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Medicine

Management of Serum Sickness in Aplastic Anemia

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Objectives

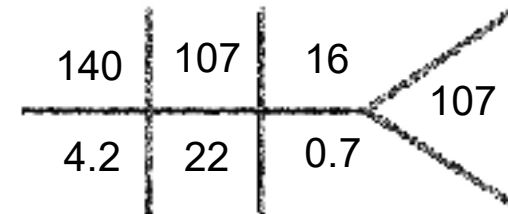
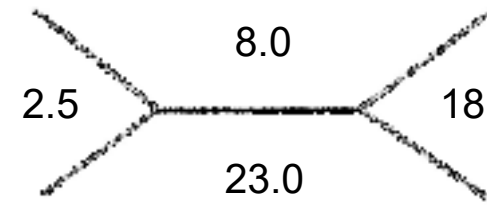
- Summarize the pathophysiology and management strategies of aplastic anemia
- Associate causes of serum sickness to the clinical presentation and management strategies
- Interpret and implement information to choose an appropriate treatment regimen to a patient case

Patient JT

- HPI: 50 year old female presenting for treatment of aplastic anemia
- PMH: antinuclear antibody and antithyroglobulin antibody elevations
- **Chief Complaint: Chronic vaginal bleeding in the setting of worsening thrombocytopenia and new diagnosis of aplastic anemia**

- Vitals:

