How I treat acquired aplastic anemia

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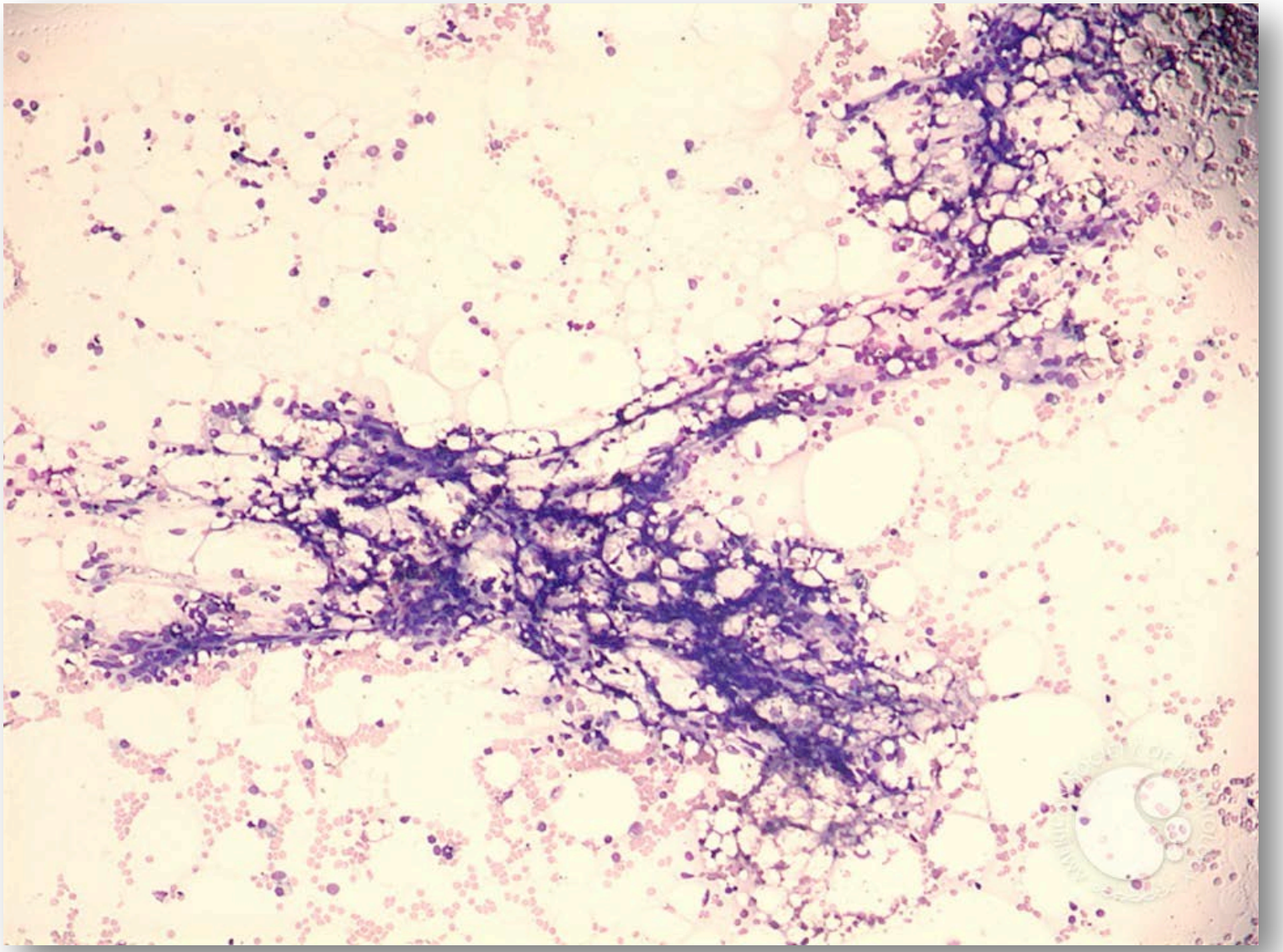
Symptoms, Signs, and Lab Findings

- Bruising, bleeding, hemorrhage
- Anemia
- Pancytopenia
- Infection – infrequent at presentation
- Prior history of chemical and medical drug exposures
- Prior history of a single lineage cytopenia, usually thrombocytopenia or anemia
- Prior history of seronegative hepatitis in the months before pancytopenia - defines posthepatitis SAA.
- If macrocytosis and mild anemia present – clue that ITP is ***not*** the correct diagnosis.

