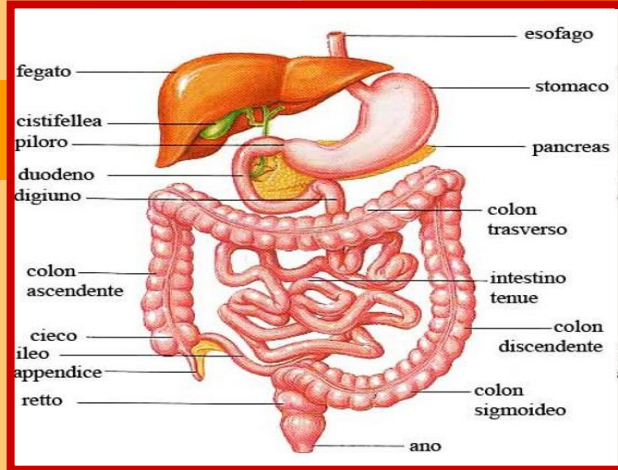


Università degli Studi di Ferrara

Corso di Laurea in Odontoiatria

Anno Accademico 2018-2019

Corso di Anatomia Patologica



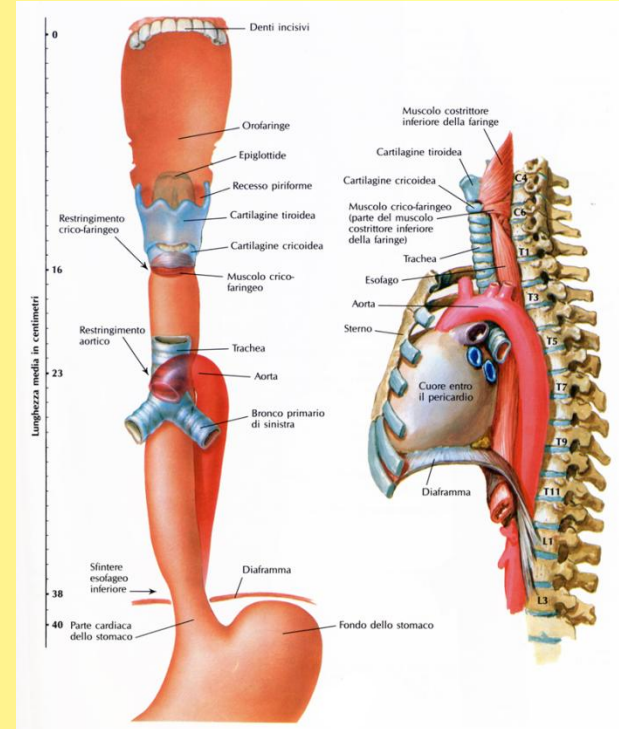
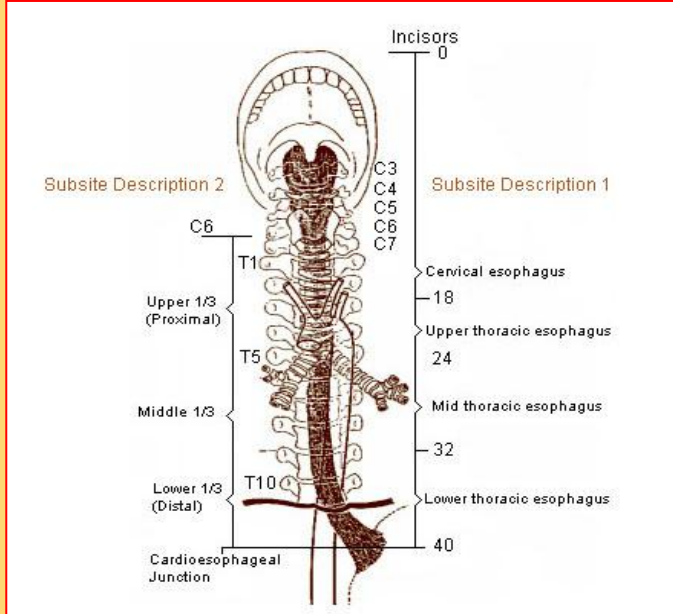
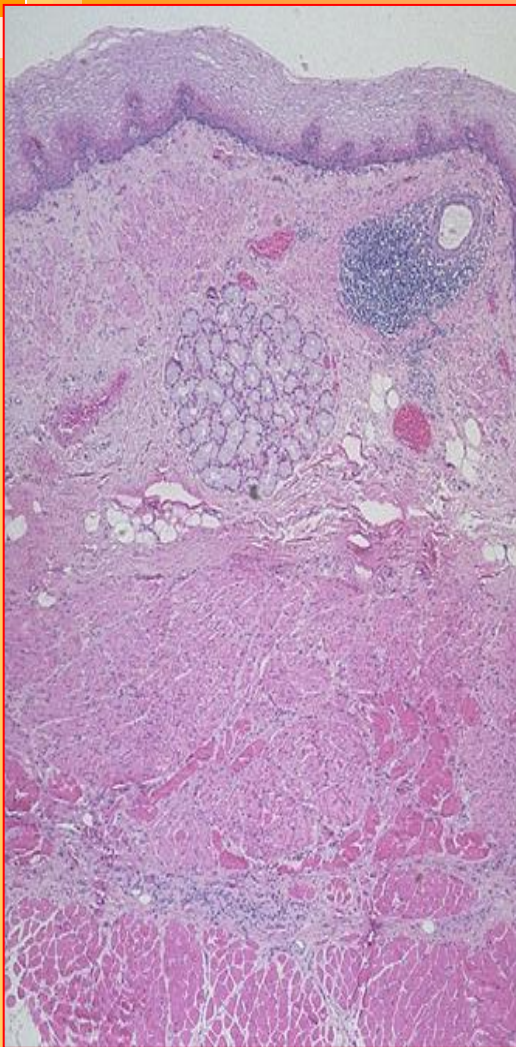
Dr. Stefano Ferretti
Dipartimento di Morfologia, Chirurgia e Medicina sperimentale
Università di Ferrara

Apparato gastroenterico
esofago, stomaco

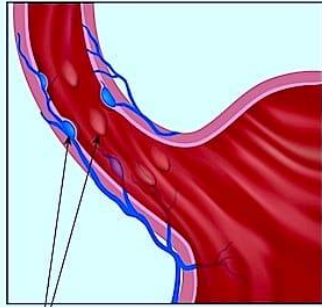


Esofago

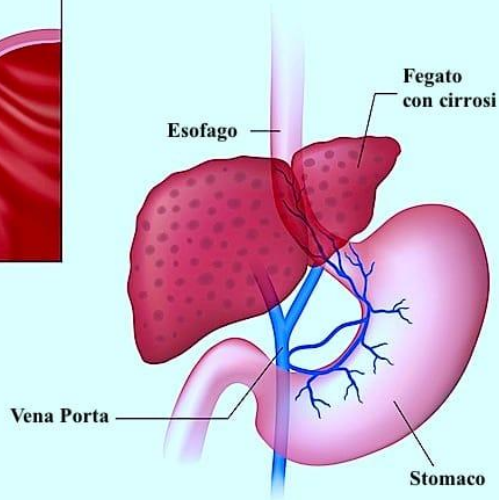
anatomia



Varici Esofagee



Varici Esofagee



varici esofagee

Clinica

- Asintomatiche
- Ematemesi post-rottura
- Prognosi generalmente infausta (50% I episodio)

Etiopatogenesi

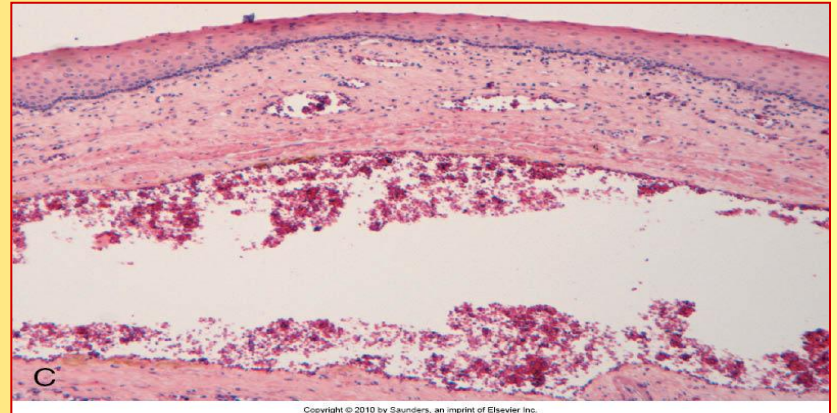
- Ipertensione portale
- Congestione anastomosi porta-cava
- Evoluzione 90% cirrosi epatica
- Schistosomiasi*



Anatomia Patologica

- Varici venose sottomucose
- Rottura, emorragia massiva

varici esofagee



Anatomia Patologica

Esofagiti “chimiche” e “fisiche”

- Infiltrazione granulocitaria
- Ulcerazioni
- Pseudomembrane
- Necrosi transmurale



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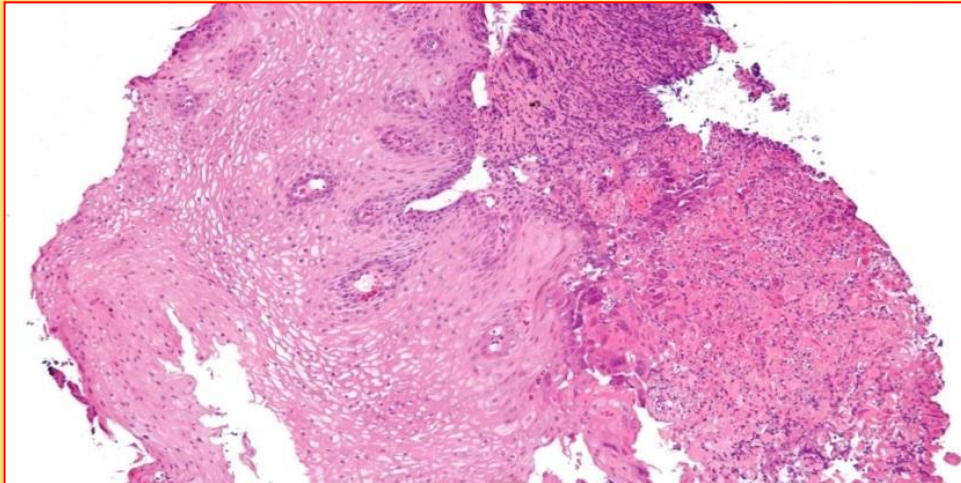
Etiopatogenesi

- Fattori fisici
- Fattori chimici
 - *Alcool*
 - *Fumo di sigaretta*
 - *Reflusso gastro-esofageo*
 - *Farmaci*
- Infezioni
 - *HPV, CMV, micosi*
- *Altre cause (patologie sistemiche)*

esofagiti

Clinica

- Dolore
- Disfagia



Etiopatogenesi

- Reflusso gastro-esofageo
- (*reflusso biliare*)

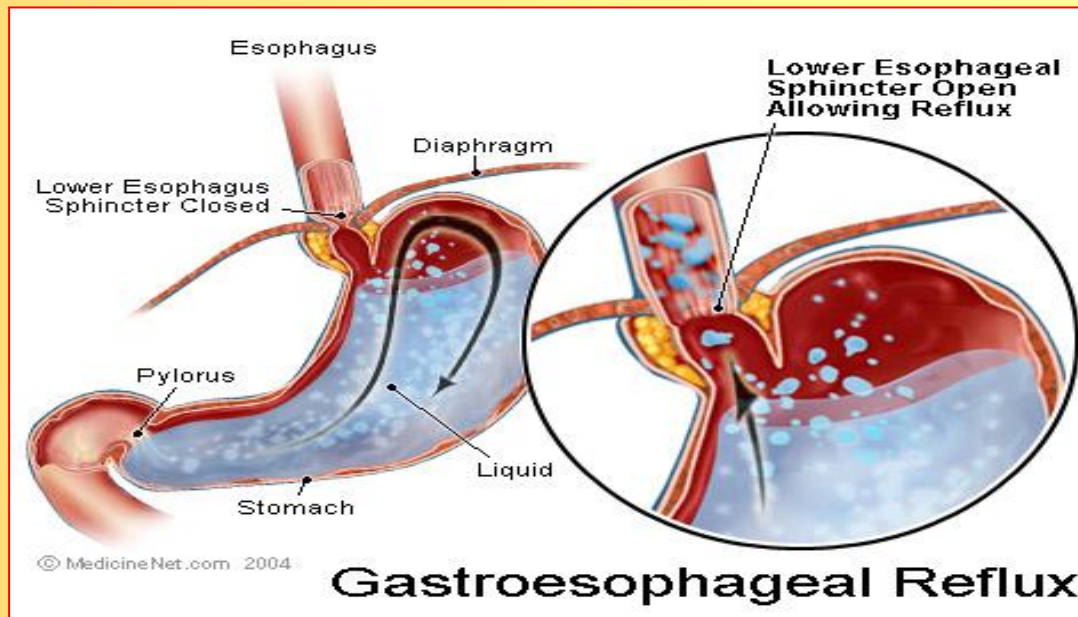
Fattori di rischio:

- Ernia iatale
- Alcool/tabacco
- Obesità
- Gravidanza
- Ritardo riempimento gastrico
- Aumento volume stomaco

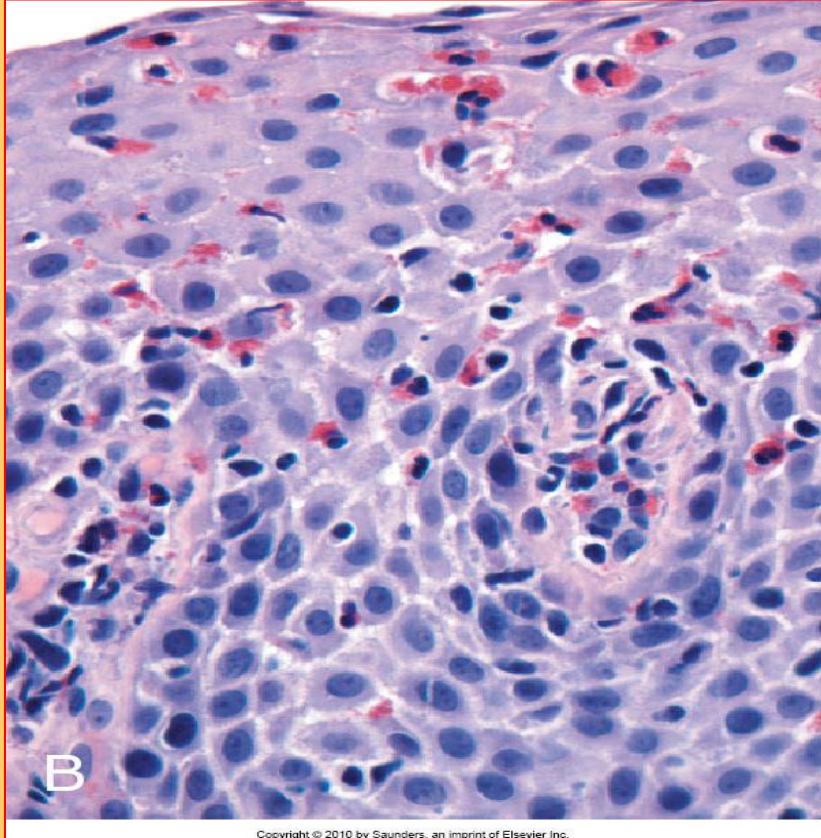
Clinica

- Età gen. > 40 aa.
- Piroisi, disfagia
- Rigurgito
- Dolore (severo)

esofagite da reflusso



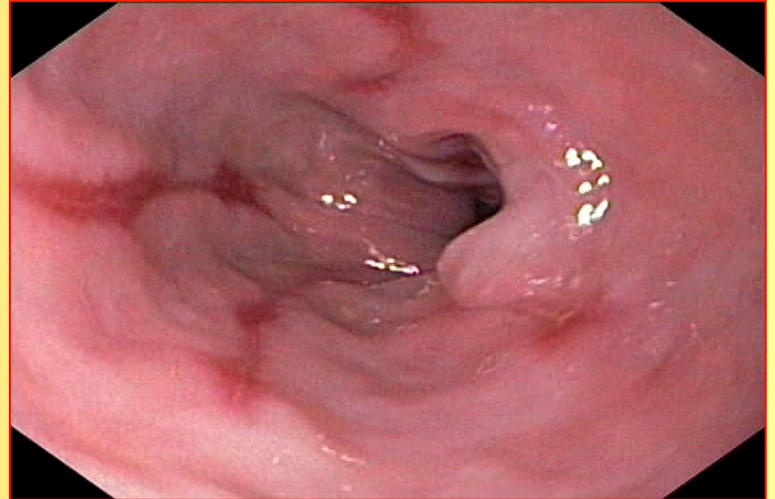
esofagite da reflusso



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Anatomia Patologica

- Iperemia
- Infiltr. gr. eosinofili e neutrofil
- Iperplasia basale (> 20%)
- Papille lamina propria

