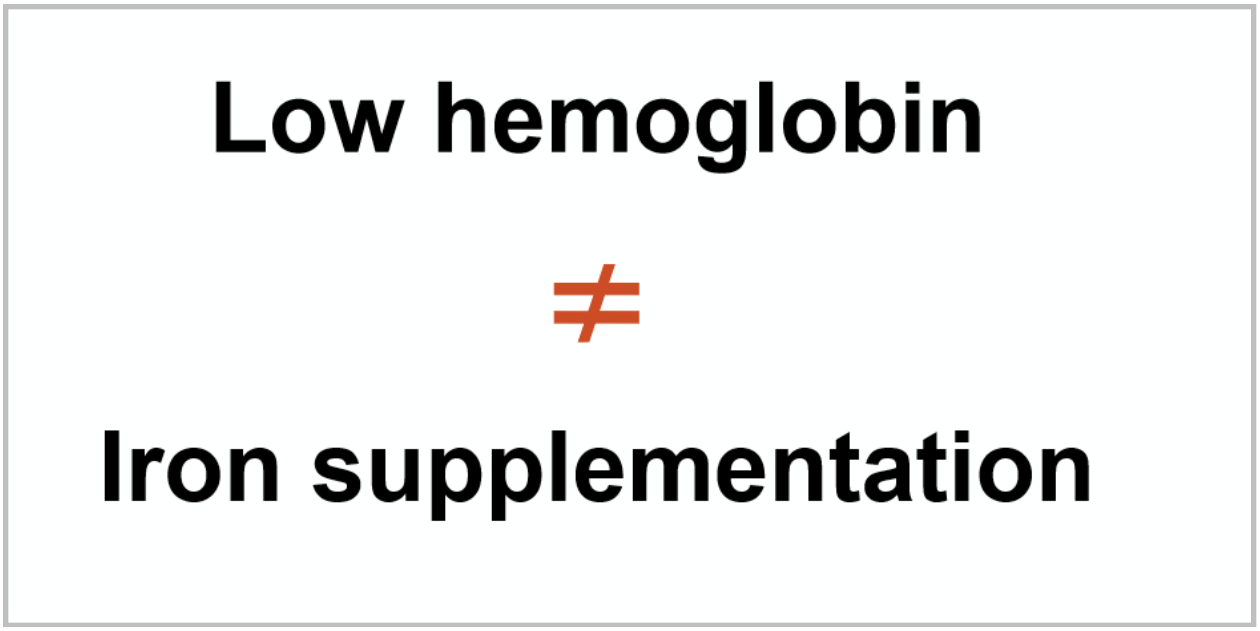
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Anemia of Chronic Disease

Hey, everyone. In this presentation, we're going to talk about anemia of chronic disease. Anemia of chronic disease, or ACD, occurs commonly, but it is the most misunderstood, under-diagnosed, and improperly treated form of anemia. In many cases, clinicians mistake it for iron-deficiency anemia and prescribe iron supplements, which not only don't provide benefit, they may actually be harmful or even fatal in some situations. ACD is also referred to as anemia of chronic inflammation, which is probably a better term because the patient doesn't have to have a life-threatening infection or disease in order to have it. It can be caused by something as simple as a viral infection, a UTI, H. pylori infection, or an autoimmune disease. Anemia of chronic inflammation is an adaptive or protective mechanism to limit the amount of iron a person absorbs when pathogens are present. All living things, including bacteria and cancer cells, depend on iron to sustain life.



The body regulates how much iron it absorbs based on two factors: it's own physiological need and the presence of any potential threats to health. If someone has normal iron metabolism and consumes more iron than they need, they will simply absorb less, but when inflammation is present, that triggers the release of chemicals that signal the iron regulation system to adopt a defense mode. The individual then absorbs only what is needed to make red blood cells but not enough to nourish pathogens or feed cancer cells. In this situation, hemoglobin levels will often decrease slightly, typically to the range of 9.5 to 10.5 g/dL, and stabilize at that level until the underlying condition is cured. Because so many clinicians wrongly assume that low hemoglobin equals iron deficiency, they will often prescribe iron supplements at this stage, which, as I mentioned, could exacerbate the problem. This can easily be avoided by running an iron panel with ferritin, as we do in the case review. Low ferritin and low iron saturation with high TIBC or UIBC would make iron-deficiency anemia apparent, and this would actually occur before hemoglobin

drops, which as you know doesn't happen until the last stage of iron deficiency, so this is a problem that is easily avoided with just routine lab testing that, unfortunately, is not a part of most basic workups in the primary care setting.

ACD and IDA iron marker comparison

	Serum iron	Serum ferritin	Iron saturation	TIBC/ UIBC	Soluble transferrin receptor	Reticulocyte hemoglobin content	Hemoglobin	MCV	RDW	White blood cell
Anemia of Chronic Disease (ACD)	Low	High	Low	Low	Normal	Normal	Low, but rarely <9.5 g/ dL	Normal to slightly low	Normal	High, low, or normal
Iron Deficiency Anemia (IDA)	Low	Low	Low	High	High	Low	Low; may be <9.5 g/dL	Low	High	Normal

Here is a comparison of lab markers for anemia of chronic inflammation or disease and iron-deficiency anemia. In ACD, serum iron and iron saturation are low because the body is trying to sequester free iron from potential pathogens or cancer cells. Serum ferritin, however, will be high because extra free iron is being collected by macrophages and stored in liver cells as ferritin. Ferritin can be used to distinguish between iron-deficiency anemia and anemia of chronic disease in about two-thirds of patients, but it is not reliable in the other third.

