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Therapeutic Plasma Exchange in TTP

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Presentation Outline

- Pertinent definitions and terminology
- Pathophysiology of TTP
- Therapeutic plasma exchange as treatment

Definitions & Terminology

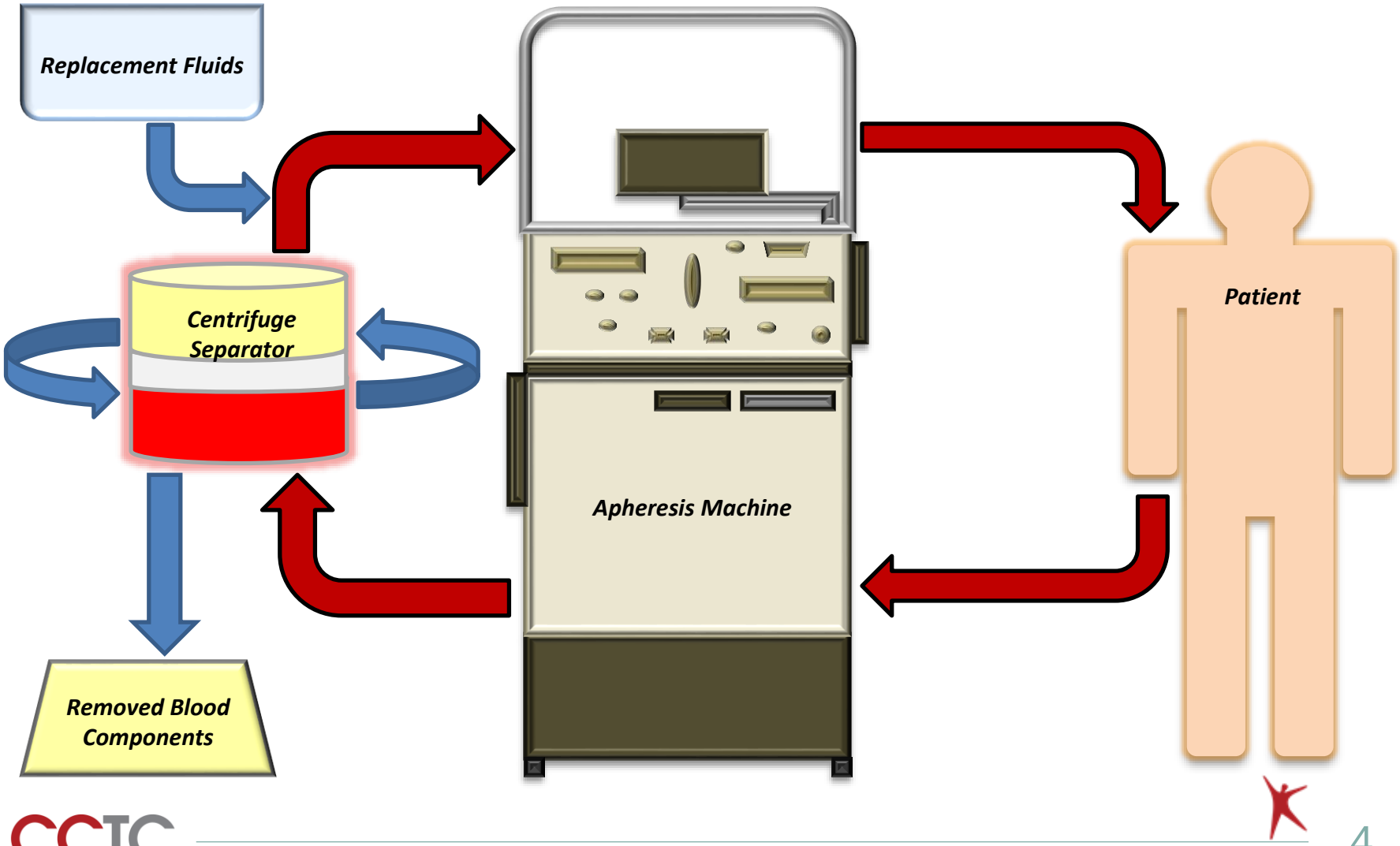
Thrombotic Thrombocytopenic Purpura (TTP)

