

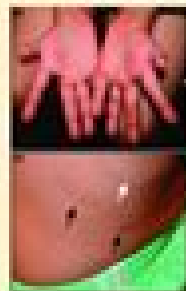
Aplastic Anemia and Bone Marrow Failure Syndromes with Pancytopenia

Common causes of pancytopenia

Impaired production	Peripheral destruction	Impaired production and peripheral destruction
Aplastic anemia - acquired and congenital	Autoimmune hemolytic pancytopenia	Paroxysmal nocturnal hemoglobinuria
Bone marrow infiltrating disorders	Spleen sequestration	Spl
- Malignancy		Drugs
- Primary and secondary myelodysplasia		Leukemia
- Granulomatous disorders		Hemophagocytic lymphohistiocytosis (HLH)
- Metabolic disorders		
Nutritional deficiencies		Transfusion-associated Graft-versus-host disease
- Vitamin B12		Infections
- Folate acid		
- Copper		
Myelodysplastic syndromes		

Fanconi Anemia

- DNA DSB repair defect, usually AR mutation in **FANCA** gene
- Bone, skin, and renal abnormalities, developmental delay
- Blood: thrombocytopenia progressing to pancytopenia by mid-childhood. Decreased retics and macrocytosis. Elevated HbF.
- BM: Initially normo- to hypocellular with megaloblastic changes ± erythroid dysplasia, progressing to aplasia. Late development of MDS or AML (~10%). +1q, +3q are characteristic
- Initial testing: mitomycin-induced chromosomal breaks



REDS: Blood Reviews 33 (2018) 365–367; Hematopathology 2nd Ed, Jaffe, Am J Clin Pathol 2013;138:9-29; Genet Med. 2010 Dec; 12(12)

Acquired Aplastic Anemia

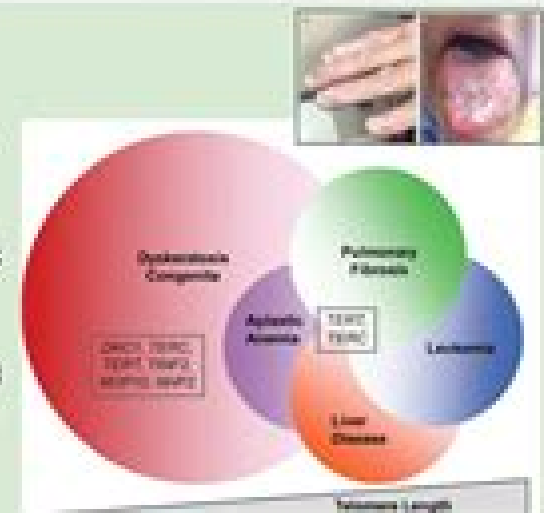
- Immune-mediated; triggered by environmental or genetic factors
- Severe AA: markedly hypocellular BM (usually <25% of normal for age) + 2 of the following: grans <0.5; platelets <20; or corrected retics <1%. Very serious disease has grans <0.2. Markedly decr. megs is a clue.
- Infection is the major cause of mortality, may also progress to MDS/AML (erythroid changes in AA are okay, megs/gran dysplasia is suspicious).
- Up to 1/3 of patients have short telomeres
- 50-60% have PNH clones, rarely progress to clinical PNH; a/w better response to rx.
- Rx is immunosuppression and/or SCT

81aureabrown



Dyskeratosis Congenita & Telomere Biology Disorders

- Most commonly X-linked recessive defect in telomere maintenance (**DKC1** gene), or very short germline telomere length (<1st percentile).
- Spectrum of presentations: skin and nail abnormalities, oral leukoplakia, increased risk of malignancies
- Blood: Gradual development of pancytopenia with decreased retics and macrocytosis. Elevated HbF. Normal platelet morph.
- BM: eventual aplasia with substantial risk of MDS/AML
- Initial test: lymphocyte telomere length



Shwachman-Diamond Syndrome

- AR defect in ribosome biogenesis due to mutation in **SBDS** gene
- Exocrine pancreatic insufficiency, bone abnormalities
- In SDS (DBA also), ribosomal stress → p53 stabilization and cell-cycle arrest/apoptosis. TP53 mutations → escape from apoptosis → improved function, but increased risk of leukemia
- Blood: neutropenia with macrocytosis is the dominant initial feature, 1/3 of cases then progress to pancytopenia with decreased retics. Elevated HbF.
- BM: Granulocyte hypoplasia/dysplasia, progressing to pancytopenia. Some develop late AML.



