World Apheresis Association

Apheresis

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Message from the Incoming WAA President

Fevzi Altuntas, M.D.
President-Elect, WAA

Dear Colleagues

I'd like to express my sincere thanks to the member societies for giving me this opportunity to be the president.

I am very grateful to the former administration, Dr. Bill Clark and the board members, for their great and valuable efforts. Needless to say, they did their best and WAA has become one of the most important organizations worldwide. As the resident, I would like to mention some of the prominent future plans on related topics: Cooperation/collaboration, research, education, industry & technology, and social responsibilities.

As an umbrella organization, we will keep covering all of the issues related to apheresis. In future the WAA will flourish by collaborating with other member societies and by establishing and developing good relationships among the member societies. In addition, we have to increase the number of member societies to spread our doctrine. After that, if we could have success in combining all member societies' databases under the WAA registry, the next step will be conducting well-organized research on therapeutic apheresis science.

As a matter of fact, education is a sine qua non event for us. So we should establish accreditation programs, seminars, and workshops either face-to-face or online regarding apheresis training in conjunction with other member societies. Without a doubt, a financially supported fellowship exchange program could be one of the other extra benefits for the apheresis world. Moreover, we should encourage other member societies to support apheresis training and activities in their countries. In this context, physicians, nurses, technicians, researchers and various industries are our targeted groups.

Currently, the developed apheresis technology has become more useful and practical with satisfactory results and evidenced safety. The WAA's collaboration with industry is extremely important in terms of having enough financial support for future activities such as congresses and educational programs. It should be kept in mind that social responsibilities lead to social activities worldwide.

Taking apheresis technology, science, knowledge and experience to developing countries using all possible means should be one of our goals. Declaration of special time frames such as 'World apheresis Day' or 'World Stem Cell Donor Day' may lead to an increase in awareness. We should maintain contact with the media by all means to gain speed in reaching our goals.

For our part, we should encourage the member societies to submit abstracts and participate. The exact date and location for the next WAA joint meeting will be announced soon. The scientific committee will be working on the schedule and programs in the following days.

While doing this, your proposals about possible topics and arguments are welcome. Finally, on behalf of the whole WAA board, I wish you all the best for the 2020 Conference and I hope to see you at the next meeting! It would be a pleasure to be working with you closely on these subjects to carry WAA one step further.

Sincerely yours.

Fevzi Altuntas, MD. President-Elect. WAA

BRIEF BIOGRAPHY

Prof. Dr. Fevzi Altuntas is a faculty member at Yıldırım Beyazıt University, Faculty of Internal Medicine, Department of Hematology, Ankara, Turkey. In addition, he is the chief physician of the Ankara Oncology Training and Research Hospital, and the director of Department of Hematology, Therapeutic Apheresis and Stem Cell Transplantation Centers. In total, more than 100 autologous, allogeneic, unrelated, cord blood and haploidentical stem cell transplants are being performed annually at the Stem Cell Transplant Center of the Ankara Oncology Training and Research Hospital. He was the pioneer in the spread of apheresis centers and stem cell transplantation centers in Turkey. There has been a significant contribution to the provision of necessary training in these areas by his efforts. In this context, he is the former president of the Turkish Apheresis Association. He is a member of the International Committee of the American Society For Apheresis.

Additionally, Dr. Altuntas is the founder and president of some respectable associations in Turkey such as Turkish Society of Hematological Rare Diseases, Turkish Blood and Bone Marrow Transplant Association and Turkish Hematological Oncology Association. Also, he is the JACIE (The Joint Accreditation Committee-ISCT & EBMT) inspector of Turkey.

He established the first stem cell transplantation unit and started the first transplantation in Uzbekistan in 2014. Some of his awards due to contribution to Turkish hematology are being the owner of the Year Physician Award by Turkish Ministry of Health, appreciation by Turkish Ministry of Health for stem cell transplantation studies, and lifetime Honor Award winner by Turkish Apheresis Association. He has been researcher and study coordinator for over 30 international Phase II/III studies.

To date, Dr Altuntas has published over 90 articles in international refereed journals and more than 40 articles in national journals. The number of published national and international abstracts is over 500. He wrote more than 30 books and book chapters. His articles were cited about 1300 times. He took part in national and international journals as an editorial board member and he is still one of the Senior Editors of "Transfusion & Apheresis Science".

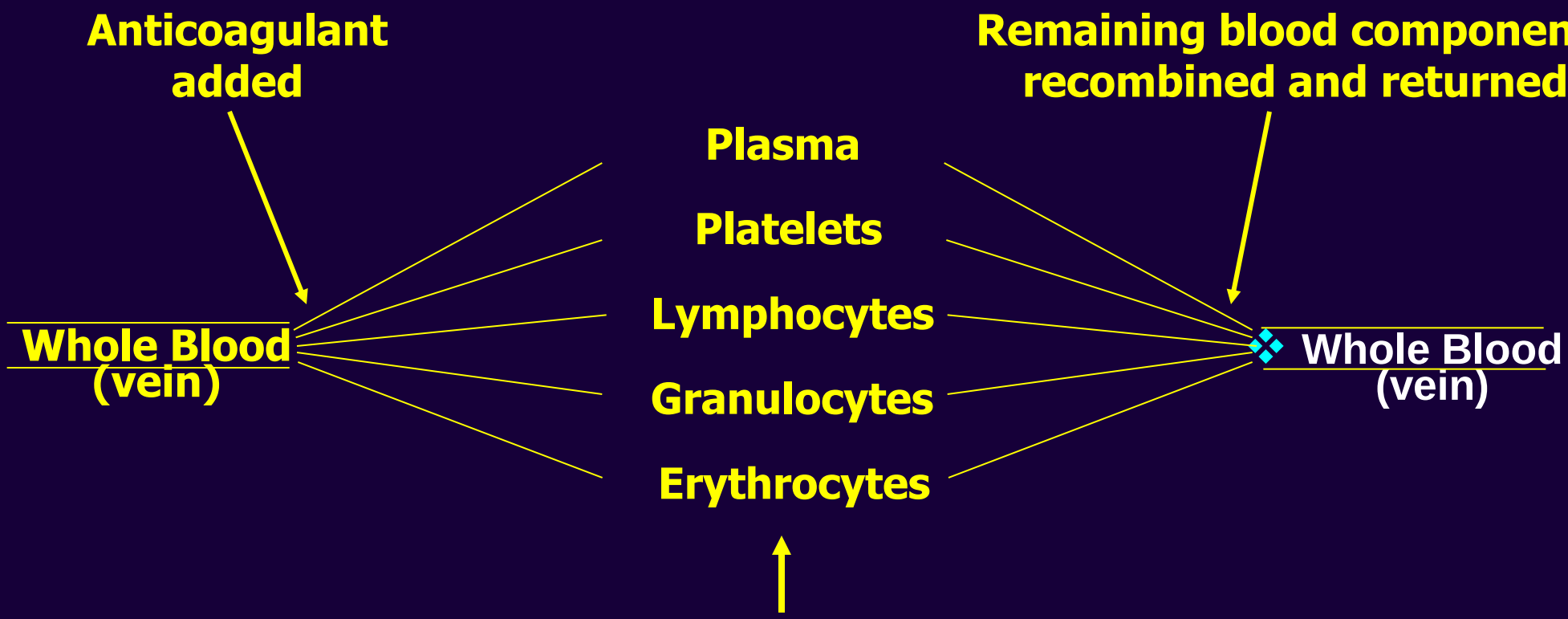
What is Apheresis?

- Collection of a particular blood component from a Donor or a patient and the remaining constituents are returned to the donor or patient.
- Apheresis is a process by which blood being removed from a subject is continuously separated into component parts, usually to allow a desired component(s) to be retained while the remainder is returned to the subject.

What is Apheresis?

- Cytapheresis - removing cell components.
  - ✓ Erythrocytapheresis - removing RBCs only.
  - ✓ Plateletapheresis – removing PLTs only.
  - ✓ Leucoapheresis- removing WBCs only
- Plasmapheresis - removing plasma only.

Principles of apheresis



Blood components separated by centifugation and selectively removed

Apheresis Methods

1) Centrifugation (specific gravity)
   a) Continuous flow (CFC)
   b) Intermittent flow (IFC)
2) Adsorption
3) Filtration
   ✓ Apheresis by membrane filtration
4) Photopheresis

Apheresis Methods

1. Centrifugation

a) Continuous flow

- One or two access points
- Continuous blood separation
- All fractions can be removed in ongoing manner
  - ❖ Do not need to empty container until end of procedure

Apheresis Methods

1. Centrifugation

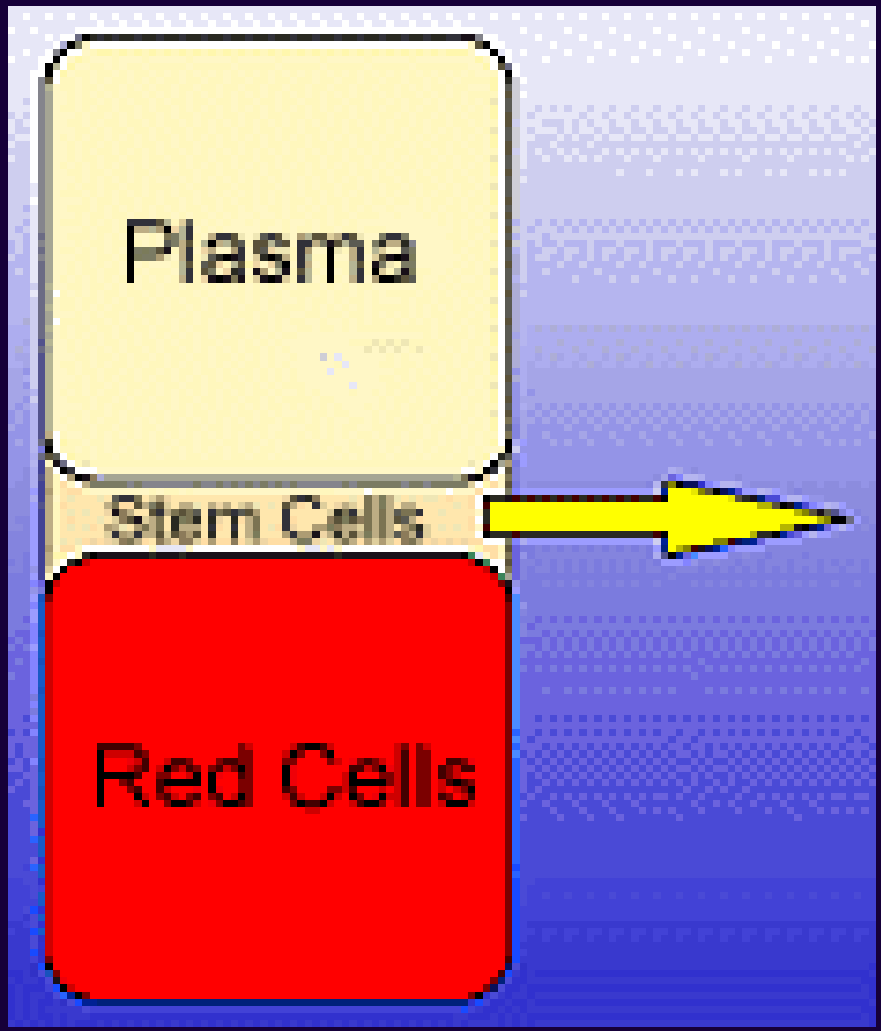
b) Intermittent flow

- One access needed
- Blood separation in cycles
- Slightly longer processing time
- Slightly larger extracorporeal volume
- Blood processed in discrete batches
- Separation until container filled with dense component (RBC)
- Needs to empty before next batch

Apheresis Methods

Centrifugation

- Cells are separated by the centrifugal technique according to **specific gravity** from each other.
- The most outward form are ranked following:
  - **Plasma** 1.025-1.029
  - **Platelets** 1.040
  - **Lymphocytes** 1070
    - Mononuclear cells-stem cells
  - **Granulocytes** 1.087-1.092
  - **Erythrocytes** 1.093-1.096
- This method is particularly suitable for cytapheresis operations.



