



Introduction:

Welcome to the clinical case-series, “Reasoning without Resources,” by Prof. Gerald Paccione of the Albert Einstein College of Medicine. These teaching cases are based on Prof. Paccione’s decades of teaching experience on the medical wards of Kisoro District Hospital in Uganda. They are designed for those practicing in low resource settings, Medicine and Family Medicine residents, and senior medical students interested in clinical global health. Each case is presented in two parts. First comes a case vignette (presenting symptoms, history, basic lab and physical exam findings) along with 4-10 discussion questions that direct clinical reasoning and/or highlight diagnostic issues. A month later, CUGH will post detailed instructors notes for the case along with a new case vignette. For a more detailed overview to this case-series and the teaching philosophy behind it, see [Introduction to “Reasoning without Resources.”](#) Comments or question may be sent to Prof. Paccione at: gpaccion@montefiore.org

About the Author:

I’m a Professor of Clinical Medicine at the Albert Einstein College of Medicine in the Bronx, New York, where my career has centered on medical education for the past 40 years – as a past residency Program Director in Primary Care and Social Internal Medicine at Montefiore Hospital, and global health advisor and program leader at the school. I’ve served on the Boards of Directors of Doctors for Global Health, Doctors of the World USA, and the Global Health Education Consortium. I spend about 3-4 months a year in Uganda working on the Medicine wards of Kisoro District Hospital which, like most hospitals in the world that serve most of the world's population, has (almost) no resources. "At the bedside", I teach Internal Medicine residents and medical students how to assimilate the elements of history, physical exam and epidemiologic probability into a diagnostic impression that, even without definitive testing, can lead to appropriate therapeutic strategies in the field.

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Case 57: The Slow Decline

A 58 year old woman from Mutumbira village in the Kisoro district, a peasant and mother of a nurse at KDH, is admitted with increasing confusion and incontinence for weeks-months.

She was well and fully functional until about 3 years ago when she began to lose her appetite. Food tasted bland, and she lost weight. According to her daughter, within a year she became very weak, unable to dig, and “very wasted”, all clothes fitting loosely. She fatigued easily and was breathless on minimal exertion, and at times couldn’t get up from the toilet. A year later (two years prior to this admission) she was admitted to Kisoro District Hospital, noted to be very pale with a hemoglobin of 6g/dl, and transfused 2 units of blood (to a post-transfusion Hb of 9). At home she felt stronger and started to do some light work. She had never been told of anemia before (though never had blood tests), bore 3 children without complications, and could not tell the color of her stools since she used a pit latrine.

Despite albendazole, iron tablets and multivitamins, within 4 months she again became very weak and “pale”, now frequently bedridden, with intermittent sharp chest pains and new “sores” on her tongue (neither were further specified). She was re-admitted with a hemoglobin of 5 and again transfused 2 units. She felt stronger and wanted to go home but her daughter insisted that she live with her a while prior to her (daughter’s) departure for advanced nursing studies in Kampala. Under her watchful eye, her daughter thought she recovered more slowly this time, but after 4 months her mother finally got her wish to go home to her village, feeling “better”. Months later she was re-admitted for incapacitating weakness, and was again re-transfused. Throughout, she noted no melena or blood in her stools, nor fever or sweats. Her menses had been normal, ended 8 years ago, and she had no vaginal bleeding since. She does not drink alcohol, and neither she nor her devoted husband had risks for HIV.

Three months post-discharge and 2 months prior to this admission, the patient developed confusion. She feared being seen, didn’t recognize people, refused to eat or drink, and was frequently found talking to herself alone. Her daughter returned from Kampala and immediately called a psychiatrist in the capital who ordered Amitriptyline 50 mg/day. However, after the first dose, the patient slept for 2 days and upon awakening refused to take any more. A month later she was totally bedridden because of weakness and inability to walk steady, and totally confused, refusing to and unable to remember eating or drinking. She began mindlessly picking at her bedding, feared noises, and felt that animals were coming to attack her. A couple of weeks after she became incontinent of both urine and feces and disoriented to place and time (hour, date and month), her family brought her to the hospital again for what they feared would be her terminal admission.