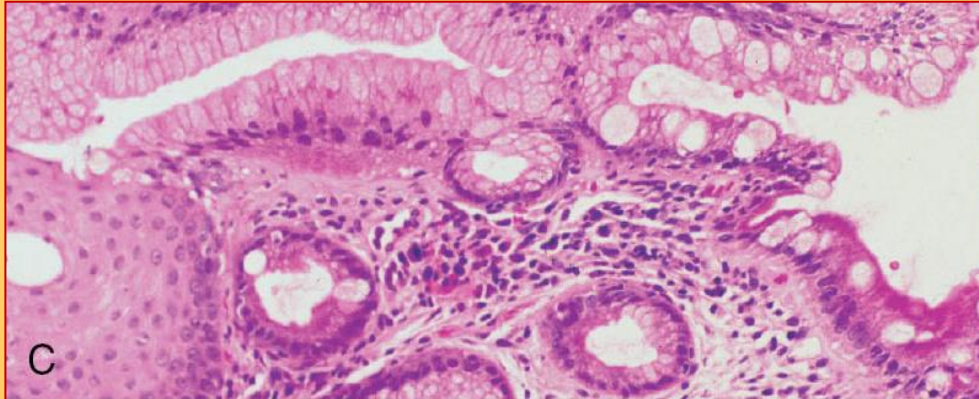
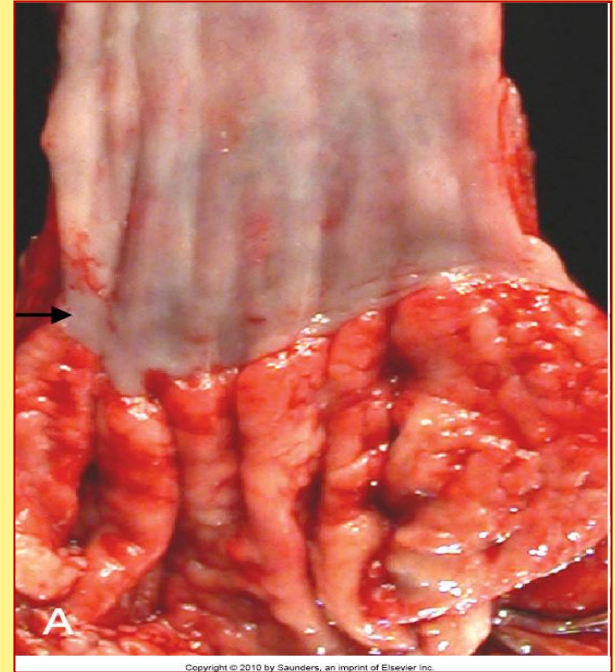


esofago di Barrett

Anatomia Patologica

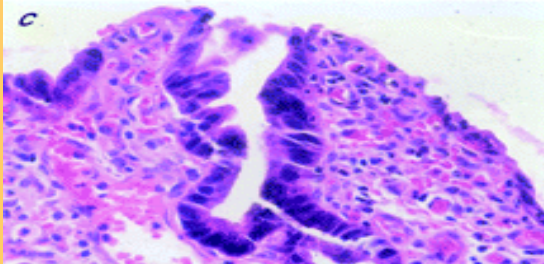
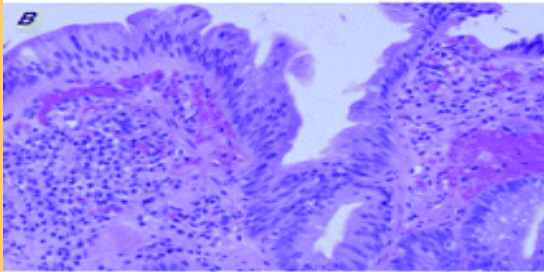
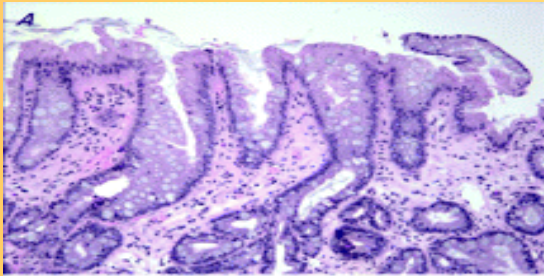
- Aree rossastre giunzionali
- Rivest. di tipo gastrico esofago distale
- Estensione \leq 3 cm
- Metaplasia intestinale (goblet cells)
- Ev. displasia basso/alto grado
- Aumento rischio neoplasia (ADK)

*metaplasia
intestinale
in mucosa
esofagea*



Metaplasia intestinale in mucosa esofagea

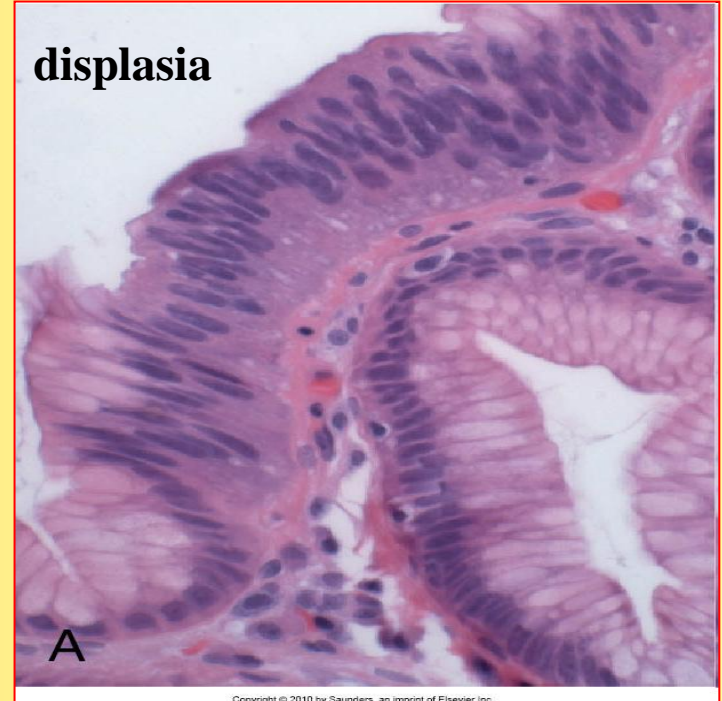
esofago di Barrett



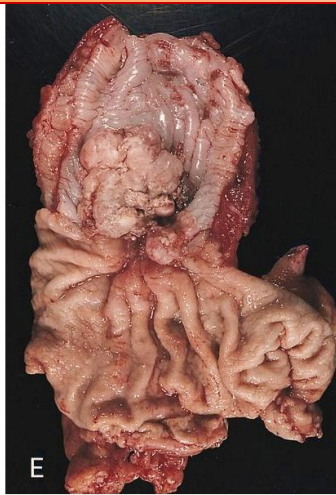
Clinica

- Diagnosi endoscopica
- Necessità di follow-up
- (resezione)

displasia



adenocarcinoma esofageo



Etiopatogenesi

- Progressione Barrett-carcinoma
- Mutazione/overespr. P53
- Amplificaz. C-erbB2, ciclina, RB, p16

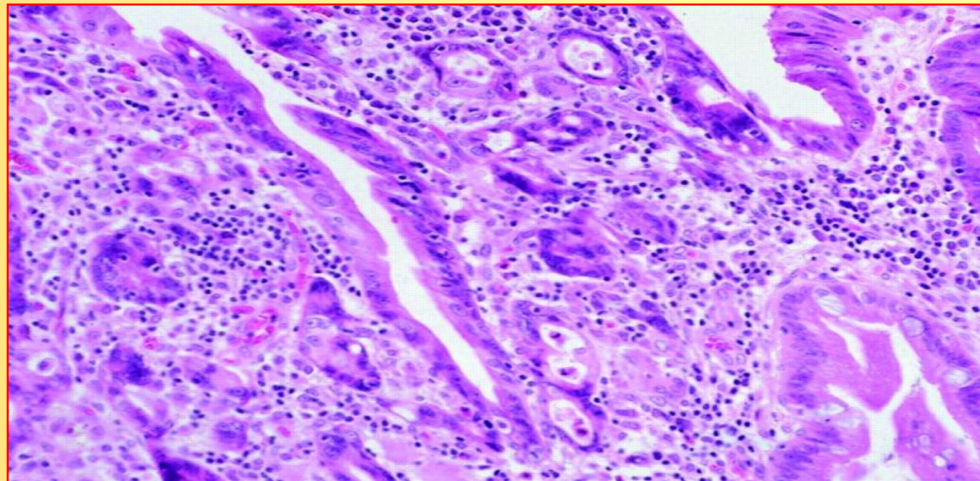
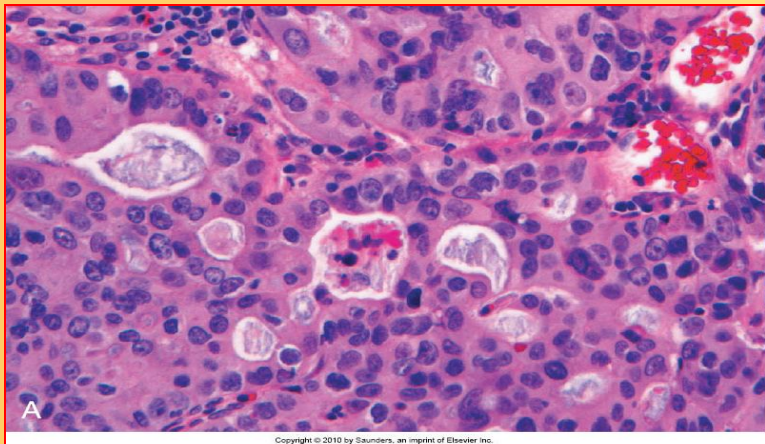
Clinica

- Reperto talora occasionale in Barrett
- Dolore
- Disfagia
- Perdita peso
- Ematemesi
- Vomito
- Prognosi infausta

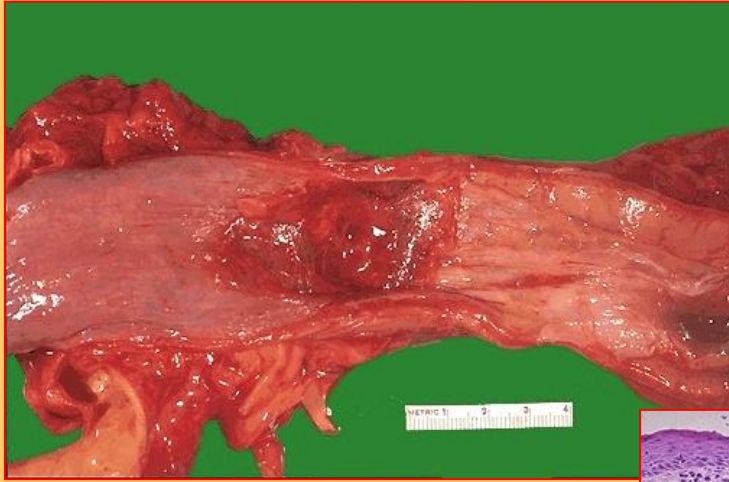
Anatomia Patologica

- III distale dell'esofago
- Sviluppo endoluminale (raro)
- Infiltrazione diffusa (freq.)
- Precedente esofago di Barrett
- Struttura ghiandolare mucinosa
- Struttura "intestinale"
- Talora forme "signet ring"
- Raramente forme indiff. (simili SCLC)

adenocarcinoma esofageo

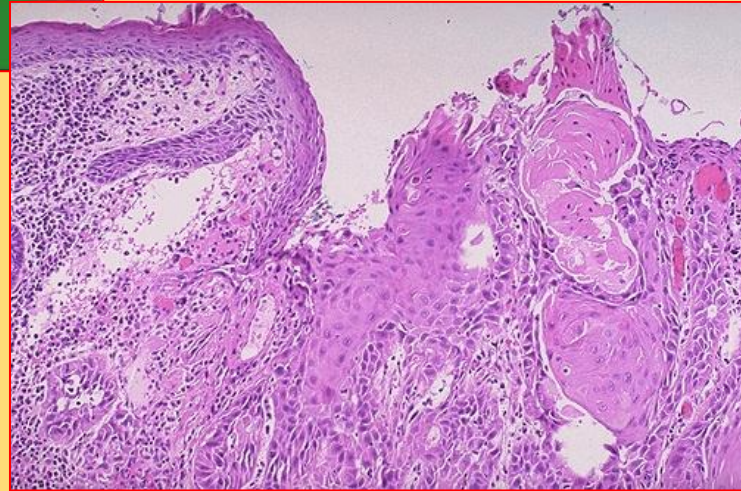


carcinoma squamoso esofageo



Etiopatogenesi

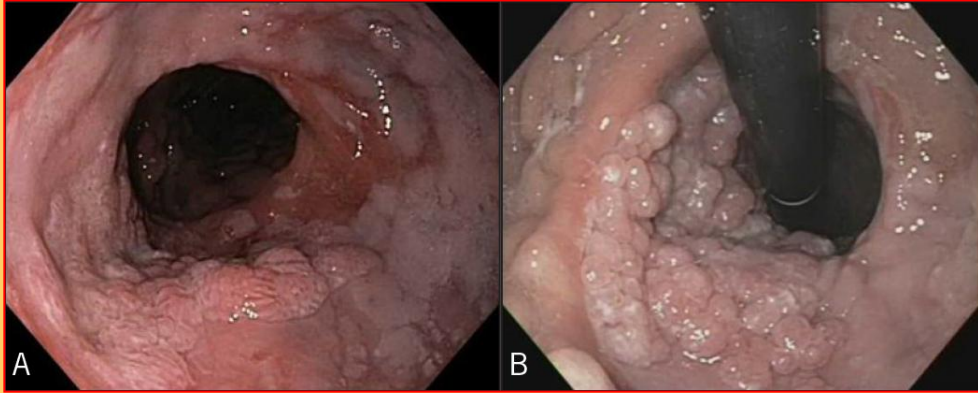
- Assunzione di alcool- tabacco
- Deficit nutrizionali
- Idrocarburi policiclici
- Nitrosamine
- Mutageni (tossine fungine)
- HPV
- Perdita p53, p16



Clinica

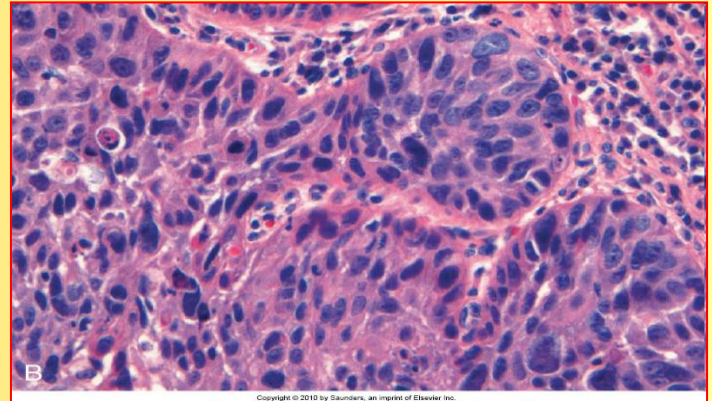
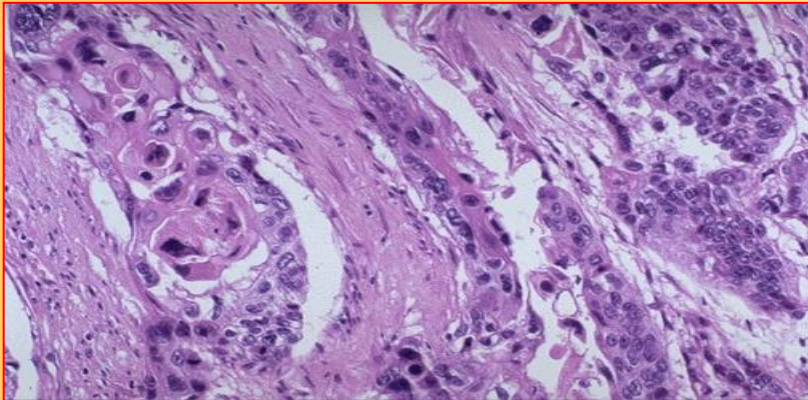
- Inizio insidioso
- Disfagia
- Odinofagia
- Perdita peso
- Emorragie
- Sepsi
- Prognosi infausta

carcinoma squamoso esofageo



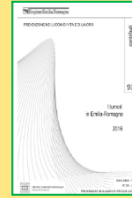
Anatomia Patologica

- Spesso forme bene-mod. differenziate
- Meno freq. forme verrucoidi, fusate
- Invasione precoce parete (ricca rete linf.)
- Infiltrazione circonferenziale (stenosi)
- Metastasi LGH cervicali/mediastinici/celiaci