- Rare, life-threatening condition
- Ischemic end-organ damage due to microvascular thrombi (thrombotic microangiopathy)

Apheresis

- Extracorporeal therapy with automated cell-separator
- Physically separates blood components
- Goal – remove pathogenic substance from circulation

Apheresis – Schematic



Definitions & Terminology (continued)

Therapeutic Plasma Exchange

- Apheresis procedure that exchanges native plasma with a replacement fluid
- Pathogenic component(s) exists within native plasma
- Extent of procedure – in terms of "plasma volumes"

1 Plasma Volume (liters) = [0.07 x weight(kg)] X [1 – hematocrit*]

*expressed as a decimal

American Society for Apheresis (ASFA)

- Guidelines on indications for therapeutic apheresis
- Systematic and evidence-based
- ASFA Categories and Grade of Recommendation

Pathophysiology of TTP

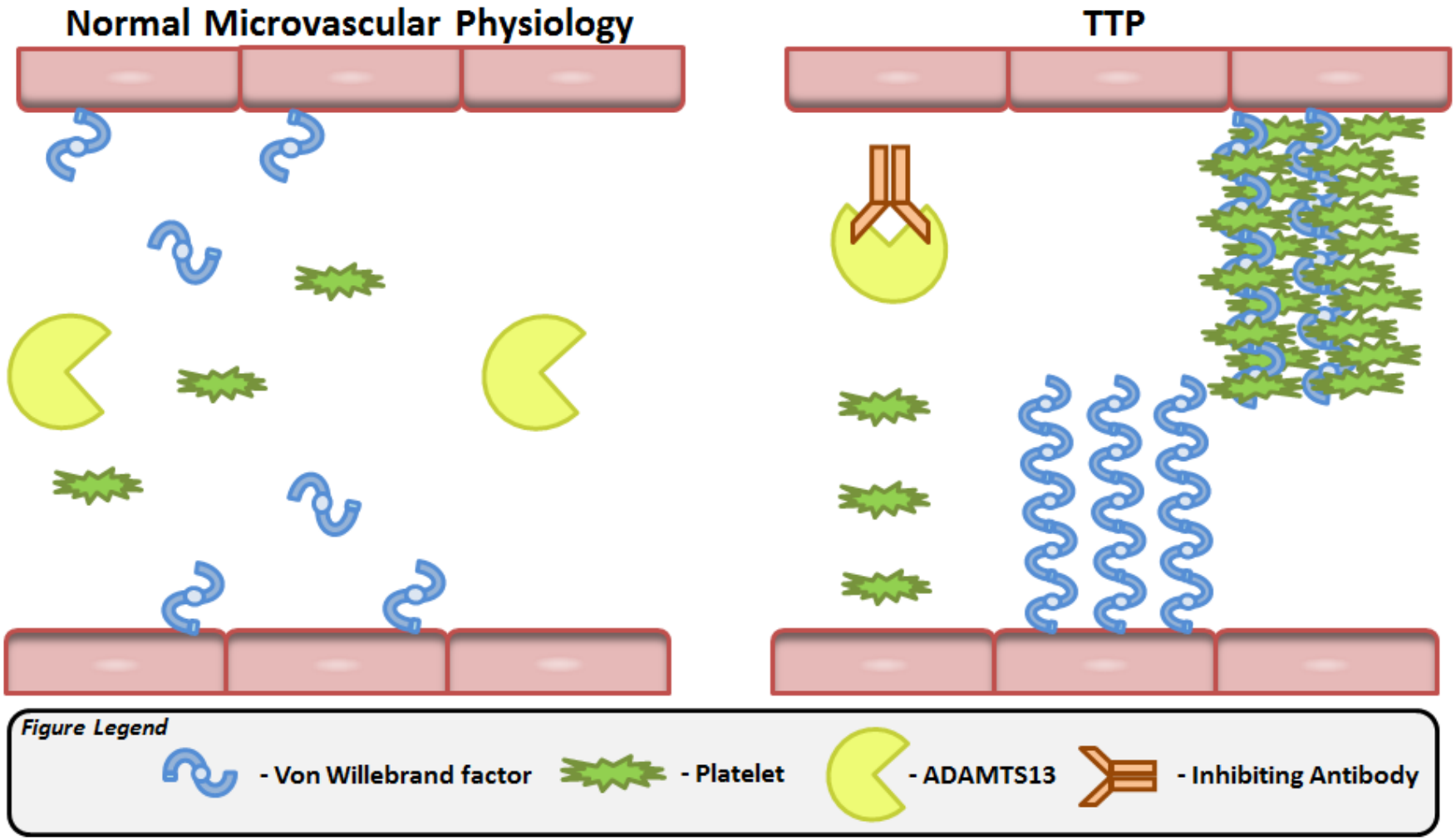
Deficiency of ADAMTS13 metalloprotease

- Normally cleaves unusually-large von-Willebrand factor multimers (UL-vWF)
- Auto-antibody formation ➔ Inhibits ADAMTS13
- Severe deficiency in the majority of cases
  - (<10% activity, with inhibiting antibodies)

Formation of microvascular thrombi

- Consequence of increased circulating UL-vWF
- Interaction of UL-vWF, platelets, endothelium, and high-shear flow (arterial microvasculature)
- Widespread ischemic end-organ damage

TTP – Schematic



Diagnosis of TTP

Classic teaching – Pentad of TTP

- Thrombocytopenia, microangiopathic hemolytic anemia (MAHA), neurologic changes, renal dysfunction, and fever
- May only see thrombocytopenia and MAHA (or other signs/symptoms) ➔ Clinical diagnosis

Laboratory abnormalities

- Thrombocytopenia, anemia (schistocytes on smear)
- ⬆Total (indirect) bilirubin, ⬆LDH, ⬇haptoglobin
- ⬇ADAMTS13 activity, (+)inhibitor antibodies

Therapeutic Plasma Exchange in TTP

Proven first-line therapy (ASFA Category I)