Physical Exam:

Middle-aged woman, looking older than her age, sitting, staring, in no distress, “pleasantly dazed”
BP: 126/75 lying to 98/70 on standing; HR 115 to 118; RR 20; T 97.0

Skin: normal, without rashes

HEENT: Eyes: PERRLA, EOM full; conjunctiva pale, non-icteric; fundi benign without hemorrhages, exudates or papilledema;

Mouth: tongue erythematous patches with linear ulcer on side, 2 cm x 0.4cm; no thrush;
Breath without musty or unusual odor; ENT: normal,

Neck: no lymphadenopathy, JVP 5 cm above angle of Louis; no HJR; thyroid palpable, normal;

Lungs clear to percussion and auscultation

Heart: PMI hyperdynamic, 1 cm lateral to MCL, 2 cm diameter; no RV lift; S1, S2 normal without S3, S4, or rubs; Gr 2/6 early peaking SEM LSB without radiation;

Abdomen: no hepato-splenomegaly, masses, tenderness; guaiac (-) brown stool; rectal tone decreased

Extremities: no edema, clubbing, pulses intact;

Neurologic: Mental Status: disoriented to time and place; unable to count to 10; recognizes daughter but not her friend, follows simple commands; 0/3 short-term memory

Cranial Nerves: intact II-XII;

Motor: 5-/5 diffusely;

Sensory: decreased vibration knees to feet with both 256 and 128 tuning fork, and fingers with 256 fork; proprioception diminished index and big toe on right, index toe on left; intact fingers;

Reflexes: + 2 upper extremities; +3 knees with myoclonus; absent ankle jerks bilaterally

Gait: unable/unwilling to stand; Romberg couldn't be tested, nor could Cerebellum be evaluated.;

1. What is the frame of this case by history (the key clinical features the final diagnosis must be consistent with)?

- 61 year old woman with a gradual 3 year decline
- Severe anemia, with transient symptomatic responses to transfusions for 2 years.
- Only 3 children (re-anemia); no melena or blood noted in stool, no vaginal bleeding; no fevers or sweats, no hepato-splenomegaly; but with significant weight loss
- No response to iron, multivitamins, albendazole.
- Confusion, disorientation, inability to walk and incontinence, progressive, weeks-months
- Unable to taste food and Tongue with erythema, atrophy and linear ulcer

The “frame” is that of a middle-aged woman with symptomatic severe anemia of >3 years duration that is later associated with florid neuropsychiatric symptoms. Of significance, despite 3 years of symptoms, there're still no other exam clues to common processes that cause anemia: no obvious sources of blood loss (GI tract, vagina), reticulo-endothelial involvement/infiltration (liver, spleen, nodes), or signs of inflammation; and no response to iron or multivitamins.

2. What are the most common causes of anemia in East Africa in women in their 50's?

Although there are no rigorous studies that address this specific demographic, the most common cause of anemia in women in East Africa is probably iron-deficiency. Multiple pregnancies and menses with inadequate dietary iron, frequently compounded by hookworm (often with guaiac (-) stools), schistosomiasis, and/or trichuris parasitic infections make iron deficiency anemia extremely common. H.Pylori is highly endemic and can cause iron deficiency via peptic ulcer disease-induced GI bleed or gastritis-achlorhydria-induced iron malabsorption; and intestinal polyps, cancers and AVMs, though less common than in the West, are also seen but go undiagnosed in rural Africa. Cervical cancer is common, indeed the most frequent cause of cancer death in Ugandan women, and can cause iron-deficiency anemia through chronic vaginal bleeding.

Common infections in Africa/Uganda - HIV, malaria and TB - all can cause anemia through multiple mechanisms including cytokine-induced "anemia of chronic inflammation", direct bone marrow suppression, hypersplenism/sequestration, and hemolysis.

Viral infections endemic in Africa induce various malignancies associated with anemia, again through various mechanisms: HIV- related lymphomas and Kaposi Sarcoma (common mechanisms being cytokine marrow suppression, splenic sequestration, and GI blood loss); HSV-8 and Kaposi Sarcoma (either related or not to HIV); HPV and cervical cancer, through vaginal bleeding (as noted above); and Hepatitis B and Hepato-cellular carcinoma which can cause either an anemia through cytokine marrow suppression or polycythemia through para-neoplastic erythrocytosis.

