ANEMIA OF INFLAMMATION / CHRONIC DISEASE (AI/ACD)

TERM DEFINITION

Anemia* associated with systemic inflammation that is typically chronic, but can occur acutely

*ANEMIA DEFINED AS

♀ Hb < 12 g/dL | ♂ Hb < 13 g/dL

CAUSES

- Infection (often chronic)
- Cancer
- Trauma
- Inflammatory bowel disease
- Connective tissue disease
- HLH

CLINICAL PEARLS

AI/ACD & iron deficiency anemia often coexist

Most common type of anemia in hospitalized patients

In critically ill patients, AI/ACD can develop within one week of admission

The severity of anemia in AI/ACD seems to have a built-in floor, such that the hemoglobin rarely falls below **7 g/dL** unless there are other contributing causes.

The absorption of oral iron is commonly impaired in diseases with systemic inflammation. In cases where AI/ACD and iron deficiency coexist, parenteral iron administration is more effective.

PRESENTATION

SIGNS & SYMPTOMS

IN AI/ACD cases, anemia is usually not severe enough to cause symptoms. Patients may present with symptoms and signs related to underlying inflammatory conditions.

LABS

HEMATOLOGICAL FINDINGS

Anemia is mild-moderate (Hb > 7g/dL) & typically normocytic, normochromic (10% are microcytic)

Other hematological findings associated with inflammation may include:

- Thrombocytosis
- Leukocytosis
- Lymphopenia

ACUTE PHASE REACTANTS

Positive acute phase reactants associated with inflammation include elevated serum:

- C-reactive protein (CRP)
- Haptoglobin
- Ferritin
- Fibrinogen

ACUTE PHASE REACTANTS

Negative acute phase reactants associated with inflammation include decreased serum:

- Albumin
- Total iron binding capacity

DIAGNOSIS

AI/ACD

=

Inflammation

+

Iron restriction that is not caused by systematic iron deficiency*

DIFFERENTIAL DIAGNOSIS

Other causes of hypoproliferative normocytic normochromic anemia:

- Anemia of chronic kidney disease
- Anemia of endocrine disorders
- Anemia of liver disease
- Anemia associated with primary bone marrow process (e.g., multiple myeloma)

Look for the following iron indices of AI/ACD: *low serum Fe, low transferrin saturation (<20%), high serum ferritin level (>100 µg/L)*

THERAPEUTIC PRINCIPLES

Transfusion only if anemia is severe and symptomatic, which is rarely the case. Treat underlying inflammatory condition, with the goal of ameliorating associated morbidity, not the anemia per se.

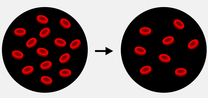
COMPARATIVE PHYSIOLOGY

Apart from blood loss, inflammation is the **MOST COMMON CAUSE OF ANEMIA** in non-mammalian vertebrates. In some cases, the anemia takes a long time to emerge because the lifespan of their RBCs can be as long as 600 days (e.g. in certain reptiles).

Veterinarians often classify anemia according to whether it is "**regenerative**" or "**non-regenerative**". The most common form of non-regenerative anemia is AI/ACD, caused by infectious, inflammatory, trauma-mediated, and neoplastic diseases. As with humans, AI/ACD in domestic animals, while typically normocytic, is microcytic in a small percentage of cases.

PROXIMATE MECHANISMS

AI/ACD is primarily a disorder of iron distribution involving suppressive effects of iron starvation and inflammation on the erythropoietic system and reduced RBC survival.



Inflammation greatly increases synthesis of the acute phase protein, hepcidin (a master regulator of iron metabolism). Hepcidin blocks export of iron from gut and erythrocyte-recycling macrophages into the blood, resulting in a functional iron deficiency*. Erythropoiesis is inhibited by the low serum iron levels as well as the presence of inflammatory mediators.

Functional iron deficiency *is the reduced availability of storage iron*

EVOLUTIONARY MECHANISMS

Iron sequestration in AI/ACD may have evolved as a means of protecting the host against iron-dependent microbes.

AI/ACD may represent an evolutionary trade off in which the benefits of starving microbes of iron outweighed the risks associated with a mild anemia.

Alternatively, the mild reduction in Hb seen in AI/ACD may actually have a beneficial effect on hemodynamics by decreasing the viscosity of blood, hence total peripheral resistance. This would result in increased cardiac output and oxygen delivery.

HISTORY OF MEDICINE

In the 1800s, anemia was divided into primary types and secondary types. **Primary anemias** (whose cause was felt to be known) included pernicious anemia and chlorosis. **Secondary anemias** included all other types of anemia, for which the etiology was poorly understood. Many of these patients with secondary anemia probably had anemia of inflammation because chronic infections (including tuberculosis, osteomyelitis, endocarditis and empyema) and cancer were highly prevalent at the time.

NOTES

ATTRIBUTIONS

Written by Dr. William Aird

Input from Dr. Stephen Stearns (*Evolutionary Medicine*)
Dr. John Harvey (*Comparative Physiology*)
Dr. Jane Maienschein & Dr. Kate McCord (*History of Medicine*)

Designed by Janie Vu

The Blood Project
ENCYCLOPEDIA OF BLOOD