



AMERICAN SOCIETY OF HEMATOLOGY

2021 L Street, NW, Suite 900, Washington, DC 20036 **ph** 202.776.0544 **fax** 202.776.0545 **e-mail** ASH@hematology.org

June 17, 2010

2010

President

Hal Broxmeyer, PhD
Walther Oncology Center
Indiana University School of Medicine
950 W. Walnut Street, Room 302
Indianapolis, IN 46202
phone 317-274-7510
fax 317-274-7592
hbroxmey@iupui.edu

President-Elect

J. Evan Sadler, MD, PhD
Washington University Medical School
660 South Euclid Avenue, Box 8125
Saint Louis, MO 63110-1093
phone 314-362-9029
fax 314-454-3012
esadler@wustl.edu

Vice President

Armand Keating, MD
Princess Margaret Hospital
610 University Avenue, Suite 5-303
Toronto, ON M5G 2M9
CANADA
phone 416-946-4595
fax 416-946-4530
armand.keating@uhn.on.ca

Secretary

Charles Abrams, MD
University of Pennsylvania
School of Medicine
421 Curie Boulevard, #912
Philadelphia, PA 19104-6140
phone 215-573-3288
fax 215-573-7400
abrams@mail.med.upenn.edu

Treasurer

Linda Burns, MD
Division of Hematology,
Oncology, and Transplantation
University of Minnesota
420 Delaware Street, SE
Mayo MC 286/Room 14-154A Moos Tower
Minneapolis, MN 55455-0341
phone 612-624-8144
fax 612-625-9988
burns019@umn.edu

Councillors

Kenneth Anderson, MD
Thomas Bensinger, MD
David Bodine, PhD
Stephanie Lee, MD, MPH
Elaine Muchmore, MD
Mohandas Narla, DSc
Marilyn Telen, MD
David Williams, MD

Editors-in-Chief

Cynthia Dunbar, MD, *Blood*
Roy Silverstein, MD, *The Hematologist*

Executive Director

Martha L. Liggett, Esq.
mliggett@hematology.org

Department of Health and Human Service
200 Independence Avenue, SW
Room 736-E
Washington, DC 20201

Dear Ms. Stevenson,

The American Society of Hematology (ASH) appreciates the opportunity to comment on the Health and Human Services (HHS) initiative on Multiple Chronic Conditions. The Society represents more than 16,000 clinicians and scientists committed to the study and treatment of blood and blood-related diseases.

There are several hematologic diseases that contribute to patients experiencing multiple chronic conditions and would benefit from being included in this HHS initiative. Below is information on four hematologic conditions ASH recommends for inclusion in the HHS list of Multiple Chronic Conditions.

Disorders of Hemoglobin

Disorders of hemoglobin including sickle cell disease and thalassemia should be considered for inclusion in the HHS Initiative on Multiple Chronic Conditions. The World Health Organization estimates that 7% of the world's population are genetic carriers of a hemoglobin disorder and that 300,000-500,000 babies are born each year with a severe hemoglobin disorder.[1] In North America, ~ 3400 conceptions each year (0.8/1000 live births) are affected by a severe hemoglobin disorder. [2] In the US specifically, the overall prevalence of the sickle hemoglobinopathies has recently been estimated to be approximately 90,000.[3,4] Patients with the sickle hemoglobinopathies are hospitalized annually between 100,000-125,000 times at an aggregate cost of nearly \$500 million.[5] Individuals with the severe forms of thalassemia and any form of sickle cell disease have complications of multiple organ systems from the disease itself, its treatment (blood transfusions with resultant iron overload), or both. Common complications of sickle cell disease include acute and chronic pain, growth failure, asthma, sleep disordered breathing, kidney disease, pulmonary hypertension, priapism and resultant erectile dysfunction, osteonecrosis, and neuropsychological complications. Because of their high prevalence in the population and their complex, multi-system array of complications, the hemoglobin disorders should strongly be considered for inclusion in the HHS Initiative on Multiple Chronic Conditions.

Hereditary Hemochromatosis

Hereditary hemochromatosis is an inherited disorder with a prevalence of approximately 1:200 among Caucasians.[1-3] Untreated, it results in iron deposition in, and damage to, the liver, heart, pancreas and other organs.[4-5] Homozygosity for a single missense mutation (G to A) at nucleotide 845 in the HFE gene on chromosome 6p21 accounts for >90% of cases and almost all cases in Caucasians of Northern European descent.[7-11] This mutation results in substitution of cysteine with tyrosine at amino acid 282 and is referred to as the C282Y mutation, [12] and results in inappropriate enteric iron uptake despite abundant iron stores in the body.[2] The accumulation of iron in the liver and other organs slowly results in liver failure (cirrhosis, hepatocellular carcinoma), diabetes, hypogonadism, hypopituitarism, arthropathy, cardiomyopathy and heart failure, and skin pigmentation.[2, 12]

Myeloproliferative Diseases

Myeloproliferative diseases excluding CML (ET, Polycythemia vera, primary myelofibrosis) affect an estimated 15,000 – 20,000 Americans annually. Although the incidence is relatively low, prevalence is much larger because of the chronic nature of the diseases. Major complications include transformation to acute leukemia, myelofibrosis (for ET and PV), and thrombohemorrhage (PV and ET). Thrombotic complications include arterial and venous thromboses, as well as microcirculatory disorders involving the skin and neurologic systems. Spontaneous bleeding episodes occur when platelet levels are generally high. Splenomegaly and hepatomegaly are common and substantial. The symptom burden in patients with myeloproliferative diseases is high, with more than 40 percent of patients reporting bone pain, night sweats, pruritis and approximately 80% reporting fatigue. One third of patients recently surveyed with these diseases required assistance with ADLs, and the majority of patients reported their symptoms limited social functions and physical activity. [1] Because of risks of complications and disease transformation, overall survival may be near-normal, or may be as short as less than 5 years.

