Gruppo di ricerca geriatrica

Seminari del Venerdì del
Gruppo di Ricerca Geriatrica
10 dicembre 2004

Caso clinico
"Neoplasia gastrica"

Ignazio Di Fazio

L.B., 88 anni

Anamnesi fisiologica e familiare:

Vedova da 19 anni

Vive con la famiglia di uno dei 3 figli coniugati, al piano terra

3 anni di scolarità, casalinga

Dieta libera, non fuma, non beve

Variazione di peso corporeo (negli ultimi 3 mesi): +3kg

Familiarità per malattie cardiovascolari (IM sorella),

negativa per ipertensione arteriosa, diabete mellito, demenza, malattie psichiatriche, neoplasie.

L.B., 88 anni

Già nota all'IDRG (2/'03) per:

- Poliartrosi (prevalente anche e ginocchia), lombalgia cronica
- Cardiopatia ischemica cronica e valvolare (lieve insufficienza mitro-aortica)
- Ipertensione arteriosa sistemica di grado 1 a rischio cardiovascolare molto elevato
- Insufficienza renale cronica lieve
- Obesità moderata
- Encefalopatia vascolare cronica, TIA ('95)

Sintesi anamnestica

- *Colecistectomia per litiasi ('65)*
- *Plastica uterina per prolasso ('70)*
- *Plastica per ernia ombelicale ('85)*
- *Iperuricemia ('96)*

Valutazione multidimensionale

MMSE 30/30, GDS 3/15,
Barthel index 95/100, IADL perse 5/8,
Tinetti 26/28, PPT 19/28

Motivo del ricovero di LB

Giunge alla nostra osservazione nel giugno ‘03 da Divisione Medica (dopo 15 giorni di ricovero) per:

“*Stato confusionale acuto, disidratazione, crisi convulsive generalizzate, aterosclerosi cerebrale, cardiosclerosi*”.

Esami strumentali recenti

(eseguiti durante il ricovero in medicina)

- TC encefalo senza mdc:

  Non alterazioni tomo-densitometriche recenti in sede sovra e sotto-tentoriale. Dilatazione ex-vacuo sistema ventricolare associato a marcata e diffusa ipodensità sostanza bianca periventricolare come da leucoaraiosi. Atrofia cortico-sottocorticale. Calcificazioni parietali arterie vertebrali. Non espansi extracerebrali.

- Rx torace:

  ampliamento ili compatibile con condizione di stasi piccolo circolo.

  Immagine cardio-mediastinica con aumento diametro trasverso.

Motivo del ricovero della Sig. LB

Il delirium è presente da circa 1 mese, ed è stato inizialmente attribuito dal MdF all'amlodipina 5mg, iniziata per scarso controllo pressorio, e subito sospesa.

Nonostante la sospensione, lo stato confusionale si è ripresentato in diverse occasioni, sempre a risoluzione spontanea, mai trattato.

La comparsa di aggressività verbale ha indotto i familiari a richiedere ricovero ospedaliero.

Durante il ricovero lo stato funzionale è notevolmente peggiorato e, constatata l'impossibilità di dimettere la paziente al domicilio in condizioni di autonomia, è stato richiesto il trasferimento in IDRG.

All'ingresso il delirium non è presente.

Anamnesi farmacologica

- Paracetamolo 500 mg 1 cp ab (PO)
- Losartan 50 mg 1 cp (h. 8, PO)
- Clonidina TTS2 1 cerotto/sett (h. 8, TD)
- Furosemide 25 mg 1 cp/gg alt.(h. 8, PO)
- Isosorbide-5-mononitrato 80 mg (R) 1 cp (h. 20, PO)
- Indobufene 200 mg 1 cp (h. 13, PO)
- Pantoprazolo 20 mg 1 cp (h. 20, PO)

Valutazione clinica all'ingresso in IDRG

Parametri vitali & stato nutrizionale

PA 155/60 mmHg (clino), 145/70 mmHg (orto) FC 80 b/m, 16 AR/min

BMI 31.1 Kg/m²

Esame obiettivo

Dentizione insufficiente**; cute e mucose** lievemente disidratate; **capo e collo:** collo non dolente, mobile, non dolorabile. Tiroide nella norma.

Cuore: toni ritmici (80 bpm), soffio sistolico 2/6 all'apice ed alla base. **Torace**: asimmetrico per scoliosi, basi noromoespansibili, MV fisiologico su tutto l'ambito. **Addome**: globoso per adipe, dolente alla palpazione profonda in ipocondrio dx, fegato 3 cm dall'arco in espirio, peristalsi presente.

Esame neurologico: vigile e collaborante, orientata nello spazio e nel tempo. Assenti tremori. Dubbia sfumata troclea a dx. Tono muscolare nella norma. Mingazzini negativo. ROT evocabili e simmetrici ai quattro arti. Romberg negativo. **Mammella**: n.d.r. **Apparato urogenitale**: Giordano negativo bilateralmente.

Apparato locomotore: dolorabilità articolare arto inferiore dx.

Sintomi riferiti:

Dispepsia di recente insorgenza

Valutazione multidimensionale all'ingresso

Premorboso (1 mese):

- BARTHEL INDEX 78/100
- ADL (perse) 1/6
- IADL (perse) 6/8
- Stato cognitivo premorboso riferito integro

All'ingresso:

- BARTHEL INDEX 57/100
- ADL (perse) 3/6 (mantiene vestirsi, continenza e alimentazione)
- IADL (perse) 6/8 (mantiene telefono e denaro)
- MMSE 29/30
- GDS 6/15
- Tinetti 14/28
- PPT 13/28

Orientamento diagnostico all'ingresso

- *Recente episodio di delirium e convulsioni generalizzate secondarie a sindrome da disidratazione (6/'03)*
- *Encefalopatia vascolare cronica, TIA ('95)*
- *Cardiopatia ischemica cronica e valvolare (insufficienza mitro-aortica lieve)*
- *Ipertensione arteriosa sistemica grado 2 a rischio cardiovascolare molto elevato*
- *Insufficienza renale cronica lieve*
- *Dispepsia in corso di valutazione*
- *Obesità moderata*
- *Poliartrosi severa (prevalente anche e ginocchia). Lombalgia cronica*
- *Disturbo dell'adattamento con tono dell'umore depresso*

Obiettivi

Clinici:

- Valutazione dello stato cognitivo e causa recente delirium
- Valutazione del disturbo del tono dell'umore
- Monitoraggio e controllo pressorio
- Valutazione e trattamento dispepsia

Riabilitativi:

- Trattamento antalgico
- Miglioramento della deambulazione

Terapia instaurata all'ingresso:

- Losartan 50 mg — 1 cp (h 8 PO)
- Indobufene 200 mg — 1 cp (h 8 PO)
- Clonidina TTS2 — 1 cerotto/sett (h 8 TD)
- Isosorbide-5-mononitrato 80 mg (R) — 1 cp (h 20 PO)
- Omeprazolo 20 mg — 1 cp (h 8 PO)
- Paracetamolo 500 mg — 1 cp (h 8, 12, 20 PO)

- **Dieta ipocalorica (1600 KCAL/die)**

Diario clinico

1° giornata

Paziente tranquilla, orientata nel tempo e nello spazio. CAM negativa.

Notte poco riposata: riferisce "tremori" durante la notte non rilevati dal personale.

Poliartralgie: paracetamolo 500 mg x 3

ECG ingresso: ritmo sinusale (FC: 80 bpm). Conduzione atrio-ventricolare normale. Asse cardiaco equilibrato. T invertita in aVL. Segni di sovraccarico ventricolare sinistro.

PA 120/60 mmHg, FC 90 bpm

Segni di disidratazione alle mucose, inizia idratazione per os e monitoraggio idrico

Dispepsia associata a rigurgito acido e nausea.

Inizia FKT.

