Parietal Cell Antibody ELISA and Intrinsic Factor Antibody

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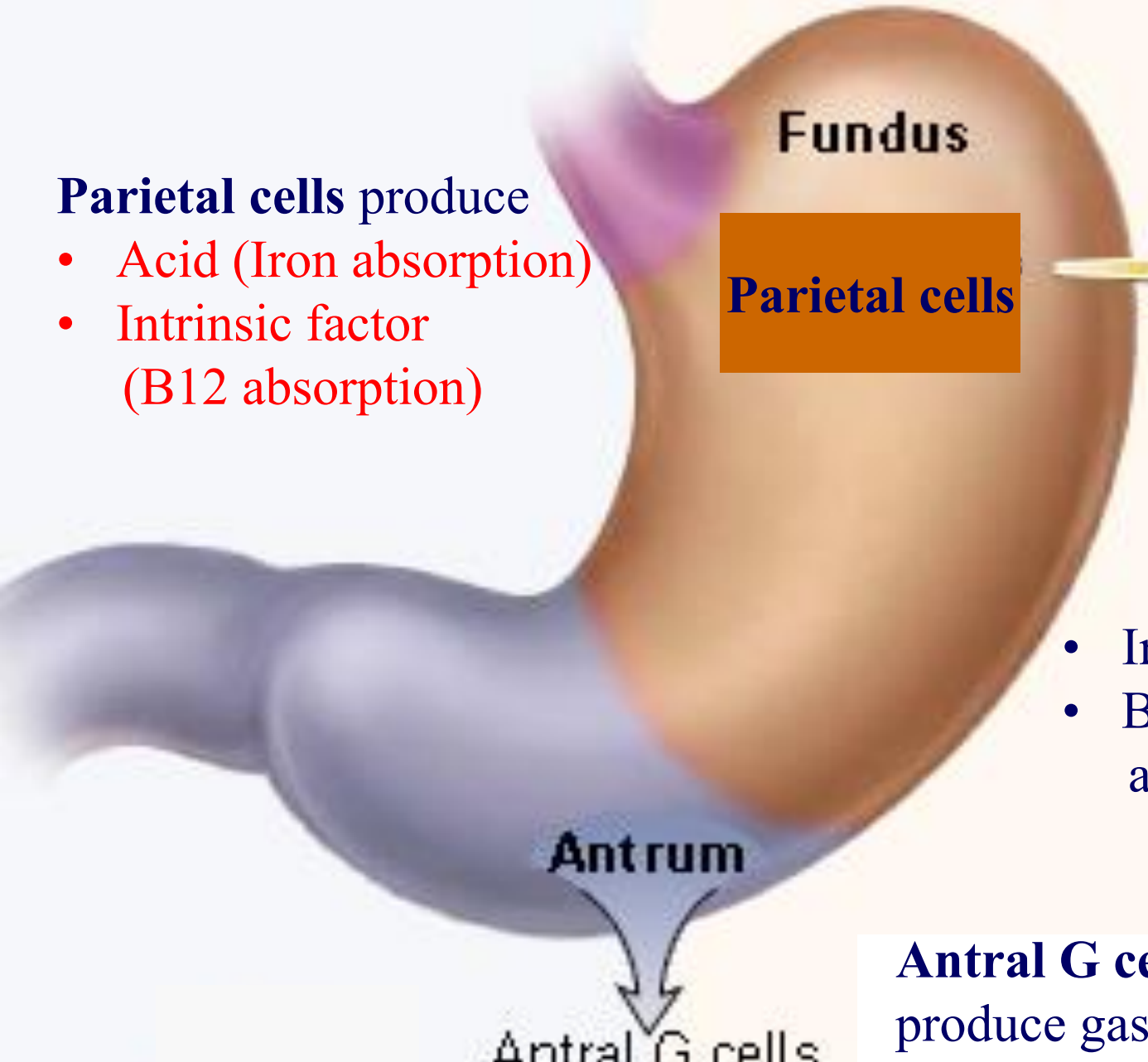
Phadia user group meeting
Rydges Sydney Airport Hotel, Dreamliner 1 Room
23rd November 2017

Parietal Cell Antibody = Autoimmune Gastritis (Asymptomatic)

Parietal cell antibody is a serum diagnostic marker for autoimmune gastritis identified by gastric biopsy

Autoimmune Gastritis affects Fundus, spares Antrum



Parietal cells produce

- Acid (Iron absorption)
- Intrinsic factor (B12 absorption)

