Therapeutic Apheresis: Vascular Access

Gagan Mathur MD, MBA

Medical Director- Transfusion Service, Saint Luke's Health System

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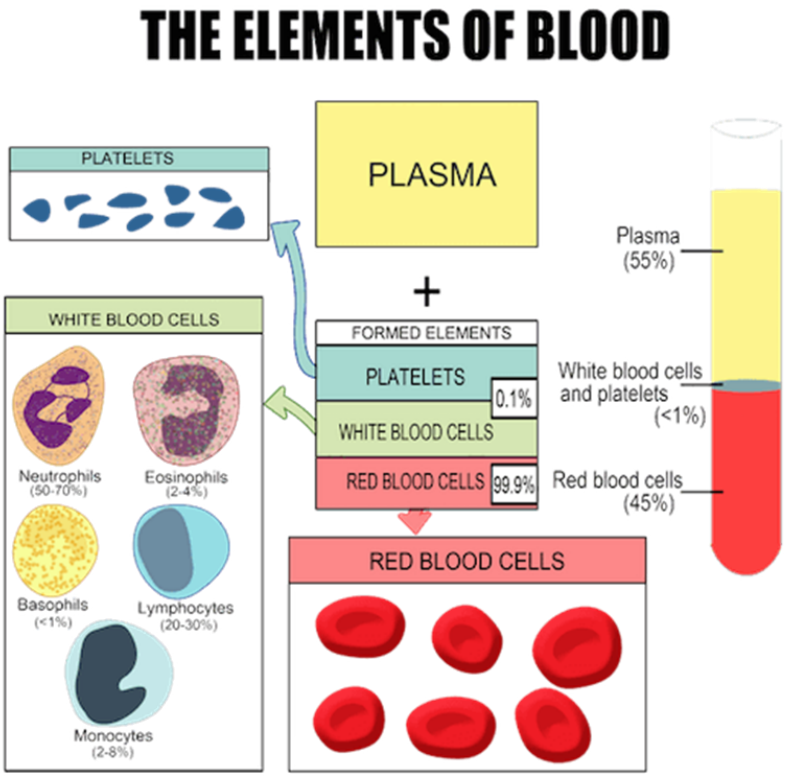
Disclosures

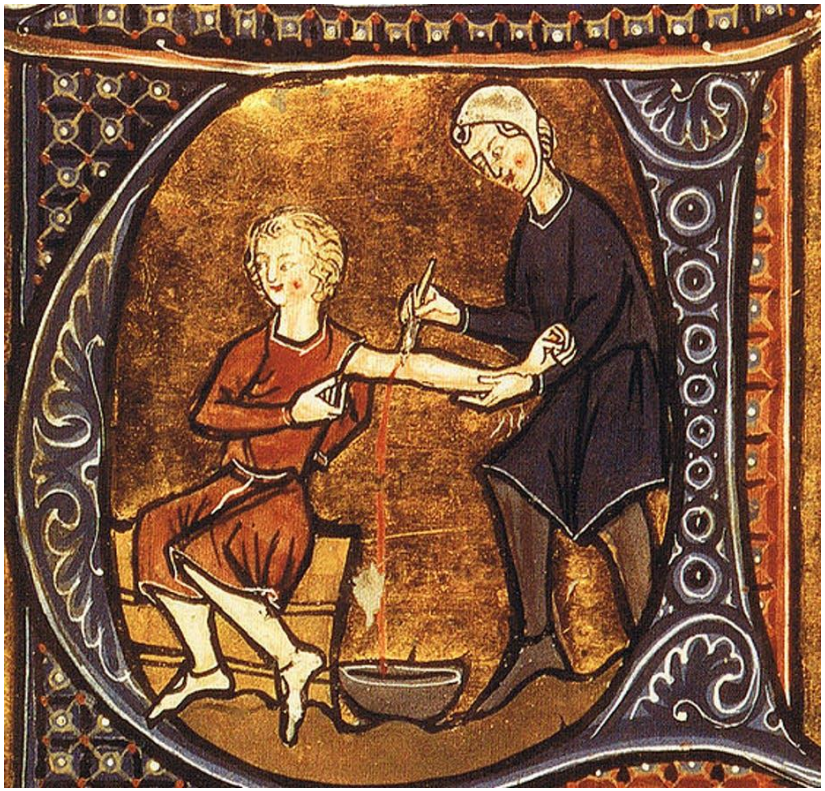
- None

Apheresis

- Greek for “to take away” or “subtract”
- Apheresis is a medical technology in which the blood of a person is passed through an apparatus that separates out one particular constituent and returns the remainder to the circulation



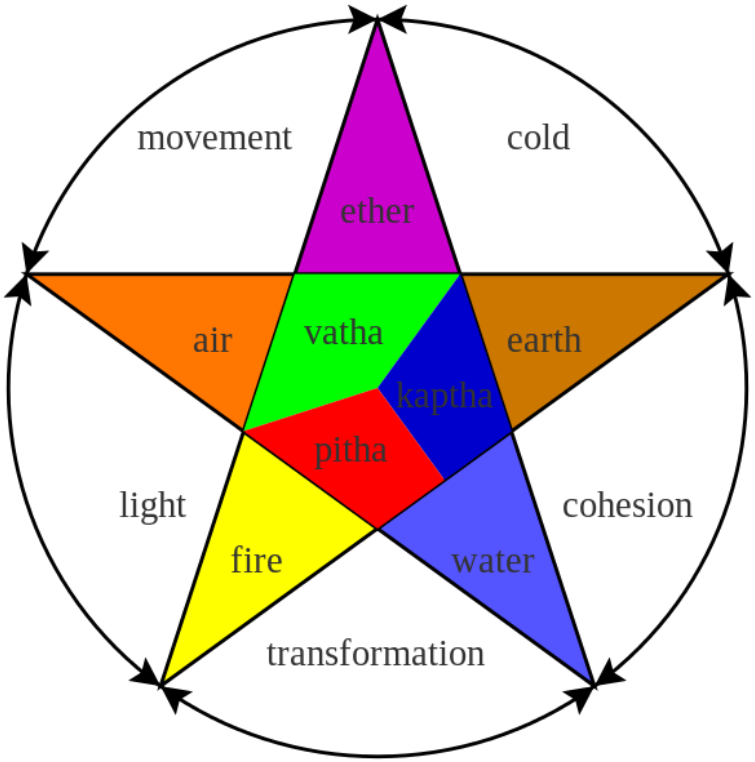
Humorism



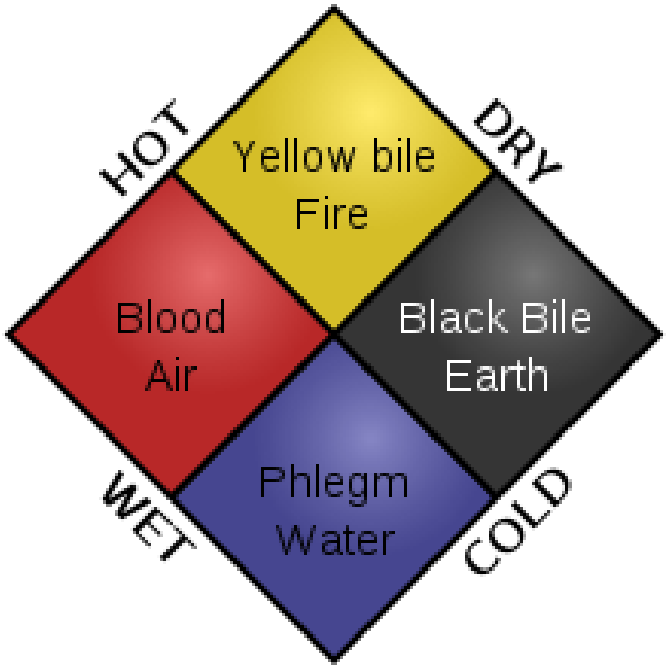
- Ancient and medieval medicine believed that poisonous substance in the blood cause diseases
- Therapeutic bleeding or bloodletting was performed in all ancient cultures to treat nearly every illness

