulties :
  - The choice of a suitable machine and method;
  - The choice of suitable vascular access andthe insertion site (jugular vein, subclavian vein, femoral vein),
  - and the type of central venous catheter to be used (tunnelling, percutaneous, long-term, short-term)
- psychological aspects(Admission to hospital, extracorporeal treatment
- physiological response/ standards :
  - Greater difficulty in metabolising citrates
  - Blood volume vs ECV

Pediatric Apheresis - Considerations

Adverse Effects

- Citrate toxicity
- Hypotension/Vasovagal
- Access related complications
  - Infection
  - Hematoma
  - Pneumothorax
  - Air emboli
  - etc
- Platelet loss
- Hemoglobin level drop
- Hypofibrinogenemia
- Transfusion reactions
- Allergic reactions

TABLE II. Adverse Reactions of Therapeutic Apheresis

Reaction	% of procedures
ACD Toxicity	3.0
Vasovagal Reactions	0.5
Vascular Access Complications	0.15
FFP Related Reactions	0.12
Hepatitis B (from FFP)	0.06
Arrhythmias	0.01
Hemolysis	0.01
Single death (from underlying disease)	0.006
Total	3.856

TABLE III. Severity of Adverse Reactions (%)

Reaction	Mild	Moderate	Severe	Fatal
ACD toxicity	85	12	3	0
Vasovagal reactions	1	73	26	0
Vascular access complications	39	49	12	0
FFP related reactions	36	53	11	0

Pediatric Apheresis - Considerations

Adverse Effects - Hypocalcemia

- paediatric patients are particularly subject to the toxicity of citrates, they have greater difficulty in metabolising citrates in critical situations
- Symptoms of citrate toxicity are nonspecific and can be difficult to detect in young children:
  Abdominal pain, vomiting, pallor, brady-, tachycardia, hypotension, anxiety, sweating, agitation, licking their lips (tingling)…
- *In infants and critically ill, semi-conscious patients, hypotension may be the first sign of hypocalcemia*

Pediatric Apheresis - Considerations

Adverse Effects - Hypocalcemia

Differences in patient sensitivity to lower calcium levels may be due, in part, to differences in:

- Magnesium levels
- Serum protein levels
- Decreased serum glucose levels
- Drop rate of ionized calcium

Pediatric Apheresis - Considerations

Adverse Effects - Hypocalcemia

Strategies to prevent Hypocalcemia according to the literature:

- In small children, obtain an ionized calcium level before and during the treatment
- High volume(>1-2V)frequent &repeated TPE: Check Serum Ca hours after session or just before the next session
- Supplement calcium
- Limit the amount of citrate delivered to 1 - 1.5 mg/kg/min[2]
- Wash RBCs used for priming
- Avoid transfusions on the same day
- Use a blood warmer
- heparin or ACD associated heparin may be used as an anticoagulant,(In the absence of any clotting disorders)

Pediatric Apheresis - Considerations

Adverse Effects - Hypocalcemia

Calcium-Supplementation Options according to the literature:

- Bolus dosing of calcium gluconate 0.5 g/10 kg at 1. and 2. hour of collection[5] OR Calcium gluconate 10% 10cc+1000 cc N/S as replacement solution
- Infusion from different vein
- Simultaneous reinfusion of calcium solution into the return line just before it reenters the patient[1]
- Older patients with vague symptoms can be treated with oral calcium carbonate, 10 mg/kg[2]

Pediatric Apheresis - Considerations

Adverse Effects – allergy & anaphylaxis

- Plasma proteins(IgA,complements,etc.)
- HES:Alternative complement activation(C3a&C5a)
- Ethylen Oxide in plasmapheresis tube set: hapten formation
- ACEI medicines:no inactivation of bradykinin by kininase I&II
  - Plasmapheresis tube sets and patient`s plasma
  - Rapid Albumin infusion increase pre-kalikrein and consequently bradykinin

(ACEI should be discontinued 48 h before TPE)

Pediatric Apheresis - Considerations

Adverse Effects - Hypotension

- Decreased Intravascular Volume:
  - High extracorpular Volume(>10.5 cc/kg)
  - Clinical condition: neurologic disorders; severely sick patients ,etc
  - Intermittent method of TPE
  - Fluid shift:
    - When blood is removed in the beginning of a procedure
    - Cristaloid replacement
  - Negative Fluid balance:
    - Anticoagulant+Replacement Fluid < Plasma Removed
- Vasovagal reflex

