Ordine dei Medici Chirurghi e degli Odontoiatri della provincia di **Belluno**

FNOMCeO
Federazione Nazionale degli Ordini dei Medici Chirurghi e degli Odontoiatri

LA SORVEGLIANZA DELLE CONDIZIONI E DELLE LESIONI PRECANCEROSE IN GASTROENTEROLOGIA

GASTRITI ATROFICHE

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UOSD Anatomia Patologica
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ULSS1 Dolomiti

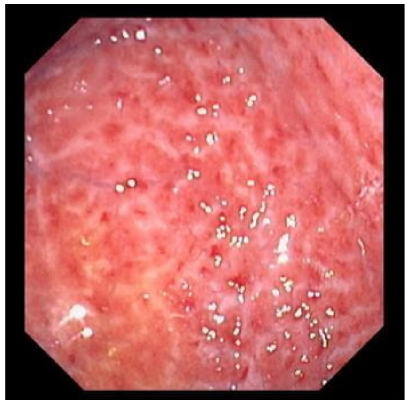
21 Ottobre 2023

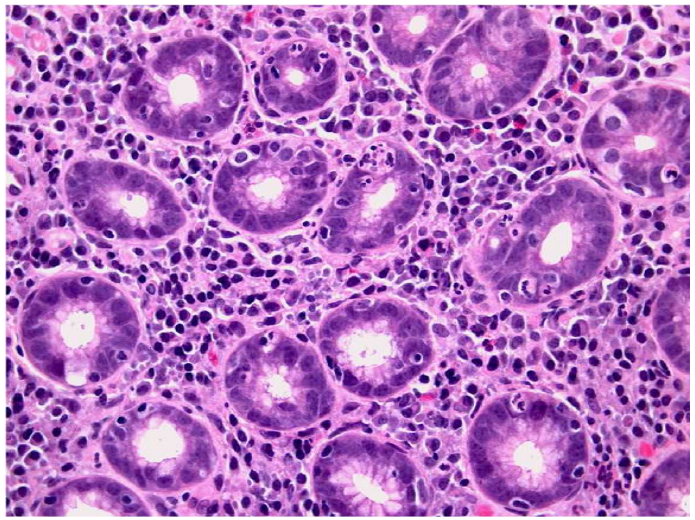
REGIONE DEL VENETO
ULSS 1 DOLOMITI

SOMMARIO

- Definizione di Gastrite
- Definizione di Atrofia
- Classificazione eziologica/Lesioni correlate
- Stadiazione e Sorveglianza
- Conclusioni

GASTRITE

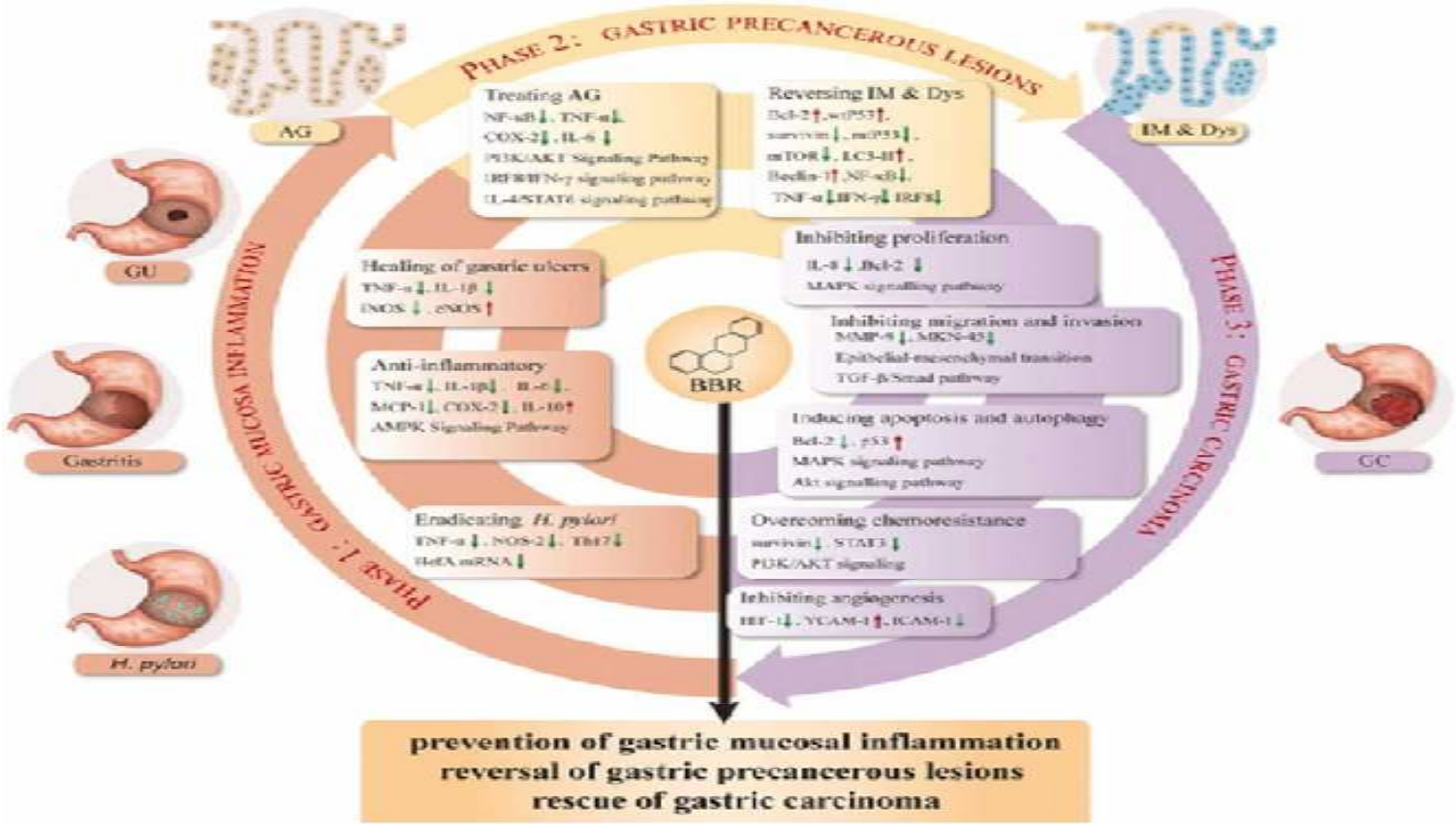




Main etiological category	Pathogenic mechanism	Agent	Specific agent
Environmental	Transmissible	Parasitic	Anisakiasis *Cryptosporidium* *Strongyloides stercoralis*
		Fungal	Mucormycosis Candidiasis *Actinomyces* Histoplasmosis
		Bacterial	*Helicobacter pylori* (A) *Enterococcus* *Treponema pallidum*
		Viral	*Cytomegalovirus* *Enterovirus* Epstein-Barr virus
	Not transmissible	Chemical	Endogenous (bile); Exogenous (alcohol, NSAIDs, doxycycline, taxol, lanthanum carbonate)
		Physical	Radiation
	Unknown		
Host-related	Autoimmune Immune-mediated	Diagnostic label	
		Autoimmune (A)	
		Allergic	
		Lymphocytic	
		Eosinophilic	
		Collagenous	
		Graft-versus-host disease	
		Congenital immune disorders	
	Associated with systemic diseases	Crohn's, vasculitis, sarcoidosis, ischemia	
	Unknown	Stress-induced	

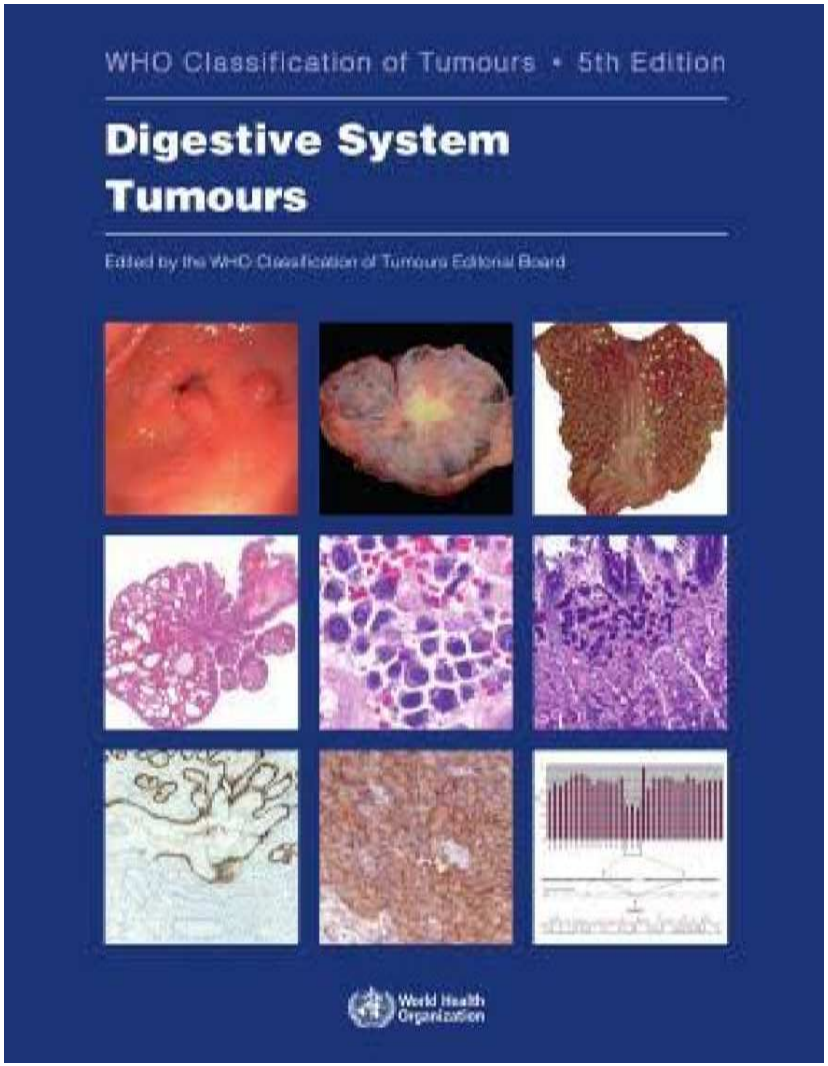
Sugano K.et al. Kyoto Global Consensus Report on H. Pylori Gastritis. Gut 2015
El-Zimaity H. et al. The differential diagnosis oh H. Pylori negative gastritis. Virchow Arch. 2018