Apheresis Methods

Filtration

- In filtration technique,
  - ✓ Cells and plasma migrated in a porous membrane are separated from each other by the diameter of the membrane pores.
  - ✓ Blood components are separated from each other by on the size (dimensions).

Apheresis Methods

Adsorption

- It is an application used for more IMMUNOADSORPTION operations.
- Required elements who are separated from plasma using bioactive membranes.

Apheresis Classification

I. Component collections (Donor apheresis)
   1) Plateletpheresis
   2) Leucopheresis
   3) Erythrocytapheresis
   4) Plasmapheresis
   5) Stem cell apheresis

II. Therapeutic Procedure (Therapeutic apheresis)
   1) Therapeutic cytapheresis
   2) Therapeutic plasmapheresis (plasma exchange)

Donor Apheresis

- Advantages
  - ✓ Select only component(s) needed
  - ✓ Return rest of blood
  - ✓ No need for component separation in lab
  - ✓ More frequent donation allowed (some)
- Disadvantages
  - ✓ Expense/equipment/training
  - ✓ Citrate exposure

Therapeutic Apheresis

- Scientific basis of treatment assumes
  - ✓ Blood contains disease causing agent
    - Autoantibodies,
    - immune complexes,
    - sometimes alloantibodies
  - ✓ This agent can be effectively removed by apheresis
  - ✓ Treatment will result in clinical improvement

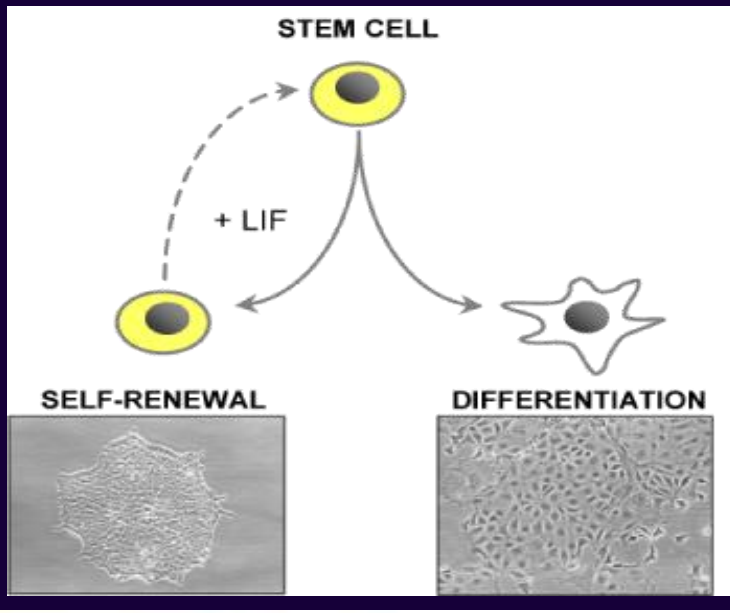
Types of Apheresis

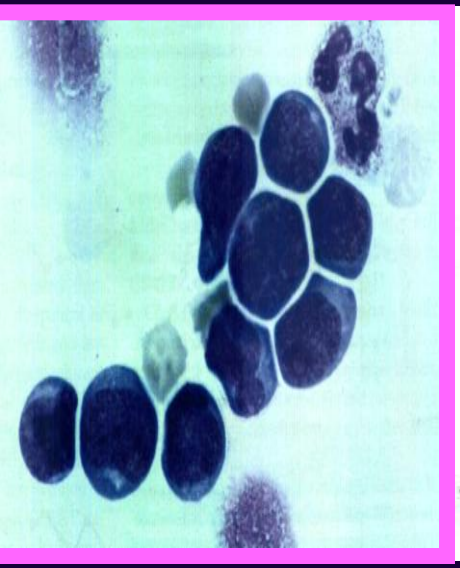
- **Plasmapheresis**
  - Plasma exchange
  - LDL apheresis
  - Immunoadsorption
- **Leukapheresis**
  - WBC reduction
  - Peripheral Blood Stem Cell collection
  - Granulocyte collection
  - Lymphocyte collection
- **Plateletpheresis**
  - Reduction
  - Collection
- **Erythrocytopheresis**
  - RBC exchange
  - RBC depletion
  - RBC collection
- **Photopheresis**

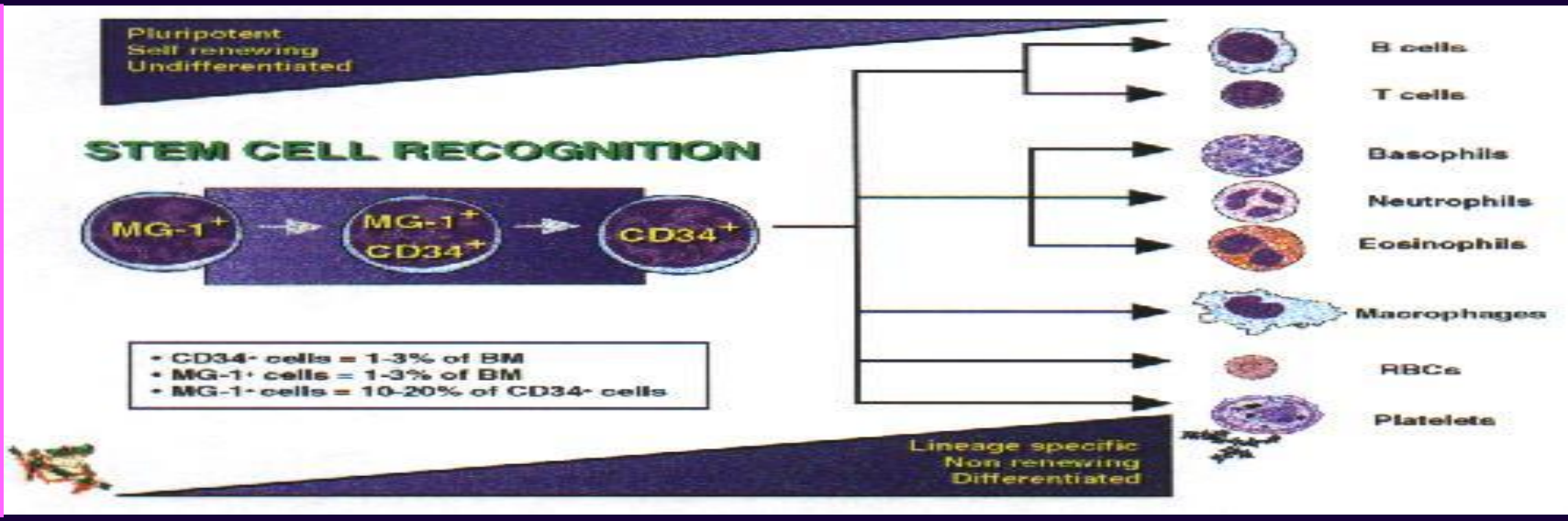
Stem cell apheresis

Hematopoietic Stem Cell

- ✓ can renew itself (Self-Renewal)
- ✓ can differentiate to a variety of specialized cells (Differentiation)
- ✓ can mobilize into peripheral blood (Mobilization)
- ✓ Clonal cells





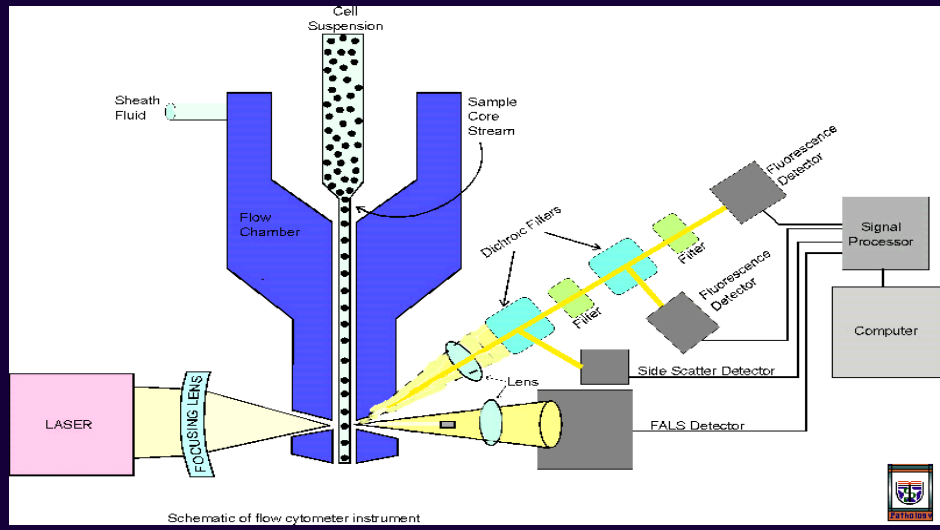


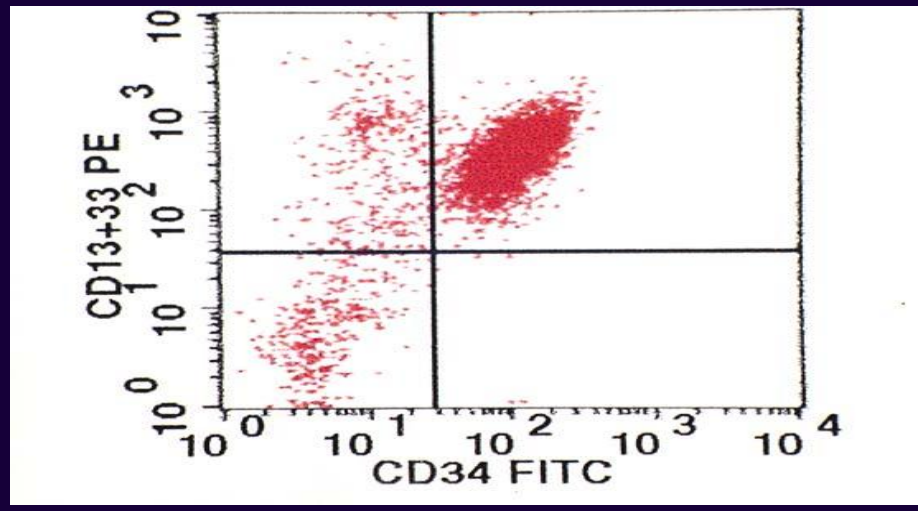
Hematopoietic Stem Cell Detection

- The only way to correctly identify stem cells that grow in their culture and show that generate all blood cell types.
- But this process is not practical because it takes time for several weeks.