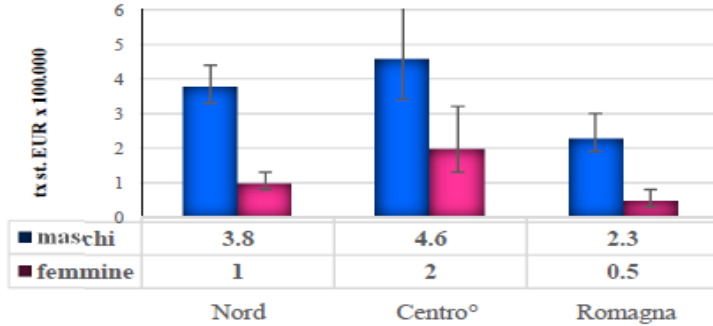


epidemiologia

Incidenza, mortalità

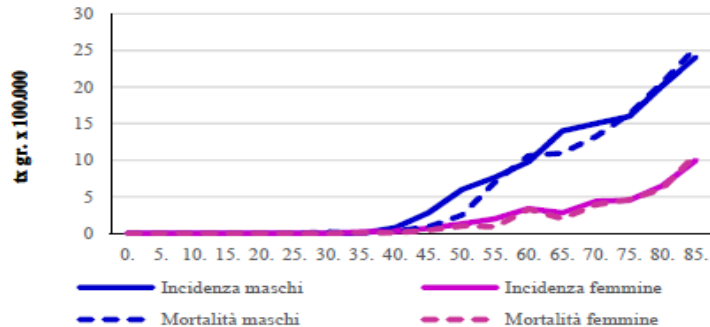


Confronti incidenza tra Aree Vaste

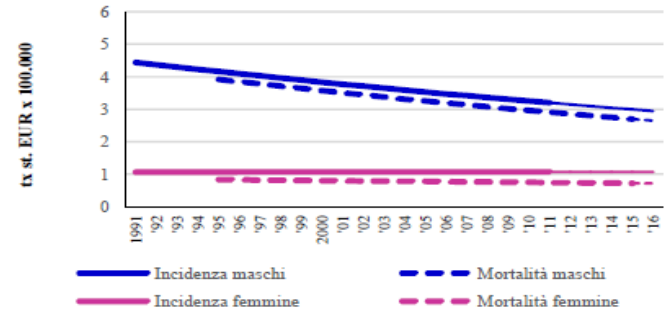


^oProvincia di Ferrara

Andamento per età



Andamenti temporali



	maschi		femmine	
	incidenza	mortalità	incidenza	mortalità
Anni	1991-2011	1995-2015	1991-2011	1995-2015
APC	-1.63*	-1.85*	+0.02	-0.72

APC: variazione percentuale annua * p<0,05

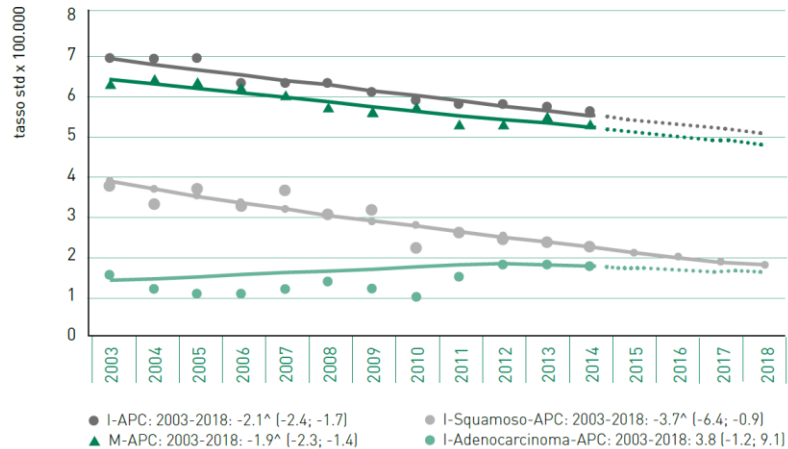


FIGURA 13A. Tumore dell'esofago, maschi. AIRTUM: stima dei trend tumorali di incidenza e mortalità 2003-2018. Tassi standardizzati nuova popolazione europea 2013

APC = Annual Percent Change (variazione percentuale media annual), I = incidenza, M = mortalità. Squamoso: ICD-O-3 = 8070-8079, Adenocarcinoma: ICD-O-3 = 8140-8149.



epidemiologia

Incidenza, mortalità

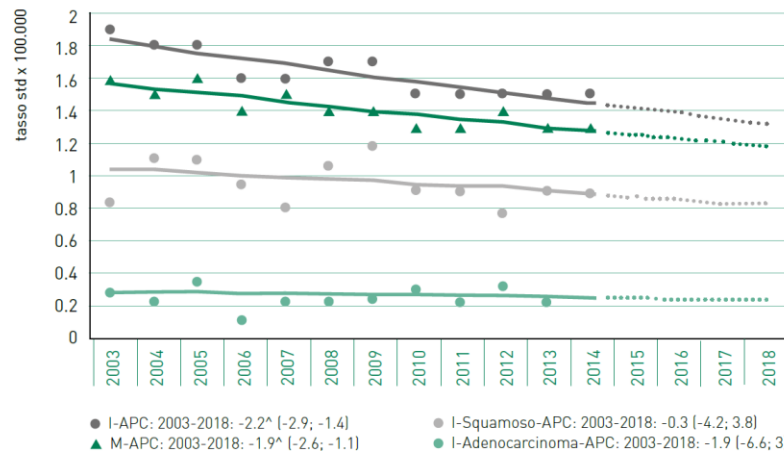


FIGURA 13B. Tumore dell'esofago, femmine. AIRTUM: stima dei trend tumorali di incidenza e mortalità 2003-2018. Tassi standardizzati nuova popolazione europea 2013

APC = Annual Percent Change (variazione percentuale media annual), I = incidenza, M = mortalità. Squamoso: ICD-O-3 = 8070-8079, Adenocarcinoma: ICD-O-3 = 8140-8149.

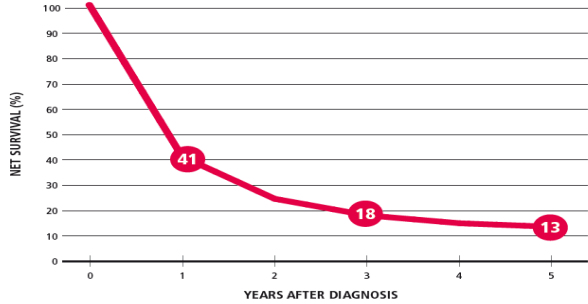


ESOPHAGUS CANCER

MALES & FEMALES

AGE-STANDARDIZED NET SURVIVAL (%), 2005-2009

POOL OF 42 CANCER REGISTRIES (5502 OBSERVED CASES)

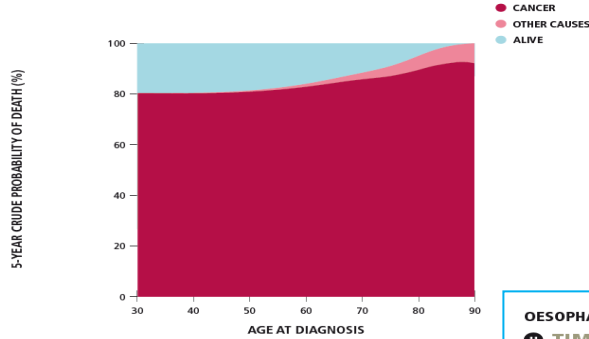


ESOPHAGUS CANCER

MALES & FEMALES

CRUDE PROBABILITY OF DEATH (%), 2005-2009

POOL OF 42 CANCER REGISTRIES (5376 OBSERVED CASES)

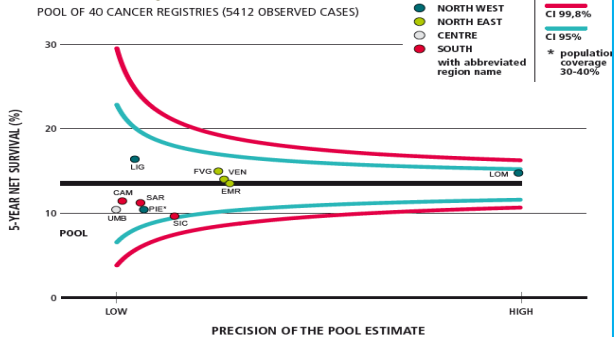


ESOPHAGUS CANCER

MALES & FEMALES

5-YEAR AGE-STANDARDIZED NET SURVIVAL (%) BY REGION, 2005-2009

POOL OF 40 CANCER REGISTRIES (5412 OBSERVED CASES)

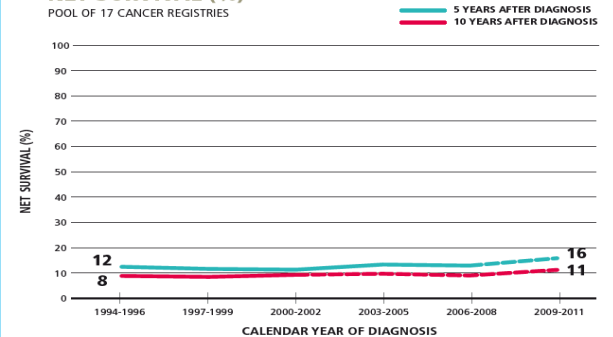


ESOPHAGUS CANCER

MALES & FEMALES

TIME TREND OF 5-, 10-YEAR AGE-STANDARDIZED NET SURVIVAL (%)

POOL OF 17 CANCER REGISTRIES



epidemiologia

Prevalenza e guarigione

CURE FRACTION AND TIME TO CURE BY AGE AT DIAGNOSIS AND SEX FOR CANCER PATIENTS DIAGNOSED IN ITALY IN 1985-2009

AGE AT DIAGNOSIS	CURE FRACTION %		AGE AT DIAGNOSIS	TIME TO CURE YEARS	
	MALE	FEMALE		MALE	FEMALE
0 - 44	11%	28%	0 - 44	7	8
45 - 59	7%	16%	45 - 59	8	9
60 - 74	4%	7%	60 - 74	8	9
75+	3%	4%	75+	8	10



Pool of Italian Cancer Registries - 1 January 2010

ESOFAGO OESOPHAGUS

(ICD-10 C15)

COMPLETE PREVALENCE BY YEARS SINCE DIAGNOSIS

YEARS →	≤ 2	(2 - 5]	(5 - 10]	(10 - 15]	(15 - 20]	> 20
No. →	1 637	942	697	431	208	265
% →	39%	23%	17%	10%	5%	6%
PROPORTION → PER 100 000	3.1	2.0	1.3	0.9	0.4	0.5
	MALE 73%			FEMALE 27%		

COMPLETE PREVALENCE BY SEX, MACRO-AREA, AND AGE

(PROPORTION PER 100 000)

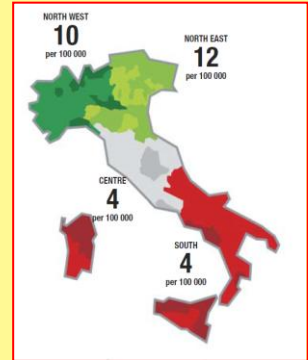
AGE CLASS →	0-44	45-59	60-74	75+	ALL AGES
MALE					
NORTH WEST	1	6	44	64	15
NORTH EAST	0	13	60	60	12

2 587 347 CANCER SURVIVORS

4 181
OESOPHAGUS
CANCER SURVIVORS

ALREADY CURED
at 1 JANUARY 2010

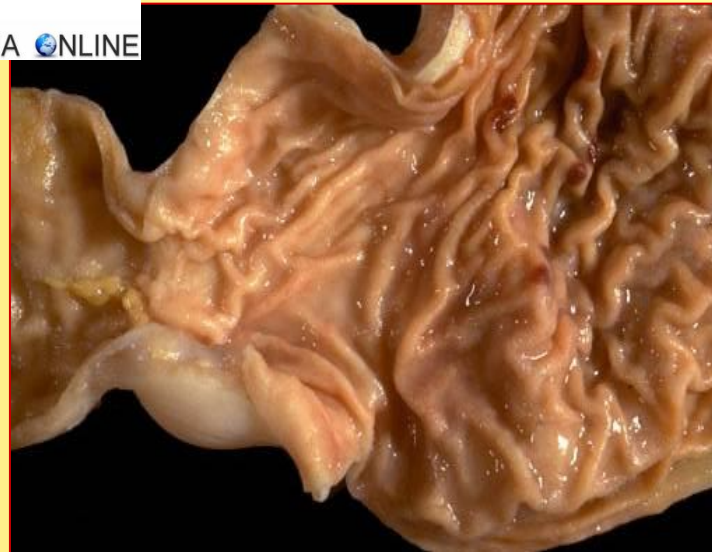
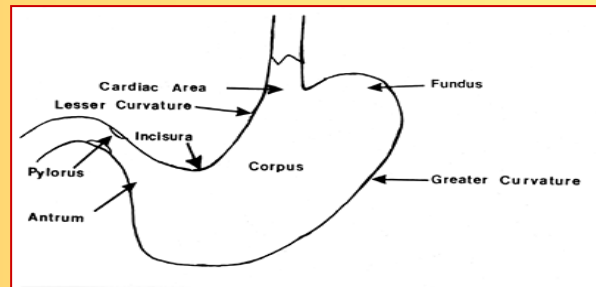
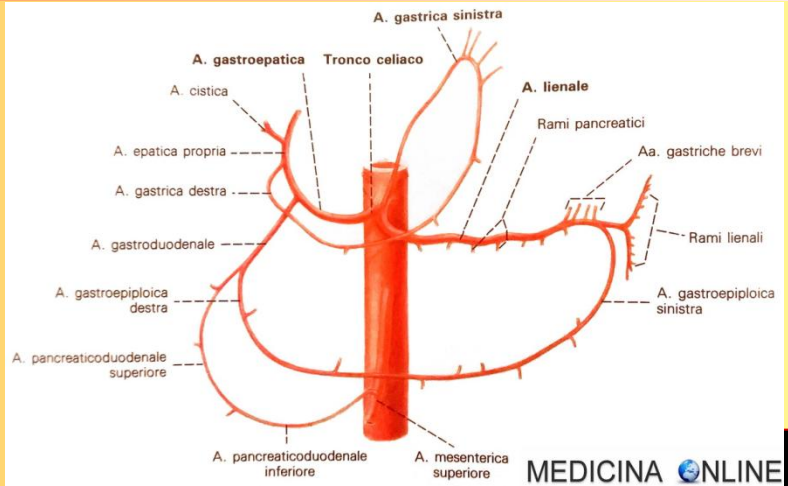
1 072 (26%)

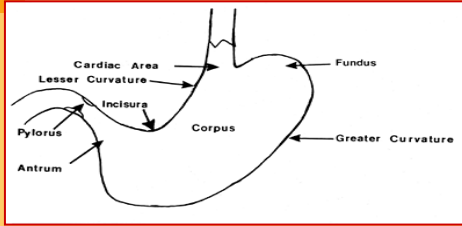




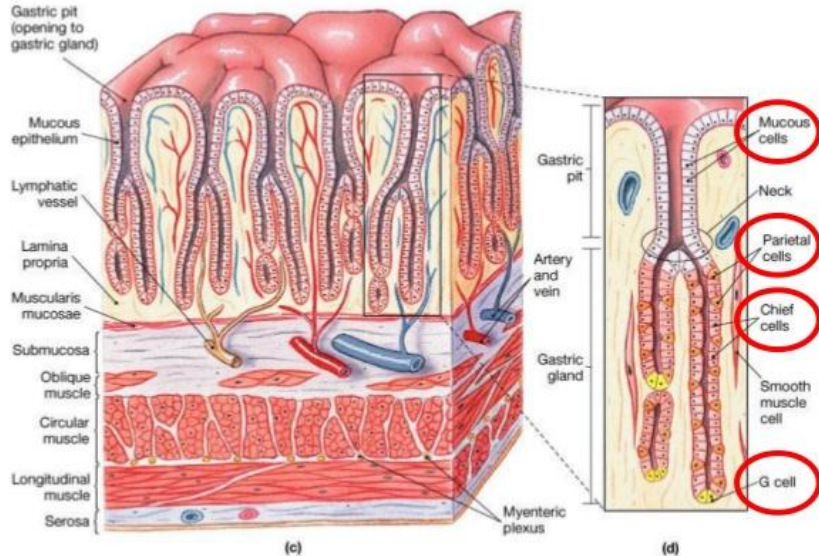
Stomaco

anatomia

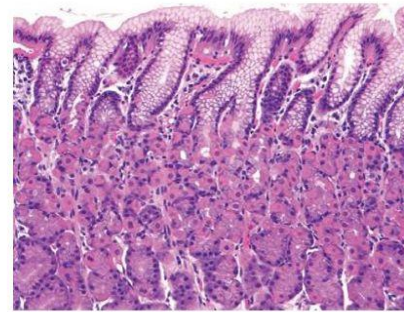




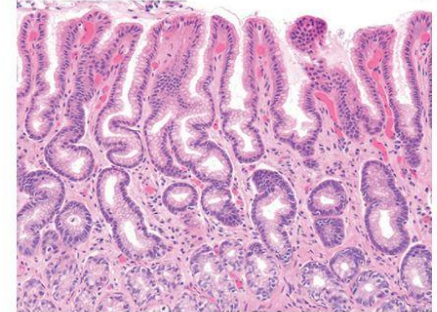
Stomaco



Stomach - Histology



Fundic mucosa with parietal & chief cells



Antral mucosa with mucin secreting glands

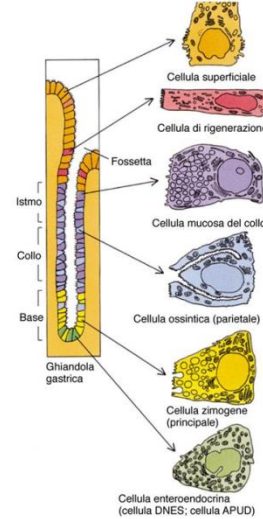
Lume dello stomaco



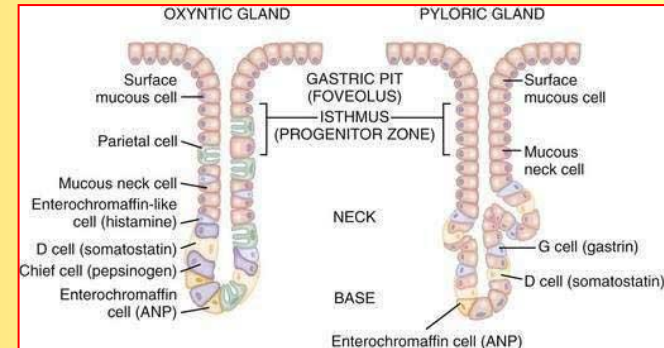
Tipi cellulari	Sostanze secrete
Cellule mucose collette	muco bicarbonato
Cellule parietale	Acido gastrico Fattore intrinseco (Ca ⁺⁺ absorption)
Enterochromaffin-like cell	istamina
Cellule principali	Pepsin(ogen) Gastric lipase
D cells	somatostatina
G cells	gastrina