Megaloblastic anemias are often undiagnosed and under-reported in Africa, but the few reports that do exist suggest that vitamin B12 deficiency is extremely common. It is usually due to Pernicious Anemia, and affects women 2-to-1, usually at a younger age than in the West. Folate deficiency is also prevalent, especially in alcoholics who are often among the poorest of a generally malnourished population whose diet incorporates few leafy green vegetables. (N.B. Ugandans drink more alcohol per capita than any other people in the world according to the WHO.)

3. What is the differential diagnosis of this patient's illness, and the pros and cons of each possibility? What's the most likely diagnosis and why?

The central theme of the differential is "anemia and mental status change". The key question is, are they linked and if so, how? Possibilities include: through the same pathophysiologic process manifesting in different organs, one process leading to increased susceptibility to another, or two separate processes occurring sequentially over time in a population with a very high burden of disease.

- HIV-associated anemia with later development of HIV-related dementia/psychosis or CNS opportunistic infections/malignancies. HIV has been prevalent in Africa for over 30 years; in some long-term survivors it can present decades after initial infection; and social history is not infrequently and not surprisingly inaccurate. HIV causes weight loss, anemia and marked weakness, and later culminate in nervous system opportunistic pathology that can mimic this presentation with dementia, psychoses, and incontinence (myelopathy). However, severe anemia is a powerful negative prognostic indicator in HIV disease, and 3 years since initial symptoms would likely be too long to survive without therapy. The absence, in the interim, of common opportunistic infections, fevers or thrush almost rules out the diagnosis clinically.*

- *Multiple myeloma complicated by CNS infection, hypercalcemia, or uremia. Myeloma can cause the weight loss and severe refractory anemia without reticulo-endothelial involvement; and indirectly, the later neuropsychiatric symptoms through infectious or metabolic complication of the disease. However, the time course is (again) long for an untreated malignancy that would have been far advanced a few years ago, she has had no bone pain or fractures that are often seen with myeloma, and myeloma wouldn't explain the dysgeusia or lingual atrophy/ulcers.*
- *“Cancer” causing anemia through GI blood loss or marrow replacement, with neurologic symptoms caused by either metastatic disease to the CNS or para-neoplastic electrolyte imbalance, e.g. hyponatremia (SIADH) or hypercalcemia. The problem with this hypothesis is the lack of history or exam evidence of a primary tumor (e.g. blood in the stool, etc.), or of metastatic disease: most cancers that cause weight loss are metastatic/widespread, and overt abnormalities (e.g. hepatomegaly with intestinal adenocarcinomas or splenomegaly/lymphadenopathy with lymphomas) 3 years post-symptom onset would be expected.*
- **Vitamin B12 Deficiency:** ... *the diagnosis in this patient.*

Vitamin B12 deficiency is the paradigmatic disease causing anemia and neuropsychiatric dysfunction. It's most commonly caused by “pernicious anemia” (PA) from autoimmune destruction of the gastric parietal cells and loss of the “intrinsic factor” necessary for vitamin B12 absorption in the ileum. In the West, B12 deficiency is more common in women (2:1 ratio), presenting at an average age of around 60. Symptoms have usually been present for more than 6 months prior to diagnosis although in Africa, as in the pre-modern era in Western medicine, the lag is considerably longer. During this time, non-hematologic complications of B12 deficiency often arise - as in this patient who finally presented with a florid case of “megaloblastic madness”.

The deficiency affects hematologic stem cell maturation and thus every cell line - erythrocytes, granulocytes and platelets, with usually the “megaloblastic anemia” coming first after erythrocyte size increases. (Thus the MCV usually enlarges before the anemia develops, the opposite of the sequence in iron-deficiency anemia in which the hematocrit falls to around 30 before the MCV decreases). By the time patients with PA become symptomatic from anemia, the MCV is usually over 110 unless complicated by a competing microcytic process.

B12 deficiency affects rapidly dividing cells in the intestines as well as the bone marrow and thus can induce secondary malabsorption of other nutrients, particularly relevant to rural populations in Africa with borderline nutritional and micronutrient intake. Thus folate is poorly absorbed compounding the megaloblastosis; and since iron requires acid for maximal absorption and patients with PA are achlorhydric, over a third of patients with PA are iron deficient in the West, probably more in Africa. (N.B. Despite cellular deficiencies, paradoxically high levels of serum folate and iron can result from their inability to enter or be utilized by B12 deficient cells, and a co-existing iron deficiency can blunt the increase in the MCV, confounding diagnosis.)