Flow Cytometry: Stem cells= CD34+

- Stem cells are expressing a particular protein on the surface of its cells:
  - ✓CD34
- CD34 + cells were measured using the current sitometer.
- However, all CD34-expressing cells are not stem cells.



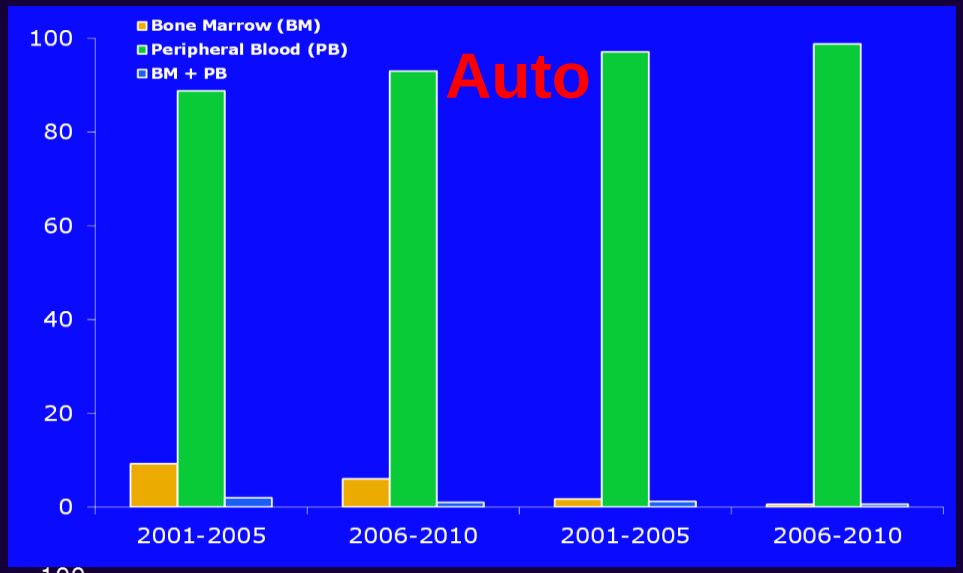


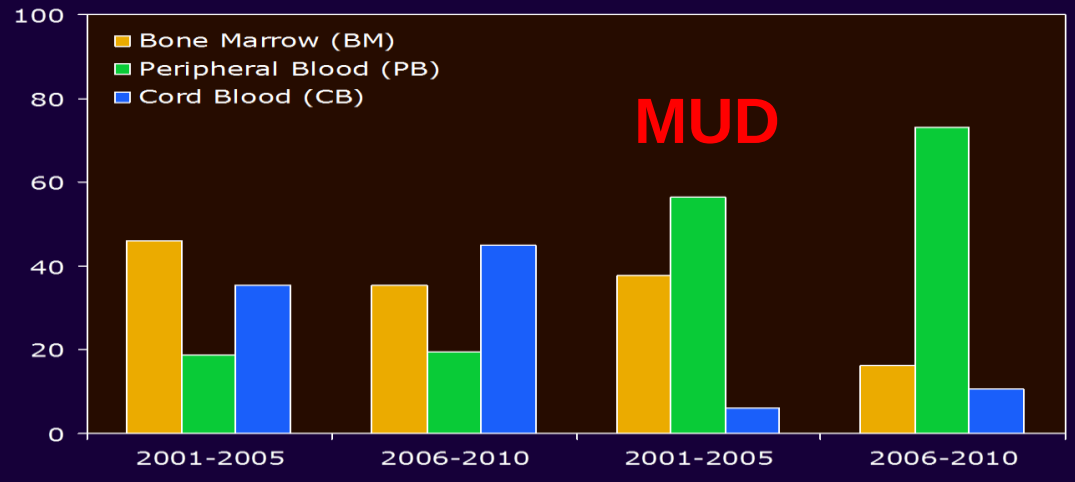
Hematopoietic Stem Cell Source

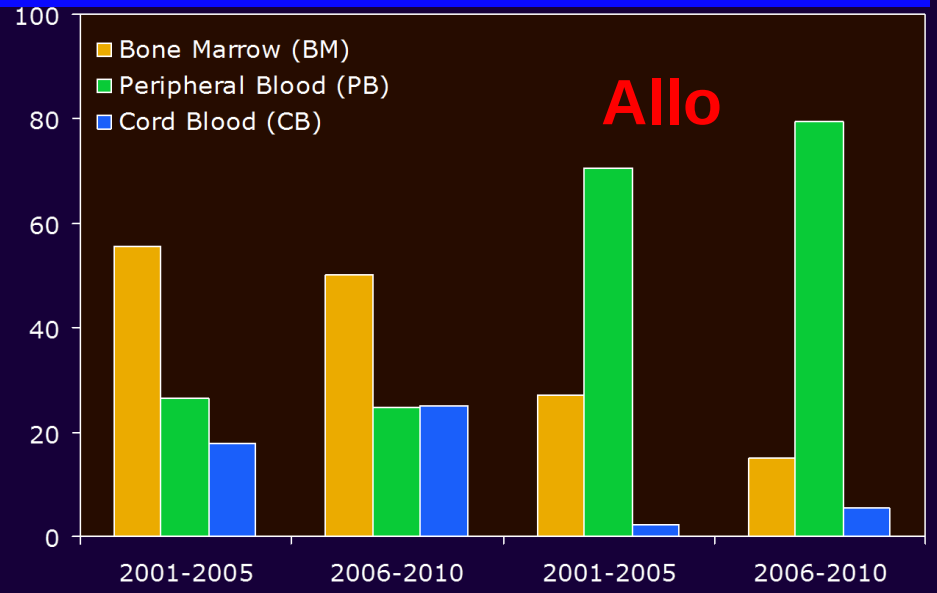
① Bone Marrow

② Peripheral Blood

③ Cord Blood







Peripheral Blood Stem Cells

- The most frequently used source of HSCs
  - ✓ Does not require general anesthesia
  - ✓ Decrease risk to donor
  - ✓ Faster engraftment compared to BM
- But
  - ✓ Need for mobilization regimen
  - ✓ Increased risk of chronic GVHD

Hematopoietic Stem Cell Mobilization

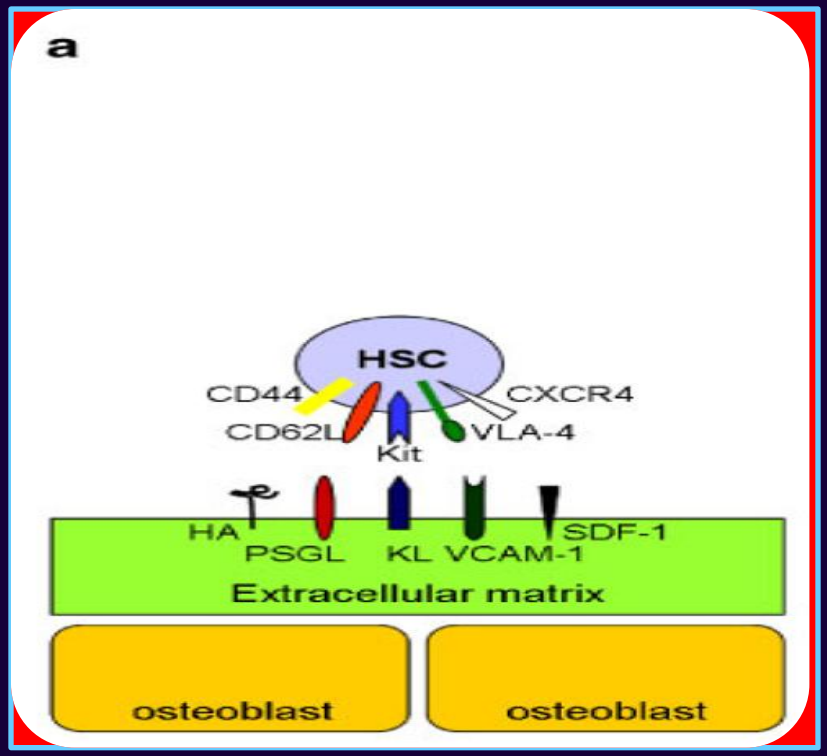
- The concentrations of HSCs are 10-100 times greater in the BM compared to the PB.
  - ✓ 0.1% of PB mononuclear cells
  - ✓ 1-4% bone marrow cells
- Therefore, methods to increase the circulating concentrations of HSCs are necessary to ensure adequate and successful collections.
- Agents used to mobilize HSCs include the administration of cytokines with or without chemotherapy prior to scheduled collection periods.