Parietal, cells Destroyed

- Iron def anemia
- B12 def (Pernicious) anemia

Antral G cells produce gastrin

Autoimmune Gastritis

Asymptomatic

10-20 yrs

Chronic Atrophic Gastritis

Parietal cell destruction

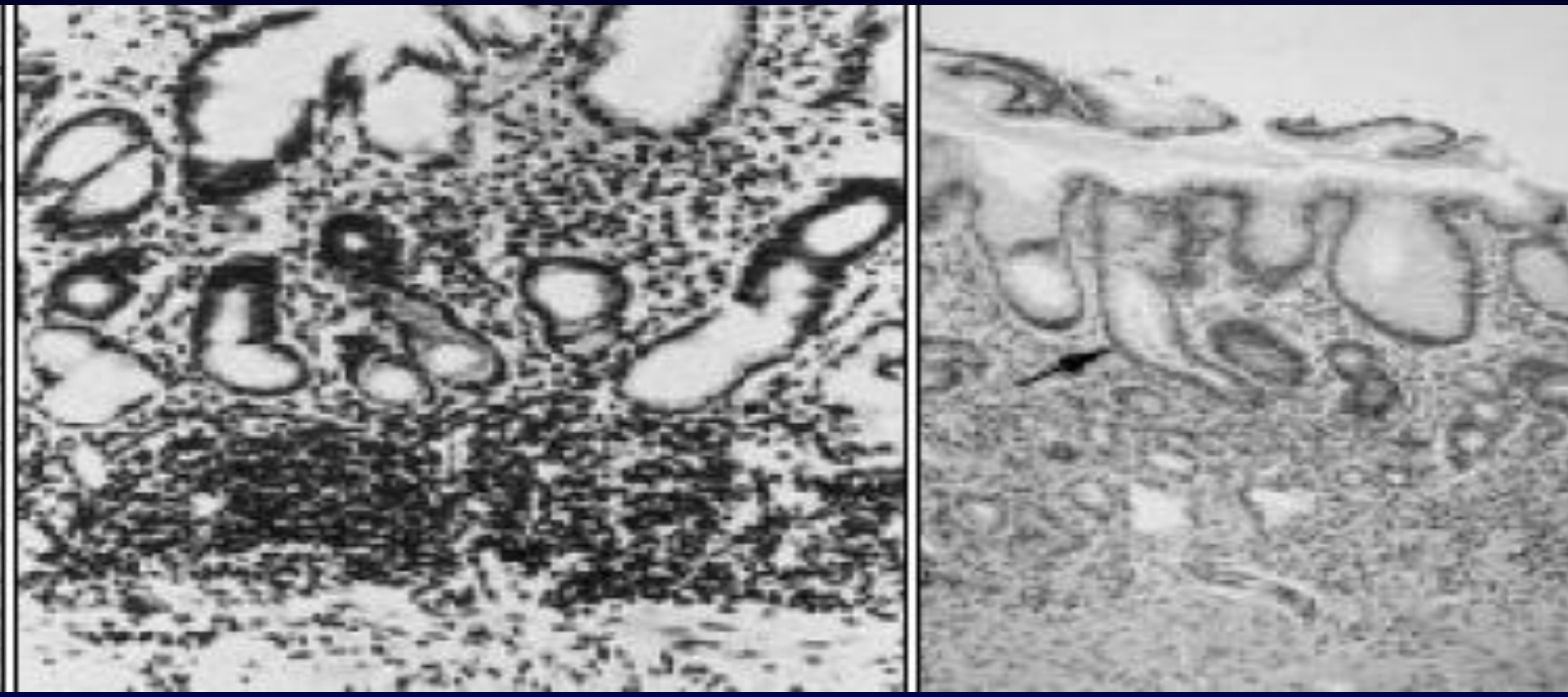
Loss of acid and intrinsic factor

Intrinsic factor antibody

Parietal Cell Antibody to gastric H/K ATPase

Fe-deficient/Pernicious/anaemia

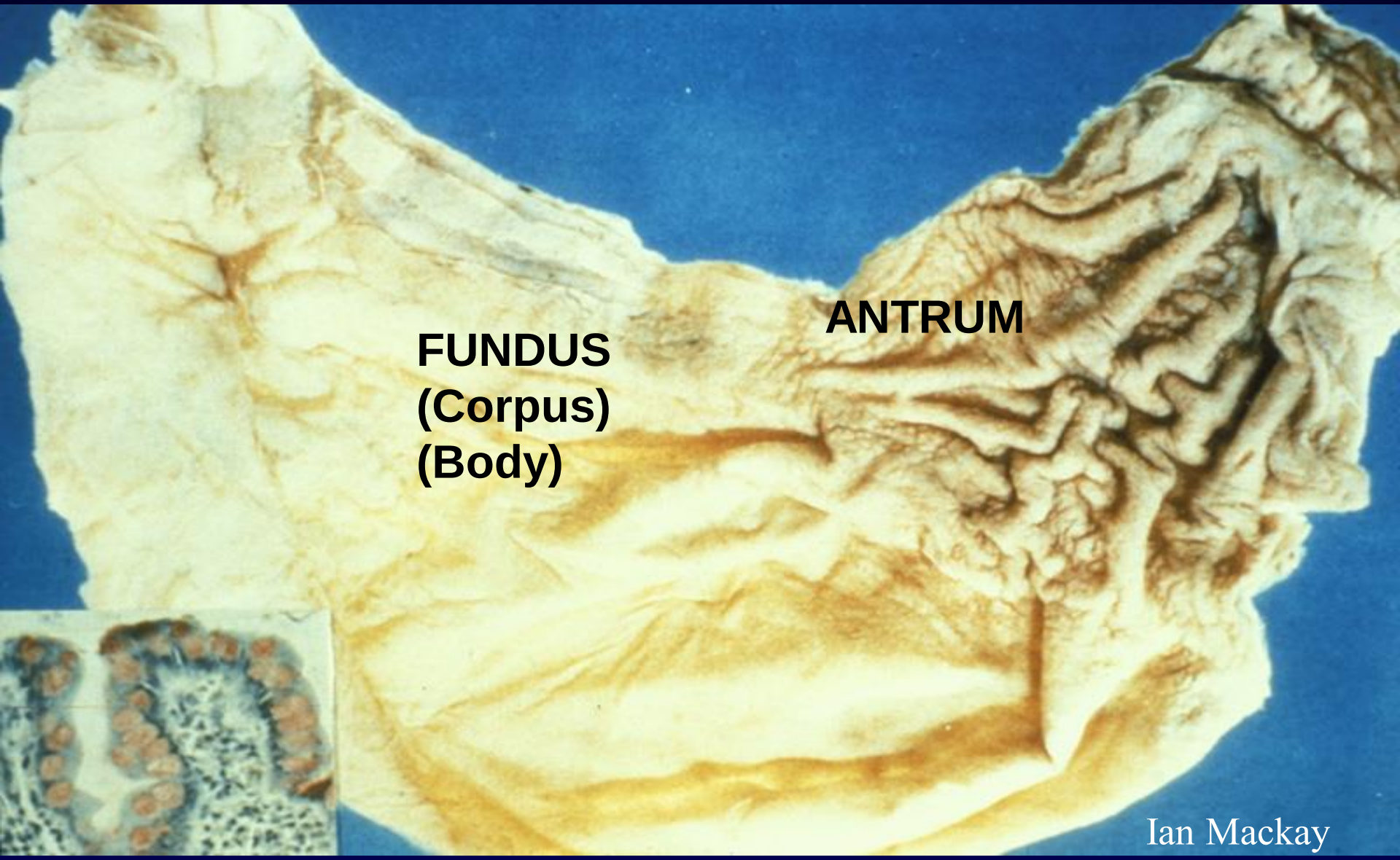
Autoimmune Gastritis progresses to Atrophic Gastritis



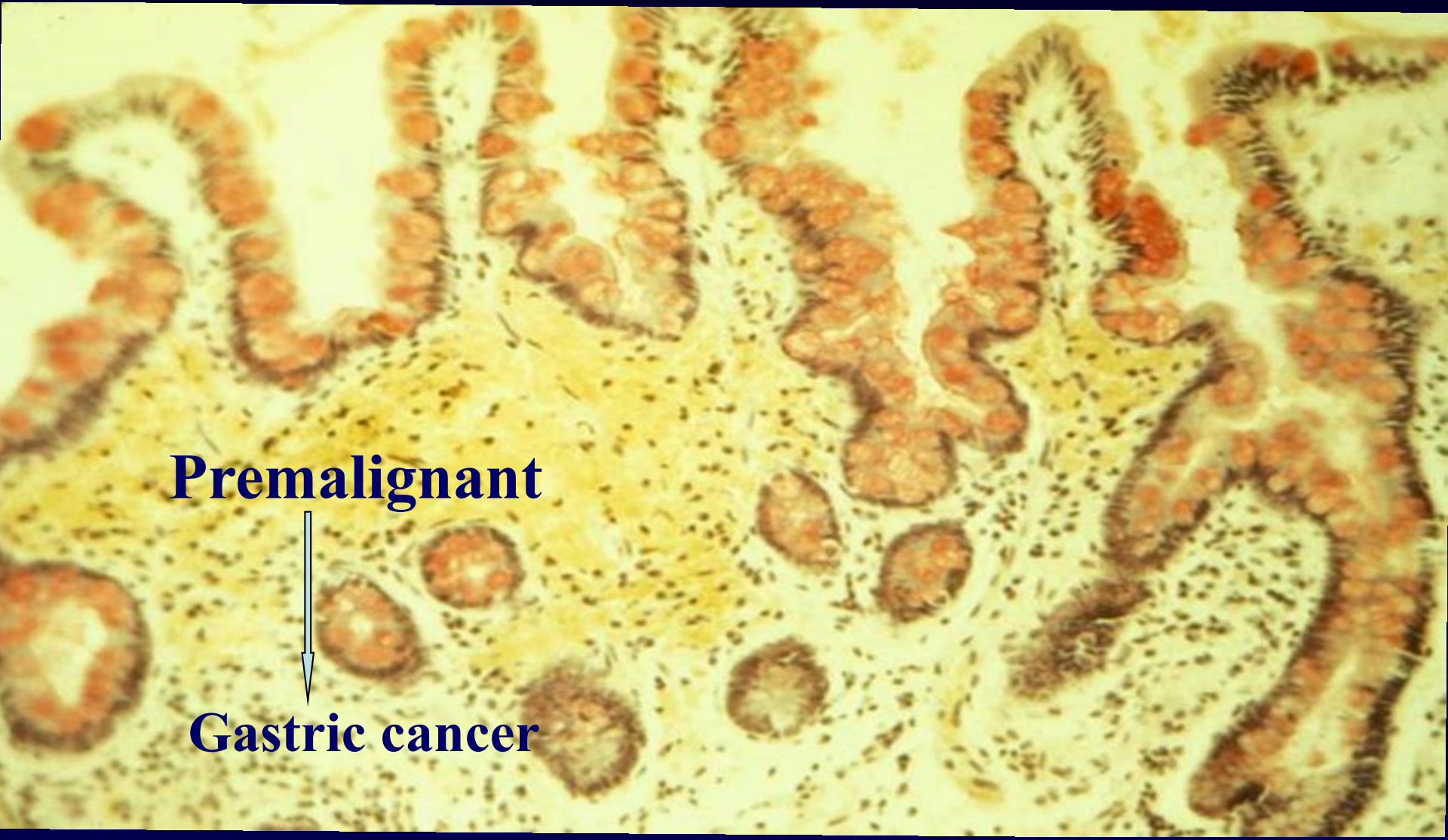
Autoimmune Gastritis → Gastric Atrophy

Whittingham S, Mackay I and Toh BH. *Current medical literature-Gastroenterology* 2007, 26: 29-36

