

# Contents

---

- iii Editors' Message
- iv Reviewers
- v Continuing Medical Education Information

## Ham-Wasserman Lecture

- 1 Gene therapy for hemophilia  
*Amit C. Nathwani*

## Acute Lymphoblastic Leukemia: Aiming High to Keep MRD Low, or Even Better, Negative

- 9 Navigating the nexus of MRD and novel agents in ALL  
*Anjali S. Advani and Edward A. Copelan*
- 17 Pediatric-inspired protocols in adult acute lymphoblastic leukemia: are the results bearing fruit?  
*Lori Muffly and Emily Curran*
- 24 Curing Ph<sup>+</sup> ALL: assessing the relative contributions of chemotherapy, TKIs, and allogeneic stem cell transplant  
*Adele K. Fielding*

## Aggressive Non-Hodgkin Lymphomas: It's Getting Personal

- 30 Molecular profiling and management of mantle cell lymphoma  
*Jia Ruan*
- 41 Emerging strategies in peripheral T-cell lymphoma  
*Neha Mehta-Shah*
- 47 Prognostication with circulating tumor DNA: is it ready for prime time?  
*David M. Kurtz*

## Aging and Hematologic Disorders: Exploring the Evidence

- 53 Ready for prime time: role for geriatric assessment to improve quality of care in hematology practice  
*Heidi D. Klepin*
- 59 Evidence-Based Minireview: Longitudinal geriatric assessment in quality care for older patients with hematologic malignancies  
*Richard J. Lin and Heidi D. Klepin*
- 63 Delivering intensive therapies to older adults with hematologic malignancies: strategies to personalize care  
*Rebecca L. Olin*

## Balancing the Scales: Management of Patients at Risk of Bleeding and Clotting in the Acute Care Setting

- 71 Managing the competing risks of thrombosis, bleeding, and anticoagulation in patients with malignancy  
*Hanny Al-Samkari and Jean M. Connors*

- 80 Management of rare acquired bleeding disorders  
*Marzia Menegatti, Eugenia Biguzzi, and Flora Peyvandi*
- 88 Bleeding in critical care associated with left ventricular assist devices: pathophysiology, symptoms, and management  
*F. W. G. Leebeek and R. Muslem*

### Bone Marrow Failure and Clonal Evolution

- 97 Idiopathic aplastic anemia vs hypocellular myelodysplastic syndrome  
*Jibrán Durrani and Jaroslaw P. Maciejewski*
- 105 Monitoring and treatment of MDS in genetically susceptible persons  
*Stella M. Davies*
- 110 Genetic predisposition to MDS: diagnosis and management  
*Elissa Furutani and Akiko Shimamura*

### Challenges in Myeloma Therapy

- 120 Roundtable: How I treat a newly diagnosed patient with high-risk myeloma  
*Jonathan L. Kaufman*
- 125 How I treat a refractory myeloma patient who is not eligible for a clinical trial  
*Siyang Leng, Divaya Bhutani, and Suzanne Lentzsch*
- 137 What to do with minimal residual disease testing in myeloma  
*Elisabet E. Manasanch*
- 142 Evidence-Based Minireview: Does achieving MRD negativity after initial therapy improve prognosis for high-risk myeloma patients?  
*Surbhi Sidana and Elisabet Manasanch*

### Coagulation Conundrum Roundtable: Case-Based Discussion on the Implications of Exogenous Estrogens in Hemostasis and Thrombosis

- 148 Case-based discussion on the implications of exogenous estrogens in hemostasis and thrombosis: the obstetrician's view  
*Andra H. James*
- 152 Case-based discussion on the implications of exogenous estrogens in hemostasis and thrombosis: the hematologist's view  
*Margaret V. Ragni*

### Combined Basic Science and Education Session on Cancer-Associated Thrombosis

- 158 What's new in the prevention and treatment of cancer-associated thrombosis?  
*Miriam Kimpton and Marc Carrier*
- 167 Update from the clinic: what's new in the diagnosis of cancer-associated thrombosis?  
*Erica A. Peterson and Agnes Y. Y. Lee*

- 175 Platelets and cancer-associated thrombosis: focusing on the platelet activation receptor CLEC-2 and podoplanin  
*Katsue Suzuki-Inoue*
- 182 Update from the laboratory: mechanistic studies of pathways of cancer-associated venous thrombosis using mouse models  
*Yohei Hisada and Nigel Mackman*

