Paradigm shift of Digestive disease spectrums in Bangladesh and emerging countries: Challenges for an Internist

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- The market based economy of Bangladesh is the 44th largest in the world in nominal terms, and 32nd largest by purchasing power parity.
- Bangladesh is classified among the next emerging market of economies.
- According to the IMF, Bangladesh's economy is the second fastest growing major economy of 2016, with a rate of 7.1%.
- Financial sector of Bangladesh is the second largest in the subcontinent

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- This progress has brought a rapid epidemiological and demographic transitions.
- In 1980, 7% of adults and 3% of children were overweight or obese. In 2013, those rates had climbed to 17% for adults but only 4.5% for children.
- In developed countries, increases in obesity that began in the 1980s and accelerated from 1992 to 2002 have slowed since 2006. Conversely, in developing countries like Bangladesh increases are likely to continue.

Global Burden of Disease (GBD) study.2014: 11-1734

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Pathway to Obesity

- Socio economic developments
- Changes in life style
- Rapid urbanization
- Change of food habit
- Processed food
- Lack of mobility

Impact of Obesity: Digestive and Liver disease

- Significant associations between obesity and a number of gastrointestinal disorders in a large sample population in various developing countries.

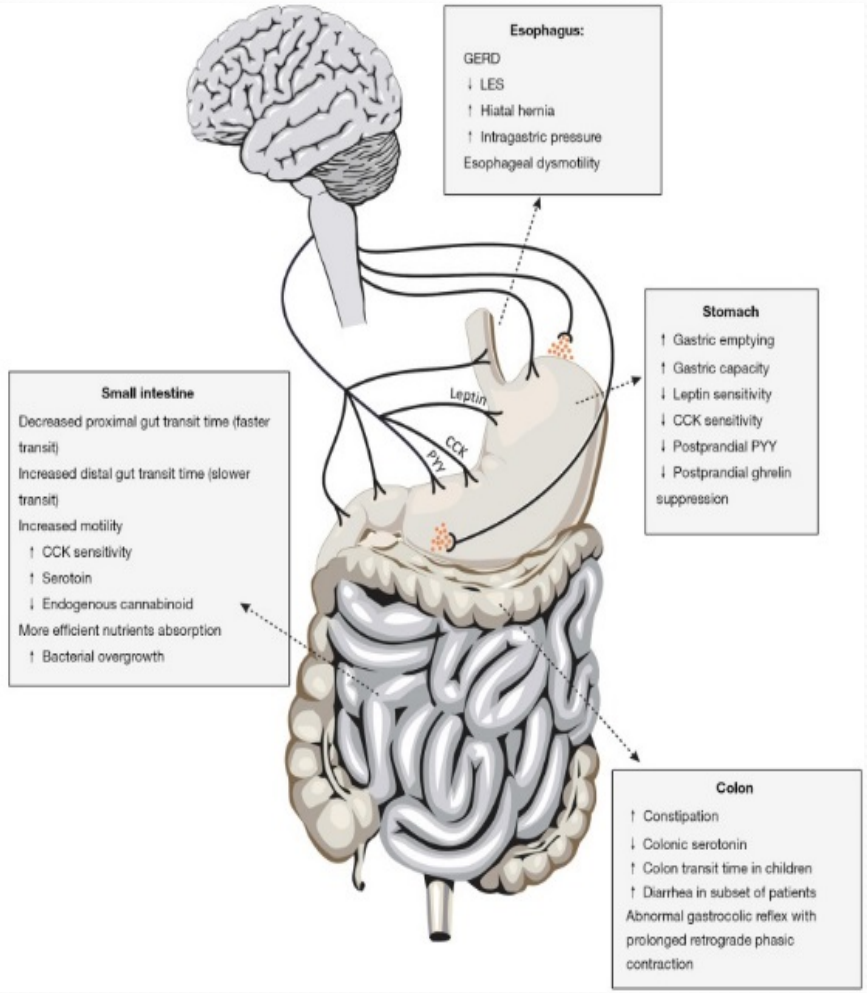
- Reflux esophagitis and hiatal hernia were strongly related to obesity (BMI > 25). In particular, obesity with young male was a high risk for these diseases.
- On the other hand, it has been reported that obesity is also associated with Barrett's esophagus and colorectal adenoma; however, obesity was not a risk factor for these diseases in our study.
- The difference of ethnicity of our subjects may partly explain why we found no data to implicate obesity as a risk factor for Barrett's esophagus.
- Arterial sclerosis associated with advanced age and hyperglycemia was accompanied by an increased risk of colorectal adenoma.

Impact of Obesity: Digestive and Liver disease

- Increase Incidence of Pancreatic and colorectal neoplasm.
- Significant Increase incidence of Functional Gastrointestinal disease.
- Increase in Inflammatory Bowel disease
- Increase in Non Alcoholic Fatty Liver Disease

Gastroenterology Research and Practice
Volume 2013 (2013), Article ID 760574

Obesity and GI motility



Obesity and GI motility

- Gastrointestinal motility is closely linked to the rate at which nutrients become systemically available.
- Regulation of gastric emptying represents the most important brake against delivery of nutrients to the intestine in excess of digestive and absorptive capacity.
- In man, gastric emptying is slowed in proportion to the energy density of the meal, which will level out the rate of energy delivery to the duodenum.
- Studies suggest a more rapid gastric emptying in obesity, although the opposite has been reported in some experimental settings.
- Gastric volume is larger in obese individuals and appropriate satiety signals are not triggered in response to gastric distension.
- Postprandial intestinal transit time in obesity is similar to that in normal-weight subjects, however, despite this fact, intestinal absorption of nutrients is more efficient in obesity.