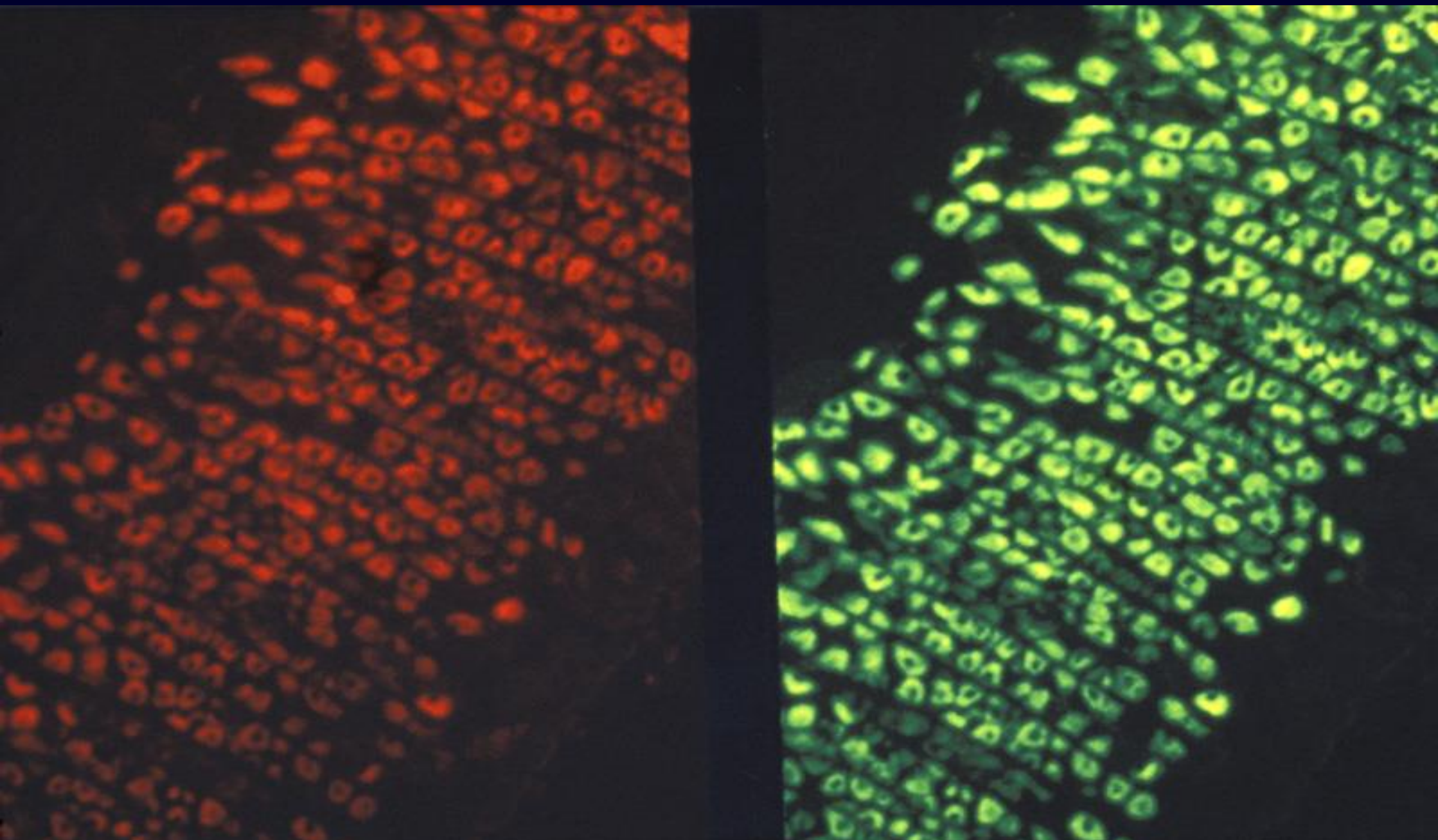
End-Stage Chronic Atrophic Gastritis of Fundus sparing Antrum



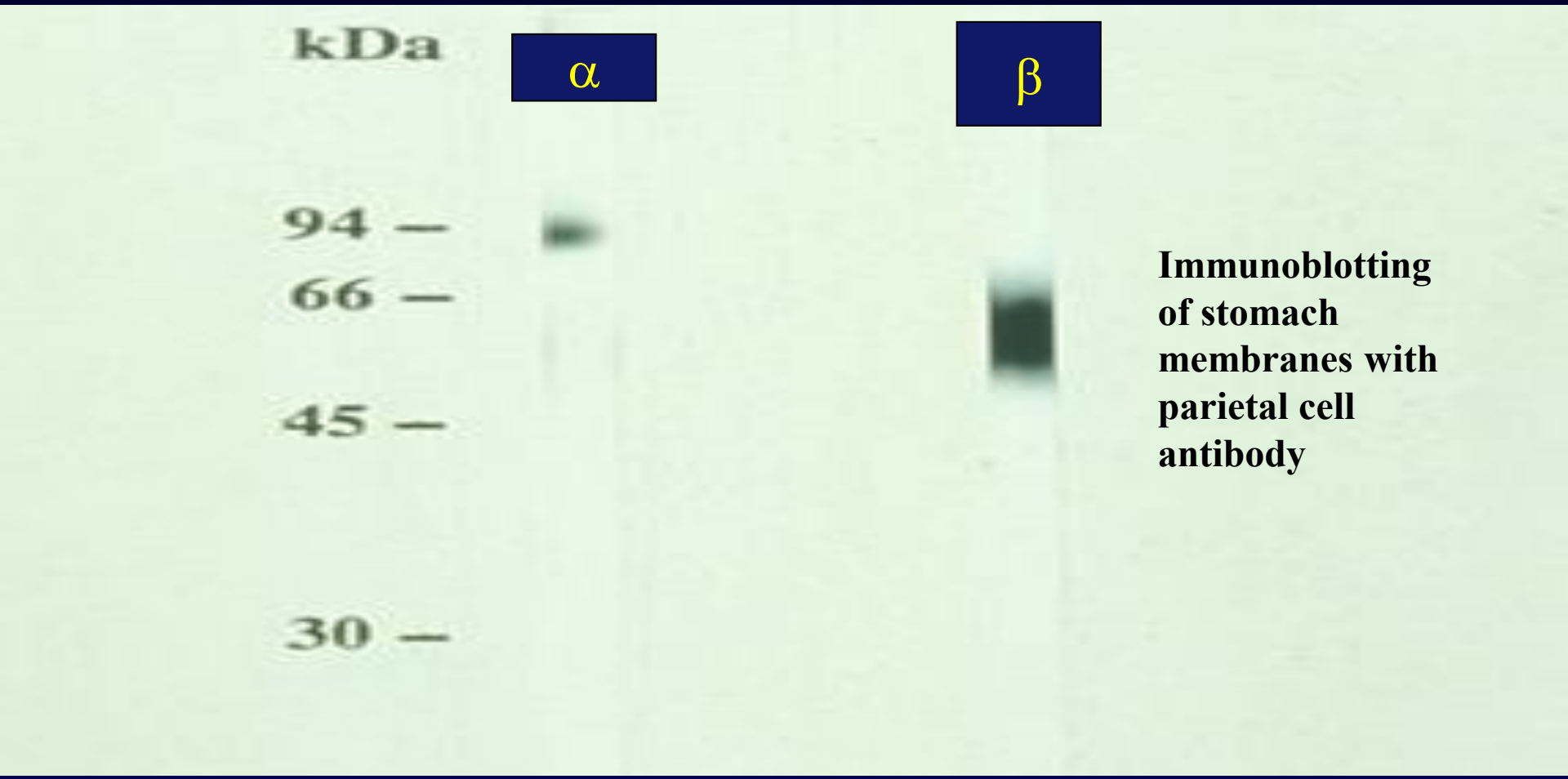
Intestinal *Metaplasia*: mucous cells replace parietal, zymogenic and ECL cells