Humorism

Ayurveda



Hippocrates



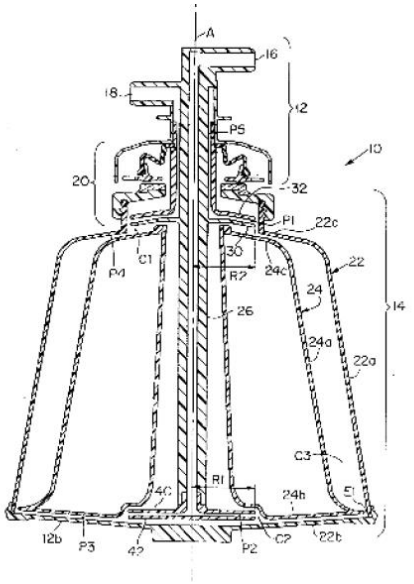
Modern Apheresis

- In 1950 Dr. Cohn, envisioned a device that would separate donor plasma for purification of albumin to be used for resuscitation of wounded soldiers in World War II
- Latham improved the design resulting in “Latham bowl”, which was used in the first apheresis instruments

Edwin Cohn

Developed cold ethanol fractionation to produce albumin

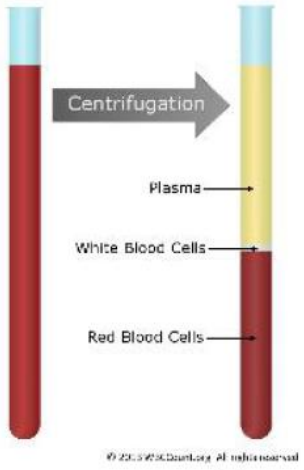
Alan (Jack) Latham, Jr.

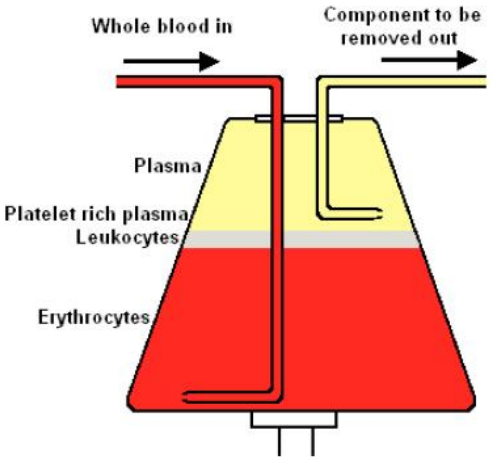


Modern Apheresis

- Originally performed discontinuously
- Now performed with continuous removal and separation of blood components
- Method of separation
  - Centrifugation
  - Membrane filtration