Common Mobilization Regimens

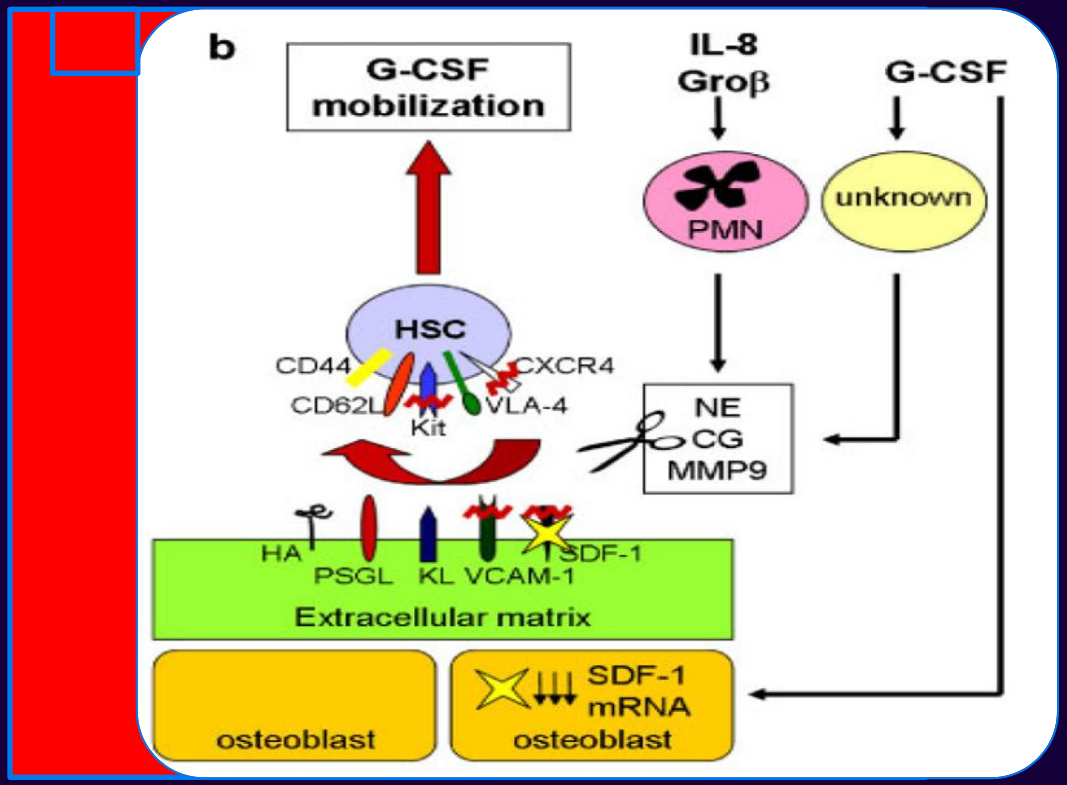
1. Hematopoietic growth factors
   a) G-CSF, GM-CSF
2. Plerixafor (in combination with G-CSF)
3. Other cytokines
   a) Pegfilgrastim, stem cell factor (SCF)
4. Chemotherapy+ Growth factors
   a) Mobilization-specific chemotherapy: Cyclophosphamide, cytarabine, etoposide, etc
   b) Disease-specific chemotherapy: ICE, IVE, VIGEPP, etc

Mechanisms of Stem Cell Mobilization with G-CSF

Adhesive interactions between HSC and matrix components in the BM



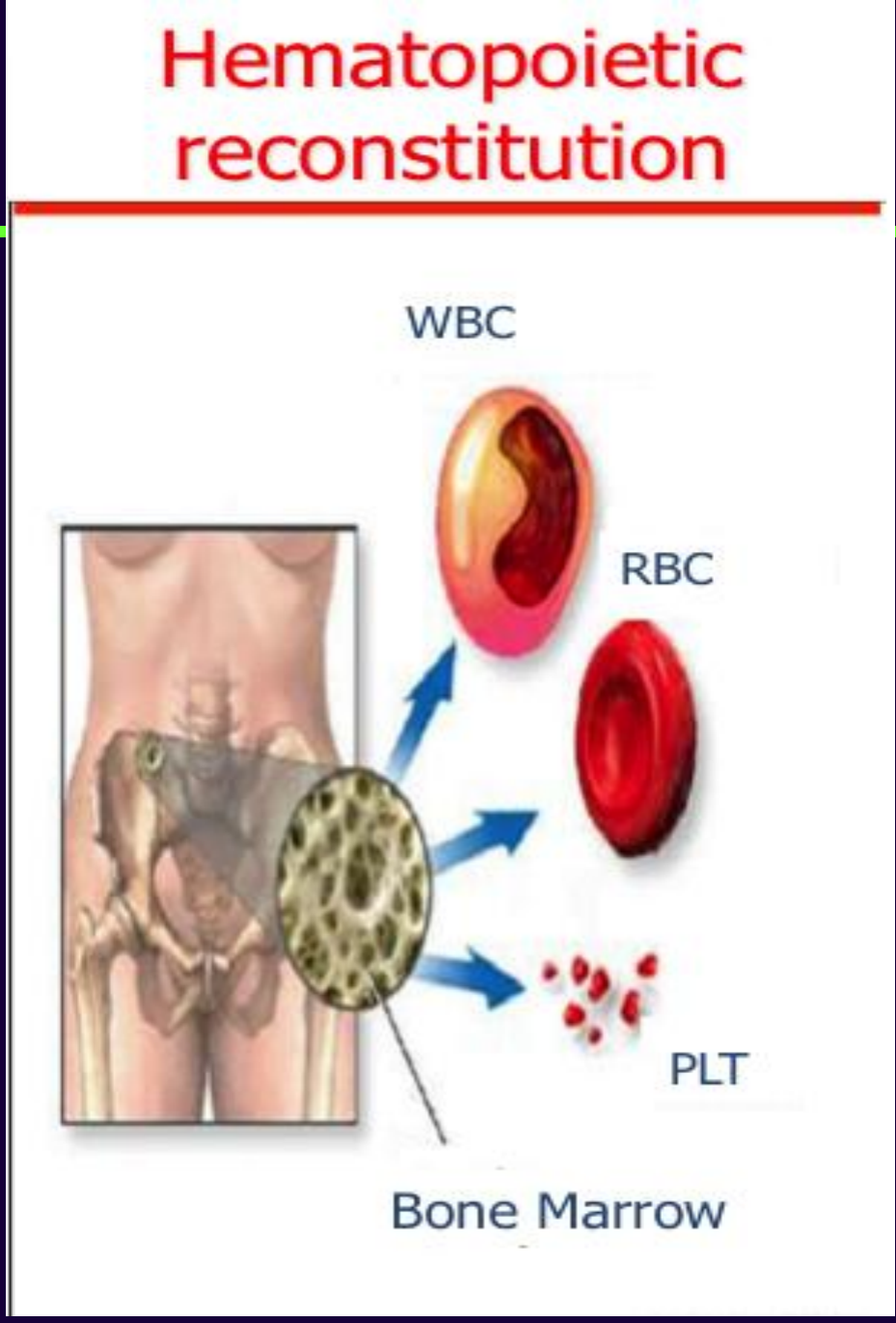
G-CSF Mobilization



G-CSF induces the release of a number of proteases into the BM which cleave several adhesion molecules thought to play an important role in HSC trafficking and mobilization.

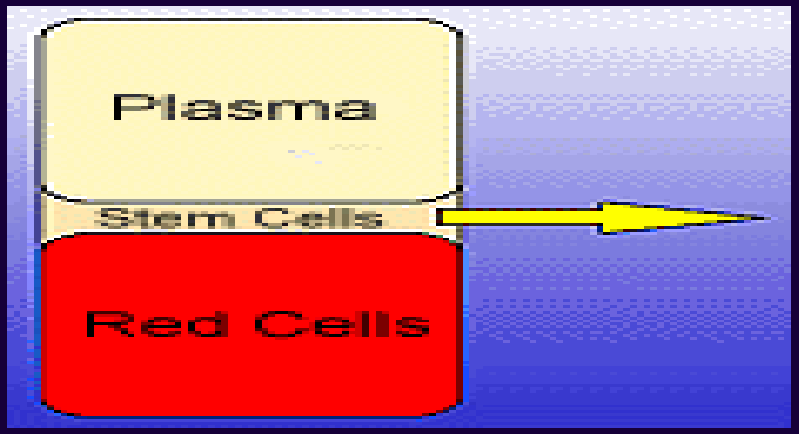
Dose of CD34

- **Dose of CD34+cell is important for hematopoietic reconstitution:**
- **Auto HSCT**
  - ✓ **> 2 x10^6 CD34+ cell/kg**
- **Allogeneic HSCT**
  - ✓ **> 5 X10^6 CD34+ cell/kg**



Stem cell apheresis

- Whole blood is separated into components under the influence of centrifugal force:
  - ✓ RBC, WBC and plasma are separated depending on their specific gravity and density.



Stem cell transplantation Indications

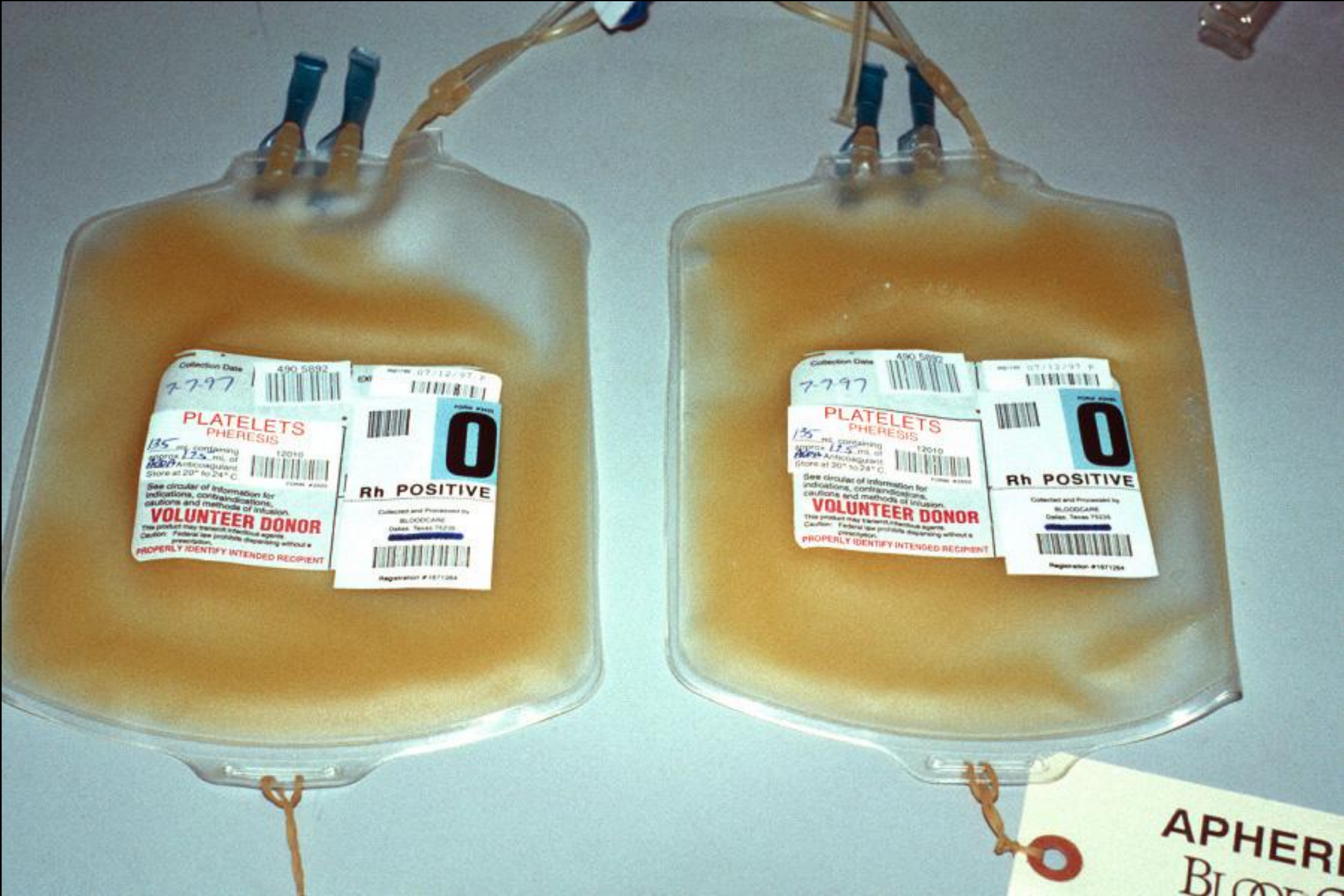
I. Hematologic malignancies
   1. Acute leukemias:
      a) AML
      b) ALL
   2. MDS
   3. Lymphomas:
      a) Hodgkin lymphoma
      b) NonHodgkin Lymphoma
   4. Multiple Myeloma
   5. Chronic leukemias:
      a) CML
      b) CLL