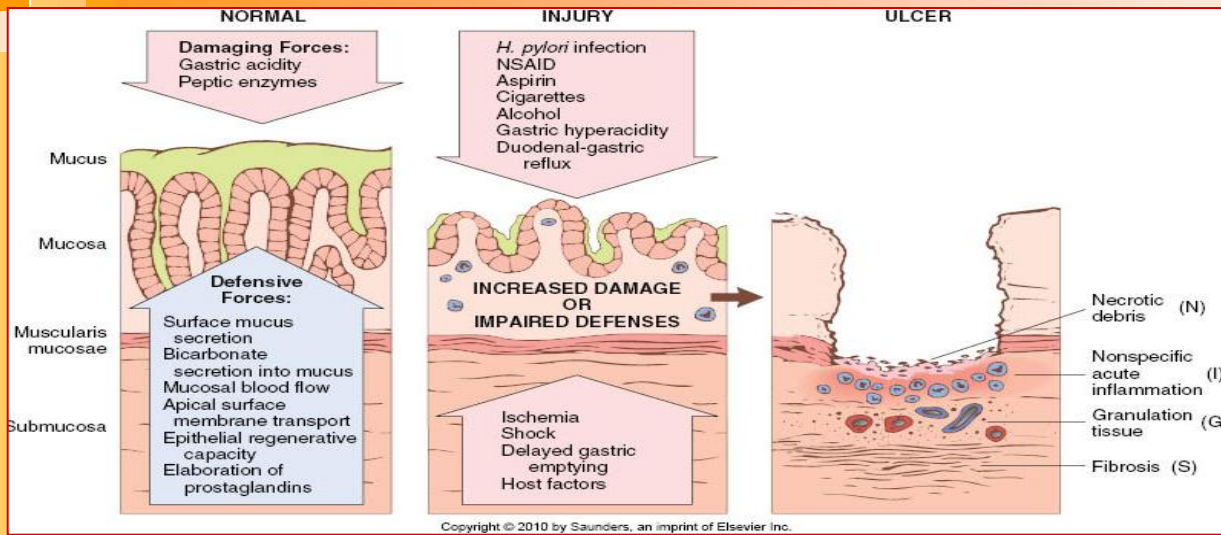
Fossette e ghiandole gastriche

- **Fossette.**
 - Invaginazioni che uniscono il dotto delle ghiandole all'epitelio dello stomaco.
- Cellule staminali che producono tutti i tipi cellulari della fossetta e della ghiandola.



anatomia





gastriti acute

- ## Clinica
- Dolore
 - Perforazione
 - Emorragie
 - *Esito variabile*

- ## Etiopatogenesi
- Alterazione della protezione della mucosa*
- Riduzione sintesi mucina
 - Fattori fisici
 - Fattori tossici
 - Fattori iatrogeni
 - Infezioni (HP)
 - Ipossia
 - Quadri sistemici (stress, ustioni, traumi cranici)
 - Reflusso biliare

- ## Anatomia Patologica
- Infiltrazione neutrofila epiteliale
 - Erosioni, ulcere
 - Emorragie
 - Occlusione
 - Estensione variabile

Etiopatogenesi – Fattori di rischio

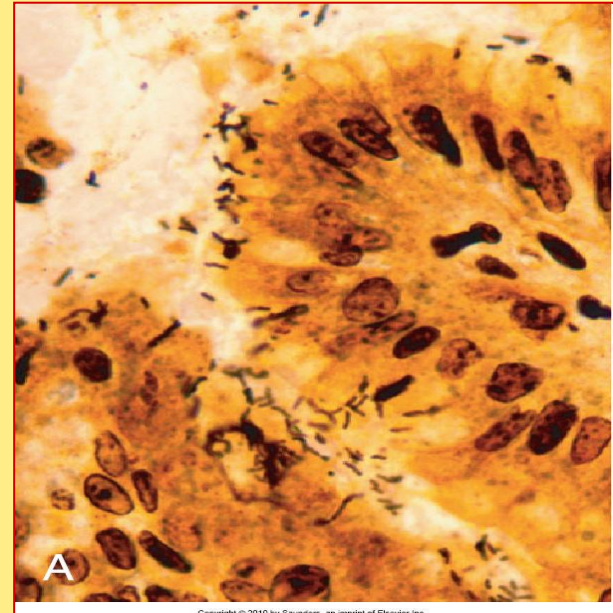
Alterazione della protezione della mucosa (90%)

- **Meccanismo lesivo cronico**
 - Fumo di sigaretta
 - Consumo di carni rosse
 - Cibi conservati con sale, nitrati, nitriti
 - Cibi conservati con affumicatura
 - Basso consumo verdura e frutta
 - Reflusso biliare
 - FANS, farmaci cortisonici
- **Infezione da HP**
 - (flagelli, ureasi, adesine, tossine)
 - Interazione batterio/ospite
 - Polimorfismo IL/1-B

Autoimmunità (10%)

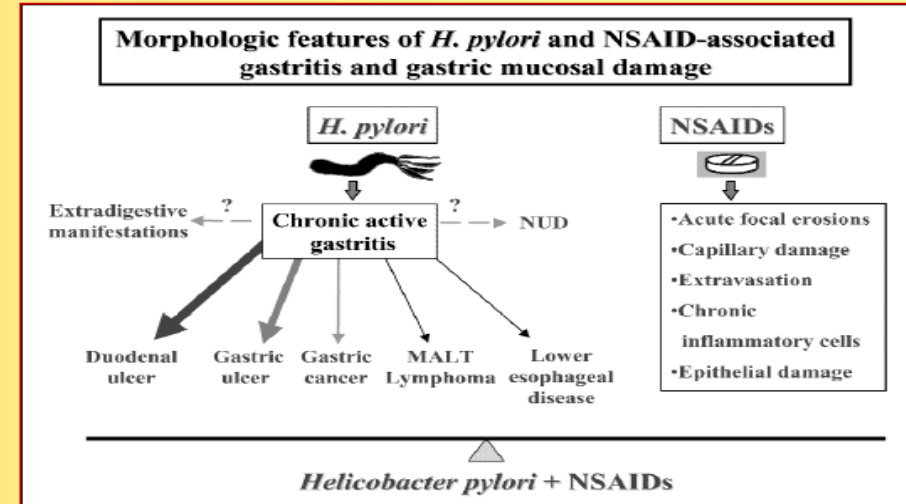
- **Reazione T CD4+ versus cellule parietali**
 - Ab versus cell. parietali e fatt. intrinseco
 - Deficit di fattore intrinseco (anemia)
 - Deficit secrezione acida

**gastriti
croniche**



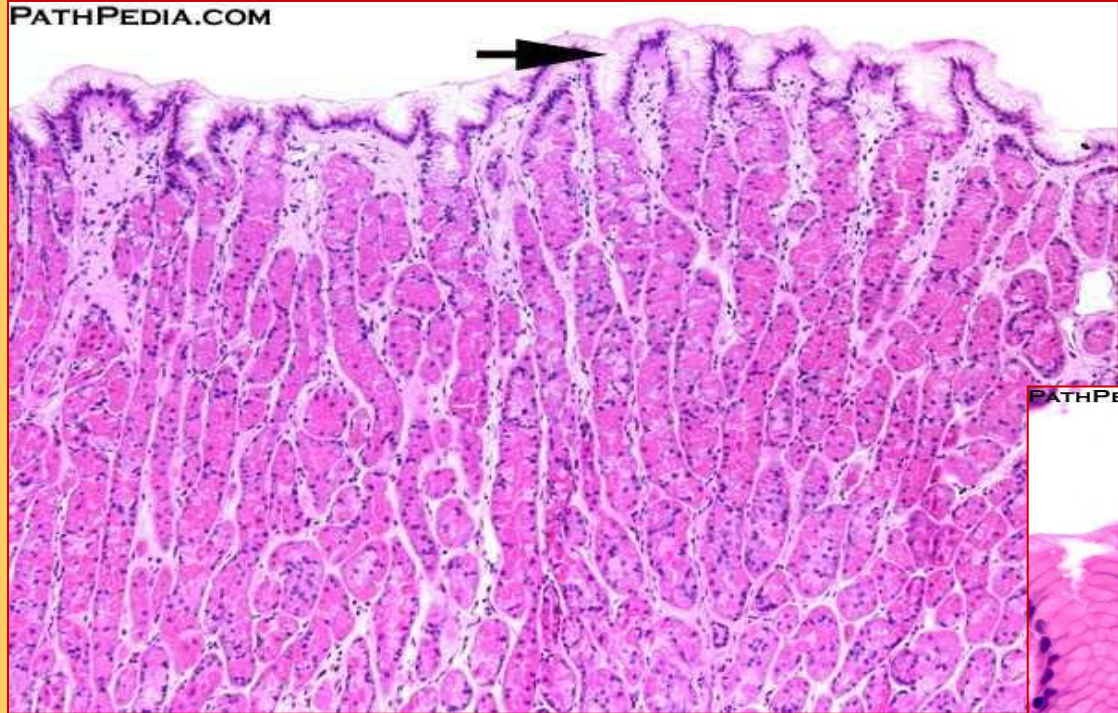
Tipo	<i>Helicobacter p. associata</i>	Autoimmune
Sede	Antro	Corpo
Infiltrato infiammatorio	Neutrofili, plasmacellule	Linfociti, macrofagi
Secrezione acida	Aumentata o liev. diminuita	Diminuita
Gastrina	Normale/diminuita	Aumentata
Altre lesioni	Pseudopolipi infiammatorii	Iperplasia neuroendocrina
Sierologia	Ab anti HP	Ab anti cell.parietali (H+,K+,ATPasi, fatt. intrinseco)
Sequela	Ulcera peptica Atrofia Adenocarcinoma "intestinale" Linfoma MALT	Anemia perniciosa Adenocarcinoma "gastrico"
Associazioni	Basso stato socio-economico Aree rurali	Malattie autoimmuni (tiroiditi, Grave's, diabete)

gastriti croniche



fisiopatologia

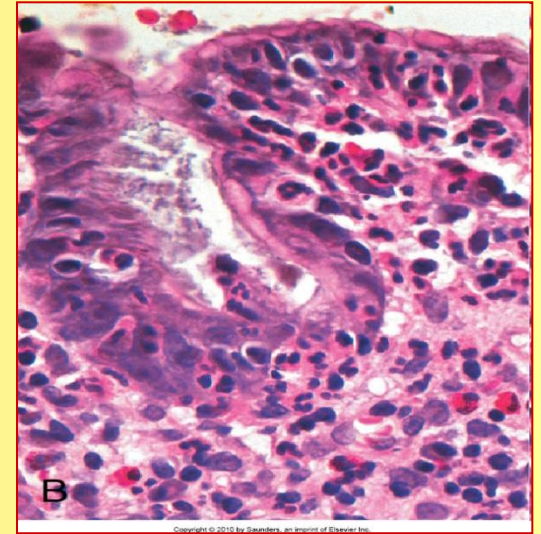
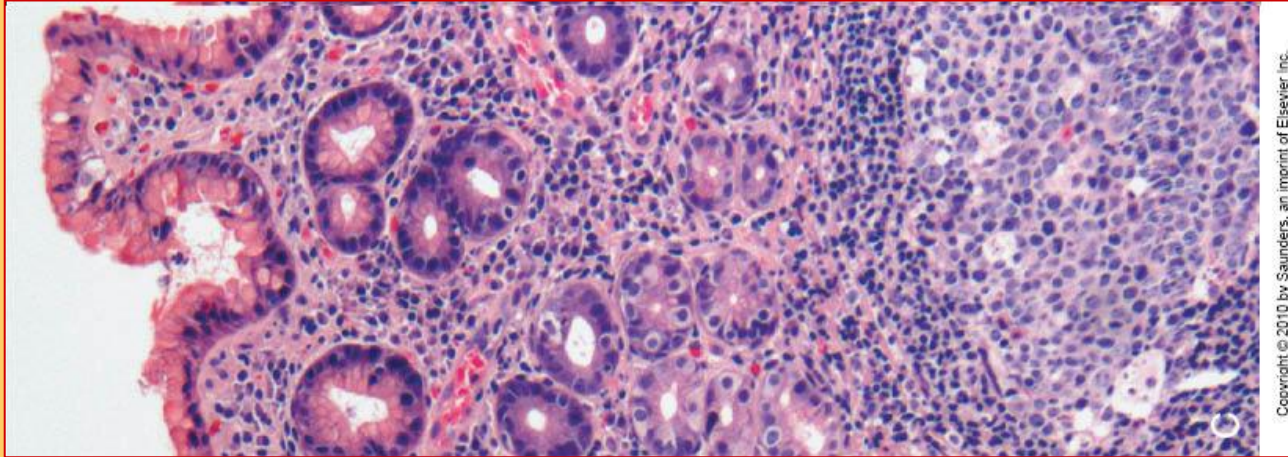
gastriti croniche



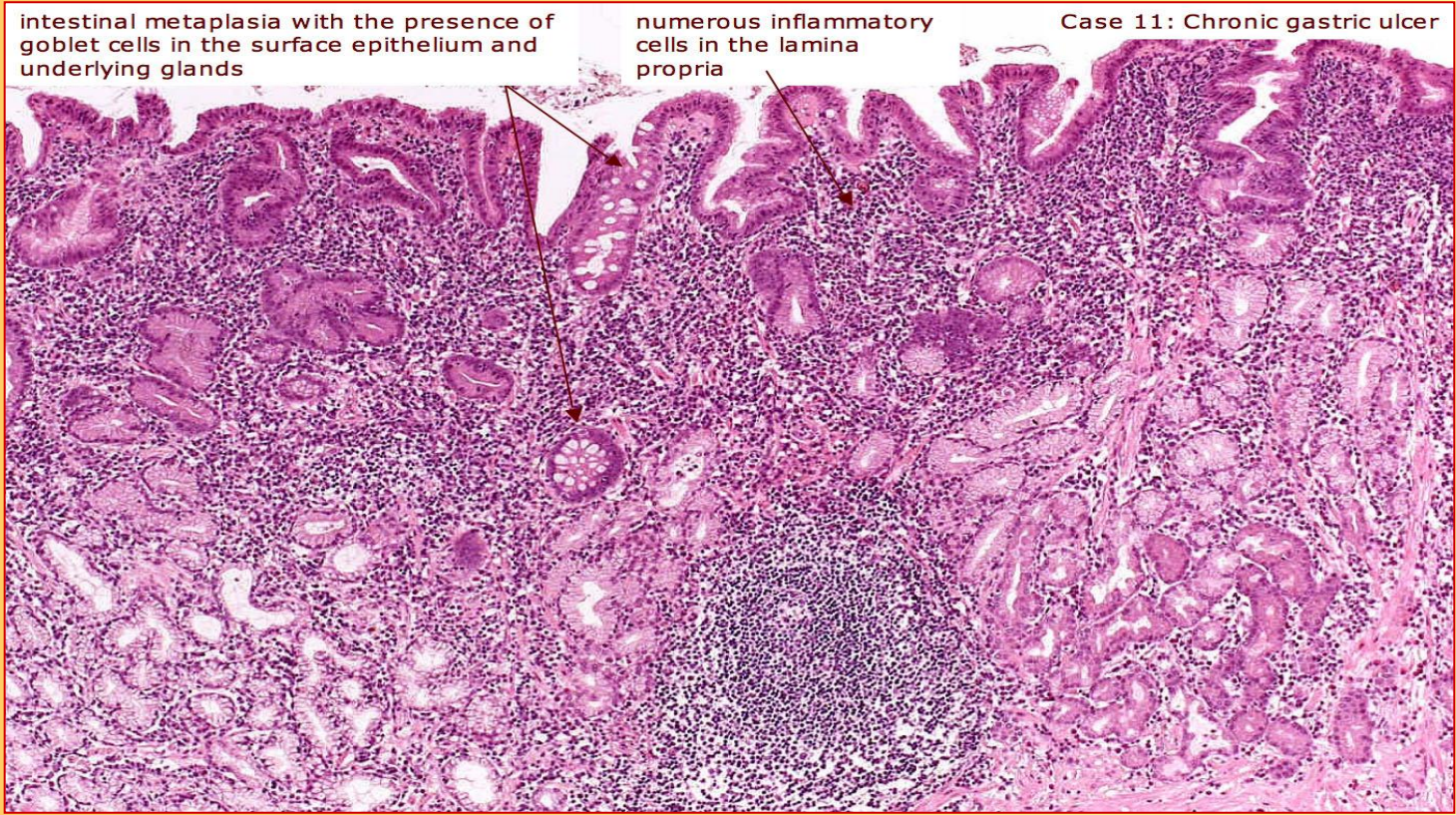
Anatomia Patologica

- Infezione HP
- Infiltrazione flogistica (neutrofila, pl cell.):
 - Fasi attive: lamina propria, epitelio
 - Fasi quiescenti: lamina propria
- Erosione della mucosa
- Interessamento foveolare
- Atrofia/iperplasia ghiandolare
- Metaplasia intestinale
- Displasia
- Rischio ca gastrico *intestinal type*