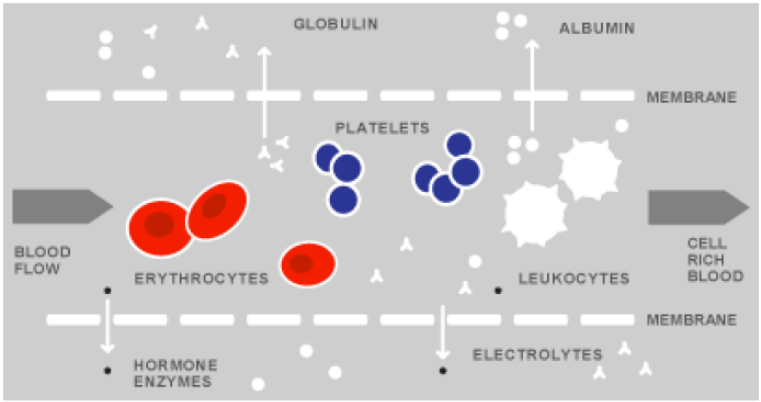
Centrifugation



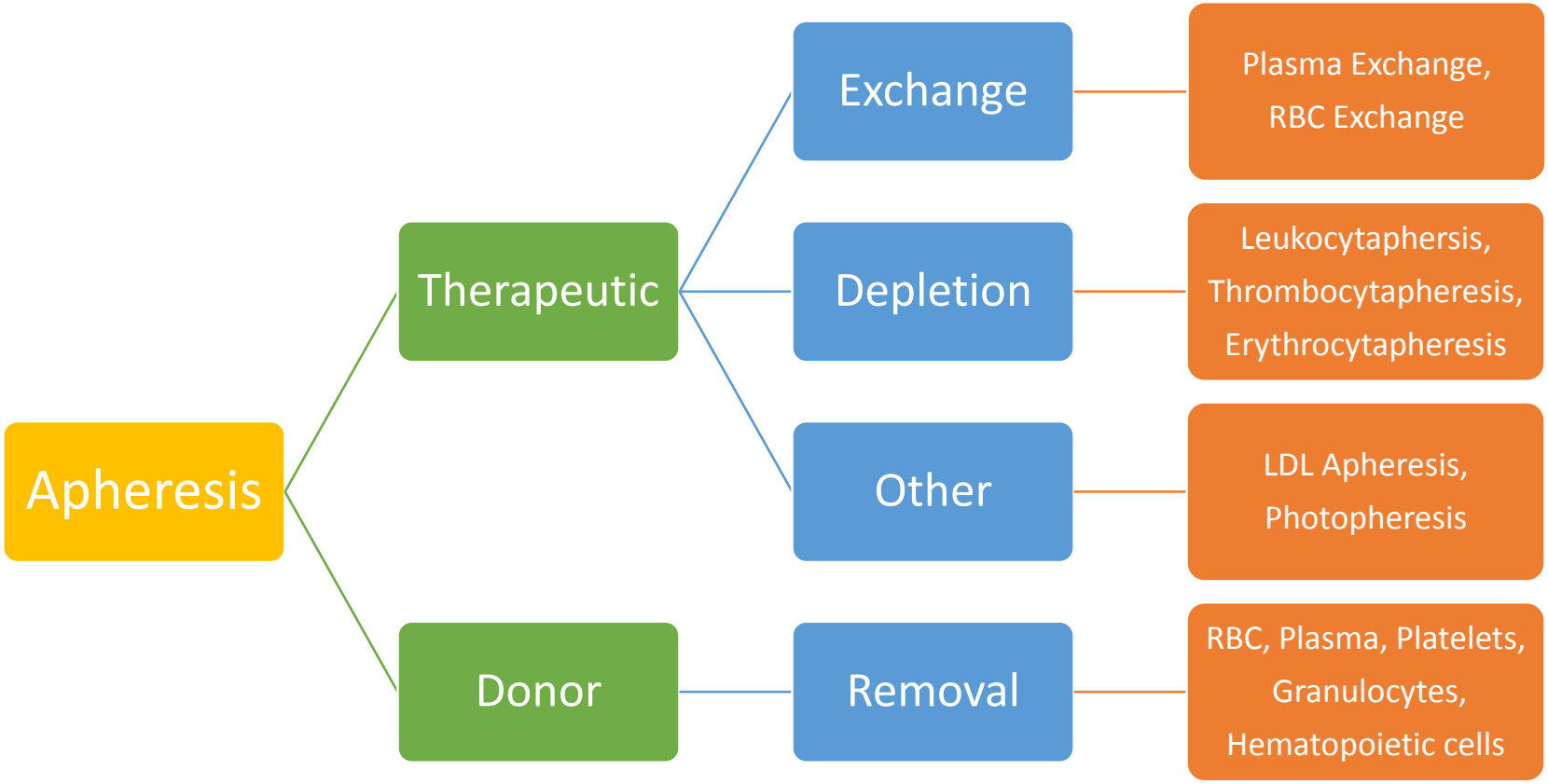


Membrane Filtration

- Only for Plasma exchange
- High flow rates to achieve transmembrane pressure
- Access via a larger vein
- Lower extraction efficiency of 27%–53%
  - 86% in centrifugation
- Less effective for higher-molecular weight proteins such as IgM, fibrinogen, and immune complexes
- Preferred by nephrologists



Apheresis Procedures



Logistics

- Clinical Issues
  - Consult for therapeutic apheresis (TA)
  - Confirm indication, procedure & rationale for TA
  - Treatment plan- number & frequency
  - Clinical & laboratory end points
- Technical Issues
  - Anticoagulant
  - Replacement Fluid
  - Volume Processed
  - Vascular Access

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TA Guidelines

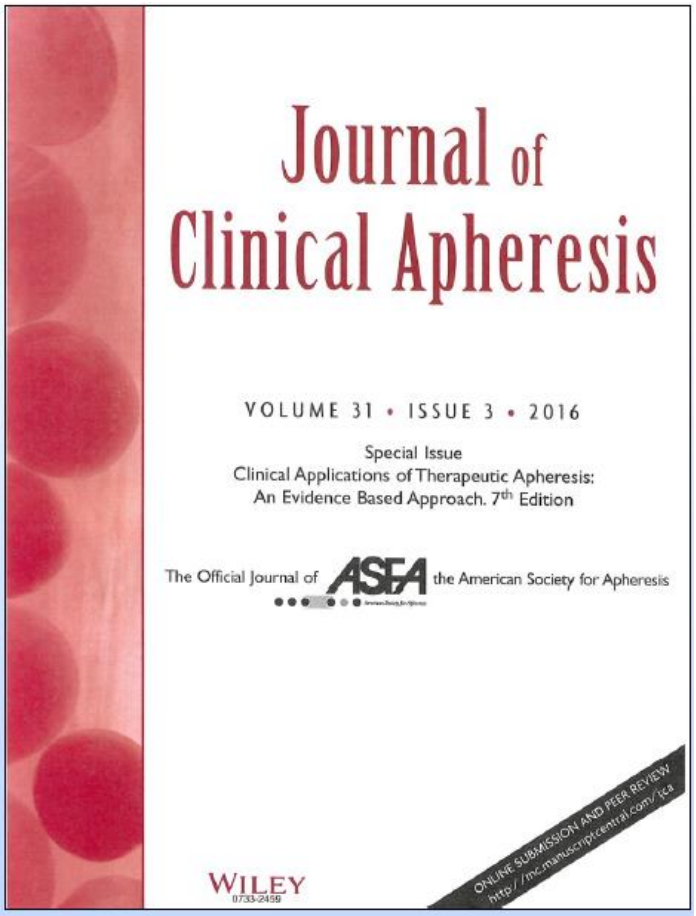

TABLE II. Category Definitions for Therapeutic Apheresis

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision making should be individualized.
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.

Common Indications

	Category	Grade
THERAPEUTIC PLASMA EXCHANGE		
Thrombotic thrombocytopenic purpura (TTP)	I	1A
Cryoglobulinemia, symptomatic/severe	II	2A
Hyperviscosity in monoclonal gammopathies, symptomatic	I	1B
Myasthenia gravis, moderate-severe	I	1B
Acute inflammatory demyelinating polyradiculoneuropathy (GBS)	I	1A
Chronic inflammatory demyelinating polyradiculoneuropathy	I	1B
Neuromyelitis optica spectrum disorders, acute	II	1B
Renal transplantation, antibody mediated rejection	I	1B
Liver transplantation, antibody mediated rejection	III	2C
Cardiac transplantation, antibody mediated rejection	III	2C
Anti-glomerular basement membrane disease, Dialysis independent or DAH	I	1B
ANCA-associated rapidly progressive glomerulonephritis, dialysis dependence or DAH	I	1A
Focal segmental glomerulosclerosis, recurrent in transplanted kidney	I	1B

Common Indications

	Category	Grade
LDL APHERESIS		
Familial hypercholesterolemia, Homozygotes	I	1A
Lipoprotein (a) hyperlipoproteinemia	II	1B
RBC EXCHANGE		
Sickle cell disease, Acute stroke	I	1C
Sickle cell disease, Stroke prophylaxis/iron overload prevention	I	1A
LEUKOCYTAPHERESIS		
Hyperleukocytosis, Symptomatic	II	1B
THROMBOCYTAPHERESIS		
Thrombocytosis, symptomatic	II	2C

Logistics

- Clinical Issues
  - Consult for therapeutic apheresis (TA)
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  - Treatment plan- number & frequency
  - Clinical & laboratory end points
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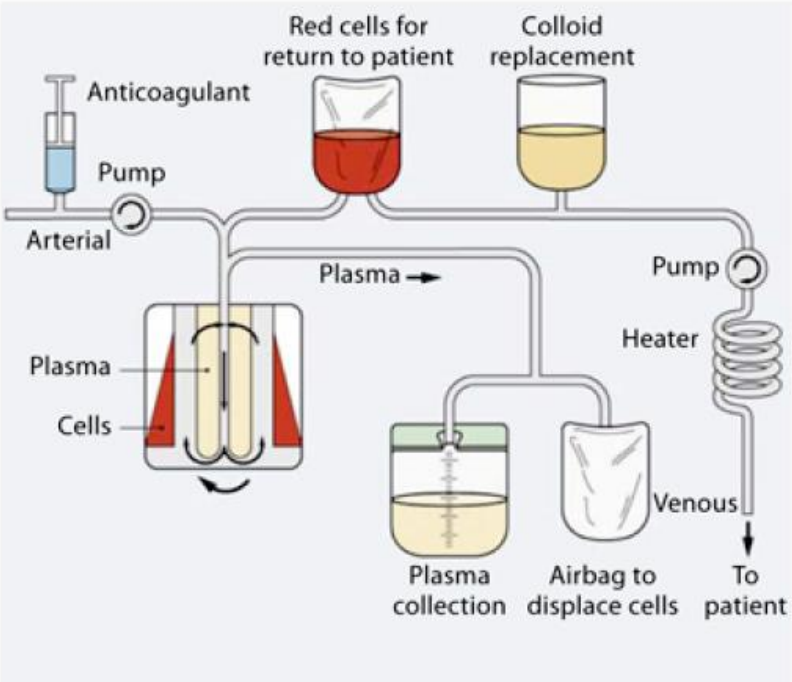
Plasma Exchange Circuit