TIBC and UIBC are decreased when iron stores are high and increased when they are low, so in ACD, they are often but not always low because there is plenty of iron, but it is not easily available, whereas in iron-deficiency anemia, they would be increased because iron stores are diminished.

As you will recall from the iron overload and iron deficiency presentations, soluble, AKA serum, transferrin receptor is not affected by inflammation, and it can be used to distinguish between iron-deficiency anemia and anemia of chronic disease. If soluble transferrin receptor is high, that would be suggestive of iron-deficiency anemia, and if it is normal, that would be suggestive of ACD.

Reticulocyte hemoglobin content, which is abbreviated as CHr or RET-He, is a new sensitive marker of iron deficiency. Reticulocytes are the earliest erythrocytes released into blood and circulate for only one to two days. Some evidence suggests it is the most sensitive marker of iron deficiency and the first to go out of range, especially in children. It is unfortunately not yet widely available and not at all through LabCorp at the time of this recording, but some Quest locations around the U.S. do have it.

Hemoglobin is often low in both anemias but typically not below 9.5 g/dL in ACD. MCV is low in frank iron-deficiency anemia but would be normal or perhaps slightly low in ACD. RDW would be normal in ACD but high in iron-deficiency anemia. Finally, white blood cell is a marker of infection

and inflammation, as you know, so it could be low or high in ACD, or normal for that matter, whereas you wouldn't expect any changes in iron-deficiency anemia. Of course, given that it can be low, normal, or high in ACD, this is not really a useful marker to distinguish between the two, but it could be part of the overall pattern.

All of these markers here on this slide except soluble transferrin receptor and reticulocyte hemoglobin content are part of my case review blood panel. If you see anemia, and you're not sure if it is iron deficiency or ACD, you can order both of these markers, soluble transferrin receptor and reticulocyte hemoglobin content, to clarify the diagnosis. We will also have a handout that summarizes these markers for you and the difference between ACD and IDA that you can just quickly refer to.

Population	Risk factors
Elderly	H. pylori, other chronic inflammatory conditions common with aging
People with chronic infections	H. pylori, tick-borne illness, reactivated viral infections, GI pathogens
People with autoimmune disease	Rheumatoid arthritis, IBD, Hashimoto's, etc.
People with other chronic, inflammatory conditions	Osteoarthritis, interstitial cystistis, etc.

Populations at risk for anemia of chronic disease or inflammation include the elderly because of things such as H. pylori and other chronic inflammatory conditions; people with chronic infections, the obvious reasons; people with autoimmune disease such as rheumatoid arthritis, IBD, Hashimoto's, both because they are inflammatory and according to some research may be associated with infections; then people with other chronic inflammatory conditions such as osteoarthritis, interstitial cystitis, etc.

Let's look at a few cases. I don't have a lot of these. It is definitely not as common in my experience as iron-deficiency anemia or B12 or folate-deficiency anemia, except in the elderly, for whom it is the most common cause of anemia.

Marker	Value	Functional Range	Lab Range
Glucose	99	75 - 90	65 - 99
Hemoglobin A1c	5.5	4.8 – 5.4	4.8 - 5.6
Uric Acid	3.1	3.2 - 5.5	2.5 - 7.1
BUN	6	13 – 18	6 - 20
Creatinine	0.47	0.85 – 1.1	0.57 - 1.00
BUN/Creatinine Ratio	13	9 – 23	8 - 20
Sodium	138	134 – 140	134 - 144
Potassium	4.6	4.0 – 4.5	3.5 - 5.2
Chloride	97	100 – 106	97 - 108
C02	25	25 – 30	18 - 29
Calcium	8.8	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.0	3.5 – 4.0	2.5 - 4.5
Magnesium	1.9	2.0 – 2.6	1.6 - 2.3
Protein, total	5.9	6.9 – 7.4	6.0 - 8.5
Albumin	3.3	4.0 – 5.0	3.5 - 5.5
Globulin	2.6	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.3	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	<0.2	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	77	42 – 107	39 - 117
LDH	109	140 - 180	119 - 226
AST	13	10 - 30	0 - 40
ALT	9	10 - 22	0 - 32
GGT	18	0 - 28	0 - 60
TIBC	159	250 – 350	250 - 450
UIBC	144	150 - 375	131 - 425
Iron	15	85 – 135	27 - 159
Iron saturation	9	15 – 45	15 - 55
Ferritin	162	15 - 120	15 - 150
Vitamin B-12	654	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	28.7	35 - 60	30.0 - 100.0
Cholesterol, total	135	150 - 250	100 - 199
Triglycerides	94	50 – 100	0 - 149
HDL	45	55 – 85	> 39
LDL	71	0 - 175	0 - 99
T. Chol / HDL Ratio	3.0	< 3	0 - 4.4
Triglycerides / HDL Ratio	2.09	< 2	< 3.8
CRP-hs	158.87	< 1.0	0.00 - 3.00
Homocysteine	7.1	< 7.0	0.0 - 15.0