Diagnosis

- Established on blood **AND** bone marrow examination
- Elevated mean corpuscular volume
- “Empty” marrow on histology
- Appearance of the marrow in inherited and acquired cases is identical
- Differential diagnosis:
  - Marked hemophagocytosis?
  - Dysplasia?
  - Increased blasts?
  - Megakaryocytes are the most reliable lineage to use in distinguishing MDS from SAA.

Pathology – Bone Marrow Aspirate

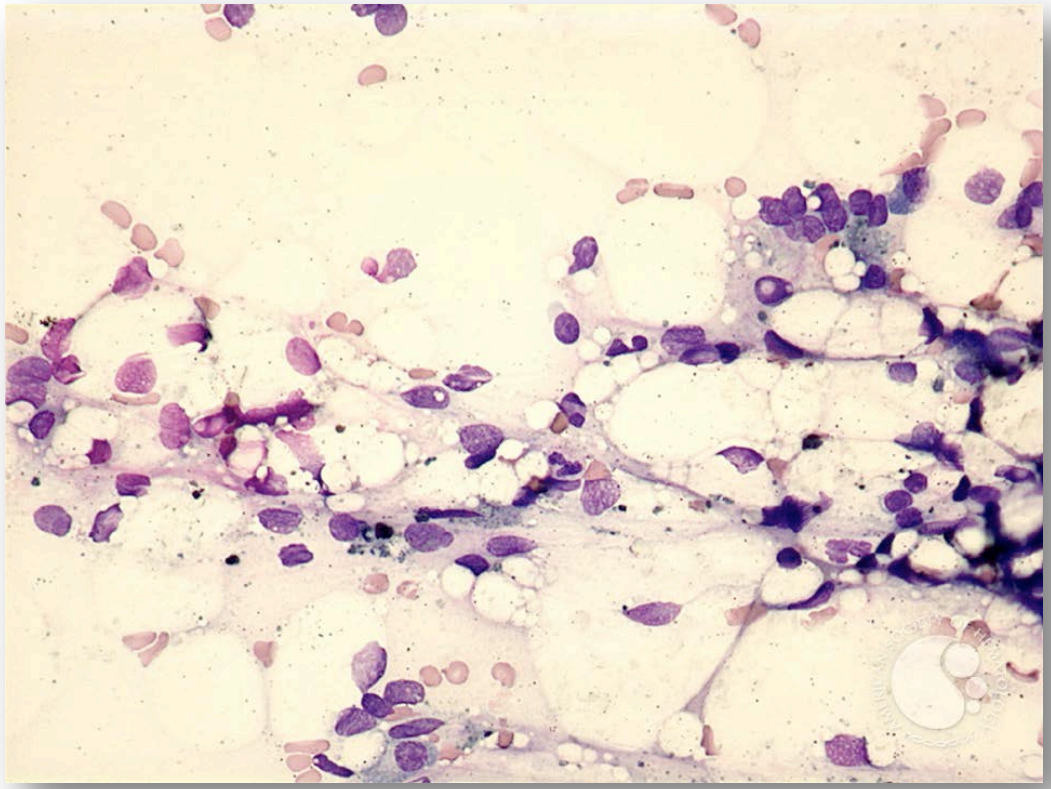


Spicules are empty and generally devoid of hematopoietic elements.

ASH Image Bank

Pathology – Bone Marrow Aspirate

1.