Bone Marrow Failure Syndromes

**Mahmoud Deeb Aljurf, Eliane
Gluckman, Carlo Dufour**



Bone Marrow Failure Syndromes:

Bone Marrow Failure Gary M. Kupfer, Gregory H. Reaman, Franklin O. Smith, 2018-09-29 This book presents the latest scientific knowledge on inherited and acquired bone marrow failure syndromes describing the advances in understanding of genetics and pathophysiology that have been achieved as a result of high throughput DNA sequencing RNA expression studies and modern biochemistry techniques The full range of relevant conditions is covered including acquired aplastic anemia Fanconi anemia ribosomopathies telomeropathies dyskeratosis congenita Shwachman Diamond syndrome Diamond Blackfan anemia and congenital neutropenias and thrombocytopenias In addition it is explained how the study of these rare diseases has uncovered important new science and elucidated the pathophysiology of more common hematological and oncological diseases A treatment specific chapter describes options ranging from the conventional to the cutting edge Bone Marrow Failure will be of value for both trainee and practicing hematologists and oncologists [Bone Marrow Failure Syndromes](#) Neal S. Young, 2000 This comprehensive and clear text familiarizes clinicians with the most recent information concerning bone marrow failure syndromes including anemia leukopenia and thrombocytopenia Twelve top experts present state of the art guidance on pathophysiology and treatment with an emphasis on chemotherapy The result is an indispensable source on the treatment of these often life threatening diseases Provides a complete understanding of individual syndromes with disease oriented chapters Offers a comprehensive chapter on Proximal Nocturnal Hemoglobinuria including its biological aspects a subject that has very little previous research Emphasizes bone marrow and stem cell transplantation protocols as well as hematologic growth factors Organizes chapters consistently to address history epidemiology clinical features differential diagnosis and treatment Includes abundant photomicrographs and diagrams to clarify complex concepts and clinical issues Features the expertise of several members of the National Institutes of Health in Bethesda MD a leading center for the research and treatment of these syndromes *Aplastic Anemia and Other Bone Marrow Failure Syndromes* Nasrollah T. Shahidi, 2012-12-06 During the past decade there have been numerous direct and indirect scientific contributions to both the etiology and therapy of aplastic anemia and related bone marrow failure syndromes Clinical observations such as autologous bone marrow recovery after conditioning with immunosuppressive agents for bone marrow transplantation failure to achieve engraftment in some identical twins without prior immunosuppressive therapy and hematologic response to immunosuppressive agents have led to the concept of immune mediated etiology of acquired aplastic anemia Such a concept was further strengthened by laboratory findings implicating the role of activated cytotoxic T lymphocytes and abnormal production of inhibitory lymphokines The immunologic mechanisms may also apply to the idiosyncratic bone marrow aplasias associated with drugs toxic chemicals and viruses These agents may alter normal cellular recognition sites by interacting with cellular components and result in loss of self tolerance Immunologic mechanisms have long been advocated in many other organ failures and the hemopoietic organ is no exception It is of interest that parallel

clinical and laboratory investigations in juvenile diabetes mellitus type I and in rodent models of this disease have yielded results compatible with the same pathogenic mechanisms The infiltration of pancreatic islets by activated T lymphocytes functional and morphological alterations of islet cells upon incubation with lymphokines such as gamma interferon and tumor necrosis factor and clinical response to cyclosporine are a few examples