Esami ematochimici

Globuli bianchi	(4-10mila/mm^3)	8.1
Globuli rossi	(4.1-5.1milioni/mm^3)	**3.5**
Hb	(12-16 g/dl)	**10.2**
Hct	(37-47%)	**30**
MCV	(82-96 fl)	87
Piastrine	(150-450 mila/mm^3)	275
Proteine totali	(6-8 g/dl)	6.3
albumina	(55-68%; >3.5 g/dl)	**49.6/3.1**
alfa1	(1.5-5%)	4.3
alfa2	(6-12%)	**14.4**
beta	(7-14%)	13.9
gamma	(11-21%)	17.8
Colesterolo	(<200 mg/dl)	165
HDL	(40-85 mg/dl)	**33**
Trigliceridi	(40-200 mg/dl)	184
AST	(1-35 U/l)	18
ALT	(5-35 U/l)	34
gamma-GT	(5-35 U/l)	34
Fosfatasi alcalina	(75-240 U/l)	186
Colinesterasi	(5.3-12.9*10 ^{3}U/l)	3.3
Bilirubina totale	(0.1-1 mg/dl)	0.5
Es.urine		
peso specifico	(1.002-1.030)	1.010
pH	(<8)	7
germi	(assenti)	**Numerosi**
proteine	(< 20 mg/dl)	**28**
Hb	(< 10 ul)	**-**
leucociti	(assenti)	**7/8 pcm**
eritrociti	(assenti)	-

Formula leucocitaria:		
neutrofili	(40-75%)	62
eosinofili	(0-5%)	1
basofili	(0-2%)	1
linfociti	(20-50%)	29
monociti	(2-12%)	8
Reticolociti	(2-20n/1000)	19
VES	(1-12 mm/ora)	**33**
PCR	(<0.5 U/dl)	**3.1**
Glucosio	(65-110 mg/dl)	**129**
Urea	(18-50 mg/dl)	**55**
Creatinina	(0.5-1.1 mg/dl)	**1.5**
Sodio	(130-146 mmol/l)	137
Potassio	(3.7-5.4 mmol/l)	4.6
Cloro	(95-110 mmol/l)	104
Ferritina	(8-140 ng/ml)	144
Ferro	(60-170 ug/dl)	**36**
Transferrina	(200-360 ug/dl)	**175**
f -T4	(0.93-1.7ng/dl)	1.7
TSH	(0.27-4.2 uU/ml)	2
SOF		Assente
PT	(70-130%)	95
PT T	(26-36sec.)	36
Fibrinogeno	(180-350 mg/dl)	**397**
SOF		Assente

Diario clinico

3° giornata

Dispepsia poco sensibile all'omeprazolo (20 mg).

Si richiede EGDS.

Iperglicemia a digiuno (129 mg/dl): curva glicemica oraria (h 8-12-18-21)

Non ottimale controllo dei valori pressori, PA 170/80mmHg, Fc 88 bpm. Inizia amiloride + hct ½ cp, prosegue monitoraggio.

Diario clinico

5° giornata

EGDS: erosioni antrali e del bulbo, piloro pervio.
Si eseguono prelievi bioptici.
Conclusione: gastro-duodenite erosiva.

Prosegue con omeprazolo 20 mg/die.

Valori glicemici non patologici, sospende monitoraggio.

Diario clinico

6° giornata

Nessun segno di stato confusionale acuto.

Mucose ben idratate, sospende monitoraggio idratazione per os.

Programma riabilitativo: deambula con un bastone con maggiore sicurezza.

Valutazione neuropsicologica: non si rileva decadimento cognitivo. Tuttavia è presente deficit isolato delle abilità di organizzazione e pianificazione visuospaziale.

Diario clinico

8° giornata

h. 9.30 PA 160/80 mmHg, fc 74 bpm. Insufficiente controllo pressorio. Aumenta amiloride + hct: 1 cp.

h. 19.30: PA 230/80 mmHg, Fc 106 bpm, cefalea, ansiosa, in assenza di angor o equivalenti, esegue ECG che è sovrapponibile all'ingresso.

OD] urgenza ipertensiva.

Si somministra furosemide 20 mg ev. + bromazepam 10gtt

h. 20: PA 180/70 mmHg, Fc 96 bpm

h. 20.30 PA 140/70 mmHg, Fc 80 bpm, sat O_2: 96% in aa.

Diario clinico

10° giornata

h. 9.00 PA 160/80 mmHg, Fc 75 bpm. Inizia amlodipina 2.5mg.

Dispepsia in miglioramento.

Riduzione dei sintomi depressivi.

Ridotto il dorore articolare, con miglioramento nella deambulazione. Non necessita di ausilio.

Diario clinico

12° giornata

h. 10.00 Bene pressione e frequenza, da 2 giorni valori stabili.

Oggi PA 140/80 mmHg, Fc 75 bpm.

Dispepsia in ulteriore regressione.

Programma riabilitativo: prosegue miglioramento nella deambulazione.

Diario clinico

16° giornata

Buon compenso emodinamico, netta riduzione del dolore articolare.
Assente dispepsia.

Terapia in atto:

losartan 50mg	1cp h 8 PO
amiloride+hct	1 cp h 8 PO
clonidina TTS2	1 cerotto/settimana
amlodipina 2.5 mg	1cp h 20 PO
Indobufene 200mg	1 cp h 13 PO
nitroglicerina 15mg	1 cerotto dalle 20 alle 8, TD
paracetamolo 500mg	1 cp h 8 - 12 – 20 PO
omeprazolo 20 mg	1 cp h 8 PO

ABPM: tutti i parametri esaminati risultano nella norma. Normale riduzione notturna della pressione media.

Migliorata la deambulazione, si programma dimissione per fine settimana.

Valutazione multidimensionale alla dimissione

MMSE	30/30	
GDS	5/15	
Barthel Index	80/100	(+23= premorboso)
BADL (perse)	1/6	(-2)
Tinetti	22/28	(+8)
PPT	20/28	(+7)
GIC	III	

Diagnosi di dimissione (23/7/'03)

- *Recente episodio di delirium e convulsioni generalizzate secondarie a sindrome da disidratazione (6/'03)*
- *Encefalopatia vascolare cronica, TIA ('95)*
- *Cardiopatia ischemica cronica e valvolare (insufficienza mitro-aortica lieve)*
- *Ipertensione arteriosa sistemica grado 2 a rischio cardiovascolare molto elevato; urgenza ipertensiva intercorrente*
- *Insufficienza renale cronica lieve*
- *Gastroduodenite erosiva (in attesa di referto biopsia gastrica)*
- *Anemia da disordine cronico*
- *Poliartrosi severa (prevalente anche e ginocchia). Lombalgia cronica*
- *Obesità moderata*
- *Disturbo dell'adattamento con tono dell'umore depresso*

Terapia alla dimissione

• PARACETAMOLO 500mg	*1 cp al bisogno, PO*
• LOSARTAN 50mg	*1 cp h 8, PO*
• CLONIDINA TTS2	*1 cerotto/sett., TD*
• AMILORIDE + HCT	*1 cp h 8, PO*
• AMLODIPINA 5 mg	½ cp h 20, PO
• NITROGLICERINA 15mg	*1 cerotto 20-8, TD*
• INDOBUFENE 200 mg	*1 cp h 13, PO*
• OMEPRAZOLO 20 mg	*1 cp h 8, PO*

Esame bioptico (25/7/'03)

Reperto macroscopico: frustoli di mucosa gastrica in parte ulcerati e sede di proliferazione adenocarcinomatosa ed a cellule ad anello con castone, focalmente interessante il terzo superiore della mucosa.

Diagnosi istologica: adenocarcinoma di tipo intestinale ed a cellule con castone. **Early Gastric Cancer, tipo II C.**

Evoluzione

Contattata la divisione di chirurgia dell'ospedale XX per la presa in carico della paziente.

TC toraco-addominale: negativa per lesioni a carico degli organi e delle linfoghiandole.

CEA e CA 19.9 nei limiti.

Viene sottoposta a **gastroresezione subtotale**.