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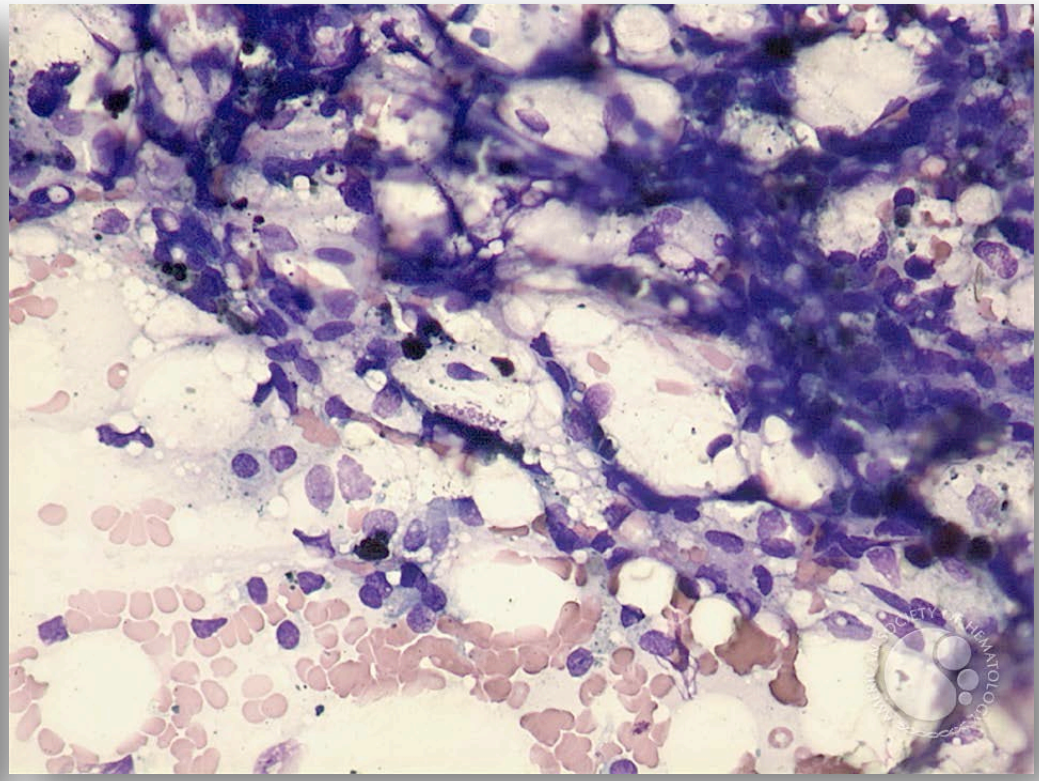