- Anticoagulant
- Replacement Fluid
- Volume Processed
- Vascular Access

Anticoagulants

- Extracorporeal circuit will clot without anticoagulants
- ACD-A (most common)
  - Binds to ionized calcium
  - Metabolized rapidly (kidney & Liver)
- Unfractioned Heparin or Combination (some centers)
  - HIT
  - Bleeding

Replacement Fluids

- Crystalloid (normal saline)
  - Cheap
  - Hypo-oncotic
  - No coagulation factors or immunoglobulins
- Colloid (albumin)
  - Expensive
  - Slightly hyper-oncotic, can result in volume expansion
  - Very low risk of infectious disease transmission
  - No coagulation factors or immunoglobulins
- Plasma
  - Cheaper than albumin
  - Iso-oncotic
  - Associated risks of all blood product transfusions (infectious disease, allergic reactions, TRALI)

Volume Processed

- Dose = Plasma volume (PV)
- PV = BV x (1-Hct)
  = (70ml/kg x Wt) x (1-Hct)
- 1 PV = ~60% removal
- No benefit in exchanging > 2 PV

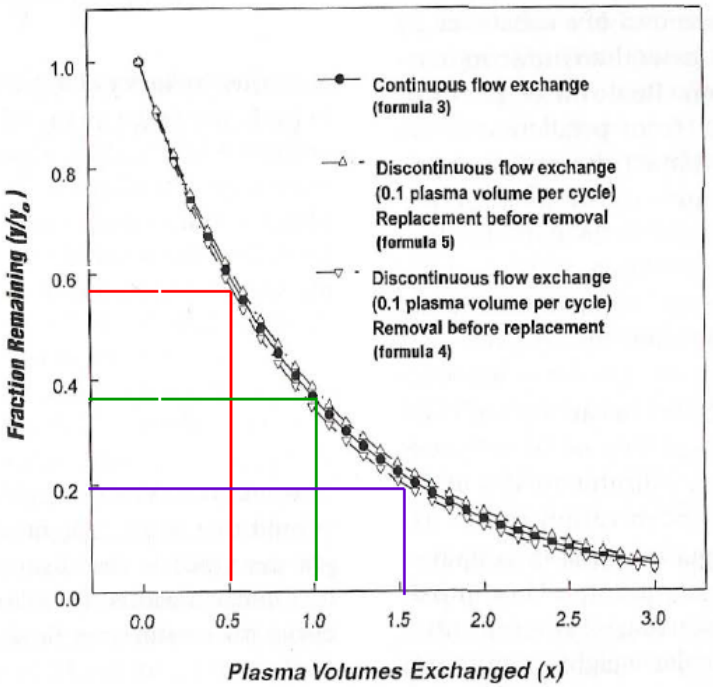
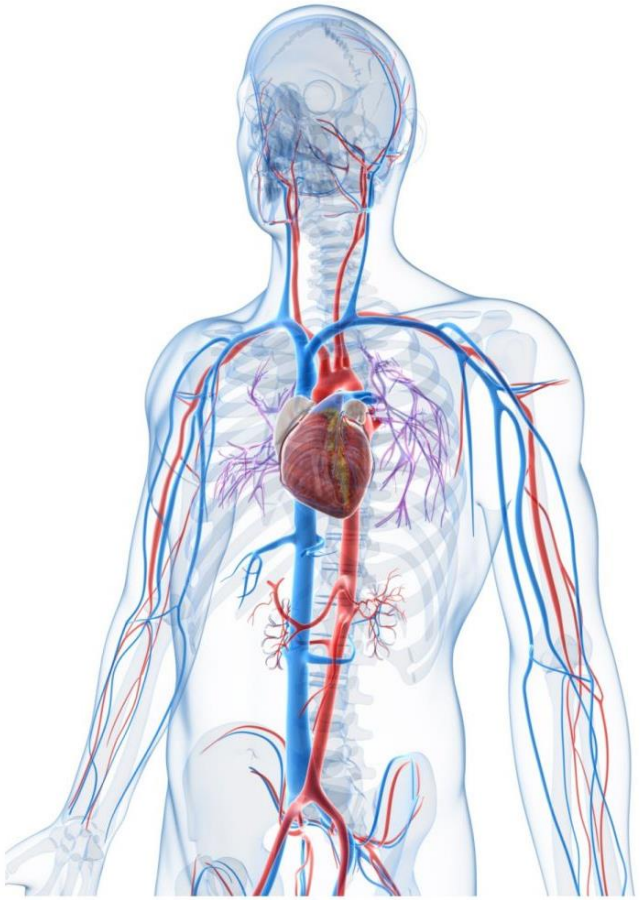


Figure 15-2. Theoretical depletion of soluble substances from the plasma by plasma exchange according to the one-compartment model. A fixed proportion of the remaining intravascular mass of the soluble substance is removed with each increment of plasma volume removed. (Adapted with permission from Chopek and McCullough.[10])