J Intern Med. 1995 Apr;237(4):411-8.

Obesity and GI Motility

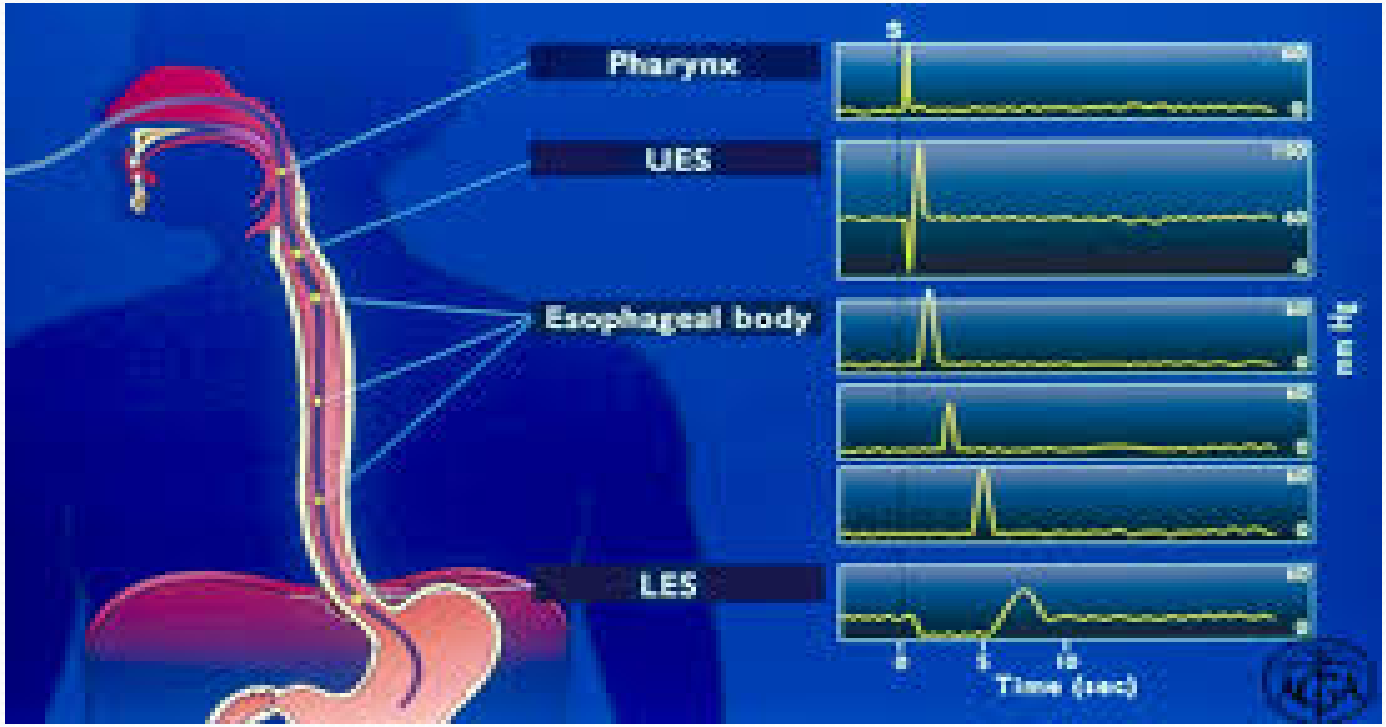
- Several regulatory mechanisms for gastrointestinal motility, such as the autonomous and enteric nervous systems and gastrointestinal regulatory peptides, are also of importance for feeding behavior and metabolism.
- Dysfunction of the autonomous nervous system has been observed, the sensitivity to cholecystokinin is decreased in obesity, and plasma concentrations of somatostatin and neurotensin are lower than in normal-weight subjects.
- These changes in regulatory mechanisms favor rapid gastrointestinal transit of ingested nutrients and promote rapid intestinal absorption in obesity and decreased satiety in response to ingested food.
- It is presently not known whether the observed changes in gastrointestinal motility in obesity represent a primary feature linked to the pathogenesis of such disease.

J Intern Med. 1995 Apr;237(4):411-8.

