



australasian society of clinical immunology and allergy inc.

## **Consensus Guidelines on Anti-Intrinsic Factor Antibody Testing**

**Prepared by ASCIA in conjunction with the  
Royal Australasian College of Pathologists (RCPA).**

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Recently anti intrinsic factor antibody has become the primary test for diagnosis of pernicious anemia. However methodology for this assay varies between laboratories. In addition it has been noticed anecdotally that there have been a number of positive results recorded in women below the age of 50 in the absence of a positive parietal cell antibody. Frequently anti intrinsic factor antibody is reported without reference to serum B12 result and anti parietal cell antibody.

Discussions at the St George Hospital meeting (2002) led to the formulation of a questionnaire which was distributed to all 26 laboratories carrying out intrinsic factor antibody via the QAP programme. Seventeen replies were returned and analysed. The consensus statement below is based on the results of this questionnaire.

### **1. Isotype of a IFA Tested**

#### 1.1 Minimum

- IgG to be measured.

### **2. Specimen Type**

#### 2.1 Comments

- Preferred specimen type is serum.

### **3. Assay Precision**

#### 3.1 Minimum

- Manufacturer or laboratory evidence of a less than 20% intra-assay and inter-assay variation required at cut off.

### **4. Assay Linearity**

Not applicable

### **5. Calibrators**

#### 5.1 Minimum

- Calibrators should be tested in duplicate for single point calibrator assays/kits

#### 5.2 Optimum

- Calibrators should be tested in duplicate for both single point and double point assays/kits

## **6. Controls**

### 6.1 Minimum

- Negative sample
- Kit controls (if using commercial kits)
- External reference material (commercial or sourced in-house, but NOT the kit control) with a value around cut-off of the assay/kit.

## **7. Samples**

### 7.1 Minimum

- If assay precision is < 20% patient samples can be performed in singles.

### 7.2 Optimum

- All patient samples should be performed in duplicate.

## **8. Reporting in association with other tests**

### 8.1 Minimum

- Results should be reported in association with parietal cell antibodies

### 8.2 Optimum

- Results should be reported in association with B12 and full blood evaluation (FBE).

## **9. Reporting values**

### 9.1 Minimum

- Results should be reported as positive, negative or equivocal

### 9.2 Optimum

- Results should be reported in a quantitative manner

## **10. Cut-offs**

### 9.1 Minimum

- Manufacturers recommended cut off should be used

### 9.2 Optimum

- The range should be determined using a normal population and a population of patients with pernicious anemia as defined by anemia, macrocytosis, atrophic gastritis on biopsy and response to parental B12.

## **Suggested Comments**

### **If both parietal cell antibody and intrinsic factor antibody are positive-**

Immunological evidence of Pernicious Anemia

### **If both parietal cell antibody and intrinsic factor antibody are negative-**

No immunological evidence of Pernicious Anemia

### **If parietal cell antibody is positive but intrinsic factor antibody is negative-**

Gastric Parietal cell antibody is associated with >90% of patients with Autoimmune Gastritis, the end result of which may be Pernicious Anemia (PA). In 20-30% of patients, relatives of patients with PA, autoimmune thyroiditis and a small

percentage of healthy persons may be positive and run an increased long term risk of pernicious anemia.

A negative Intrinsic Factor antibody result does not exclude the diagnosis of PA as only 60% of patients with PA will have this antibody.

**If parietal cell antibody is negative but intrinsic factor antibody is positive**

Immunological evidence of Pernicious Anemia (if the patient has low Hb macrocytosis and low B12 levels)

**or** (if only low B12)

The clinical significance of these results is uncertain in the absence of anaemia or macrocytosis. Suggest repeating in 6 mths with serum gastrin, full blood count and fasting B12.

**If parietal cell antibody is negative but intrinsic factor antibody is positive-  
(if >50 yrs old)**

Immunological evidence of Pernicious Anemia

**(if <50 yrs old)**

Suggest confirmation of diagnosis of Pernicious Anemia with Gastric Biopsy.

**If intrinsic factor antibody is positive and parietal cell antibody not done-  
(if >50 yrs old)**

Immunological evidence of pernicious anemia

**(if <50 yrs old)**

Suggest testing for Gastric Parietal Cell antibody to confirm diagnosis of Pernicious Anemia

**If intrinsic factor antibody is negative and parietal cell antibody is not done-**

Suggest testing for Gastric Parietal Cell antibody (GPC) because Intrinsic Factor Antibodies (IFA) are found only in about 60% of patients with Pernicious Anemia (PA) whereas GPC is an excellent marker for Autoimmune Gastritis associated with PA.

**If parietal cell antibody is positive and intrinsic factor antibody is not done-**

Gastric Parietal Cell antibody is associated with >90% of patients with Autoimmune Gastritis, the end result of which may be Pernicious Anemia (PA). 20-30% of relatives of patients with PA, autoimmune thyroiditis and a small percentage of patients may be positive and never reach the stage of PA. If PA is suspected, we suggest testing for antibodies to intrinsic factor.