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Pernicious anemia: What are the actual diagnosis criteria?

Daniel Cattan

Daniel Cattan, Department of Internal Medicine and Hepato-Gastroenterology, Centre Hospitalier, 94195 Villeneuve Saint George, France
Author contributions: Cattan D contributed to all of this letter.
Correspondence to: Daniel Cattan, Professor, Department of Internal Medicine and Hepato-Gastroenterology, Centre Hospitalier, 94195 Villeneuve Saint George, France. danielcattan@yahoo.fr
Telephone: +33-1-60470829 Fax: +33-1-43310249
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Abstract

A gastric intrinsic factor output under 200 U/h after pentagastrin stimulation (*N* > 2000 U/h) is specific for pernicious anemia. The other findings are either variable or non specific. Serum intrinsic factor antibodies, considered as specific in general practice, are present only in half of the patients with pernicious anemia. In their absence, since the disappearance of the Schilling tests, the gastric tubage currently used for the study of gastric acid secretion, is obligatory for the simultaneous study of intrinsic factor output. This study is important to eliminate another disease much more frequent than pernicious anemia, the protein bound to cobalamin malabsorption was observed in achlorhydric simple atrophic gastritis in the presence of intrinsic factor secretion.

Key words: Pernicious anemia; Intrinsic factor; Achlorhydria; Schilling test; *Helicobacter pylori*

Peer reviewer: Yu-Yuan Li, Professor, Department of Gastroenterology, First Municipal People's Hospital of Guangzhou, 1 Panfu Road, Guangzhou 510180, Guangdong Province, China

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TO THE EDITOR

The recent article entitled "new insights in pernicious anemia (PA) from a gastroenterological point of view" published in issue 41 of the *World Journal of Gastroenterology* 2009[1], does not clearly describe the actual diagnosis criteria for PA. The recent disappearance of Schilling tests and the difficulties in finding a laboratory able to appreciate the intrinsic factor (IF) output have raised the question about the secure diagnosis of this disease.

A gastric IF output under 200 U/h post pentagastrin stimulation (*N* > 2000 U/h) is specific for PA. The other findings are either variable or non specific. Variable findings include elevated serum gastrin, serum IF antibodies (considered specific in current general practice), normal antral mucosa, normal or elevated serum level of folate and reduced level of erythrocyte folate. Non specific findings include fundic atrophic gastritis, achlorhydria, and hypergastrinemia[2]. Hyperplasia of enterochromaffin-like cells exists in atrophic gastritis with hypergastrinemia, achlorhydria with conservation of good IF secretion[3]. Parietal cells antibodies (PCA) are observed in a high proportion of normal middle aged women.

In fact, PA diagnosis is easily feasible in half of the patients in the presence of IF serum antibodies and hypergastrinemia. The absence of any these findings does not eliminate the diagnosis. Replacement of hypergastrinemia by a fundic atrophic gastritis is perhaps admissible. However, this gastritis alone and hypergastrinemia alone are not sufficient. PCA have no place[4].

In old patients with cobalamin deficiency, the demand is evidently less once intestinal diseases (gluten enteropathy being not forgotten) are eliminated.

In scientific studies, particularly in those on the relation between *Helicobacter pylori* and PA, however, the demand has to be greater than in recent articles[5,6] to make sure that the patient does not have a simple atrophic gastritis with achlorhydria and conservation of good IF secretion, a disease much more frequent than PA and responsible for a non dissociation of alimentary cobalamin from protein nutriments. In this disease (food bound to cobalamin malabsorption[7]), the most common disorder of cobalamin absorption[4], cobalamin deficiency is moderate (the role of chlorhydric acid

in the dissociation of cobalamin from alimentary proteins varies with the nature of these proteins. Moreover IF secretion is important for the reabsorption of cobalamins from bilio-pancreatic and intestinal secretions), the anemia is discrete and sometimes only macrocytosis is observed. Schilling tests show a good absorption of cristalline cobalamin and a malabsorption of various proteins bound to cobalamins[8]. Treatment can be oral cobalamin[4]. Longitudinal studies[4,9] showed that the frequency of the evolution of this gastritis toward PA is very low. This disease is another disease rather than PA. The presence of cobalamin deficiency in these simple achlorhydric gastritis can explain the demand of the earliest authors[2,9,10] for the diagnosis tests of PA in patients without IF serum antibodies. These diagnosis tests include either gastric tubage with study of the IF output by 15 min fractions in the hours before and after stimulation or Schilling test done in good conditions, that is using the two- stage test (with then without oral administration of IF eventually repeated for the elimination of cobalamin malabsorption due to the cobalamin deficiency's effect itself on the intestinal mucosa)[10].

Since Schilling tests are no longer available, the diagnostic criteria have changed[4,11]. In the absence of serum IF antibodies in a patient with a low serum cobalamin level, the gastric tubage for study of IF output is obligatory for scientific purposes.

Deficiency in IF secretion is the "gold standard" for the diagnosis of PA, which should be used to evaluate the value of associations between serological markers, including eventually new PCA.

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