II. Severe aplastic anemia

III. Congenital immunodeficiency syndromes & metabolic diseases

IV. Autoimmune diseases

DONOR APHERESIS


PLATELETS
PHERESIS
VOLUNTEER DONOR
Rh POSITIVE
O
PROPERLY IDENTIFY INTENDED RECIPIENT
APHERE

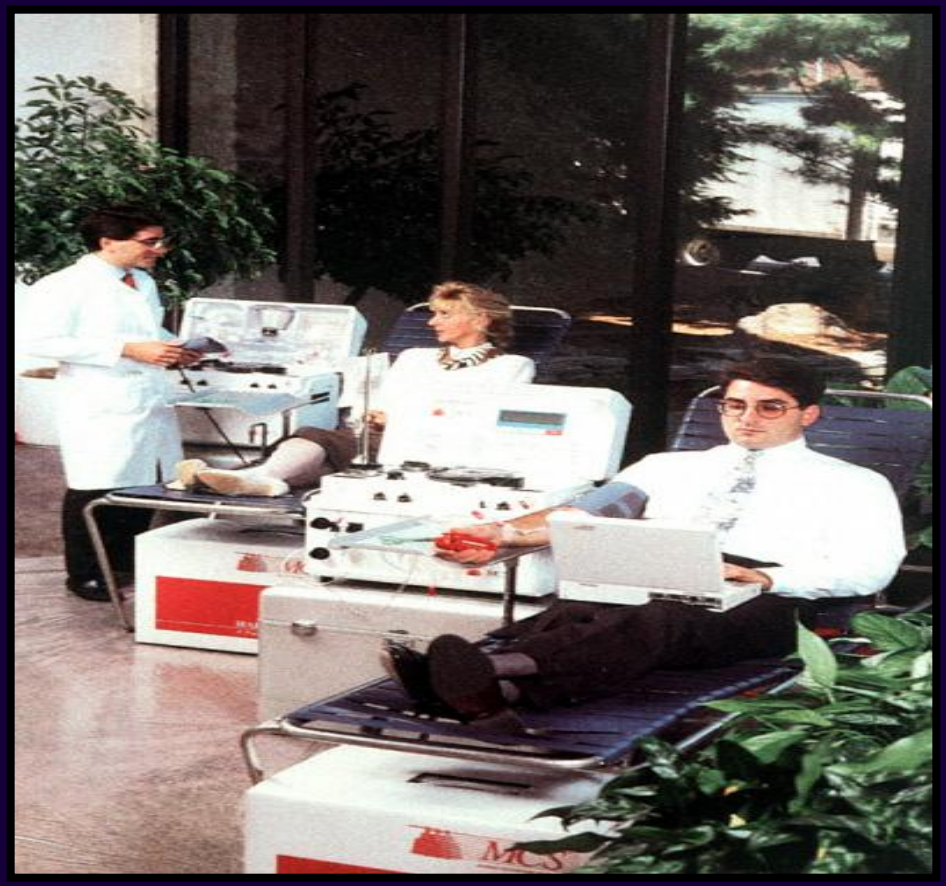
Platelet concentrations

1) Random donor platelets =

- ✓ One unit of whole blood were prepared by centrifugation method

2) Apheresis platelets =

- ✓ It is collected from a donor apheresis
- ✓ platelet product containing 3 x 10^{11} and above



Platelet concentrations

- **Unit:**
  - ✓ Single apheresis donor unit: platelets contain ~ 3 x10^{11}
- **The risk of infection:**
  - ✓ The risk of bacterial contamination is high
  - ✓ They are pooled risk is further increased (1%)
- **Storage:**
  - ✓ + 20/24ºc agitation in / horizontal shaking <u>up to 5 days</u>
    - Longer-term storage increases the risk of bacterial proliferation and septicemia

Platelet concentrations

- **Dosage:**
  - ✓Therapeutic dose = 1 apheresis unit
    - Should increase platelet counts 20-40 x 10^9 / L
- **Practice principles:**
  - ✓ABO and Rh should be given appropriate platelet suspension
  - ✓You do not need cross-match test before transfusion
  - ✓Platelets should never be put in the refrigerator
  - ✓They are pooling should be used within 4 hours
  - ✓It should be infused over 30 minutes -1 hour

Who can Donate Platelet

Age:	**17th – 61st birthday (first time donor)**
Weight:	**At least 50 kg (110 lbs)**
Hemoglobin:	**Must meet requirements** ≥12.5 gr/dL and ≥ 38%
Donation frequency:	**every 3 days, 2 times a week, 24 times a year**
	RBC: 56 days
	Plasma: 1 month
Health:	**In good health and feeling well.**
Screening:	**At time of donation, a number of questions are asked to determine donor eligibility, e.g.:**

If donor has	*To wait for donor*
The tooth examination:	*3 days later rounds*
Colds, flu or sore throat:	*will be fully recovered*
Ear piercing / body tattoos:	*6 months*

Donation Criteria

- Donors for apheresis procedure must meet the criteria applicable as the donors for normal donation.
- CBC, ABO and Rh typing, antibody screening and testing for transfusion and transmitted diseases (VDRL, anti-HIV I&II, HIV-1 RNA, anti-HCV, HCV-RNA, HBsAg, ANTI-HTLV I&II, RPR, anti-HBc and Anti-HBs if Anti-HBc positive) SHOULD BE DONE.
- A drug history should be obtained; donors who have taken aspirin or aspirin containing medications within 3 days of donation should be temporarily deferred.

Donation Interval

- The interval between platelet donations should be at least 48 hours, with no more than two donations in a week and 24 donations in a year.
- Plasmapheresis donors may donate as often as every 48 hours but not more than twice in a 7-day period.
- If it becomes impossible to return the donor's red cells during apheresis, at least 8 weeks shall elapse before subsequent apheresis procedure, unless the red cell loss was less than 200 mL.

DONOR ELIGIBILITY - PLATELET APHERESIS

- No whole blood donation for 8 weeks
- No platelet donation for 48 hours
- No aspirin in last 36 hours
- Platelet count >150,000/uL
- No more than 2 times per week
- No more than 24 donations in one year


Collection Date
05/09/00
Q 1736
740 8079
EXPIRES
05/10/00
Q 1736
GRANULOCYTES
PHERESIS
16411
indications, contraindications,
cautions and methods of infusion.
VOLUNTEER DONOR
LOT NO 0222
11E15200

Granulocyte apheresis

- Granulocytes from donors to achieve under normal circumstances is very difficult.
- In contrast, Sufficient granulocytes (>1x 10^{10} / kg) can be obtained 12 hours later from apheresis donors taking G-CSF 10 mg / kg sq together with 8 mg dexamethasone.

Granulocyte concentrations

- Description:
  - ✓ > 1 x 10^{10} granulocytes is prepared by a single donor apheresis (75%)
- content:
  - ✓ Different amounts of lymphocytes, includes platelets and red blood cell
- storage:
  - ✓ Stored for 24 hours at +20/24 ˚ C
- Indication:
  - ✓ Gram-negative sepsis (yeast infection) that has been shown +
  - ✓ Absolute neutropenia (neutrophil count <500 / □l) +
  - ✓ It did not respond to antibiotics and other treatments +
  - ✓ Patients with hypoplasia and the chance to return on bone marrow function

Granulocyte concentrations

- The dosage and duration of treatment:
  - ✓ At least 4 days, > 1-4 x 10^{10} granulocyte transfusions
- Practice principles:
  - ✓ ABO and Rh appropriate product should be used
  - ✓ RBC transfusion compatibility testing should be done
  - ✓ Irradiating should be given
  - ✓ Standard 170µ blood filter must be used
  - ✓ As quickly as possible should be transfused (<6 hours)

Therapeutic Apheresis

Therapeutic Cytapheresis

1. Leucopheresis
2. Erythrocytapheresis
3. Plateletpheresis (thrombocytopheresis)

Common Diseases Treated with Cytapheresis

- Leukemia with WBC count >100,000/mL
- Sickle Cell Anemia
- Hyperparasitemia (e.g., malaria)
- Life-threatening hemolytic transfusion reactions
- Symptomatic Thrombocytosis

Therapeutic- Leucopheresis

Disease	Indications
AML	leukostasis; >100.000/mL
ALL	leukostasis;>200.000/mL
CML	leukostasis;>300.000/mL
CLL	leukostasis;>400.000/mL; treatment resistant

Therapeutic- Leucopheresis

- Leukostasis syndrome
  - ✓ Usually WBC> 100,000/μL (blast)
  - ✓ Rarely <100,000/μL
  - ✓ Pulmonary and CNS symptoms
- CML (blastic phase)
- T-ALL
  - ✓ To prevent tumor lysis syndrome