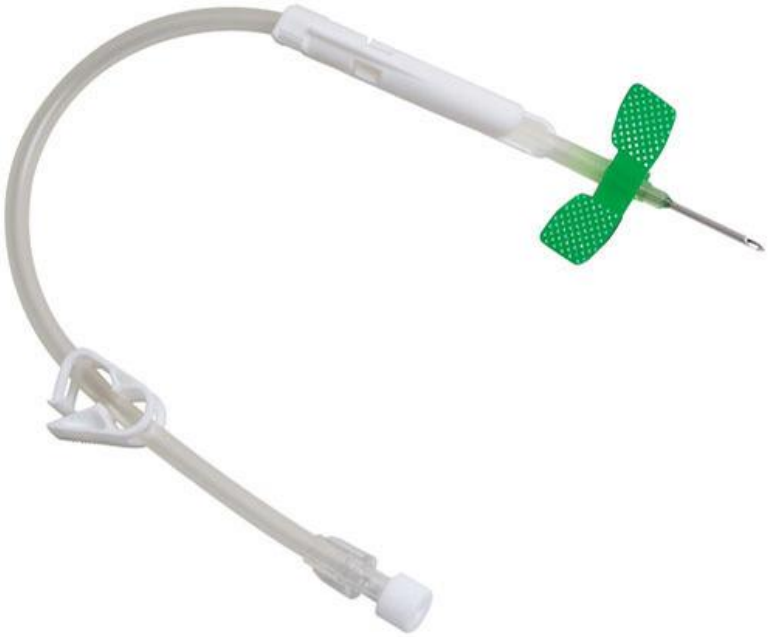
Vascular Access



- Inlet and outlet for blood flow

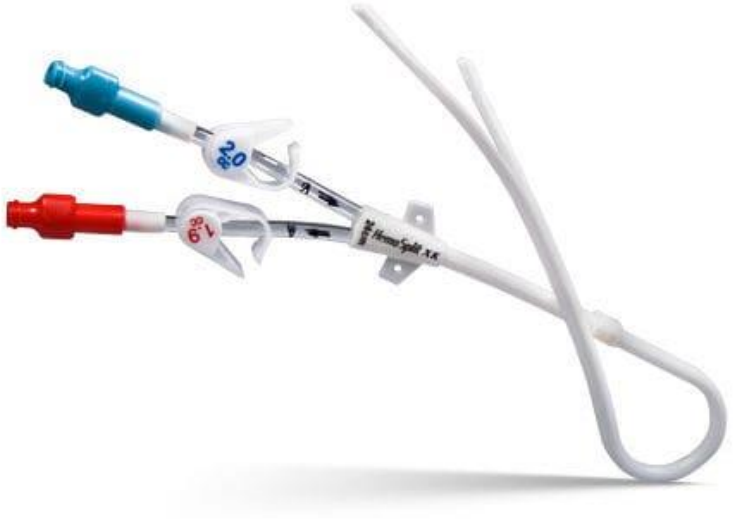
Options

- Peripheral Veins
- Arteriovenous Fistulas & Grafts



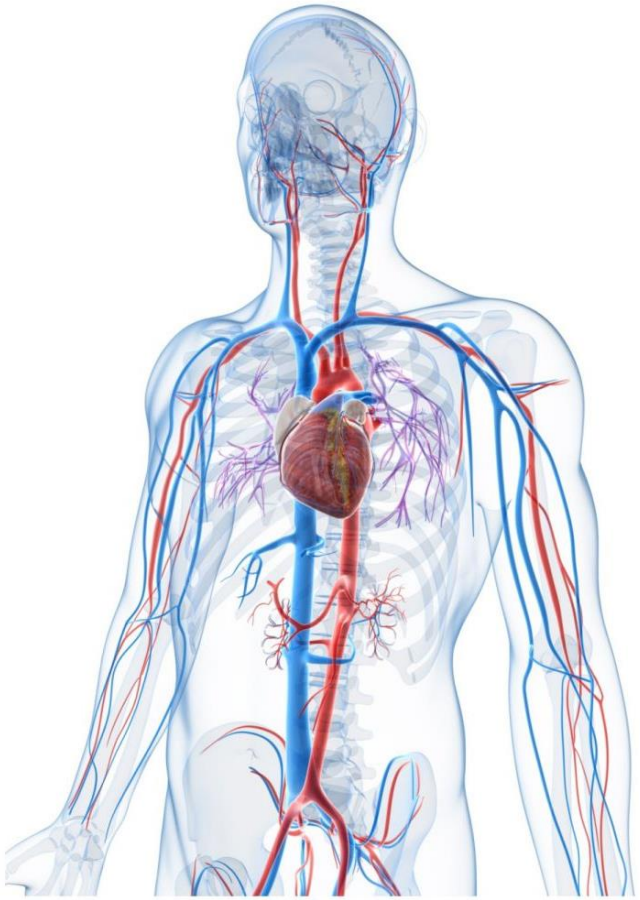
Peripheral

- Central Venous Catheters
- Venous Access Ports



Central

Vascular Access



- Why is vascular access so important?

Adverse Reactions

- Overall well tolerated by most patients
- Rate 4-5% of TA procedures
- Common adverse reactions
  - Citrate toxicity
  - Hypotension/vasovagal
  - Transfusion reactions

Adverse Reactions

- Citrate toxicity
  - Temporary decrease in Ca_i^{2+}
  - Tingling, numbness, nausea
  - Calcium supplementation: calcium carbonate, calcium gluconate, calcium chloride

Adverse Reactions

- Vaso-vagal reactions
  - Pallor
  - Hypotension
  - Diaphoresis
  - Bradycardia
  - Nausea/vomiting
- More common with plasmapheresis than with cytapheresis
- ACE inhibitors exacerbate

Adverse Reactions

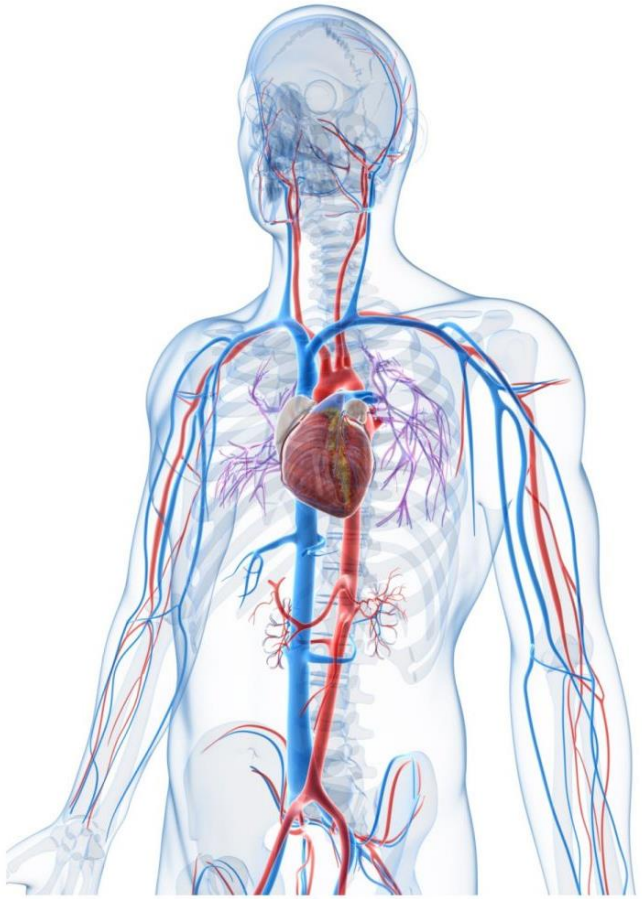
- Coagulation alterations
  - Daily TPE without plasma replacement can deplete coagulation factors and increase bleeding
  - Consider Plasma replacement with daily exchange and in patients with coagulation abnormalities
  - Monitor fibrinogen

Adverse Reactions

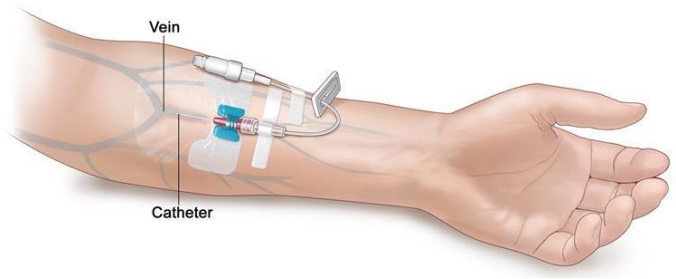
- Vascular Access
  - Hematoma
  - Clotting of line
  - Insufficient for pressures required
- Infections/sepsis
  - More problematic with central lines than with peripheral access

Vascular Access

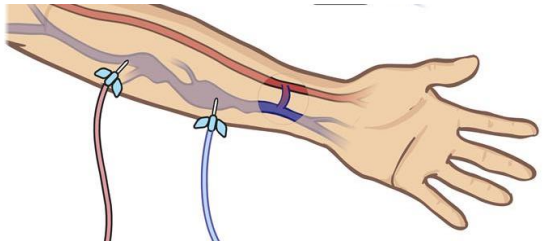
- Associated with serious TA adverse reactions
- Can be a logistic bottle neck
- Without adequate vascular access cell separation for TA is not possible



