Chronic Feed Intolerance Management in Geriatric Palliative Care

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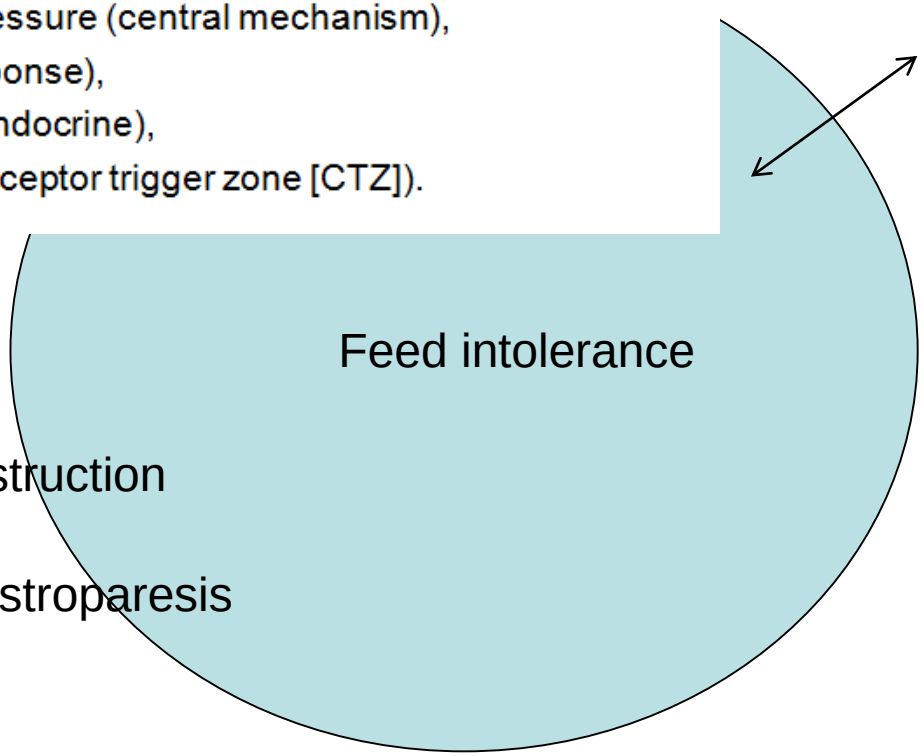
Beit Balev Nesher

Gastrointestinal disorders (e.g., bowel obstruction, gastroenteritis)
Visceral pain
Systemic illness (e.g. myocardial infarction, sepsis, shock)

Increased intracranial pressure (central mechanism),
Toxins (homeostatic response),
Motion sickness (neuroendocrine),
Chemotherapy (chemoreceptor trigger zone [CTZ]).

Acute and transient?
Chronic?

Anorhexia
Early satiety
GE reflux
Aspiration
Vomiting



- The expression „feed intolerance“ is frequently used in daily clinical practice, but there is no consensus on its definition.

- The materialization of feed intolerance is an increased gastric residual volume (no consensus on its magnitude)

- Feed intolerance constitutes an unmet therapeutic challenge – consensus no doubt.

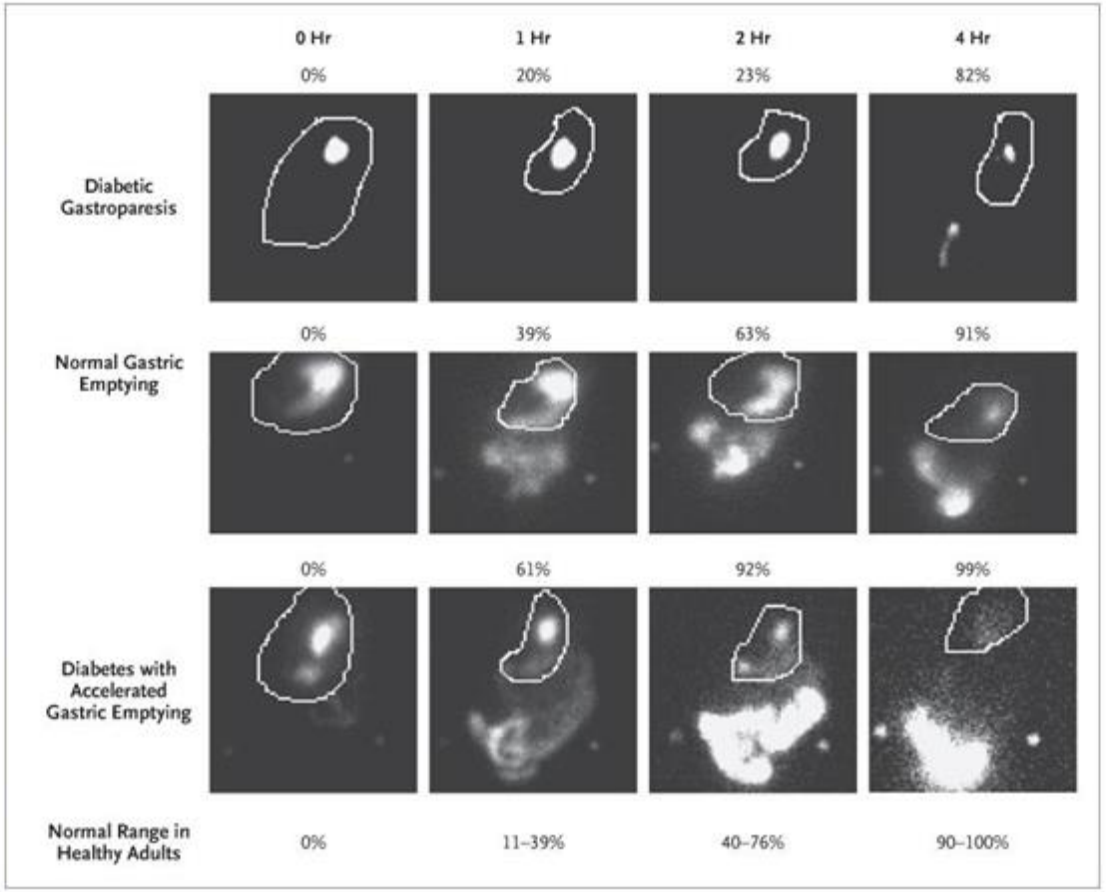
Tests for assessment of **chronic** feed intolerance

- Obstruction?
  - gastroscopy,
  - CT
- Gastroparesis?

  Assessment of gastric emptying:
  - scintigraphy
  - breath test
  - gastric residual volume

Gastric scintigraphy with radiolabeled **solid food** - gold standard

Scintiscans of Residual Gastric Contents



The white areas represent the isotope, and the white outlines indicate the region of interest for quantification of radioactivity in the stomach. The percentage of solid food consumed that was emptied from the stomach at each time point after the meal is shown above each scintiscan.

Camilleri M. N Engl J Med 2007;356:820-829

Breath test for diagnosing feed intolerance

Nouven NQ, Bryant LK, Burgstad CM, Chapman M, Deane A et al.
Gastric emptying measurement of liquid nutrients using the (13)C-octanoate breath test in critically ill patients: a comparison with scintigraphy.
Intensive Care Med 2013;39:1238-1346.

- The (13)C-octanoate breath test ((13)C-OBT) is a simple, non-invasive technique that does not involve radiation exposure.
- **AIM:** To evaluate the performance of the (13)C-OBT in the assessment of GE in critically ill patients.
- **METHODS:** meal retention was determined and the gastric emptying coefficient (GEC) and half emptying time [t50(BT)] were calculated for the (13)C-OBT. Delayed GE was defined as meal retention >13 % at 180 min.
- **RESULTS:** Delayed GE was identified in 27/33 patients. Meal retention correlated well with GEC ($r = -0.63$ to -0.74; $P < 0.0001$).
- **CONCLUSION:** There was a correlation between (13)C-OBT and gastric scintigraphy, with GEC performing as a better and more sensitive marker of detecting delayed GE than t50. However the relatively wide 95 % confidence intervals suggest that (13)C-OBT is more suitable for research studies rather than for individual patients in clinical practice.

The gastric residual volume – one protocol out of many

- Upon clinical suspicion, in patients with tube feeding
- The gastric residual volume (GRV) is measured **thirty minutes after administration of enteral formula** has been terminated, by aspirating the gastric content with a 50-mL syringe. Feeding can be given at original rate if GRV <100 mL.

Phillips LK, Rayner CK, Jones KL, Horowitz M. Measurement of gastric emptying in diabetes. J Diabetes Complications 2014 pii: S1056-8727(14)00185-8.

Hsu CW, Sun SF, Lee DL, Lin SL, Wong KF et al. Impact of disease severity on gastric residual volume in critical patients. World J Gastroenterol 2011;17:2007-2012.

What is known:

- Studies about feed intolerance come from **critical care medicine**. None could be located in the geriatric literature.

- **Gastric emptying** (GE) is commonly impaired during critical illness with up to 50% of mechanically ventilated patients have delayed GE (i.e. “gastroparesis”).
- **Antro-pyloro-duodenal as well as intestinal motilities** are also frequently impaired in these patients.