Parietal cell antibodies



Parietal cell antibodies target gastric H/K ATPase α and β subunits

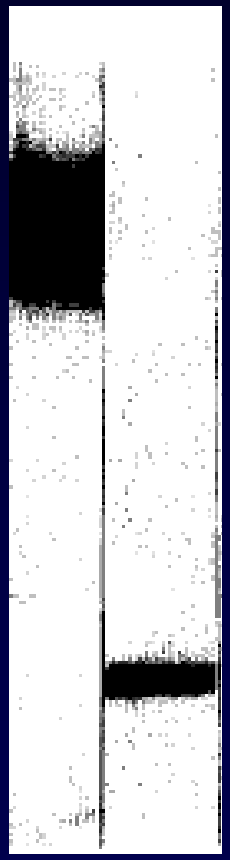


Immunoblotting of stomach membranes with parietal cell antibody

Callaghan J, Khan A, Alderuccio F, van Driel I Gleeson P, Toh BH. *Autoimmunity*. 1993;16:289

β subunit of the gastric H/K ATPase is a heavily glycosylated 35 kDa core protein

60–90 kd
β subunit



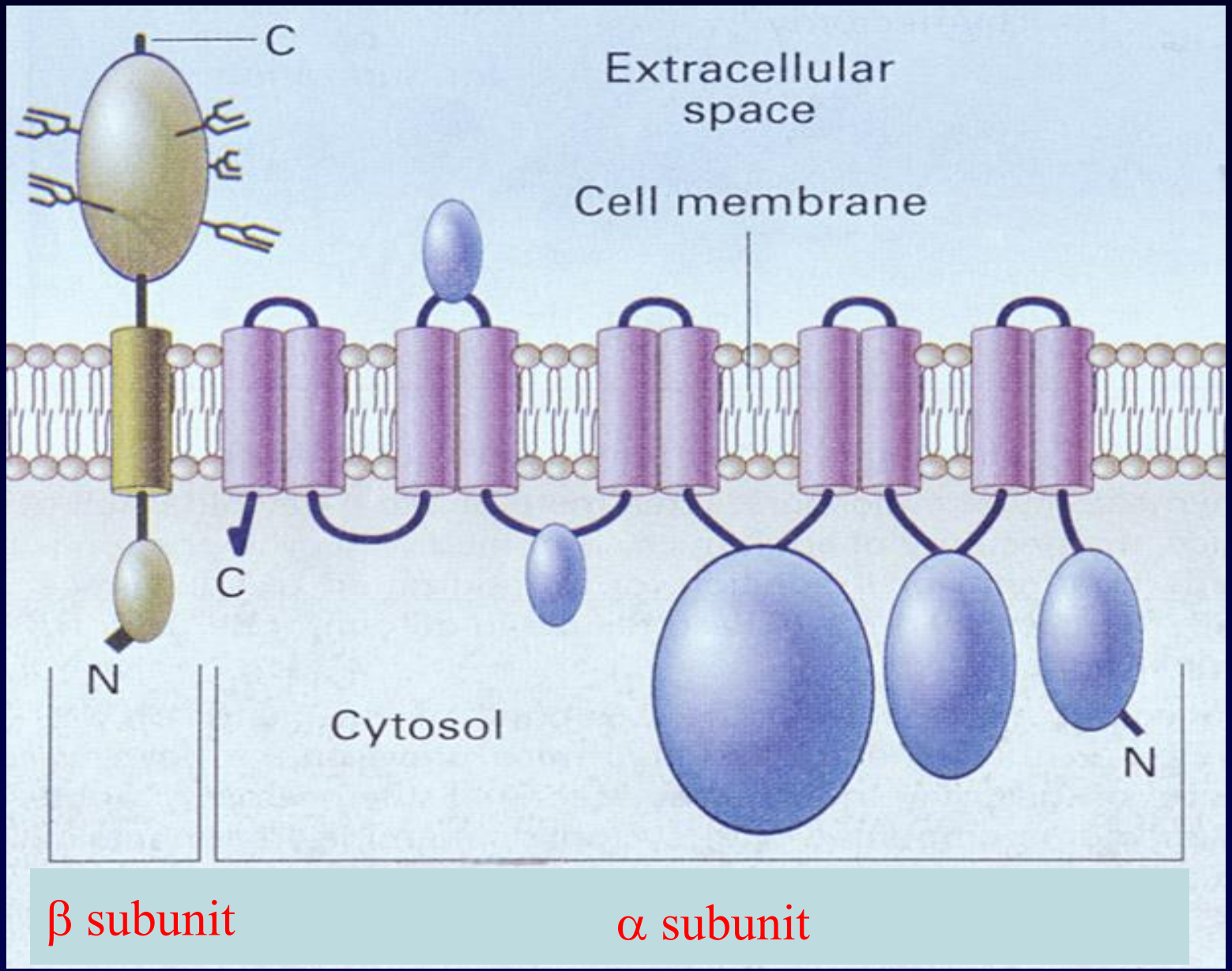
35 kd core protein

Proc Nat Acad Sci, 1990; 87, 6418-6422

The 60-90 kDa parietal cell autoantigen associated with autoimmune gastritis is a β subunit of the gastric H/K ATPase (proton pump)