- Temp 36.7° C, HR 86, RR 18, BP 102/70, SpO2 99%
- CrCl: 108 mL/min



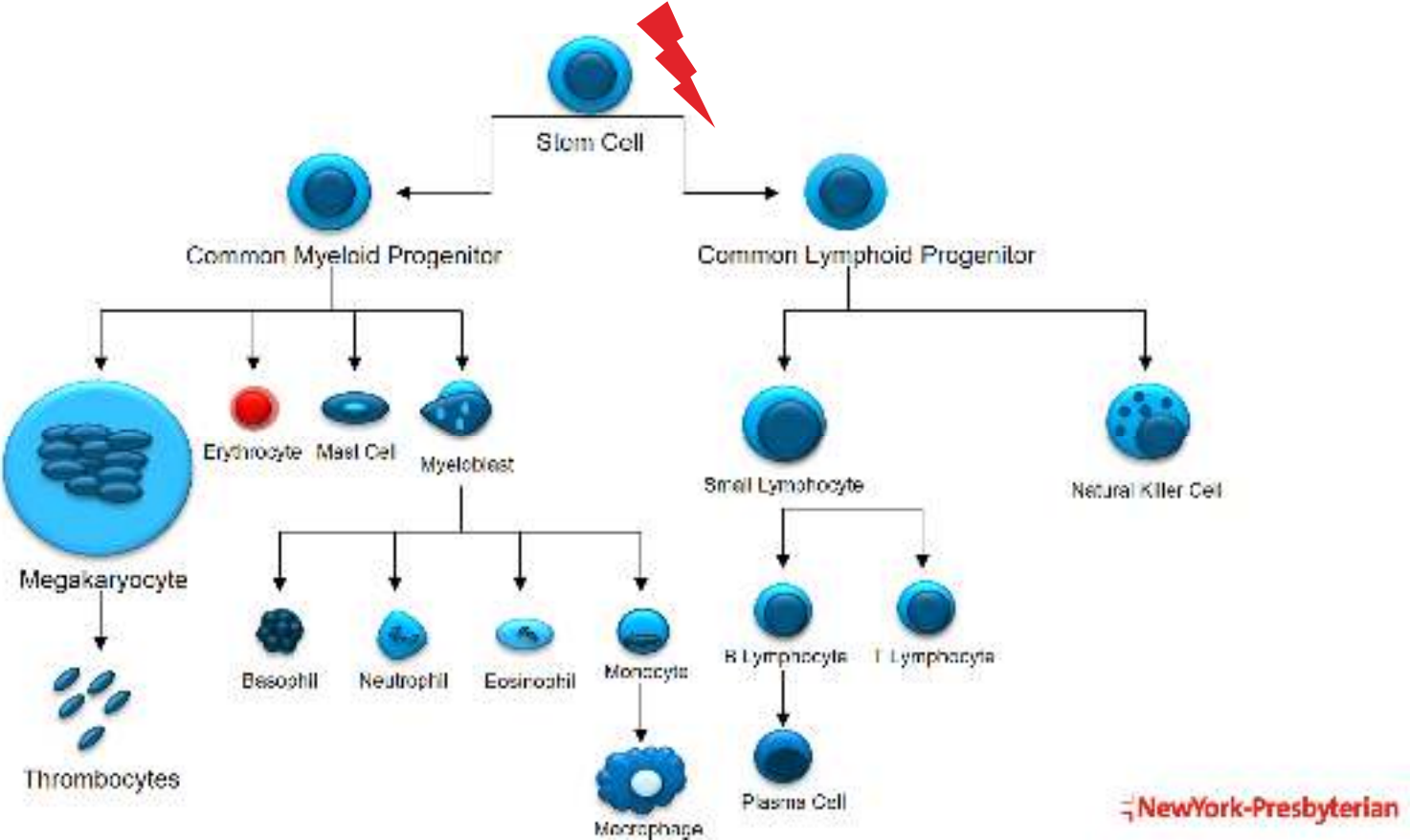
- ANC: 0.36×10^3 u/L

Bone Marrow Biopsy

- Hypocellular marrow (10-15%)

Aplastic Anemia

- Bone marrow pancytopenia
- Misnomer, aplasia
- Rare disorder, affects 1 in 100,000 individuals
- Typically presents with



Rixe N, et al. Serum Sickness. [Updated 2022 May 2]. In: StatPearls [Internet].

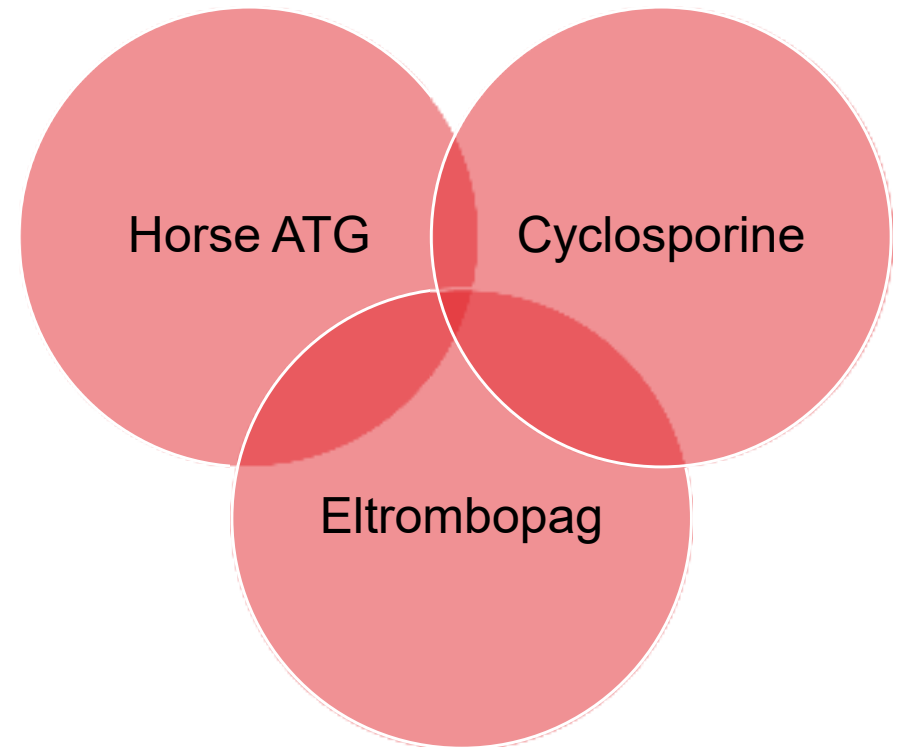
Management

- **Medically fit (<40 years old)**

- If matched donor available → allogeneic stem cell transplant
- Triple immunosuppressive therapy