## DOACs in the Real World

- 187 Is there a role for low-dose DOACs as prophylaxis?  
*Alexander T. Cohen and Beverley J. Hunt*
- 194 Direct oral anticoagulant monitoring: what laboratory tests are available to guide us?  
*Ravi Sarode*
- 198 What we have learned about direct oral anticoagulant reversal  
*Deborah M. Siegal*
- 204 Evidence-Based Minireview: Mortality and thrombosis in patients receiving prothrombin complex concentrates or andexanet alfa for the management of direct oral factor Xa inhibitor-associated major bleeding  
*Miriam Kimpton and Deborah M. Siegal*

## Expanding Horizons for Immunotherapy in Pediatric Leukemia

- 209 Moving immunotherapy into the front line in ALL  
*Amanda Winters and Lia Gore*
- 218 Opportunities for immunotherapy in childhood acute myeloid leukemia  
*Adam J. Lamble and Sarah K. Tasian*
- 226 Mechanisms of and approaches to overcoming resistance to immunotherapy  
*Liora Schultz and Rebecca Gardner*

## Hodgkin Lymphoma: Celebrating 200 Years since Thomas Hodgkin Entered Medicine

- 233 Management of older Hodgkin lymphoma patients  
*Andrew M. Evens, Jordan Carter, Kah Poh Loh, and Kevin A. David*
- 243 Novel agents and immune invasion in Hodgkin lymphoma  
*Reid W. Merryman and Ann LaCasce*
- 249 Evidence-Based Minireview: What is the optimal timing of anti-PD-1 antibodies in relapsed classical Hodgkin lymphoma?  
*Pamela Blair Allen and Ann S. LaCasce*
- 252 Cure at what (systemic) financial cost? Integrating novel therapies into first-line Hodgkin lymphoma treatment  
*Scott F. Huntington*

## Immunotherapy in Myeloma

- 260 CAR T-cell therapy: is it prime time in myeloma?  
*Surbhi Sidana and Nina Shah*

266 Myeloma: next generation immunotherapy  
*Adam D. Cohen*

## Indolent Lymphomas: The Marathon Has a New Course

273 Targeting CD20: teaching an old dog new tricks  
*Jeff P. Sharman*

279 Indolent lymphomas: pushing the pace with novel agents  
*Caron A. Jacobson*

287 Where does transplant fit in the age of targeted therapies?  
*Victor A. Chow and Ajay K. Gopal*

## Inflammation and Hematopoiesis: The Impact of Inflammation on the Bone Marrow Microenvironment

294 Inflammatory bone marrow microenvironment  
*Nils B. Leimkühler and Rebekka K. Schneider*

303 Microbiota modification in hematology: still at the bench or ready for the bedside?  
*Christopher J. Severyn, Ryan Brewster, and Tessa M. Andermann*

## Iron: How to Manage When There Is Too Much or Too Little of It

315 Management of iron deficiency  
*Shuoyan Ning and Michelle P. Zeller*

323 Evidence-Based Minireview: The role of IV iron in management of patients with iron-deficiency anemia presenting to the emergency department  
*Julia G. Ramos and Michelle P. Zeller*

327 New diagnostic tools for delineating iron status  
*Yelena Z. Ginzburg*

337 Iron overload in transfusion-dependent patients  
*Thomas D. Coates*

## Management of Sickle Cell Disease Complications Beyond Acute Chest

345 Management of liver complications in sickle cell disease  
*Abid R. Suddle*

351 Osteonecrosis in sickle cell disease: an update on risk factors, diagnosis, and management  
*Oyebimpe O. Adesina and Lynne D. Neumayr*

359 Complications in pregnant women with sickle cell disease  
*Kim Smith-Whitley*

## Myelodysplastic Syndromes: From Mild-Mannered to Lurking Leukemia

367 Lowering the boom on lower-risk myelodysplastic syndromes  
*Mikkael A. Sekeres and Bhumika J. Patel*

373 Integrating patient-centered factors in the risk assessment of MDS  
*Rena J. Buckstein*

381 In MDS, is higher risk higher reward?

*Guillermo F. Sanz*

## Myeloproliferative Neoplasms: Managing the Cup That Runneth Over

391 Diagnostic workflow for hereditary erythrocytosis and thrombocytosis

*Mary Frances McMullin*

397 From Budd-Chiari syndrome to acquired von Willebrand syndrome: thrombosis and bleeding complications in the myeloproliferative neoplasms