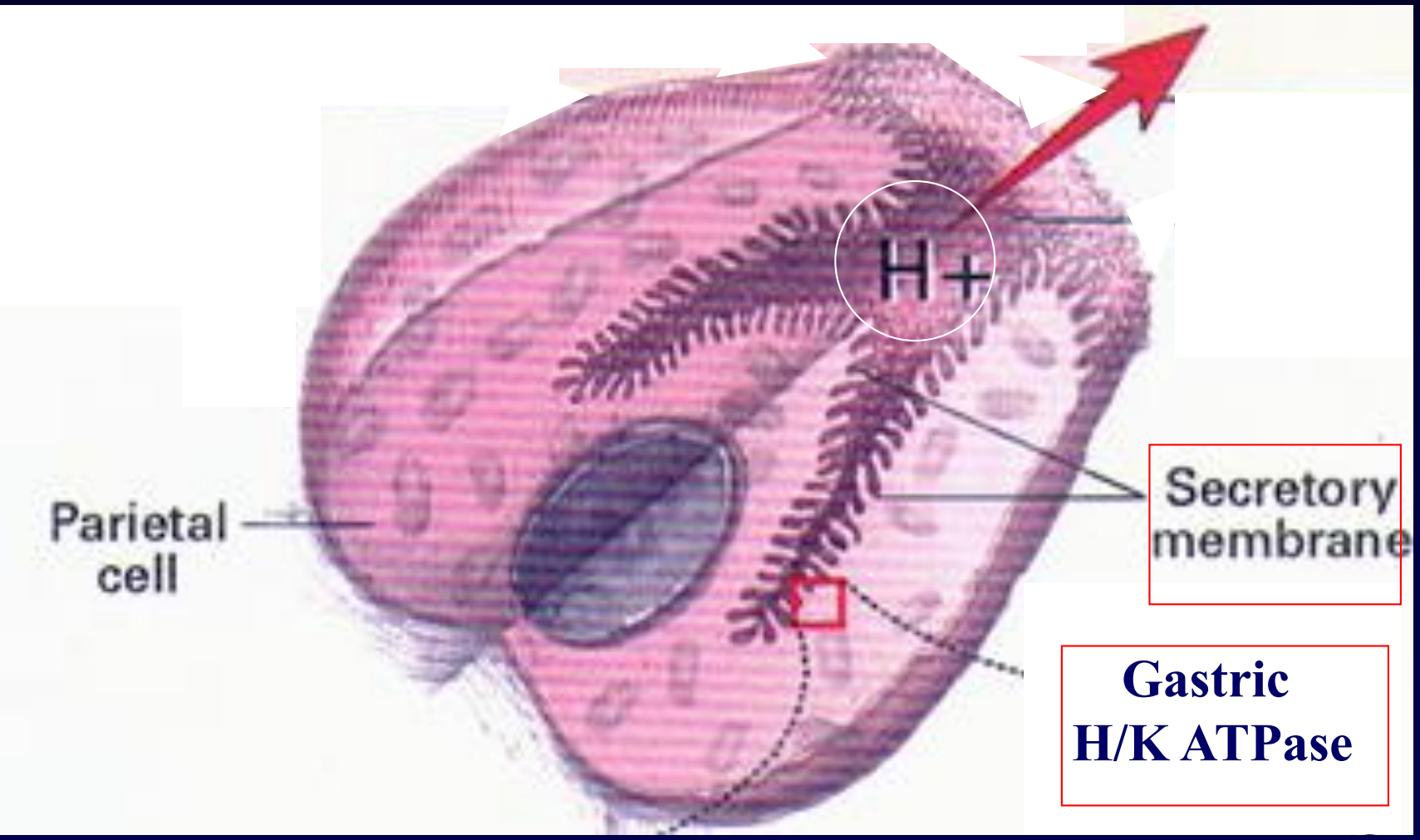
Toh BH et al

Gastric H/K ATPase



Toh BH et al. *N Engl J Med.* 1997;337:1441-8.

Gastric H/K ATPase is located on secretory membranes



Toh BH et al. *N Engl J Med.* 1997;337:1441-8.

Haematologic complications of gastric atrophy

- Iron-deficiency anemia 40yr
- B12-deficiency pernicious anemia 60yr

Iron-deficiency Anemia

- 21 yr younger than B12-deficient patients
- Females mostly
- K. Faber >100 yr ago: "Achylia gastrica mit Anämie", Medizinishe Klinik, vol. 5, 1909,1310–1325.
- *Gastric autoimmunity causes 20-25% of obscure/refractory iron deficiency anemia and is 4-6x more common than coeliac disease*
- Progresses to B12 deficiency anemia

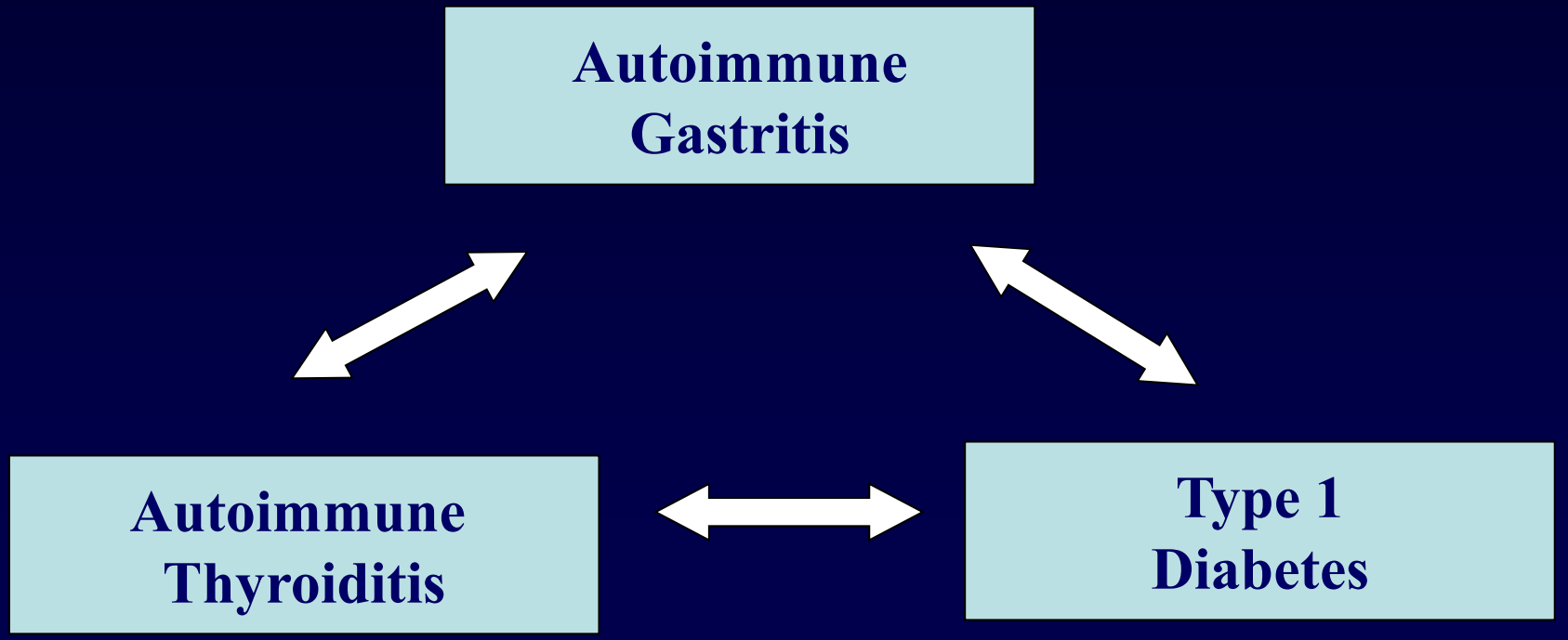
Hershko et al, *Blood,* 2006, 107, 1673

Associated Endocrinopathies

- **Autoimmune Thyroiditis: 40%**
  (*Thyro-gastric autoimmunity)*
- **Type 1 Diabetes Mellitus: 10%**

Lahner E et al *Am J Med.* 2008;121:136-41.
Tsirogianni et al. *Autoimmun Rev*. 2009, 8:687-91.