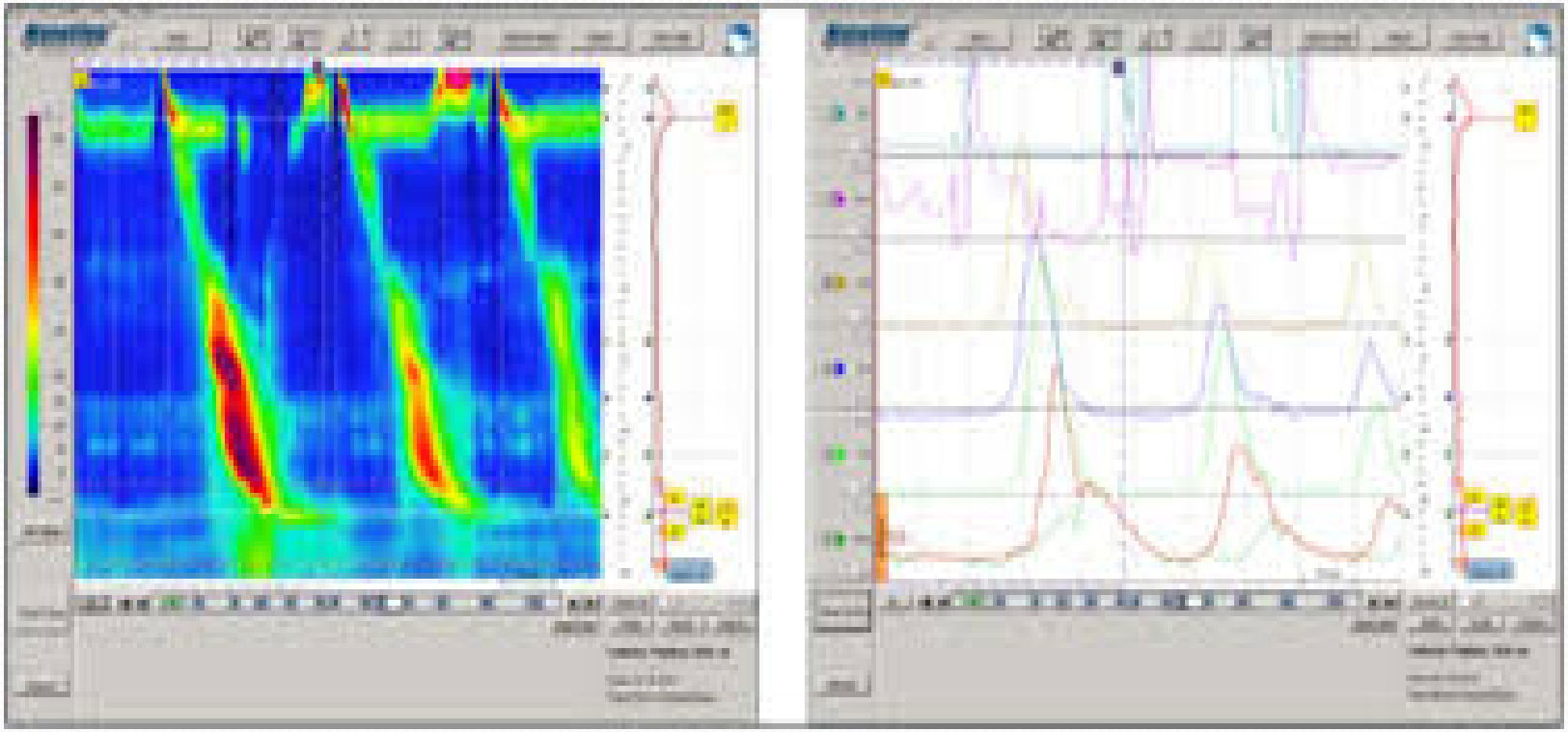
Esophageal Manometry with Impedance

Esophageal manometry (EMS) with Impedance

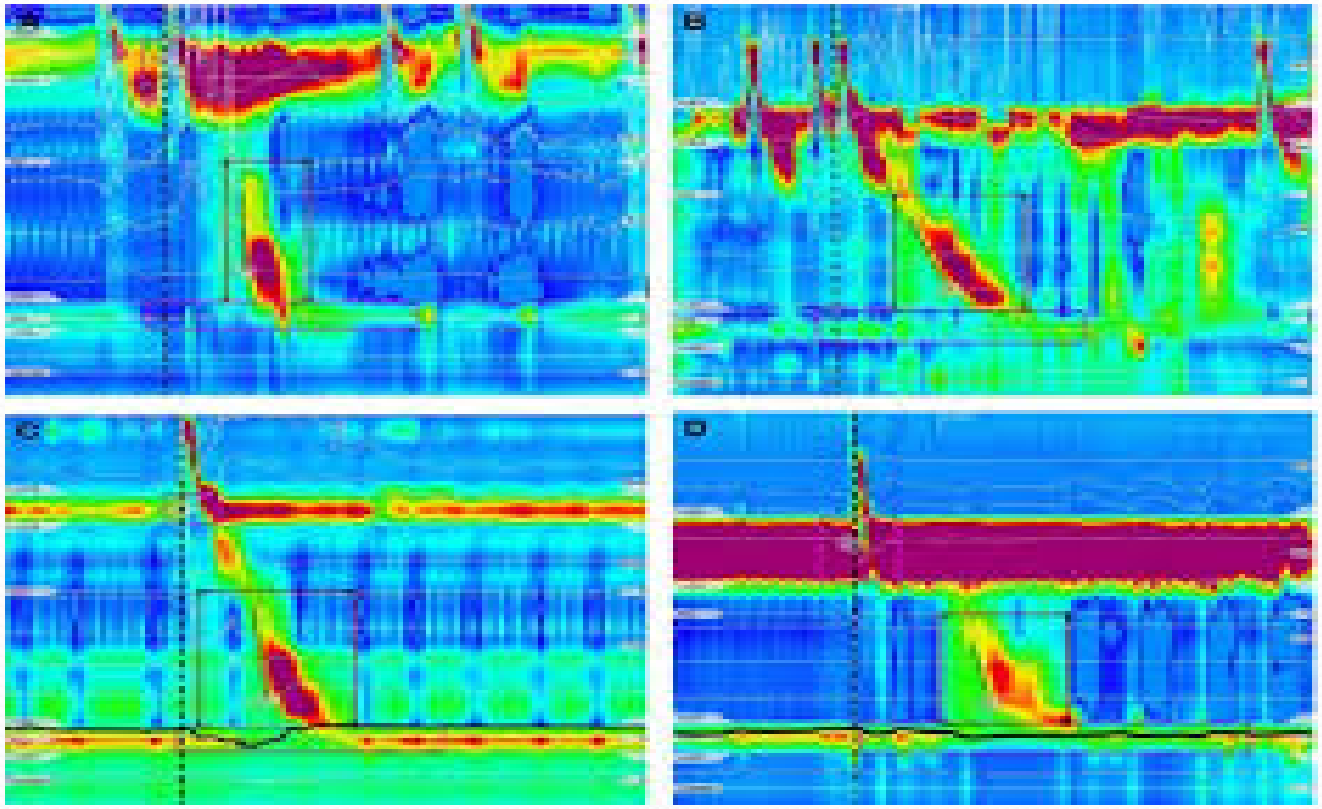
EMS



EMS and Impedence



