**Question 77**
For which of the following immunological disorders would fresh frozen plasma be the replacement fluid of choice during plasmapheresis?

A. Myasthenia gravis  
B. Thrombotic thrombocytopenic purpura  
C. Guillain Barre syndrome  
D. Chronic inflammatory demyelinating polyneuropathy  
E. Waldenstrom’s macroglobulinaemia

**Answer:**

**Plasmapheresis/ Plasma exchange**
- Extra-corporeal blood purification system to remove *large molecular weight (>150000)* substances of *long half-life (> 21 days)* from plasma
- Centrifugation allows *cytapheresis*: selective cell removal
- Principle is that removal of these substances can  
  - Halt/ reverse the pathological process  
  - Unload the reticuloendothelial system thus facilitate natural removal  
  - Infusion of large amounts of plasma without risk of fluid overload
- Replacement fluids dependant on condition  
  - *Albumin +/- saline* for most conditions (no risk of infection transmission but net loss of immunoglobulins)  
  - *Saline* for hyperviscosity  
  - *FFP/ cryo-poor plasma* for TTP (replaces normal proteins removed, so immunoglobulins and clotting factors not depleted)
- Duration and frequency dependant on condition  
  - 75% IgM is intravascular so quicker compared to IgG (45% intravascular)

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<tr>
<th>Pathological substance</th>
<th>Disease</th>
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| Autoantibodies         | Myasthenia gravis  
                        | Anti GBM antibody disease (Goodpasture’s)  
                        | Thrombotic thrombocytopenic purpura (TTP)  
                        | Guillian Barre syndrome/ CIPD  
                        | SLE (uncommon)  
                        | Systemic vasculitis  
                        | Factor VIII inhibitors |
| Immunoglobulins        | Hyperviscosity syndrome  
                        | Waldenstrom’s macroglobulinaemia  
                        | Multiple myeloma (light chains) |
| Lipoproteins           | Hypercholesterolaemia |
| Leucocytes             | Hyperleukaemic leucostasis |
| Platelets              | Severe thrombocytosis |
| Erythrocytes           | Sickle cell crisis |
| Circulating immune complexes | SLE  
                        | Immune complex glomerulonephritis |
### Systemic vasculitis

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<tr>
<th>Protein bound substances/ toxins</th>
<th>Thyroid storm</th>
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<td>Amanita phylloides toxins</td>
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### Complications of plasmapheresis
- Hypotension (↓ plasma volume)
- Dyspnoea (fluid overload; allergic reactions to FFP)
- Citrate induced (used as anticoagulant):
  - Hypocalcaemia (binds to form calcium citrate)
  - Alkalosis in renal failure (citrate -> bicarbonate which is poorly excreted)
- Infection
- Vascular access related complications
- Reaction if on ACEi (hypotension, abdominal pain, flushing - ?kinins generated) so withhold 24 hours prior
- Therapeutic drug removal (especially those protein bound eg pheytoin)

A. Myasthenia gravis
- Weakness and muscle **fatiguability** due to neuromuscular junction dysfunction
- Autoantibodies against Ach receptor (Anti AchR Ab) in 80%, seronegative in 20% (but still responds to plasma exchange – suggesting other autoantibodies at work)
- Treat with acetylcholinesterase inhibitors (eg pyridostigmine), immune modulators (eg steroids, AZA), plasma exchange, IV Ig or thymectomy
- Plasma exchange works by **direct removal of Anti AchR Ab**
  - Effective within days
  - Duration of action 3-4 weeks (new Ab forms especially if no concurrent immunosuppression)
  - Used in **myasthenic crises or a bridge to thymectomy**
  - Since used to remove antibodies, it doesn’t matter what replacement fluid is used – thus mainly albumin/ saline
- IV Ig as effective as plasma exchange
  - ↑ infection risk as pooled donors
  - Uncertain mechanism of action

B. TTP
- Deficiency of/ autoantibodies against a specific vWF cleaving protease (ADAMTS13)
- Leads to accumulation of ultra large vWF multimers -> platelet aggregation
- Plasma exchange removes the ultra large vWF multimers and the autoantibodies
- The replacement fluid is important as using **FFP can presumably supply the missing/ deficient ADAMTS13 enzyme**
- In conjunction with immunosuppression (eg steroids/ rituximab/ cyclosporine)
- Pentad:
  - Fever
  - Renal failure
  - Neurological complications eg seizures
  - Thrombocytopenia
  - Microangiopathic haemolytic anaemia (deposition of fibrin/ platelets on vessel wall -> high shear forces)
- Only HUS post diarrhoea in children, and TTP secondary malignancies do not respond to plasma exchange

C. Guillian Barre syndrome (GBS)
- Acute immune-mediated polyneuropathy
- Infection triggers immune response which cross reacts with peripheral nerve components (either myelin or axon) due to molecular mimicry
- Associated infections include campylobacter, HIV, CMV/EBV or with vaccinations (influenza/ meningococcal)
- Treat with plasma exchange, IV Ig or IFN (effective in some studies)
  o Plasma exchange removes antibodies and complement
- **Steroids NO LONGER recommended** (I think this was one of the neuro questions!)

D. CIPD
- Similar to GBS

E. Waldenstrom's macroglobulinaemia (WM)
- Macroglobulinaemia refers to a group of disorders where there is proliferation of B cells/plasma cells which produce an **IgM monoclonal protein**
  o MGUS (IgM variant)
  o CLL
  o Some lymphomas
  o Primary amyloidosis
  o WM
- Malignant lymphoproliferative disorder of B cells exhibiting plasmacytoid/ plasma cell-like differentiation -> Ig M secretion -> paraprotein accumulates -> hyperviscosity
- Plasma exchange works by **direct removal of paraprotein** thus again type of replacement fluid is immaterial