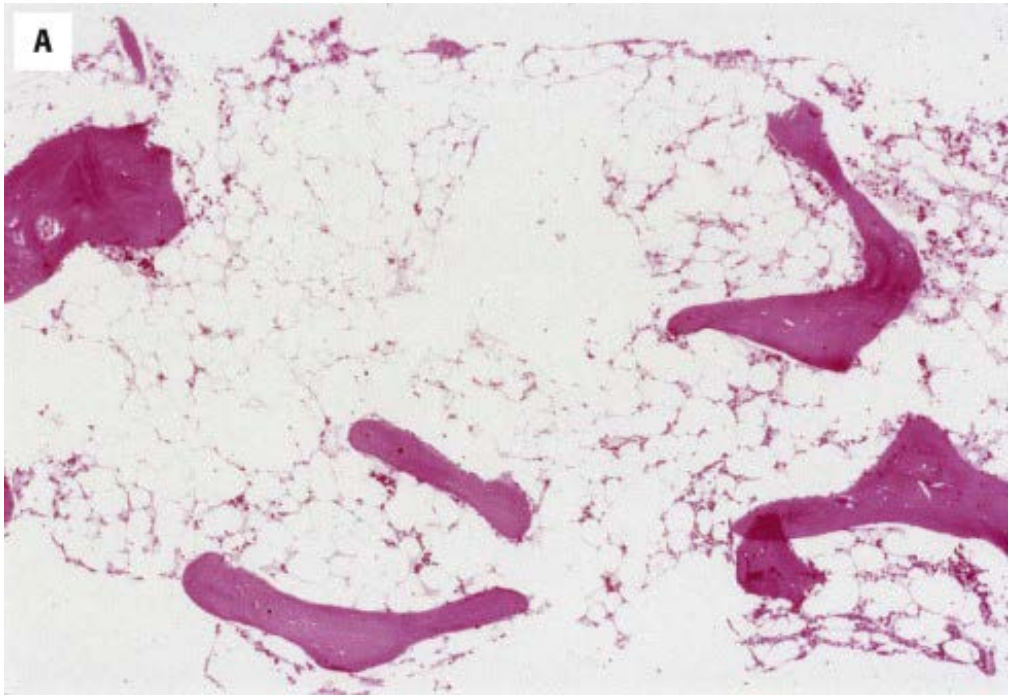
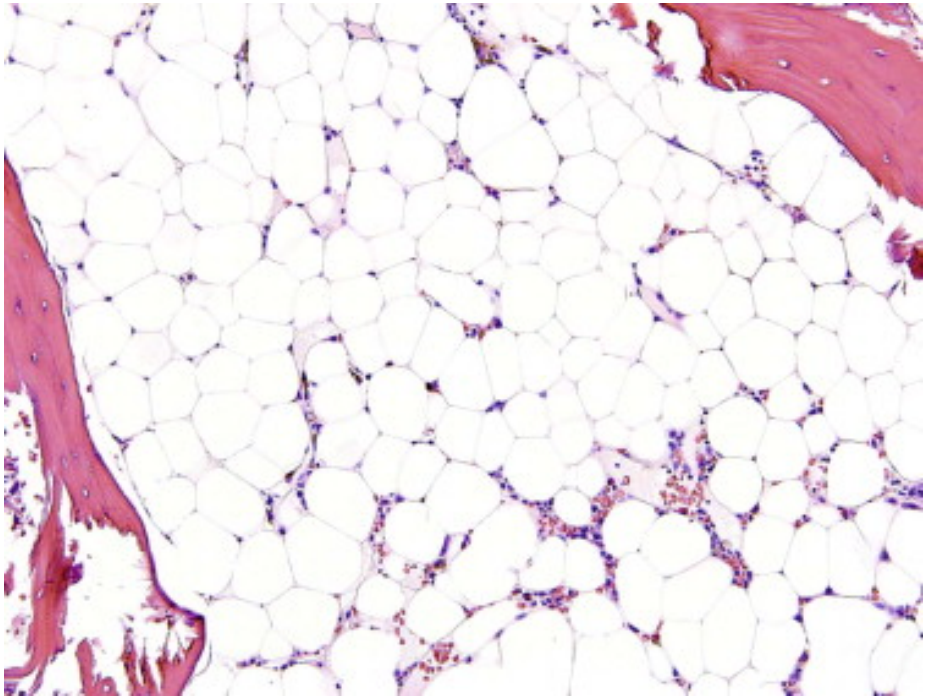