CORREA'S CASCADE



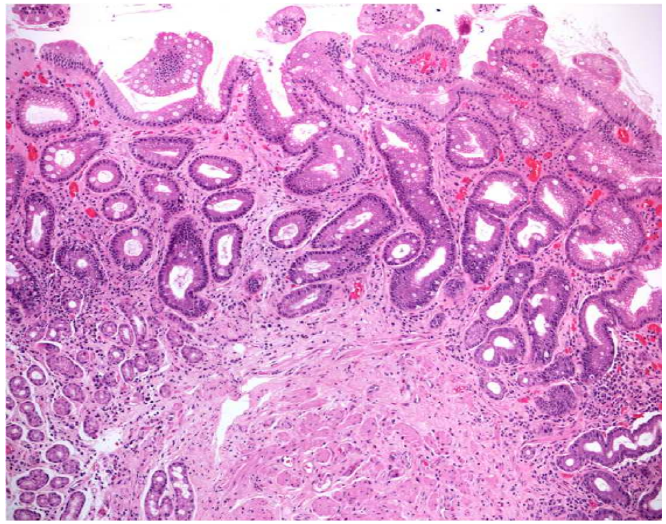
Qingsong Liu . Pharmacological Research 2022

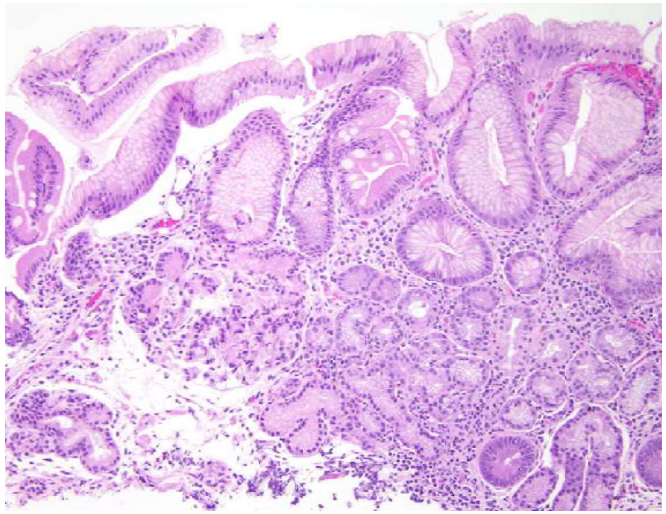
Gastriti e metaplasia: precursori del carcinoma gastrico (GC)



Rugge M. (2019)

GASTRITE ATROFICA
- Definizione -





- Perdita delle ghiandole native
- GA non metaplasica /metaplasica
- Causa di modificazioni funzionali

Environmental Metaplastic Atrophic Gastritis (**EMAG**)
- Eziologia-

- H. Pylori, alcool, fumo, sale, reflusso biliare
- Asintomatici/Dispepsia
- Pepsinogeno
- Gastrina sierica a digiuno/Ab cellule parietali

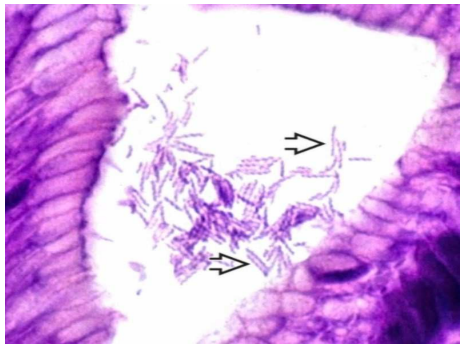
Multifocal atrophic gastritis

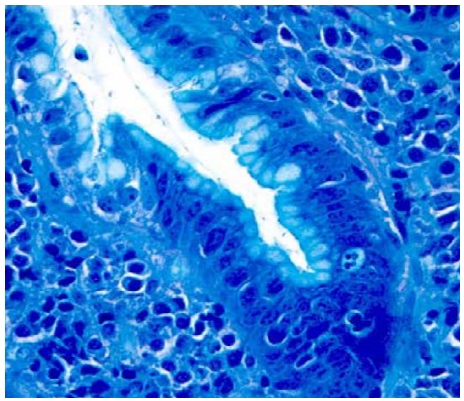
INFEZIONE da HP

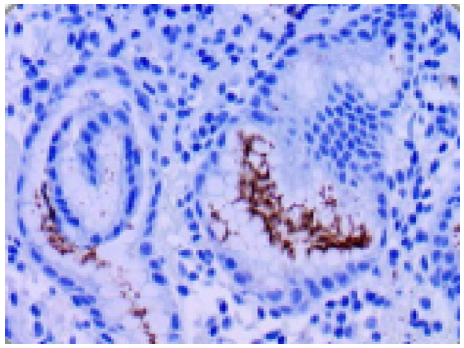
UNIDENTIFIED CURVED BACILLI IN THE STOMACH OF PATIENTS WITH GASTRITIS AND PEPTIC ULCERATION*

BARRY J. MARSHALL J. ROBIN WARREN

Departments of Gastroenterology and Pathology, Royal Perth Hospital, Perth, Western Australia



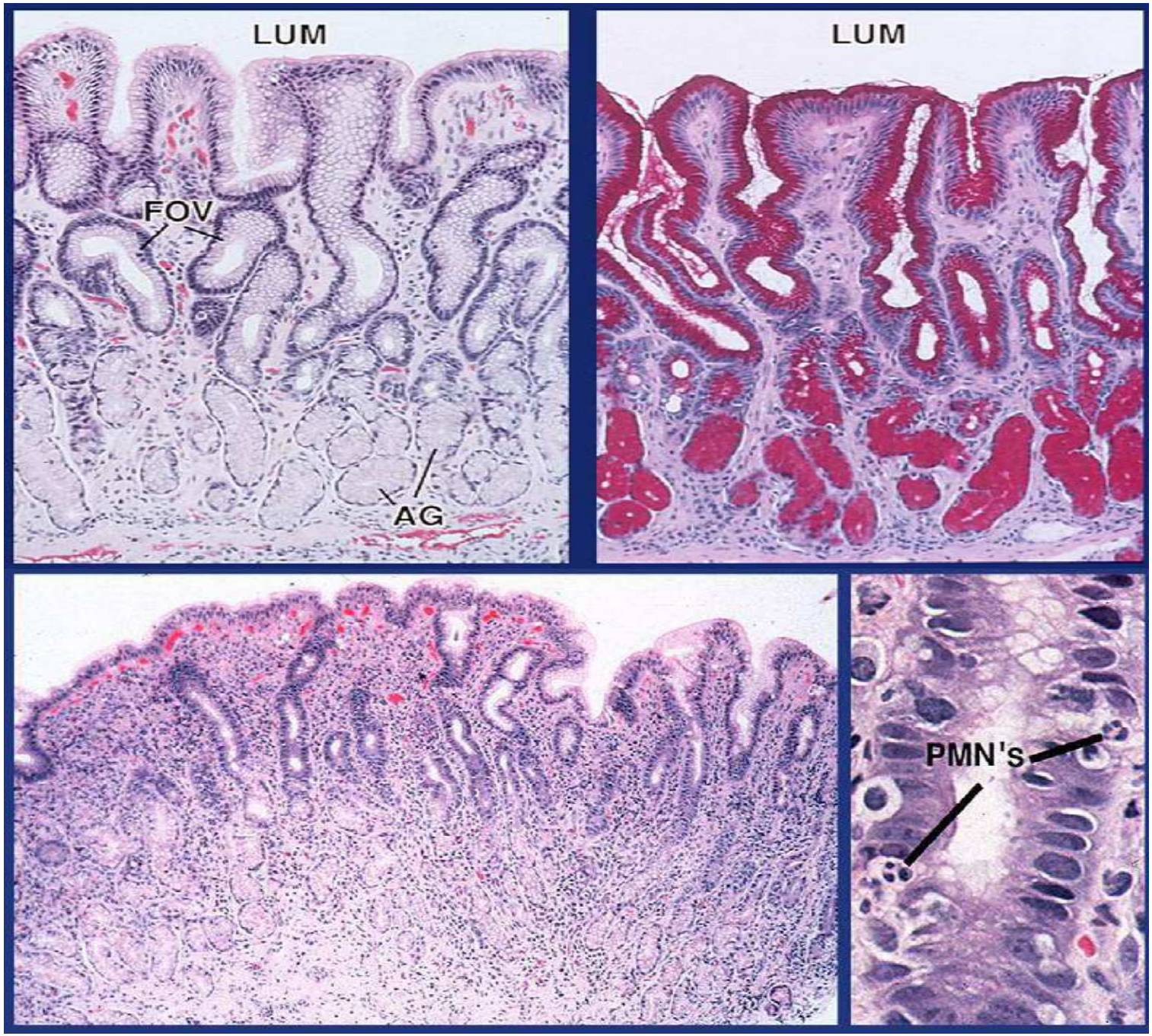


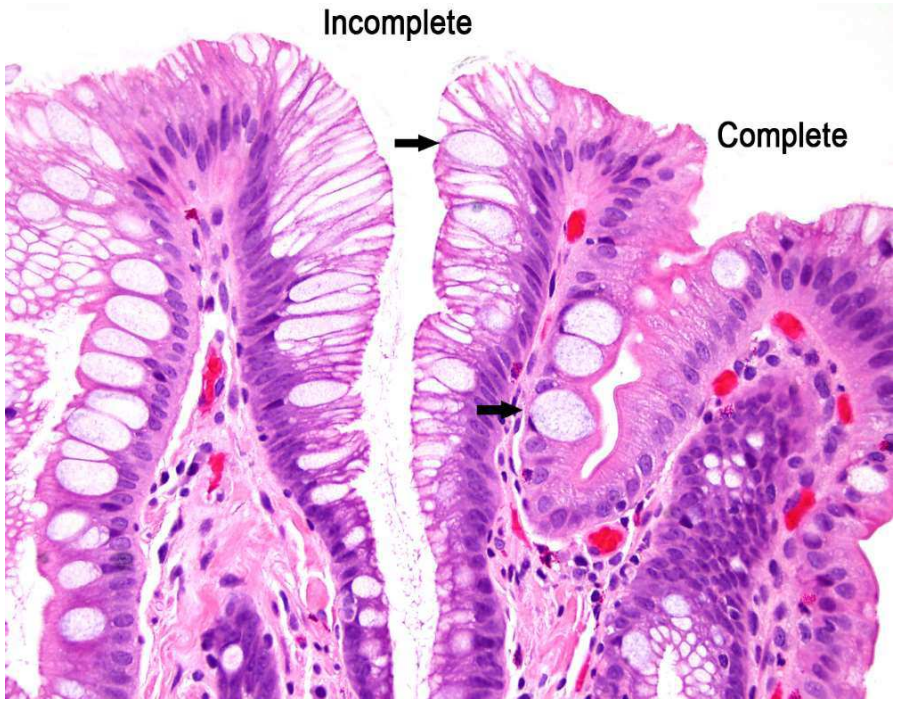


1982 Isolamento
1994 Cancerogeno gruppo I

CONSEGUENZE DI INFEZIONE da HP

- Ulcera peptica
- Atrofia e metaplasia intestinale (HpAG)
- Adenoma gastrico (intestinale)
- Adenocarcinoma (tipo intestinale)
- Linfoma MALT
- Correlazione a gastrite autoimmune (?)


