

Anemia in the Elderly

A Survey of Physicians' Approaches to Diagnosis and Workup

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Anemia is one of the most common clinical problems encountered by physicians caring for elderly patients. There is controversy about whether anemia should be regarded as a "normal" concomitant of the aging process. A survey of 232 Maryland physicians was conducted to examine how they approach this problem. The levels of both hemoglobin and hematocrit at which practicing physicians diagnose and perform an anemia workup on elderly patients were lower than currently recommended. Physicians who see more elderly patients used significantly lower values of hemoglobin and hematocrit for the diagnosis and workup of anemia. There were no significant differences between family physicians and internists in their approach to diagnosis or workup of anemia in the elderly.

Anemia is one of the most common clinical problems in elderly patients. There is a recurrent controversy whether patients older than the age of 65 years have an age-related decline in red blood cell values, a so-called anemia of senescence.¹⁻³ If this decline represents a physiological response to aging, then it has been suggested that new hematologic norms are necessary when examining elderly individuals.^{1,4,5} This position is further supported by work that suggests the majority of cases of elderly anemic patients cannot be explained after standard laboratory investigation.^{1,6} In contrast, advocates of the opposing viewpoint believe that while anemia is very common in the aged, it should never be regarded as a normal concomitant of aging.⁷ Several authors^{2,8,9} caution against the establishment of new geriatric norms, concluding that health status, socioeconomic status, race, and attitude are more important considerations than age itself when evaluating abnormal hematologic values in the elderly patient.

To provide information about the actual use of the anemia of senescence theory by practicing physicians, a sample of physicians in Maryland was surveyed to ascertain their approach to diagnosing anemia in otherwise healthy elderly patients. Of specific interest was the determination

of what levels of hemoglobin and hematocrit were used for making the diagnosis of anemia, the levels that would prompt an anemia workup, and the content and extent of a workup for elderly anemic patients who had normal red blood cell indices.

METHODS

A random sample of 500 physicians was generated from the 1432 physicians registered with the Medical and Chirurgical Faculty of Maryland (the state medical society) who had identified either family medicine or internal medicine as their primary specialty. A one-page questionnaire on anemia in otherwise healthy elderly patients was mailed to these physicians together with a cover letter explaining the study and requesting participation. Each questionnaire had a confidential code number so that a follow-up mailing could be sent to nonrespondents. The questionnaire had been pretested on a small sample of physicians to refine the questions and the format.

Each physician was asked to identify cutoff levels for hemoglobin and hematocrit below which male and female patients would be identified as having anemia, and to identify levels of hemoglobin and hematocrit below which they would carry out further investigations. For those elderly patients with anemia and normal red blood cell indices, the questionnaire asked which further test would be ordered (options included blood smear, reticulocyte count, stool for

Submitted, revised, February 21, 1989.

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TABLE 1. CHARACTERISTICS OF THE SAMPLE OF MARYLAND PHYSICIANS

Characteristics	Number	Percent
Total number of surveys mailed	500	
Response	232	46.4
Specialty		
Family practice	70	38.7
Internal medicine	111	61.3
Board certification	142	72.1
Type of practice		
Solo practice	93	40.1
Group practice	66	28.4
Practice location		
Metropolitan	143	74.9
Nonmetropolitan	48	25.1
Number of patients seen per week	80 ± 47	(mode 100)
Number of patients > 65 y seen per week	34 ± 23	(mode 30)
Number of nursing home patients per month	12 ± 30	(mode 0)

blood, serum iron levels, iron-binding capacity, serum ferritin levels, serum vitamin B₁₂ levels, folate levels, or other). If the cause for anemia was still unclear after this workup, the physicians were then asked whether a further workup was indicated, and if so, to list in order of importance the following tests: barium enema, upper gastrointestinal series, gastroduodenoscopy, colonoscopy, proctoscopy, sigmoidoscopy, bone marrow aspirate or biopsy, or other. Finally, there was a question asking whether, and why, a hematologist or gastroenterologist would be consulted in the case of an elderly anemic patient.

Each physician was asked to provide the background information listed in Table 1. Frequencies, cross-tabulations using chi-square as a measure of statistical significance, and correlations were used to describe and analyze the data.¹⁰ Pearson's correlation coefficient shows the direction, strength, and statistical significance of a relationship, and was used to examine the relationship between values for diagnosis and workup and percentage of physicians' patients over 65 years with anemia. Negative values indicate inverse relationships.

