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Iron, Vitamin B12, and Folate Deficiencies Have “Dreadful Consequences,” but Treatments Are Available

By Christine Kilgore

Anemia is not a normal consequence of aging — it is an overlooked sign of underlying illness, so the approach should be to evaluate, delineate, and address the cause or causes, said T.S. Dharmarajan, MD, at the Annual Conference of AMDA – The Society for Post-Acute and Long-Term Care Medicine.

Causes of anemia include renal insufficiency, chronic inflammation and disease, deficiencies of iron, folate, and/or B12, and unexplained causes. “And they’re not mutually exclusive. You should not be satisfied with eliminating one cause,” said Dr. Dharmarajan, professor of medicine at Albert Einstein College of Medicine and vice chairman of the Department of Medicine and clinical director of the Division of Geriatrics at Montefiore Medical Center (Wakefield campus) in the Bronx.

“Anemia has dreadful consequences” that are well-documented in the literature, he said, including lethargy and weakness, reduced lower muscle strength, impaired gait and mobility, falls and fractures, worsened cognition, increased hospitalizations and lengths of stay, and worsened coronary artery disease (CAD) and left ventricular hypertrophy. Anemia is also now believed to worsen and predispose patients to chronic kidney disease, he said.

Across studies, “anemia consistently increases the size of the heart, increases left ventricular hypertrophy, and worsens the manifestations of CAD and heart workload until you get heart failure,” Dr. Dharmarajan said, during a session on the management of chronic conditions.

A 2017 prospective cohort study of over 32,000 outpatients with stable CAD in 45 countries showed that over four years of follow-up evaluations, low hemoglobin was an independent predictor of cardiovascular events and mortality, he noted (Am J Med 2017;130:720–730). “I’ve had a lot of experience with heart failure readmissions in quality improvement projects. About 30% to 40% of them are severely anemic, with a hemoglobin between 8 and 10 [g/100 mL]. Why are we not treating a basic [contributor] to heart failure?”

A basic evaluation for anemia includes a history and physical examination; review of medications and dietary habits; assessment of stool for occult blood; renal function review through estimated glomerular filtration rate, ferritin levels, and transferrin saturation; assay of serum B12 and folic acid; and measure of reticulocyte count and indirect bilirubin. “This is very simple and within our means!” as primary care providers and geriatricians, he said.

An assessment of thyroid function is also now considered more of a standard than something to be individualized, he noted. Other components of the evaluation can be individualized, and may include the Coombs test to detect antibodies against red blood cells, serum protein electrophoresis, bone marrow studies, and upper and lower endoscopy.

Endoscopy, he said, “comes up on the top of this list.” “I’m a primary care doctor, not a hematologist, and in at least 80% of my patients with anemia, I don’t need to make a referral. If I have to, the most common referral I make is to the gastroenterologist,” he said.

Testing serum ferritin is important, but the results should be interpreted with caution because liver disease, pressure ulcers, and inflammatory conditions...
The year 2020 has been filled with surprises, if not bewilderment, for us all. It is unlikely that any of us could have predicted a year ago — or six months ago, or even three months ago — what our world would be like today. COVID-19 has truly turned the planet on its ear. My previous watershed event for before and after used to be the attack on the World Trade Center on September 11, 2001. I measured my thoughts by what life had been like before 9/11 versus afterward. My frame of reference has now changed to what the world was like “pre-COVID-19” and will be measured by “since COVID-19” in the future.

Just today I was trying to remember the last time I stood in line at my favorite Greek restaurant, went for a haircut, was able to fly to Florida to visit my grand-children — or even bought toilet paper freely. These things are small in comparison to the risks everyone on the front lines of the coronavirus battle faces, but they have become significant measures in my world today. It seems a lifetime of the coronavirus battle faces, but they have become significant measures in my world today. It seems a lifetime of the risks everyone on the front lines of the coronavirus battle faces, but they have become significant measures in my world today. It seems a lifetime of COVID-19 versus afterward.

My epiphany from this is how everything we regard as so constant and consistent is quite fragile. In December, the worry was whether the presents for your loved ones would arrive in time for Christmas. Now it is whether we all will be alive for next Christmas in this age of COVID-19.

How to survive, if not thrive, in the current environment has been taught to me by those I admire the most: AMDA — The Society for Post-Acute and Long-Term Care Medicine itself, and you — the membership. The answer is to be nimble. Let me provide examples. I have watched the Society’s membership in 2020 recognize the threat of COVID-19 to the vulnerable residents in our facilities and move into attack mode. You pivoted to meet the threat of a disease never encountered before. Without proven treatments, vaccines, adequate testing, or sufficient personal protective equipment, you nimbly changed into some of the most informed clinicians in the country in treating this coronavirus scourge. You have worked tirelessly to keep staff and residents protected. In your medical director role, you have helped skilled nursing facilities to be nimble themselves and revise their processes to battle COVID-19.

The responsiveness of the Society’s staff to the demands induced by the pandemic was as stunningly impressive as we were able to observe as it was instructive. Our nimbleness was an Olympic sport, you each would be gold medal winners.

Your Foundation salutes each of you, your facilities, and your courageous staffs, along with Chris Laxton and the amazing Society staff. Your selfless shifting in response to the threat and changes posed by COVID-19 has been remarkable. Without strict vegetarianism, the use of metals in food, and the combination of the two — with time to a SNF admission and time to an adverse cardiovascular event (CV) in older adults with a new diagnosis of Alzheimer’s disease (JAMA Neurol Open 2019;2:190213). The three AChEI inhibitors included in the study were donepezil hydrochloride, rivastigmine tartrate, and galantamine hydrobromide. The study was conducted in a 5% random sample of Medicare beneficiaries (N = 73,475).

There was no difference in the time to SNF admission between the groups. An increased risk of a CV event due to bradycardia and syncope was observed in the AChEI and combination therapy groups versus the memantine treatment group. In pairwise comparisons of individual AChEI groups, combination therapy, and memantine, the only statistically significant difference for CV events was found in the comparison between memantine monotherapy versus donepezil monotherapy. The difference was again driven by bradycardia and syncope. The study’s limitations included possible exclusion of diagnoses other than Alzheimer’s disease, the use of claims data, and selection of new prescriptions only.

“We need to be cautious in the setting of CV disease and fall and syncope risk and weigh the risks of these medications against a potentially small benefit,” said Mila Little, DO, CMD, an associate professor at Duke University, who presented the study. Paraphrasing a beloved cartoon character, Daniel Tiger, she sang, “First, do no harm, but what is the actual benefit?” — an adage that would resonate with so many providers working in PALTC.

Dr. Boyum is the managing editor of Caring for the Ages.

Unlike B12, folate is present in virtually all foods, but its availability falls when food is cooked with heat. Malnutrition/malabsorption is one cause of folate deficiency; others include excess utilization (e.g., psoriasis, hemolysis), excess loss (e.g., dialysis, liver disease), and heavy alcohol use, which inhibits enterichepatic circulation.

Folate deficiency can be treated with 1 mg of folic acid daily, but cobalamin deficiency should be ruled out before treatment. “Make sure they’re not B12 deficient. If they are, the deficiency will be masked [by folic acid supplementation] and will progress,” he said.

A blunted erythropoietin response to anemia is a primary reason for anemia caused by chronic disease, making it important to distinguish between anemia of chronic disease and iron deficiency, Dr. Dharmarajan said. In patients with chronic kidney disease, erythropoietin deficiency is the primary cause for anemia, though other causes may exist and should be ruled out, he said.

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