LUM
FOV
AG
LUM
PMN's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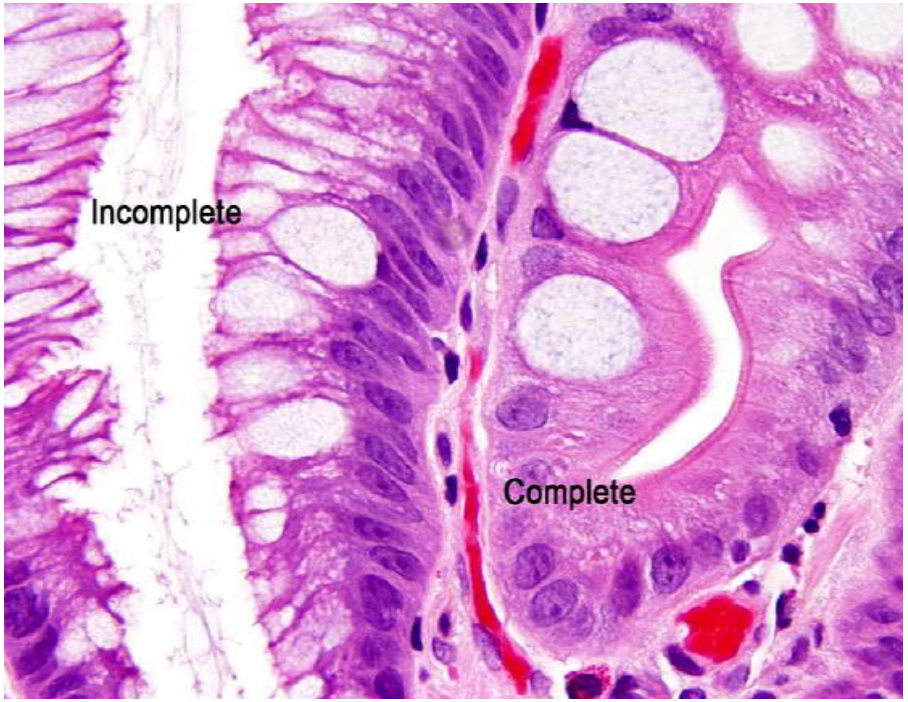
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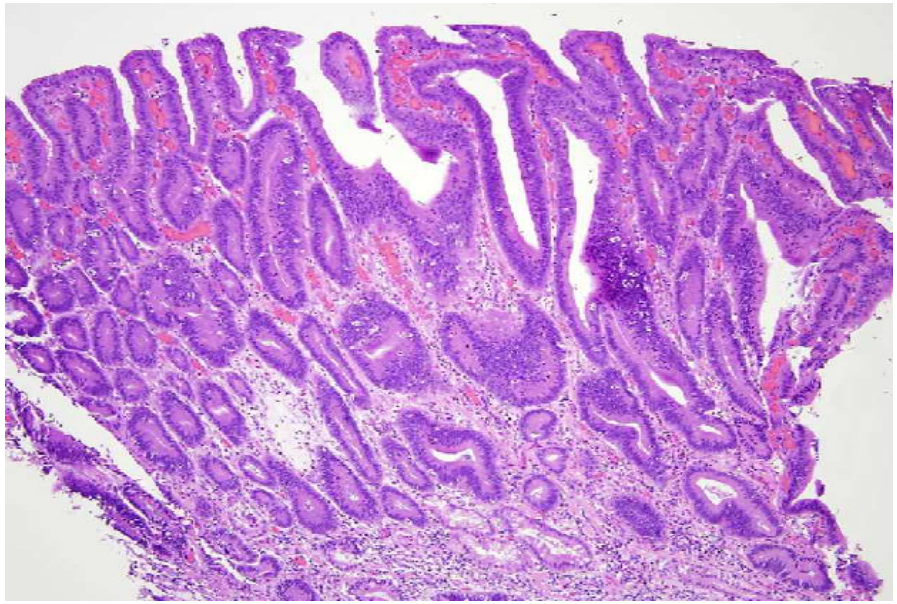
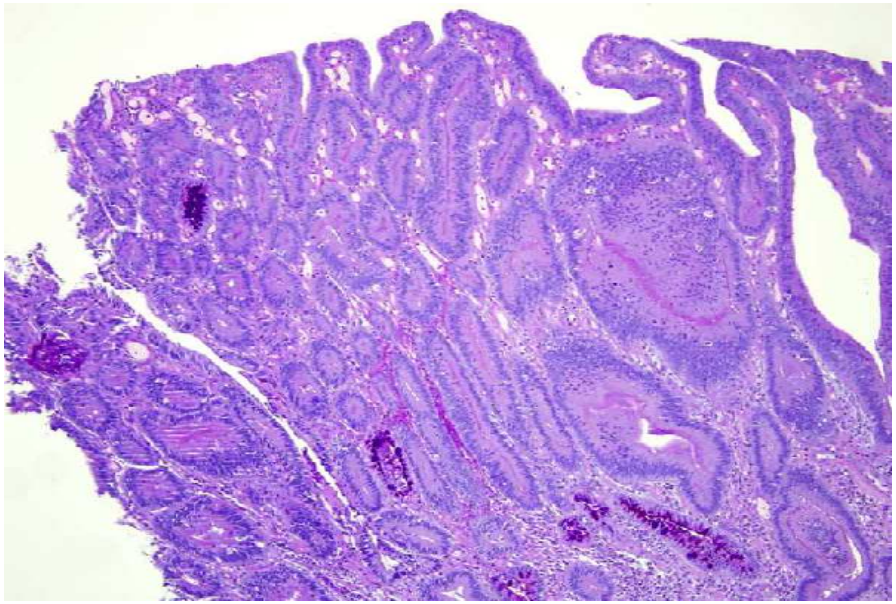
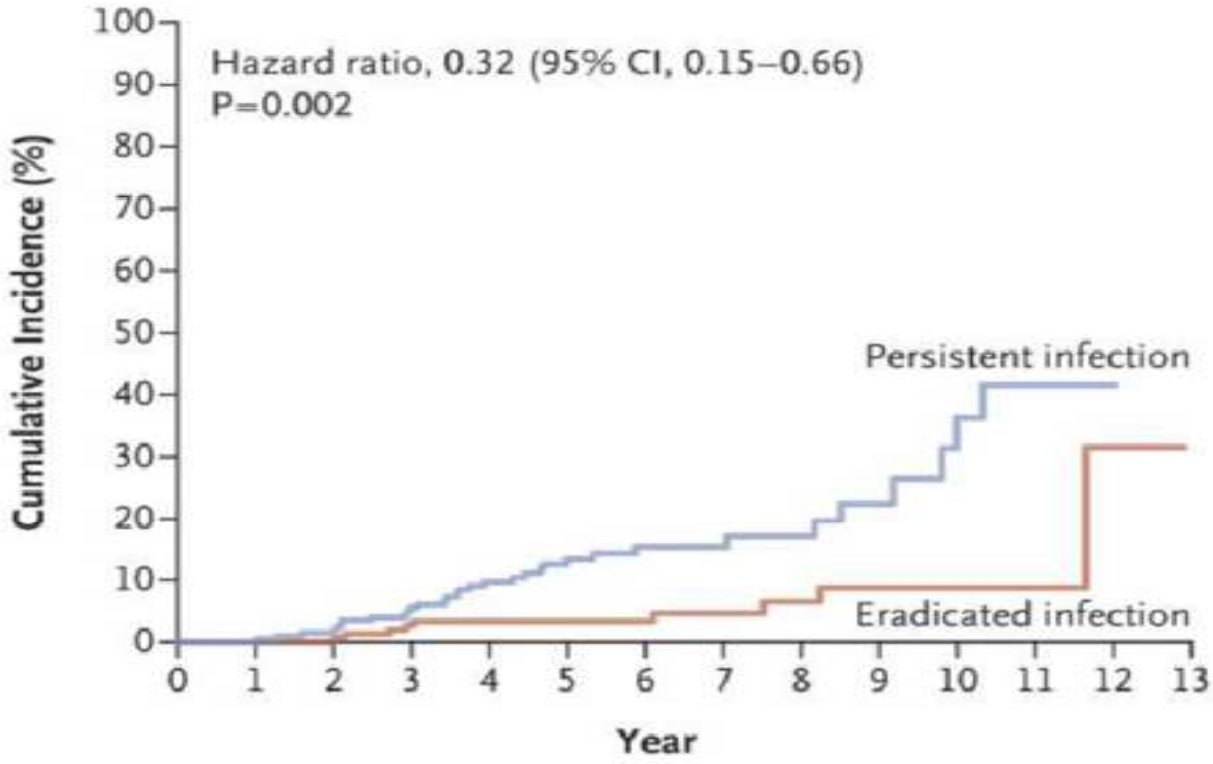






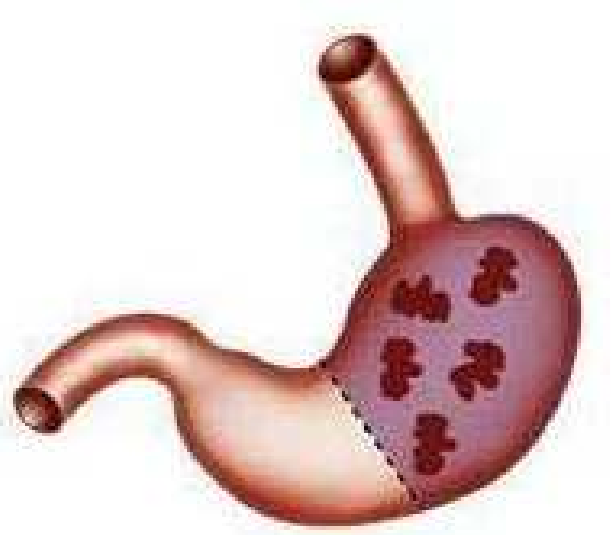
No. at Risk

Persistent infection	228	211	196	176	137	102	70	51	33	23	13	7	1	0
Eradicated infection	167	164	154	144	116	89	76	62	45	28	10	8	2	0

Choi IJ, Kook MC, Kim YI, Cho SJ, Lee JY, Kim CG, Park B, Nam BH. Helicobacter pylori Therapy for the Prevention of Metachronous Gastric Cancer. N Engl J Med. 2018 Mar 22;378(12):1085-1095.. PubMed PMID: 29562147.

Autoimmune Metaplastic Atrophic Gastritis (**AMAG**) - Eziologia-

- Prevalenza 0.5-4.5%
- Disordine immuno-mediato T cell
- Asintomatici/56% sintomi GI/70% dispepsia
- Associazione Hashimoto (40%)
- Elevati livelli di gastrina sierica
- Riduzione ratio pepsinogeno I/pepsinogeno II
- Anemia ferro carenziale
- Carenza di B12/anemia perniciosa
- HP infezione?



Diffuse corporal atrophic gastritis

E. Orgler. Autoimmune Gastritis: Update e new perspectives in therapeutic management. Curr Treat Opinions Gastro (2023) 21:64-77

Autoimmune gastritis: long-term natural history in naïve *Helicobacter pylori*-negative patients

WHAT IS ALREADY KNOWN ON THIS SUBJECT?

⇒ Autoimmune gastritis (AIG) is an immunomediated inflammation of oxyntic mucosa, mostly diagnosed in its atrophic stage. Due to the possible concurrence of previous or current H. pylori infection, the risk of AIG-associated gastric cancer (GC) remains unclear.