Learning at bedside

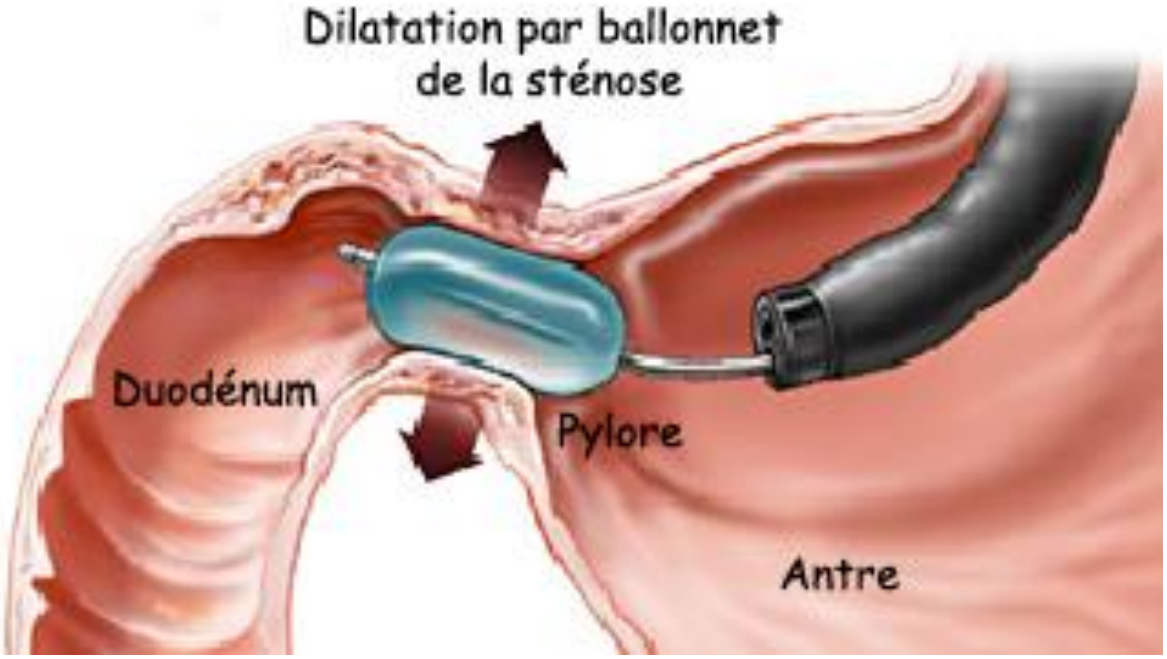
- Three case histories from our institution (Long-term Geriatric Care including palliation and hospice) illustrate the variety of etiologies of chronic feed intolerance, the eclectic diagnostic workup, and unpredictable (sometimes) success in the treatment.

Case 1

- A 84-year-old woman was admitted on May 7th 2015 for hospice care with the diagnosis of terminal stage carcinoma.

Patient history:

- 2013: carcinoma of breast ER positive,
- 2013: left mastectomy, radio-chemo-hormonal therapy
- 2014: treatment discontinued because of adverse effects and poor compliance.
- 2014: Weight loss about 20 kg, BMI 19, abdominal pain, vomiting
- **2014 December:** gastroscopy showed diffuse infiltration of the gastric mucosa by tumor, narrowing of the antrum and severe pyloric stenosis; **balloon pyloroplasty performed**


Dilatation par ballonnet
de la sténose
Duodénum
Pylore
Antre

- Biopsy samples from the gastric mucosa showed lobular **carcinoma of mammary origin:** ER positive, CDGEP15 rare postive cells, CK7 focally positive
- 20.4 – 6.5.2015 - readmitted to the acute care hospital with the same symptoms: early satiety, frequent vomiting
- Gastroenterology consultation: decision not to repeat pyloroplasty, stenting the pylorus thought not to be feasible. Proposed surgical jejunostomy, which the patient refused to undergo.
- May 2015: Referral for hospice care as “terminal stage cancer”.
- Treatment to be continued with fulvestrant (third-generation nonsteroidal aromatase inhibitor) 500 mg i.m. 1/28 days.

On physical examination:

- Vital signs within the normal range, wasting, sarcopenia, no palpable abdominal mass

nothing of the extraordinary

51			mg/dl	UREA
0.56	0.67	0.65	mg/dl	CREATININE
0.56			mg/dl	CREATININE
3.6	4.7	5.5	mg/dl	URIC ACID
3.6			mg/dl	URIC ACID
4.5	4.6	4.3	mmol/l	POTASSIUM - K
4.5			mmol/l	POTASSIUM - K
133	136	136	mmol/l	SODIUM - NA
133			mmol/l	SODIUM - NA
8.3	8.5		mg/dl	CALCIUM - CA
8.3			mg/dl	CALCIUM - CA
3.5	2.1		mg/dl	PHOSPHORE - P

אבחנה	ת.התחלה
PALLIATIVE CARE [hospice]	07/05/2015
BREAST CARCINOMA [2013, Lt, mastectomy, chemo and radiation therapy]	
PYLORIC STENOSIS ACQUIRED [due to gastric metastases of mammary origin (ER positive) diffusely infiltrating the stomach, baloon pyloroplasty]	14/12/2014
VOMITING [and weight loss 20 kg, gastroparesis	
HYPERTENSION [remitted nil antihypertensive medication]	
HYPERLIPIDEMIA	
CHRONIC ISCHEMIC HEART DISEASE UNS [stable]	
CONGESTIVE HEART FAILURE (CHF) [TTE - moderately reduced LVEF, mild mitral regurgitation]	
SCHIZOPHRENIA UNS [severe behavikoral disorder, refusal to be examined and refusal to submit to blood tests]	
HYPOALBUMINEMIA [2.2 g/dL improved to 3 g/dL Dec 2015]	08/05/2015
CONSTIPATION	10/05/2015
SYNCOPE [vaso-vagal]	22/07/2015
POLYPHARMACY	
URINARY INCONTINENCE	

צורת הגשה	דרך מתן	התרופה	מינון	ימים	ת.התחלה	שעות	ת.סיום
PATC	PATCH	FENTA 12MCG [FENTANYL 12.5mcg]	12.5mcg X1	כל 3 ימים	26/07/2015	12:00	
TAB	P.O	ATZIRUT X [BISACODYL 5mg]	10mg X1		19/07/2015	20:00	
SUS	P.O	EASY MEAL K-2 COFFEE	125ml X2		12/07/2015	08:00, 14:00	
SUP	P.R	GLYCERIN [GLYCERIN 2.7g]	2sup X1	כל 2 ימים	05/07/2015	06:00	
TAB	P.O	PERCOCET-5 [OXYCODONE HCL 5mg, PARACETAMOL 325mg]	1TAB X0		28/06/2015		25/09/2015
TAB	P.O	FOLIC ACID(REKAH) [FOLIC ACID 5mg]	5mg X1		23/06/2015	12:00	
AMP	I.M	PRAMIN [METOCLOPRAMIDE 10mg]	10mg X0		17/06/2015		14/09/2015
TAB	P.O	PRAMIN [METOCLOPRAMIDE 10mg]	10mg X3		08/06/2015	08:00, 12:00, 18:00	
PWD	P.O	HADASSA WHEY	7.5g X2		08/05/2015	08:00, 18:00	

TAB	P.O	NOZINAN [LEVOMEPROMAZINE 25mg]	12.5mg X1		26/05/2015	21:00		
TAB	P.O	NOZINAN [LEVOMEPROMAZINE 25mg]	6.25mg X1		26/05/2015	08:00		
TAB	P.O	OLANZAPINE [OLANZAPINE 5mg]	2.5mg X1		07/05/2015	20:00		
TAB	P.O	LORIVAN [LORAZEPAM 1mg]	1mg X1		07/05/2015	21:00		
TAB	P.O	PAPAVERINE [PAPAVERINE 40mg]	40mg X0		01/06/2015			
DROP	P.O	OPTALGIN LIQ [DIPYRONE 500mg]	1000mg X0		07/05/2015			

- Management: Pramin tb 10 x 3 before meals and small volume feeding, usual medications continued
- Patient progressively improved, acceptable food tolerance, no nausea or vomiting, able to sit, walks with a rolling walker 20 - 30 meters, participates on cultural activities.

- On admission: gastric outlet stenosis by tumor, feed intolerance,
- Successful palliation: gastric outlet stenosis by tumor, feed tolerance.

Pathophysiology of feed intolerance in the patient

- Gastic outlet obstructed by tumor?
- Obstruction relieved by pyloroplasty; late in course oral intake is tolerated through June 2015 – January 2016.

- Compression by tumor from outside? None on CT.

Gastroparesis?

- Gastroparesis (GP) is a chronic neuromuscular disorder of the upper gastrointestinal tract.
- The pathophysiology of GP is diverse. Abnormalities in fundic tone, antroduodenal dyscoordination, a weak antral pump, gastric dysrhythmias, and abnormal duodenal feedback all contribute to delays in gastric emptying .