1. High-power view shows naked nuclei and debris-laden histiocytes
2. Spicules are composed almost entirely of stromal elements

ASH Image Bank

Pathology - Bone Marrow Biopsy

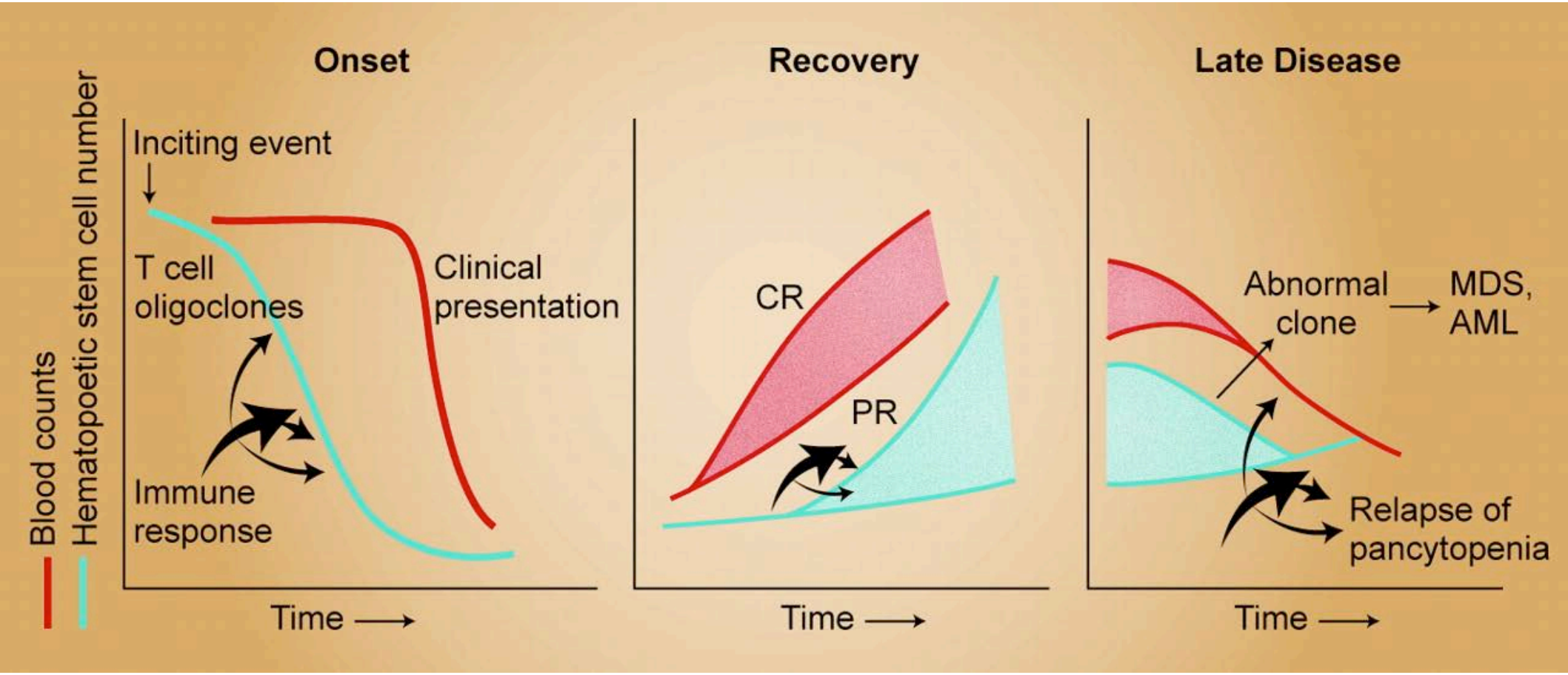




- In severe cases, the cellularity is typically <25% of expected for age and predominantly composed of plasma cells and lymphocytes
- The biopsy **must** be of adequate length to ensure that marrow **deep** to the physiologic subcortical hypocellular region is sampled.

Aster JC, et al. Hematopathology. 2013
Hsi E, et al. Hematopathology: Foundations in Diagnostic Pathology 2nd ed. 2012