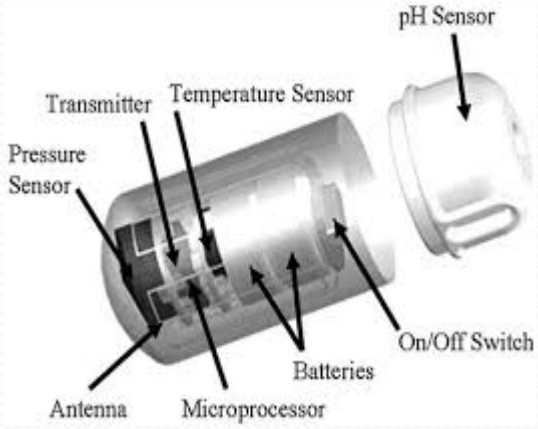
Impedance



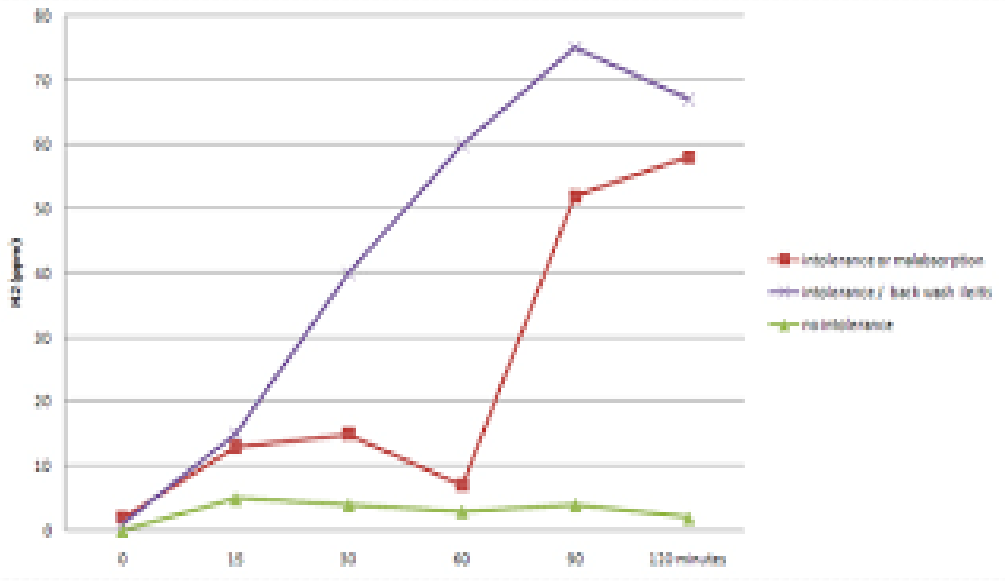
Gi motility and Obesity

Smart Pill

Smart Pill

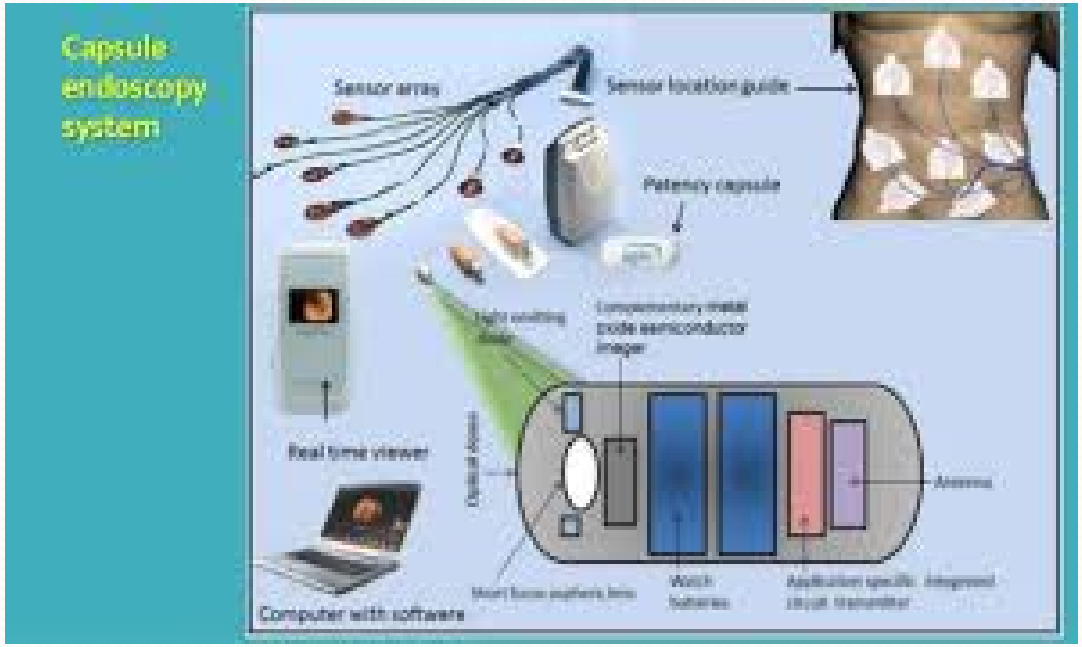


Smart Pill



Capsule Endoscopy