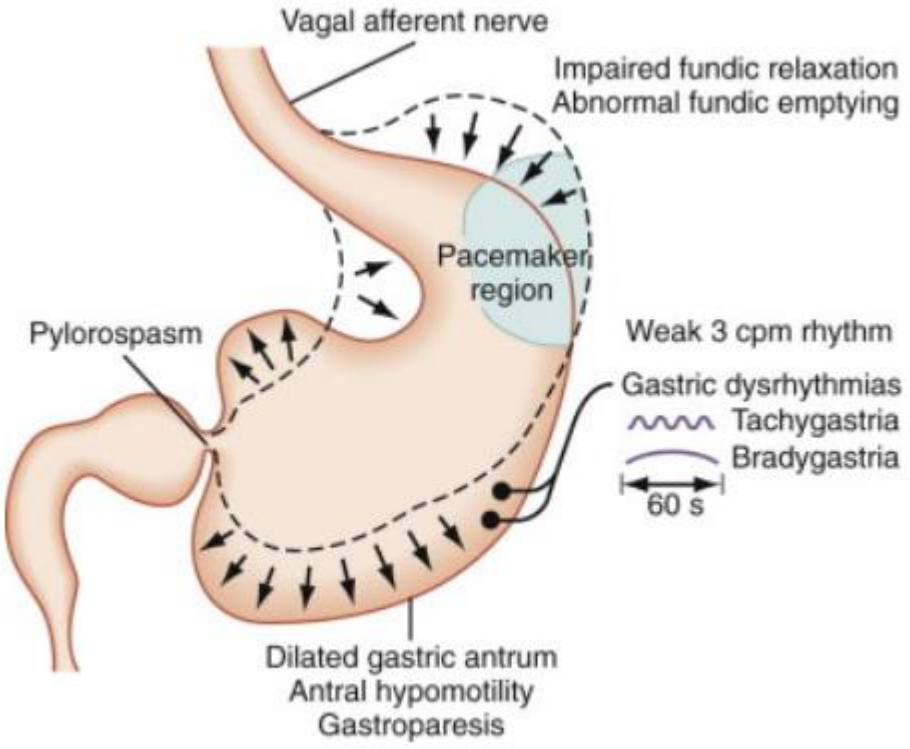
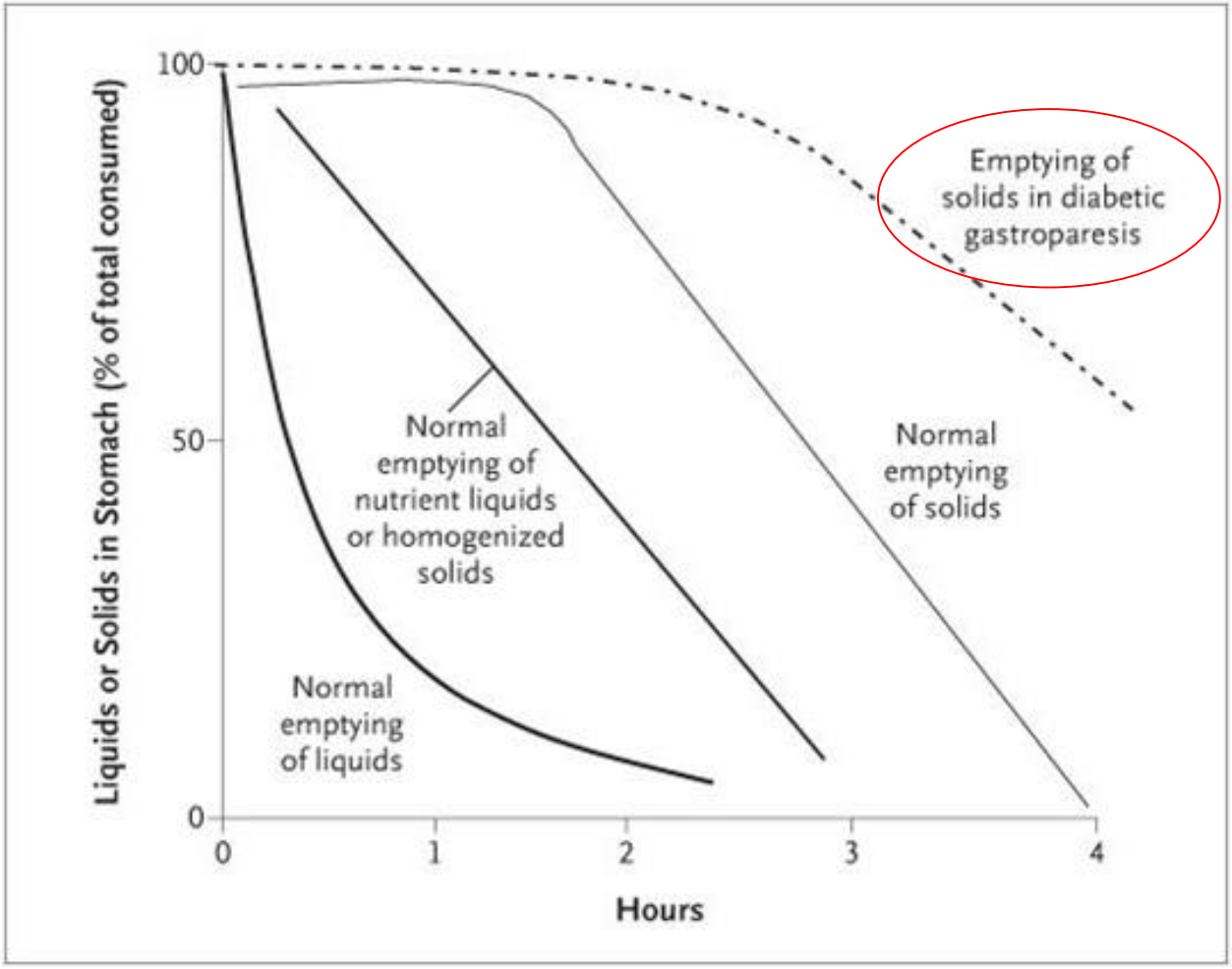


Figure 48-20. Spectrum of gastric neuromuscular disorders. Gastric

Patterns of Gastric Emptying in Healthy People and in Patients with Diabetic Gastroparesis



Camilleri M. N Engl J Med 2007;356:820-829

The NEW ENGLAND JOURNAL of MEDICINE

What may be relevant to this patient?

Causes of delayed gastric emptying

Mechanical causes

- Peptic ulcer disease, scarred pylorus.
- → Malignancy: gastric cancer, gastric lymphoma, pancreatic cancer.
- Gastric surgery: vagotomy, gastric resection, roux-en-Y anastomosis.
- Crohn's disease.

Endocrine and metabolic causes

- Diabetes mellitus.
- Hypothyroidism.
- Hypoadrenal states.
- Electrolyte abnormalities.
- Chronic renal failure.
- Medications.
- Anticholinergics.
- → Opiates.
- Dopamine agonists.
- Tricyclic antidepressants.

Abnormalities of gastric smooth muscle

- Scleroderma.
- Polymyositis, dermatomyositis.
- Amyloidosis.
- Pseudo-obstruction.
- Myotonic dystrophy.
- Neuropathy.
- Scleroderma.
- Amyloidosis.
- Autonomic neuropathy.

Central nervous system or psychiatric disorders

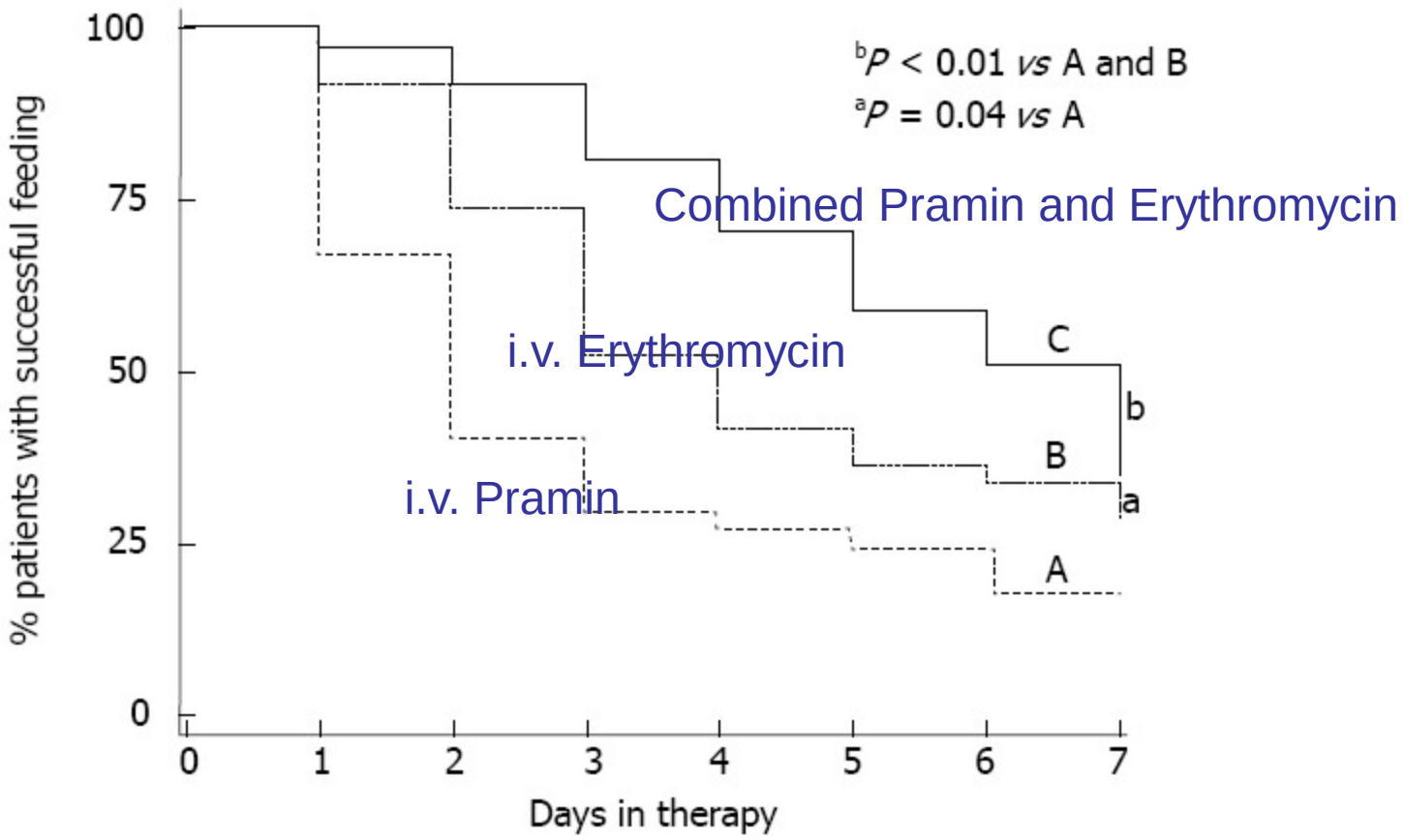
- Brain stem tumors.
- Spinal cord injury.
- Anorexia nervosa.
- → Stress.

Miscellaneous

- Idiopathic gastroparesis.
- Gastroesophageal reflux disease.
- Nonulcer (functional) dyspepsia.
- → Cancer cachexia or anorexia.

Management of gastroparesis

- Improve the gastric motility: metoclopramide (Pramin), domperidone (*Motilium*), erythromycine



Efficacy of metoclopramide (A), erythromycin (B) and combined erythromycin and metoclopramide (C) in the treatment of feed intolerance of critical illness over 7-d period.

Nguyen NQ. **Pharmacological therapy of feed intolerance in the critically ills**. World J Gastrointest Pharmacol Ther. 2014;3:148-155.

- **The current first line treatment for feed intolerance** is prokinetic therapy with erythromycin and metoclopramide (alone or in combination), which are highly effective and free of significant adverse effects.

- Additional therapies are gastric bypass surgery, invasive procedures under endoscopy, jejunostomy.

Recent guidance on the use of metoclopramide and domperidone from the *British National Formulary*

- The risks of neurological effects with metoclopramide such as extrapyramidal disorders and tardive dyskinesia outweigh the benefits in long term or high dose treatment.
- Recommended used for short period (5 days) at maximum dose of 30 mg/24 hours. In practice sometimes used for longer durations and higher doses in palliative care but only if benefit outweighs risk.