The development of severe anemia explains this patient's initial symptoms of dyspnea, weakness and fatigue and the cycles of improvement and relapse after transfusion (and possibly treatment with multivitamins), and a nutritional etiology of the anemia explains the absence of blood loss, signs of inflammation or organ infiltration. As is common in areas without physicians or diagnostic resources, she lived with the anemia for over 2 years before manifesting clear-cut neurologic complications of the vitamin deficiency state.

Neuropsychiatric manifestations affect 30-40% of those with B12 deficiency and are protean, affecting the peripheral nerves, posterior columns of the spinal cord, and the brain. It used to be thought that the neurologic manifestations always followed the hematologic ones, but classic studies from New York in the '90's (Lindenbaum, et al; Healton et al) of a large series of 143 patients with neuropsychiatric manifestations of B12 deficiency demonstrated that in 80% of those who develop them, the neurologic symptoms came first. Studies in this cohort also revealed the following:

- the most common symptom, in >70%, was "pins and needles" paresthesias bilaterally in the feet and hands;*
- gait ataxia was present in ~25%;*
- other symptoms included leg weakness, autonomic dysfunction (orthostasis, incontinence) in 7% and mental status changes (global dementia, memory loss, psychosis) in 10-15%;*
- of those with mental status changes, 95% had other exam findings of B12 deficiency, and 80% had decreased vibratory sensation;*
- progression of disease occurs slowly, over weeks to months.*

Our patient developed almost all of the neuropsychiatric manifestations of B12 deficiency: leg weakness, inability to walk due to unsteady gait, incontinence, and finally psychosis, "megaloblastic madness", so-called in the initial reports of the disease.

4. Explain the neurologic and oral examinations in this patient (in light of the likely diagnosis).

B12 deficiency causes both peripheral nerve and spinal cord dysfunction: peripheral nerve disorders are characterized by distal, symmetric sensory loss and diminished reflexes, while spinal cord disease manifests spasticity, extensor plantar reflexes, hyperactive reflexes, and segmental vibratory or sensory levels. Either one or both together can cause impaired proprioception, non-segmental vibratory loss, or autonomic symptoms such as orthostasis without compensatory increase in heart rate (Healton, et al, Medicine, 1991).

In this patient with incontinence, orthostasis without a compensatory rise in HR was noted on exam.

Neurologic exam revealed disorientation, memory loss and inattention - all signs of advanced dementia. The history told a story of paranoid psychosis, well-described in B12 deficiency. (N.B. The dementing illness, having evolved over months, is too rapid for Alzheimers).

The motor exam revealed diffuse, mild weakness seen in B12 deficiency.

The sensory exam, which was challenging and possibly inaccurate because of the patient's dementia, showed loss of vibration below the knees to both 256 and 128 tuning forks, and in the hands to the

256 fork. Vibration sense is diminished in ~70% of those with B12 neurologic disease; the 256 fork is the more sensitive instrument to assess early loss. (So the deficit in the legs was more severe.) Proprioception is abnormal in ~50% of those with B12 neurologic disease, always accompanied by diminished vibratory sensation. Loss in the index toe is more sensitive than the big toe, thus sometimes the index toe is the only location that reveals the dysfunction.

The Reflexes are hyperactive with knee myoclonus consistent with B12 myelopathy, and the loss of ankle jerks suggests an associated peripheral neuropathy.

Gait could not be tested, but the history of unsteadiness suggests ataxia.

Neither could Romberg test be done. However, of note, only about 10% of those with B12 neurologic disease have a positive Romberg test.

Oral exam: B12 deficiency frequently causes oral symptoms and signs, and loss of taste was one of the first symptoms the patient complained of 3 years ago. B12 deficiency can cause glossitis with red patches of inflammation, lingual atrophy involving 50% of the tongue, oral ulcers, stomatitis, and cheilitis – all considered non-specific and seen in other nutrient deficiencies. Our patient had patches of inflammatory glossitis, and linear ulcers. Linear ulcers have been described (Grells, et al J.Am.Acad.Derm 2009, p.498), as seen in this patient, and proposed as a specific and possibly early manifestation of B12 deficiency (though not “early” in this case!).