Ultimo ricovero (aprile '04)

- ***Poliartrosi severa (prevalente anche e ginocchia). Lombalgia cronica***
- ***Ipertensione arteriosa sistemica grado 2 a rischio cardiovascolare molto elevato. Urgenza ipertensiva intercorrente***
- ***Cardiopatia ischemica cronica. Insufficienza mitro-aortica lieve***
- ***Esiti gastrectomia subtotale per adenocarcinoma (early gastric cancer tipo 2C; 9/'03)***
- ***Insufficienza renale cronica lieve***
- ***Anemia da disordine cronico***
- ***Obesità moderata***
- ***Disturbo dell'adattamento con tono dell'umore depresso***

Valutazione multidimensionale:
MMSE 29/30, GDS 6/15,
Barthel Index 92/100, IADL perse 5/8, Tinetti 21/28, PPT 21/28

Follow - up (aprile 2004)

Eco-addome: fegato nei limiti morfovolumetrici ed ecostrutturali. Non lesioni focali ripetitive. Esiti di colecistectomia. Pancreas e retroperitoneo non esplorabili. Rene destro di volume ridotto. Marcato assottigliamento dello spessore parenchimale compatibile con nefropatia. Piccole cisti parapieliche.

Rx torace: normale trasparenza dei campi polmonari con ili di normale morfologia. Diaframma regolare con seni costo-frenici liberi. Immagine cardiaca lievemente ingrandita sul versante di sinistra con aortosclerosi.

CEA: 2.5 (v.n. <3.4 ng/ml)

CA 19.9: 15.4 (v.n. <34 UI/ml)

Esami ematochimici (aprile 2004)

Body Mass Index	(18.5-24.9)	**32.3**
Esami di laboratorio:		
Globuli bianchi	(4-10mila/mm^3)	5.8
Globuli rossi	(4.1-5.1milioni/mm^3)	**3.3**
Hb	(12-16 g/dl)	**10.3**
Hct	(37-47%)	**31**
MCV	(82-96 fl)	94
Piastrine	(150-450 mila/mm^3)	275
Proteine totali	(6-8 g/dl)	6.5
albumina	(55-68%; >3.5 g/dl)	57 / 3.7
alfa1	(1.5-5%)	3
alfa2	(6-12%)	10
beta	(7-14%)	12
gamma	(11-21%)	18
Colesterolo	(<200 mg/dl)	189
HDL	(40-85 mg/dl)	**38**
Trigliceridi	(40-200 mg/dl)	**233**
AST	(1-35 U/l)	18
ALT	(5-35 U/l)	20
gamma-GT	(5-35 U/l)	32
Fosfatasi alcalina	(75-240 U/l)	221
Colinesterasi	(5.3-12.9*10 ^{3}U/l)	4.9
Bilirubina totale	(0.1-1 mg/dl)	0.2
FT4	(0.93-1.7 ng/ml)	1.4
TSH	(0.27-4.2 uU/ml)	1.7

Formula leucocitaria:		
neutrofili	(40-75%)	42
eosinofili	(0-5%)	2
basofili	(0-2%)	1
linfociti	(20-50%)	40
monociti	(2-12%)	**15**
Reticolociti	(2-20‰)	12
VES	(1-12 mm/ora)	**23**
PCR	(<0.5 mg/dl)	**1.6**
Glucosio	(65-110 mg/dl)	101
Urea	(18-50 mg/dl)	**54**
Creatinina	(0.5-1.1 mg/dl)	**1.7**
Sodio	(130-146 mmol/l)	137
Potassio	(3.7-5.4 mmol/l)	4.7
Cloro	(95-110 mmol/l)	106
Ferro	(50-150 ug/dl)	65
Transferrina	(200-360 mg/dl)	**177**
Ferritina	(8-140 ng/ml)	**169**
PT	(70-130%)	91
PTT	(26-36sec.)	36
CEA	(< 3.4 ng/ml)	2.5
CA 19/9	(< 34 U/ml)	15.4
SOF		Assente

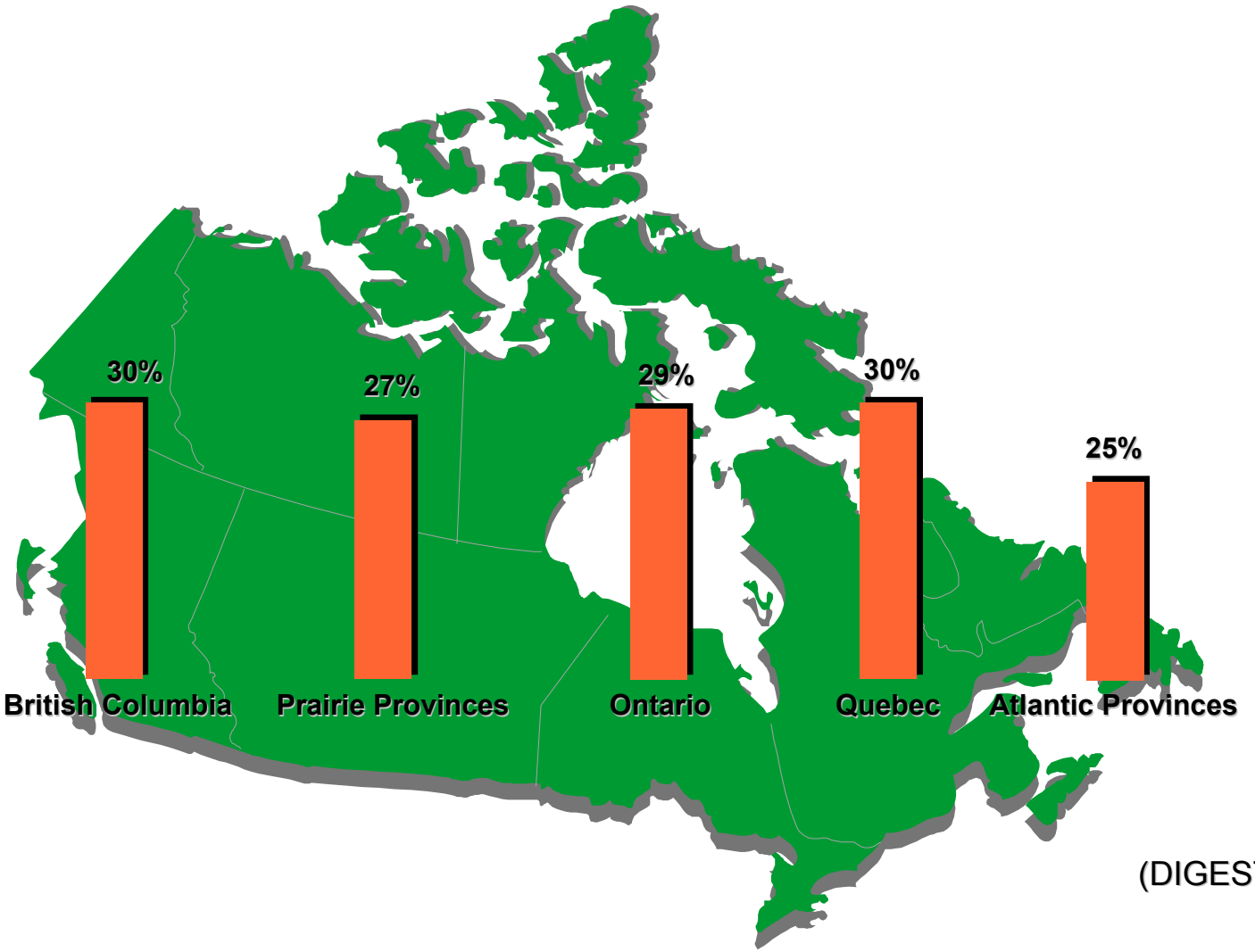
Dyspepsia

Dyspepsia - Definition

- Painful, difficult, or disturbed digestion, which may be accompanied by symptoms such as nausea and vomiting, heartburn, bloating and stomach discomfort.
- A group of symptoms which alert clinicians to consider disease of the upper gastrointestinal tract