WHAT ARE THE NEW FINDINGS?

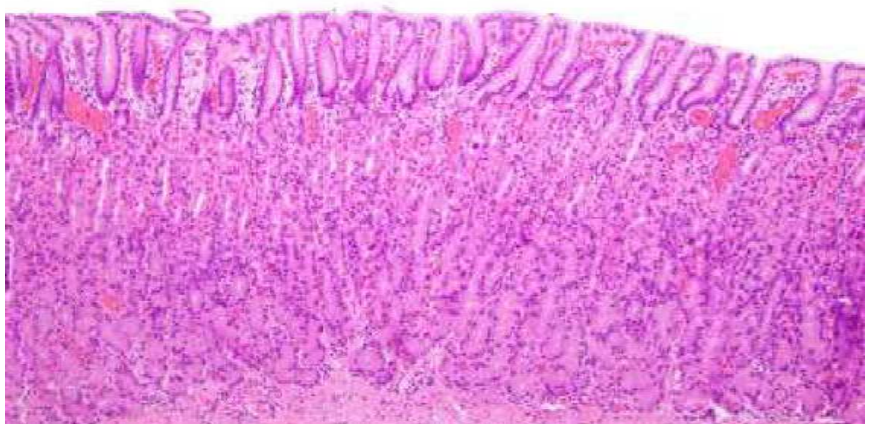
⇒ When previous or current H. pylori infection is rigorously excluded, the long-term follow-up of AIG does not reveal any excess risk for malignancy, except for thyroid cancers. In the natural history of AIG, the initial extensive pseudopyloric metaplasia is slowly replaced by focal gland intestinalisation.

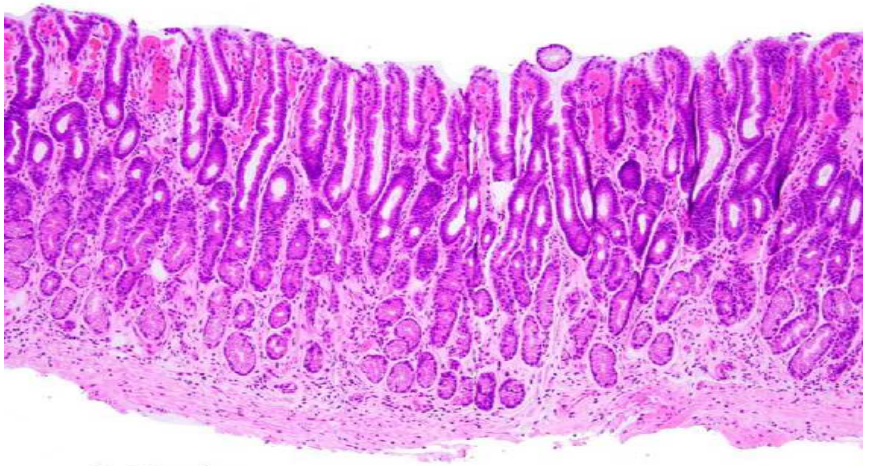
⇒ Enterochromaffin-like-cell hyperplasia, an essential feature of AIG, progresses from diffuse to adenomatoid, the latter being significantly associates with type 1 neuroendocrine tumours.

HOW MIGHT IT IMPACT ON CLINICAL PRACTICE IN THE FORESEEABLE FUTURE?

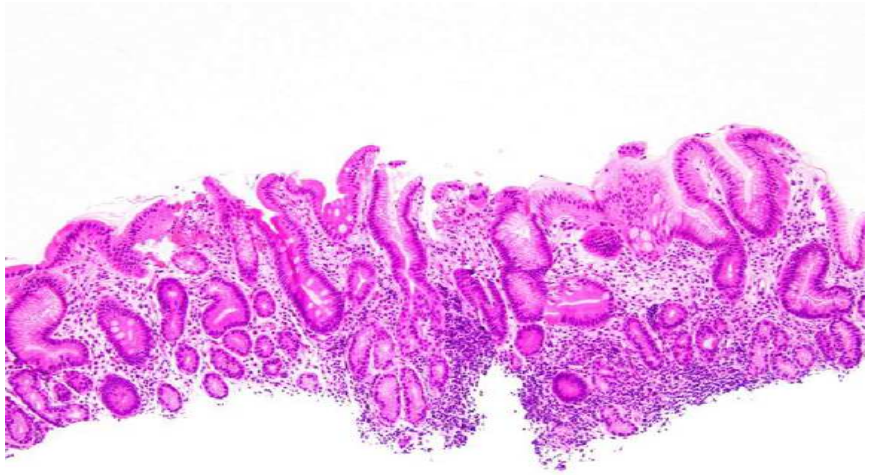
⇒ In naïve H. pylori-negative patients, neuroendocrine neoplasia, not GC secondary prevention, prioritises the clinical, endoscopic and histopathological surveillance of AIG.

Rugge M, *et al*. *Gut* 2023;**72**:30–38. doi:10.1136/gutjnl-2022-327827

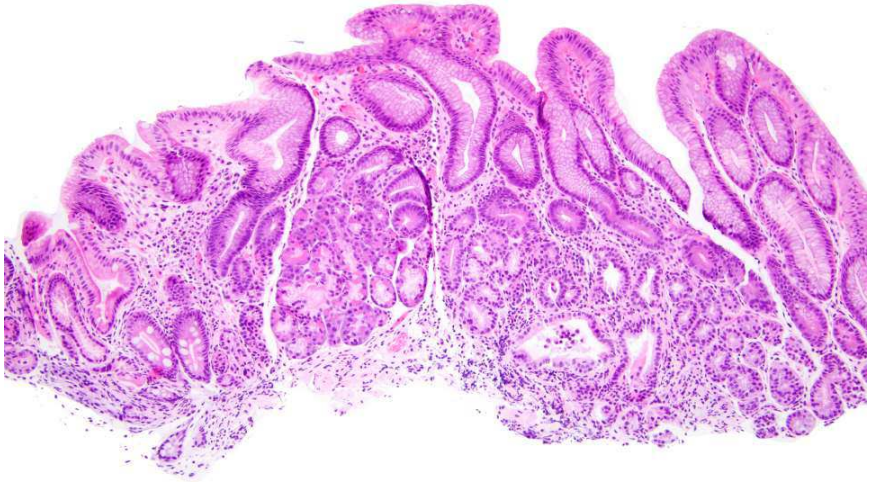


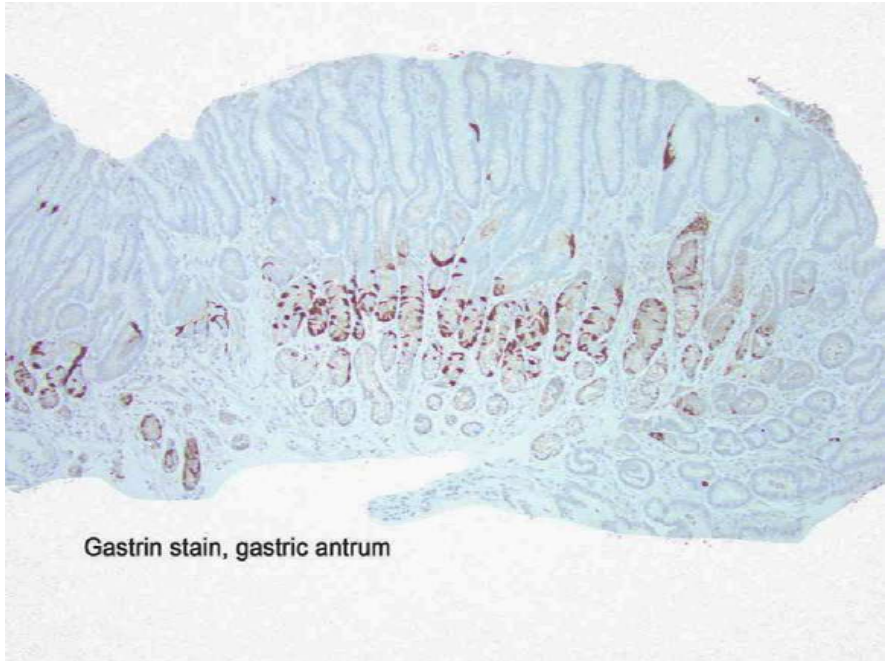


Gastric antrum

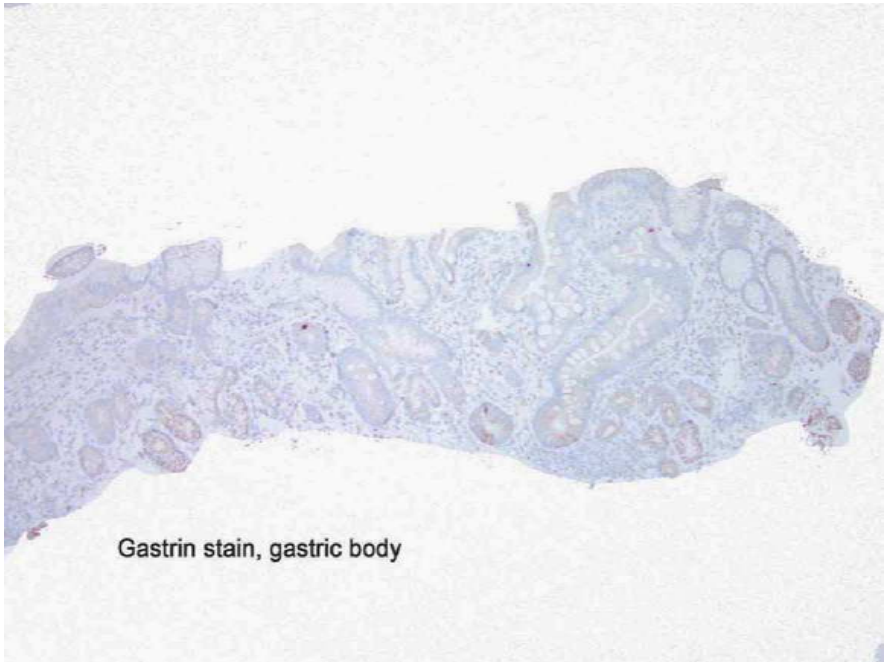


Gastric body with absent parietal cells and intestinal and (pseudo)pyloric metaplasia (antralization)