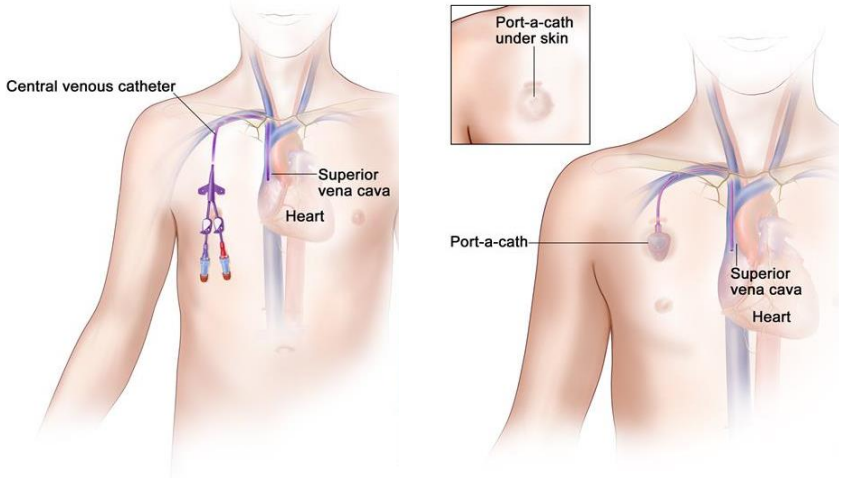
Options



- Peripheral Veins



- Arteriovenous Fistulas & Grafts



- Central Venous Catheters

- Venous Access Ports

Determinants

- Indication for TA
- Type of TA system used
- Number and frequency of treatments needed
- Anticipated duration of treatment

Pt. already has a line, Pick One!

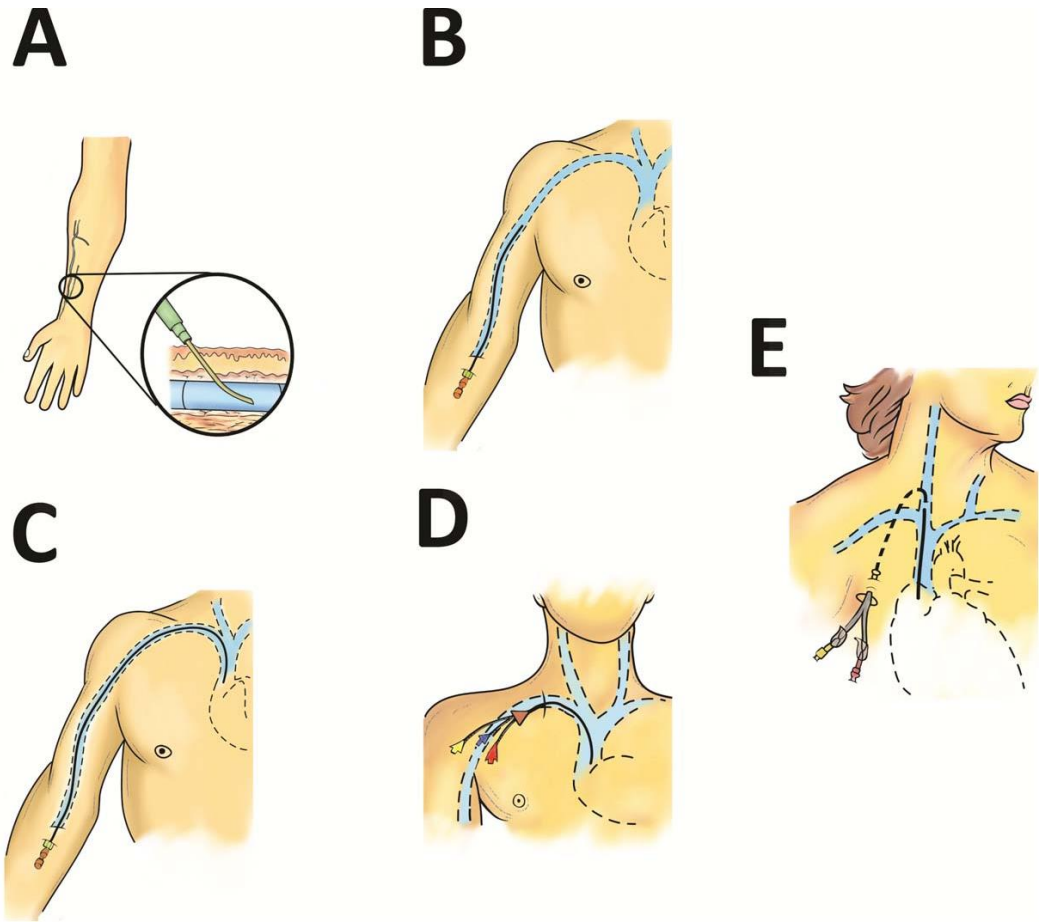
(A) Peripheral intravenous

(B) Midline catheter

(C) Peripherally inserted central catheter

(D) Nontunneled centrally inserted central catheter

(E) Tunneled centrally inserted central catheter



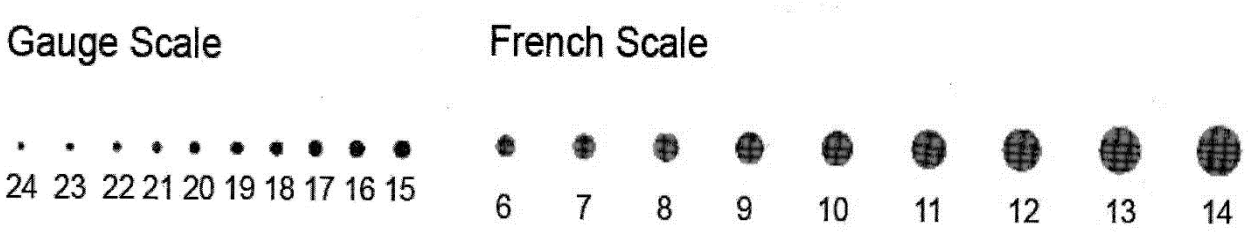
Things to Consider

- Catheter Size
  - Minimum for adequate flow rate
  - Prevent mechanical hemolysis

