PERNICIOUS ANEMIA

Autoantibodies to intrinsic factor

Intrinsic factor (IF), a sialic acid containing 60 kD glycoprotein, plays a vital role in the transport and absorption of vitamin B_{12} in the intestine. After secretion by parietal cells of the stomach mucosa IF binds to **vitamin B_{12}** ingested with food. This vitamin B_{12}-IF complex is carried to the intestine where it allows absorbtion of vitamin B_{12} via binding to a **specific IF receptor**. Subsequently vitamin B_{12} is released into the blood binding to another protein (transcobalmin).
Reduced production of the IF and / or impairment of its transport function in the digestive system bring about a deficiency in vitamin B_{12} leading to the development of **pernicious anemia** (Biermer`s anemia). Patients suffering from atrophic **chronic gastritis of type A** exhibit autoantibodies to both parietal cell H^+/K^+-ATPase and the intrinsic factor produced by parietal cells. According to their binding sites these autoantibodies are divided into two types.
Type 1 antibody (blocking antibody) prevents the attachment of vitamin B_{12} to IF in the stomach. In contrary **type 2 antibody** (binding antibody) interacts with both IF and IF-vitamin B_{12} complex and prevents their absorption in the intestine by reacting with the IF region recognized by the mucosa.

Etiopathogenesis of pernicious anemia

Pernicious anemia is the result of chronic atrophic gastritis of type A. Contrary to gastritis type B this disease is an autoimmune process with a progressive destruction of the gastric mucosa. Whilst type A gastritis involves the fundus and corpus of the stomach, type B gastritis affects the antrum as well and is usually associated with Heliobacter pylori infections.

Clinical pattern

Histopathology

- Loss of gastric mucosa folds
- Submucosal infiltration of mononuclear cells
- Loss of parietal cells and replacement by mucus-containing cells
- Intestinal metaplasia

Progression

Typically type A gastritis progresses to an atrophic gastritis combined with pernicious anemia within 20-30 years.
Clinical symptoms of pernicious anemia occur in most cases after the age of 40.

Intestinal complications

- Patients with pernicious anemia face a higher risk to develop an adenocarcinoma.

Neurological complications

- Peripheral neuropathy
- Demyelation, axonal degeneration and neuronal death
- Sensory ataxia
- Memory loss
- Psychosis

Type A gastritis

- autoimmune pathogenesis
- fundus, corpus
- pernicious anemia
- autoantibodies to parietal cells (H+/K+-ATPase)
- autoantibodies to intrinsic factor
- achlorhydria
- low serum pepsinogen I
- hypergastrinemia

Type B gastritis

- non-autoimmune pathogenesis
- fundus, antrum, corpus
- Helicobacter pylori infection
- hypogastrinemia

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Diagnostic methods

- *Gastric biopsy*
- *Hematology*
  - Megaloblastic anemia
  - Macrocytosis with polymorphonuclear leucocytosis
- *Serology*
  - Low vitamin B_{12} level
  - Antibodies to parietal cells
  - Antibodies to H^+/K^+-ATPase
  - Antibodies to intrinsic factor **(highly specific)**
  - Hypergastrinemia
  - Low level of serum pepsinogen I
- *Schilling test*
  - Confirmation of vitamin B_{12} deficiency due to intrinsic factor deficiency

Epidemiology

The overall prevalence of pernicious anemia has been estimated at 0.1% of the population. However, the incidence of pernicious anemia is age related.

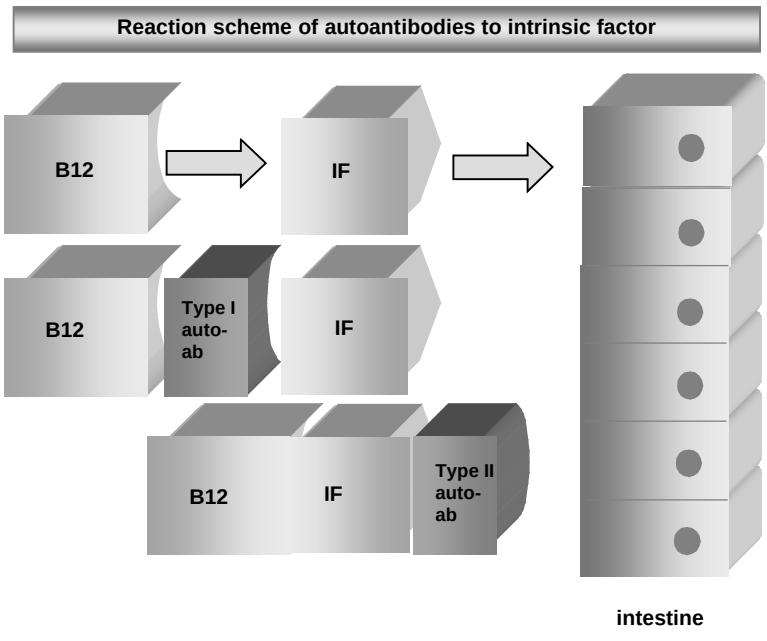
A recent population study revealed that 1.9 percent of persons older than 60 years suffer from undiagnosed pernicious anemia (Carmel et al., 1996).

Therapy

- Monthly intramuscular injection of 100 µg vitamin B_{12}
- Daily oral intake of vitamin B_{12} for people older than 60 years with diagnosed gastric atrophy

The detection of megaloblastic anemia and vitamin B_{12} deficiency beside antibodies to intrinsic factor meet the criteria for differential diagnosis of pernicious anemia. Additional parameters (e.g. Schilling test) increase costs and expenditure of human labor.

Detection of antibodies to parietal cells is not specific for pernicious anemia exclusively, because they are also detectable in other autoimmune diseases. Antibodies to the intrinsic factor are highly specific for pernicious anemia.



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Anti-intrinsic factor (Order Code: 3600)

Technical data:

Assay	96 determinations
Disorder	Pernicious anemia
Parameters	IgG antibodies to intrinsic factor (type 1 and type 2)
Antigen	Intrinsic factor (human, recombinant)
Principle of the test	Enzyme-linked immunosorbent assay (ELISA), semi-quantitative
Results	Binding index (BI), positive: B > 1; negative BI < 0,8
Incubation scheme	30 min RT – 30 min RT – 15 min RT
Substrate	Tetramethylbenzidine (TMB), 450 nm
Sample	human serum, 1 + 100

Sensitivity and specificity

A specifity of 99% and a sensitivity of 98% has been established for GA Generic Assays GmbH Anti-intrinsic factor by investigating serum samples from healthy persons (n=110) and patients suffering from pernicious anemia (n=49)

Precision

The coefficient of variation in 6 serums (15 pilot batches) was:

Intra-assay: < 7%
Inter-assay: < 10%

Literature

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Additional products for the differential diagnosis of pernicious anemia

Order Code	Product	Results	Determinations
3600	Anti-intrinsic factor (IF)	semi-quantitative	96
4020	BiermAK Dot (PCA, IF)	qualitative	24 x 2

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