- **Less fit (>40 years old)**

- Triple immunosuppressive therapy



ATG: antithymocyte globulin

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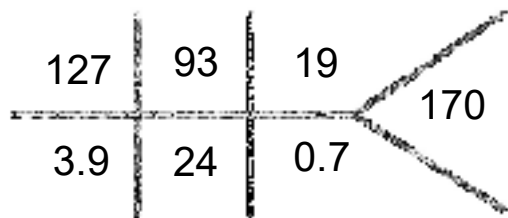
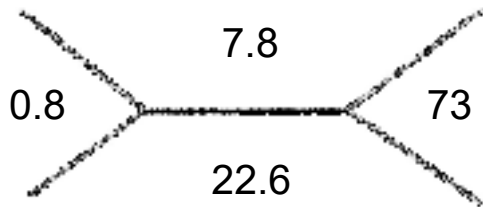
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JT Labs – Day 14

- Vitals:

- Temp 39.3° C, HR 68, RR 18, BP 118/78, SpO2 96%
- CrCl: 119 mL/min



- Notable Labs:

- ANC: 0.6×10^3
- CH50: <12.8 U/mL (RR: 38.7-89.9 U/mL)
- C3: 39 mg/dL (RR: 80-162 mg/dL)
- C4: <4 mg/dL (RR: 14-47 mg/dL)
- ESR: 122 mm/hr (RR: 1-20 mm/hr)
- CRP: >300 mg/L (RR: <3 mg/L)

CH50: total complement 50; C3: complement 3; C4: complement 4;
ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RR:
reference range

Serum Sickness

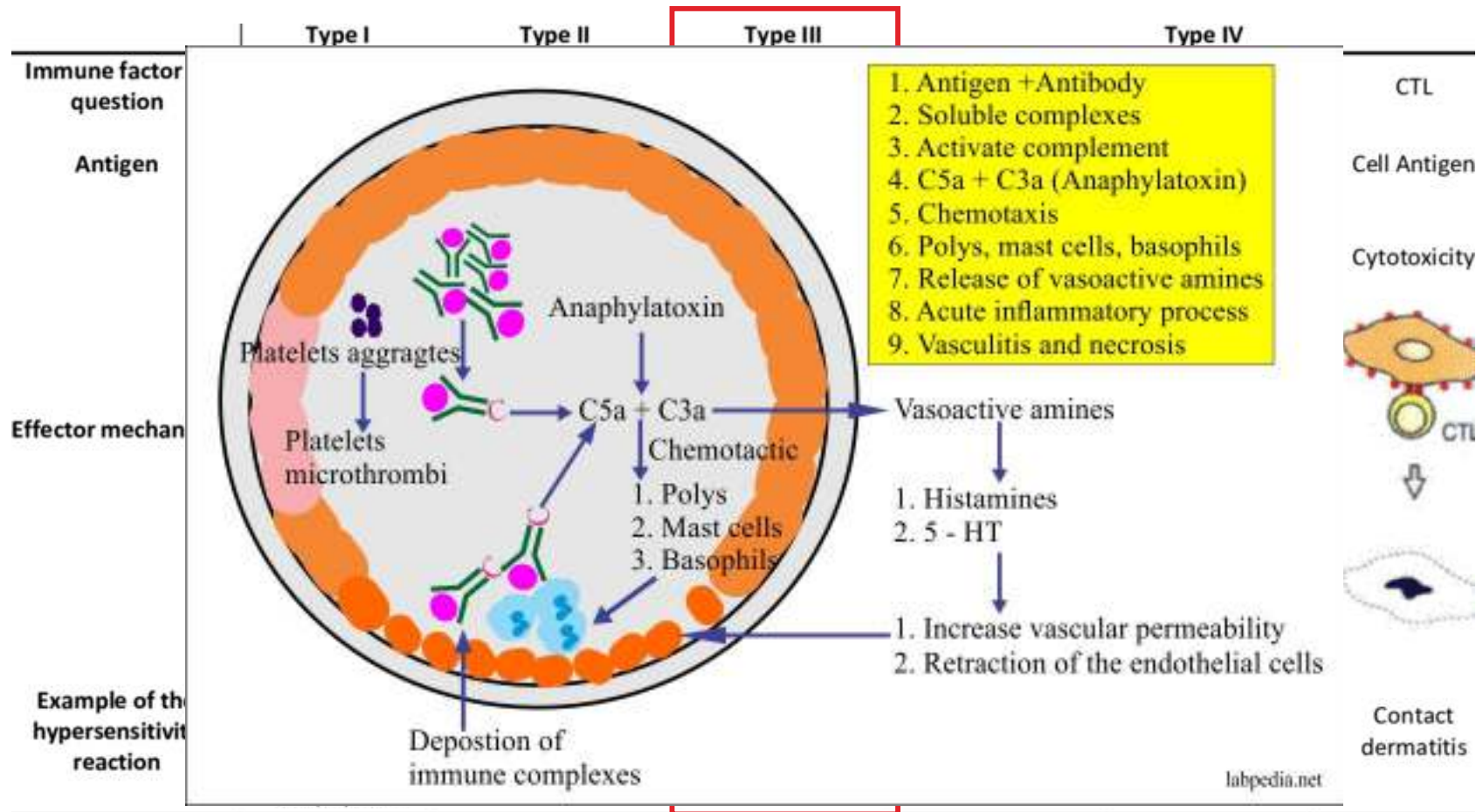
- History:

- First described in 1905 by von Pirquet and Schnick
- Patient had a reaction to horse serum for treatment of diphtheria and scarlet fever
 - Published book “Die Serumkrankheit”

- An immune-complex-mediated hypersensitivity reaction to medications that contain proteins

- Rare reaction with not well defined incidences for common offending agents

Pathophysiology

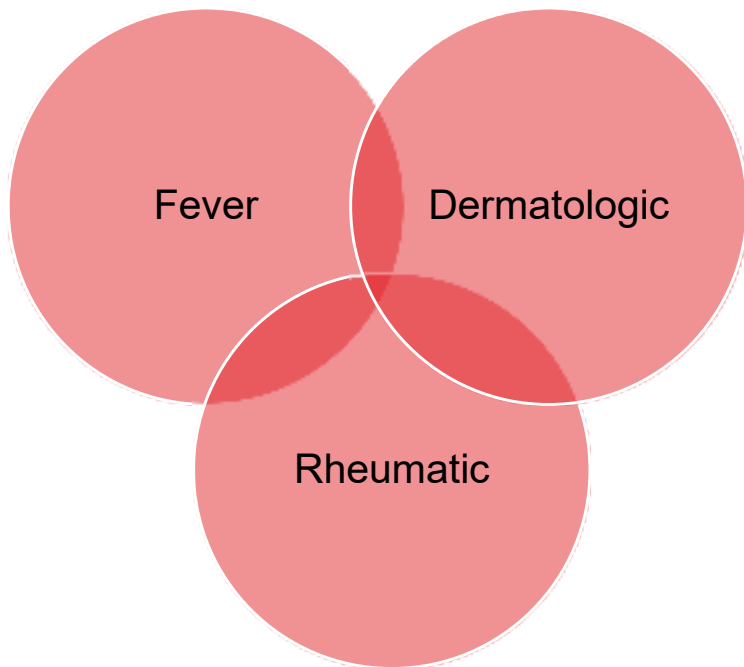


Source: (F. Blanc, 2008)

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Clinical Manifestations

- Present about 1-2 weeks after administration of offending agent (unless previously exposed)



Less Common Features
Headache/blurred vision
Edema
Splenomegaly
Lymphadenopathy
Gastrointestinal symptoms
Neuropathy
Vasculitis