- **Domperidone**, due to small increased risk of serious cardiac side effects, should be used at the lowest effective dose for the shortest possible duration. The maximum treatment duration for domperidone is one week. Recommended dose 30 mg/24 hours.
- Domperidone is contra-indicated in conditions where cardiac conduction is, or could be, impaired, underlying cardiac disease, concomitant prescription of drugs that prolong the QTc interval, potent CYP3A4 inhibitors, or severe hepatic impairment

Collis E, Mather H. Nausea and vomiting in palliative care. BMJ 2015;351:h6249

The patient, by January 2016

SUP	P.R	CONTALAX [BISACODYL 10mg, BUTYLATED HYDROXYANISOLE 2mg]	2sup X1		25/09/2015	06:00
ENEMA	P.R	EASY GO ENEMA [SORBITOL 80%, GLYCERIN 20%]	180ml X1	כל 3 ימים	01/09/2015	06:00
TAB	P.O	ATZIRUT X [BISACODYL 5mg]	10mg X1		19/07/2015	20:00
TAB	P.O	FOLIC ACID(REKAH) [FOLIC ACID 5mg]	5mg X1		23/06/2015	12:00
PWD	P.O	HADASSA WHEY	7.5g X2		08/05/2015	08:00, 18:00
TAB	P.O	NOZINAN [LEVOMEPROMAZINE 25mg]	12.5mg X1		26/05/2015	21:00
TAB	P.O	NOZINAN [LEVOMEPROMAZINE 25mg]	6.25mg X1		26/05/2015	08:00
TAB	P.O	OLANZAPINE [OLANZAPINE 5mg]	2.5mg X1		07/05/2015	20:00
TAB	P.O	LORIVAN [LORAZEPAM 1mg]	1mg X1		07/05/2015	21:00

Comment

- Gastroparesis was transient
- Improvement can be attributed to discontinuation of opiate?, improvement of constipation?, relief of stress?, estrogen receptor antagonism?

- זה לא ניגמר עד שזה ניגמר
- פליאציה זה יותר מאשר לתת נוזלים בעירוי תת-עורי

Patient prognosis?

Doria MT. Gastric metastasis as the first manifestation of an invasive lobular carcinoma of the breast. Autops Case Rep 2015;5:49-53.

- **Systemic therapy** is the treatment for breast cancer that is metastatic to the stomach and other sites.
- The choice of systemic treatment (**chemotherapy, hormonal therapy, or both**) is based upon symptoms, age, performance status, and previous systemic treatments.
- Taal et al. reported a **46% response rate** (17 out of 37 patients with gastric metastasis) in their patients treated with systemic therapy. **The response to hormonal treatment and chemotherapy was similar in their group of patients.**
- **Palliative surgery is only recommended in cases of gastric obstruction.**
- **I**n the McLemore et al. series, 64% (47 out of 73 patients) underwent palliative surgical interventions for obstructive symptoms or mass effect. However, surgical **palliation did not significantly improve the overall survival.**
- Median overall **survival** of patients with gastric metastasis of breast cancer is equivalent to that of all women with metastatic breast disease, **ranging from 24 to 36 months.**

Case 2

A 83-year-old woman was admitted to our department December 2014 with the diagnoses

- carcinoma of the pancreas,
- gastric outlet obstruction,
- feed intolerance.

PALLIATIVE CARE [hospice]
PANCREAS PRIM MALIGNANT TUMOR [MODERATELY DIFFERENTIATED DUCTAL ADENOCARCINOMA', GASTRIC OUTLET OBSTRUCTION
DIABETES MELLITUS TYPE II
HYPERTENSION
ANEMIA
DEPRESSIVE DISORDER NOS [and cognitive decline]
OBESITY (30 =< BMI < 35)
SKIN - MALIGNANT NEOPLASM NOT MELANOMA [SCAMOUS CELL CARCINOMA WELL DEFERNTIATED]

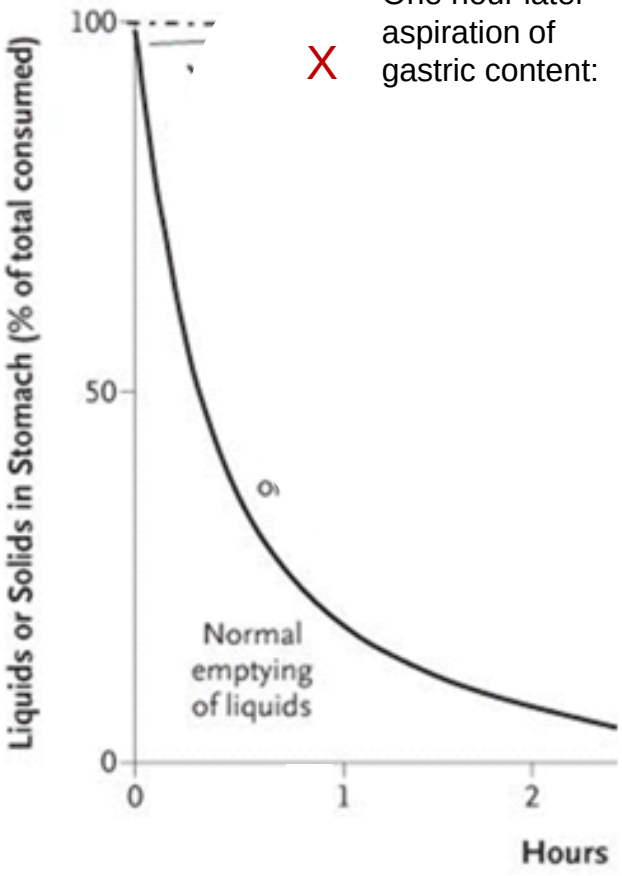
I.V	SODIUM CHLORIDE [SODIUM CHLORIDE .9%]	500mL X2		21/12/2014	06:00, 22:00	23/12/2014
PATCH	FENTA 50 MCG [FENTANYL 50mcg]	50mcg X1	כל 3 ימים	15/12/2014	17:00	
P.R	ABROLET FORTE NEW [PARACETAMOL 250mg]	4sup X0		15/12/2014		
S.L	ACERIL [CAPTOPRIL 12.5mg]	12.5mg X0		13/12/2014		
B.E	LYTEERS [BENZALKONIUM CHLOR .1mg, POTASSIUM CHLORIDE 1.5mg, SODIUM CHLORIDE 6.5mg]	1DRP X3		11/12/2014	08:00, 12:00, 18:00	24/12/2014
INH	AEROVENT RES 20ML [IPRATROPIUM BROMIDE .25mg/ml]	1ml X0		11/12/2014		24/12/2014
S.C	CLEXANE [ENOXAPARIN 40mg]	40mg X1		07/12/2014	20:00	

Vomiting, ‘feed intolerance’

Evaluation of GRV **and t**rial of enteral feeding

- **8.12** , in fasting state nasogastric tube inserted
- Aspiration by a 50-mL syringe the gastric content, i.e. 400 mL containing remnants of solid food ingested the day before.
- In the following, slow instillation in the stomach of 200 mL water. One hour later emptying the gastric content by syringe: volume 200 mL.

- Enteral feeding discontinued, s.c. saline ordered. Metoclopramide i.v. 10 mg x 3 started.



10.12. Reassessment of feed tolerance

- 11.30: through nasogastric tube 100 mL Osmolite by slow drip followed by 100 mL water.
- 13.30 aspiration of gastric content = 200 mL
- Veto to oral and enteral feeding

11.12. In the morning fasting state aspiration of the gastric content: 600 mL containing remnants of solid food (interdiction not respected)

Another trial of feed tolerance – result reproducible?

- 100 mL Osmolite by slow drip followed by 100 mL water, 3 hours later examination of the gastric residual volume = 300 mL.
- Isotonic saline or glucose total 2000 mL/day provided plus KCl and $MgSO_4$ i.v.

- **23.12.2014** On insistence of the patient's daughters she was referred to an acute care hospital for additional assessment.

- The test consisted of **gastrographin follow-through**. It showed a slightly enlarged stomach, which quickly emptied in the duodenum; there was no reflux.
- Patient discharge from the ER with the diagnosis **'transient gastroparesis'.**

- **23. 12.** The patient and proxies insisted on reinstitution of oral feeding. This went from bad to worse.

- Vomiting, coffee ground – enoxaparin discontinued, i.v. Pramin continued, i.v. ranitidine started.
- **24.12.** Morning gastric residual volume 200 mL. Later vomiting.
- **25.12.** Trials of enteral feeding of small volumes by slow drip.
- **26.12.** Hypotension, tachycardia, exitus

Comment:

- Obstruction of the gastric outlet and jejunum were excluded on gastrographin follow-through.
- The feed intolerance was functional, i.e. gastroparesis.
- Fast emptying of the radiocontrast material from the stomach does not exclude gastroparesis.

Case 3

- An 81-year-old woman was referred in November 2014 for palliative care
- DX: Catastrophic outcome of neurosurgery for trigeminal neuralgia, vegetative state (UWS), weaned from mechanical ventilation, tracheostomy care.
- PEG, pulmonary aspirations – MD's diagnosed gastroparesis
- Laparoscopic jejunostomy performed and patient fed through the jejunostomy: the gastrostomy tube was left in place.

- 4.12. The jejunostomy tube pulled out , the cutaneos entrance obliterated.

  Assessment of feed tolerance
- 150 mL water administered through the gastrostomy tube – 30 minutes later GRV = 0
- Continuous drip feeding was instituted and is successfully provided without complications till present (January 2016)

Comment

- Gastroparesis was transient.

DeLegge MH. Managing gastric residual volumes in the critically ill patient: an update. Curr Opin Clin Nutr Metab Care 2011;14:193-196.

Case summaries - conclusions

- Three case histories illustrate the variety of etiologies of chronic feed intolerance: gastroparesis associated with malignancy, neurogenic gastroparesis, and duodenal obstruction by pancreatic tumor.