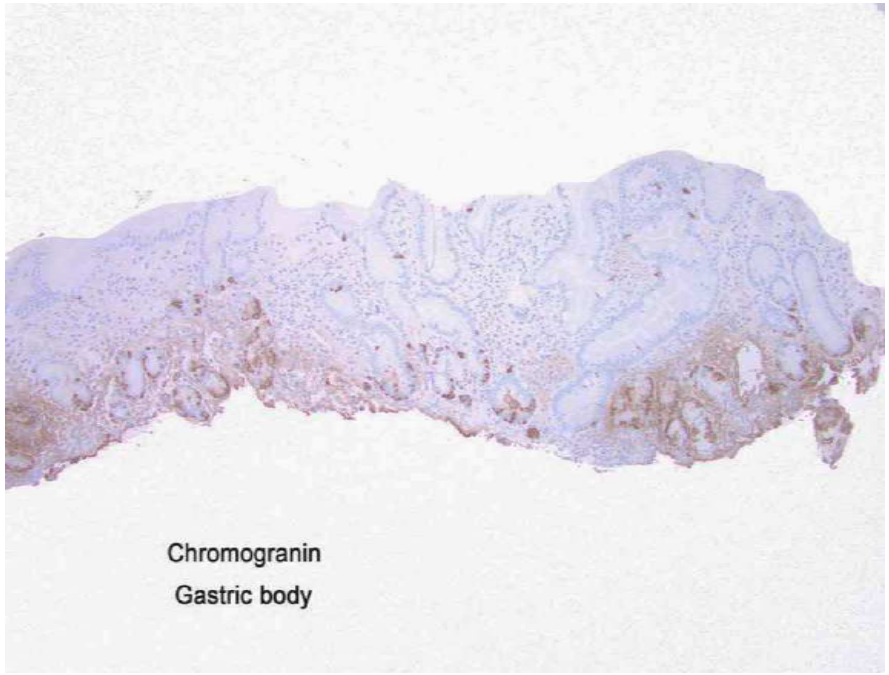




Gastrin stain, gastric antrum

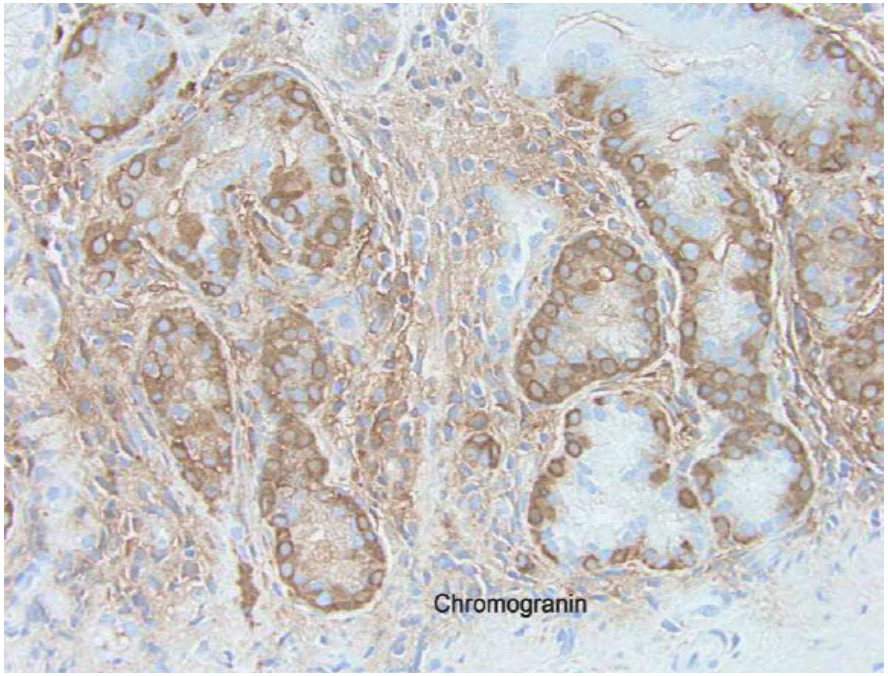


Gastrin stain, gastric body



Chromogranin

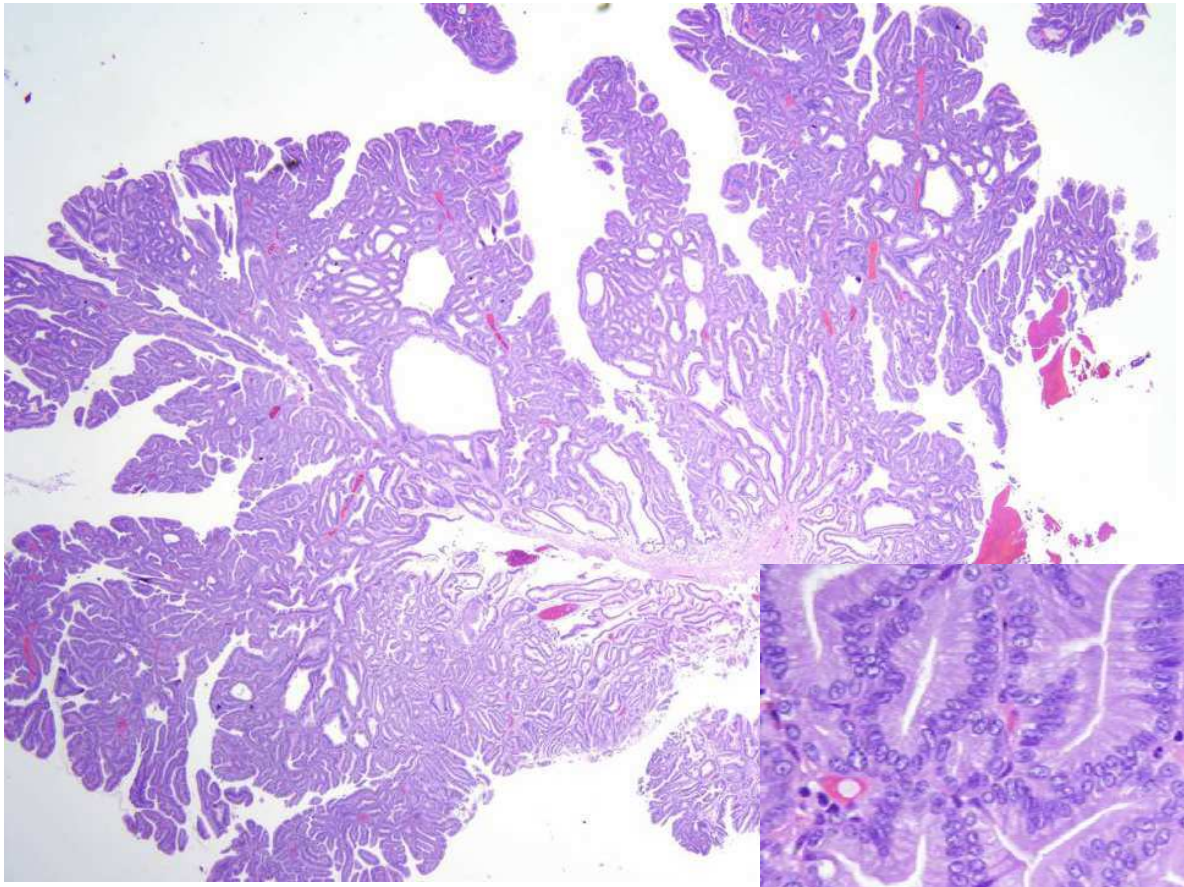
Gastric body



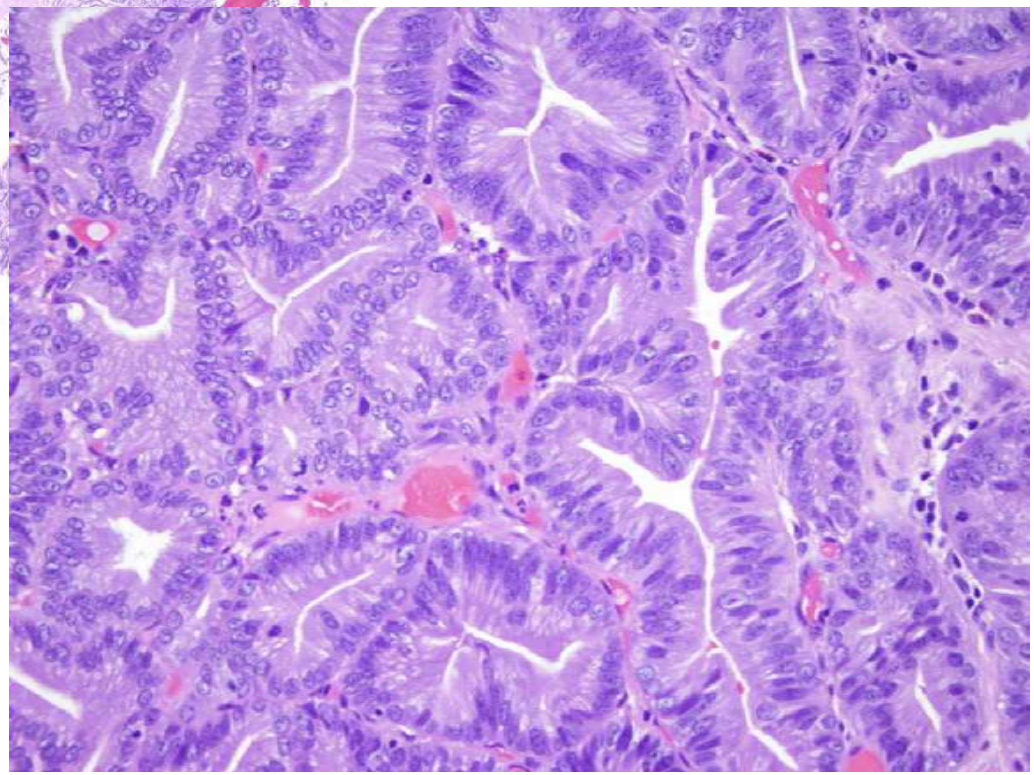
Chromogranin

CONSEGUENZE DELLA GASTRITE AUTOIMMUNE

- Atrofia della mucosa ossintica (AIG)
- Anemia perniciosa
- Adenoma gastrico (intestinale vs pilorico)
- NET tipo 1
- Polipo iperplastico
- Adenocarcinoma (?)