Bone Marrow Failure, An Issue of Hematology/Oncology Clinics of North America Colin A Sieff, 2018-07-15 This issue of Hematology Oncology Clinics edited by Dr Colin A Sieff will focus on Bone Marrow Failure Topics include but are not limited to Acquired and Inherited Bone Marrow Failure Kickapoo Joy Juice and Somatic Mutations in the Pathogenesis of AA Somatic Mutations in Aplastic Anemia Recent Advances and Long term Results of Medical Treatment of AA Upfront Matched Unrelated Donor Transplantation in AA Significance of Clonal Mutations in the Diagnosis and Management of Myelodysplastic Syndrome Alternate Haploidentical Donor Transplantation in AA Management of Diamond Blackfan Anemia and Prospects for Novel Treatment MDS AML and Cancer Surveillance in Fanconi Anemia Diagnosis Treatment and Molecular Pathology of Shwachman Diamond Syndrome Clinical Implications of Clonal Hematopoiesis in Dyskeratosis congenita and Germline GATA2 Mutations and Bone Marrow Failure

Congenital and Acquired Bone Marrow Failure Mahmoud Deeb Aljurf, Eliane Gluckman, Carlo Dufour, 2016-12-23 Congenital and Acquired Bone Marrow Failure is a comprehensive guide to congenital and acquired bone marrow failure in adult and pediatric patients Chapters are divided into two sections acquired aplastic anemia and inherited bone marrow failure syndromes Content ranges from the basic to the translational and from the epidemiology of acquired aplastic anemia and telomere biology to the management treatment and supportive care of pediatric adult and geriatric patients Contributors are world leading experts in the field of bone marrow failure The book is required reading for residents fellows clinicians and researchers across hematology oncology pathology bone marrow transplantation pediatrics and internal medicine Provides an overview of all congenital and acquired bone marrow failure syndromes Focuses on the molecular pathogenesis clinical manifestation and diagnosis laboratory features and treatment of each disease within the syndromes Features the area of supportive care which is a topic of great interest to infectious disease physicians and those involved in transfusion services

Aplastic Anemia and Bone Marrow Failure Syndromes Adrian Wiestner, 2022 ***Aplastic Anemia and Other Bone Marrow Failure Syndromes*** Nasrollah T. Shahidi, 1990

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Orkin, David G. Nathan, 2009-01-01 To address the exponential growth in the fields of pediatric hematology and oncology this classic reference has been separated into two distinct volumes With this volume devoted strictly to pediatric hematology and another to pediatric oncology you ll keep you on the cutting edge of these two specialties The completely revised 7th edition of Nathan and Oski s Hematology of Infancy and Childhood is now in full color and provides you with the most comprehensive authoritative up to date information for diagnosing and treating children with hematologic disorders It brings together the pathophysiology of disease with detailed clinical guidance on diagnosis and management for the full range of blood diseases that you encounter in everyday practice Written by the leading names in pediatric hematology this resource is an essential tool for anyone involved in caring for children with hematologic disorders And as an Expert Consult title this thoroughly updated 7th edition comes with access to the complete contents online fully searchable Balances summaries of relevant pathophysiology with clear practical clinical guidance to help you thoroughly understand the underlying science of diseases Offers comprehensive coverage of all hematologic disorders including newly recognized ones along with the latest breakthroughs in diagnosis and management Uses many boxes graphs and tables to highlight complex clinical diagnostic and management guidelines at a glance Presents an all new full color design that includes clear illustrative examples of relevant science and clinical problems for quick access to the answers you need Provides access to the complete contents online fully searchable enabling you to consult it rapidly from any computer with an Internet connection Your purchase entitles you to access the web site until the next edition is published or until the current edition is no longer offered for sale by Elsevier whichever occurs first If the next edition is published less than one year after your purchase you will be entitled to online access for one year from your date of purchase Elsevier reserves the right to offer a suitable replacement product such as a downloadable or CD ROM based electronic version should access to the web site be discontinued

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