gastriti
croniche

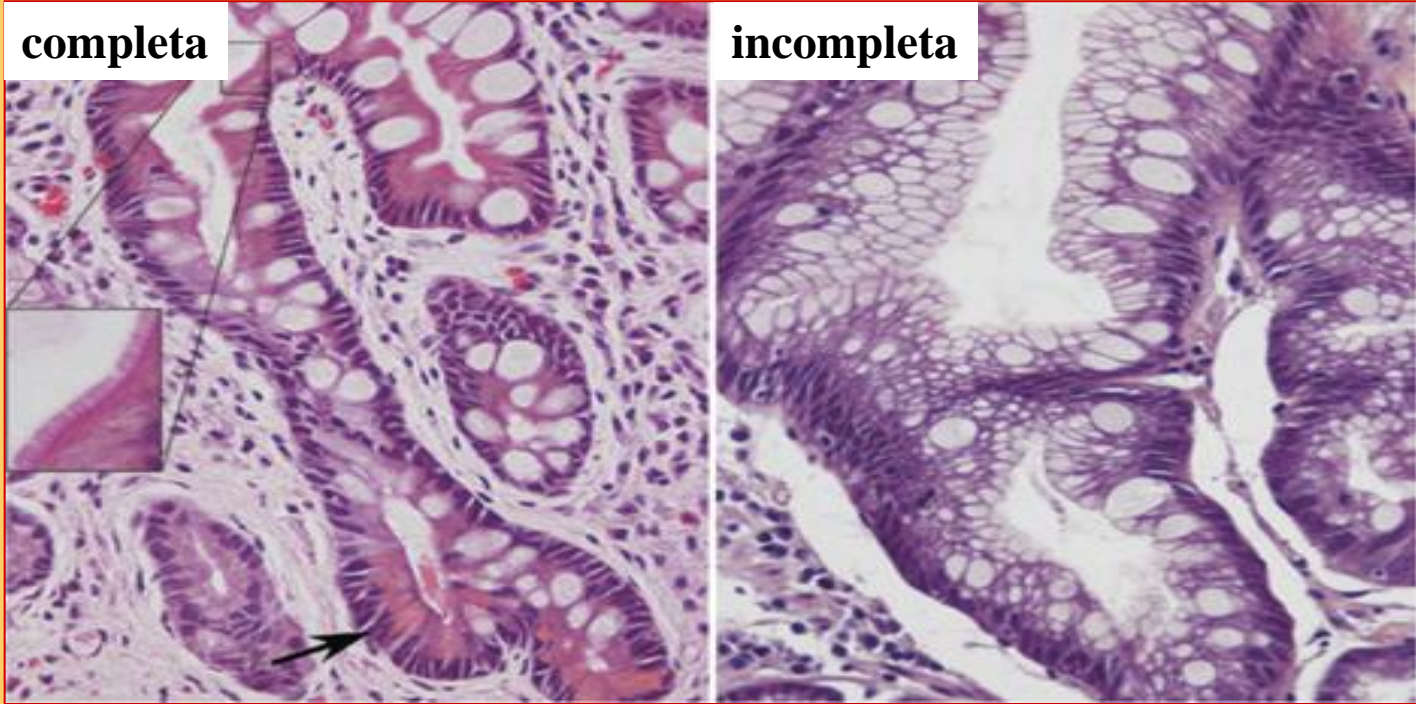


gastriti croniche



metaplasia intestinale

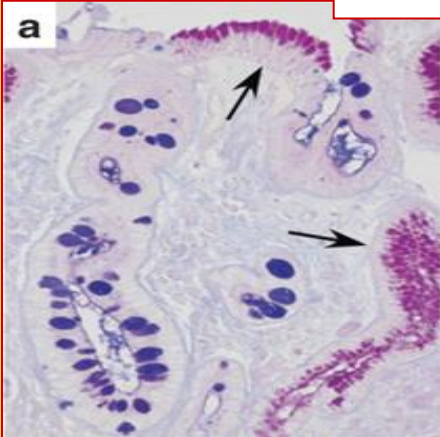
**gastriti
croniche**



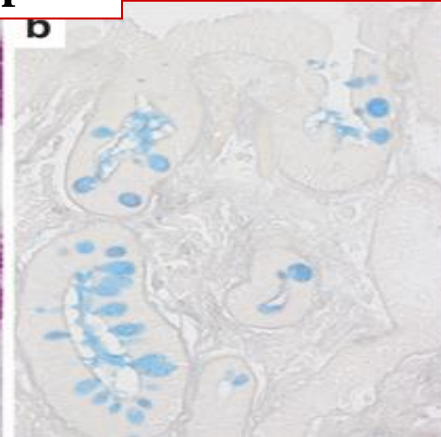
metaplasia intestinale

gastriti
croniche

completa

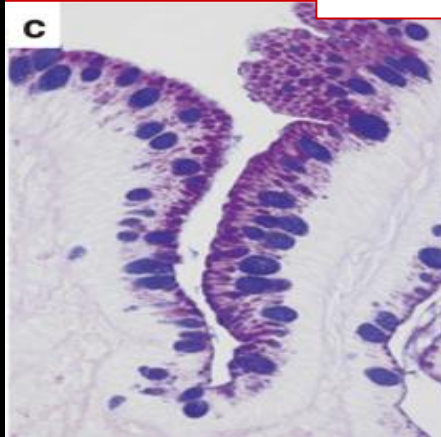


mucine
neutre
acide

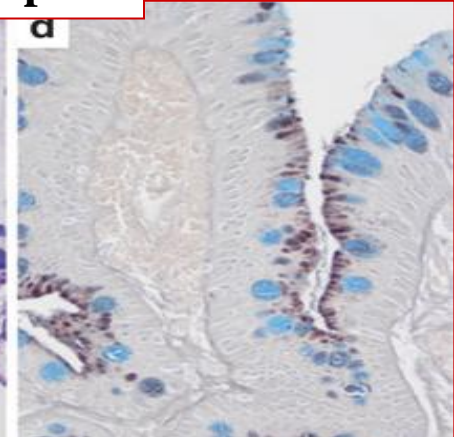


mucine acide
sialomucine
solfomucine

incompleta

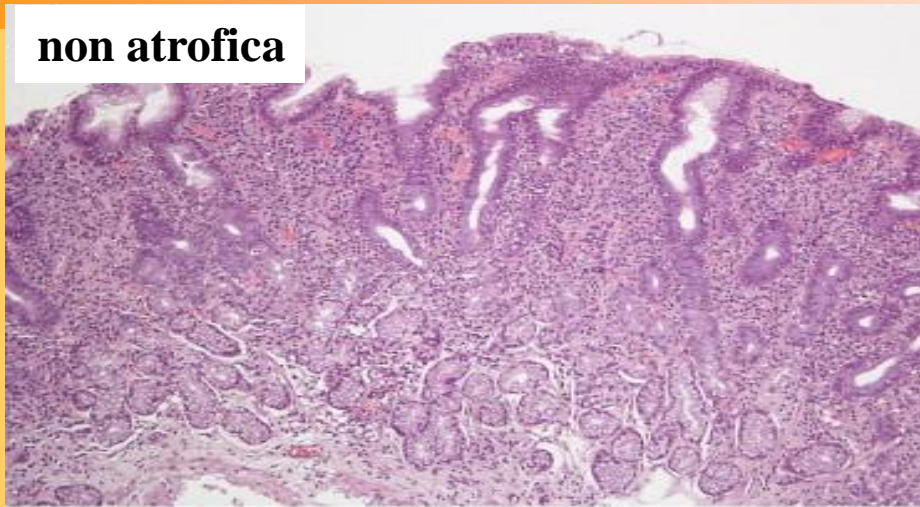


mucine
neutre
acide

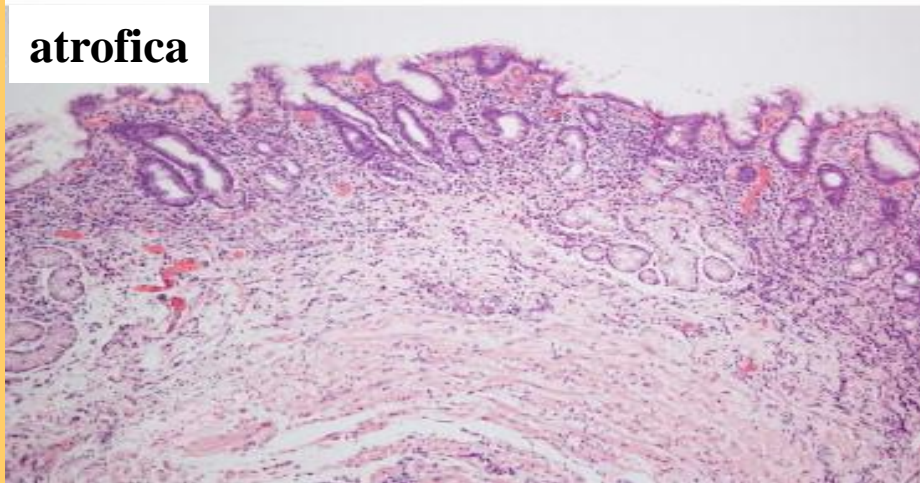


mucine acide
sialomucine
solfomucine

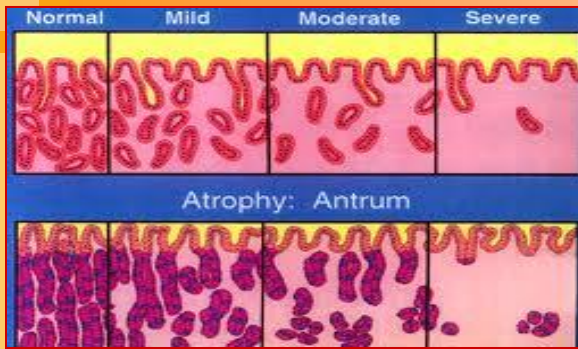
non atrofica



atrofica

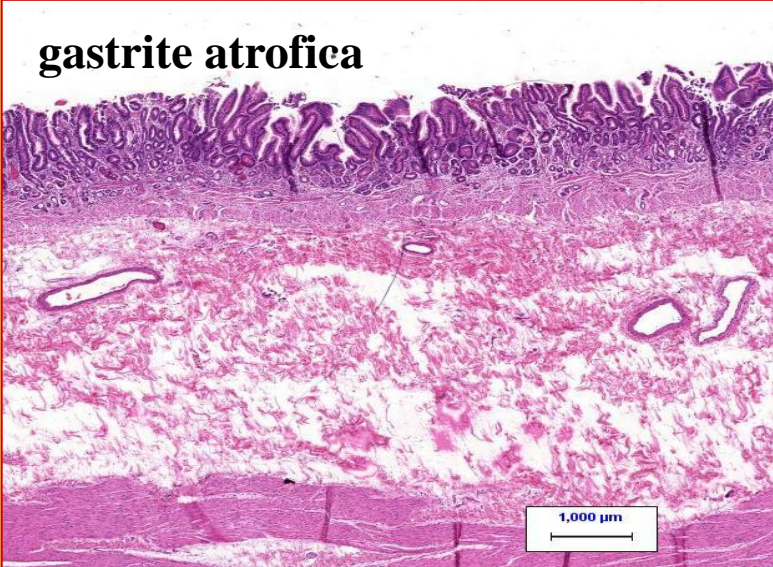


**gastriti
croniche**



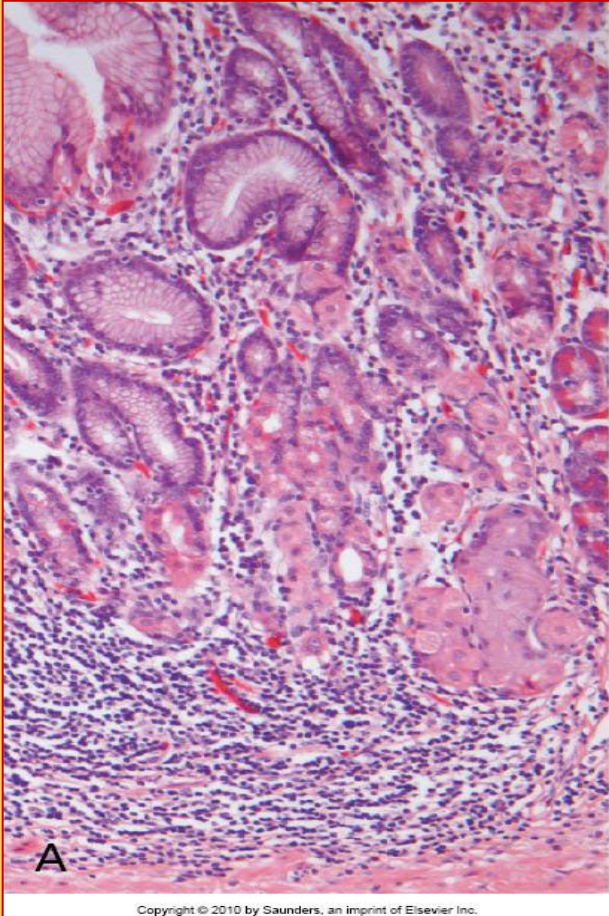
gastriti atrofiche

gastriti croniche

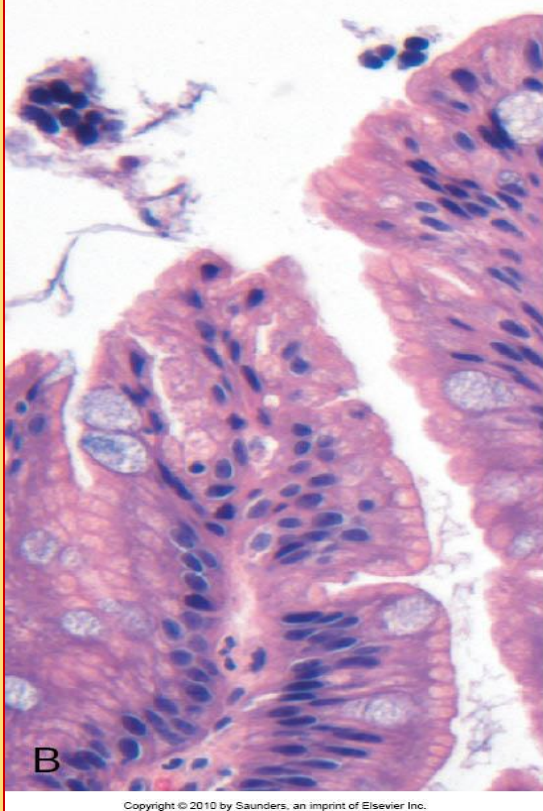


gastriti autoimmuni

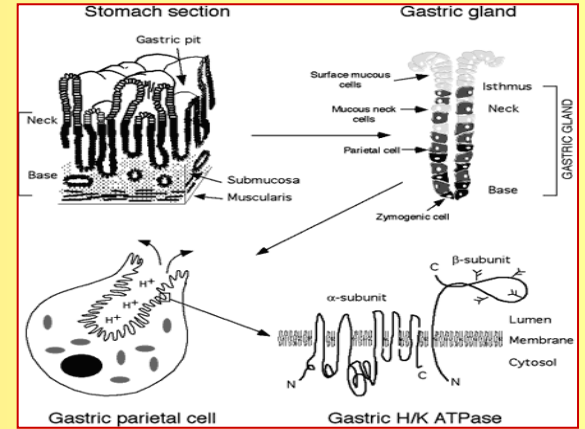
gastriti croniche



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adenocarcinomi

Fattori di rischio

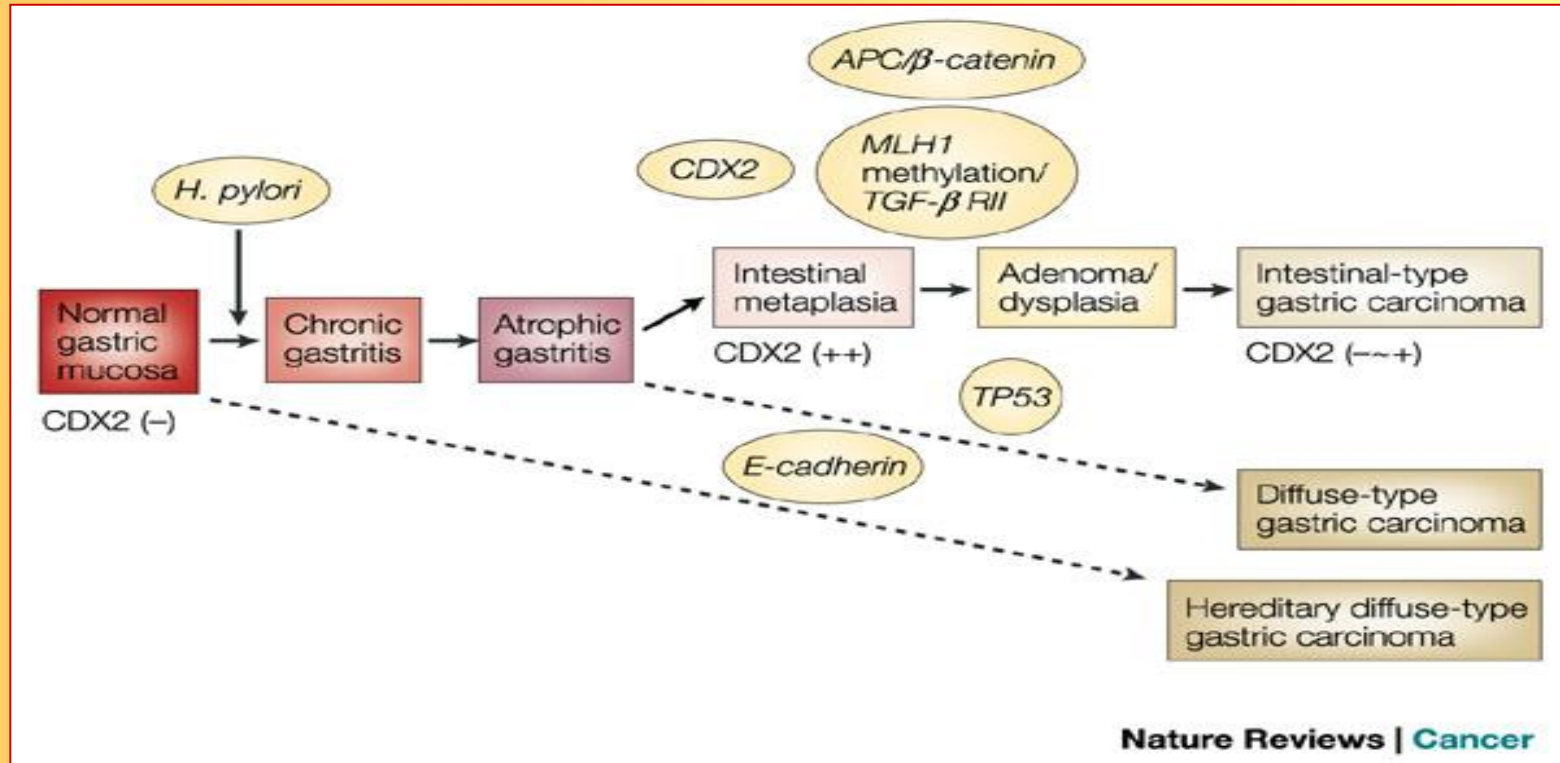
- Infezione da *Helicobacter pylori*
- Abitudine al fumo