Polipo del corpo gastrico in donna di 72 anni con Gastrite autoimmune

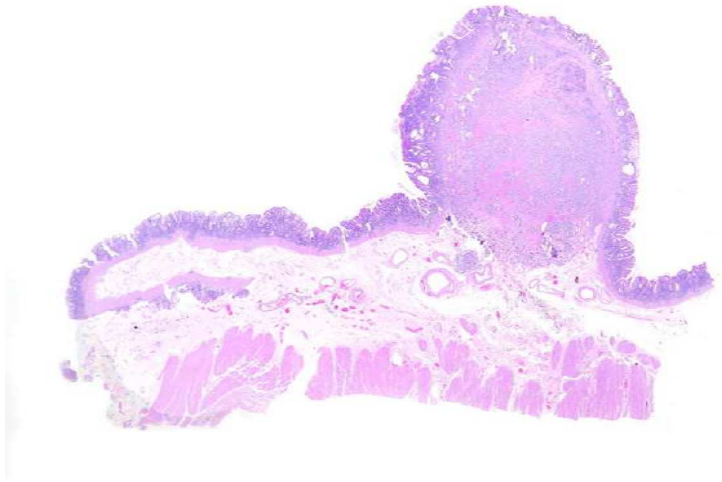


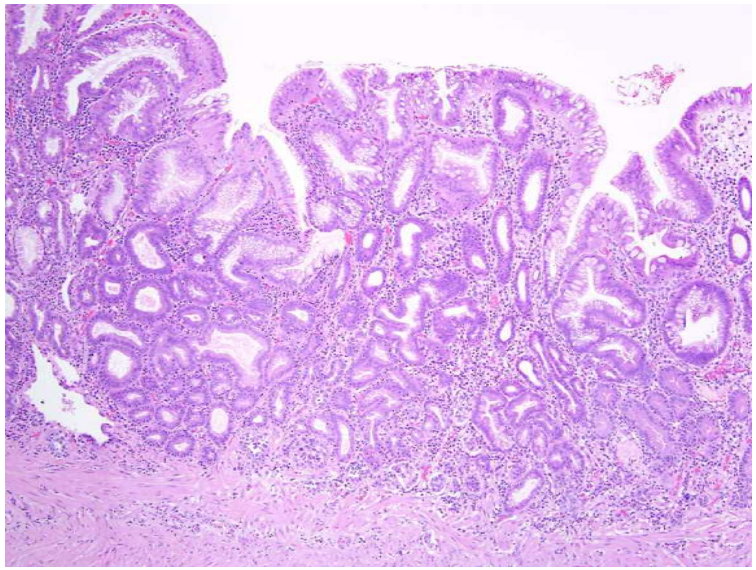
Pyloric Gland Adenoma – Defining series, Vieth et al. - Virchows Arch. 2003 Apr;442(4):317-21

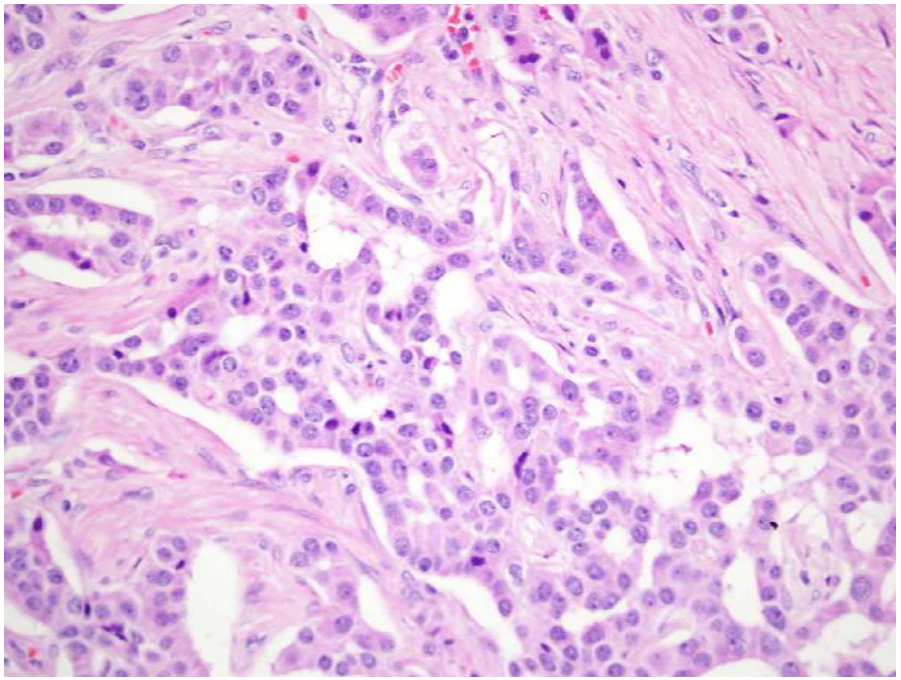
- 2.7% of all gastric polyps
- Adults (73+/-12.8 years),
- **Women (75%).**
- **In stomach, mostly in body (64%),often found in patients with autoimmune gastritis (36%).**
- Some showed transition to adenocarcinoma

- Now known to have *GNAS** mutations, both sporadic and syndromic examples (familial adenomatous polyposis), which they share with oxyntic gland adenoma/chief cell adenoma.
- *guanine nucleotide-binding protein (G protein), alpha subunit

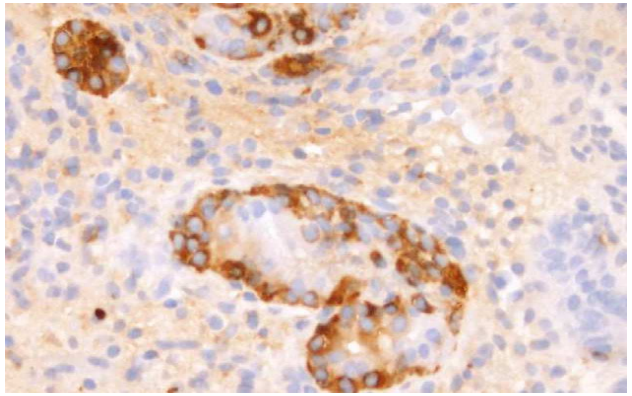
Donna di 50 anni
con storia di diabete di tipo 1







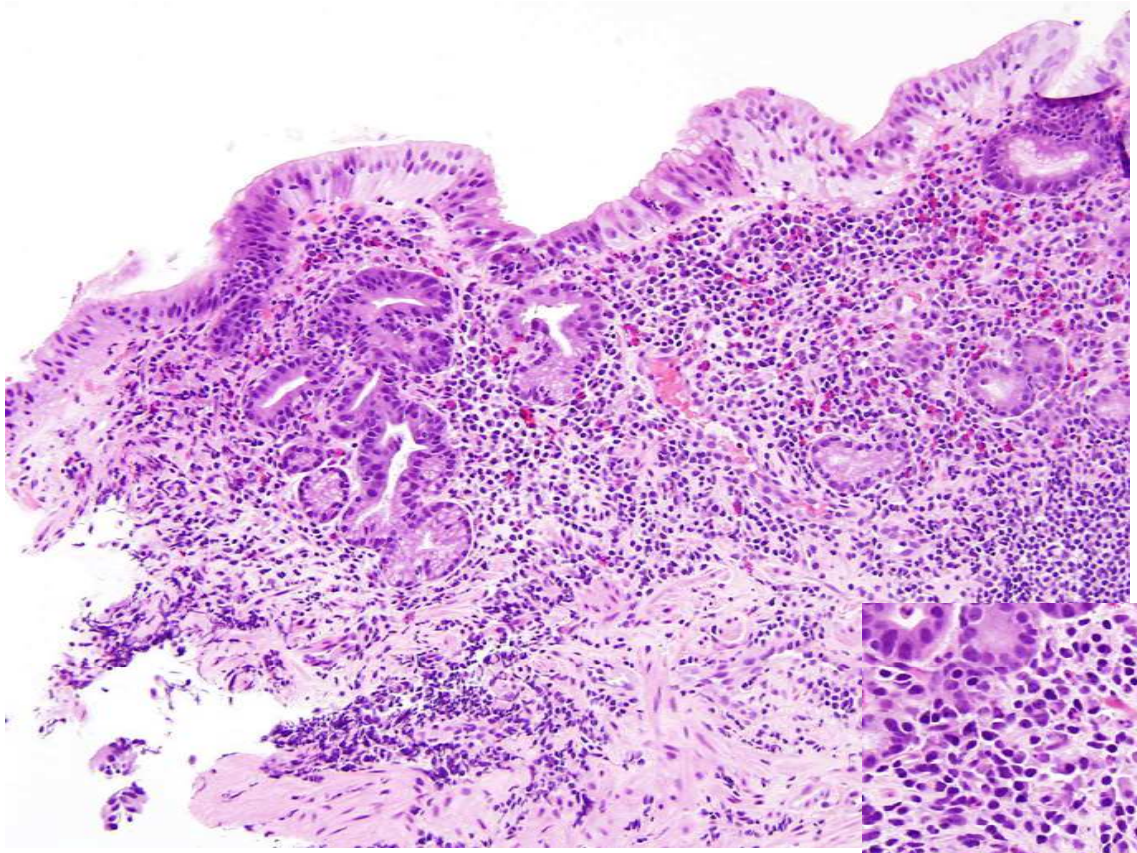
Macro polipi multipli/noduli inferiori a 1cm