- The following observations warrant emphasis:

  1. Even in the presence of an anatomical obstacle, a functional element may be present which may be reversible,

  2. Quick passage of gastrographin the stomach does not rule out gastroparesis,

  3. Recovery of gastric emptying after pyloroplasty can take time,

  4. Gastroparesis, whether idiopathic or neurogenic, may be transient. Patience and perseverance can be rewarding.

Chronic Feed Intolerance
Management in Geriatric Palliative Care

- PubMed no items
- No guidelines.
- What should/what can we do?
- The simplest first,
- Strive for a diagnosis,
- Recognize that palliation may provide comfort for many months.

Feed intolerance - the simplest to be done first

- Less formula or longer feeding times (controlling the feeding time) may reduce the risk of aspiration.
- The patient should be positioned in Fowler’s or semi-Fowler’s position before feeding, during feeding and for one to two hours after feeding. This promotes gastric emptying.
- Left-sided lying during feeding, which alters emptying of the stomach into the duodenum, should be avoided.
- Treat constipation
- Discontinue unnecessary medications, in particular those which may affect the gastric and intestinal motility.

In selected cases

Suspected gastroparesis

Step 1: Diagnosis: 4 h Gastric emptying by scintigraphy

Step 2: Exclude iatrogenic disease
Dietary: low fat, low fiber diet
Glycemic control among diabetics

Step 3: Pharmacological Rx:
- Prokinetics: metoclopramide, erythromycin, domperidone
- Antiemetics: anti-histamine$_1$ receptors; 5-HT$_3$ antagonists

Step 4: Nutritional support: Enternal formula

Step 5: Non-pharmacological Rx
Pyloric injection of botulinum toxin
Venting gastrostomy, feeding jejunostomy
Parenteral nutrition
Gastric electrical stimulation
Pyloroplasty
Partial gastrectomy

- Making a proper diagnosis is mandatory: by endoscopy, measurement of gastric transit time and or GRV.

Learning points

- Feed intolerance, with main symptoms anorhexia, early satiety, esophageal reflux and pulmonary aspiration, constitutes a major therapeutic challenge.

- The cause of feed intolerance may be an anatomic obstruction of the stomach or jejunum, or neuro-muscular dysfunction of the upper GI tract (‘gastroparesis’). A variety of additional factors may be involved.

- Making a proper diagnosis is mandatory: by endoscopy, measurement of gastric transit time and or GRV.

- Pharmacologic treatment of chronic gastroparesis with Pramin® or Motilium® is often disapointing.

- There are promising techniques for palliation of impaired gastric emptying, either delivered endoscopically or via minimal invasive surgery. Their utility may be narrowed by disorganized peristalsis and faulty nursing.

- In the recent literature, indications for withholding enteral feeding and initiating TPN were **three consecutive GRV measurements > 500 mL** within a period of 24 hours (Soroksky A), and, at variance, GRV >250 mL (Reignier J).

Mllave SA, et al. Use of residual volume as a marker for enteral feeding intolerance: prospective blinded comparison with physical examination and radiographic findings. JPEN J Parenter Enteral Nutr 1992;16:99-105

Soroksky A et al. A simplified approach to the management of gastric residual volumes in critically ill mechanically ventilated patients: a pilot prospective cohort study. Isr Med Assoc J 2010;12:543-548.

Reignier J. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial**. JAMA 2013;209:249-256.**

- **Metoclopramide [10 mg x 4/day *iv*]** has been shown to improve feed intolerance during critical illness but its therapeutic efficacy declines progressive over the 7 d (from 85% in the first days of therapy to less than 35% after 7 d of treatment[32]. Metoclopramide, however, is not effective[33] and, in fact, contraindicated[34] in patients with brain injury, as it can raise intracranial pressure further.

- **Erythromycin** is the only available motilin agonist uses in clinical practice. Given at a low dosage, ranging **between 3 to 7 mg/kg per day**, erythromycin has been shown to increase both gastric emptying and improve feed intolerance in critically ill patients. Low dose erythromycin (**200 mg x 2/day**) was found to be more efficacious than metoclopramide

- **Metoclopramide** (Pramin) is used as a **prokinetic** drug showing also strong antiemetic action. It functions as an antagonist of dopaminergic receptor D2.
- Unfortunately, lack of selectivity causes metoclopramide to stimulate receptors present in the central nervous system and can trigger unpleasant side effects in the form of extrapyramidal disorders

- **Domperidone** (*Motilium*) is a drug of similar action to metoclopramide. It has an affinity for the same D2 receptor, but with greater selectivity for the gastrointestinal tract, which reduces the risk of side effects.
- ***EGG (electro gastrogram)*** - in patients with diabetic gastroparesis and dysrhythmia the administration of domperidone ***normalises gastric motility in some patients***.

- **Understanding of the neurochemistry of the emetic reflex** has been important in developing antiemetic agents with new mechanisms of action.

- In the area postrema there are receptors for a large number of neuroactive agents (e.g., dopamine, histamine, acetylcholine, norepinephrine, and substance P). Pharmacologic agents that block specific sets of receptors (e.g., dopamine and neurokinin-1 [NK1]) has resulted in the identification of valuable antiemetic drugs.

- Type 3 serotonin receptors are present in large quantities on vagal and splanchnic afferents within the gastrointestinal tract. These peripheral receptors are pivotal in the initiation of the acute nausea and vomiting caused by cisplatin and other strongly emetogenic chemotherapeutic agents. Inhibition of this pathway by specific 5-HT3 receptor antagonists results in highly effective antiemetic therapy.

WHAT IS CURRENT KNOWLEDGE

- ✓ Tube feeding of bedridden PEG patients often results in complications such as vomiting, aspiration, and resulting in aspiration-induced pneumonia.
- ✓ Which types of diet might have higher and lower risks of aspiration pneumonia has not been clarified in these patients.

WHAT IS NEW HERE

- ✓ Low-lipid-containing elemental diets significantly facilitated gastric emptying compared with a standard liquid diet and were associated with a reduced risk of aspiration pneumonia in bedridden PEG patients.

Crit Care. 2007;11(6):R132.

The relationship between gastric emptying, plasma cholecystokinin, and peptide YY in critically ill patients.

Nguyen NQ[1], Fraser RJ, Bryant LK, Chapman MJ, Wishart J, Holloway RH, Butler R, Horowitz M.

- Cholecystokinin (CCK) and peptide YY (PYY) are released in response to intestinal nutrients and play an important physiological role in regulation of gastric emptying (GE). Plasma CCK and PYY concentrations are elevated in critically ill patients, particularly in those with a history of feed intolerance.
- GE was delayed in 64% (25/39) of the patients. Baseline plasma CCK (8.5 +/- 1.0 versus 6.1 +/- 0.4 pmol/L; P = 0.045) and PYY (22.8 +/- 2.2 versus 15.6 +/- 1.3 pmol/L; P = 0.03) concentrations were higher in patients with delayed GE and were inversely correlated with GEC (CCK: r = -0.33, P = 0.04, and PYY: r = -0.36, P = 0.02).
- The pathogenetic role of these gut hormones in delayed GE requires further evaluation with specific antagonists.

23 REFERENCES ‘FEED INTOLERANCE – ELDERLY’
NONE ‘FEED INTOLERANCE – PALLIATIVE/PALLIATION’

Summers MJ, Bartolomeo AE, Zaknic AV, Chapman MJ et al.

Endogenous amylin and glucagon-like peptide-1 concentrations are not associated with gastric emptying in critical illness.

Acta Anaestheosol Scand 2014;58:2350242.

- The aims of this study were to determine amylin and **GLP-1 concentrations in the critically ill** and their relationship with GE, glucose absorption and glycaemia.
- **METHODS:** In fasted critically ill and healthy subjects (n = 26 and 23 respectively), liquid nutrient, containing 100 mg (13) C-sodium octanoate and 3 g 3-O-methlyglucose (3-OMG), was administered via a nasogastric tube. Amylin, GLP-1, glucose and 3-OMG concentrations were measured in blood samples taken during fasting, and 30 min and 60 min after the 'meal'. **Breath samples were taken to determine gastric emptying coefficient (GEC). Intolerance to intragastric feeding was defined as a gastric residual volume of ≥ 250 ml** and/or vomiting within the 24 h prior to the study.
- **RESULTS: GLP-1 concentrations were increased in the critically ill and were greater in feed intolerant** when compared with those tolerating feed [3.7 (0.4-7.2) vs. 1.2 (0.7-4.6) pmol/l; P = 0.02],

Mancini SA et al. **Pyloroplasty for Refractory Gastroparesis**.
Am Surg 2015;81:738-746.

- Pyloroplasty is beginning to emerge as a successful drainage procedure for refractory gastroparesis.
- Diabetic and nondiabetic **gastroparesis**, 46 patients
- Gastric emptying – by scintigraphy
- **Laparoscopic pyloroplasty** was performed in 42 patients, open pyloroplasty in three, and one patient was converted from laparoscopic to open pyloroplasty.
- The postoperative gastric emptying scintigraphy improved in 90 per cent of patients and normalized in 60 per cent.

Summary of endoscopic therapies for refractory gastroparesis

Endoscopic therapies	Technique/mechanism	Advantages	Disadvantages
Intrapyloric botulinum toxin injection	Radial or direct injection of 100-200 U of toxin around the pylorus	Safe and well tolerated	No clear benefit in RCTs
	Toxin binds to cholinergic receptors resulting in decreased acetylcholine release	Easy to perform	Need for repeat treatments
		Observational studies report high response rate	
Gastric electric stimulation	Miniature wireless device placed through over-tube and secured to the gastric mucosa with endoclips	Proof of concept design with proven benefit	Lack of human studies
	Device stimulates gastric muscle resulting in more regular, constant amplitudes	Currently used prior to definitive surgical placement	No comparative data to surgically placed gastric pacers
		Less invasive compared to surgical placement	
Transpyloric stenting	Through-the-scope self-expandable metal stents placed across the pyloric channel	Small case series demonstrating a proven benefit in symptoms	Limited data Potential for stent migration
Endoscopic pyloromyotomy	Submucosal dissection and tunneling with full separation of the pyloric ring (myotomy)	Less invasive alternative to traditional surgical pyloromyotomy	Limited data Technically challenging with limited expertise Potential for complications:
Endoscopic decompression or bypass	Percutaneous endoscopic jejunostomy (PEJ) and direct PEJ	Safe and effective	Limited success
	Direct post-pyloric enteral nutritional support		Technical difficulty
endoscopic ultrasound-guided gastrojejunostomy	Transluminal anastomosis using self-expanding, lumen-apposing metal stents	Decreased morbidity and mortality compared to surgical approach	Lack of human trials Unknown long-term safety and patency issues

- **Direct percutaneous endoscopic jejunostomy** (DPEJ) offers another approach to provide direct postpyloric enteral nutritional support. The main limitation of DPEJ is technical difficulty as the jejunum is narrow, making it more difficult to advance a needle directly into the lumen.