- Storia familiare
- Abitudini alimentari
 - salagione/affumicatura (nitrati/nitriti)
 - carni rosse,
 - basso consumo frutta e verdura
 - reflusso biliare

Forme di predisposizione ereditaria

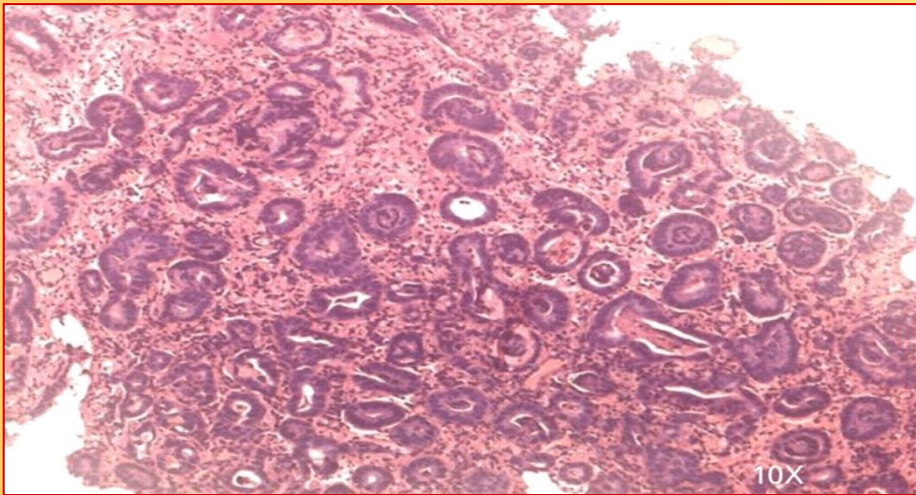
- Poliposi adenomatosa familiare
- S. di Linch
- S. di Li-Fraumeni
- S. di Peutz-Jeghers



adenocarcinomi

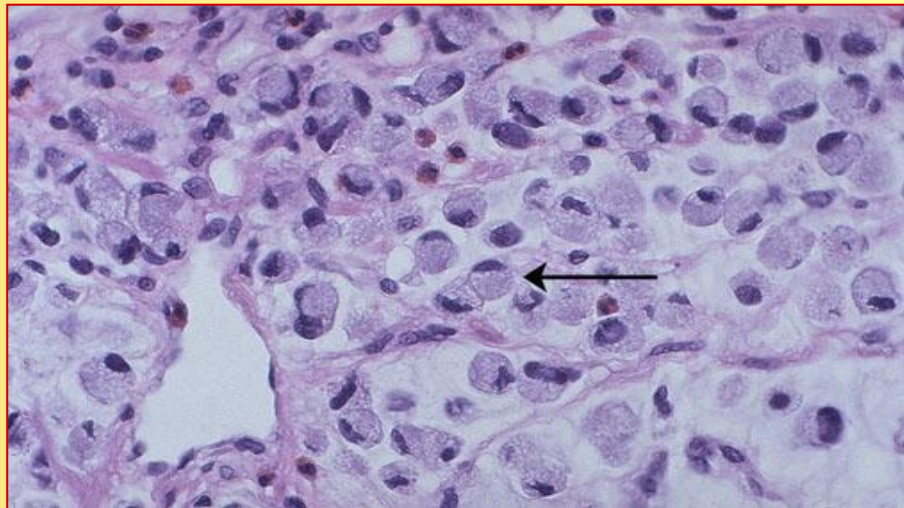


intestinale

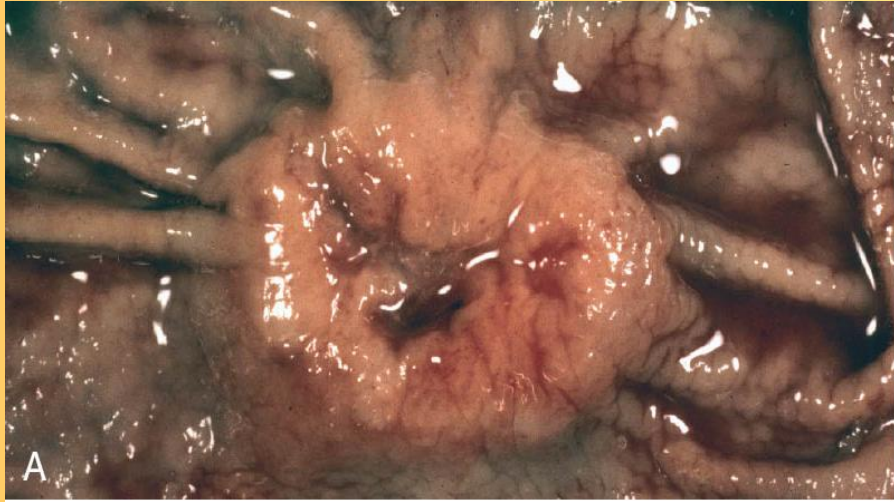


adenocarcinomi

diffuso

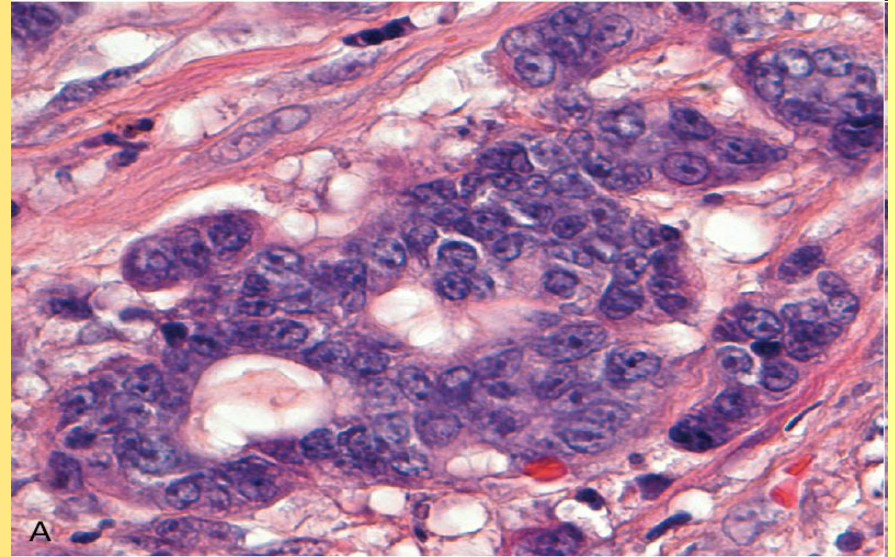


intestinale



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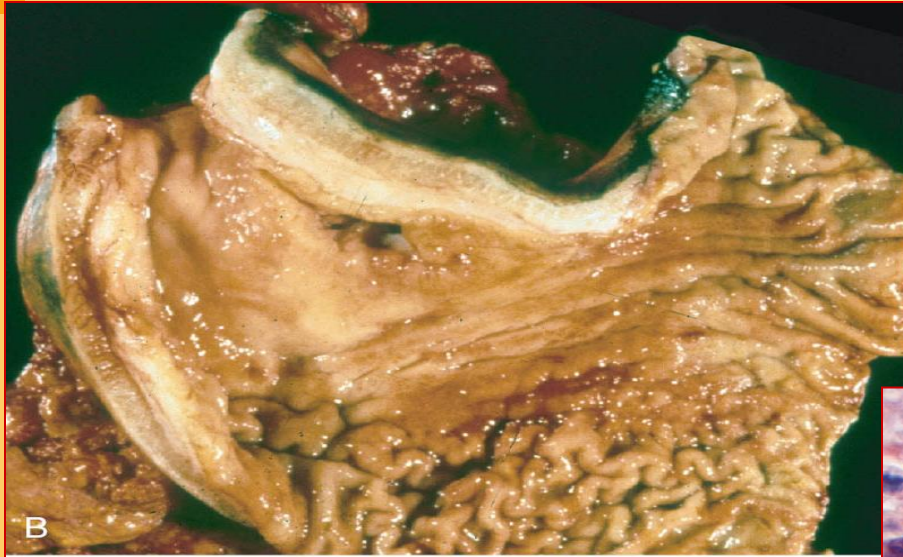
adenocarcinomi



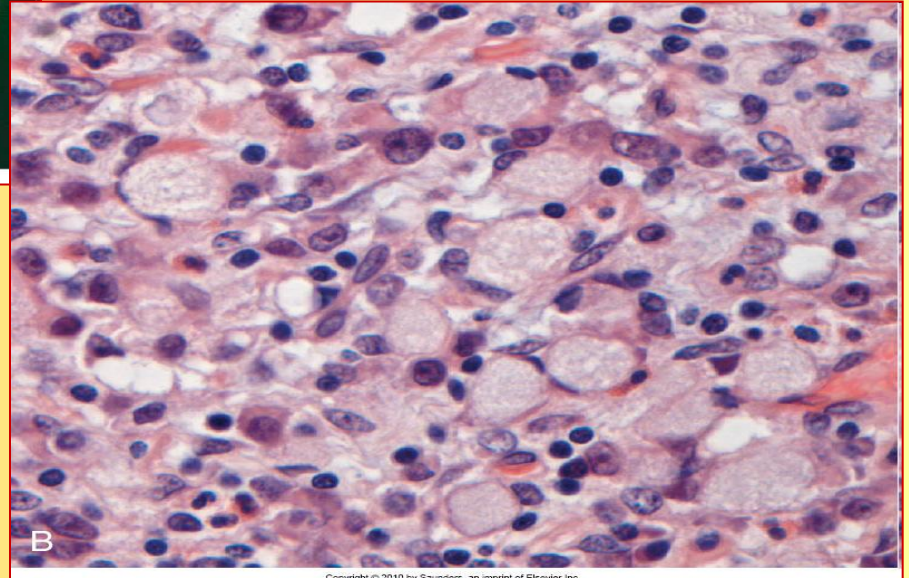
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adenocarcinomi

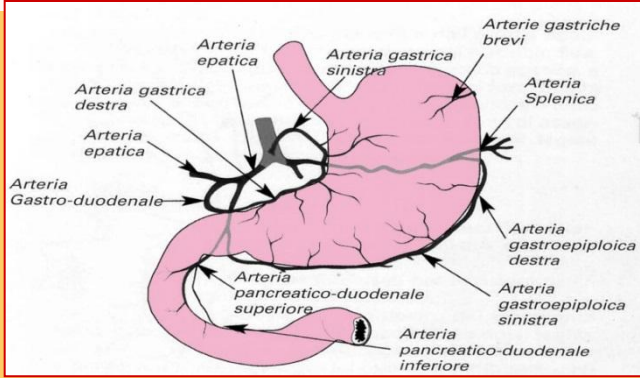
diffuso



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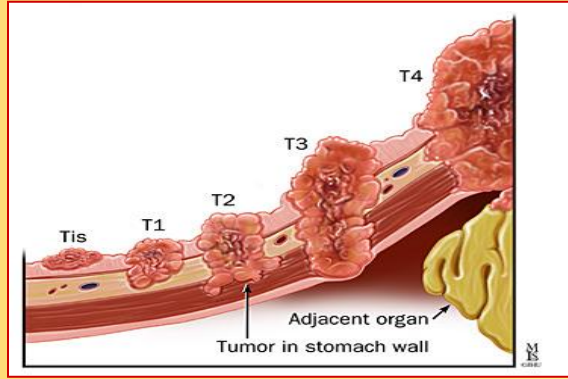
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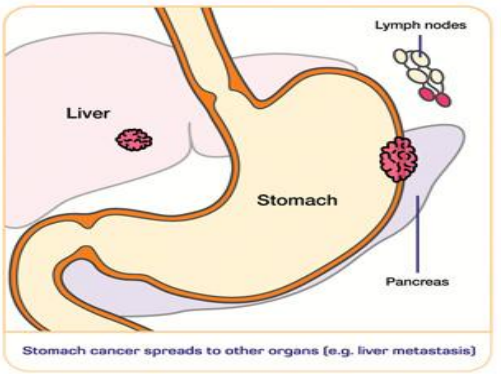
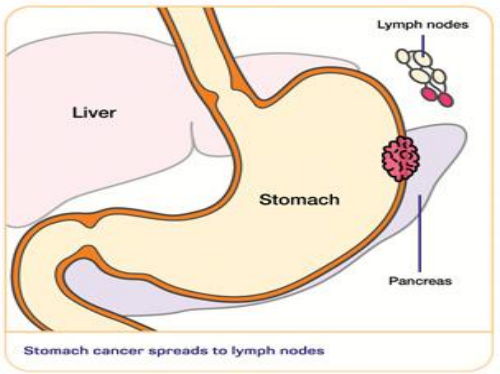
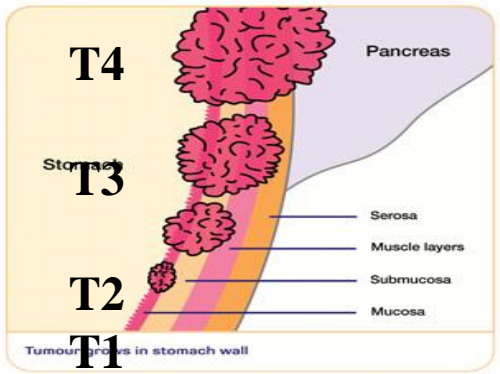
adenocarcinomi