To minimize the risk of hypovolemia and fluid shift:

- Limit the patients extracorporeal (ECV) to <15% of patients TBV at all times:
  - ECV: the “dead spaces” (tubing, chambers) of an instrument. (Range 150-500ml) that need to filled to complete the apheresis circuit
- Priming the instrument with colloid solution or RBCs (washed RBCs diluted with 5% albumin) may be necessary for a pediatric/small pt
- Hct during TPE should be > or = 24%
- Start at a slow inlet flow rate of 10 ml/min, then increase flow rate in increments of 5 ml/min[2]

Pediatric Apheresis - Considerations

Adverse Effects – catheter complications

- Infection
- Thrombosis
- Nerve insults
- Hematoma and bleeding
- AV fistula
- Air emboli(acute dyspnea, cyanosis,tachycardiaand hypotension)

Pediatric Apheresis - Considerations

Adverse Effects – hypokalemia

- Albumin: 35% dilutional decrease in serum potasium

Journal of Clinical Apheresis 28:145–284 (2013)

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice—Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Sixth Special Issue

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Aphresis Indication Categories (ASFA/AABB)

- **Category I:** First line therapy –proven to be effective
- **Category II:** Adjunct therapy –proven to be beneficial in some instances
- **Category III:** May be-evidence is conflicting but there is some suggestion of benefit, can be considered if conventional therapy is failing
- **Category IV:** Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful.IRB approval is desirable if apheresis treatment is undertaken in these circumstances.
- **Category P:** Pending

ANCA- associated rapidly progressive glomerulo-	TPE	Dialysis dependence	I	1A
nephritis (Granulomatosis with polyangiitis;	TPE	DAH	I	1C
Wegener's Granulomatosis)	TPE	Dialysis independence	III	2C
Anti-glomerular basement membrane disease	TPE	Dialysis dependent and no DAH	III	2B
(Goodpasture's syndrome)	TPE	DAH	I	1C
	TPE	Dialysis independence	I	1B
Aplastic anemia; pure red cell aplasia	TPE	Aplastic anemia	III	2C
Focal segmental glomerulosclerosis	TPE	Recurrent in transplanted kidney	I	1B
Hemolytic uremic syndrome, atypical	TPE	Complement gene mutations	II	2C
	TPE	Factor H antibodies	I	2C
	TPE	MCP mutations	IV	1C
Hemolytic uremic syndrome,infection-associated	TPE	Shiga toxin associated	IV	1C
	TPE	S. pneumonae associated	III	2C
Henoch-Schonlein purpura	TPE	Crescentric	III	2C
	TPE	Severe extrarenal disease	III	2C
Immunoglobin A nephropathy	TPE	Crescentic	III	2B
	TPE	Chronic progressive	III	2C
Nephrogenic sytemic fibrosis	ECP		III	2C
	TPE		III	2C

Renal transplantation, ABO compatible	TPE	Antibody mediated rejection	I	1B
	TPE	Desensitization, living donor, positive crossmatch due to donor specific HLA antibody	I	1B
	TPE	Desensitization, high PRA deceased donor	III	2C
Renal transplantation, ABO incompatible	TPE	Desensitization, live donor	I	1B
	TPE	Humoral rejection	II	1B
	TPE	Group A2/A2B into B, deceased donor	IV	1B
Thrombotic microangiopathy, drug associated	TPE	Ticlopidine	I	1B
	TPE	Clopidogrel	III	2B
	TPE	Cyclosporine/ Tacrolimus	III	2C
	TPE	Gemcitabine	IV	2C
	TPE	Quinine	IV	2C
Thrombotic microangiopathy, HSCT associated	TPE	Refractory	III	2C
Thrombotic thrombocytopenic purpura	TPE		I	1A

TABLE V. General Issues to be Considered When Evaluating a New Patient for Therapeutic Apheresis Initiation

General	Description
Rationale[a]	Based on the established/presumptive diagnosis and history of present illness the discussion could include the rationale for the procedure, brief account of the results of published studies, and patient-specific risks from the procedure.
Impact	The effect of therapeutic apheresis on comorbidities and medications (and vice-versa) should be considered.
Technical issues[a]	The technical aspects of therapeutic apheresis such as type of anticoagulant, replacement solution, vascular access, and volume of whole blood processed (e.g., number of plasma volumes exchanged) should be addressed.
Therapeutic plan[a]	Total number and/or frequency of therapeutic apheresis procedures should be addressed.
Clinical and/or laboratory end-points[a]	The clinical and/or laboratory parameters should be established to monitor effectiveness of the treatment. The criteria for discontinuation of therapeutic apheresis should be discussed whenever appropriate.
Timing and Location	The acceptable timing of initiation of therapeutic apheresis should be considered based on clinical considerations (e.g., medical emergency, urgent, routine etc). The location where the therapeutic apheresis will take place should be also addressed (e.g., intensive care unit, medical ward, operating room, outpatient setting). If the timing appropriate to the clinical condition and urgency level cannot be met, a transfer to a different facility should be considered based on the clinical status of the patient.