Marker	Value	Functional Range	Lab Range
TSH	1.010	0.5 – 2.5	0.45 - 4.500
T4, total	6.5	6.0 – 12	4.5 - 12.0
T3 Uptake	27	28 - 35	24 - 39
T3, Total	121	100 – 180	71 - 180
Copper	134		72 - 166
Zinc	68		56 - 134
Zinc / Copper Ratio	0.51	> 0.85	
Serum Methylmalonic Acid (MMA)	80	0 - 325	0 - 378
WBC	7.3	5.0 – 8.0	3.4 - 10.8
RBC	4.04	4.4 – 4.9	3.77 - 5.28
Hemoglobin	11.8	13.5 - 14.5	11.1 - 15.9
Hematocrit	36.1	37 - 44	34 - 46.6
MCV	89	85 – 92	79 - 97
MCH	29.2	27.7 – 32.0	26.6 - 33.0
MCHC	32.7	32 – 35	31.5 - 35.7
RDW	13.6	11.5 – 15.0	12.3 - 15.4
Platelets	417	150 – 415	150 - 379
Neutrophils	66	40 – 60	
Lymphocytes	18	25 – 40	
Monocytes	14	4.0 – 7.0	
Eosinophils	2	0.0 – 3.0	
Basophils	0	0.0 – 3.0	

This patient is a 31-year-old female with ulcerative colitis. She was in a severe postpartum flare when she came to see me. Red blood cell, hemoglobin, and hematocrit are all low, suggestive of anemia. If we relied only on hemoglobin, as many clinicians do, we might assume iron deficiency and prescribe iron. Look at her ferritin. It is high at 162. Her C-reactive protein is extremely high at 159. Yes, that's not a typo. Her platelets were also high at 417, and zinc-to-copper ratio was very low at 0.51, so there is definitely significant inflammation here. Her serum iron and iron saturation are low. Her iron was 15, and her iron saturation was 9, as you'd expect in ACD. Her TIBC is low at 159 rather than high, and that is also as you'd expect. This is a pretty classic textbook case of ACD, and giving this patient iron would absolutely be the wrong thing to do and could make her much worse.

Another similar case is a 29-year-old male with a very long list of complaints, 20 or so years of suffering with severe psoriasis, arthritis, swelling, SIBO, candida, leaky gut, potentially parasites, toxic overload, heavy metals, depression, anxiety, insomnia, headaches, hormonal imbalance, trouble gaining weight, food sensitivities, and methylation and detoxification issues. Those were the patient's own words on the intake form.

Marker	Value	Functional Range	Lab Range
Glucose	96	75 - 90	65 - 99
Hemoglobin A1c	5.4	4.4 – 5.4	4.8 - 5.6
Uric Acid	7.0	3.7 – 6.0	3.7 - 8.6
BUN	7	13 – 18	6 - 20
Creatinine	0.50	0.85 – 1.1	0.76 - 1.27
BUN/Creatinine Ratio	14	8 – 19	8 - 19
Sodium	139	135 – 140	134 - 144
Potassium	3.9	4.0 – 4.5	3.5 - 5.2
Chloride	99	100 – 106	97 - 108
C02	29	25 – 30	18 - 29
Calcium	8.9	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.9	3.5 – 4.0	2.5 - 4.5
Magnesium	2.0	2.0 – 2.6	1.6 - 2.3
Protein, total	7.6	6.9 – 7.4	6.0 - 8.5
Albumin	3.3	4.0 – 5.0	3.5 - 5.5
Globulin	4.3	2.4 – 2.8	1.5 - 4.5
A/G ratio	0.8	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.3	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	68	42 – 107	39 - 117
LDH	114	140 - 180	121 - 224
AST	9	10 - 30	0 - 40
ALT	7	10 - 29	0 - 44
GGT	12	0 - 40	0 - 65
TIBC	218	250 – 350	250 - 450
UIBC	192	150 - 375	111 - 343
Iron	26	85 – 135	38 - 169
Iron saturation	12	15 – 45	15 - 55
Ferritin	137	30 - 150	30 - 400
Vitamin B-12	776	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	116	35 - 60	30.0 - 100.0
Cholesterol, total	159	150 - 240	100 - 199
Triglycerides	57	50 – 100	0 - 149
HDL	37	55 – 85	> 39
LDL	111	0 - 175	0 - 99
T. Chol / HDL Ratio	4.3	< 3	0 - 5.0
Triglycerides / HDL Ratio	1.54	< 2	< 3.8
CRP-hs	139.94	< 1.0	0.00 - 3.00
Homocysteine	7.1	< 7.0	0.0 - 15.0