Capsule Endoscopy



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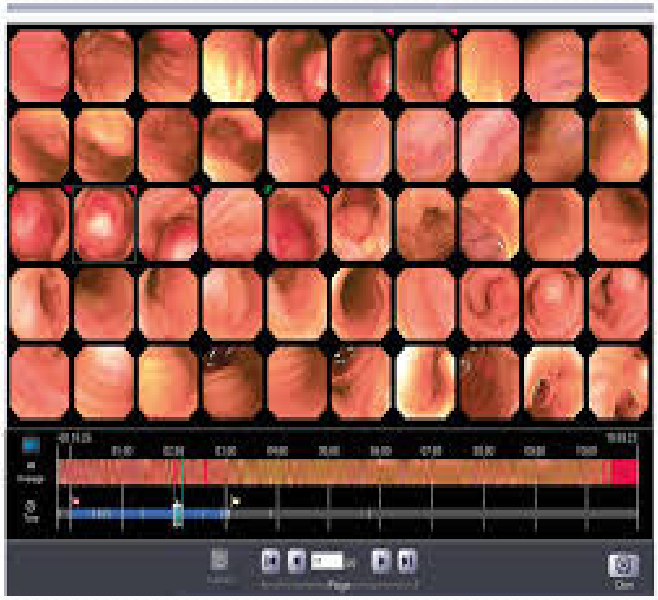
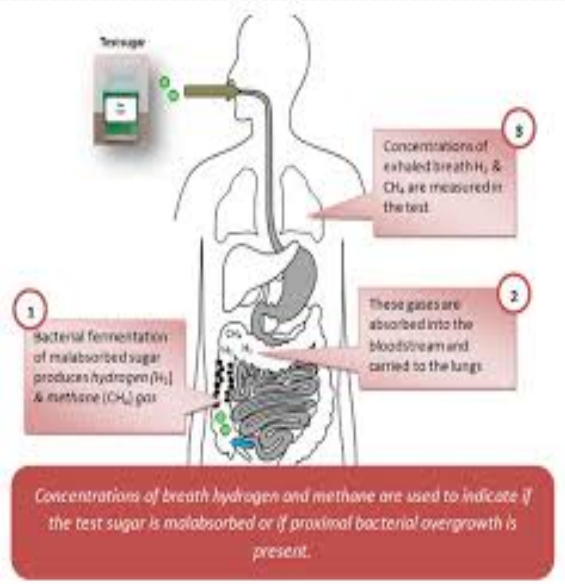
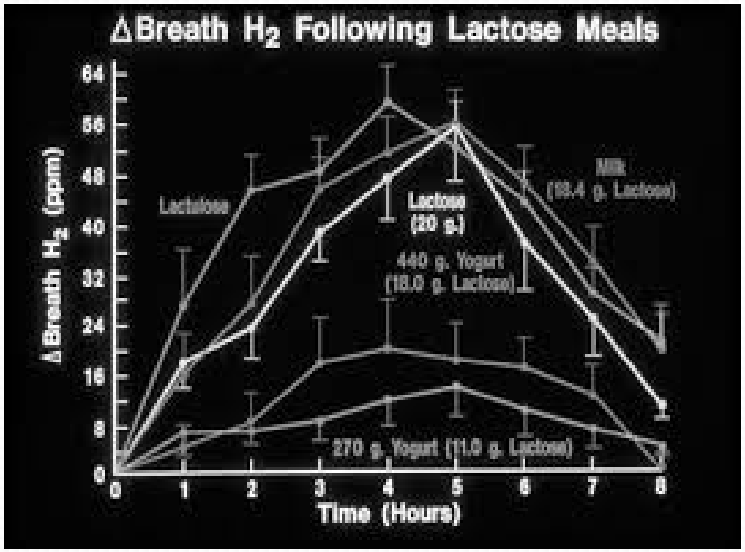