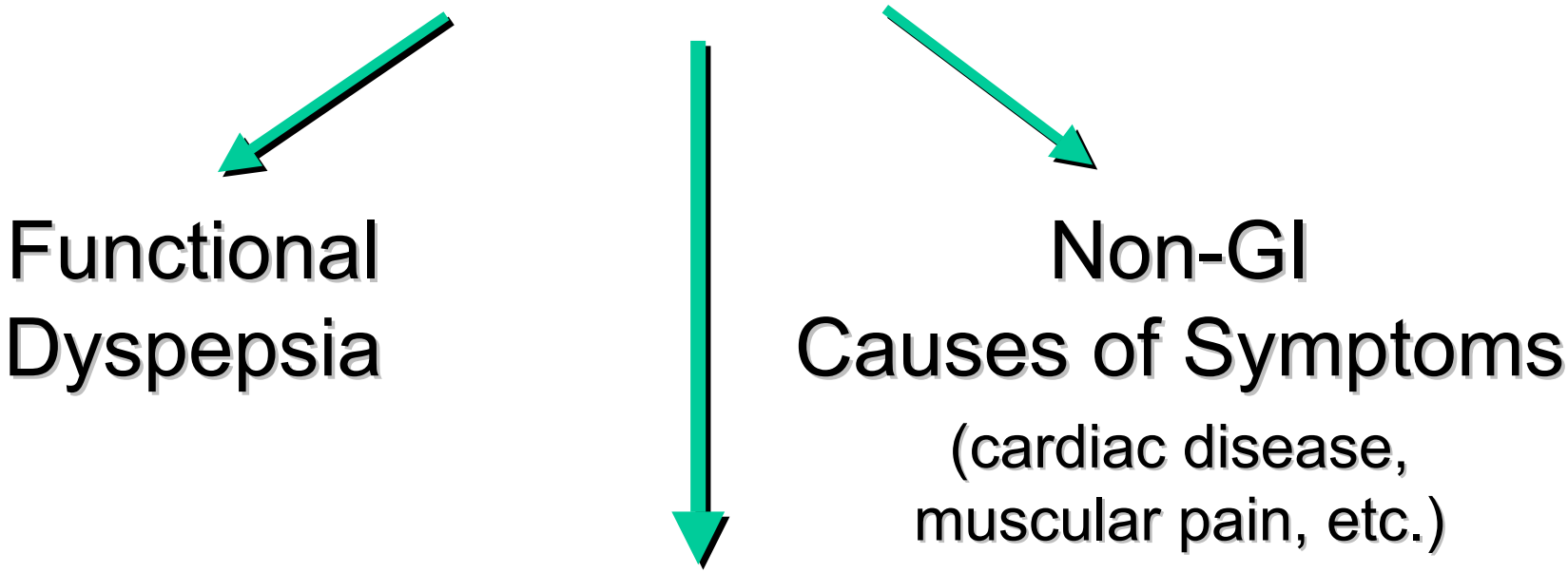
(British Society of Gastroenterology, 1996)

Overall Prevalence of Dyspepsia in Canada



(DIGEST, 1996)

Dyspepsia

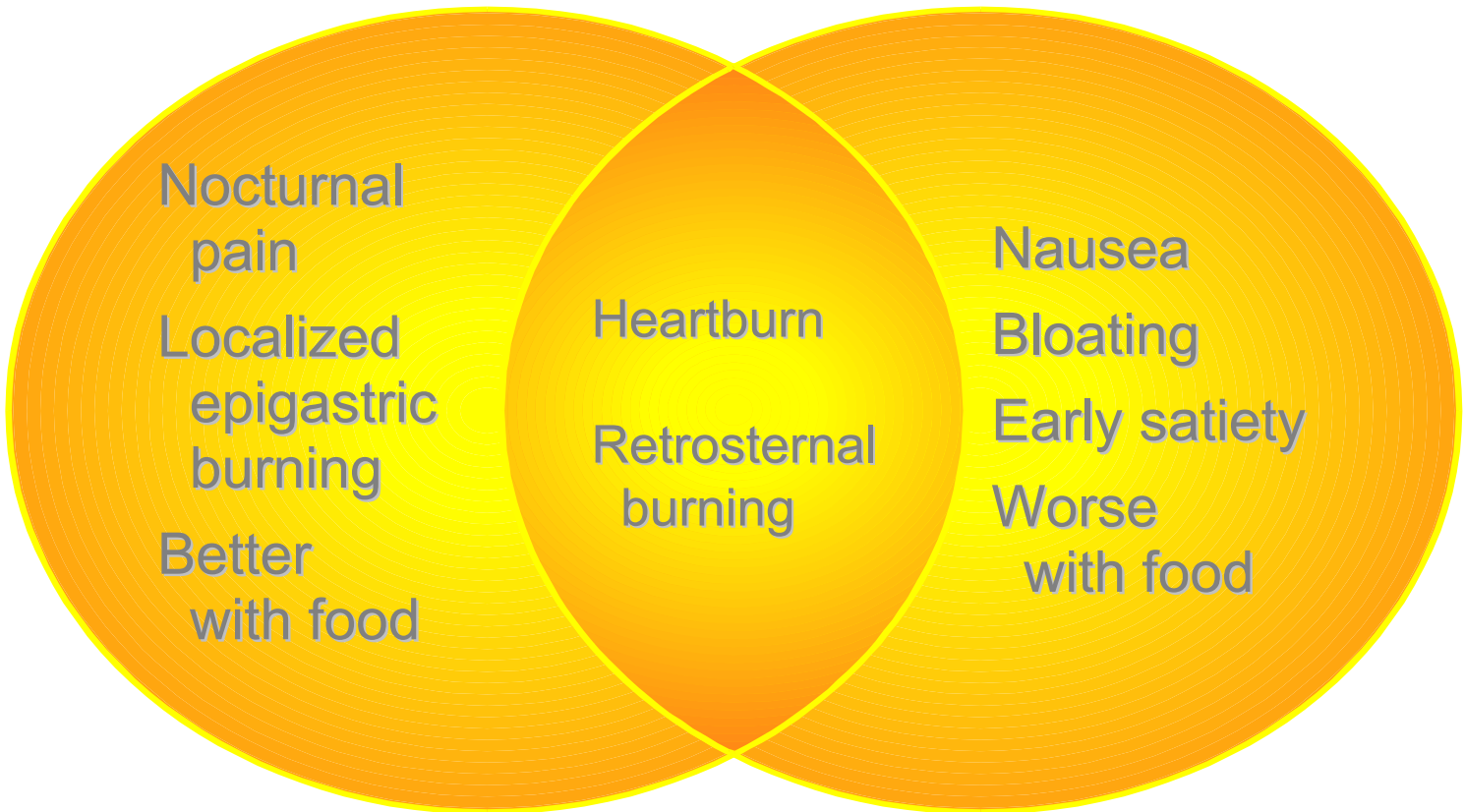

Functional Dyspepsia
Non-GI Causes of Symptoms
(cardiac disease, muscular pain, etc.)
Structural Dyspepsia
(GERD, PUD, pancreatic disease, gallstones, etc.)

Functional Dyspepsia - Definition

- Chronic or recurrent upper GI symptoms not explained by biochemical or structural abnormalities (does not imply that there is no physiological basis)
- Appropriate evaluation using standard diagnostic tests reveals no abnormalities
- Also known as non-ulcer dyspepsia, essential dyspepsia, idiopathic dyspepsia