Lab Findings/Diagnosis

Complete blood count with differential

- Thrombocytopenia, neutropenia, and possible eosinophilia

Erythrocyte sedimentation rate and C-reactive protein

- Elevated

Urinalysis

- Mild proteinuria

Complement studies

- CH50, C3, and C4 decreased

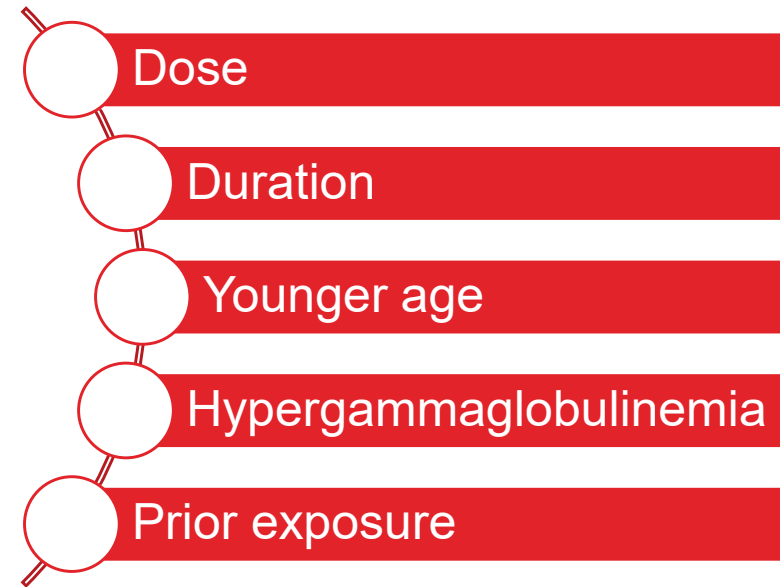
Offending Agents

- Medications that contain protein antigens from nonhuman species

Medications
Horse and rabbit antithymocyte globulin
Anti-toxins
Murine monoclonal antibodies (ex. Rituximab and Infliximab)
Rare: vaccination, fully humanized monoclonal antibodies, immunotherapies

- Symptoms begin to resolve when offending agent is discontinued

Risk Factors



Management

Mild to Moderate

Withdrawal of offending agent



- Symptoms typically resolve within 48 hours of discontinuation
- Supportive care with analgesics, non-steroidal anti-inflammatory drugs, and antihistamines as needed

Severe

Withdrawal of offending agent



Steroids

Penicillin Induced Serum Sickness

▪ Case Report:

- 19 year old woman presenting with fever, chills, anorexia, and myalgias one week after penicillin G benzathine depot injection
- Infectious disease and rheumatologic workup were unremarkable
- Labs:
 - CRP: 24 mg/dL (reference range 0-1 mm/hr)
 - ESR: 95 mm/hr (reference range 0-15 mm/hr)
 - Complements decreased
- Initial management:
 - Unable to withhold agent (depot)
 - Analgesics and antipyretics, but symptoms persisted and rash formed
 - Prednisone 50mg daily initiated (tapered over months)

Rabbit ATG Serum Sickness

▪ Case Report:

- 45 year old received 1.5 mg/kg thymoglobulin prior to liver transplant.
- Post-op day 9, she presented to emergency room with left lower quadrant abdominal pain.
 - Three days into hospitalization, she developed polyarthritis involving her neck, jaw, knees, elbows, and wrists, manifested as arthralgia, stiffness, edema, and warmth of the skin overlying each joint
- Negative infectious work-up and low complement levels present → Serum sickness diagnosis
- Started on methylprednisolone 3 mg/kg/day x 3 days with rapid clinical improvement
 - Followed by prednisone taper

Refractory ATG Associated Serum Sickness

▪ Case Series:

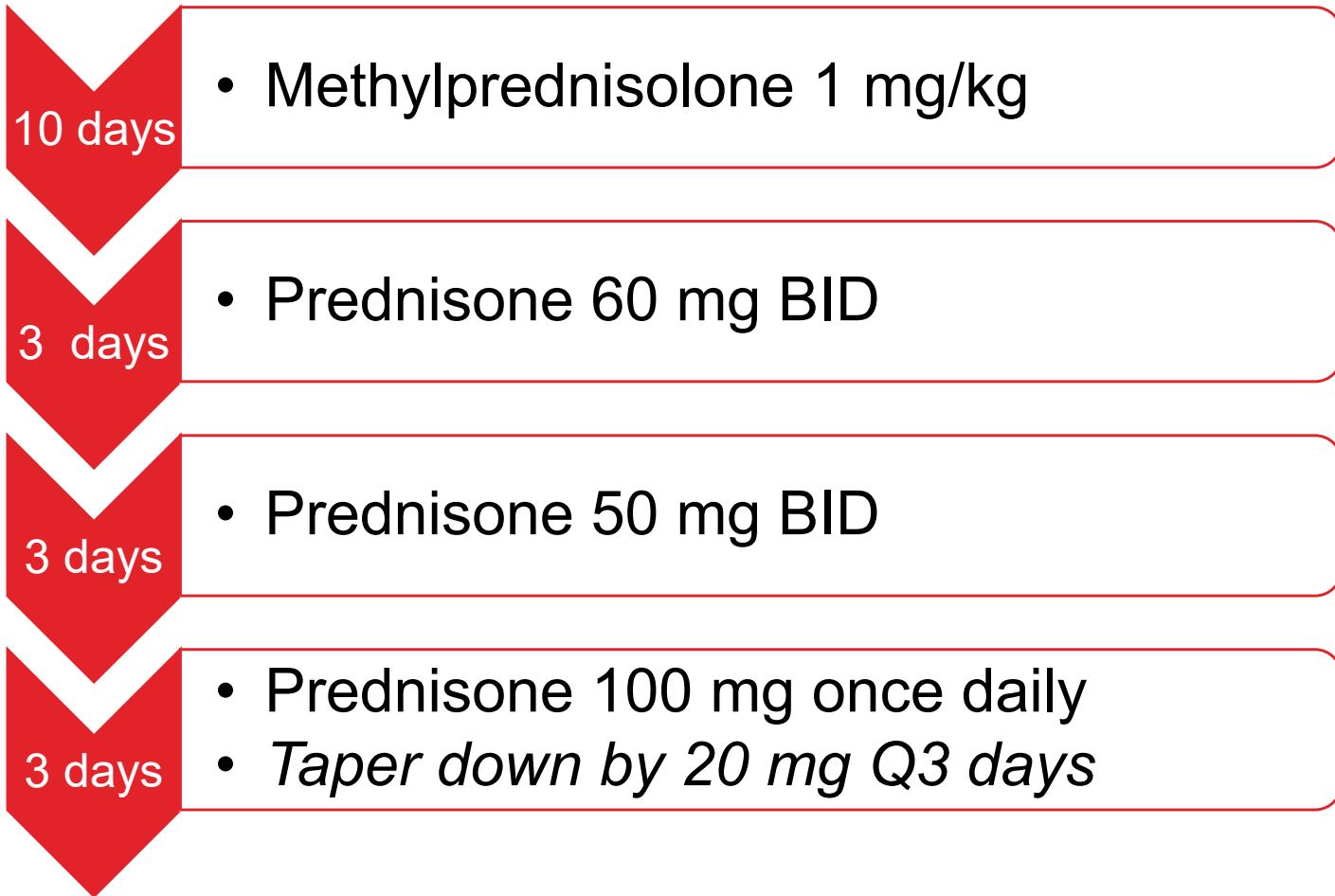
- 5 renal transplant recipients with serum sickness secondary to ATG dosed 1.5 mg/kg/day
- All presented 10-17 days after ATG with non-specific signs and symptoms of serum sickness
- All patients received 1-2 mg/kg/day of prednisone:
 - All had persistent symptoms after two full days of steroids and were initiated on therapeutic plasma exchange
 - Three patient's symptoms resolved after one session and the other two after two sessions
- Therapeutic plasma exchange may be a potential option for refractory serum sickness

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Treatment



Takeaway Points

- The management of aplastic anemia includes the utilization of horse ATG
- Administration of horse ATG is associated a risk of serum sickness
- Serum sickness typically resolves after removal of the offending agent, but in cases such as aplastic anemia therapy can't be withdrawn
- Steroids are the mainstay of the management of serum sickness, but optimal dosing strategies have yet to be determined



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