RESULTS

Of the 500 questionnaires mailed, 232 responses were received for a 46.4% response rate. Not all respondents answered all questions. Forty of these questionnaires were returned uncompleted, 26 (65%) citing retirement as a reason for noncompletion. These respondents were excluded from further analysis.

TABLE 2. REPORTED HEMOGLOBIN AND HEMATOCRIT VALUES FOR DIAGNOSING AND WORKING UP ANEMIA IN MEN AND WOMEN

	Men	Women
Hemoglobin		
Diagnosis	7.67 ± 0.71 mmol/L (12.36 ± 1.14 g/dL)	7.12 ± 0.55 mmol/L (11.48 ± 0.89 g/dL)
Workup	7.23 ± 0.72 mmol/L (11.65 ± 1.16 g/dL)	6.78 ± 0.6 mmol/L (10.93 ± 0.96 g/dL)
Difference*	0.36 ± 0.5 mmol/L (0.58 ± 0.81 g/dL)	0.3 ± 0.39 mmol/L (0.48 ± 0.63 g/dL)
Hematocrit		
Diagnosis	0.3742 ± 0.0323	0.3504 ± 0.0280
Workup	0.3543 ± 0.0398	0.3340 ± 0.0329
Difference*	0.0175 ± 0.0284	0.0150 ± 0.0240

*Difference is the value for diagnosis minus value for workup.

The modal year of graduation from medical school was 1977. Most (61%) respondents listed internal medicine as their specialty, with about 25% of the total identifying a medical subspecialty. The majority (72%) were board certified. The type of practice and the characteristics of their patient population are presented in Table 1. The mean estimated percentage of anemic patients over the age of 65 years was 13.9 percent.

The mean levels of hemoglobin and hematocrit at which the diagnosis of anemia was made and the levels of hemoglobin and hematocrit that triggered a workup for anemia are presented in Table 2. The table also includes the mean differences between the levels used for making the diagnosis and levels that triggered a workup. Fifty percent of those surveyed used the same value for diagnosis and workup, while a further 46.6% were willing to tolerate a difference of up to 1.24 mmol/L (2 g/dL) before initiating a workup. The mean hematocrit difference between diagnosis and workup was 0.02 ± 0.03 (1.75% ± 2.84%). Again, one half of the physicians used the same value for diagnosis and workup, while a further 45% were willing to tolerate a 6% difference before initiating a workup.

The relative importance of other tests in the initial workup of a patient with normochromic, normocytic anemia below the level each physician specified as a trigger for initial investigation (which they reported above) was as follows: stool for occult blood (177 of 189, 94%), blood smear (161 of 184, 87%), reticulocyte count (154 of 1984, 84%), serum iron (136 of 180, 76%), serum iron-binding capacity (117 of 177, 66%), serum folate (97 of 176, 55%), serum B₁₂ (94 of 174, 54%), and serum ferritin (92 of 175, 52%). Other tests mentioned were serum protein electrophoresis, blood urea nitrogen (BUN), and erythrocyte sedimentation rate.

A total of 164 of 181 physicians (91%) believed that if

the cause of anemia was still unclear after the above workup, then further testing was indicated. When asked to rank the order of performance of other tests from first to seventh, mean ranking values were: sigmoidoscopy 2.9 ± 2.4 , proctoscopy 3.8 ± 2.6 , barium enema 3.8 ± 2.7 , upper gastrointestinal series 4.2 ± 2.3 , colonoscopy 4.6 ± 1.9 , gastroduodenoscopy 5.3 ± 1.4 , and bone marrow aspirate or biopsy 5.3 ± 2.3 . There was no difference in physicians' rankings of these tests for male or female patients.

Among the most important reasons for consulting a gastroenterologist were heme-positive stools, iron deficiency anemia, and whether a procedure (eg, colonoscopy) was indicated. The most frequent reasons given for consulting a hematologist were for a puzzling case or to perform a bone marrow aspirate or biopsy.

There was no statistically significant difference between family physicians and internists in responses to any questions in this survey, nor were there any differences between physicians practicing in metropolitan and nonmetropolitan areas.