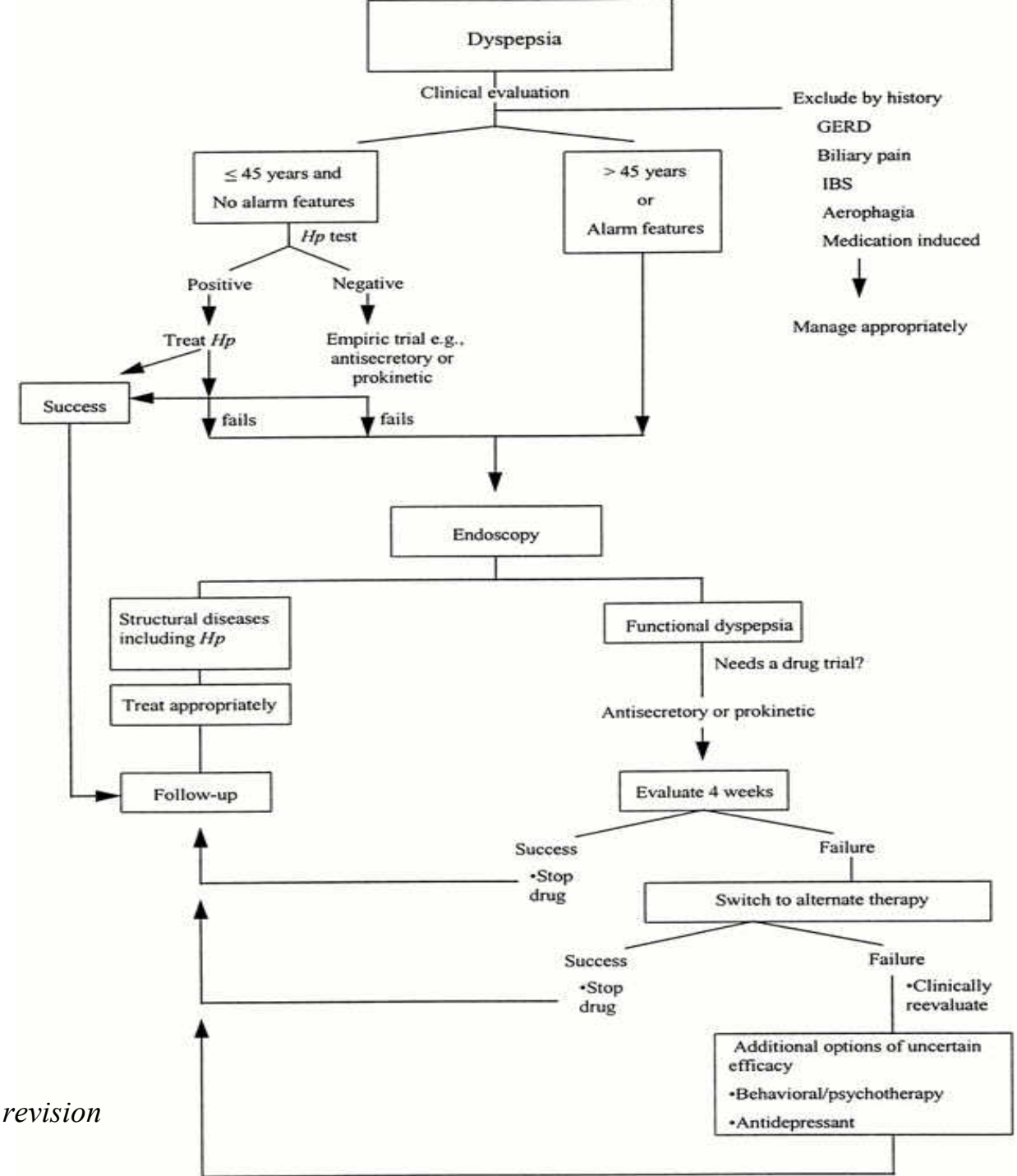
Symptoms of Functional Dyspepsia

Ulcer-like Dominant ⟷ Dysmotility-like Dominant



American Gastroenterological Association medical position statement: Evaluation of dyspepsia

Referral for early upper endoscopy is always indicated in older patients presenting with **new-onset dyspepsia**.



Gastroenterology March 1998, under revision

Age and alarm symptoms do not predict endoscopic findings among patients with dyspepsia: a multicentre database study

M B Wallacea et al. Gut 2001

Major endoscopic findings among 3815 patients undergoing upper endoscopy	
Ulcer	692/3815 (18%)
Cancer	81/3815 (2%)
Stricture	14/3815 (0.3%)

The American Gastroenterological Association recommendation and common clinical practice is to perform endoscopy on patients with new-onset dyspepsia or "alarm" symptoms or over the age of 45. Younger patients without alarm symptoms can be treated empirically, with endoscopy reserved for when symptoms fail to resolve.

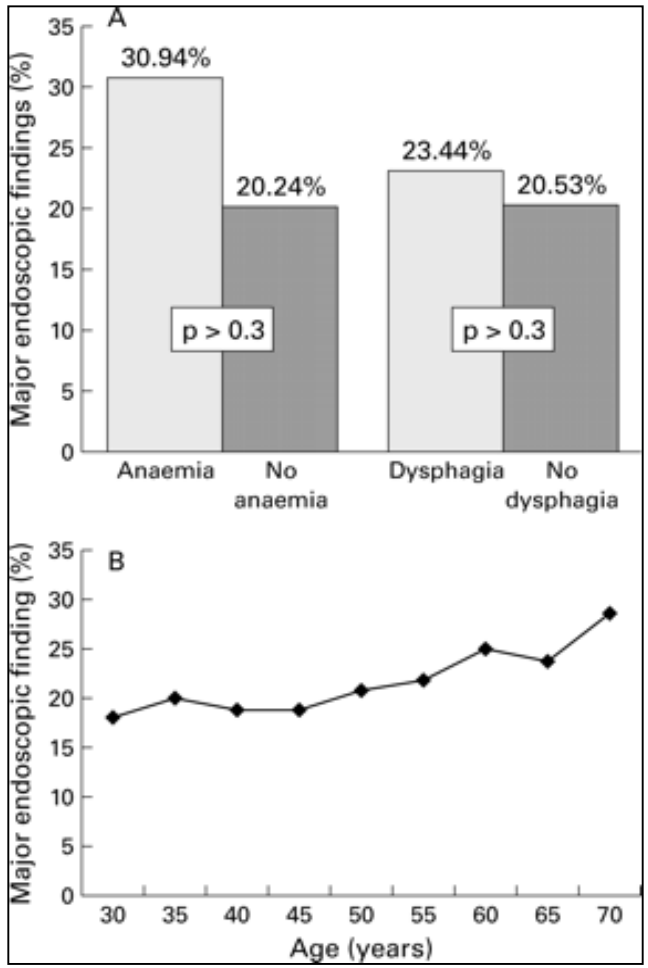


Table 2 Multivariate risk factors for predicting major upper gastrointestinal pathology

Variable	*Parameter estimate*	*Odds ratio*	*OR CI*
Intercept	−1.9493	—	—
Age (⩾45)	0.5401	1.716	1.331-2.221
Sex (male)	0.3360	1.399	1.089-1.801
Anaemia	0.8218	2.274	1.249-4.042
Bleed	1.0642	2.899	1.889-4.419

Model: probability of a major endoscopic finding = −1.9493 + (0.5401×age) + (0.3360×sex) + (0.8218×anaemia) + (1.0642×bleed), where age, sex (f/m), anaemia (n/y), and bleed (n/y) are coded 0 or 1.

OR, odds ratio; CI, confidence interval.

We have found that age and the presence of "high risk" symptoms are poor predictors of the presence of major endoscopic findings in the upper gastrointestinal tract.

The use of these variables to identify patients who do not require upper endoscopy would likely result in high false negative rates (that is, significant under diagnosis or delayed diagnosis) of important conditions.

These findings demonstrate the **need for better clinical predictors** of upper gastrointestinal pathology.

In the absence of better clinical predictors, the study also demonstrates the need for less invasive and thus more widely applicable endoscopy.

Wallacea MB et al. Gut 2001

Journal of Gerontology: MEDICAL SCIENCES
2000, Vol. 55A, No. 3, M163–M167

Copyright 2000 by The Gerontological Society of America

Noninvasive Diagnosis of *Helicobacter pylori* Infection in Older Subjects: Comparison of the ^{13}C-Urea Breath Test With Serology

Alberto Pilotto,[1] Marilisa Franceschi,[1] Gioacchino Leandro,[4] Mario Rassu,[2] Rocco Maurizio Zagari,[5] Loredana Bozzola,[3] Francesca Furlan,[2] Franco Bazzoli,[5] Francesco Di Mario,[6] and Gianni Valerio[1]

In older subjects, the ^{13}C-UBT had a significantly higher diagnostic accuracy than serology without influence of cognitive function, disability, comorbidity and cotreatments.

This method may be considered an excellent, clinically useful, noninvasive test for the diagnosis of Hp infection in older subjects.

Table 3. Sensitivity, Specificity, and Diagnostic Accuracy of the ^{13}C-UBT Versus the Assaying of IgG anti-Hp Antibodies in Serum in Older Subjects

Data	^{13}C-UBT	IgG Anti-Hp Antibodies*
Sensitivity	49/49 (100%)	35/47 (74.4%)
False negatives	0	12/47 (25.5%)
Specificity	45/47 (95.74%)	26/44 (59.09%)
False positives	2/47 (4.25%)	18/44 (40.9%)
Diagnostic accuracy	94/96 (97.9%)	61/91* (67.0%)
p value	.001	

Notes: ^{13}C-UBT = ^{13}C-urea breath test, IgG = immunoglobulin G, Hp = *Helicobacter pylori*.