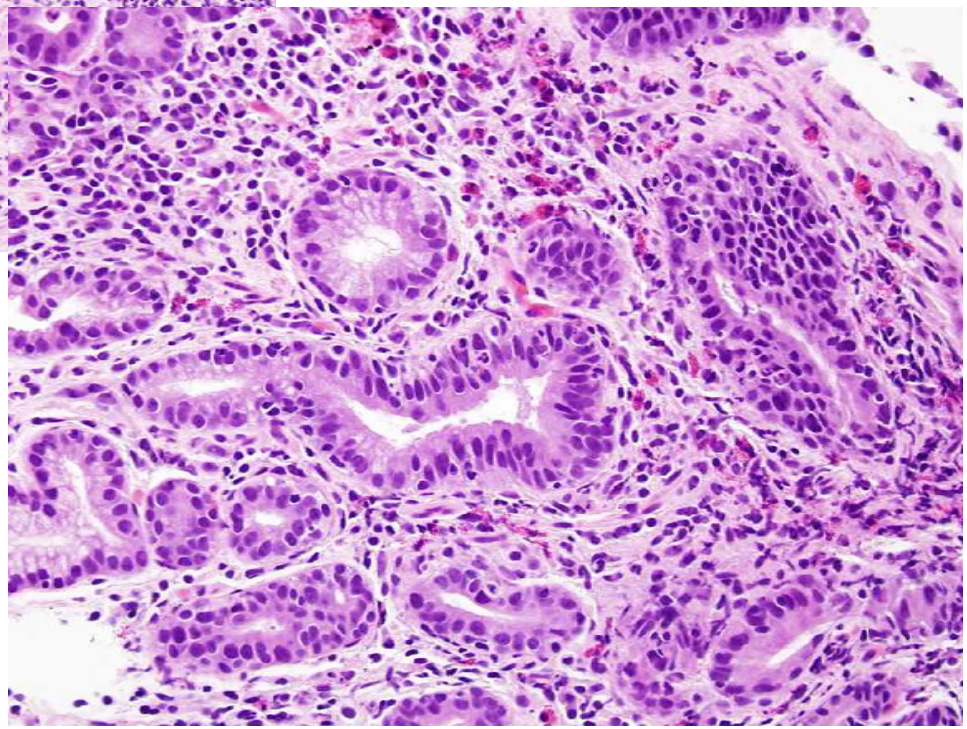


Biopsia su noduli visibili

Uomo 70 anni

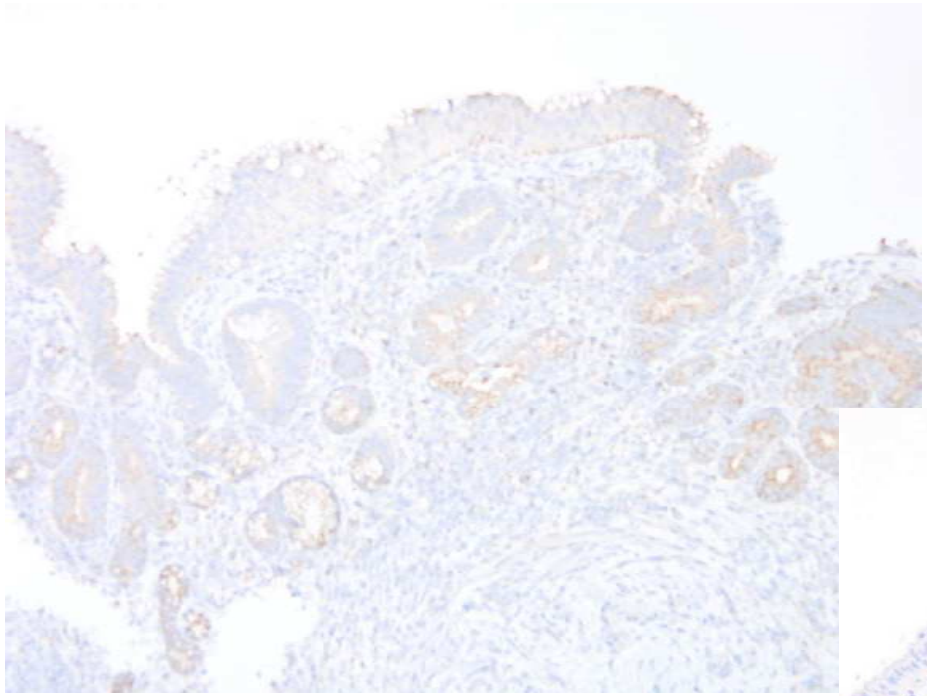
Biopsia corpo gastrico

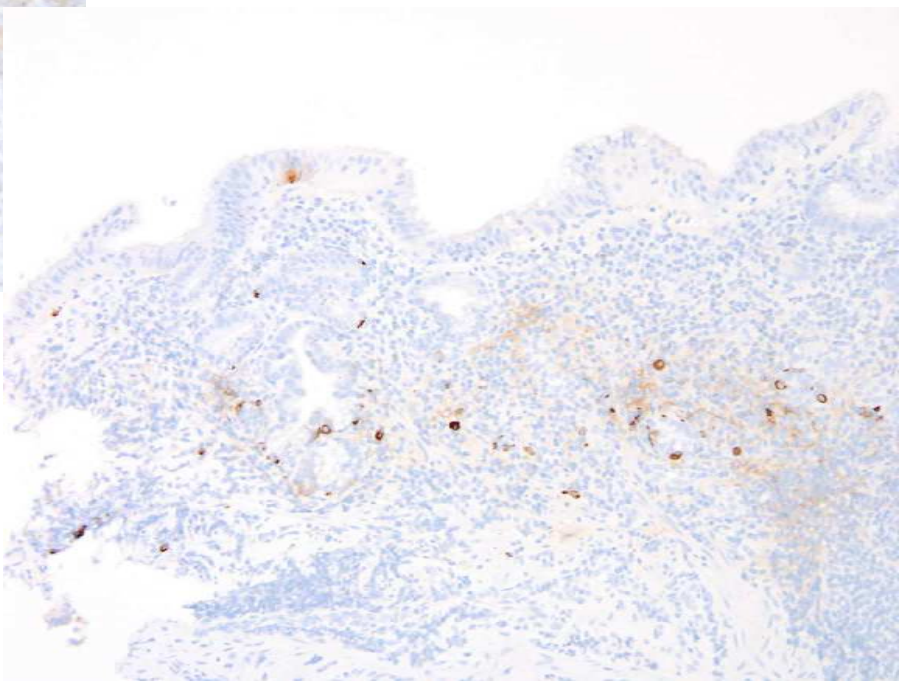




GASTROPATIA DA OLMESARTAN

ICH GASTRINA





ICH CROMOGRANINA

Classificazione dei fenotipi istologici coinvolti nella cancerogenesi gastrica

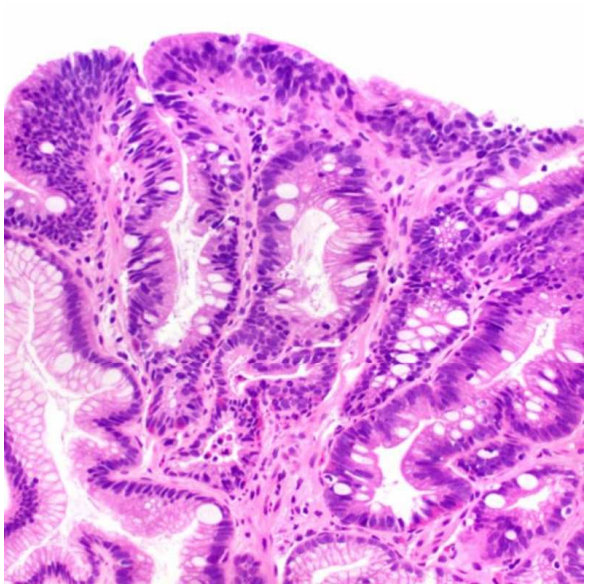
Table 3.02 Classifications of the histological phenotypes involved in gastric carcinogenesis, each listing the categories in order of increasing risk of malignancy

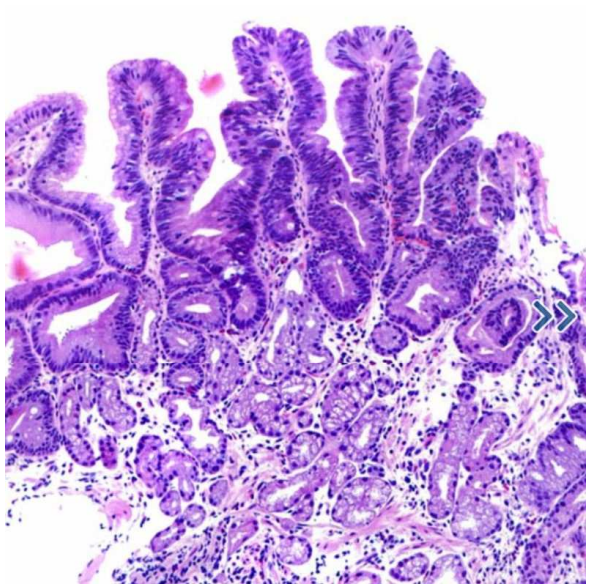
Padova International	Vienna	Revised Vienna	Japanese Diagnostic Framework for Forceps Biopsy	WHO (2019)
Category 1: Negative for dysplasia	**Category 1:** Negative for dysplasia	**Category 1:** Negative for dysplasia	**Group 1:** Normal/non-neoplastic	**Negative for dysplasia/IEN**
Category 2: Indefinite for dysplasia	**Category 2:** Indefinite for dysplasia	**Category 2:** Indefinite for dysplasia	**Group 2:** Indefinite for neoplasia	**Indefinite for dysplasia/IEN**
Category 3.1: Low-grade dysplasia (low-grade NiN)	**Category 3:** Non-invasive low-grade neoplasia (low-grade adenoma/dysplasia)	**Category 3:** Low-grade adenoma/dysplasia	**Group 3:** Adenoma	**Low-grade dysplasia/IEN** (low-grade adenoma/dysplasia)
Category 3.2: High-grade dysplasia (high-grade NiN)	**Category 4:** High-grade neoplasia **4.1:** High-grade adenoma/dysplasia **4.2:** Non-invasive carcinoma **4.3:** Suspicious for invasive carcinoma	**Category 4:** High-grade neoplasia **4.1:** High-grade adenoma/dysplasia **4.2:** Non-invasive carcinoma **4.3:** Suspicious for invasive carcinoma	**Group 4:** Suspicious for carcinoma	**High-grade dysplasia/IEN** (high-grade adenoma/dysplasia)
Category 4: Suspicious for invasive carcinoma		**4.4:** Intramucosal carcinoma	**Group 5:** Carcinoma (non-invasive or invasive)	
Category 5: Invasive adenocarcinoma	**Category 5:** Invasive neoplasia **5.1:** Intramucosal carcinoma			**Intramucosal invasive neoplasia** (intramucosal carcinoma)

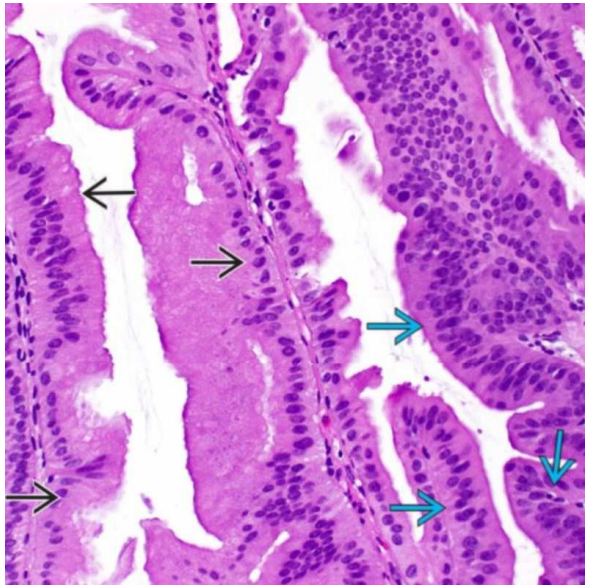
IEN, intraepithelial neoplasia; NiN, non-invasive neoplasia.