Triad of "*Thyro-Gastric Autoimmunity*" and Type 1 diabetes



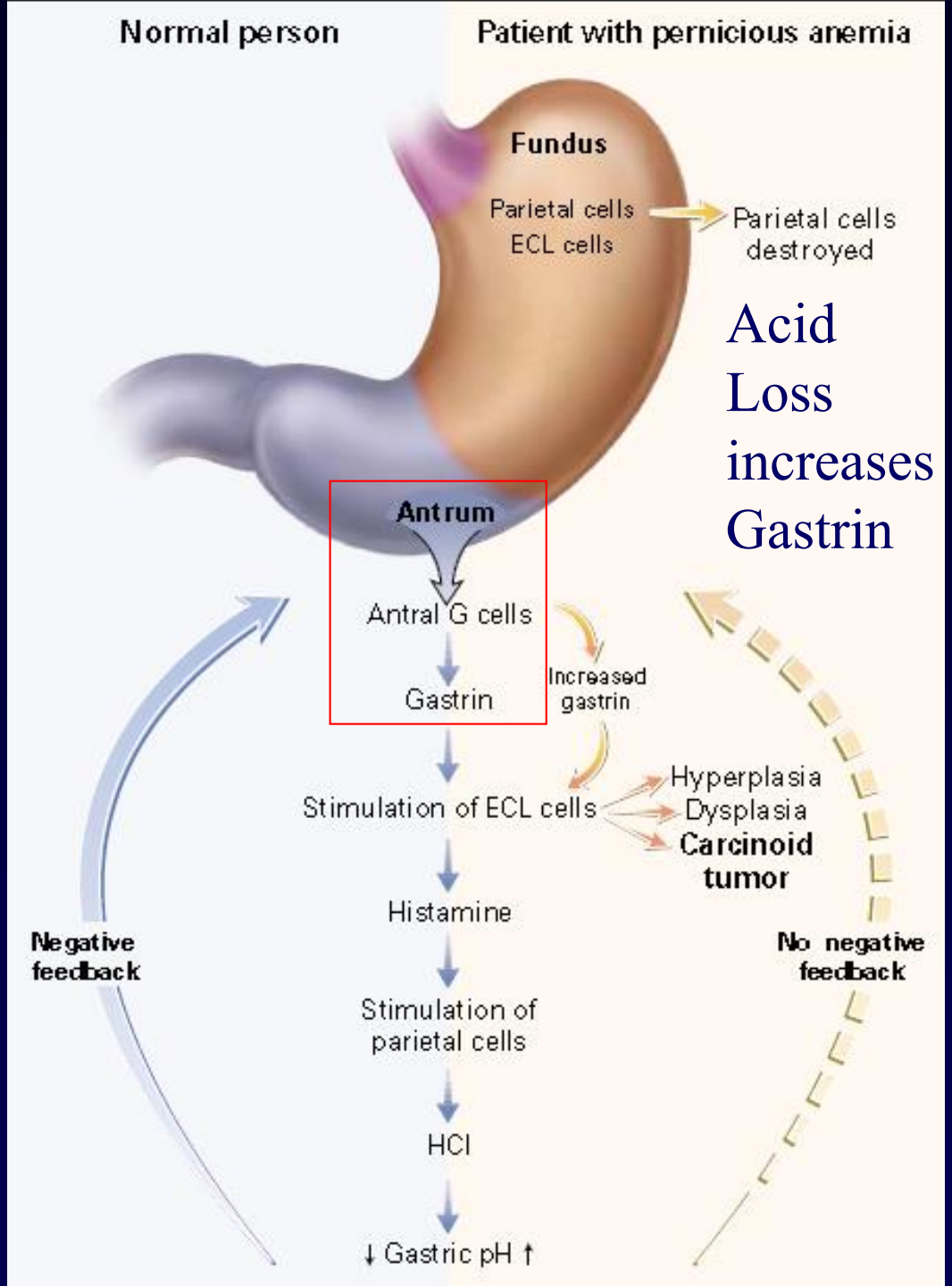
Serum Biomarkers

Autoimmune gastritis

- Parietal cell antibody to gastric H/K ATPase
- Intrinsic factor antibody

Chronic atrophic gastritis

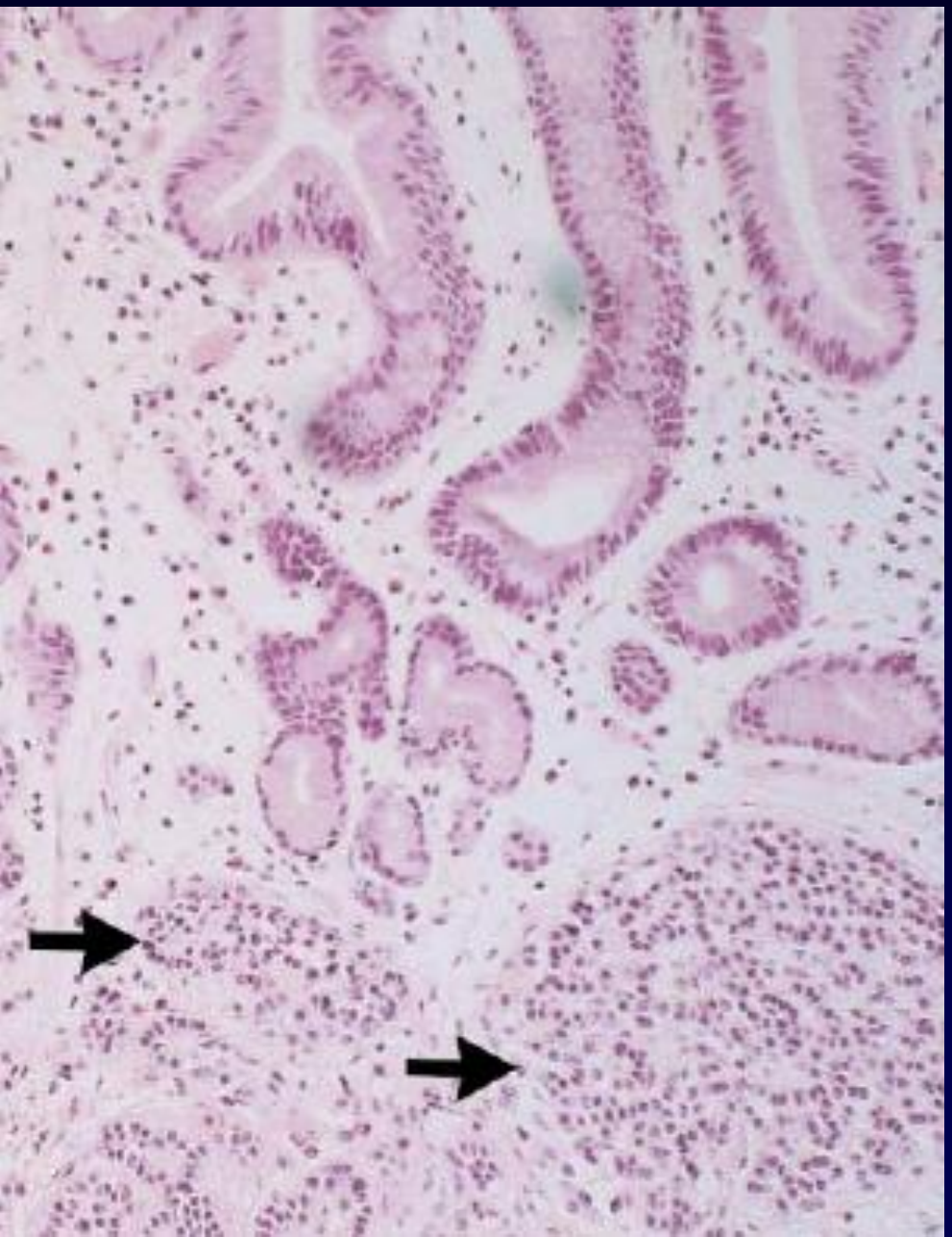
- Gastrin

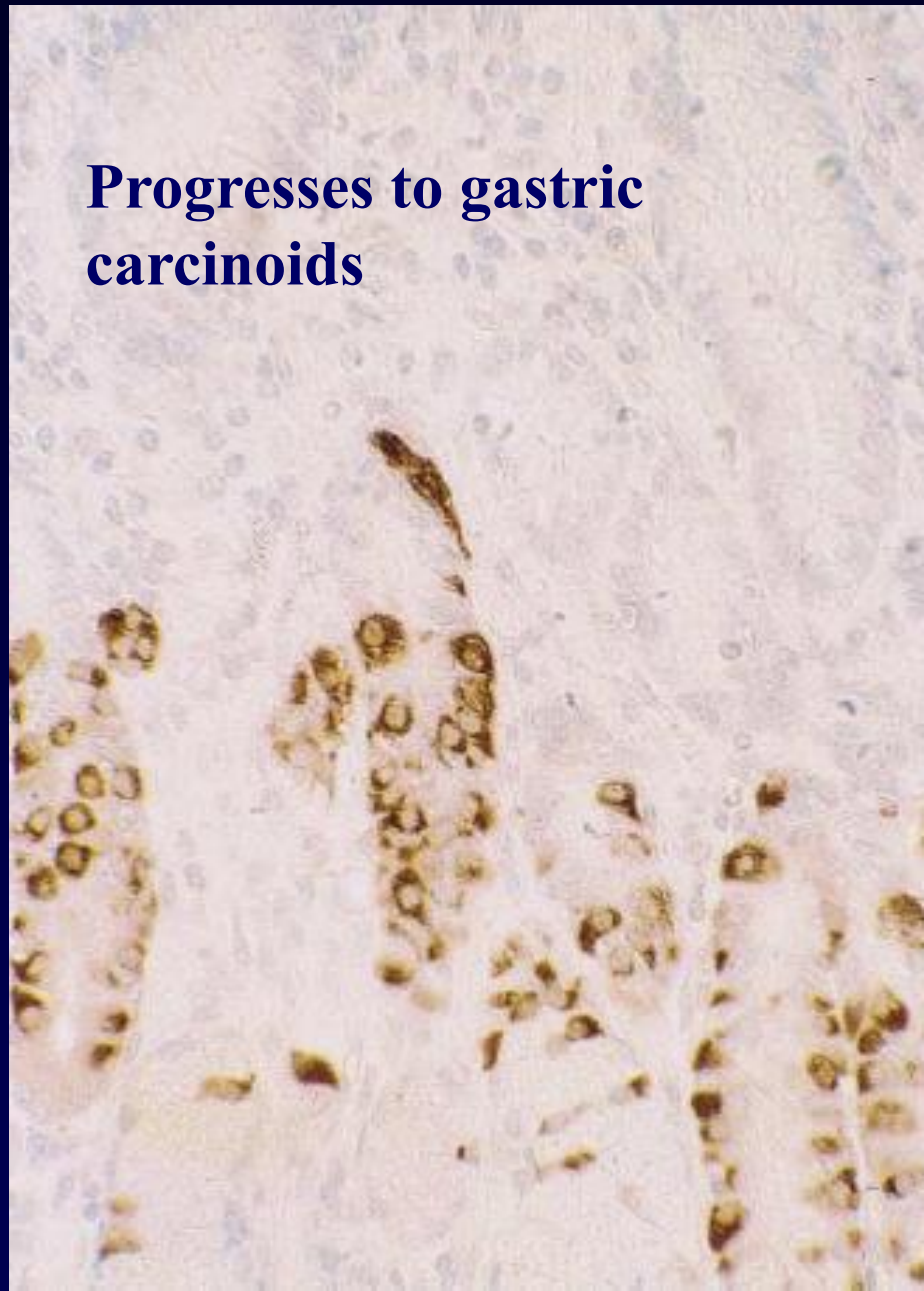


Acid Loss increases Gastrin

Case records Mass Gen
N Eng J Med
1997, 336; 861

Neuroendocrine G (Gastrin) cell Hyperplasia





Progresses to gastric carcinoids

Serum Biomarker for Gastric Atrophy "Serological Gastric Biopsy"

	Sensitivity	Specificity
• Gastrin	90%	100%

Autoimmunity, 1992, Vol. 12, pp. 1–7
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DIAGNOSTIC ELISA FOR PARIETAL CELL AUTOANTIBODY USING TOMATO LECTIN-PURIFIED GASTRIC H^+/K^+-ATPASE (PROTON PUMP)

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Predictive value of parietal cell antibody

Predicts development of gastric atrophy and pernicious anemia in *Autoimmune Thyroiditis and Autoimmune Diabetes*

Parietal Cell Antibody

- *Diagnostic* for asymptomatic autoimmune gastritis
- *Predictive* for development of chronic atrophic gastritis and symptomatic Fe/B12 deficiency