Marker	Value	Functional Range	Lab Range
TSH	2.410	0.5 – 2.5	0.45 - 4.50
T4, total	8.7	6.0 – 12	4.5 - 12
T3 Uptake	31	30 - 38	24 - 39
T3, Total	107	100 – 180	71 - 180
Copper	226		72 - 166
Zinc	57		56 - 134
Zinc / Copper Ratio	0.25	> 0.85	
Serum Methylmalonic Acid (MMA)	106	0 - 325	0 - 378
WBC	5.9	5.0 – 8.0	3.4 - 10.8
RBC	4.06	4.4 – 4.9	4.14 - 5.8
Hemoglobin	10.3	14 - 15	12.6 - 17.7
Hematocrit	32.4	40 - 48	37.5 - 51.0
MCV	80	85 – 92	79 - 97
MCH	25.4	27.7 – 32.0	26.6 - 33.0
MCHC	31.8	32 – 35	31.5 - 35.7
RDW	15.3	11.5 – 15.0	12.3 - 15.4
Platelets	362	150 – 415	150 - 379
Neutrophils	63	40 – 60	
Lymphocytes	24	25 – 40	
Monocytes	10	4.0 – 7.0	
Eosinophils	2	0.0 – 3.0	
Basophils	1	0.0 – 3.0	

Red blood cells, hemoglobin, and hematocrit are all low below the lab range, so clinical anemia here. MCV is borderline low at 80. MCH is lab-low. MCHC is borderline low, and RDW is borderline high. These markers are somewhat mixed. MCV can be low-normal in ACD, but you wouldn't expect RDW to be high in ACD, nor would you expect MCH or MCHC to be low. Serum iron, iron saturation, and TIBC are all low as expected in ACD. Ferritin is borderline high. CRP is super high at 140, another very high CRP value here. Copper is lab-high, and zinc-to-copper range is one of the lowest I've seen at 0.25. Vitamin D, 25(OH)D, is in the toxic range at 116. There is a lot of evidence of inflammation here, and this is most likely ACD.

Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	4+ Alpha hemolytic strep	4+ Citrobacter freundii complex
3+ Bifidobacterium spp.	2+ Beta strep, group B	4+ Klebsiella pneumoniae ssp pneumoniae
NG Escherichia coli	4+ Beta strep, not group A or B	4+ Staphylococcus aureus
NG Lactobacillus spp.	4+ Gamma hemolytic strep	
NG Enterococcus spp.		
2+ Clostridium spp.		

NG = No Growth

BACTERIA INFORMATION

Expected /Beneficial bacteria make up a significant portion of the total microflora in a healthy & balanced GI tract. These beneficial bacteria have many health-protecting effects in the GI tract including manufacturing vitamins, fermenting fibers, digesting proteins and carbohydrates, and propagating anti-tumor and anti-inflammatory factors.
Clostridia are prevalent flora in a healthy intestine. Clostridium spp. should be considered in the context of balance with other expected/beneficial flora. Absence of clostridia or over abundance relative to other expected/beneficial flora indicates bacterial imbalance. If *C. difficile* associated disease is suspected, a Comprehensive Clostridium culture or toxigenic *C. difficile* DNA test is recommended.
Commensal (Imbalanced) bacteria are usually neither pathogenic nor beneficial to the host GI tract. Imbalances can occur when there are insufficient levels of beneficial bacteria and increased levels of commensal bacteria. Certain commensal bacteria are reported as dysbiotic at higher levels.
Dysbiotic bacteria consist of known pathogenic bacteria and those that have the potential to cause disease in the GI tract. They can be present due to a number of factors including: consumption of contaminated water or food, exposure to chemicals that are toxic to beneficial bacteria; the use of antibiotics, oral contraceptives or other medications; poor fiber intake and high stress levels.