The NEW ENGLAND JOURNAL of MEDICINE

TABLE 2. CURRENT GUIDELINES FOR THE TREATMENT OF *H. PYLORI* INFECTION, ACCORDING TO THE MAASTRICHT 2–2000 CONSENSUS REPORT.*

Indications for which treatment is strongly recommended
Duodenal or gastric ulcer (active or not, including complicated peptic ulcer disease)
MALT lymphoma
Atrophic gastritis
Recent resection of gastric cancer
First-degree relative of patient with gastric cancer
Desire of the patient (after full consultation with the physician)
Indications for which treatment is advised
Functional dyspepsia
Gastroesophageal reflux disease (in patients requiring long-term profound acid suppression)
Use of NSAIDs (*H. pylori* infection and the use of NSAIDs or aspirin are independent risk factors for peptic ulcer disease)†

*Data are from Bazzoli.[79] MALT denotes mucosa-associated lymphoid tissue, and NSAIDs nonsteroidal antiinflammatory drugs.

†In patients taking NSAIDs, *H. pylori* eradication before NSAID use reduces the incidence of ulcer but is insufficient by itself to prevent recurrent ulcer bleeding in NSAID users at high risk. Eradication of *H. pylori* does not enhance healing of gastric or duodenal ulcers in patients receiving antisecretory therapy who continue to take NSAIDs.

S. Suerbaum, NEJM 2002

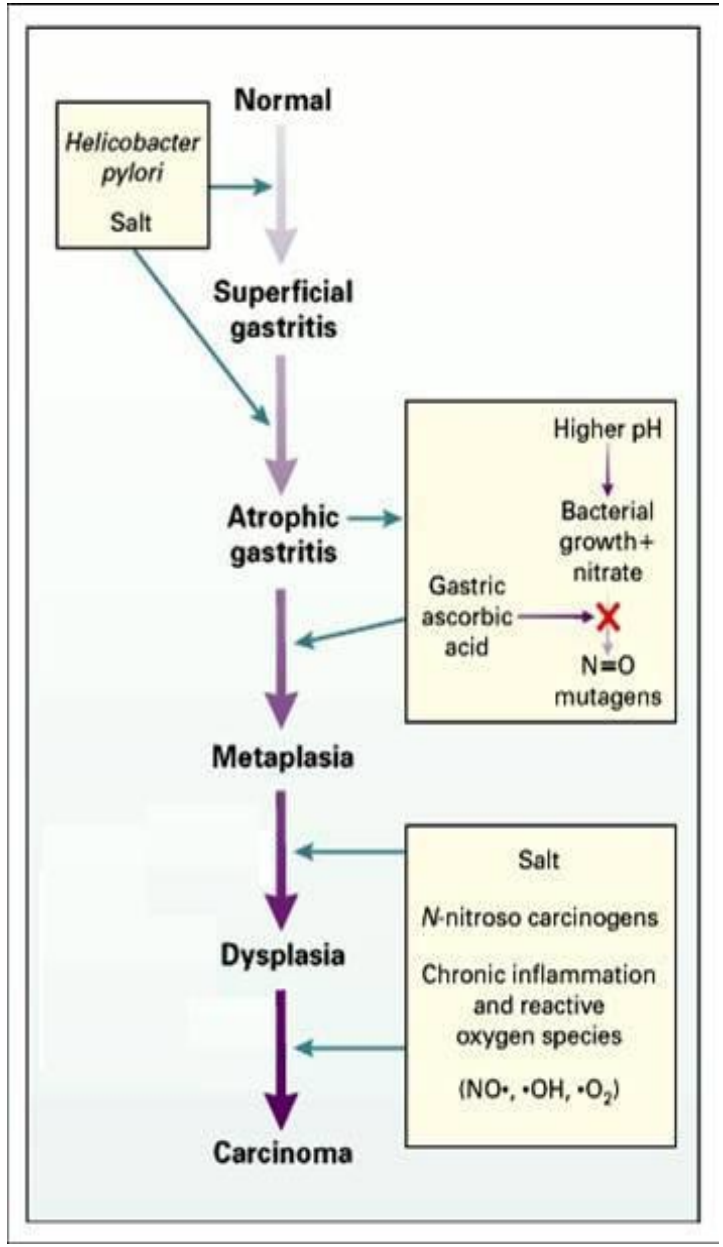
Gastric cancer

Incidence/Prevalence

- 3rd most common GI malignancy (after colorectal and pancreatic)
- 14th cause of cancer related death in U.S.
- 85-95% are caused by adenocarcinoma
- 15% are caused by Non-Hodgkin's lymphoma & leiomysosarcomas

Proposed Cascade of Pathologic Events in Gastric Adenocarcinoma

- The accepted pathway involves transitions from gastritis to gastric atrophy to metaplasia to dysplasia and, finally, to cancer. Several dietary and environmental factors may influence this pathway.
- Dietary nitrates: Bacteria in the stomach break down nitrites to compounds (eg, *N*-nitroso compounds) that are carcinogenic in animals.
- Hypochlorhydria: This condition occurs in gastric atrophy and promotes bacterial colonization of the stomach. It leads to increased nitrite formation, which may have a mutagenic effect on the atrophic gastric mucosa.
- *Helicobacter pylori*: Antral gastritis caused by *H pylori* has been linked to the development of gastric cancer. Patients with *H pylori gastritis* are 3-6 times more likely to develop gastric cancer than individuals without the infection.
- Certain foods: Salted fish and meat, smoked foods, and salt have all been implicated.
- Cigarette smoking: Those who smoke more than 30 cigarettes per day have a 5-fold increased risk of gastric carcinoma.



Fox, J. G. NEJM, 2001

Will eradication of Helicobacter pylori infection influence the risk of gastric cancer?

Hunt RH *Am J Med, 2004*

Studies suggest that cure of H pylori infection may be associated with retardation of glandular atrophy and intestinal metaplasia but not reversal of dysplasia.

Theoretically, it is attractive to believe that eradication of H pylori infection might prevent gastric cancer; however, studies supporting this hypothesis are not yet available.

Public policy strategies for the identification of patients at risk for H pylori-related gastric malignancy are likely to be complex, but testing and treating for the infection earlier rather than later in life is anticipated to be the more beneficial approach.

Location & Onset

- 37% in the proximal third of the stomach
- 30% in the distal stomach
- 20% in the midsection
- Remaining 13% in the entire stomach
- Insidious (slowly developing)
- Usually discovered in advanced stages
- Men>Women
- Occurs between the ages of 50-70

Physical Assessment

- Early gastric cancer
  - Indigestion
  - Abdominal discomfort initially relieved with antacids
  - Feeling of fullness
  - Epigastric, back, or retrosternal pain
  - NOTE: most people will show no clinical manifestations
- Advanced stage:
  - Nausea/vomiting
  - Obstructive symptoms
  - Iron deficiency/anemia
  - Palpable epigastric mass
  - Enlarged lymph nodes
  - Weakness/fatigue
  - Progressive weight loss