Aim- Therapeutic Leucopheresis

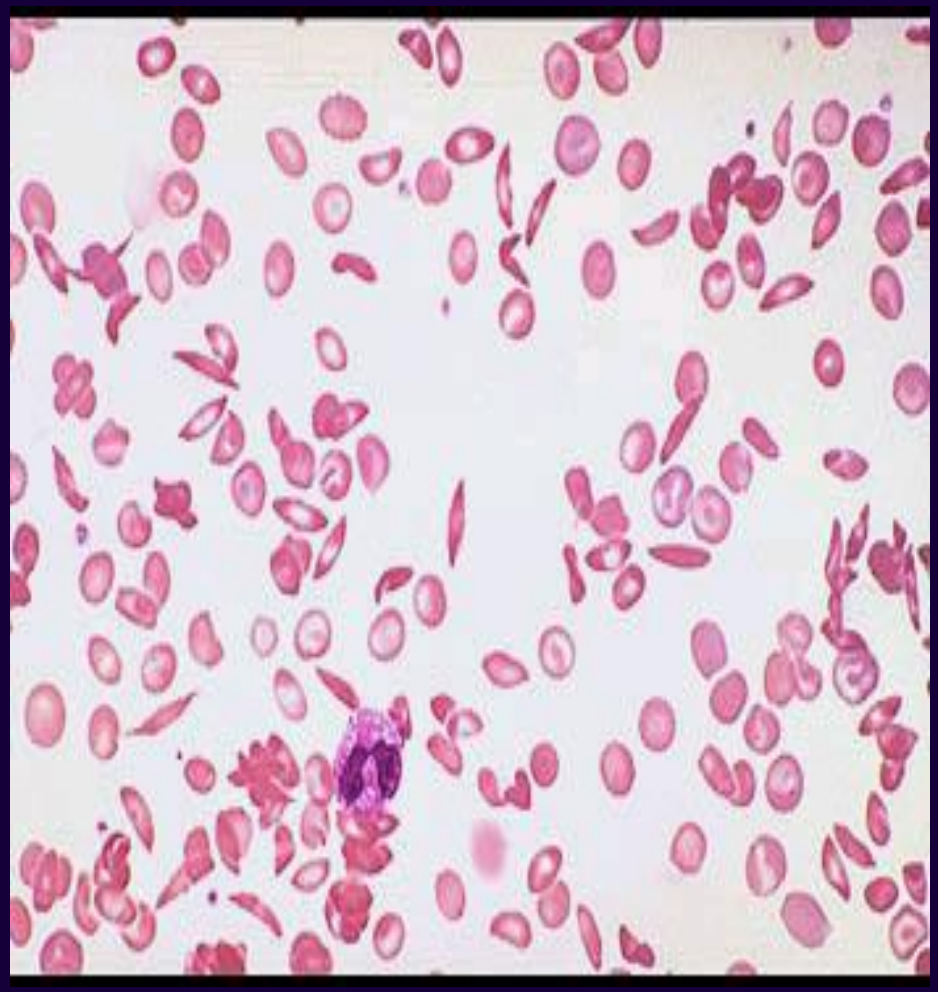
- WBC count of <100,000/μL lower
- To prevent damage to the CNS
- To correct hypoxemia
- To prevent tumor lysis syndrome
- Emergency treatment

Therapeutic RBC Exchange

- Sickle cell anemia
  - Acute chest syndrome
  - Cerebral infarction (Stroke)
  - Resistant priapism
  - perioperative
  - Standard treatment-resistant prolonged pain crises
- Protozoal Infections
  - malaria
  - Babesiosis
- Mismatch blood transfusion
  - Giving Rh positive blood Rh-negative patients
  - ABO incompatible bone marrow transplantation
  - Passenger lymphocyte syndrome
- Polycythemia
- Intoxication:
  - CO poisoning
  - methemoglobinemia

Therapeutic RBC Exchange
Sickle cell anemia

- To prevent recurrence in patients with cerebral infarction
- Acute infarction during the first 48 hours
- Acute chest syndrome
- priapism
- Prolonged painful vazooclussive crises
- Pregnancy and preoperative



Sickle cell anemia

Crisis Management

- Pain Crisis: analgesics, hydration
- Stroke: RBCx
- Acute Chest Syndrome: RBCx
- Persistent Priapism:
  - ✓ Conservative management
  - ✓ If no response within 24 hrs → RBCx
- Hemolytic/aplastic crisis: RBC Tx
- Megaloblastic crisis: folic acid

Sickle cell anemia

Chronic Red Cell Transfusion

- Simple transfusion of 10-15 mL/kg RBC every 3 - 4 wks
- Prevents recurrent stroke
- Allows “healing” of sickle cell related events
- Easy to perform in any hospital
- Needs only a single venous access

Sickle cell anemia

Acute Chest Syndrome

- Sudden onset dyspnea
- Hypoxemia - cyanosis
- Infection or stress pulls the trigger
  - ✓ Lung x-ray: pneumonia
- You may need to intubate
- Lung erythrocyte sickling due to sudden drop-Htc

Sickle cell anemia

Plan for RBCx

- Assume 100% HbS
  - ✓ Unless recently transfused
- Goal: to reduce HbS <30%
- Raise Hct to baseline + maybe 3% more
- Never raise Hct >30%
  - ✓ Concern for hyperviscosity

Advantages of Automated RBCx

- Prevents recurrent stroke
- Effective method to remove HbS cells and replenish with HbA cells
- Equal amount of red cells are removed and transfused
- No significant net iron accumulation
  - ✓ Decreased iron stores with chelation
  - ✓ Stabilized stores without chelation

Disadvantages of RBCx

- Higher cost than simple transfusion
- Increased red cell utilization
- Greater donor exposure
- Difficulty in obtaining antigen negative units
- Requires two venous accesses

Red Cell Requirements

- Pre-storage leukoreduced
- Fresh (<7 days)
  - ✓To provide 2-3 DPG immediately
  - ✓Longer surviving red cells
- Partial phenotype matched (Rh and Kell)
- Screened for sickle cell trait

Sickle cell anemia
Acute Stroke Management

- Emergent RBCx
- Sooner the better
  - ✓ To prevent permanent brain damage
- Goal: to rapidly reduce HbS and prevent further hemolysis and sickling
- Avoid simple transfusion
  - ✓ Will not reduce HbS <50%
  - ✓ Will further increase viscosity

Recurrent Stroke in SCD

- 67% (47-93%) recurrence rate within next three years, if untreated
- Incidence reduced significantly by chronic transfusion therapy to <10%
- Goals of chronic transfusion therapy
  - ✓ HbS <30% for first 3 - 4 years
  - ✓ HbS <50% – indefinitely

Therapeutic- Thrombocytopheresis

- Applied in essential thrombocythemia.
- Platelet count> 1,000,000/μL, which is done in preparation for symptomatic patients and for surgery.
- Pregnant women may also apply.

Plateletapheresis

- Platelet count> 1,000,000/uL
  - ✓ Rarely lower number of symptomatic
- Symptomatic
  - ✓ CNS events
  - ✓ Thrombotic events
- Platelet function
  - ✓ Hyper or hypo
    - Clot or bleeding
- Two blood volume is processed (~ 3 to 4 hours)
- AC ratio should be set

Therapeutic Plasma Exchange

- It is the removal and retention of the plasma with return of all cellular components to the patient.

- Recommended 1-1.5 plasma volumes be exchanged
- One volume exchange (2-4 L) → unwanted plasma component to 30% of its initial value .

Therapeutic Plasma Exchange

- Reducing plasma components that play a role in the pathogenesis of various diseases, to reduce the damage caused by the organism or pathological process is reversible to an extent of this damage.
  - ✓ Monoclonal Protein
  - ✓ Cryoglobulins
  - ✓ Immunocomplexes
  - ✓ Lipoproteins
  - ✓ Autoantibodies - alloantibodies
  - ✓ Toxins

Factors Removed by Plasmapheresis

- Immune Complexes (SLE)
- Auto- or Allo- Ab (factor VIII inhibitors).
- Ab causing hyperviscosity (Waldenström's).
- Ab blocking normal function of the immune system.
- Inflammatory Mediators (fibrinogen, complement).
- Protein-bound toxins (barbiturate poisoning).
- Lipoproteins.
- Platelet-aggregating factors (? Role in TTP).

The Efficacy of Plasma Exchange

is related to the amount of plasma removed

- A 1-volume exchange should reduce the unwanted plasma component to 30%.
- A 2-volume exchange reduces the unwanted component to only 10%.
- The actual plasma volume removed varies between 2-4 L /procedure.
- Typically, only 1-1.5 plasma volumes are exchanged per procedure

Replacement Fluids for Plasmapheresis

- 5% Human Albumin
- Albumin and Saline (70:30)
- Fresh Frozen Plasma (FFP)
- Cryopoor plasma
- Hidroksyetilstarch (HES)
- Pentastarch

TPE INDICATIONS CATEGORY-I

❖ STANDARD TREATMENT

1. TTP (thrombotic thrombocytopenic purpura)
2. Cryoglobulinemia
3. anti-GBM disease (Goodpasture Syndromes)
4. Guillain-Barre Syndromes
5. Familial Hypercholesterolemia (LDL apheresis)
6. Hyperviscosity syndromes
7. Myasthenia Gravis
8. Post Transfusion Purpura
9. Chronic inflammatory demyelinating polyneuropathy

TPE INDICATIONS CATEGORY-II

- ACCEPTABLE TREATMENT

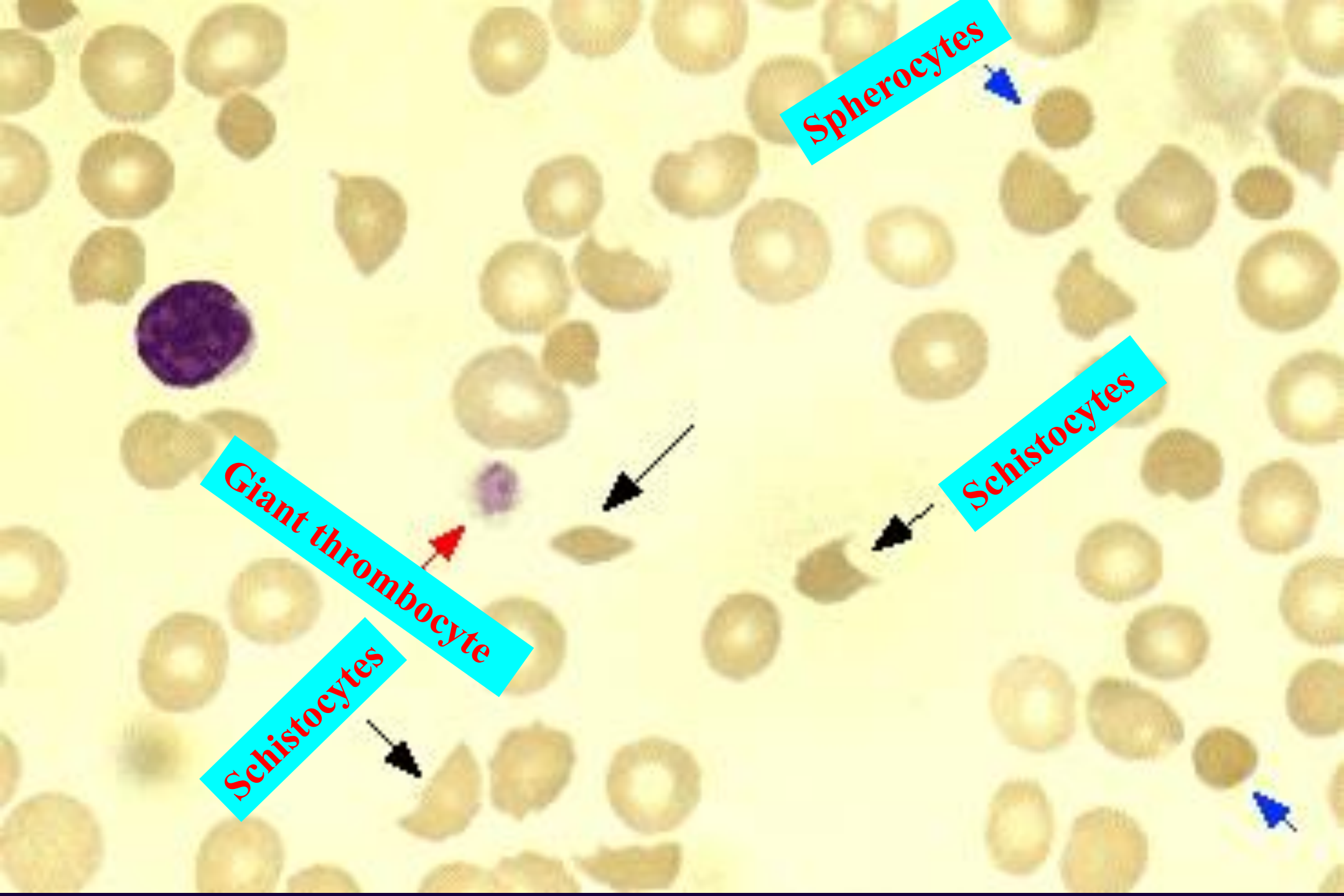
1. Cold agglutinin disease
2. Protein-bound toxins (drug overdose, poisoning)
3. Hemolytic Uremic Syndrome (HUS)
4. Rapidly Progressive Glomerulonephritis
5. Systemic vasculitis (primary or secondary to SLE and RA)
6. acute renal failure secondary to myeloma