NOTE: The above issues should be considered in addition to a routine note addressing patient's history, review of systems and physical examination.

[a]ASFA Fact Sheet for each disease could be helpful in addressing these issues.

HEMOLYTIC UREMIC SYNDROME, ATYPICAL

Incidence: 3.3/1,000,000/yr (<18 yo); 7/1,000,000/yr (children in European community)

Condition	Procedure	Recommendation	Category
Complement factor gene mutations	TPE	Grade 2C	II
Factor H autoantibodies	TPE	Grade 2C	I
MCP mutations	TPE	Grade 1C	IV

# of reported patients*: >300

	RCT	CT	CS	CR
Complement factor gene mutations	0	0	4(23)	21(26)
Factor H autoantibody	0	0	2(6)	2(2)

MCP = membrane cofactor protein

Volume treated: 1–1.5 TPV **Frequency:** Daily

Replacement fluid: Plasma; albumin (T activation associated HUS)

- Rationale for therapeutic apheresis:
  - TPE can effectively remove the autoantibody or mutated circulating complement regulators while replacing absent or defective complement regulators
  - TPE over PLx: benefits without risk of volume overload, development of hyperproteinemia, or refractoriness to regular plasma infusion
- Duration and discontinuation/number of procedures:
  - no standardized approach : based upon patient response and condition
  - vascular access, RBC prime, and calcium supplementation are of special concern.
  - 5 times per week for 2 weeks, then 3 times per week for 2 weeks with outcome evaluated at day 33 (Sanchez)
  - neither continued treatment after initial therapy failure nor ongoing prophylactic treatment for patients with remission

THROMBOTIC THROMBOCYTOPENIC PURPURA

Duration and discontinuation/number of procedures:

- TPE is generally performed daily until the platelet count is above 150 ×10^9/L, and LDH is near normal for 2 to 3 consecutive days.
- The median number of TPE procedures to establish hematologic recovery is 7–8 days.
- The role of tapering TPE over longer duration has not been s tudied prospectively but is used frequently.
- Persistence of schistocytes alone on peripheral blood smear, in the absence of other clinical features of TTP, does not preclude discontinuation of treatment.

THROMBOTIC MICROANGIOPATHY, HEMATOPOIETIC STEM CELL TRANSPLANT ASSOCIATED

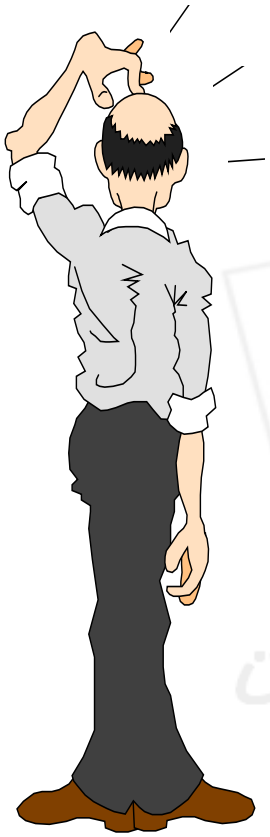
Incidence: 1-year cumulative 13% (non-myeloablative) versus 15% (high-dose); **Prevalence:**10–25%	**Condition**	**Procedure**	**Recommendation**	**Category**
	Refractory	TPE	Grade 2C	III

# of reported patients*: >300			
RCT	**CT**	**CS**	**CR**
0	0	23(345)	6(6)

Volume treated: 1–1.5 TPV
Frequency: Daily, or as indicated for chronic management
Replacement fluid: Plasma, plasma cryoprecipitate removed

- plasma ADAMTS13 protease levels are not severely deficient nor are ADAMTS13 inhibitors detectable in patients with TATMA. Therefore, a therapeutic rationale is undefined and consistent with the uncertain clinical efficacy.

Pediatric Apheresis - Considerations



Any Questions?