Stadiazione

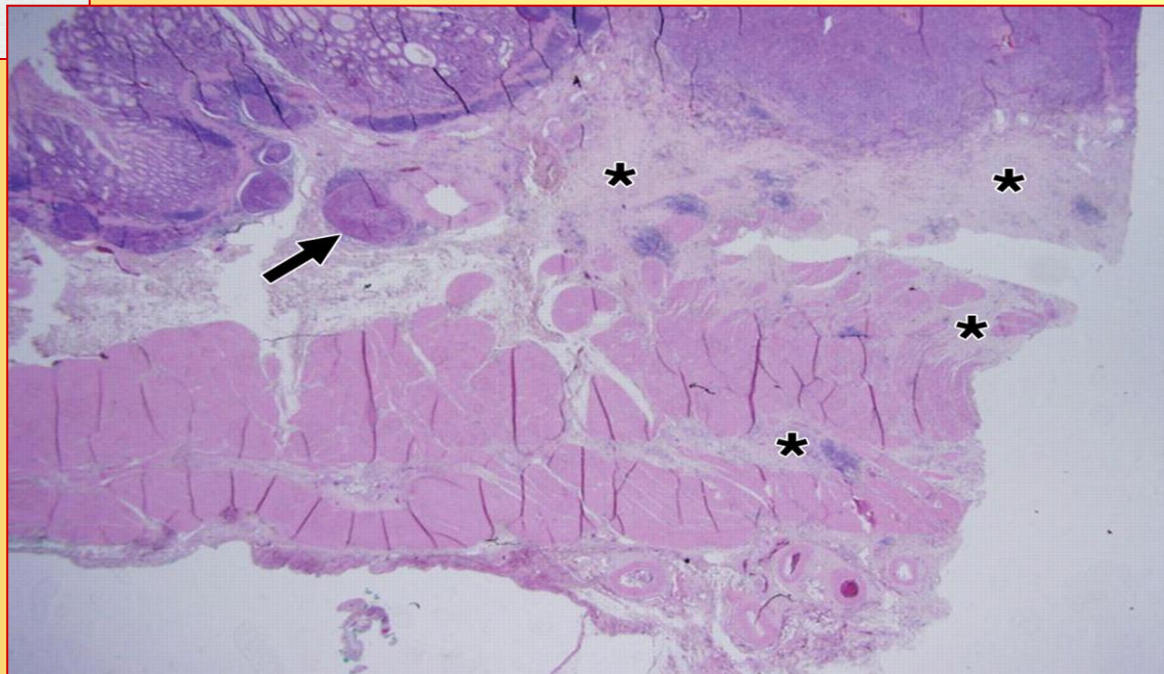
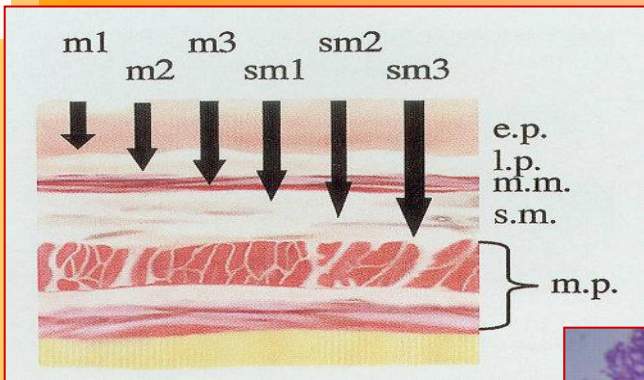
(TNM 7a ed.)



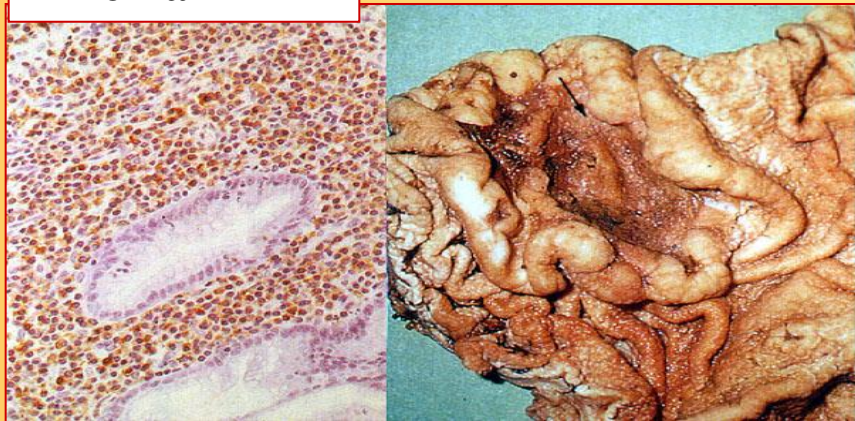
- N0=non metastasi**
- N1=1-2 LGH**
- N2=3-6 LGH**
- N3a=7-15 LGH**
- N3b=16+ LGH**



early gastric cancer

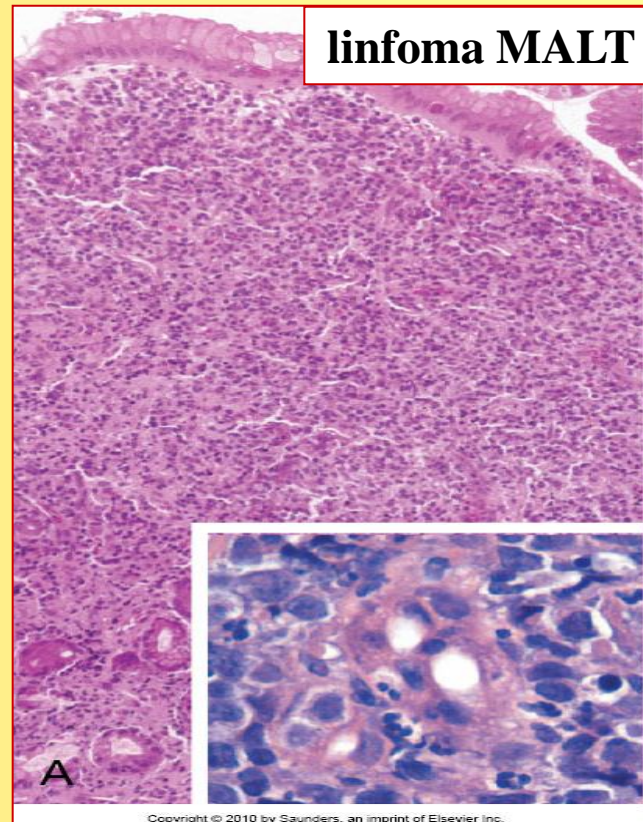


linfoma MALT

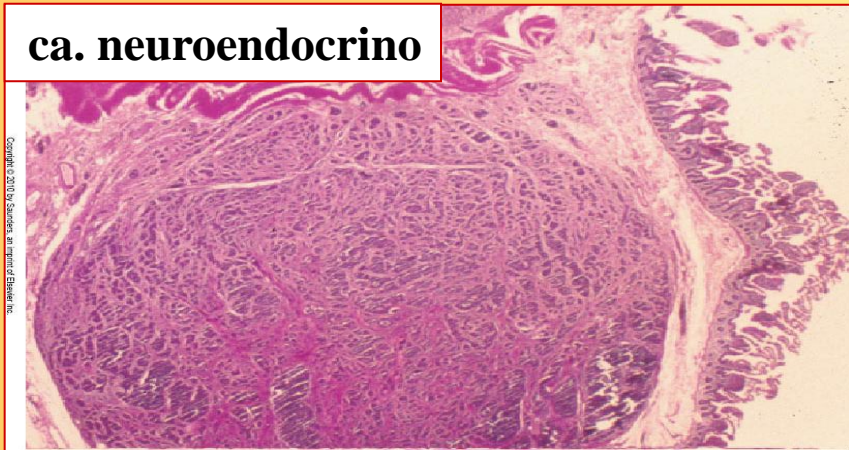


altre neoplasie

linfoma MALT



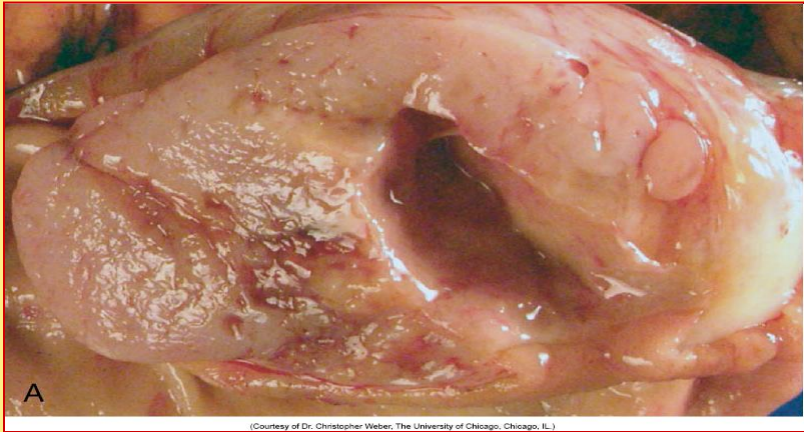
ca. neuroendocrino



altre neoplasie

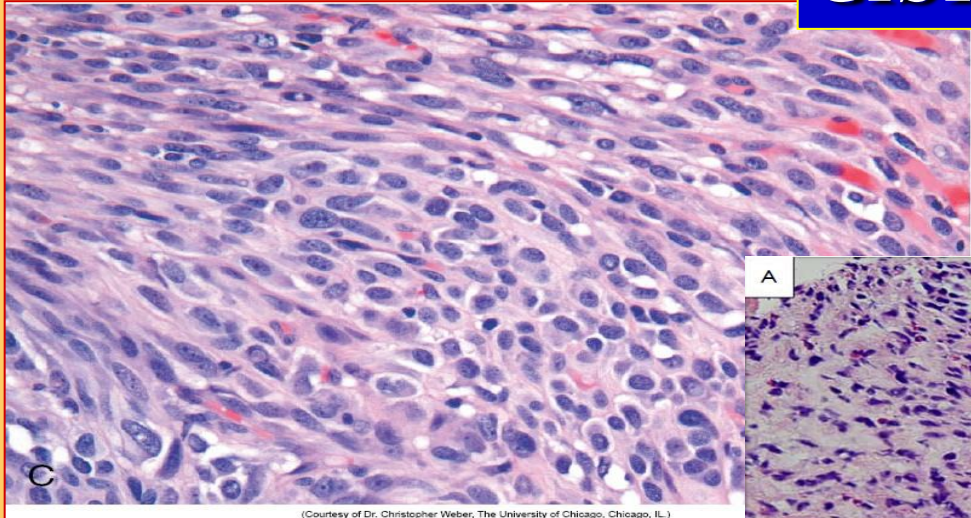


(Courtesy of Dr. Christopher Weber, The University of Chicago, Chicago, IL.)

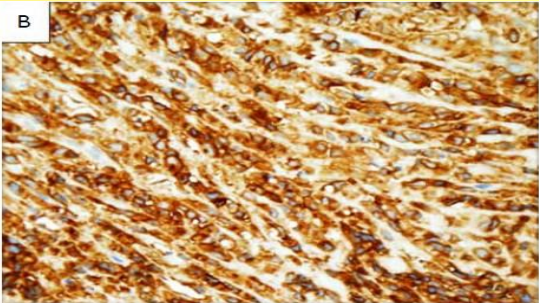
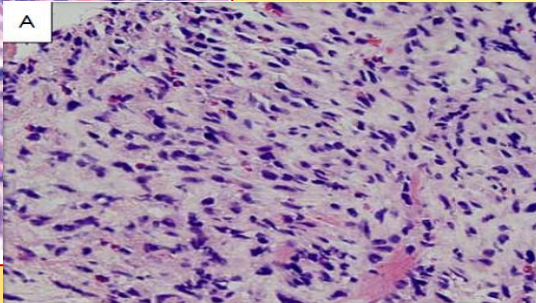


(Courtesy of Dr. Christopher Weber, The University of Chicago, Chicago, IL.)

GIST



(Courtesy of Dr. Christopher Weber, The University of Chicago, Chicago, IL.)



epidemiologia

Tumore dello stomaco

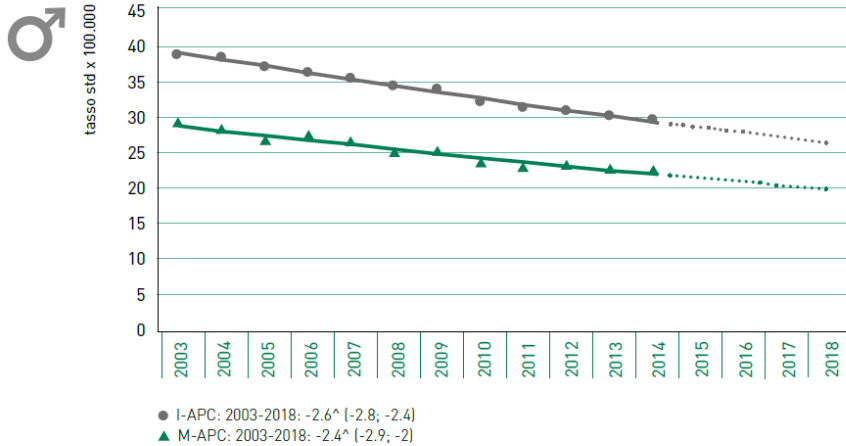


FIGURA 14A. Tumore dello stomaco, maschi. AIRTUM: stima dei trend tumorali di incidenza e mortalità 2003-2018. Tassi standardizzati nuova popolazione europea 2013

APC = Annual Percent Change (variazione percentuale media annua), I = incidenza, M = mortalità.

*incidenza
mortalità*

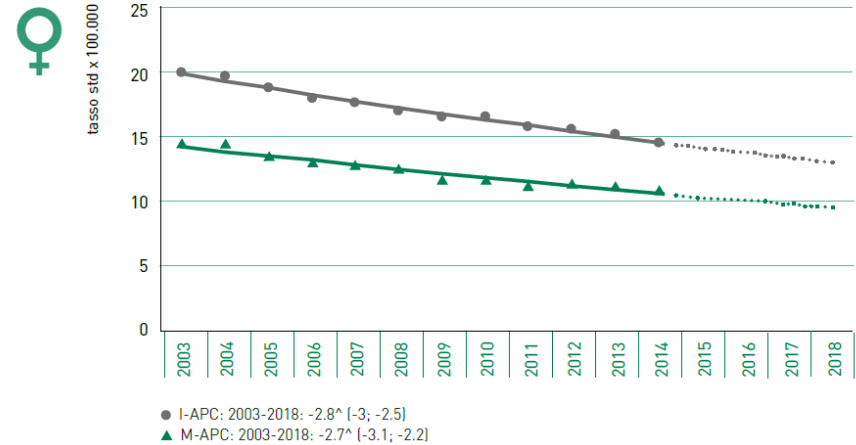


FIGURA 14B. Tumore dello stomaco, femmine. AIRTUM: stima dei trend tumorali di incidenza e mortalità 2003-2018. Tassi standardizzati nuova popolazione europea 2013

APC = Annual Percent Change (variazione percentuale media annua), I = incidenza, M = mortalità.

Rango	Maschi	Femmine	Tutta la popolazione
1°	Prostata (18%)	Mammella (29%)	Mammella (14%)
2°	Colon-retto (15%)	Colon-retto (13%)	Colon-retto (14%)
3°	Polmone (14%)	Polmone (8%)	Polmone (11%)
4°	Vescica* (11%)	Tiroide (6%)	Prostata (9%)
5°	Fegato (5%)	Utero corpo (5%)	Vescica* (7%)

TABELLA 6. Primi cinque tumori più frequentemente diagnosticati e proporzione sul totale dei tumori (esclusi i carcinomi della cute) per sesso. Stime per l'Italia 2018

* Comprende sia tumori infiltranti sia non infiltranti.