To ascertain whether physicians who are more involved with the elderly approach anemia differently, correlations between involvement with elderly patients and values for diagnosis and workup of anemia were examined (Table 3). The inverse correlations show that physicians who saw more patients older than 65 years were significantly more likely to use lower hemoglobin values to diagnose anemia and to use lower hemoglobin and hematocrit values when working up anemia. Physicians who saw more nursing home patients used significantly lower hematocrit values for working up anemia.

DISCUSSION

These results suggest that in otherwise healthy elderly patients, physicians frequently use values of hemoglobin and hematocrit for the diagnosis and workup of anemia that are lower than those recommended in the literature.^{2,3,8,9} It also is evident that up to 50% of the physicians surveyed were prepared to tolerate a difference of up to 1.24 mmol/L (2 g/dL) between the value they indicated as a diagnosis of anemia and that which initiates a workup. These findings support the view that physicians in practice act as though there exists an anemia of senescence and that they believe that the workup of a low-grade anemia in their healthy elderly patients is unrewarding. The finding that physicians who are more involved with elderly patients tolerate lower values of hemoglobin before diagnosing and working up anemia also supports the existence of the concept of an age-related decline in red cell values in the practice behavior of physicians. Using lower cutoff values may occur because physicians believe that while their elderly patients otherwise appear healthy, underlying low-grade chronic disease may account for the reduction in hemoglobin levels.

TABLE 3. CORRELATIONS OF PHYSICIAN INVOLVEMENT WITH ELDERLY AND NURSING HOME PATIENTS WITH DIAGNOSIS AND WORKUP VALUES FOR ANEMIA

	Number of Patients > 65 Years		Number of Nursing Home Patients	
	Men	Women	Men	Women
Diagnosis values				
Hemoglobin	-.28*	-.25*	-.14	-.04
Hematocrit	-.20	-.15	-.15	-.15
Workup values				
Hemoglobin	-.31*	-.27*	-.07	-.00
Hematocrit	-.27*	-.24*	-.24*	-.23*

Note: Negative correlations show an inverse relationship in which physicians seeing more elderly patients use lower values for anemia diagnosis and workup.

*P < .05

The confounding effects of chronic and inapparent disease, dietary problems, and environmental factors so prevalent in the elderly and the effects of these conditions on bone marrow function make studies of anemia in so-called healthy elderly difficult to interpret. Community-based studies involving large numbers of randomly selected patients include many patients with both treated and untreated conditions, and therefore will include some values for hemoglobin that are pathologically low.^{9,11}

There is evidence to suggest that in carefully selected populations, screened for concurrent disease, race, education, and socioeconomic status, no elderly women will have a hemoglobin of less than 7.45 mmol/L (12 g/dL), and 2.3% of men will have a hemoglobin of less than 8.69 mmol/L (14 g/dL).⁸ Garry et al⁸ state that "a slight upward adjustment in hemoglobin level may be necessary to account for altitude" in this sample. Their work is supported by recent data showing only a small fluctuation of the hemoglobin value over time in healthy very old people who lived at sea level.² In another study of 292 individuals unselected for health status, only 17 had a hemoglobin value less than 7.45 mmol/L (12 g/dL).⁹ When these patients were excluded, the new means were all within the laboratory's normal range.

Others^{9,11} would suggest that the workup of anemia is rewarding, and that most cases have a treatable underlying cause. Htoo et al⁹ found a cause for anemia in 71% of 17 patients with hemoglobin values less than 7.45 mmol/L (12 g/dL) in their unselected population of 292 patients. McLennan et al,¹¹ using 7.45 mmol/L (12 g/dL) as a cutoff value for making the diagnosis of anemia, found that 45% of their anemic patients had an identifiable cause for their anemia, with iron deficiency being the most common. Their sample was randomly selected from the general population and therefore included people with untreated conditions. Furthermore, their definition of iron deficiency (serum iron-binding saturation $\leq 16\%$) was probably over-inclusive because recent studies show that a transferrin

saturation ratio of $\leq 11\%$ and a serum ferritin of $< 45 \mu\text{g/L}$ are more specific predictors of iron deficiency.¹² The high prevalence of positive workups in patients with significant anemias is supported by other research, which shows that in the healthy elderly population there is little evidence of iron deficiency.¹³ These authors reiterate the need for a clearer understanding of the physiological and nutritional factors responsible for lower hemoglobin values in older people, if found.