Gastric Cancer: Morphology

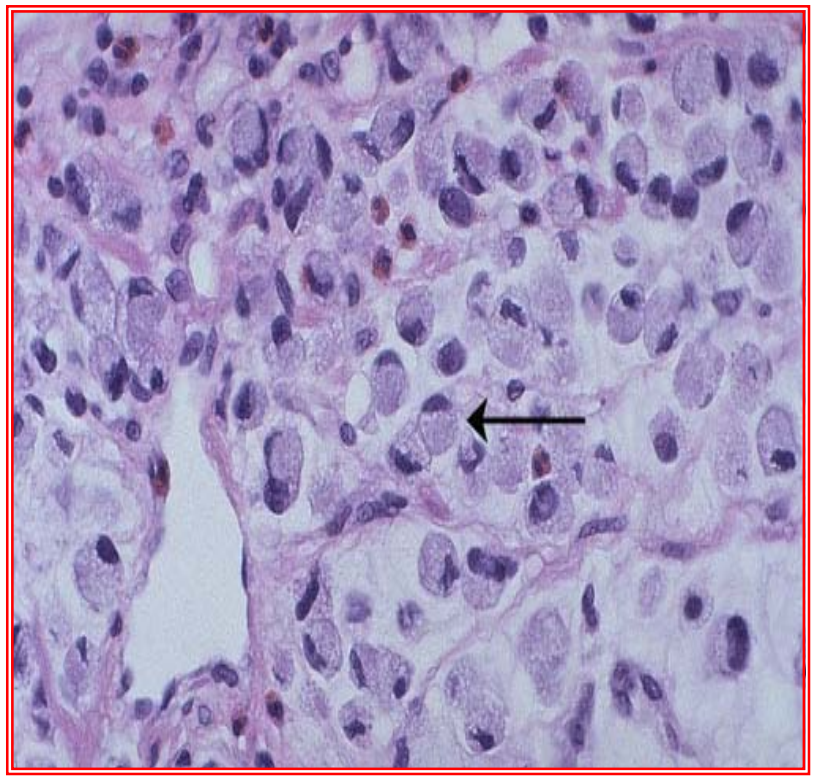
- Early gastric cancer
  - primary lesion of mucosa/submucosa
  - 90% survival after resection
- Ulcerating Carcinoma
  - deep, penetrates through all layers and adjacent organs
  - shallow edges
- Polypoid carcinoma
  - late metastasis
- Superficial Spreading Carcinoma
  - confined to mucosa/submucosa
  - good prognosis after gastrectomy
- Linitis Plastica
  - stomach loses pliability
  - poor prognosis
- Advanced Carcinoma
  - originate in early groups
  - inflammatory reaction at borders

Early gastric cancer

- These lesions are confined to the mucosa or submucosa and are classified into 3 types:
  - Type I lesions are elevated and protrude more than 5 mm into the lumen.
  - **Type II** tumors are superficial lesions that are elevated (IIa), flat (IIb), or **depressed (IIc).**
  - Type III early gastric cancers are shallow, irregular ulcers surrounded by nodular, clubbed mucosal folds.
- In Western counties, early gastric cancers account for only 5-20% of all gastric cancers. In Japan, they represent 25-46% owing to the population-screening program that was implemented to combat the high incidence of the disease.

Gastric Cancer: Histology

- Usually adenocarcinomas
  - intestinal: resembles colorectal cancer
  - diffuse: signet ring cells
- Varying differentiation
- Reactive fibrosis often present, affecting entire stomach
- Most common form is poorly differentiated:
  - mucin-filled cells with nuclei displaced to margin = signet ring cell



American Joint Committee on Cancer Staging for Gastric Cancer (2002)

American Joint Committee on Cancer Staging for Gastric Cancer†

Tumor (T) stage

TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1s		Carcinoma in situ: intra-epithelial tumor without invasion of the lamina propia
T1		Tumor invades lamina propria or submucosa
T2		Tumor invades muscularis propria or subserosa
	T2a	Tumor invades muscularis propria
	T2b	Tumor invades subserosa
T3		Tumor penetrates serosa (visceral peritoneum) without invasion of adjacent structures*
T4		Tumor invades adjacent structures*

* The adjacent structures of the stomace include the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum. Intramural extension to the duodenum or esophagus is classified by the depth of the greatest invasion in amy of these sites, including the stomach.

Nodal (N) stage

NX	Regional lymph node(s) cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 6 regional lymph nodes
N2	Metastasis in 7 to 15 regional lymph nodes
N3	Metastasis in more than 15 regional lymph nodes

Metastasis (M) stage

MX	Presence of distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage grouping

Stage 0	Tis N0 M0
Stage IA	T1 N0 M0
Stage IB	T1 N1 M0, T2a/b N0 M0
Stage II	T1 N2 M0
	T2a/b N1 M0
	T3 N0 M0
Stage IIIA	T2a/b N2 M0
	T3 N1 M0
	T4 N0 M0
Stage IIIB	T3 N2 M0
Stage IV	T1-3 N3 M0
	T4 N1-3 M0
	Any T Any N M1

†Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Sixth Edition (2002) published by Springer-Verlag New York, Inc.

Spread

Spread directly, via lymphatics, or hematogenously.

- Direct extension into the omenta, pancreas, diaphragm, transverse colon or mesocolon, and duodenum is common.
- The abundant lymphatic channels within the submucosal and subserosal layers of the gastric wall allow for easy microscopic spread.
- Lymphatic drainage is through numerous pathways and can involve multiple nodal groups (eg, gastric, gastroepiploic, celiac, porta hepatic, splenic, suprapancreatic, pancreaticoduodenal, paraesophageal, and paraaortic lymph nodes).
- Spreads hematogenously, and liver metastases are common.

Ruolo dei marker (1)

Obiettivo clinico	*prima scelta*	*seconda scelta*	*Tempi*	*Criterio di interpretazione*
diagnosi differenziale con malattia benigna	Nessuno	nessuno	-	-
bilancio di base (estensione)	CA19.9	CEA	prima della chirurgia o radioterapia o chemioterapia	livelli decisionali
risposta al trattamento primario	CA19.9	CEA	a un mese dal trattamento primario	variazioni rispetto al valore di base
riconoscimento precoce della progressione	CA19.9	CEA	regolarmente durante il follow-up (prima di ogni controllo)	variazioni rispetto al valore precedente
monitoraggio terapia malattia avanzata	CA19.9	CEA	prima di ogni nuovo ciclo terapeutico	variazioni rispetto al valore precedente

Livello di raccomandazione: tipo C

Ruolo dei marker (2)

- Si tratta di markers tumore-associati e non tumore specifici.
- FSA: antigene sialoglicoproteico fetale, 96% dei pazienti e nel 14% dei pazienti non oncologici
- CA19.9: utile nella diagnostica del cancro gastrico e pancreatico CEA: strutturalmente identico al cancro del colon, viene estratto dal cancro gastrico in proporzioni nettamente inferiori
- Vale la pena di ricordare non esistono prove scientifiche a favore dell'efficacia dei markers nella fase diagnostica.
- Essi rappresentano un contributo importante nella fase di follow-up, quando il loro innalzamento può precedere anche di mesi l'obiettivazione clinico-radiologica della ripresa della malattia.

G. Bonadonna, Medicina Oncologica, VII ed. 2003

The 5-year survival rates for stomach cancer by stage

- **Stage 0:** 89%
- **Stage IA:** 78%
- **Stage IB:** 58%
- **Stage II:** 34%
- **Stage IIIA:** 20%
- **Stage IIIB:** 8%
- **Stage IV:** 7%

Annals of Surgical Oncology, 7(7):515–519
Published by Lippincott Williams & Wilkins © 2000 The Society of Surgical Oncology, Inc.

Clinicopathological Characteristics of Gastric Carcinoma in Young and Elderly Patients: A Comparative Study

Heriberto Medina-Franco, MD,
Martin J. Heslin, MD, and Ruben Cortes-Gonzalez, MD

Conclusions: Young patients represent a significant proportion of patients with gastric cancer in Hispanic populations. There were **no significant differences in clinicopathological characteristics and outcome** of gastric adenocarcinoma between young and elderly patients. Survival was determined by the stage of the tumor and the possibility of complete surgical resection.

TABLE 1. *Presentation symptoms of gastric cancer in young and elderly patients*

Symptom	Young group No. (%)	Elderly group No. (%)	*P*
Abdominal pain	28 (73.7)	27 (70.0)	NS
Weight loss	22 (56.4)	23 (60.5)	NS
Hemorrhage	19 (50.0)	13 (34.2)	NS
Dysphagia	9 (23.1)	8 (21.0)	NS
Early satiety	5 (13.2)	5 (13.2)	NS
Vomiting	7 (17.9)	10 (26.3)	NS
Jaundice	2 (5.1)	1 (2.6)	NS
↑ Abdominal girth	2 (5.1)	1 (2.6)	NS

NS, not significant.