- JAMA. 2013 Jan 16;309(3):249-56. doi: 10.1001/jama.2012.196377.
- **Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial.**
- Reignier J[1], Mercier E, Le Gouge A, Boulain T, Desachy A, Bellec F, Clavel M, Frat JP, Plantefeve G, Quenot JP, Lascarrou JB; Clinical Research in Intensive Care and Sepsis (CRICS) Group.

- **IMPORTANCE:** Monitoring of residual gastric volume is recommended to prevent ventilator-associated pneumonia (VAP) in patients receiving early enteral nutrition. However, studies have challenged the reliability and effectiveness of this measure.
- **OBJECTIVE:** To test the hypothesis that the risk of VAP is not increased when residual gastric volume is not monitored compared with routine residual gastric volume monitoring in patients receiving invasive mechanical ventilation and early enteral nutrition.
- **DESIGN, SETTING, AND PATIENTS:** Randomized, noninferiority, open-label, multicenter trial conducted from May 2010 through March 2011 in adults requiring invasive mechanical ventilation for more than 2 days and **given enteral nutrition within 36 hours after intubation** at 9 French intensive care units (ICUs); 452 patients were randomized and 449 included in the intention-to-treat analysis (3 withdrew initial consent).
- **INTERVENTION:** Intolerance to enteral nutrition was based only on regurgitation and vomiting in the intervention group and based on **residual gastric volume greater than 250 mL at any of the 6 hourly measurements** and regurgitation or vomiting in the control group.
- **MAIN OUTCOME MEASURES:** Proportion of patients with at least 1 VAP episode within 90 days after randomization,
- **CONCLUSION AND RELEVANCE:** Among adults requiring mechanical ventilation and receiving early enteral nutrition, the absence of gastric volume monitoring was not inferior to routine residual gastric volume monitoring in terms of development of VAP

- Isr Med Assoc J. 2010 Sep;12(9):543-8.
- **A simplified approach to the management of gastric residual volumes in critically ill mechanically ventilated patients: a pilot prospective cohort study.**
- Soroksky A[1], Lorber J, Klinowski E, Ilgayev E, Mizrachi A, Miller A, Ben Yehuda TM, Leonov Y.

- **BACKGROUND:** Enteral nutrition in the critically ill patient is often complicated by gastrointestinal intolerance, manifested by a large gastric residual volume. The frequency of GRV assessment and the intolerant level above which feeding is stopped is controversial.
- **OBJECTIVES:** To evaluate a novel approach to EN by **allowing high GRV and once-daily assessment that was correlated with the paracetamol absorption test.**
- **METHODS:** We conducted a pilot prospective study in an 18 bed general intensive care unit. The study group comprised 52 consecutive critically ill mechanically ventilated patients. Enteral nutrition was started at full delivery rate. Once-daily assessment of GRV with three consecutively repeated threshold volumes of 500 ml was performed before stopping EN. The paracetamol absorption test was performed and correlated to GRV**. Patients were divided into two groups: low GRV (< 500 ml) and high GRV (at least one measurement of GRV > 500 ml).** Clinical outcome included maximal calories delivered, incidence of pneumonia, ICU length of stay, and ICU and hospital mortality.
- **RESULTS:** There were 4 patients (9.5%) with ventilator-associated pneumonia in the low GRV group and 3 (30%) in the high GRV group (P = 0.12). **GRV was inversely correlated to paracetamol absorption; however, neither GRV nor paracetamol absorption was associated with the development of pneumonia.** Both groups had similar ICU length of stay (11.0 +/- 8.2 vs. 13.8 +/- 14.4 days, P = 0.41), and similar ICU (21% vs. 40%, P = 0.24) and hospital mortality (35% vs. 40%, P = 1.0).
- **CONCLUSIONS:** In critically ill mechanically ventilated patients, allowing larger gastric residual volumes, measured once daily, enables enteral feeding with fewer interruptions which results in high calorie intake without significant complications or side effects

- The current first line treatment for feed intolerance is prokinetic medication - results are disappointing.
- Pyloroplasty (by endoscopy or surgery) emerges as a promising drainage procedure for refractory gastroparesis.
- Gastroparesis, idiopathic or neurogenic, may be transient.
- Three case histories illustrate the spectrum of etiologies, diagnostic workup, therapeutic challenge and variable success in the management of chronic feed intolerance.

- **Normal Gastric Emptying**

- The proximal stomach serves as the reservoir of food, and the distal stomach as the grinder.[11] The physical nature, particle size, and fat and caloric content of food determine its emptying rate.

- Non-nutrient liquids empty rapidly; the rate is fastest when there is a large volume. If there are increased calories in the liquid phase of the meal, emptying is relatively constant over time,[11,12] with a maximum rate of 200 kcal per hour.[12]

- Solids are initially retained in the stomach and undergo churning[13] while antral contractions propel particles toward the closed pylorus. Food particles are emptied once they have been broken down to approximately 2 mm in diameter. Thus, solids empty during two phases over 3 to 4 hours: an initial lag period (during which retention occurs), followed by a phase of relatively constant emptying.[11]

Gastroparesis:

- Approximately 25% of cases are associated with diabetes,
- nearly 50% are classified as idiopathic - many of these latter cases likely represent a postinfectious process.

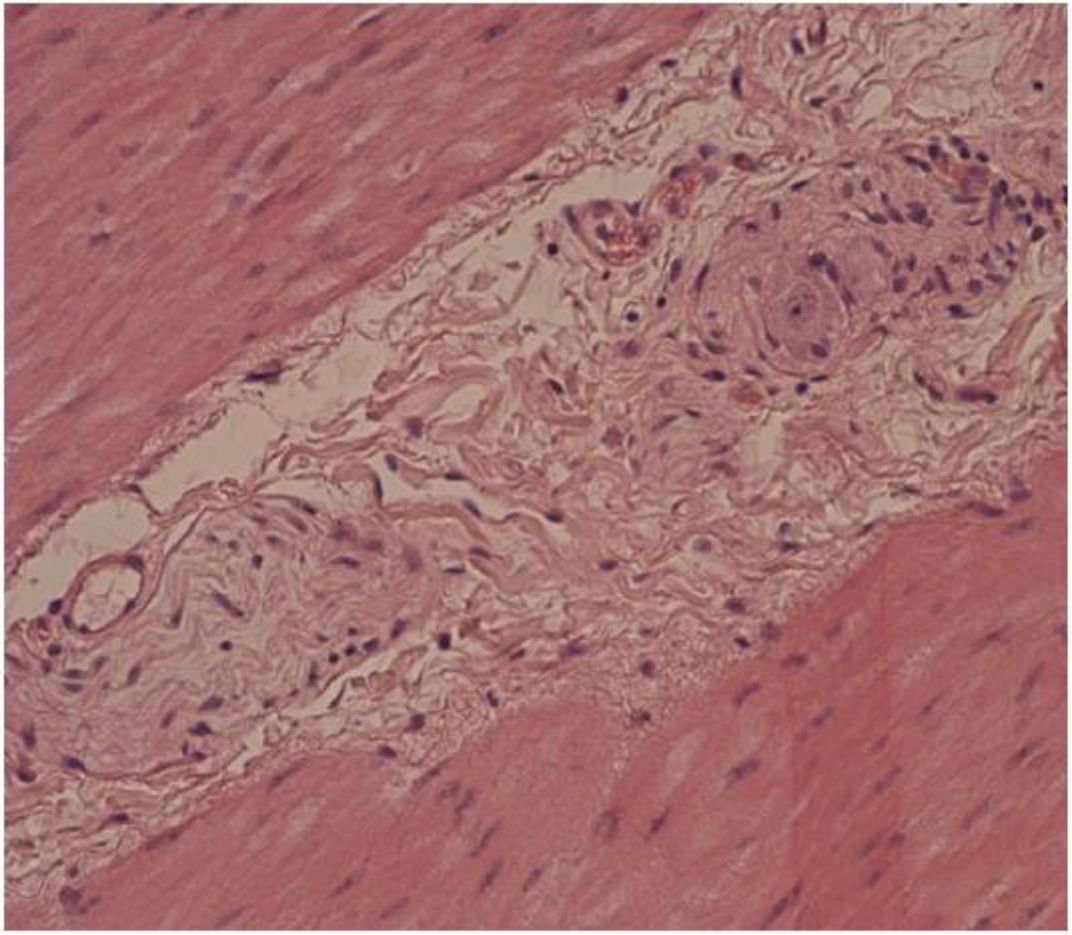
- Connective tissue disorders, autoimmune disorders, priorgastric surgery, ischemia, and medications make up the vast majority of the remaining cases.

Paraneoplastic gastroparesis?

- A disorder occurring at a distance from the tumor, caused by the tumor through circulating proteins, cytokines or other mediators, potentially reversible after cure of the neoplasia.