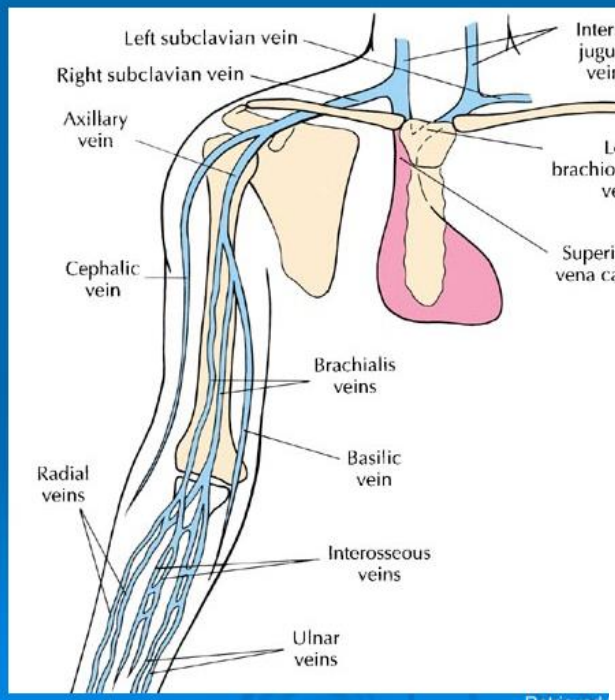
- Flow Rate (depends on size and length)
  - The Apheresis System's software/ Automatic Interface Management (AIM) system controls pump flow rates and centrifuge speed to establish and maintain the required RBC/plasma interface
  - 50 mL/min (5 to 150 mL/min)
  - Determines time needed to establish interface
  - Determines time needed to complete procedure

Size x Length = Flow Rate

	Size x length	~Flow Rate	Use
Standard IV	20 G x 30 mm	50 mL/min	Fluids
Standard IV	18 G x 30 mm	50-100 mL/min	Blood
Standard IV	16 G x 30 mm	200 mL/min	Resuscitation
Double/Triple Lumen CVC	16-18 G x 125-500 mm	100-500 mL/min	CV Access
PICC	18-20 G X 550-600 mm	6-30 mL/min	CV Access
Midline	22-18 G X 80-100 mm	120-420 mL/min	Midline Access
Port	14-16 G x 450 mm	50-300 mL/min	CV Access



Anatomy



Vein Measurements

	Length	Diameter	Flow Rate
Cephalic	38cm	6mm	40-90ml/min
Basilic	24cm	8mm	90-150 ml/min
Axillary	13cm	16mm	150-350ml/min
Subclavian	6cm	19mm	350-800ml/min
Innominate	2.5cm	19mm	800-1500ml/min
SVC	7cm	20mm	2000ml/min

General Rule of Thumb

- A large bore cannula is preferable to a narrow
- A shorter cannula is preferable to a longer
- A larger proximal vein is preferable to smaller distal vein
- Upper limbs are preferable to lower limbs
- Maintain integrity of vein
- Adequate flow rate
- Avoid hemolysis due to excessive pressure
- Avoid clotting due to sluggish flow

Peripheral Veins

- Antecubital and forearm veins evaluated for adequate vascular access
- Patient preparation, hydration, warming extremity, distractions, relaxation, etc.
- Skill of RN is paramount (vein choice, access skills, warming extremity)
- Access (16-17 G, antecubital vein)
- Return (18-20 G, non-antecubital vein)

Peripheral Veins

- Centrifugation based TA
- Acute or inttermitent TA
- Short-term, less frequent & shorter treatments (1-3 treatments, over 1-2 weeks)
- Outpatient treatments
- Patient’s vascular anatomy, mobility, and hygiene
- Experience/comfort level of providers
- Low rate of infections and adverse reactions, less invasive

Central Venous Catheters

Non-Tunneled CVC

- Short term (< 2 weeks) treatments
- Risk of infection/sepsis if kept for longer time
- Patient cannot bathe or swim
- Invasive
- Acute or intermittent TA

Tunneled CVC

- Long term (weeks to months) treatments
- Comparatively lower infection rates
- Patient cannot bathe or swim
- Invasive

Placement of Apheresis CVCs

- Anatomic locations:
  - Most common choices: great vessels (chest); femoral veins
  - Right IJ >> Right SC >> Left SC > Left IJ
  - Catheter tip: junction of SVC and right atrium; proximal right atrium
  - Preparation (NPO for ≥8 hours)
  - Placement verification (fluoroscopy; CXR; ultrasound; TEE)
- Who places apheresis CVCs:
  - Interventional radiologists (IR suite: scheduled; weekend: emerg only)
  - Surgeons (OR suite; scheduled: often delayed due to other surgeries)
  - Intensivists (ICU; ultrasound guidance; may be faster than IR or OR
  - Other (residents; nephrologists)
  - Tunneled CVCs (currently interventional radiologists or surgeons only)

Care of Apheresis CVCs

- Inpatient care (for nurses):
  - Intra-luminal catheter-locking agents (port patency):
    - Heparin: usually 1000-5000 U/ml (total of 5-6 ml)
    - Studies using 100U/ml; 10,000 U/ml
    - Citrate (4%)(5, 30, 47%): similar efficacy; ↓ bleeding risk & cost; no risk of HIT
    - rt-PA (recombinant tissue plasminogen activator)
    - Tego caps (non-heparin)
  - Dressing changes:
    - usually after each treatment
    - antiseptic technique (mask, etc)
    - protection of line

- Outpatient care (for patients):
  - Temporary lines (keep dressing dry/no showers; care with dislodging line)
  - Tunneled lines (first 2-3 weeks: keep dressing dry/no showers)
  - Monitoring for site infection
  - Compliance with catheter flush schedule

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WILEY Journal of Clinical Apheresis ... ASFA

RESEARCH ARTICLE

Tissue plasminogen activator vs heparin for locking central venous catheters between apheresis procedures

Gagan Mathur[1] | Sarah L. Mott[2] | Laura Collins[3] | Annette J. Schlueter[3]

TABLE 1 Cost associated with performing locks

Lock	Packaging	Costs	Dose per port	Cost per lock (two ports)
Recombinant tissue plasminogen activator	2 mg vial	$38 per vial	2 mg	$76
Heparin	10 000 units/10 mL vial	$1 per vial	2 mL	$0.50[a]
Intervening line locking procedure	-	$90 per lock	-	$90[b]

[a]Approximately two locks per vial (8 mL for locks plus wastage).
[b]Approximately 60% of $151 charge per lock.

TABLE 3 Cost of locks based on interval between extracorporeal photopheresis (ECP) procedures

Interval between procedures (days)	Recombinant tissue plasminogen activator (rt-PA)				Heparin			
	Cost of rt-PA	IF[a] needed	Cost of IF	rt-PA total cost	Cost of heparin	IF needed	Cost of IF	Heparin total cost
1-7	$76	0	$0[b]	$76	$0.50	0	$0[b]	$0.50
8-14	$76	0	$0	$76	$1	1	$90	$91
15-21	$76	0	$0	$76	$1.50	2	$180	$181.50
22-28	$76	0	$0	$76	$2	3	$270	$272

[a]IF = intervening flush/lock (between procedures).
[b]Charge for the initial flush is included in the ECP procedure performed.