Breathing test : H Pylori, Motility, malabsorption and Bacterial overgrowth



Breathing test : H Pylori, Motility, malabsorption and Bacterial overgrowth

Figure 3. Urea Breath Test Instrumentation
$^{13}CO_2$ levels are collected and measured before (blue pouch) and after (pink pouch) ingestion of ^{13}C-labeled urea.



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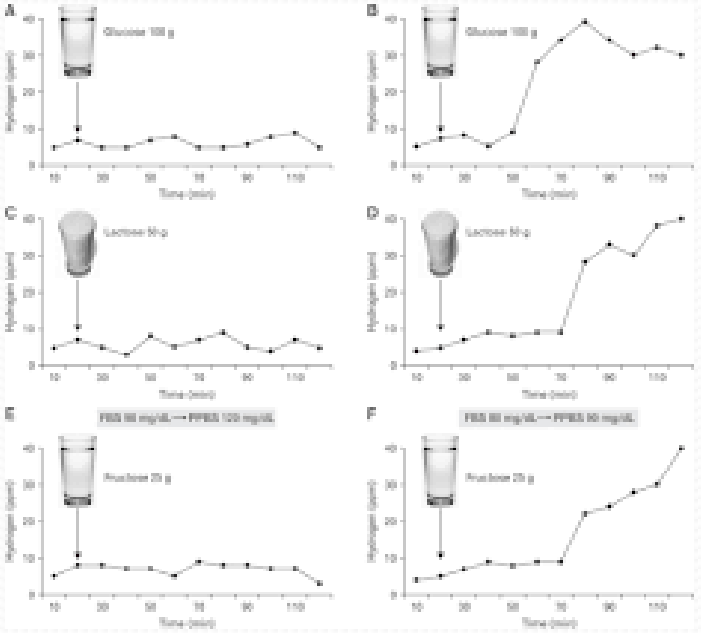

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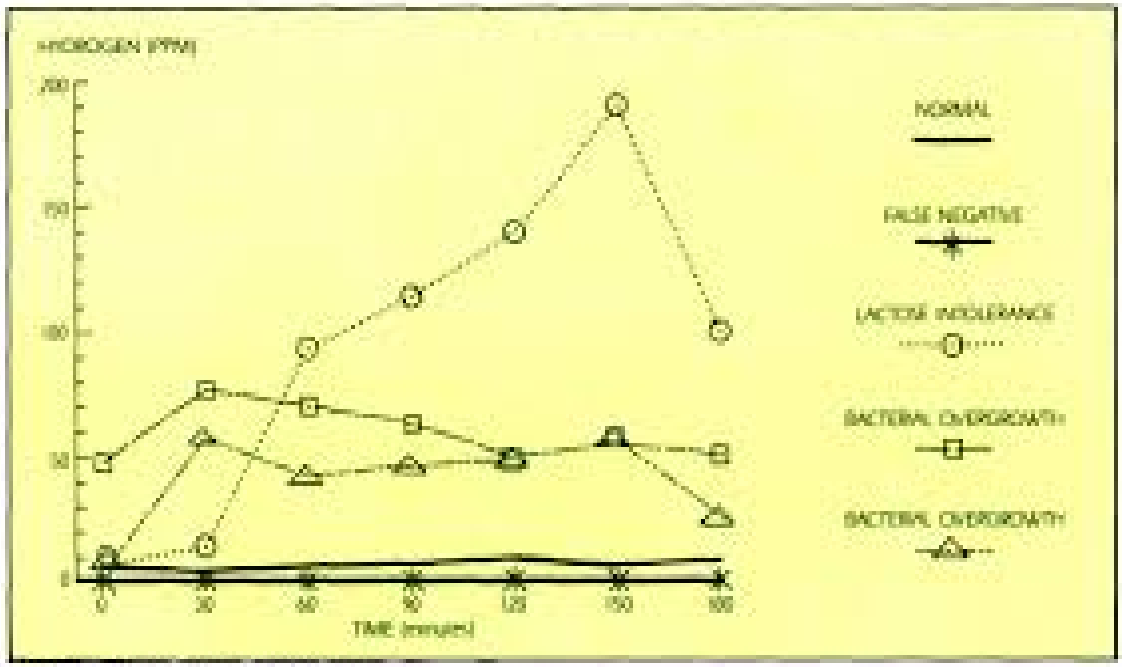