YEAST CULTURE

Normal flora	Dysbiotic flora
No yeast isolated	

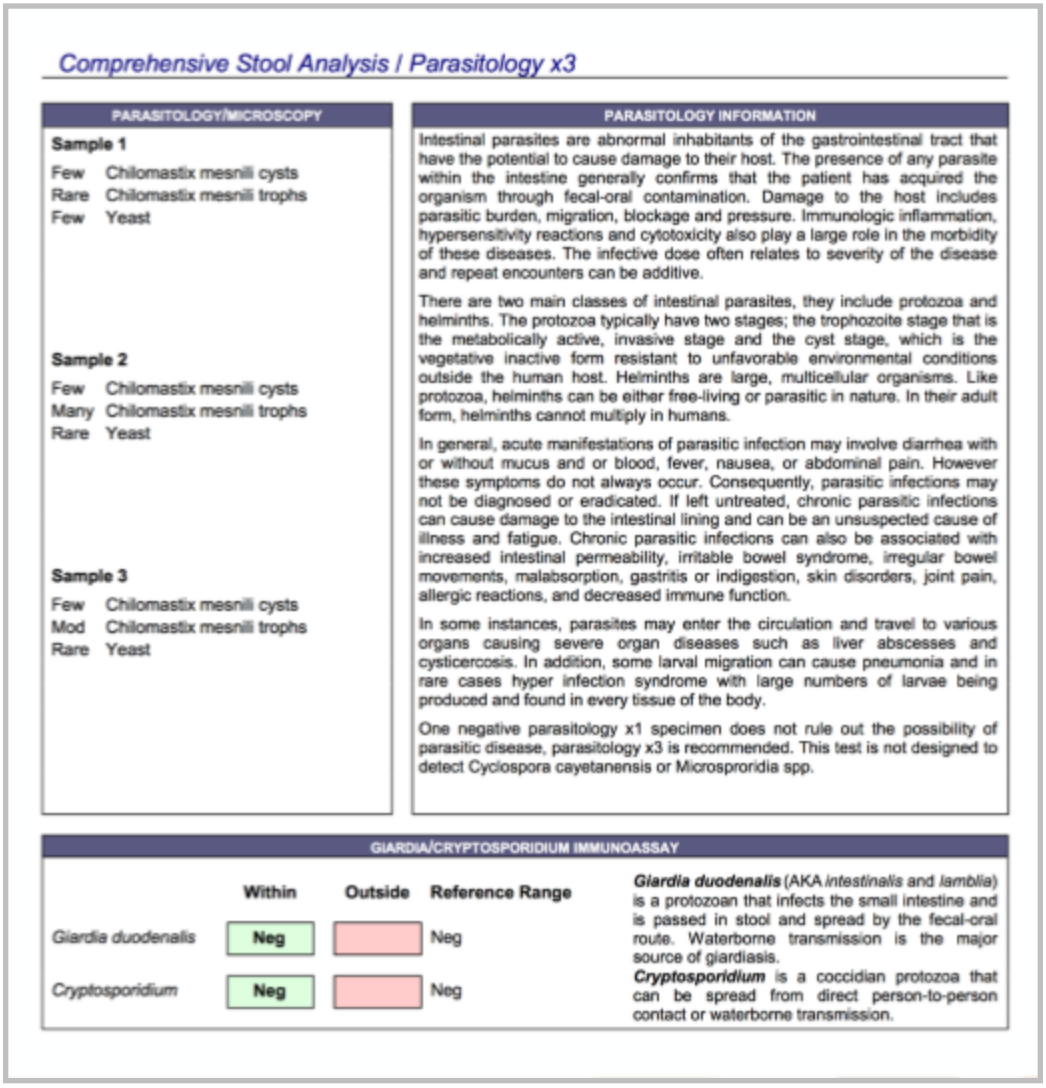
MICROSCOPIC YEAST

Result:	Expected:
Few	None - Rare

The microscopic finding of yeast in the stool is helpful in identifying whether there is proliferation of yeast. Rare yeast may be normal; however, yeast observed in higher amounts (few, moderate, or many) is abnormal.

YEAST INFORMATION

Yeast normally can be found in small quantities in the skin, mouth, intestine and mucocutaneous junctions. Overgrowth of yeast can infect virtually every organ system, leading to an extensive array of clinical manifestations. Fungal diarrhea is associated with broad-spectrum antibiotics or alterations of the patient's immune status. Symptoms may include abdominal pain, cramping and irritation. When investigating the presence of yeast, disparity may exist between culturing and microscopic examination. Yeast are not uniformly dispersed throughout the stool, this may lead to undetectable or low levels of yeast identified by microscopy, despite a cultured amount of yeast. Conversely, microscopic examination may reveal a significant amount of yeast present, but no yeast cultured. Yeast does not always survive transit through the intestines rendering it unviable.



Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY

Sample 1

Few Chilomastix mesnili cysts
Rare Chilomastix mesnili trophs
Few Yeast

Sample 2

Few Chilomastix mesnili cysts
Many Chilomastix mesnili trophs
Rare Yeast

Sample 3

Few Chilomastix mesnili cysts
Mod Chilomastix mesnili trophs
Rare Yeast

PARASITOLOGY INFORMATION

Intestinal parasites are abnormal inhabitants of the gastrointestinal tract that have the potential to cause damage to their host. The presence of any parasite within the intestine generally confirms that the patient has acquired the organism through fecal-oral contamination. Damage to the host includes parasitic burden, migration, blockage and pressure. Immunologic inflammation, hypersensitivity reactions and cytotoxicity also play a large role in the morbidity of these diseases. The infective dose often relates to severity of the disease and repeat encounters can be additive.

There are two main classes of intestinal parasites, they include protozoa and helminths. The protozoa typically have two stages; the trophozoite stage that is the metabolically active, invasive stage and the cyst stage, which is the vegetative inactive form resistant to unfavorable environmental conditions outside the human host. Helminths are large, multicellular organisms. Like protozoa, helminths can be either free-living or parasitic in nature. In their adult form, helminths cannot multiply in humans.

In general, acute manifestations of parasitic infection may involve diarrhea with or without mucus and or blood, fever, nausea, or abdominal pain. However these symptoms do not always occur. Consequently, parasitic infections may not be diagnosed or eradicated. If left untreated, chronic parasitic infections can cause damage to the intestinal lining and can be an unsuspected cause of illness and fatigue. Chronic parasitic infections can also be associated with increased intestinal permeability, irritable bowel syndrome, irregular bowel movements, malabsorption, gastritis or indigestion, skin disorders, joint pain, allergic reactions, and decreased immune function.

In some instances, parasites may enter the circulation and travel to various organs causing severe organ diseases such as liver abscesses and cysticercosis. In addition, some larval migration can cause pneumonia and in rare cases hyper infection syndrome with large numbers of larvae being produced and found in every tissue of the body.