Intrinsic factor antibody

- Combined with Parietal Cell Antibody, increases sensitivity for pernicious anemia
- Limited value for Parietal Cell Antibody negative patients

Limited value of intrinsic factor antibody

	Parietal cell antibody	Intrinic factor antibody
Retrospective (n=847)	86.3%	0.04%

PCA by immunofluorescence

Khan S et al *J Clin Pathol*. 2009 ;62:439-41

Autoimmunity. 2012;45:527-32

Parietal cell antibody identified by ELISA is superior to immunofluorescence, rises with age and is associated with intrinsic factor antibody

BAN-HOCK TOH[1,2], T KYAW[1], ROBERTA TAYLOR[2], WENDY POLLOCK[2], & WOLFGANG SCHLUMBERGER[3]

Table I. Gastric H/K ATPase antibody identified by *Euroimmun* ELISA compared with Parietal Cell Antibody identified by immunofluorescence in a *retrospective set* of 138 sera assessed for intrinsic factor antibody.

ELISA is 32% more sensitive than immunofluorescence

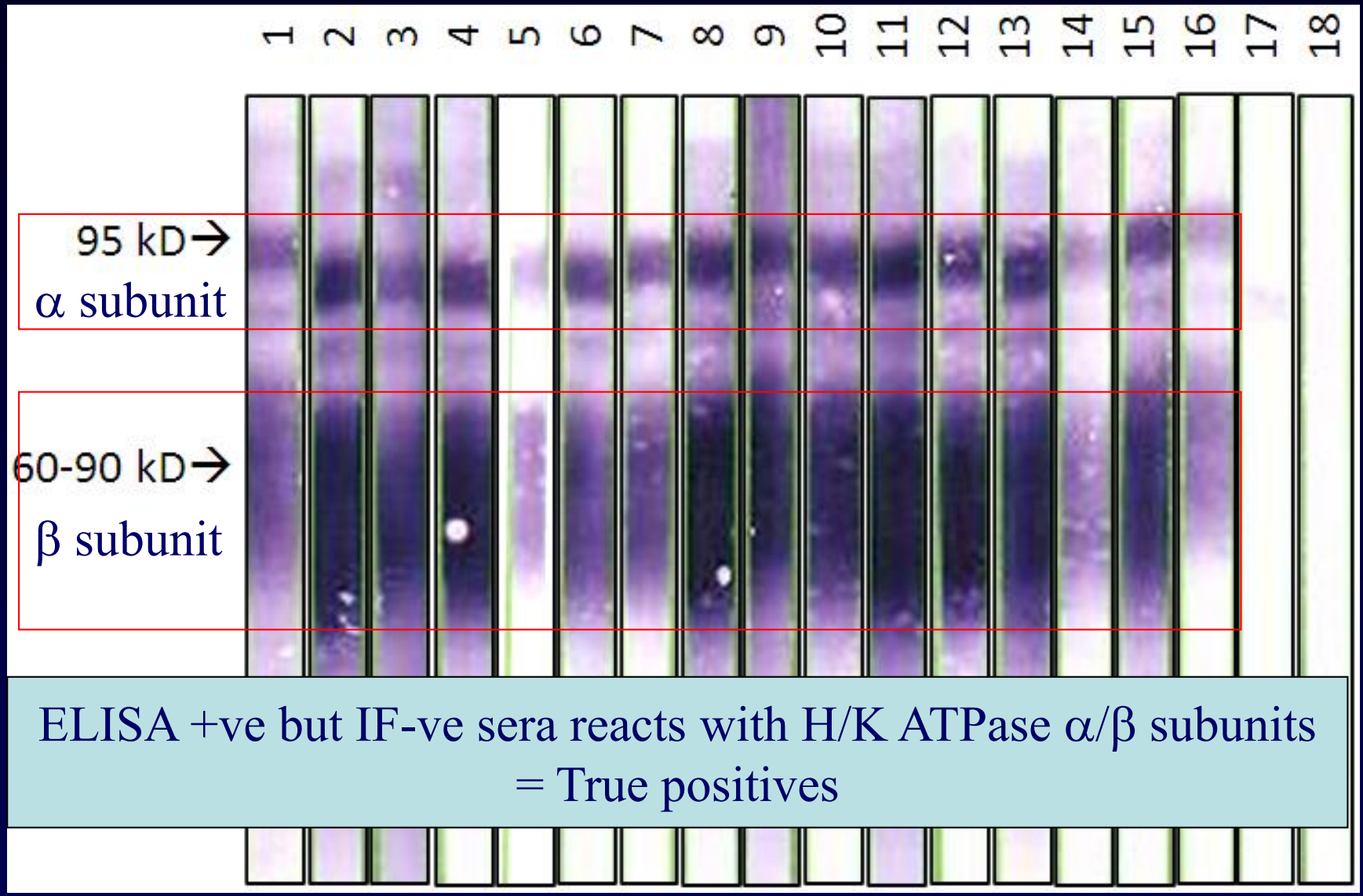
		Gastric H/K ATPase antibody (*Euroimm* ELISA)		
		Positive	Negative	Total
Parietal Cell Antibody (Immunofluorescence)	Positive	59	3	62
	Negative	28	48	76
Total		87	52	138