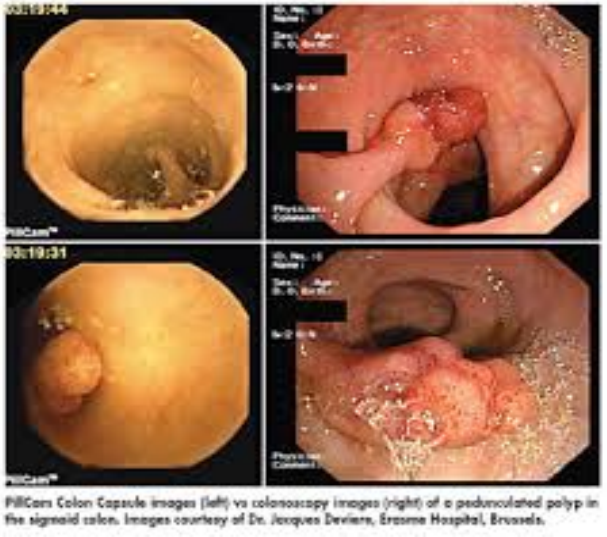
Figure. Lactose Breath Hydrogen Test

IRRITABLE BOWEL SYNDROME

- Studies have shown a significant increase in some IBS symptoms (constipation, diarrhea, straining, and flatus) in obese patients
- One study demonstrated a threefold increase in the risk of IBS with obesity

Amer J of Gastro 1994

Colon Capsule Endoscopy



PillCam Colon Capsule images (left) vs colonoscopy images (right) of a pedunculated polyp in the sigmoid colon. Images courtesy of Dr. Jacques Devriere, Erasme Hospital, Brussels.

Esophageal Disease

- GERD – Increased risk ranging from 1.5- to 3-fold

Am J Medicine 1999 Alimentary Pharmicological Therapy 2004

GERD-related complications – Erosive esophagitis • Association examined in multiple case-control, cross-sectional,and cohort studies

Positive association with adjusted odds ratios ranging from 1 to 2.1 in overweight and 1.6 to 14.6 in obese patients

Am J Gastroenterology1999 Gastroenterology Clin North America 2005

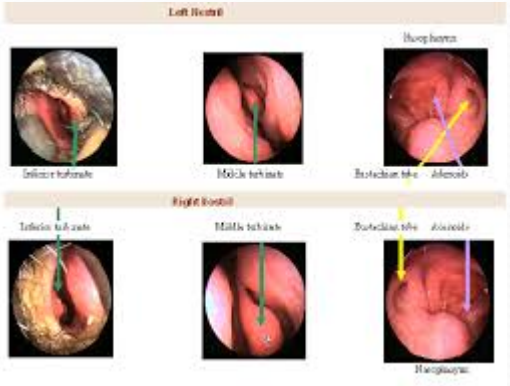
Esophageal Disease

- GERD-related complications – Barrett esophagus : 2 fold increase associated with GERD.
- Esophageal adenocarcinoma : Pooled studies demonstrate a 2.1-fold increase in the overall risk of esophageal adenocarcinoma in patients with a BMI greater than 25 compared to subjects with a normal BMI