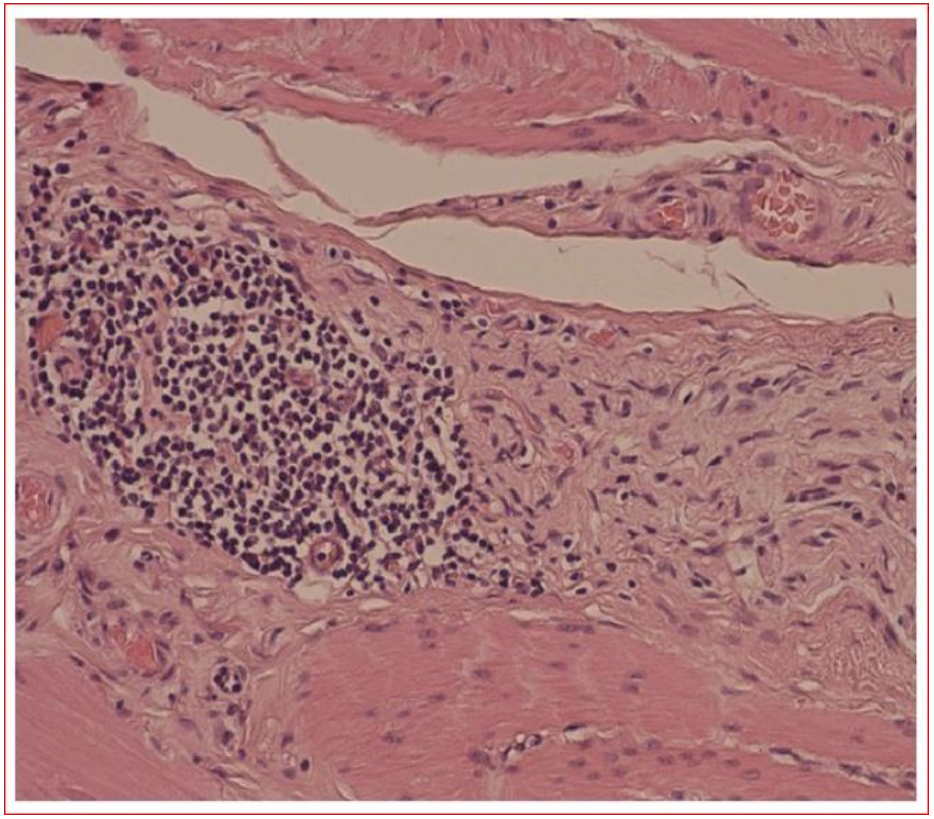
Argyriou KN, Peters M, Ishtiaq J, Enaganti S. **A Rare Case of Paraneoplastic Syndrome Presented with Severe Gastroparesisdue to Ganglional Loss.** Case Rep Med. 2012;2012:894837.

- Gastroparesis is the result of an **autoimmune destruction of the nerve plexus of the stomach** that causes nonspecific gastrointestinal symptoms such as intractable vomiting and abdominal discomfort that interfere with patients' quality of life and are often ascribed to psychological factors.
- We present the case of a 70-year-old Caucasian female who presented in our hospital with severe gastroparesis that was later proven to be associated with an overt small cell lung cancer (SCLC)



Intermesenteric plexus of a normal stomach. Normal nerve and a ganglion cell. (Haematoxylin-Eosin, ×200).

Pathogenesis of paraneoplastic gastroparesis

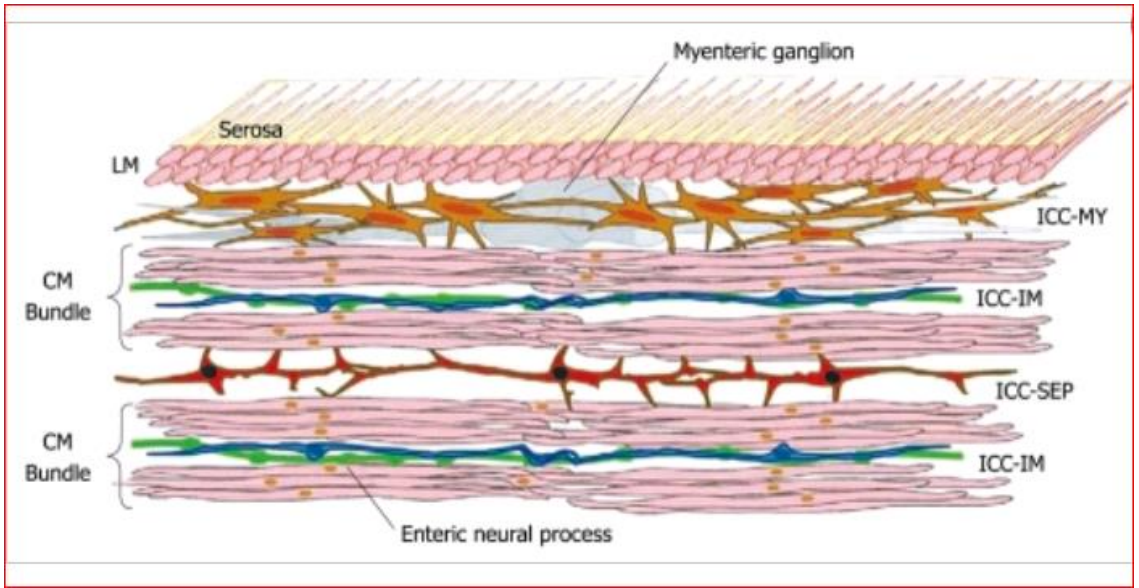


Intermesenteric plexus of the abnormal stomach. Nerve infiltrated by lymphocytes and devoid of ganglion cells. (Haematoxylin-Eosin, ×200).

Argyriou KN, Peters M, Ishtiaq J, Enaganti S. A rare case of paraneoplastic syndrome presented with severe gastroparesis due to ganglional loss. *Case Reports in Medicine*. 2012;2012:4 pages.894837

Chopin’s case

- Paraneoplastic ?
- Does not match the definition of a PNS, since the disorder occurs by direct involvement by tumor
- Destruction of the gastric nerve plexus by tumoral invasion – a hypothesis



- משקל חודש אפריל: 63.5 ק"ג. BMI=26.1 - בטווח הנורמה. ישנה עליה קלה במשקלה במהלך 3 החודשים האחרונים.
- בבדיקות דם מה- 14/4: אוריאה- 67, **אלבומין- 3.2,** TP- 6.1.
- **מקבלת נפח הזנה קטן, בשל בעיות של אספירציות על רקע רפלוקס**, דרך PEG, **שולבת אוסמולייט וג'ביטי** בנסיון להיטיב עם היציאות:
- 2 פחיות אוסמולייט (237 מ"ל*2) + 2 פחיות ג'ביטי (237מ"ל*2) +3 כפות הדסה שייק (15 גר* 3) + 6 מנות הדסה ווי (15 גר* 3) + 1000 מ"ל מים (250 מ"ל מים* 4).
- **בקצב טפטוף איטי של 33 טיפות/ דקה : כ-1400 קק"ל**
- (22.5 קק"/ק"ג נוכחי), כ-85 גר חלבון (1.37 גר/ק"ג נוכחי) וכ-1796 מ"ל מים (29 מ"ל/ק"ג נוכחי). N:NPC- 1:78.

להמשך באותה תוכנית הזנה, כולל מעקב אחר יציאות, שקילות חודשיות ובדיקות דם. מעקב חוזר בעוד כחודש

Feed intolerance in palliative care

- **Feed intolerance manifests** with early satiety, vomiting, feed reflux or regurgitation, and pulmonary aspiration

The “vomiting center” is not anatomically discrete but the initiation of the vomiting reflex is controlled by a complex system of networks located in the brainstem

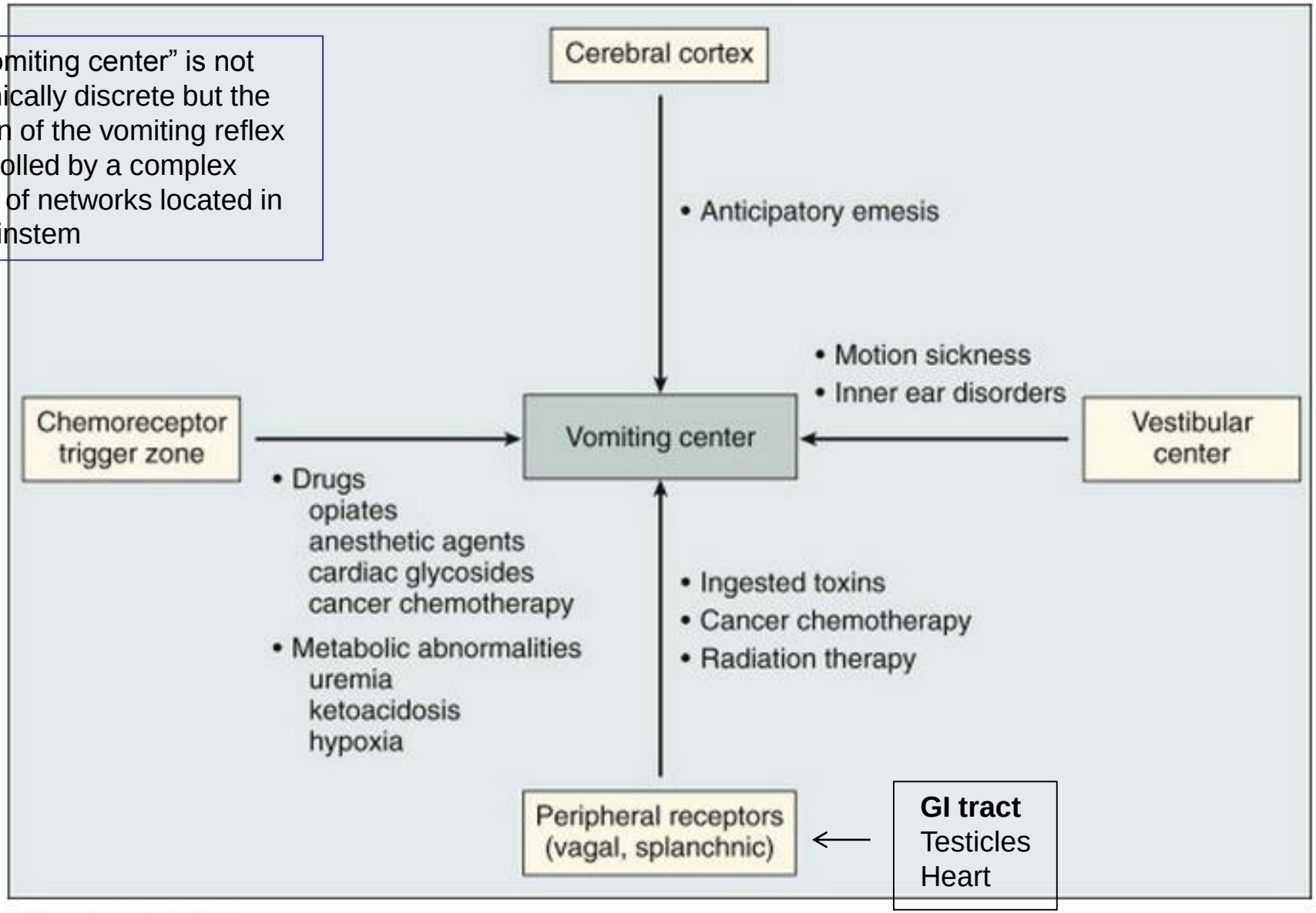


Figure 42-1

Schematic diagram of the various pathways for initiation of the vomiting reflex. Clinical syndromes mediated by each mechanism are illustrated.