One negative parasitology x1 specimen does not rule out the possibility of parasitic disease, parasitology x3 is recommended. This test is not designed to detect Cyclospora cayetanensis or Microsproridia spp.

GIARDIA/CRYPTOSPORIDIUM IMMUNOASSAY

	Within	Outside	Reference Range
Giardia duodenalis	Neg		Neg
Cryptosporidium	Neg		Neg

Giardia duodenalis (AKA *intestinalis* and *lamblia*) is a protozoan that infects the small intestine and is passed in stool and spread by the fecal-oral route. Waterborne transmission is the major source of giardiasis.
Cryptosporidium is a coccidian protozoa that can be spread from direct person-to-person contact or waterborne transmission.

We did some stool testing on him during the case review, and a few things popped up. He had significant pathogenic dysbiosis with Citrobacter, Klebsiella, and Staph aureus at 4+; a lot of commensal imbalance flora; and then no growth of E. coli, Lactobacillus, and Enterococcus, so insufficiency dysbiosis as well. Then, he had Chilomastix mesnili cysts and trophs. This is considered by the CDC to be nonpathogenic, but it is also considered to be an indicator of fecal oral transmission. We talked about this with some other nonpathogenic organisms in the gut unit. You might want to consider doing additional testing for parasites when you see this. It is entirely possible that he has another parasite that is causing iron withholding, his symptoms, and the ACD, or it is possible that even just the Citrobacter, Klebsiella, and staph are causing that.

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Immunoglobulins A/E/G/M, Serum					
Immunoglobulin G, Qn, Serum	778		mg/dL	700 - 1600	01
Immunoglobulin A, Qn, Serum	273		mg/dL	91 - 414	01
Immunoglobulin M, Qn, Serum	92		mg/dL	40 - 230	01
Immunoglobulin E, Total	**407**	**High**	IU/mL	0 - 100	01
Thyroid Antibodies					
Thyroid Peroxidase (TPO) Ab	<6		IU/mL	0 - 34	01
Thyroglobulin Antibody	<1.0		IU/mL	0.0 - 0.9	01
Thyroglobulin Antibody measured by Beckman Coulter Methodology					
Soluble Transferrin Receptor	14.9		nmol/L	12.2 - 27.3	02

Because his RDW was borderline high, and the clinical picture wasn't completely textbook for ACD, I ran soluble transferrin receptor and some other tests. STFR was low-normal, suggesting he is definitely not iron deficient. His total IgE was high, which can happen in parasitic infections, triggering an immune response. Given all this, the parasite is perhaps the most likely cause of ACD in this case.

Lab ordered:	Lab mnemonic:	Ordered on:	Ordered by:	Ordered at:
Vitamin B12	001503	03/08/2012 10:01:00 AM	Kresser C	LabCorp

Lab Name	Lab Mnemonic	Abnormal Flag	Result	Unit	Normal Range	Result Time	Status
Vitamin B12	001503		269	pg/mL	211-946	03/09/2012 6:48:51 AM	

Lab ordered:	Lab mnemonic:	Ordered on:	Ordered by:	Ordered at:
CMP14+LP+TP+TSH+SAC+TIBC+CB...	346041	03/08/2012 10:01:00 AM	Kresser C	LabCorp