Hemophilia

Hemophilia is a chronic, lifelong disorder characterized by a predisposition to hemorrhage and is due to congenital deficiencies in the synthesis or function of coagulation factors. Severe hemophilia (defined as factor levels less than 1% of normal and spontaneous bleeding in the absence of treatment) is characterized by spontaneous joint bleeding resulting in debilitating joint disease, major bleeding at other sites (such as intracerebral) and the need for intermittent or chronic replacement of coagulation factors. With directed and extended duration prophylaxis clinical manifestations such as joint disease may be avoided at significant financial cost and inconvenience. Prior to the development of virally inactivated coagulation factors infection such as HIV, hepatitis B and hepatitis C developed in the majority of patients requiring regular coagulation factor replacement. Modern coagulation factors have not been demonstrated to transmit such diseases however the specter of either an as yet undefined illness or errors leading to the reintroduction of known illnesses remain possible. Patients with moderate (factor levels of more than 1% and less than 5% and bleeding in response to challenges) and mild hemophilia (infrequent spontaneous bleeding and the bleeding in response to severe vascular challenges)

constitute a larger proportion of the population and although less clinically affected are at lifelong risk of catastrophic bleeding complications resulting in anxiety, the need for intermittent and expensive coagulation factor concentrate and the risk of viral infection at the time of administration of such products. As a disease which predominantly affects young people, has lifelong implications for the care of patients, entails treatment with expensive interventions and can cause instantaneous and lifelong debility (or in fact death) hemophilia is a true chronic disease which begins in infancy and is present throughout the patient's life.

Again, ASH appreciates the opportunity to make these recommendations. The Society is interested in working with the HHS on this initiative. If you have any questions or require any additional information, please contact ASH Senior Manager of Policy and Practice Carol Schwartz at or 202-776-0544.

Sincerely,



Lawrence A. Solberg, Jr., MD, PhD
Chair, Committee on Practice

CITATIONS: Disorders of Hemoglobin

1. Weatherall DJ. Hemoglobinopathies worldwide: present and future. *Curr Mol Med* 2008;8(7):592-599.
2. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. *Bull World Health Organ* 2008;86(6):480-487.
3. Brousseau DC, Panepinto JA, Nimmer M, et al. The number of people with sickle-cell disease in the United States: national and state estimates. *Am J Hematol*:85(1):77-78.
4. Hassell KL. Population estimates of sickle cell disease in the U.S. *Am J Prev Med*:38(4 Suppl):S512-521.
5. Steiner C. and Miller J. Sickle Cell Disease Patients in U.S. Hospitals, 2004. Agency for Healthcare Research and Quality, Rockville, Md 2006:HCUP Statistical Brief #21(December):1-9.

CITATIONS: Hereditary Hemochromatosis

1. Cogswell ME, McDonnell SM, Khoury MJ, et al. Iron overload, public health, and genetics: evaluating the evidence for hemochromatosis screening. *Ann Int Med* 1998;129:971-79.
2. Bacon BR, Powell LW, Adams PC, et al. Molecular medicine and hemochromatosis: at the crossroads. *Gastroenterology* 1999;116:193-207.
3. Bacon BR, Olynyk JK, Brunt EM. HFE genotype in patients with hemochromatosis and other liver diseases. *Ann Int Med* 1999;130:953-62.
4. Barton JC, McDonnell SM, Adams PC, et al. Diagnosis and management of hemochromatosis. *Ann Int Med* 1998;129:932-9.
5. Pietrangelo A. Hereditary hemochromatosis – a new look at an old disease. *N Engl J Med* 2004;350:2383-97.

6. Brissot P, Guyader D, Loréal O, et al. Clinical aspects of hemochromatosis. *Transfus Sci* 2000;23:193-2000.
7. Bacon BR, Powell LW, Adams PC, et al. Molecular medicine and hemochromatosis: at the crossroads. *Gastroenterology* 1999;116:193-207.
8. Bacon BR, Olynyk JK, Brunt EM. HFE genotype in patients with hemochromatosis and other liver diseases. *Ann Int Med* 1999;130:953-62.
9. Burke W, Imperatore G, McDonnell SM, et al. Contribution of different HFE genotypes to iron overload disease: a pooled analysis. *Genet Med* 2000;2:271-7.
10. Hanson EH, Imperatore G, Burke W. HFE gene and hereditary hemochromatosis: a HuGE review. *Am J Epidemiol* 2001;154:193-206.
11. Steinberg KK, Cogswell ME, Chang JC, et al. Prevalence of C282Y and H63D mutations in the hemochromatosis (HFE) gene in the United States. *JAMA* 2001;285:2216-22.
12. Feder JN, Gnirke A, Thomas W. A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis. *Nat Genet* 1996;13:399-408.

CITATIONS: Myeloproliferative Diseases

1. *Cancer*, Jan 1 2007; 68-76: RA Mesa et al.