5. How common is this disease in Africa, and what factors contribute to its prevalence and/or symptomatic expression?

Since little clinical research has been done on diseases other than malaria, HIV and TB in Africa, the prevalence of megaloblastic anemia is unknown outside a few reports (e.g. from the Gambia, Trans.R.Soc.Trop.Med.Hyg 1986, 80:557; Nigeria, Clin Lab Hematol 1996, 14:33; Zimbabwe, Br.J.Hematol 1994, 86:844). All suggest that B12 deficiency is quite common but under-recognized. The most common cause is Pernicious Anemia, found in ~80% of megaloblastic anemias in Africa, and consistent with reports from the U.S. in African Americans in which a prevalence of B12 deficiency due to P.A. was found to be slightly higher in blacks than in whites, and often presenting at a younger age.

Besides (possibly) genetics, many other factors conspire to make B12 deficiency prevalent in Uganda:

- AIDS: low B12 levels have been reported in from 10-40% of patients infected with HIV probably due to AIDS enteropathy and malabsorption, poor nutrition, etc. The number is probably higher in Uganda.

- Poverty, diet and pregnancy: B12 is found in meat and dairy products, which are expensive in rural Uganda and infrequently consumed. In the Mt. Kenya region of Kenya, B12 intake was inadequate in 44% of toddlers and 86% of school-aged children and associated with megaloblastic anemia in 4-8% of children.

Borderline B12 intake can become overt deficiency when “stressed” by increased requirements such as pregnancy: in one study in Malawi, 33% of pregnant women had a low serum B12 level, and in 16% it was severe (<50pmol/L!).

- H.Pylori infection: H.Pylori gastritis diminishes acid production and with it, iron absorption and iron stores independent of (infrequent) HP-related peptic ulcer bleeding. One hypothesis holds that HP causes P.A. by inducing autoimmune gastritis which then leads to first iron and then B12

malabsorption. *H. Pylori* infection is highly prevalent in Africa, and if these hypotheses hold, may contribute to the prevalence of B12 deficiency.

- Medications: omeprazole decreases gastric acid, needed to release dietary B12 from protein binders and allow the IF-B12 complex to form. It is often prescribed for non-specific gastric ailments. Pyrimethamine and trimethoprim, both commonly used prophylactic drugs in HIV, (weakly) inhibit dihydrofolate reductase and the resulting interference with folate metabolism could precipitate megaloblastic anemia.

- TB ileitis: TB is highly prevalent in Uganda, and involvement of the ileum a common location of extra-pulmonary, intestinal TB. Although infrequent overall, and with ensuing symptoms clearly dominated by the intestinal TB, ileal disease causes malabsorption of the IF-B12 complex and B12 deficiency.

6. Why is this diagnosis infrequently made in rural Africa?

What test(s) can be done to support the diagnosis?

B12 deficiency is very much a laboratory diagnosis until it's advanced, lab resources aren't available in most district hospitals for more than a hematocrit or sometimes a CBC; there are many competing and more common causes of anemia (discussed above), some of which mask the diagnosis; and neither district health providers nor physicians are familiar with the disease since its prevalence in Africa has been unknown and the disease under-reported.

By the time the patient is symptomatic from anemia (and even sooner), a careful examination of the peripheral blood smear should be diagnostic in the hands of hematologists: the most sensitive marker is neutrophil hypersegmentation: >5% 5-lobed polies, or 1% 6-lobe polies is considered diagnostic of megaloblastic anemia with a sensitivity of >95%, although this finding is missed in ~1/3 of routine lab evaluations. (Chronic renal failure rarely causes hypersegmentation.)

Other findings on smear include macro-ovalocytes (a normal RBC on smear is about the size of a lymphocyte nucleus), poikilocytosis, and possibly thrombocytopenia (seen in only 20% however).

The best test, and the "gold standard" of diagnosis, is response to therapy. (In the U.S., elevated levels of serum methylmalonic acid and total homocysteine are useful in confirming the physiologic relevance of low serum B12 levels).

7. What are the most common pitfalls in the diagnosis of this disease?

The most common diagnostic pitfalls include:

- causes of microcytosis are present simultaneously, thus masking the increase in MCV expected in megaloblastic anemias. The most common of these are iron-deficiency and alpha-thalassemia, both of which are common in African women. In nearly all cases of "normocytic" anemia due to B12 or folate deficiencies, a co-existing cause of microcytosis is present.