- When gastrointestinal motility is impaired (acute or chronic dysmotility) naso-gastric **feeding is not tolerated.**

- Furthermore, antro-pyloro-duodenal as well as intestinal motilities during both fasting and fed stage are also frequently impaired in these patients, therefore **routine use of post pyloric feeding is not recommended**

Nguyen NQ. Pharmacological therapy of feed intolerance in the critically ills. World J Gastrointest Pharmacol Ther. 2014;3:148-155.

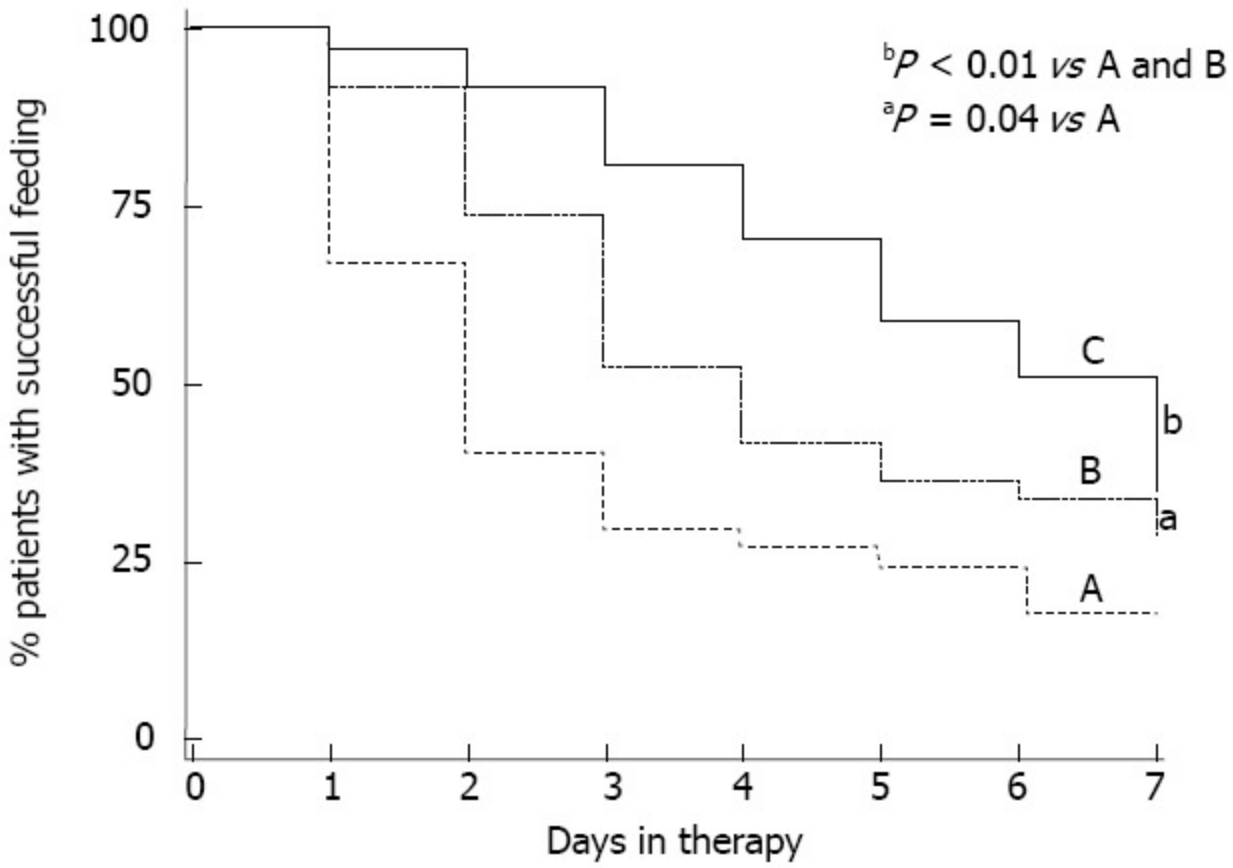
- **The current first line treatment for feed intolerance** is prokinetic therapy with erythromycin and metoclopramide (alone or in combination), which are highly effective and free of significant adverse effects.

- Although diarrhea occurs commonly after combination prokinetic therapy, it is not associated with Clostridium difficile colitis and settled shortly after stopping the treatment.

- The use of prokinetic therapy over a long period must be avoided.

- **Metoclopramide [10 mg x 4/day *iv*]** has been shown to improve feed intolerance during critical illness but its therapeutic efficacy declines progressive over the 7 d (from 85% in the first days of therapy to less than 35% after 7 d of treatment[32]. Metoclopramide, however, is not effective[33] and, in fact, contraindicated[34] in patients with brain injury, as it can raise intracranial pressure further.

- **Erythromycin** is the only available motilin agonist uses in clinical practice. Given at a low dosage, ranging **between 3 to 7 mg/kg per day**, erythromycin has been shown to increase both gastric emptying and improve feed intolerance in critically ill patients. Low dose erythromycin (**200 mg x 2/day**) was found to be more efficacious than metoclopramide



Efficacy of metoclopramide (A), erythromycin (B) and combined erythromycin and metoclopramide (C) in the treatment of feed intolerance of critical illness over 7-d period.

Feed intolerance

Three case histories from Bait Balev Nesher

	PALLIATIVE CARE [hospice]	
	VEGETATIVE STATE [PERSISTENT]	10/08/2014
	TRIGEMINAL NEURALGIA - RIGHT [S/P neurosurgery, MICROVASCULAR DECOMPRESSION]	10/08/2014
	S/P CRANIOTOMY [EVD INSERTION' RT. FRONTAL BURR HOLE]	19/08/2014
	VENTRICULOSTOMY - RIGHT	23/08/2014
	TRACHEOSTOMY	20/08/2014
	JEJUNOSTOMY gastrostome]	13/11/2014
	DIARRHEA [CDT and CDA positive]	16/12/2014
	ASPIRATION PNEUMONIA - LEFT	21/11/2014
	MECHANICAL VENTILATION	
	URETERAL CATHETERIZATION	
	URINARY RETENTION	
	INJURY OPEN WOUND ABDOMINAL WALL [surgical]	
	KLEBSIELLA PNEUMONIA [September 2014]	
	CONJUNCTIVITIS ACUTE	17/11/2014

	דרך מתן	התרופה	מינון	ימים	ת.התחלה	שעות	ת.סיום
	P.G	HADASSA WHEY	7.5g X3		23/12/2014	06:00, 12:00, 18:00	
	P.G	OSMOLITE HN	237ml X4		23/12/2014	06:00, 12:00, 18:00, 22:00	
	P.G	FLAGYL [METRONIDAZOLE 250mg]	500mg X3		23/12/2014	06:00, 12:00, 18:00	05/01/2015
	טפטוף	DEXAMYCIN [DEXAMETHASONE 1mg, NEOMYCIN SULPH 5mg]	1DRP X3		22/12/2014	08:00, 12:00, 18:00	28/12/2014
	P.G	HADASSA SHAKE VANIL	15g X3		14/12/2014	06:00, 12:00, 18:00	

Palliative gastric bypass surgery – to be implemented?

Table III. Studies that compared palliative resection and bypass surgery.

	Reinders et al. 1995 [46]		Lillemoe et al. 1996 [47]		Kuhlmann et al. 2005 [48]	
Study	**Resection *n*=36**	**Bypass *n*=24**	**Resection *n*=64**	**Bypass *n*=62**	**Resection *n*=80**	**Bypass *n*=90**
Median tumour size (cm)	4.30	4.25	3.6	NS	2.9	3.5
Morbidity (%)	44	33	42	32	41	31
Hospital mortality (%)	3	0	1.6	1.6	0	2
2-year survival (%)	24	2	16	8	24	2
Hospital stay (days)	25	18	18	15	16	10
Chemoradiation (%)	17	17	78	48	14	44

NS, not stated in the article.

- To palliate obstructive jaundice, a biliary bypass should be performed **on relatively fit patients.** In addition to the biliary bypass, gastric bypass should be performed routinely to prevent gastric outlet obstruction due to tumor ingrowth or compression of the duodenum.

  Mann CD et al. Combined biliary and gastric bypass procedures as effective palliation for unresectable malignant disease. ANZ J Surg 2009;79:471-475.

- 26.7- דו"ח דיאטנית: המטופלת אוכלת בכמויות קטנות, לפי יכולותיה והעדפותיה. משיחה עם המטופלת ניכר כי חל שיפור בתיאבון בשבועיים האחרונים. קיים שיתוף פעולה טוב עם העשרות: איזימילק (125 מל*2), הדסה ווי (7.5 גר*2), מעדנים וארוחה חלבית בצהריים (אוכלת בחדרה). לבקשתה תקבל בנוסף גבינת צפתית בארוחת הצהריים (חלבית). המשך מתן מענה תזונתי לפי יכולותיה והעדפותיה של המטופלת. מעקב חוזר בעוד כחודשיים.

Non-calorie liquids empty from the stomach more quickly than calorie liquids

Gastric emptying in the elderly Soenen S, Rayner CK, Horowitz M, Jones KL. Clin Geriatr Med 2015;31:339-353.