Table II. Gastric H/K ATPase antibody identified by *Inova* ELISA compared with Parietal Cell Antibody identified by immunofluorescence in a *retrospective set* of 138 sera assessed for intrinsic factor antibody.

		Gastric H/K ATPase antibody (*Inova* ELISA)		
		Positive	Negative	Total
Parietal Cell Antibody (Immunofluorescence)	Positive	58	4	62
	Negative	20	56	76
Total		78	60	138

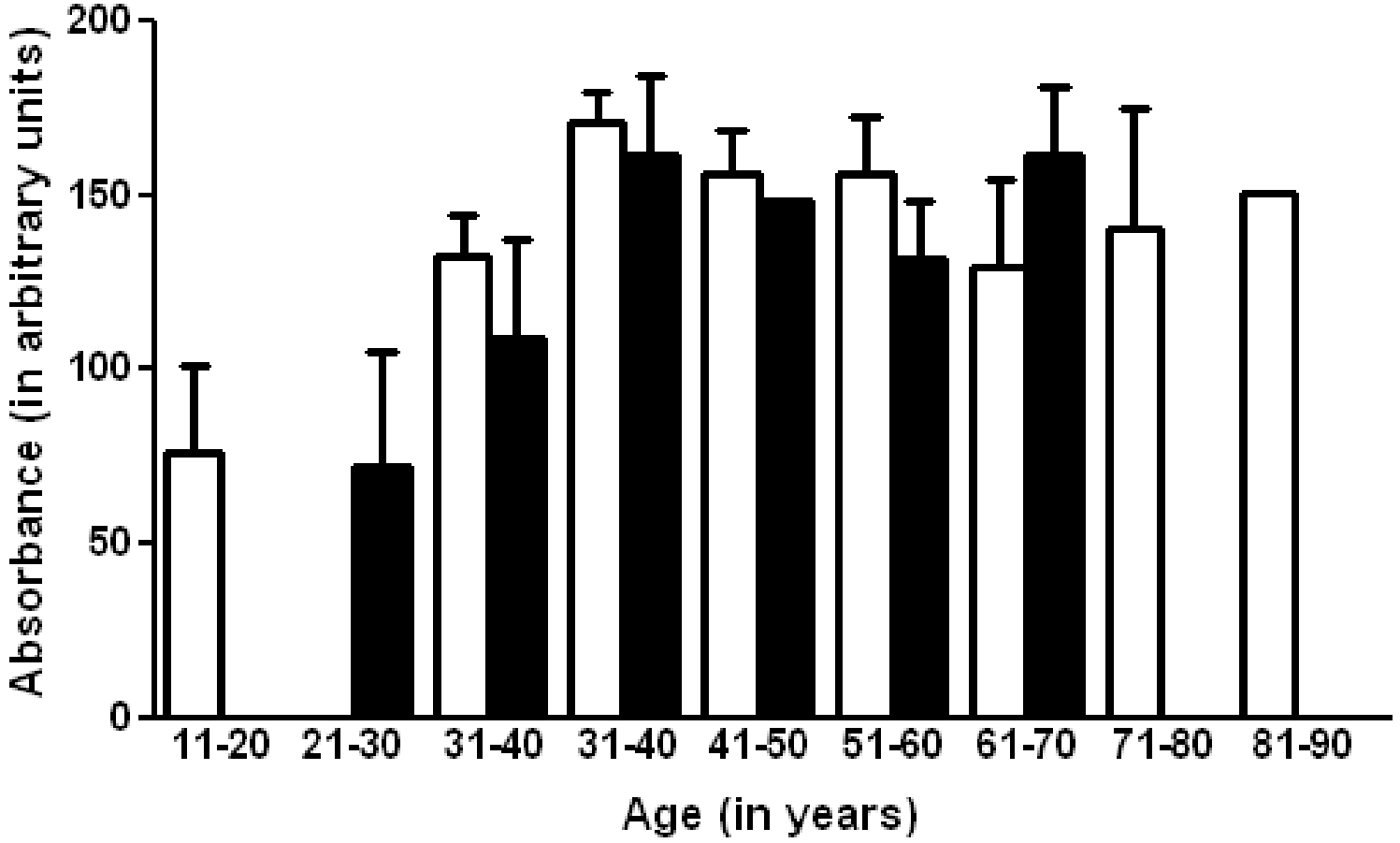
Table III. Gastric H/K ATPase antibody identified by *Euroimmun* ELISA compared with Parietal Cell Antibody identified by immunofluorescence in 161 *prospective* sera sent for testing for tissue-reactive antibodies.

		Gastric H/K ATPase antibody (*Euroimm* ELISA)		
		Positive	Negative	Total
Parietal Cell Antibody (Immunofluorescence)	Positive	21	3	24
	Negative	8	129	137
Total		29	132	161



ELISA +ve but IF-ve sera reacts with H/K ATPase α/β subunits = True positives

Comparison between ELISA+/IIF+ and ELISA+/IIF-



Practical Implications

- Patients with one member of the triad of autoimmune gastritis, thyroiditis and type 1 diabetes should be screened for presence of the other partners

- Aymptomatic patients should be followed up yearly for progression to organ failure

Indications for yearly testing

- Asymptomatic subjects with Parietal Cell Antibody
- Autoimmune thyroiditis
- Type 1 diabetes mellitus

Yearly Assessments

Gastric Autoimmunity
Parietal cell antibody
Intrinsic factor antibody

↓

Biomarker of Corpus Atrophy
gastrin

↓

Haematologic Sequelae
Serum iron, B12 and FBE

ELISA for Parietal Cell Antibody

- Automated
- Objective
- Quantitative
- **Enhanced sensitivity of 25-30%**
- **Early detection of Asymptomatic Autoimmune gastritis at risk of developing Symptomatic Atrophic gastritis**

Chronic Atrophic Gastritis

- **Antral Gastritis**
- *Helicobacter pylori*

- **Corpus Gastritis**
- *Autoimmune*

Atrophic corpus gastritis is the end-stage of autoimmune gastritis

H.Pylori as "trigger" for autoimmune gastritis?

H. Pylori prevalence decreases with age

- < 20 yr 87.5 %
- 20-40 yr 47 %
- 41-60 yr 37.5 %
- > 60 yr 12.5 %

Hershko et al, *Blood,* 2006, 107, 1673

H.Pylori:"Hit and Run" Hypothesis

Antral Gastritis:

H.pylori *infection*

Molecular mimicry between H.pylori & Gastric H/K ATPase

Corpus Gastritis

Autoimmune Gastritis

Corpus Atrophy

H.Pylori *loss*

References

1: Toh BH. Pathophysiology and laboratory diagnosis of pernicious anemia. *Immunol Res.* 2017;65:326-330.

2: Toh BH. Diagnosis and classification of autoimmune gastritis. *Autoimmun Rev.* 2014;13:459-62.