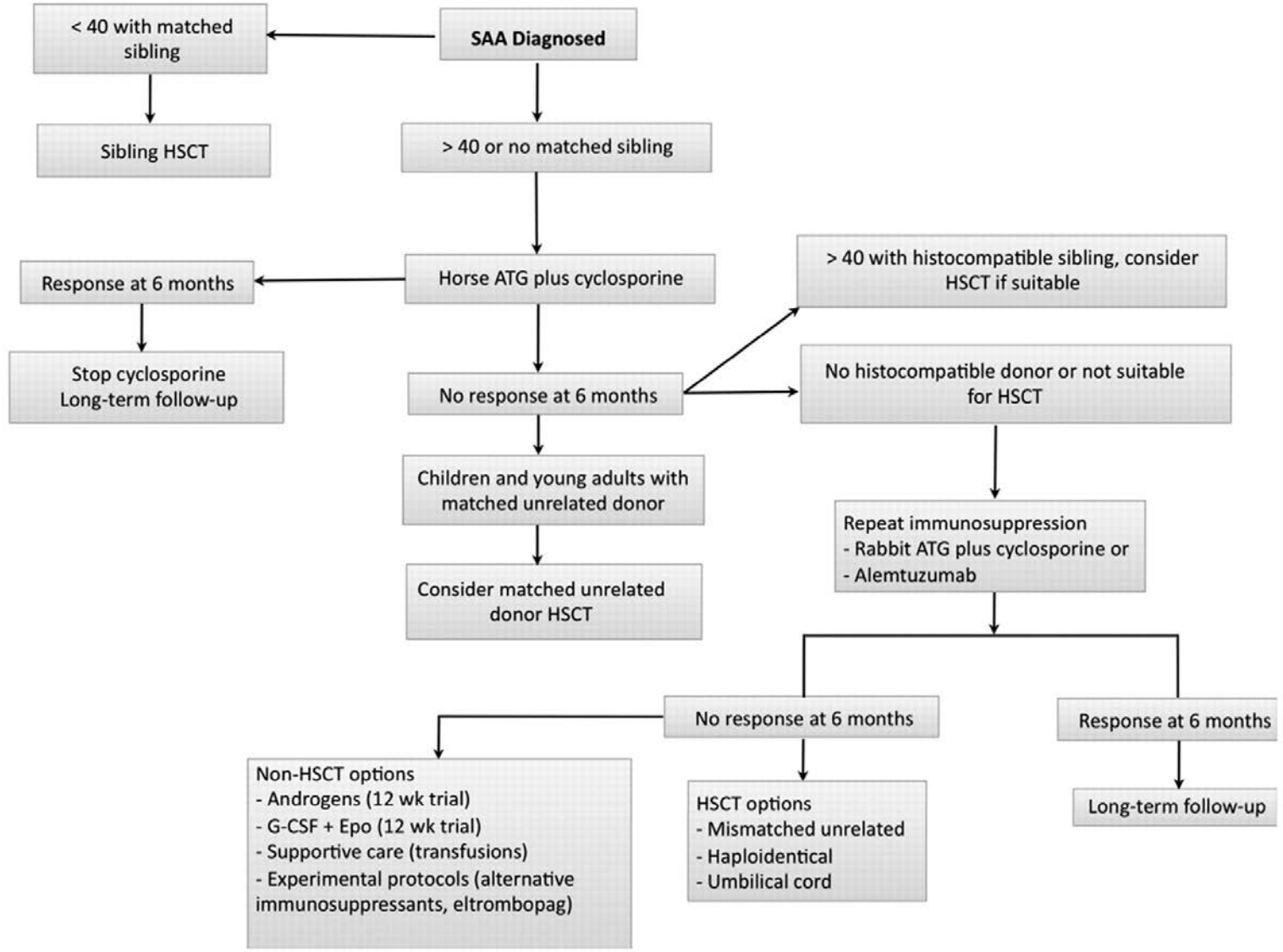
Pathophysiology of acquired aplastic anemia



Treatment (1)

- Moderate cases (lack of blood count criteria for SAA) - observation is appropriate when transfusion is not required
- Transfusion-dependent can be treated according to Fig. 1
- Antibiotics when fever or documented infection occurs in the presence of severe neutropenia (ANC <500/μL)
- Immunosuppressive therapies are widely used due to lack of transplantation
- ATG-based regimen in combination with cyclosporine
- 60% of patients are responders at 3 or 6 months after initiation of horse ATG

Algorithm for initial management of SAA. In patients who are not candidates for a matched related HSCT, immunosuppression with horse ATG plus cyclosporine should be the initial therapy.