TABLE 2 Extracorporeal photopheresis procedure flow rate issues with heparin vs recombinant tissue plasminogen activator (rt-PA) line locks

	n	Percentage
Heparin		
Significant issues	9	13
Some issues	24	34
No issues	37	53
rt-PA		
Significant issues	3	13
Some issues	4	17
No issues	16	70

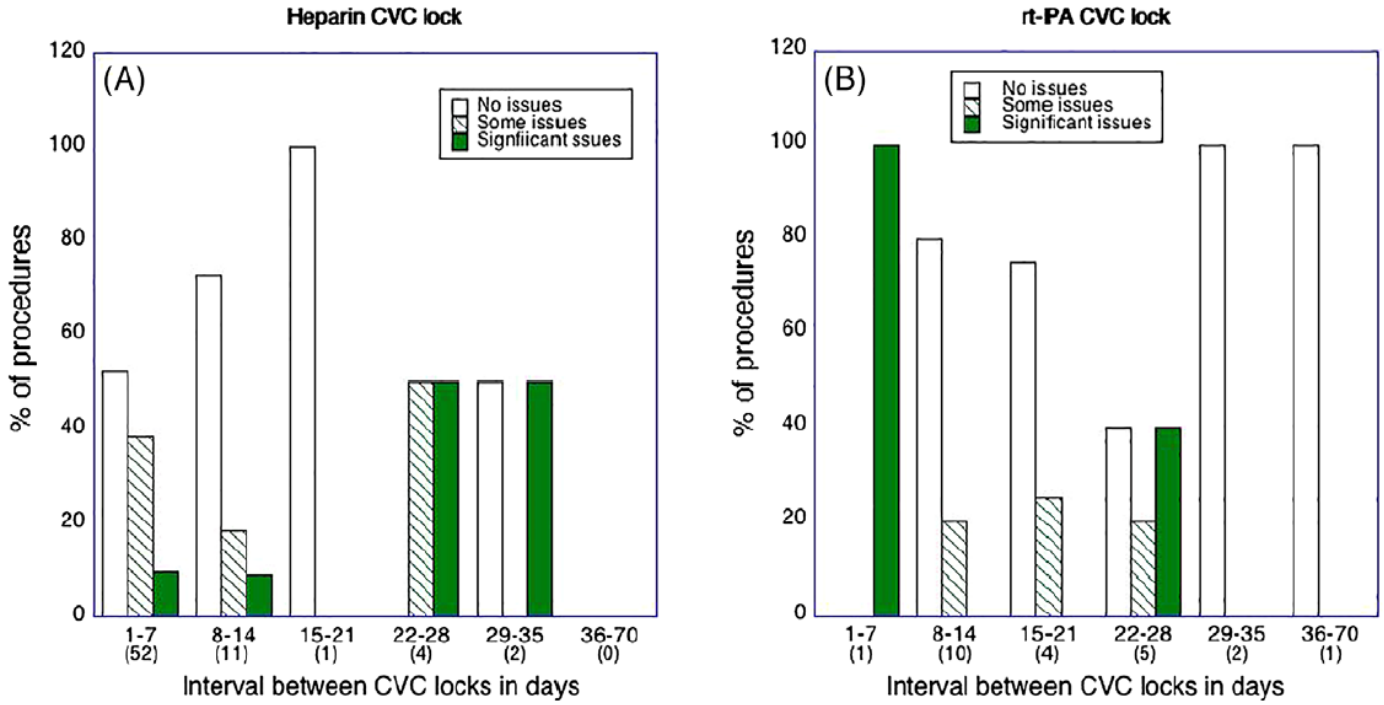

FIGURE 1 Lack of association between central venous catheter lock interval and flow rate issues for (A) heparin locks and (B) recombinant tissue plasminogen activator locks. The numbers in parentheses below each interval (on the *x* axes) represent the total number of procedures within that interval

Arteriovenous Fistulas & Grafts

- Long-term (years) treatments
- Requires trained staff for cannulation
- Requires surgery & adequate patient vascular anatomy
- 2-3 months “to mature”
- Issues with maturity & maintenance
- Lowest complications, cost & mortality rates

Venous Access Ports

- Long-term (weeks to months) treatments
- Lower infection & dysfunction rates
- Requires trained staff for cannulation
- Requires surgical placement, 2-3 weeks to heal
- Patients are free to bathe, swim, or exercise
- Can get Infected & thrombosed
- Typically used for red cell exchanges & extracorporeal photopheresis

Summary

TABLE II. Option of Vascular Access for TA

Access Type	Use	Advantage	Disadvantage
Peripheral Vein	Short-term, less frequent and shorter treatments, large veins	Lower side effects, less invasive	Thrombophlebitis, not suitable for cases with high platelet or WBC counts, not suitable for filter-based systems
Nontunneled CVC	Short-term treatments, filter-based and centrifugation-based systems	Better BFR compared to peripheral veins	Risk of infection, not suitable for prolonged TA, patients cannot bathe or swim
Tunneled CVC	Long-term (weeks to months) treatments, filter-based and centrifugation-based systems	Lower infection rates compared to nontunneled CVC	Higher infection, malfunction and mortality rates compared to AVF, patients cannot bathe or swim
Totally implantable ports	Long-term (weeks to months) treatments, filter-based and centrifugation-based systems	Lower infection rates compared to tunneled CVC, patients can bathe, swim and exercise	Infection and thrombosis
AVF	Long-term (years) treatments	Lowest complication, cost and mortality rates	Issues with maturity and maintenance

Journal of Clinical Apheresis DOI 10.1002/jca

Kalantari, Kambiz. "The choice of vascular access for therapeutic apheresis." *Journal of clinical apheresis* 27.3 (2012): 153-159.

Summary

TABLE III. A Comparison of the Advantages and Disadvantages Associated With Vascular Access Types Used in Therapeutic Apheresis (TA) Procedures

Vascular access type	Indications for use	Advantage	Complications
Peripheral Veins	Centrifugal based TA	Low rate of infections	Patient discomfort
	Acute or intermittent TA	Immediate use	Infiltration and sclerosis of veins
Non-tunneled central venous catheters	Short term use only (<2 weeks)	Easy to place at bedside	Risks inherent to catheter insertion
	Acute or intermittent TA	Blood flow rate high	Dysfunction
	Centrifugal or filter based TA		Infection, including sepsis, and metastatic infections
			Central vein stenosis
Tunneled central venous catheters	Short or long term use	Reduced infection rate when compared to non-tunneled catheters	Risks inherent to catheter insertion
	Centrifugal or filter based TA	Blood flow rate high	Dysfunction
			Infection, including sepsis, and metastatic infections
			Central vein stenosis
Arteriovenous Fistula (AVF)	Chronic TA (>3 months)	Lowest infection and dysfunction rates compared to other vascular access types	Requires surgery and adequate patient vascular anatomy
	Centrifugal or filter based TA		Requires a maturation period before use (~6–8 weeks)
			May be associated with primary maturation failure and subsequent need for additional procedures
			Requires trained staff for cannulation
Arteriovenous grafts (AVG)	Chronic TA (> 3 months)	Lower infection and dysfunction rates compared to catheters	Requires surgery
	Centrifugal or filter based TA	Most AVGs may be used within 2 weeks of placement	Requires trained staff for cannulation
			Higher infection/thrombosis rates compared to AVFs

Golestaneh, Ladan, and Michele H. Mokrzycki. "Vascular access in therapeutic apheresis: update 2013." *Journal of clinical apheresis* 28.1 (2013): 64-72.

Conclusions

- Therapeutic apheresis is frequently use for management of various disease processes
- Vascular access is important logistic & clinical issues to consider when evaluating a new patient for TA
- Main determinants of vascular access for TA depend on type of procedure; acuity; number, frequency, and anticipated duration of treatment; patient's vascular anatomy; and providers' comfort level
- Proper maintenance of peripheral & central access is needed to maintain adequate access and minimized adverse reactions

Questions

Thank You....