TTP - Diagnostic Criteria

- Amorosi and Ultmann (1996)
  - ✓Microangiopathic hemolytic anemia (Schistocytes, -LDH)
  - ✓Thrombocytopenia
  - ✓Neurological symptoms
  - ✓Renal involvement
  - ✓Fever
- Moake JL (2002)
  - ✓ Diagnostic criteria= Thrombocytopenia and MAHA (schistocyt, elevated LDH)

Amorosi EL, Ultman JE. Thrombotic thrombocytopenic purpura: report of 16 cases and review of literature. Medicine 1966; 45:139-59

Moake JL. Thrombotic Microangiopathies. N Engl J Med 2002; 347:589–600


Spherocytes
Schistocytes
Giant thrombocyte
Schistocytes

Clinical Features

Initial symptoms	Altuntas et al	Literature
Anemia	100%	100%
Thrombocytopenia	100%	100%
Neurological problem	66%	60-86%
Renal impairment	52%	34-58%
Fever	31%	23-86%
Classical “pentad”	23%	10-30%

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vWF-Cleaving Protease

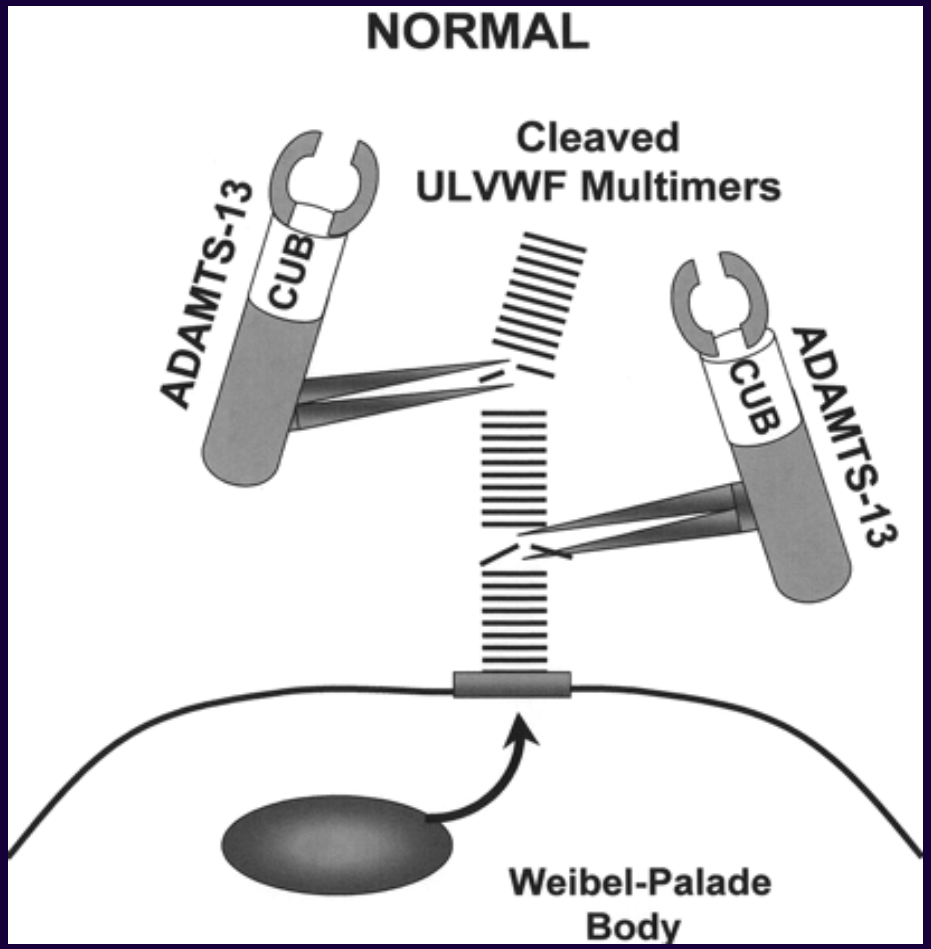
- A metalloproteinase
- Normal range 75-125%
- In majority of TTP patients <15%
- In Congenital TTP 2-32%
- Probably long half life 2-3 days

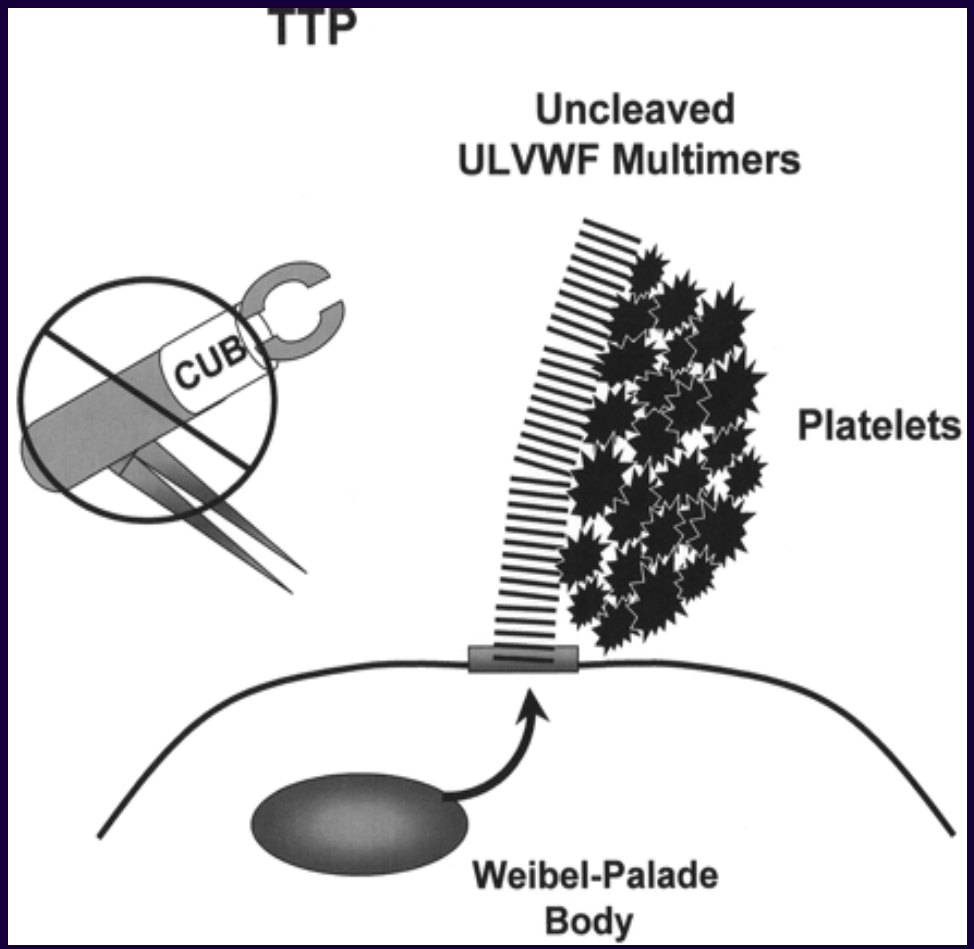
Deficiency of VWF Protease

1) Congenital In chronic relapsing TTP
2) Acquired

- In Primary TTP
  - ✓ Spontaneous auto antibody
    - IgG purified from plasma
  - ✓ Transient
- In secondary TTP
  - ✓ Triggered by infection/drugs/malignancy/pregnancy/stem cell transplantation
    - Bacteria/virus (HIV/HTLV-I/Brucella), ticlodipins,clopidogrel, simvastatin, atorvastatin, cytotoxic agents, cyclosporin-A, tacrolimus (FK506), penicillamine, carcinoma, lymphoma
  - ✓ Deranged Immune system (SLE, Sjogren's syndrome, HIV)