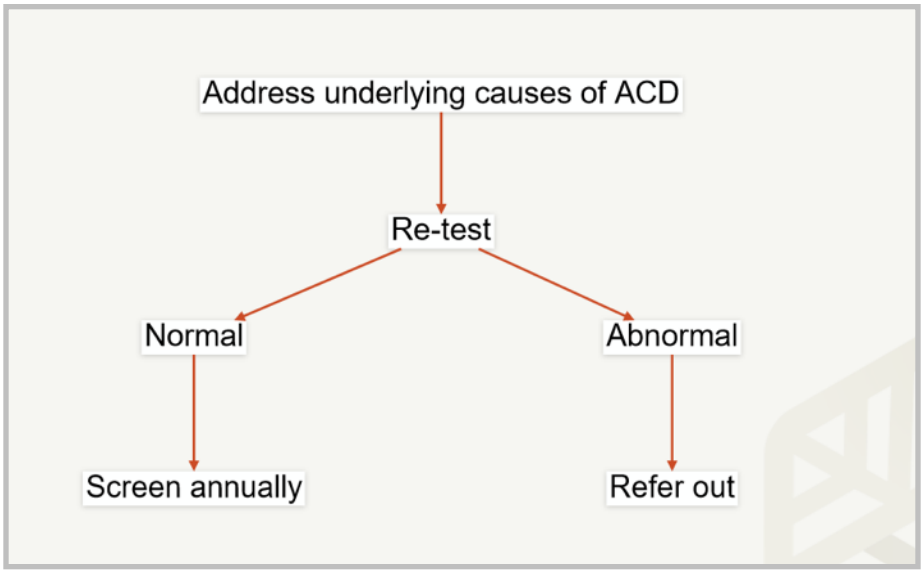
Lab Name	Lab Mnemonic	Abnormal Flag	Result	Unit	Normal Range	Result Time	Status
Chemistries	321866					03/08/2012 12:44:58 PM	
Glucose, Serum	001032		93	mg/dL	65-99	03/09/2012 5:40:52 AM	
Hemoglobin A1c	001464		5.3	%	4.8-5.6	03/09/2012 6:28:07 AM	
*** . *Increased risk for diabetes: 5.7 - 6.4 Diabetes: >6.4 Glycemic control for adults with diabetes: <7.0*							
Uric Acid, Serum	001057		5.4	mg/dL	2.5-7.1	03/09/2012 5:40:52 AM	
Please Note:	001061					03/08/2012 5:40:52 AM	
*** *Therapeutic target for gout patients: <6.0*							
BUN	001040		10	mg/dL	8-27	03/09/2012 5:40:52 AM	
Creatinine, Serum	001370		0.84	mg/dL	0.57-1.00	03/09/2012 5:40:52 AM	
eGFR If NonAfricn Am	100791		70	mL/min/1.73	>59	03/09/2012 5:40:53 AM	
eGFR If Africn Am	100792		80	mL/min/1.73	>59	03/09/2012 5:40:53 AM	
*** *Note: A persistent eGFR <60 mL/min/1.73 m2 (3 months or more) may indicate chronic kidney disease. An eGFR >59 mL/min/1.73 m2 with an elevated urine protein also may indicate chronic kidney disease. Calculated using CKD-EPI formula.*							
Sodium, Serum	001198		137	mmol/L	134-144	03/09/2012 5:40:52 AM	
Potassium, Serum	001180		4.2	mmol/L	3.5-5.2	03/09/2012 5:40:52 AM	
Chloride, Serum	001206		100	mmol/L	97-108	03/09/2012 5:40:52 AM	
Carbon Dioxide, Total	001578		21	mmol/L	20-32	03/09/2012 5:40:52 AM	
Calcium, Serum	001016		9.2	mg/dL	8.6-10.2	03/09/2012 5:40:52 AM	
Phosphorus, Serum	001024		3.9	mg/dL	2.5-4.5	03/09/2012 5:40:52 AM	
Magnesium, Serum	001537		2.2	mg/dL	1.6-2.6	03/09/2012 5:40:52 AM	
Protein, Total, Serum	001073		7.8	g/dL	6.0-8.5	03/09/2012 5:40:52 AM	
Albumin, Serum	001081	L	3.3	g/dL	3.5-4.8	03/09/2012 5:40:52 AM	
Globulin, Total	012039		4.5	g/dL	1.5-4.5	03/09/2012 5:40:53 AM	
A/G Ratio	012047	L	0.7	1	1.1-2.5	03/09/2012 5:40:53 AM	
Bilirubin, Total	001099		0.5	mg/dL	0.0-1.2	03/09/2012 5:40:52 AM	
Alkaline Phosphatase, S	001107		100	IU/L	25-165	03/09/2012 5:40:52 AM	
LDH	001115		104	IU/L	0-214	03/09/2012 5:40:52 AM	
AST (SGOT)	001123		11	IU/L	0-40	03/09/2012 5:40:52 AM	
ALT (SGPT)	001545		4	IU/L	0-40	03/09/2012 5:40:52 AM	
GGT	001958		12	IU/L	0-60	03/09/2012 5:40:52 AM	
Iron Bind.Cap.(TIBC)	001347	L	218	ug/dL	250-450	03/09/2012 5:40:53 AM	
UIBC	001348		204	ug/dL	150-375	03/09/2012 5:40:52 AM	
Iron, Serum	001339	L	14	ug/dL	35-155	03/09/2012 5:40:52 AM	