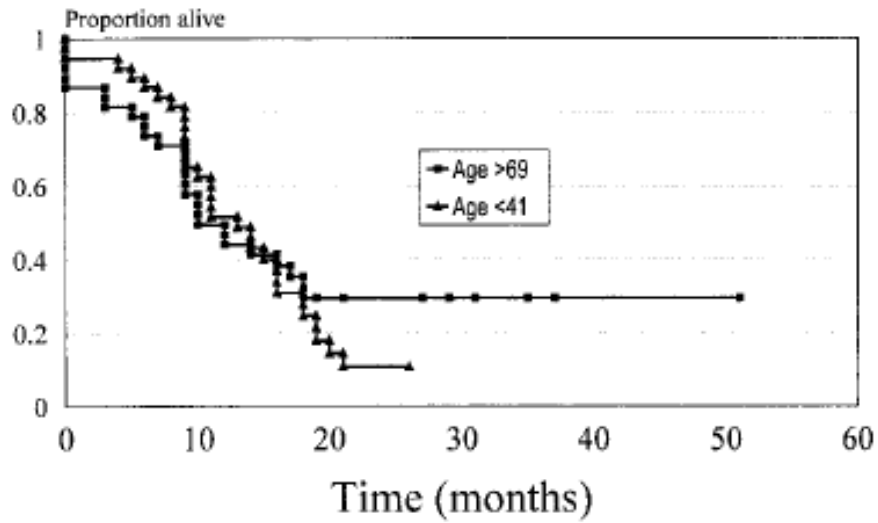
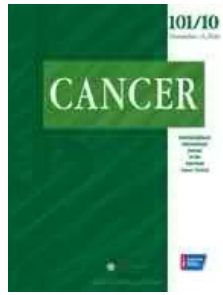


FIG. 2. Survival of patients according to age group ($P = .38$).

Gastric Cancer: Treatment

- Surgical resection
- 6 cm margin is required for resection
- Tumor in antrum: distal gastrectomy
- Proximal tumor: total gastrectomy with splenectomy (Roux-en-Y)
- Tumor in cardia: esophagogastrectomy with splenectomy

American Cancer Society Treatment Guidelines by stage



- **Stage 0:**
  - because stage 0 cancers are limited to the lining layer of the stomach and have not invaded the underlying tissue of the stomach, they are treated by **surgery alone**. **No chemotherapy or radiation therapy is needed.**
- **Stage I:**
  - cancer surgically removed by a total or partial gastrectomy (the complete or partial removal of the stomach), and removal of the omentum (fatty tissue in the abdomen) and nearby lymph nodes.
  - No additional therapy is usually required.
- **Stage II**:
  - surgical removal of all or part of stomach and an extended lymphadenectomy (removal of more lymph nodes).
  - A recent study has shown that adjuvant chemotherapy (treatment given after surgery) with 5-FU and radiation therapy
- **Stage III:**
  - surgery (unless they have other medical conditions that make them too ill for surgery) because up to 15% may be successfully treated. Also, the surgery may help relieve symptoms from the cancer. A recent study has shown that adjuvant chemotherapy with 5-FU and radiation therapy (treatments in addition to surgery) help people with stage III stomach cancer to live longer.
- **Stage IV:**
  - because stage IV stomach cancer has spread to distant organs, a cure is usually not possible. Patients with advanced stomach cancer often need surgery to prevent stomach and/or intestinal obstruction (blockage) or to control bleeding.

Gastric Cancer: Palliation

- If life expectancy is more than 1-2 months
- Stomach must be movable
- Remove lesion that is causing obstruction

Neoplasia in the Elderly: dimension of the problem

P.Boyle-Joint NCI-EORTC Meeting 1990, Venice

"Prediction for year 2000 are that approximately 60-70% of the cancer will occur in person aged 65 years or older: neoplasia in the elderly is an oncological time bomb"

2004 >60% of all tumors in persons ≥ 65 years

>45% of all tumors in persons ≥ 70 years

Neoplasia in the Elderly: in Italy

- 270.000 new patients per year
- 165.000 (61%) age >65
- 90.000 (33%) age 65-74
- 75.000 (28%) age >75

S. Monfardini SIGG 2004

The three classes of elderly patients, from Balducci et al. (Cancer Control, 2000)

	MGA parameters	Therapeutic indication
Class 1: Fit patients	• No functional dependence in ADLs and IADLs • No relevant comorbidities • No geriatric syndromes	The same of younger patients
Class 2: Intermediate or vunerable patients	• Dependence in one or more IADLs but not ADLs • Comorbidities present but not life threatening • Mild memory disorder and depression • No Geriatric Syndrome	Adapted or attenuated treatments (e.g.: chemotherapy dose reductions)
Class 3: Frail	• Age $\geq$ 85 years • Dependence in one or more items of ADL •One or more geriatric syndromes • 3 or more grade 3 comorbidities (CIRS-G) or one severe comorbidity with constant limitation of daily life	Only supportive cares for palliation

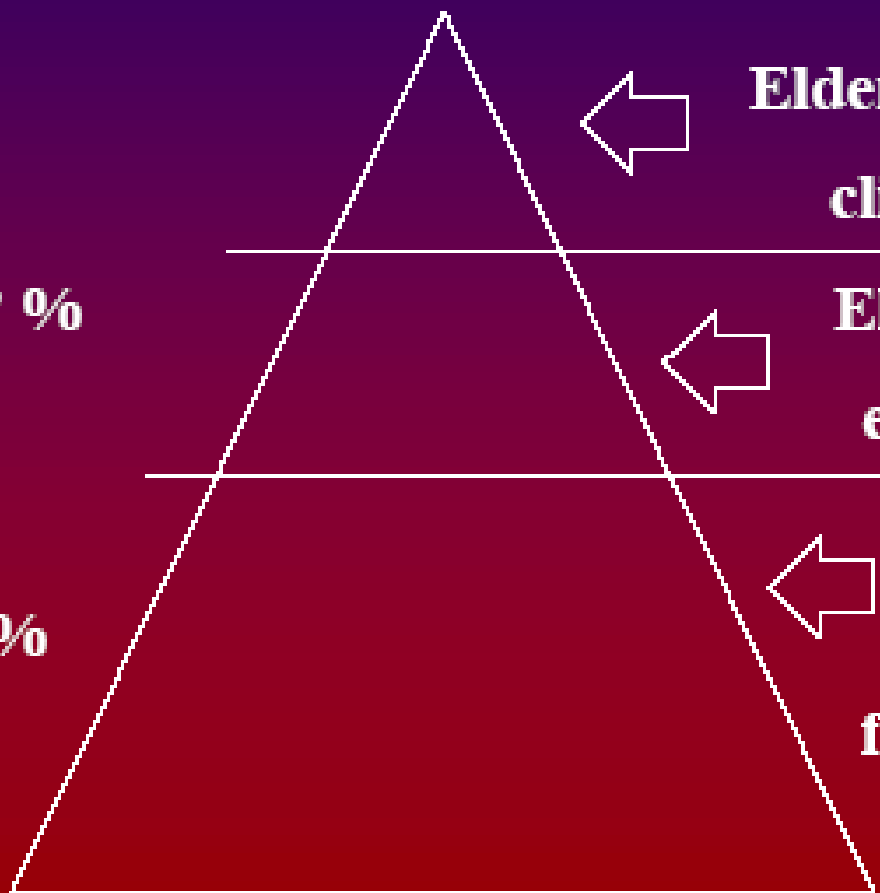
Exclusion of older patients from clinical studies

(16.369 pts in 164 studies from 1993 to 1996)

HUTCKINS, NEJM 1999

	Selected for Trials	General population	p
Pts >65 years	25 %	65%	< 0.001
Pts.>70 years	13 %	47%	< 0.001

TREATMENT OF ELDERLY CANCER PATIENT : WE PROBABLY ONLY KNOW THE TOP OF THE ICEBERG



Elderly selected for clinical studies

? %

Elderly selected for empirical treatment

? %

Elderly not receiving any treatment because of frailty, lack of family support

S. Monfardini SIGG 2004

CANCER IN THE ELDERLY (1983-2004)

- 1980: Empirical dose reduction of anticancer agents
- 1983: Retrospective evaluation of toxicity in ECOG studies
- 1985-2004: Specific trials, supportive therapy
- 1996-2004: MGE studies in cancer patients
- 2000-2004: clinical cooperation with Geriatricians

- EGDS a tutti i pazienti dispeptici?
- Attendere i segni di “allarme”?
- L’età è una discriminante?
- New-onset dyspepsia?

“The most fruitful lesson is the conquest of one’s own error. Whoever refuses to admit error may be a great scholar, but he is not a great learner.”

Johann Wolfgang von Goethe
Maxims and Reflections