ADENOMA/DISPLASIA ASSOCIATI A GA

-Istopatologia -



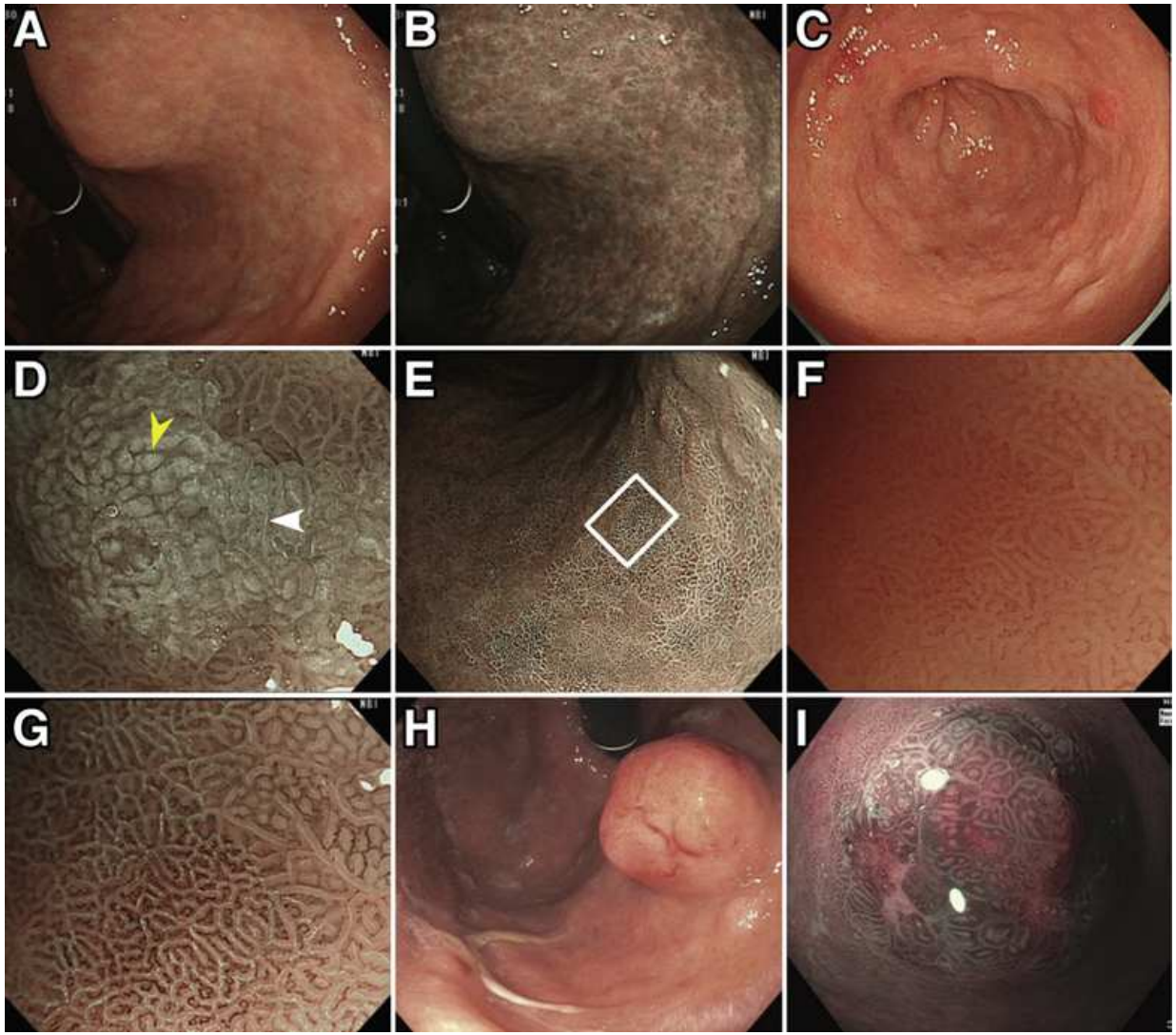




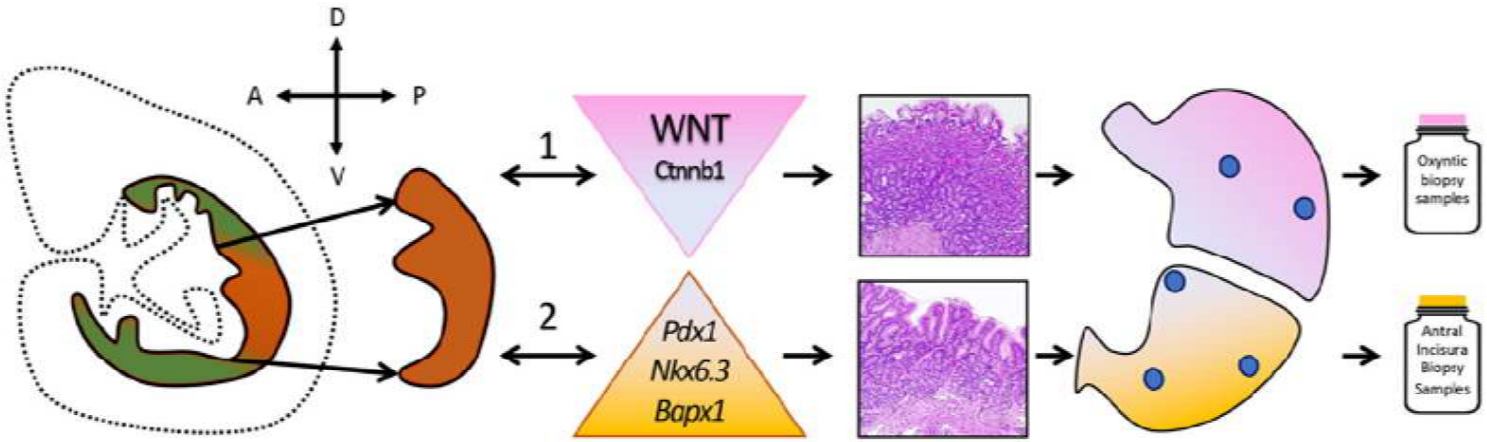
Rischio di progressione di LGD ➡ GC 4%-9%
Rischio di progressione di HGD ➡ GC 69%
Indefinito per displasia ➡ LGH in 11% dei casi

Rugge et al. Gut 2003

SORVEGLIANZA E PREVENZIONE



SORVEGLIANZA E PREVENZIONE



- WNT/beta catenina: promuove differenziazione ossintica
- Bapx1: promuove la differenziazione antrale mucosecernente

BIOPSIE GASTRICHE DEI DUE COMPARTIMENTI INVIATE SEPARATAMENTE

BIOPSIA SU LESIONI VISIBILI

STADIAZIONE sec. OLGA SYSTEM

Operative Link on Gastritis Assessment

A.

Atrophy Score		Corpus			
		No Atrophy (score 0)	Mild Atrophy (score 1)	Moderate Atrophy (score 2)	Severe Atrophy (score 3)
Antrum	No Atrophy (score 0) (including *incisura angularis*)	STAGE 0	STAGE I	STAGE II	STAGE II
	Mild Atrophy (score 1) (including *incisura angularis*)	STAGE I	STAGE I	STAGE II	STAGE III
	Moderate Atrophy (score 2) (including *incisura angularis*)	STAGE II	STAGE II	STAGE III	STAGE IV
	Severe Atrophy (score 3) (including *incisura angularis*)	STAGE III	STAGE III	STAGE IV	STAGE IV

B.

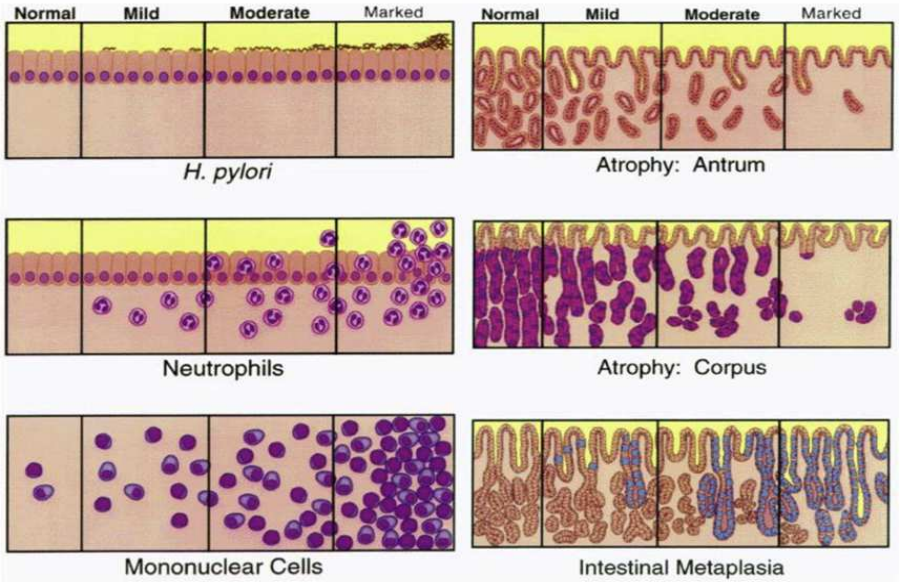


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Table 3. Gastric cancer risk associated with OLGA stages of gastritis

OLGA stage of gastritis (%) at enrollment	Follow-up in months: mean (range)	Incident neoplasia	Incident neoplasia: rate/10^3 person-years (neoplastic lesions include both intraepithelial and infiltrating types)	95% Confidence interval
0 (80.8%)	53.6 (76.6–79.2)	1/6005	Rate/10^3 person-years = 0.03	0.004–0.19
I (12.6%)	53.6 (76.6–79.2)	2/934	Rate/10^3 person-years = 0.34	0.09–1.36
II (4.3%)	38.6 (76.6–79.2)	3/322	Rate/10^3 person-years = 1.48	0.48–4.58
III (2.0%)	35.5 (70.8–74,4)	17/152	Rate/10^3 person-years = 19.1	11.9–3 0.7
IV (0.3%)	39.4 (63.6–63.6)	5/23	Rate/10^3 person-years = 41.2	17.2–99.3
Patients	considered 7436[40]	52.7 (11.573.0)	LG-IEN = 17 HG-IEN = 4 GC = 7	Rate
	10^3/person-years = 0.60			
0 (77.6%)	53.6	0/1362	Rate/10^3 person-years = 0.0	0–0.4
I (14.4%)	(11.5–70.3)	0/253		
II (5.1%)	38.6 (5.9–64.3)	0/88		
III (2.1%)	35.5 (15.8–60.7)	4/37	Rate/10^3 person-years = 36.5	13.7–97.4
IV (0.85%)	34.8 (23.3–58.1)	3/15	Rate/10^3 person-years = 63.1	20.3–195.6
Patients	considered 1755[61]		LG-IEN = 4 HG-IEN = 1 GC = 2	
0	(62.3.6%)	149 (144–204)	0/58	OLGA stages III/IV (as assessed at initial biopsy) were associated with a significantly higher risk of GC (at end of follow-up) than stages 0/I/II (Kaplan-Maier log-rank test; $p = 0.0001$; RR = 58.00; 95% CI =
	I (17.2%)		0/16	
	II (9.6%)		0/9	
	III (6.4%)		2/6	

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Stomach (P Malfertheiner, Section Editor)

Gastritis: An Update in 2020

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CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on the Diagnosis and Management of Atrophic Gastritis: Expert Review

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Endoscopic	Non-endoscopic
• Obtain topographical biopsies to determine anatomic extent and histologic severity for risk stratification	• Test for *H pylori*, treat if positive and confirm eradication
• Surveillance endoscopy should be considered in patients with* ◦ Advanced AG: every 3 years ◦ AIG: interval based on individualized assessment (see text)	• Evaluate for anemia
• In patients with newly diagnosed PA, upper endoscopy should be considered for risk stratification and to evaluate for prevalent gastric neoplasia and NETs	• Evaluate for micronutrient deficiencies, such as iron and vitamin B12 (irrespective of anemia)
• Evaluate for NETs and manage accordingly (see text)	• In patients with AIG ◦ Screen for autoimmune thyroid disease ◦ Low threshold to evaluate other autoimmune diseases based on clinical presentation (e.g. type I diabetes)
	• Check PCA and IFA in patients with endoscopic/ histologic findings consistent with AIG**

*For AIG and advanced AG, surveillance should be based on shared decision-making and individual risk assessment. Advanced AG is defined based on 1) anatomic extent and 2) histological grade.

**Endoscopic findings include corpus-predominant pattern with antral sparing; histological findings include oxyntic mucosa atrophy with lymphoplasmacytic infiltrate.

CONCLUSIONI

- GC è mediato dall'infiammazione
- GA rappresenta la cancerizzazione di campo
- OLGA permette di stratificare i pazienti in base al rischio di GC
- Nei pazienti stadio III/IV il f.u. endoscopico è una affidabile strategia di prevenzione secondaria
- L'approccio multidisciplinare consente di adattare il f.u. al profilo clinico del ss paziente