Iron Saturation	011362	LX	6	%	15-55	03/09/2012 5:40:53 AM
Ferritin, Serum	004598	H	157	ng/mL	13-150	03/09/2012 6:48:51 AM
.	321854					03/08/2012 12:44:58 PM
Lipids	321869					03/08/2012 12:44:58 PM
Cholesterol, Total	001065		166	mg/dL	100-199	03/09/2012 5:40:52 AM
Triglycerides	001172		84	mg/dL	0-149	03/09/2012 5:40:52 AM
HDL Cholesterol	011817		45	mg/dL	>39	03/09/2012 5:40:52 AM
Comment	011822					03/08/2012 5:40:52 AM
*** According to ATP-III Guidelines, HDL-C >59 mg/dL is considered a negative risk factor for CHD.						
VLDL Cholesterol Cal	011916		17	mg/dL	5-40	03/09/2012 5:40:53 AM
LDL Cholesterol Calc	012054	H	104	mg/dL	0-99	03/09/2012 5:40:53 AM
T. Chol/HDL Ratio	100065		3.7	ratio units	0.0-4.4	03/09/2012 5:40:53 AM
LDL/HDL Ratio	011849		2.3	ratio units	0.0-3.2	03/09/2012 5:40:53 AM
.	321855					03/08/2012 12:44:58 PM
Thyroid	321870					03/08/2012 12:44:58 PM
TSH	004264	L	0.318	uIU/mL	0.450-4.500	03/09/2012 6:51:15 AM
Thyroxine (T4)	001149		5.6	ug/dL	4.5-12.0	03/09/2012 5:40:52 AM
T3 Uptake	001156		32	%	24-39	03/09/2012 5:40:52 AM
Free Thyroxine Index	001164		1.8	1	1.2-4.9	03/09/2012 5:40:53 AM
Triiodothyronine (T3)	002188		71	ng/dL	71-180	03/09/2012 6:51:15 AM
.	321877					03/08/2012 12:44:58 PM
Immunoassay	321878					03/08/2012 12:44:58 PM
Vitamin D, 25-Hydroxy	081953	L	19.0	ng/mL	30.0-100.0	03/09/2012 9:20:05 AM
*** Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-OH vitamin D less than 20 ng/mL (1,2). The Endocrine Society went on to further define vitamin D insufficiency as a level between 21 and 29 ng/mL (2). 1. IOM (Institute of Medicine). 2010. Dietary reference intakes for calcium and D. Washington DC: The National Academies Press. 2. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. JCEM. 2011 Jul; 96(7):1911-30. . **Effective March 5, 2012, Vitamin D, 25 Hydroxy specimen** requirements will change to serum only.						
.	321856					03/08/2012 12:44:58 PM
CBC, Platelet Ct, and Diff	321871					03/08/2012 12:44:58 PM
WBC	005025		8.5	x10E3/uL	4.0-10.5	03/09/2012 4:48:23 AM
RBC	005033		4.52	x10E6/uL	3.80-5.10	03/09/2012 4:48:23 AM
Hemoglobin	005041	L	11.0	g/dL	11.5-15.0	03/09/2012 4:48:23 AM
Hematocrit	005058		35.2	%	34.0-44.0	03/09/2012 4:48:23 AM
MCV	015065	L	78	fL	80-98	03/09/2012 4:48:23 AM
MCH	015073	L	24.3	pg	27.0-34.0	03/09/2012 4:48:23 AM
MCHC	015081	L	31.3	g/dL	32.0-36.0	03/09/2012 4:48:23 AM
RDW	105007	H	15.1	%	11.7-15.0	03/09/2012 4:48:23 AM
Platelets	015172	H	559	x10E3/uL	140-415	03/09/2012 4:48:23 AM
Neutrophils	015107		65	%	40-74	03/09/2012 4:48:23 AM
Lymphs	015123		25	%	14-46	03/09/2012 4:48:23 AM
Monocytes	015131		9	%	4-13	03/09/2012 4:48:23 AM
Eos	015149		1	%	0-7	03/09/2012 4:48:23 AM
Basos	015156		0	%	0-3	03/09/2012 4:48:23 AM

The last patient is a 77-year-old female. Again, this is the population for whom ACD is the most common cause of anemia, so if you have an elderly patient with anemia, make sure that you are thinking about this. Her primary complaints were GERD, bloating, pain after eating, constipation, and severe fatigue. Hemoglobin is lab-low. RBC and hematocrit are normal. MCV is slightly low. TIBC, serum iron, and iron saturation are low, and ferritin and platelets are high. All of that so far is consistent with ACD.

However, MCH and MCHC were lab-low, and RDW was high, and you would expect that more in iron deficiency. Note that her B12 was almost lab-low, so given her upper GI symptoms, age, low serum B12, high platelets, and ACD, I was concerned about stomach cancer. I referred her to a gastroenterologist, and she was, in fact, diagnosed with gastric lymphoma. It would have been a very bad thing to give her iron in this case. Even though she does have some markers of iron deficiency,

she had stomach cancer, and those stomach cancer cells would thrive on something such as an iron supplement. This just highlights the importance of understanding this distinction and doing the necessary testing to make sure that you don't do something that will harm your patient.



To summarize, if you see markers of anemia such as low serum iron or iron saturation, check TIBC and ferritin. If TIBC is low and ferritin is high, it is likely that it is ACD. That's especially true if RDW is normal, MCV is normal or low normal, and white blood cells are high or low. If there is any question, you can run soluble transferrin receptor and reticulocyte hemoglobin content. If those are normal, it is virtually certain you're looking at ACD.

The next step is to address any underlying causes you've identified that can result in ACD. That is the only treatment for this condition. Do not use iron. If the patient has ACD and iron deficiency concurrently, which is possible, you want to do what you can to resolve the ACD first, particularly if there is a pathogen present, because if you feed that pathogen iron, it could get worse. If you are absolutely certain there is no pathogen and it is just inflammation that is present and causing that elevation, it is a little less clear cut. In those cases, I would still try to get the inflammation under control before going on to use iron, or I would just focus on more iron-rich foods.

If ACD doesn't resolve after addressing the underlying causes you identify, or if there are signs of more serious disease present, as with the last patient, don't hesitate to refer to a hematologist, a gastroenterologist, or a nephrologist. It depends on the signs and symptoms and what particular underlying condition they have. They will pursue blood loss, kidney function, bone marrow function, cancer, and chronic hemolysis as potential causes of these abhorrent lab markers.

Okay, that's it for the ACD presentation. Make sure to review this a couple of times so you really understand it because it is an area where the stakes are high, and as I said, there is a lot of misunderstanding in this diagnosis. Okay, that's it for now. See you next time.