Hematology, ASH, and the anemia of the aged

Last year when I served as ASH president, during the society’s regular meetings with several institutes of the National Institutes of Health (NIH), we learned that the National Institute on Aging (NIA) had just completed the Third National Health and Nutrition Examination Survey (NHANES III), which was subsequently published in Blood. The study focused on community-dwelling subjects and had elements of a wake-up call for primary care physicians, geriatricians, and hematologists, because it showed that 10 percent of men and women older than 65 years of age were anemic. Perhaps more important, although only a very small number of these subjects had hemoglobin (Hgb) levels lower than 11 g/dL, prior studies had shown that such “trivial” levels of anemia resulted in decline in objective measures of physical performance, higher 30-day mortality rates for patients with acute myocardial infarction, and poorer outcomes in patients with heart failure. These clinically important revelations led ASH to cosponsor a research-agenda-setting conference for NIA, attended by about 20 hematologists and geriatricians, in March 2004. The conference considered some of the issues raised by NHANES III and suggested areas for further investigation.

The conference found that the definition of anemia is an unresolved problem. The World Health Organization (WHO) and NHANES III used the same criteria for anemia: Hgb values lower than 13 g/dL for men and 12 g/dL for women. It is understandable that in androgen-secreting, childbearing years women might normally have lower Hgb values than men, but it is not clear that this should continue to be the case after age 65. If the same Hgb value of less than 13 g/dL were used for women, 30 percent would be considered anemic, presumably with the consequences in morbidity noted previously. Ethnic differences also need to be considered, because by WHO criteria almost 30 percent of African-American men and women have anemia, and the difference cannot be explained by an increased prevalence of iron deficiency or alpha thalassemia.

NHANES III was not designed to do a classical hematologic differential diagnosis of the underlying cause of the anemia, but most cases appeared to be production defects, with the leading causes being iron deficiency, anemia of chronic inflammation (ACI), and “nutritional deficiencies.” ASH’s conference noted the difficulty in diagnosing iron deficiency, particularly in the setting of inflammatory disease.

The problem is complicated further because the geriatricians informed the surprised hematologists that there was evidence for cytokine dysregulation in the elderly. The distinction is critical because, in a study of 100 consecutive patients with confirmed iron deficiency, of those who underwent endoscopy 16% had colon cancer or premalignant polyps. The conference also noted the difficulty in diagnosing ACI/ACD (anemia of chronic disease) and wondered if new information regarding the central role of hepcidin in inflammation may improve our diagnostic ability in future.

Many elderly subjects had borderline serum values of vitamin B₁₂, but the conference noted that there were technical problems with the assay and that the number of patients who actually had a Hgb response to vitamin B₁₂ therapy was very low. The issue of marginal vitamin B₁₂ levels and neuropathy was not considered in detail.

In the NHANES III study, about one-third of the patients with anemia were undiagnosed, leading to the hypothesis that there might be a new entity: “anemia of the aged.” Before the existence of such an entity can be proven, all other forms of anemia have to be excluded. The difficulties in diagnosing iron deficiency anemia and ACI are noted above. Furthermore, myelodysplastic syndrome (MDS) is increasingly prevalent in the elderly and is a recognized cause of anemia and other cytopenias. The conference noted that there was no simple, inexpensive, definitive test for MDS and debated the value of the peripheral smear as a screening method. There is increasing recognition of the importance of diagnosing MDS, in part because there are now effective forms of treatment including erythropoietic agents, 5-azacytidine, and lenalidomide (Revlimid, Celgene, Summit, NJ).

The conference focused on the cause of the morbidity of even “mild” anemia: was it the anemia per se, its underlying etiology, the associated comorbidities and polypharmacy, or all of the above? This is clearly an area ready for clinical research, where the anemia alone could be improved (to what level?) by either red blood cell (RBC) transfusion or administration of agents that enhance erythropoiesis.

As this was an agenda-setting conference, recommendations were made regarding future research initiatives, which could include: definitions of severe and mild anemia; a physiologic measurement of anemia; direct measurements of RBC mass and plasma volume to more accurately ascertain the extent of the anemia; assessment of marrow stem cell and erythropoietic reserve in the elderly; more accurate measures of renal, thyroid, and androgen functions; and development of screening tests for ACI, iron deficiency, and MDS.

Finally, there were thoughts about what could constitute an appropriate work-up for an elderly patient with anemia, and when to refer the patient to a hematologist. Certainly, given the potentially large number of subjects involved, there are serious cost-benefit issues.

Given the obvious clinical importance of the anemia of aging for patients and hematologists, the ASH Practice Committee’s Subcommittee on Quality of Care is sponsoring a special symposium at the 2005 ASH Annual Meeting on this subject, in order to explore the issues and problems noted. The symposium “Anemia and the Elderly: A Public Health Crisis in Hematology?” will take place on Saturday, December 10, 2005, from 2:00 pm to 3:45 pm, in the Georgia World Congress Center, Room B206. This symposium will be supported in part by a generous grant from the Association of Subspecialty Professors, the John A. Hartford Foundation, and the Merck Institute of Aging and Health.

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References


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