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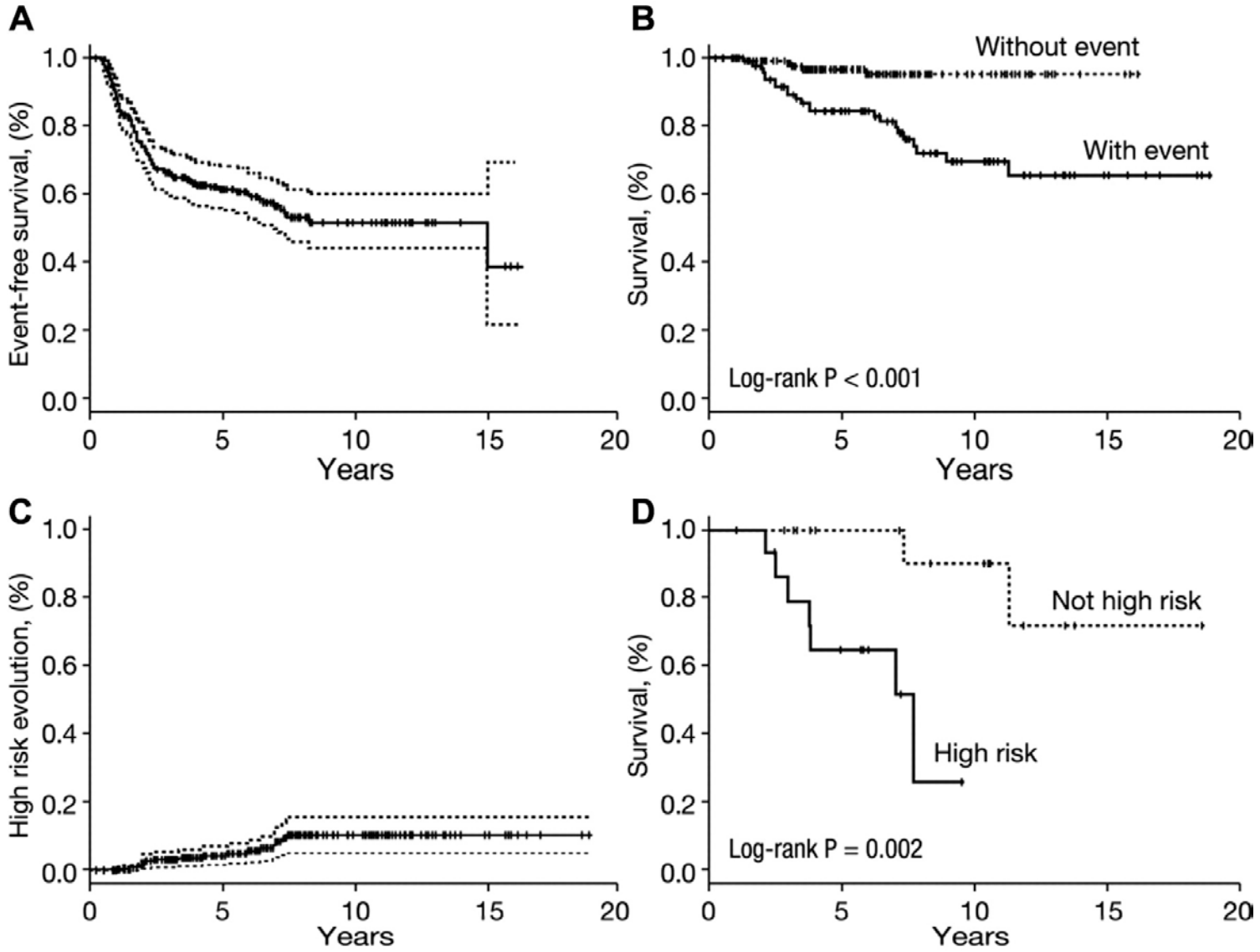
Treatment (2)

- Perform ATG skin test if available for hypersensitivity to horse serum and desensitize those by intradermal injection
- Platelets should be maintained at more than 20,000/μL during ATG administration
- Patients need to be free of infection before initiating ATG
- ATG administered at a dose of 40 mg/kg over 4 hours, daily for 4 days
- Prednisone 1 mg/kg is started on day 1 and continued for 2 weeks as prophylaxis for serum sickness
- Acetaminophen and diphenhydramine are conventional premedications for treatment with ATG

Durability of response after horse ATG. (A) Time to first late event among responders.