** Comprende rene, pelvi e uretere.



Rango	Maschi	Femmine	Tutta la popolazione
1°	Polmone (26%)	Mammella (17%)	Polmone (19%)
2°	Colon-retto (11%)	Colon-retto (12%)	Colon-retto (11%)
3°	Prostata (8%)	Polmone (11%)	Mammella (7%)
4°	Fegato (7%)	Pancreas (8%)	Pancreas (6%)
5°	Stomaco (6%)	Stomaco (6%)	Fegato (6%)

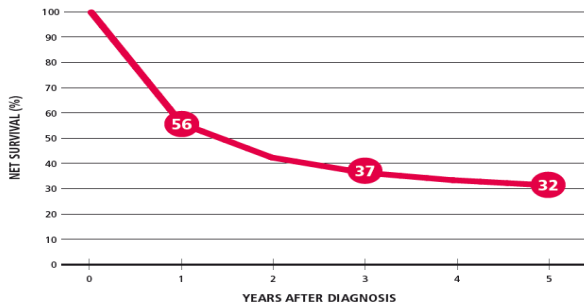
TABELLA 9. Prime cinque cause di morte oncologica e proporzione sul totale dei decessi oncologici per sesso. Pool AIRTUM 2010-2014

STOMACH CANCER

MALES & FEMALES

C AGE-STANDARDIZED NET SURVIVAL (%), 2005-2009

POOL OF 42 CANCER REGISTRIES (35217 OBSERVED CASES)

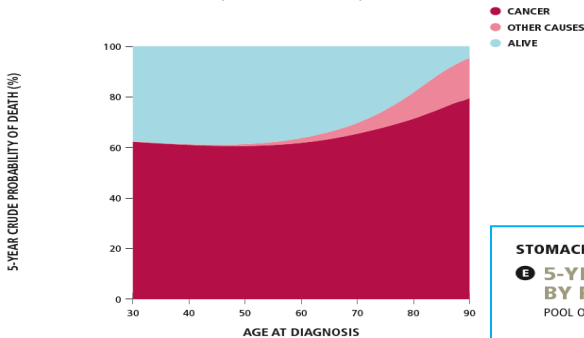


STOMACH CANCER

MALES & FEMALES

D CRUDE PROBABILITY OF DEATH (%), 2005-2009

POOL OF 42 CANCER REGISTRIES (33896 OBSERVED CASES)



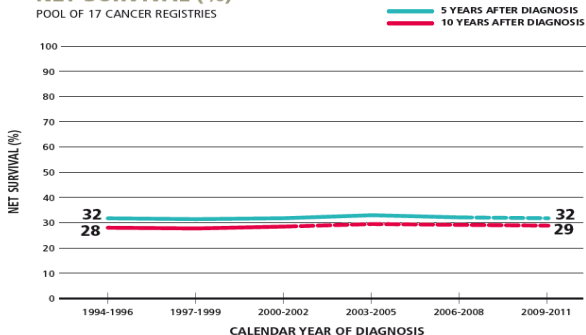
epidemiologia

STOMACH CANCER

MALES & FEMALES

H TIME TREND OF 5-, 10-YEAR AGE-STANDARDIZED NET SURVIVAL (%)

POOL OF 17 CANCER REGISTRIES

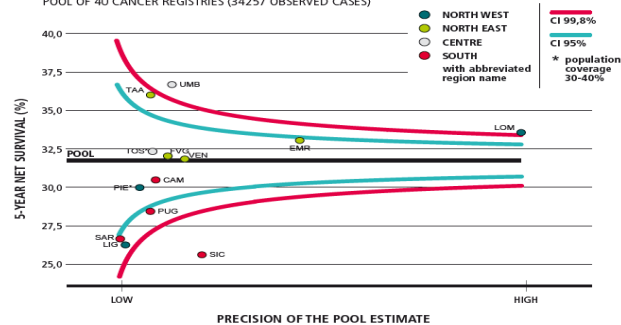


STOMACH CANCER

MALES & FEMALES

E 5-YEAR AGE-STANDARDIZED NET SURVIVAL (%) BY REGION, 2005-2009

POOL OF 40 CANCER REGISTRIES (34257 OBSERVED CASES)



LIFE EXPECTANCY AT A GIVEN AGE OF DIAGNOSIS

GENERAL POPULATION
 CANCER

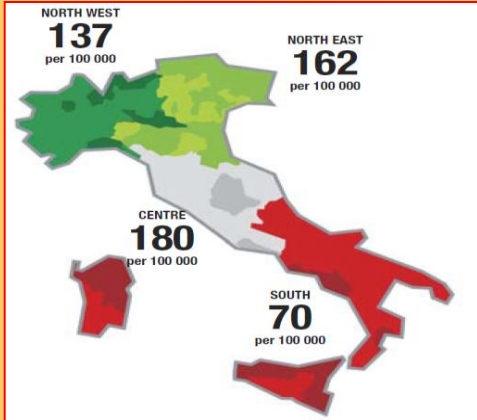


sopravvivenza

CURE FRACTION AND TIME TO CURE BY AGE AT DIAGNOSIS AND SEX FOR CANCER PATIENTS DIAGNOSED IN ITALY IN 1985-2009

AGE AT DIAGNOSIS	CURE FRACTION %	
	MALE	FEMALE
0 - 44	40%	42%
45 - 59	29%	32%
60 - 74	18%	22%
75+	13%	17%

AGE AT DIAGNOSIS	TIME TO CURE YEARS	
	MALE	FEMALE
0 - 44	8	8
45 - 59	9	9
60 - 74	10	10
75+	11	11



Pool of Italian Cancer Registries - 1 January 2010

STOMACO STOMACH (ICD-10 C16)

COMPLETE PREVALENCE BY YEARS SINCE DIAGNOSIS

YEARS →	≤ 2	(2 - 5]	(5 - 10]	(10 - 15]	(15 - 20]	> 20
No. →	14 396	12 347	15 306	10 975	7 062	14 331
% →	19%	17%	21%	15%	9%	19%
PROPORTION PER 100 000 →	25	21	26	19	12	25
	MALE 55%			FEMALE 45%		

COMPLETE PREVALENCE BY SEX, MACRO-AREA, AND AGE

(PROPORTION PER 100 000)

AGE CLASS →	0-44	45-59	60-74	75+	ALL AGES
MALE					
NORTH WEST	3	81	374	855	159

2 587 347 CANCER SURVIVORS

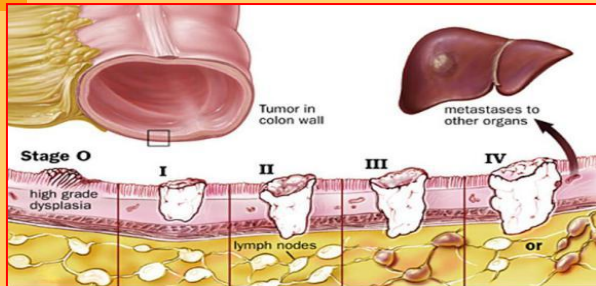
74 418
STOMACH
CANCER SURVIVORS

ALREADY CURED
at 1 JANUARY 2010

31 485 (42%)

colon

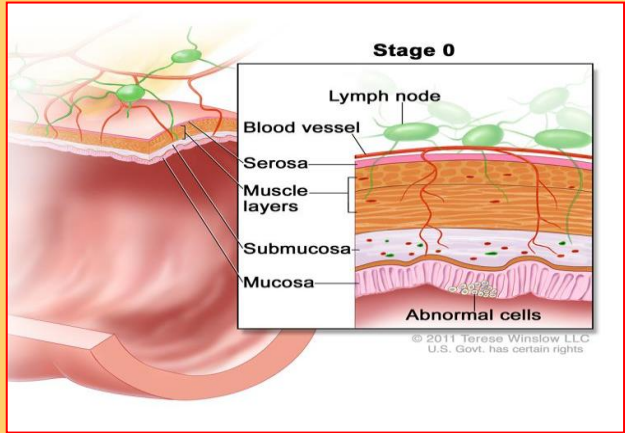
stadiazione dei carcinomi



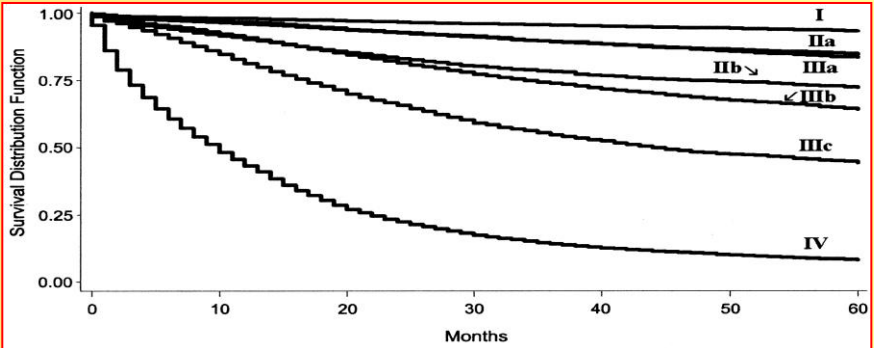
Correlazione tra classificazione TNM e DUKES (Modificata Astler-Coller, MAC)

	TNM			DUKES
Stadio 0	Tis	N0	M0	
Stadio I	T1	N0	M0 (r)	A
	T2	N0	M0	B1
Stadio II	T3	N0	M0 (r)	B2
	T4	N0	M0	B3
Stadio III	Ogni T	N1	M0 (r)	C1(T2) - C2(T3)- C3(T4)
	Ogni T	N2, N3	M0	C1(T2) - C2(T3)- C3(T4)
Stadio IV	Ogni T	Ogni T	M1	D

NOTA: la corretta stadiazione patologica dell'invasione linfonodale (N) richiede l'asportazione di almeno 12 linfonodi.



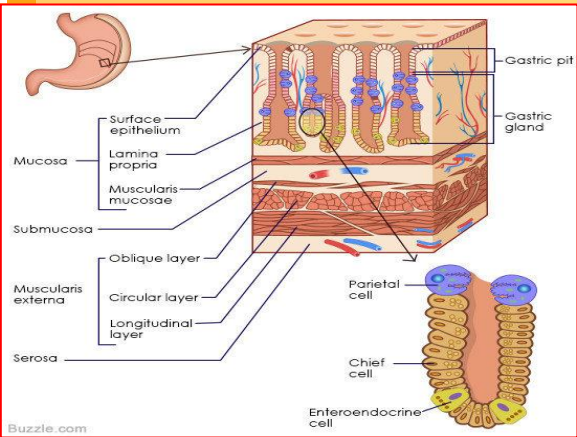
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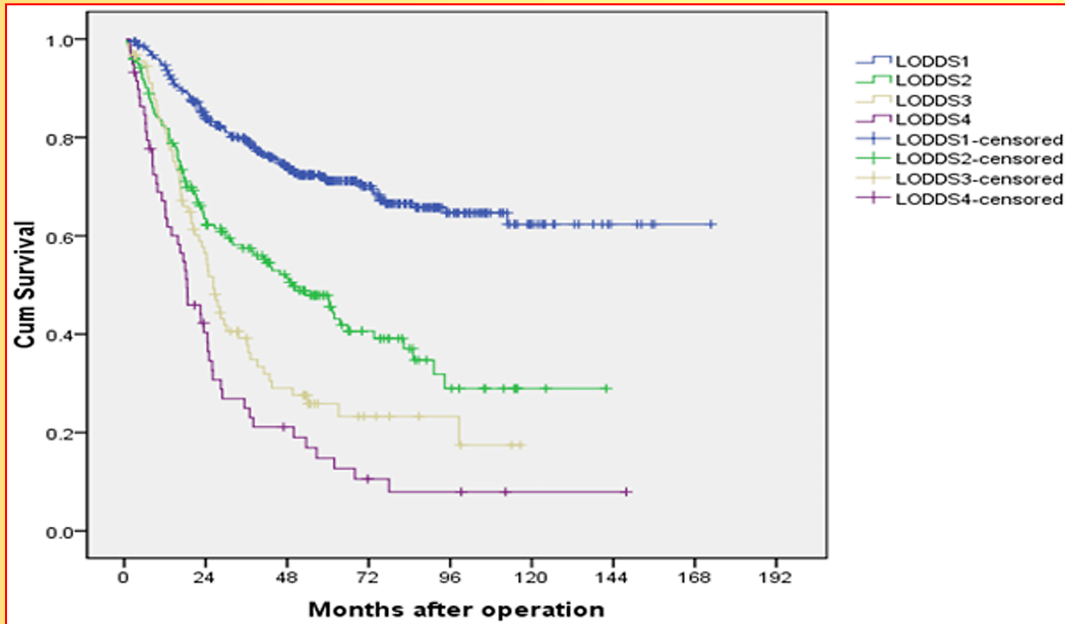
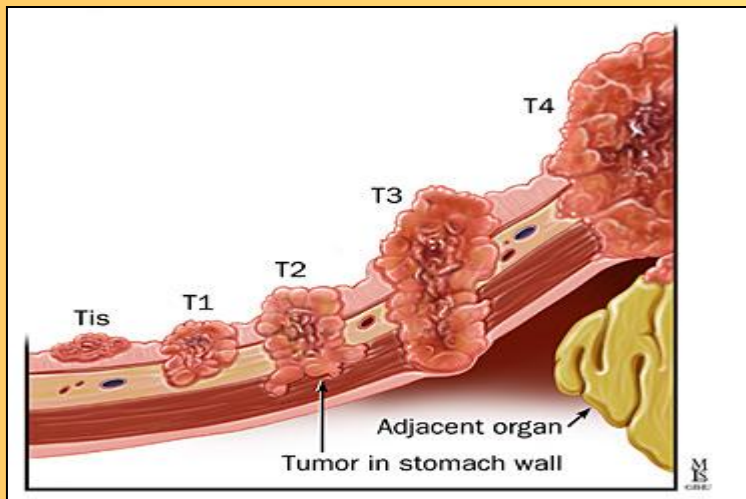
Stage	0 mo		30 mo		P	60 mo		P
	Survival, %	No.	Survival, %	No.		Survival, %	No.	
I	100	14500	96.1	8,581	—	93.2	4514	—
IIa	100	28535	91.0	2,105	<.001	84.7	8494	<.001
IIb	100	5826	80.2	3,060	<.001*	72.2	1611	<.001*
IIIa	100	1989	91.4	1,120	NS†	83.4	551	NS†
IIIb	100	15946	77.3	7,786	<.001‡	64.1	3579	<.001‡
IIIc	100	8600	59.1	3,039	<.001	44.3	1250	<.001
IV	100	20802	17.3	1,832	<.001	8.1	432	<.001

stadiazione dei carcinomi

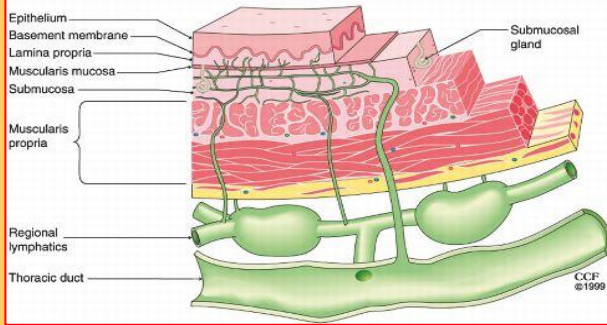
stomaco



Buzzle.com

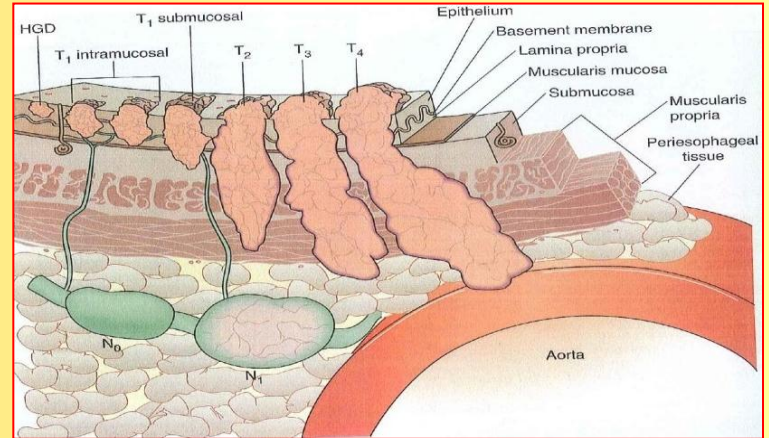


The Esophageal Wall

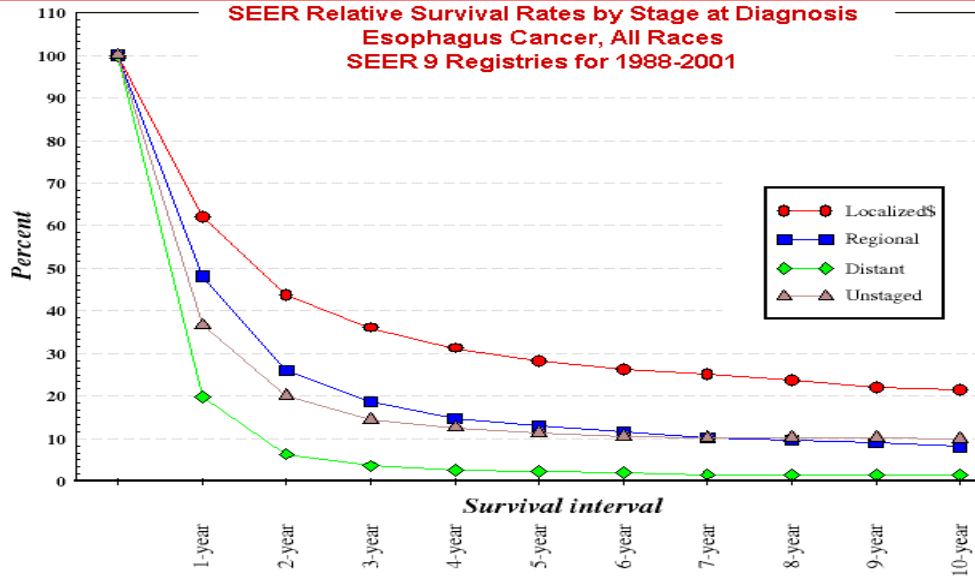


esofago

stadiazione dei carcinomi



**SEER Relative Survival Rates by Stage at Diagnosis
Esophagus Cancer, All Races
SEER 9 Registries for 1988-2001**





Continua...

