



## Endoscopic Diagnosis of Occult Bleeding in Patients with Iron Deficiency Anemia

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**Abstract:** Endoscopic measures include upper endoscopy, colonoscopy, deep enteroscopy, or capsule endoscopy. CT colonography, CT, and magnetic resonance (MR) enterography are some of the radiographic studies used in the evaluation of patients with chronic occult gastrointestinal bleeding. The role of barium enema, small bowel series, enteroclysis, standard computed tomography or magnetic resonance imaging, and nuclear scanning has declined significantly due to their poor diagnostic performance and the advent of capsule endoscopy.

**Keywords:** anemia, capsule endoscopy, iron deficiency anemia, hemoglobin synthesis, iron metabolism parameters, colonoscopy.

Anemia is defined as systemic hypoxia associated with a decrease in the content of the oxygen carrier in the body. Anemia is established when the hemoglobin concentration is less than 120 g/l in women and less than 130 g/l in men [8]. According to WHO, 2 billion inhabitants of the Earth suffer from anemia, 80–90% of these conditions are associated with iron deficiency (iron deficiency syndromes), and more than half is iron deficiency anemia (IDA) [7, 8]. IDA is absolute iron deficiency, leading to the development of sideropenic syndrome and anemia (the most common anemia in the world).

Iron deficiency leads to disruption of hemoglobin synthesis in bone marrow erythrokaryocytes, a decrease in the content of myoglobin in muscles, the activity of cytochromes and catalases in cell mitochondria, and myeloperoxidase in neutrophils [12].

Currently, there are several stages of iron deficiency [11]:

1. Predisposition – a high risk of developing iron deficiency (vegetarianism, adolescence (in combination with menstrual irregularities in girls), frequent childbirth, the presence of chronic gastrointestinal diseases, diseases of the female reproductive system associated with blood loss).
2. Pre-latent iron deficiency. At this stage, there are no laboratory criteria for iron deficiency, however, an increase in the absorption of trivalent iron in the gastrointestinal tract is determined, which can exceed 50% (normal - 10-15%).

3. Latent iron deficiency is characterized by the development of sideropenic syndrome and a decrease in iron stores in the body according to laboratory tests.

4. IDA.

Clinical manifestations of IDA are associated both with symptoms of systemic hypoxia (dizziness, flashing of “flies” before the eyes, drowsiness, decreased performance), and with the development of sideropenic syndrome, which is characterized by severe muscle weakness, violation of the integrity of the mucous membranes, skin, its appendages (fragility and delamination of nails, hair loss), decreased immunity.

The most characteristic laboratory signs of IDA are hypochromia, erythrocyte microcytosis, and anisocytosis. The hypochromia of erythrocytes is indicated by a color index of less than 0.8 (according to the old calculation), the average content of hemoglobin in an erythrocyte is less than 28 pg. Microcytosis is referred to when the average erythrocyte diameter is less than 7 mkm, and the average erythrocyte volume is less than 80 fl [12].

Iron metabolism parameters are widely used in clinical practice, but due to the lack of well-defined values that prove the presence of IDA, the high cost of the study and the large number of patients, their use is not always justified. Thus, the minimum normal values of serum ferritin (FS) as the only marker reflecting iron stores in the body and used for verification and differential diagnosis of IDA, according to different researchers [12], vary from 15 to 100 µg/L. It is known that the PS index is a positive marker of inflammation, and its amount is determined by the protein-synthetic function of the liver.

Currently, to establish the diagnosis of IDA, it is considered to be a reliable indicator of FS less than 30 µg/L [10]. The level of such a transport protein as transferrin, as a rule, is increased in iron deficiency, however, in the presence of infection, its content decreases and cannot be used in the diagnosis of IDA [12]. Variable parameters of iron metabolism, such as iron-binding capacity (total and latent) and the coefficient of saturation of transferrin with iron, since are calculated based on the content of transferrin and serum iron. The latter indicator has no connection with the iron content in the body and depends on the time at which the study was conducted and food intake [9].

Options for the investigation of acute GI bleeding include upper endoscopy and/or colonoscopy, nuclear scintigraphy, CT angiogram and catheter angiography. The investigation of choice would be guided by the suspected location of bleeding (upper vs lower GI) based on clinical presentation. In most circumstances, the standard of care for the initial diagnostic evaluation of suspected acute GI bleeding is urgent upper endoscopy and/or colonoscopy, as recommended by guidelines from the American College of Gastroenterology and the 2010 International Consensus Recommendations [6, 27]. As investigations are being planned, infusions of proton pump inhibitor or octreotide should be initiated for suspected bleeding peptic ulcer and varices respectively [1, 30].

In patients with acute upper GI bleeding, upper endoscopy is considered the investigation of choice [1]. Early upper endoscopy within 24 h of presentation is recommended in most patients with acute upper GI bleeding to confirm the diagnosis and has the benefit of targeted endoscopic treatment, resulting in reduced morbidity, hospital length of stay, risk of recurrent bleeding and the need for surgery [2]. Endoscopic evacuation of hematoma or blood clot may enable visualization of underlying pathology such as a visible vessel in a peptic ulcer and allows directed endoscopic hemostatic therapy [5, 37]. The reported sensitivity and specificity of endoscopy for upper gastroduodenal bleeding are 92%-98% and 30%-100%, respectively [4]. Risks of upper endoscopy include aspiration, side-effects from sedation, perforation, and increased bleeding while attempting therapeutic intervention. The airway should be secured by endotracheal intubation in the case of massive upper GI bleeding.

Risk factors and patient preferences should also be taken into account when choosing a study. In general, colonoscopy and upper endoscopy are the initial investigations of choice in chronic gastrointestinal occult bleeding.

The 2007 American Gastroenterological Association guidelines for unclear gastrointestinal bleeding recommend that the evaluation of a patient with a positive FOBT be contingent on the presence of iron deficiency anemia. Patients with a positive FOBT result and without anemia should be evaluated first by colonoscopy (if upper GI symptoms are present, then upper GI endoscopy as well), while patients with iron deficiency anemia should undergo both upper endoscopy, as well as colonoscopy.

Patients with negative upper endoscopy and colonoscopy without anemia do not need further testing, but anemic patients should be referred for further small bowel examination. The initial examination of the small intestine of choice, if available, is wireless capsule endoscopy.

Wireless capsule endoscopy is a simple, non-invasive examination of the small intestine to assess occult gastrointestinal bleeding from the small intestine.

Diagnostic efficacy in patients with chronic occult and unclear gastrointestinal bleeding (after negative upper endoscopy and colonoscopy) ranges from 55% to 92% for capsule endoscopy compared to 25%-30% for push endoscopy.

Capsule endoscopy also avoids the higher morbidity and mortality associated with push enteroscopy. Capsule endoscopy is less useful in evaluating sources of colonic bleeding due to delayed stools, battery life, and poor visual field due to the large diameter of the colon. Complications associated with the procedure are rare and include capsule retention and obstruction.

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