- neurologic manifestations of B12 deficiency can occur independent of hematologic manifestations. The hematocrit is normal in ~25% of patients with B12-neurologic dysfunction, the MCV normal in 25%, and both are normal in 15-20%. (However most of these patients (>95%) will have hypersegmentation on experienced review of the smear.) Thus, absence of anemia does not mean that B12-induced neurologic disease is not present.

- response to therapy as a diagnostic test can be blunted by co-existing deficiencies in iron and folate, which are common.

- in B12 deficiency, a rise in hematocrit may be seen if folate alone is given, but this may worsen the neurologic sequelae of the B12 deficiency.
- pancytopenia is a late manifestation of B12 deficiency. Anemia frequently exists without granulocytopenia or thrombocytopenia.
- as discussed above, normal serum folate and iron levels can be misleading if ordered soon after the diagnosis of B12 deficiency. If one is interested in documenting coexisting deficiencies (instead of simply treating for them), RBC-folate should be ordered and iron stores measured only after 3 weeks of B12 therapy.

8. How is the disease treated, and what response can be expected?

What are the predictors of therapeutic response?

Treatment of symptomatic disease is with parenteral B12 IM, 1000 micrograms for days to a week, followed by monthly injections of 250 or q 2-3 monthly injections of 1000 micrograms - for life. If particularly anemic, a brisk reticulocytosis is expected and hypokalemia can occur. Folate and iron should be co-administered, certainly in Africa.

About 1% of a large oral dose is absorbed by passive diffusion, and thus maintenance dosing can also be through the oral route aiming to supply about 5 micrograms daily. Thus oral doses of 500-1000 micrograms/day can also be administered.

Hematologic disease responds to therapy, and indeed is the gold standard of diagnosis of B12 deficiency anemia/pancytopenia.

Neurologic disease completely responds in ~50% of cases, and the other 50% of patients usually have an incomplete, partial response to therapy. Overall, ~75% of deficits resolve. In Lindenbaum's series, 11/18 with changes in mental status fully recovered.

The severity of the preceding dysfunction, and its duration are inversely correlated with the completeness of the response (i.e. the longer and more severe the dysfunction, the less likely to have a complete response. Most severe neurologic compromise responds partially.) Almost paradoxically but probably based on patient selection and the reason patients come to medical attention, the higher the hematocrit the more severe the neurologic disease and the less likely they are to have a complete neurologic response.

Paresthesias often respond within days; other deficits usually take 2-4 weeks with the maximum response occurring within 6 months (all who will respond will show some response within 3 months). Rare patients continue to improve beyond 6 months of therapy, up to a year.

9. What are some of the key themes in clinical diagnosis illustrated by this case?

This patient's case history is a good example of important diagnostic themes in medicine:

a) the importance of timing: as noted, many diagnoses in the differential of "anemia and neuro-psychiatric symptoms" in this patient are nearly ruled out clinically, in the context of her symptoms' severity, by the duration and evolution of her illness. i.e. her course was too long for cancers or HIV without other manifestations appearing, and too short for Alzheimers, etc.

- b) the severities of the anemia and neuro-psychiatric symptoms in this middle-aged patient are extreme and thus more “specific”, suggesting that they were likely to be manifestations of a single disease process despite their separation in time;*
- c) the relevance and importance of the “frame”: i.e. of sitting back, thinking, and defining the key clinical elements that the final diagnosis had to be consistent with. The frame of this patient’s case is diagnostic of B12 deficiency, but if not synthesized and evaluated in the context of the whole, each feature alone could be considered “non-specific”.*
- d) health disparities in Africa vs. “modern Western medicine” exposed: this patient would never have gotten to this stage of illness and near death in the U.S. - simply because of the (glaring) results of lab tests that would have been done “routinely” at some point in her ambulatory follow-up, revealing a state likely never suspected by the physician who ordered it!*

The patient’s Hb was 4.2, MCV 128, RDW 26, WBC 1.9; platelets 46,000

Post-treatment epilogue: the patient began treatment with IM B12, and after about 1-2 weeks confusion began to subside. After a month he was no longer incontinent. She began to acquire an appetite, and to remind her daughters to cook! After 6 weeks she was well-oriented to time and place, her neighbors and visitors, and began to walk again. Her CBC normalized.

Suggested Readings:

- Hershko C, Ronson A, Souroujon M, et al. Variable hematologic presentation of autoimmune gastritis: age-related progression from iron deficiency to cobalamin depletion. *Blood* 2006; 107:1673
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