- Significantly reduces overall mortality
- Initiate ASAP following diagnosis
- Exchange with donor plasma (FFP, FP24, etc.)
- ADAMTS13 testing – Do NOT delay treatment!

Physiology of plasma exchange

- Repletion of uninhibited ADAMTS13 enzyme
- Removal of inhibitor antibodies

Therapeutic Plasma Exchange in TTP (continued)

Treatment regimen

- Daily plasma exchange procedures
- Exchange 1 to 1.5 plasma volumes per procedure

Example: 70kg male, 45% hematocrit

1 Plasma Volume (liters) = [0.07 x 70] X [1 – 0.45*] = 2.7 liters

*expressed as a decimal

- Donor plasma infusion ➔ Temporizing measure only

Monitoring response to treatment

- Platelets sustained at >150,000 /µL, LDH near-normal for 2-3 consecutive days (without plasma exchange)
- Improved clinical signs and symptoms

Therapeutic Plasma Exchange in TTP (continued)

Supplemental treatment options

- Corticosteroids
- Rituximab
- Other immunosuppression

Special Considerations

Blood component transfusion

- RBC's – Transfuse judiciously, if medically necessary
- Platelets – Generally contraindicated

Cryoprecipitate-poor plasma (Cryosupernatant)

- For plasma exchange
- Rationale ➔ Cryoprecipitate contains UL-vWF
- No definitive proof of improved outcomes

Practical Considerations

Difficulties initiating treatment

- Availability of apheresis services
- Vascular access
- Machine accessibility

Potential adverse events

- Allergic reactions to donor plasma
- Any other transfusion reactions
- Reactions to supplemental treatment
- Complications of vascular access

Summary

TTP is a complex disease – Clinical diagnosis made with laboratory support

Therapeutic plasma exchange – Apheresis treatment is first-line in TTP

Clinical decision-making – Critical throughout the treatment course

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Disclosures/Potential Conflicts of Interest

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