If patients with iron deficiency are excluded, large population-based studies show that median hemoglobin values remain constant up until the age of 74 years, and the prevalence of anemia is extremely low.^{14,15} This work confirms the postulate that few otherwise healthy elderly people should have hemoglobin values below the 95th percentile reference range (median value 9.25 mmol/L [14.9 g/dL] for men, 8.63 mmol/L [13.9 g/dL] for women). These authors suggest that age-specific reference standards should be applied to elderly men, but keep the lower limit of the reference range constant for women.^{14,15} This study would suggest that physicians in Maryland tend to work up patients with hemoglobin levels that are lower than the absolute lower limit of the 95th percentile reference range found in the above studies.

Lipschitz et al¹ studied 196 healthy geriatric patients and found 42 women (21.4%) had a hematocrit of less than 0.36 (36%) and 9 men (34%) less than 0.40 (40%). After careful evaluation, the cause for the anemia could only be found in five patients (three had iron deficiency and two had anemia of chronic disease). The high prevalence of anemia in this study may in part be explained by the high proportion of black female patients and the relatively low socioeconomic status of this group. Blacks have lower hemoglobin levels than whites even after adjusting for transferrin saturation, income, education, and other socioeconomic variables.¹⁶ The percentage of women with low hemoglobin levels is lower than that of men. A critical review that looked at studies of both selected and unselected populations concludes that once health factors that might affect erythropoiesis, socioeconomic status, and race are excluded, then older women have no higher incidence of anemia and have an iron status comparable to or better than younger women.⁸ This finding would further support the argument that lower cutoff levels for diagnosis and workup should not be adopted for elderly women. The lower level of hemoglobin in elderly men may be due to an altered end-organ receptor response to testosterone, since reduced levels of testosterone have not been found in elderly male anemic patients.¹

In a later study of elderly white men, Lipschitz et al⁶ reported a 19.5% (38 of 195) prevalence of anemia, and 66% (26 of 38) of the anemic group had no identifiable cause found after an extensive workup that included testosterone assay, 2, 3-diphosphoglycerate acid, and bone marrow examination. Assessment of hematopoiesis in these individuals revealed significant decreases in differentiated bone marrow cells of the myeloid, erythroid, and megakaryocyte lines. The level of the most primitive erythroid

precursor cells (BFU-E) was not reduced, suggesting an abnormality of cellular proliferation in the elderly patients with anemia. Animal studies¹⁷ confirm the postulate of a reduced level of responsiveness to stress rather than a disorder of basal hematopoiesis. Thus, from this work it would appear that the yield is low in working up low-grade anemias in elderly patients.

Limitations of the study are that the response rate was low and therefore the findings may not reflect the beliefs of all physicians. Because these were self-reported data, the survey may not accurately reflect what actually takes place in practice behaviors of physicians. Further surveys of a larger population of physicians may yield different results.

There is no "cookbook" approach to an anemic elderly patient, and the workup for anemia is a highly individualized process. These data show that tests such as stool testing for occult blood, blood smear, and reticulocyte count are highest in priority for the initial workup of healthy elderly patients with anemia. Less priority was given by the physicians surveyed to serum folate, serum B₁₂, ferritin level, protein electrophoresis, sedimentation rate, and BUN. Bone marrow examinations are rarely felt to be indicated.

Does the entity of anemia of senescence really exist, or should physicians be doing complete workups on all otherwise healthy elderly patients with hemoglobins of less than 8.69 mmol/L (14 g/dL) in men, or 7.45 mmol/L (12 g/dL) in women? In an elderly patient, there is a tendency to ascribe an abnormal hematologic value merely to the aging process. This clinical determination is difficult, and requires a knowledge of all the confounding diseases and social variables before it can be made about appropriate evaluation. Only through further study of relatively healthy elderly individuals with anemia of undetermined cause will it be possible to feel secure in the diagnosis of anemia of senescence and its significance, if any. The real question, as yet unanswered, is of the clinical significance of anemia of undetermined cause, not whether it exists. In the current climate of scientific debate about whether an anemia of senescence exists, however, practicing physicians, especially those who see many elderly patients, act as though there is an anemia of senescence.

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