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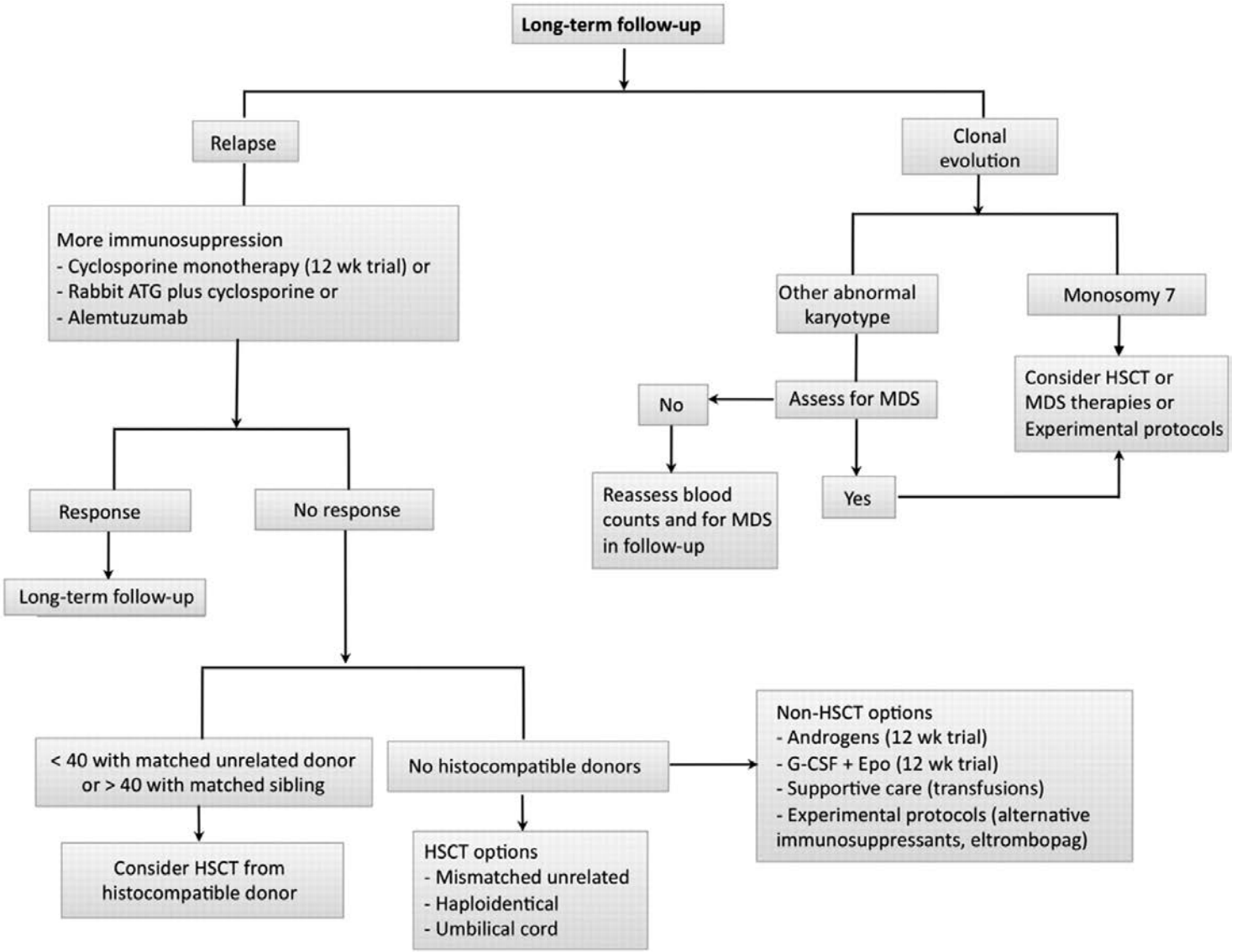
Treatment (3)

- Responders have better survival prospects than do nonresponders
- Long-term prognosis is predicted by the robustness of the early blood count response
  - Defined as either platelets or reticulocytes > 50 X 10^9/L [50,000/μL] 3 months after treatment.
- Corticosteroids are of unproven benefit, and inferior in efficacy, to conventional immunosuppression regimens
- Should not transfuse platelets prophylactically in SAA patients who have a platelet count more than 10,000/μL and who are not bleeding

Long-term follow-up after immunosuppression.



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Relapse and Long Term Follow-up

- Defined as requirement for additional immunosuppression & not necessarily recurrent pancytopenia
- Does not by itself indicate a poor prognosis
- Major reason for relapse - incomplete eradication by ATG of pathogenic clones
- Second course of ATG therapy can be administered to patients with relapsed or refractory disease
- Cyclophosphamide has been used to treat relapsed/refractory SAA, and is associated with a response rate of about 50%
  - Toxicity of high-dose cyclophosphamide: prolonged neutropenia and susceptibility to infection
  - Higher death rates have been reported with use of cyclophosphamide

References

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- *Young, N. S., Calado, R. T., & Scheinberg, P. (2006). Current concepts in the pathophysiology and treatment of aplastic anemia. Blood, 108(8), 2509-2519. Accessed August 10, 2016. http://dx.doi.org/10.1182/blood-2006-03-010777.*

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