*Brady L. Stein and Karlyn Martin*

407 Beyond JAK-STAT: novel therapeutic targets in Ph-negative MPN

*Aaron T. Gerds*

## New Diagnostic and Treatment Strategies for Antiphospholipid Syndrome

415 Improvements in diagnosis and risk assessment of primary and secondary antiphospholipid syndrome

*Michelle Petri*

421 What's new in obstetric antiphospholipid syndrome

*D. Ware Branch*

426 Is there a role for immunosuppression in antiphospholipid syndrome?

*Ecem Sevim, Rohan Willis, and Doruk Erkan*

## Patients, Borders, Money, and Mission: A Global Perspective of Chronic Myeloid Leukemia

433 Meeting the needs of CML patients in resource-poor countries

*Hemant Malhotra, Jerald Radich, and Pat Garcia-Gonzalez*

## Primary Immunodeficiencies: Finding the Needle in the Haystack

443 Primary immunodeficiencies: novel genes and unusual presentations

*Luigi D. Notarangelo, Gulbu Uzel, and V. Koneti Rao*

449 Common variable immune deficiency: case studies

*Charlotte Cunningham-Rundles*

457 Treatment of primary immunodeficiency with allogeneic transplant and gene therapy

*Sung-Yun Pai*

## Response Comes of Age in Chronic Lymphocytic Leukemia

466 Clonal dynamics in chronic lymphocytic leukemia

*Catherine Gutierrez and Catherine J. Wu*

476 Treatment-naïve CLL: lessons from phase 2 and phase 3 clinical trials

*Jennifer A. Woyach*

482 Relapsed disease and aspects of undetectable MRD and treatment discontinuation

*Barbara Eichhorst, Moritz Fürstenau, and Michael Hallek*

## Sickle Cell Disease in Young and Old: A Time for Re-Evaluation

- 490 Sickle cell disease: a comprehensive program of care from birth  
*Mariane de Montalembert, Léon Tshilolo, and Slimane Allali*
- 496 A program of transition to adult care for sickle cell disease  
*Anjelica C. Saulsberry, Jerlym S. Porter, and Jane S. Hankins*
- 505 Optimal disease management and health monitoring in adults with sickle cell disease  
*Jo Howard and Swee Lay Thein*

## Spoiled for Choice: Donor Selection for Allogeneic Stem Cell Transplantation

- 513 How we perform haploidentical stem cell transplantation with posttransplant cyclophosphamide  
*Shannon R. McCurdy and Leo Luznik*
- 522 Optimizing cord blood selection  
*Annalisa Ruggeri*
- 532 Selection of matched unrelated donors moving forward: from HLA allele counting to functional matching  
*Katharina Fleischhauer*

## Therapy of Acute Myeloid Leukemia: Adapting to Change

- 539 The growing landscape of FLT3 inhibition in AML  
*Catherine C. Smith*
- 548 Single-agent and combination biologics in acute myeloid leukemia  
*Guillaume Richard-Carpentier and Courtney D. DiNardo*
- 557 MRD evaluation of AML in clinical practice: are we there yet?  
*Sylvie D. Freeman and Christopher S. Hourigan*

## Transfusion Medicine: Optimizing Patient Blood Management (PBM)

- 570 Preoperative anemia-screening clinics  
*Yulia Lin*
- 577 Clinical decision support and improved blood use in patient blood management  
*Lawrence Tim Goodnough and Marie A. Hollenhorst*
- 583 Patient blood management as the standard of care  
*Michael F. Murphy and Antony Palmer*

## What's New in the Diagnosis and Management of von Willebrand Disease?

- 590 New therapies for von Willebrand disease  
*Pier Mannuccio Mannucci*
- 596 New advances in the diagnosis of von Willebrand disease  
*Ruchika Sharma and Sandra L. Haberichter*
- 601 Evidence-Based Minireview: Perioperative management of the VWD patient at elevated thrombotic risk  
*Holleh D. Husseinzadeh and Sandra Haberichter*

604 Perioperative management of patients with von Willebrand disease  
*James S. O'Donnell and Michelle Lavin*

## Why Patients Fail after Allogeneic Stem Cell Transplantation

610 Clonal evolution and immune evasion in posttransplantation relapses  
*Luca Vago*

617 Minimal residual disease and stem cell transplantation outcomes  
*Jacqueline Cloos, Gert J. Ossenkoppele, and Richard Dillon*

626 Cause-specific late mortality after allogeneic stem cell transplantation  
*Smita Bhatia*

## Erratum

630 Scherber RM, Mesa RA. Managing myelofibrosis (MF) that “blasts” through: advancements in the treatment of relapsed/refractory and blast-phase MF. *Hematology Am Soc Hematol Educ Program*. 2018;2018:118-126.  
*Robyn M. Scherber and Ruben A. Mesa*