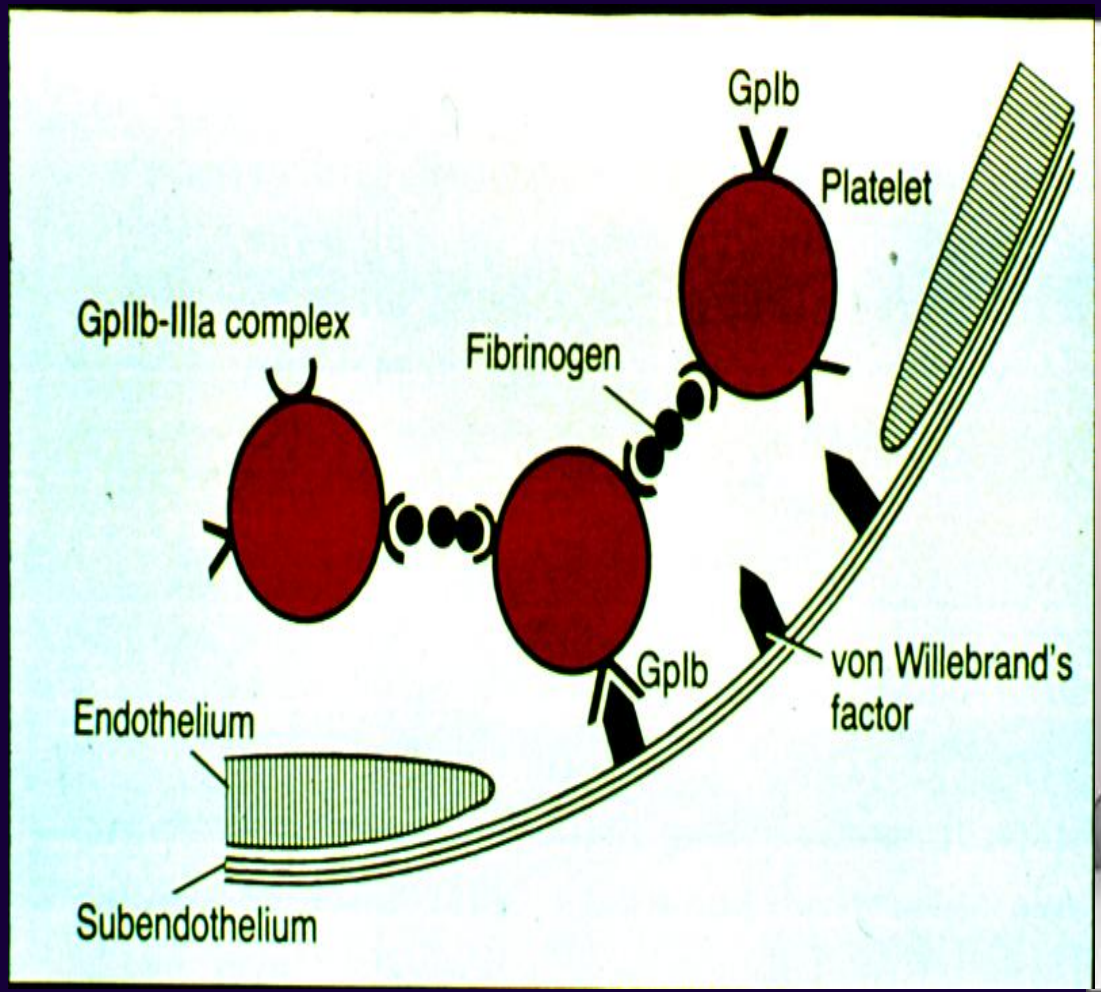
TTP pathophysiology: Deficiency of VWF Protease

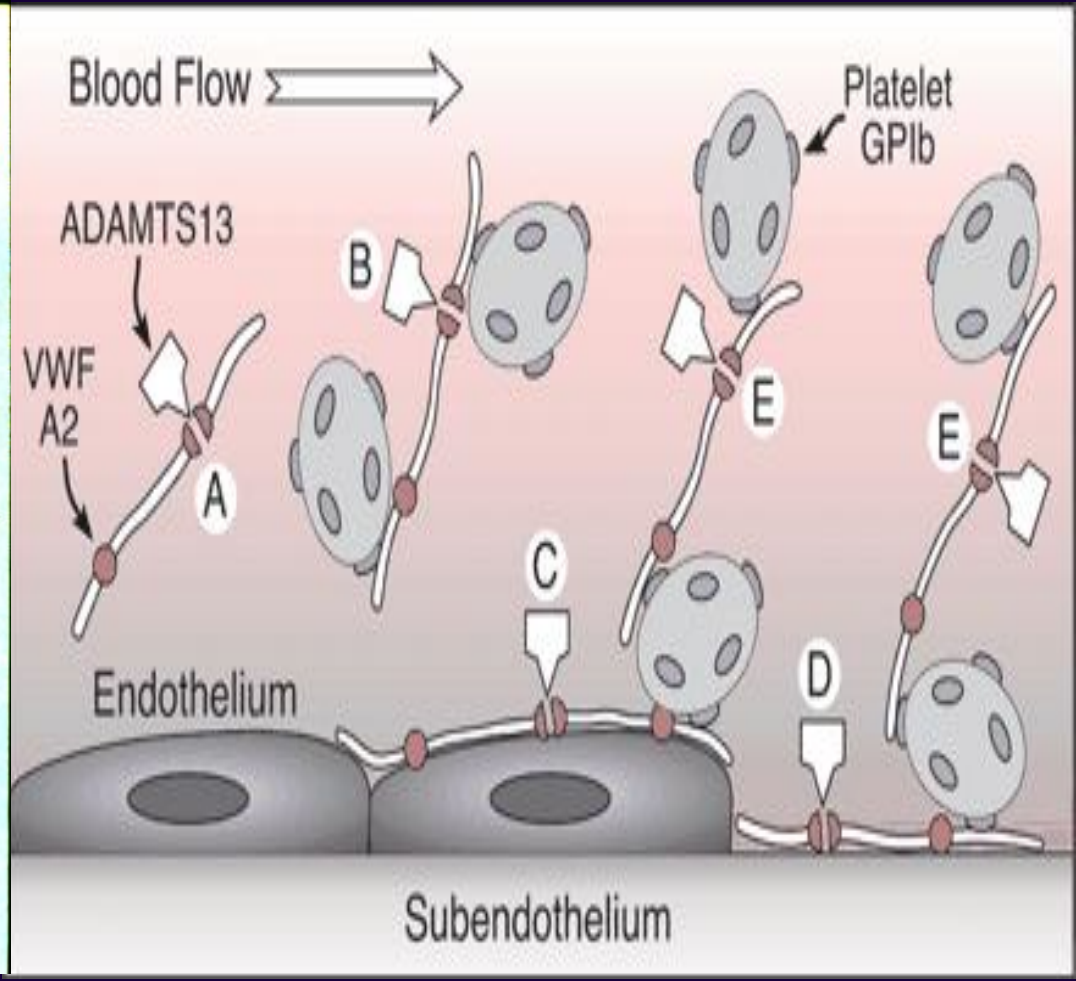




Levy GG, et l. Nature 2001; 413:488-94.

TTP: pathophysiology





Treatment of TTP

- VWF Cleaving Protease to be replaced:
  - ✓ Fresh frozen plasma (FFP)
  - ✓ Cryo poor plasma (infusion or TPE)
- Antibodies cleaning:
  - ✓ Therapeutic plasma exchange (TPD)
  - ✓ Immunoadsorption
- Suppression of antibody production:
  - ✓ Steroid
  - ✓ Immunosuppressive drugs (vincristine, cyclophosphamide, azotiopurins)
  - ✓ Rituximab
  - ✓ Splenectomy

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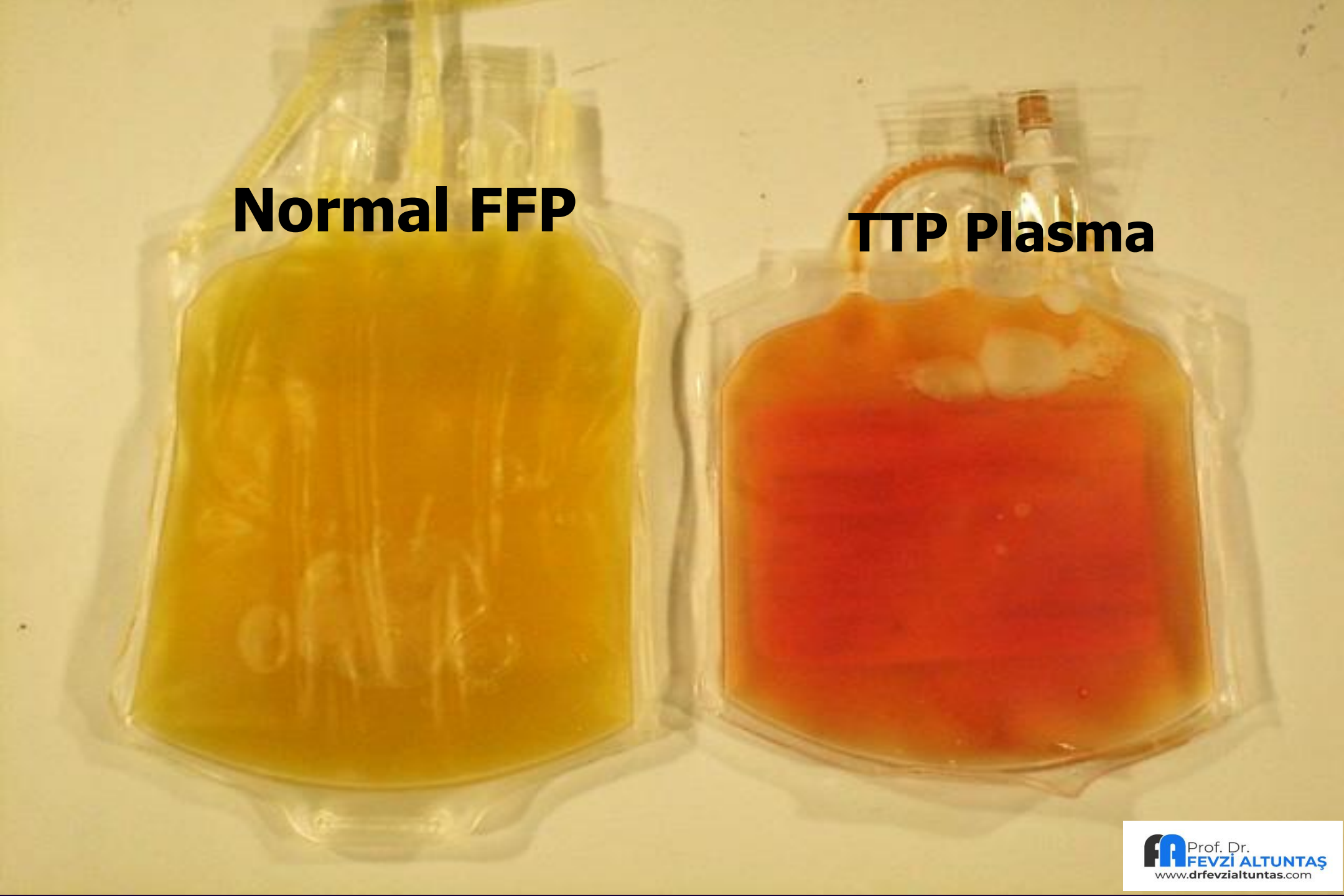

Photopheresis

- Peripheral blood mononuclear cells Interact with psoralen is irradiated with ultraviolet-A.
  - ✓ Pt ingests psoralen
  - ✓ Psoralen intercalates within DNA & RNA
  - ✓ Collected Leukocytes are exposed to UV light which activates psoralen
- Indications
  - ✓ Cutaneous T-cell Lymphoma
  - ✓ The prevention of graft rejection in solid organ transplantation (heart)
  - ✓ GVHD treatment and prophylaxis

Complications

- Citrate Toxicity
- Vascular access complications (hematoma, sepsis, phlebitis, neuropathy)
- Vasovagal reactions
- Hypovolemia
- Allergic Reactions
- Hemolysis
- Nausea, vomiting, abd pain
- Headache
- Chest pain, hypotension
- Air embolus
- Circulatory and Respiratory distress
- Transfusion-transmitted disease
- Lymphocyte loss
- Depletion of clotting factors
- Depletion of proteins and immunoglobulins

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