Gastroenterol Clin North Am 2005 J Natl Cancer Inst 1995 J Natl Cancer Inst 1998

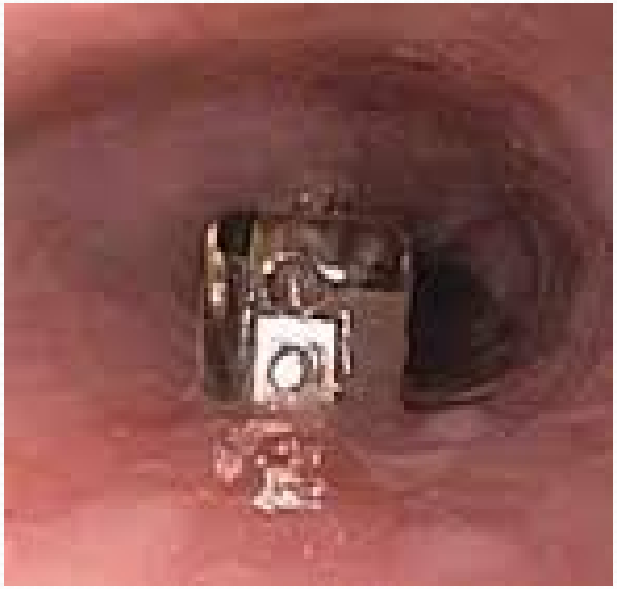
Transnasal Endoscopy

Transnasal Endoscopy

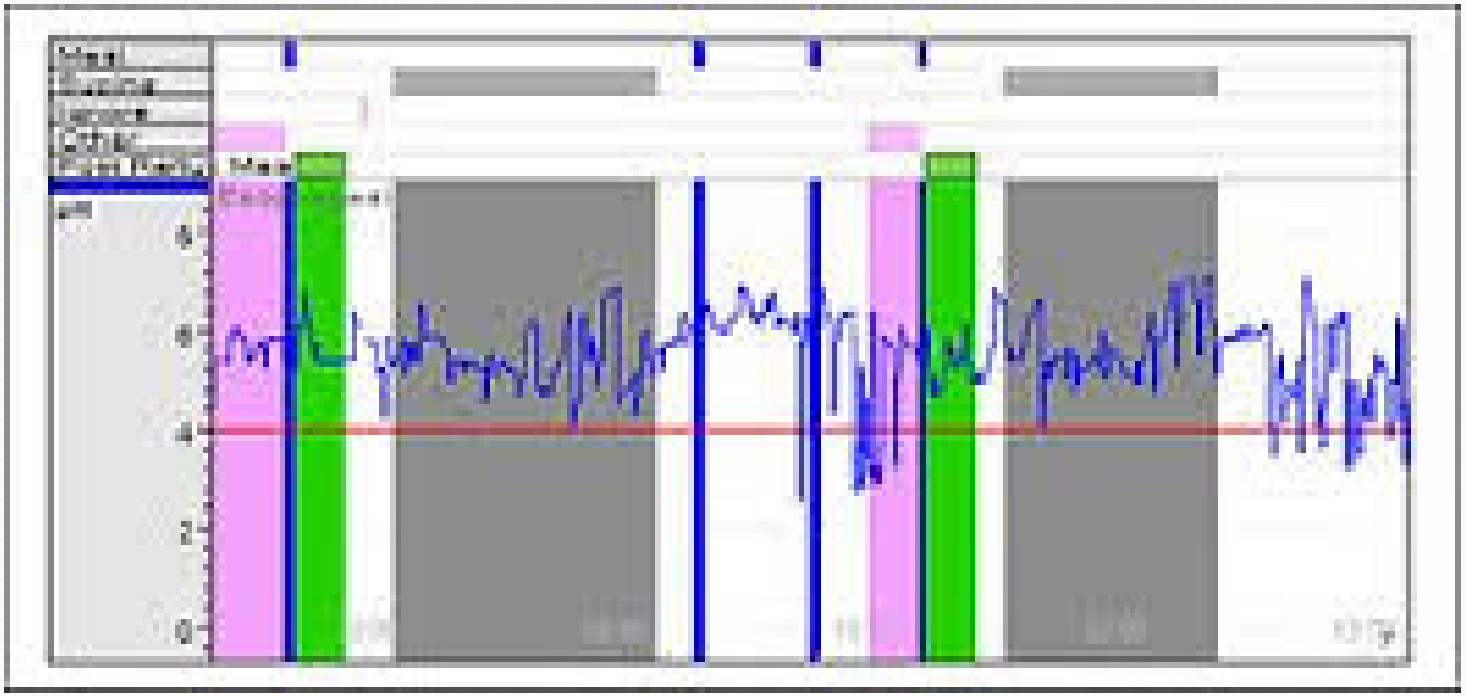


Bravo Ph Probe

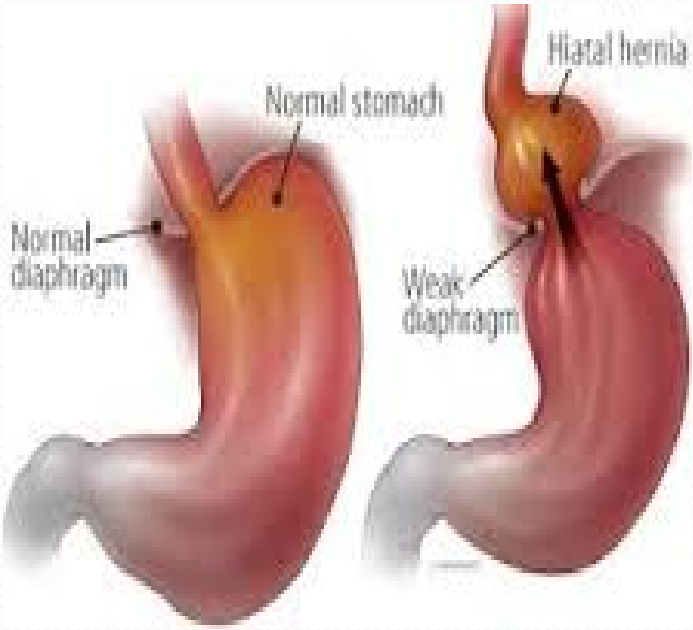
Bravo Ph Study



Bravo Ph study



Hiatal Hernia and LINKS



Gallbladder Disease

- Obesity is an important risk factor for gallbladder disease
- Risk for symptomatic gallstones increases linearly with BMI – Increase in risk for symptomatic gallstones was noted in women
- Two fold with BMI greater than 30
- Seven fold with BMI greater than 45 Nurses Health Study

Am J Clinical Nutrition 1992

Gallbladder Disease

- Risk for symptomatic gallstones increases linearly with BMI – Increase in risk for symptomatic gallstones was also noted in men
- Waist circumference > 40.4 in had a relative risk of 2.29

J Obes Relat Metab Disord 1999

- The mechanism of gallstone formation in obese individuals involves an increase in cholesterol saturation index and a decreased response to cholecystokinin

Clin Science 1985

GALLBLADDER DISEASE

- Risk of gallbladder cancer increases with gallstones –
- Obesity increases risk of cancer

PANCREATIC DISEASE

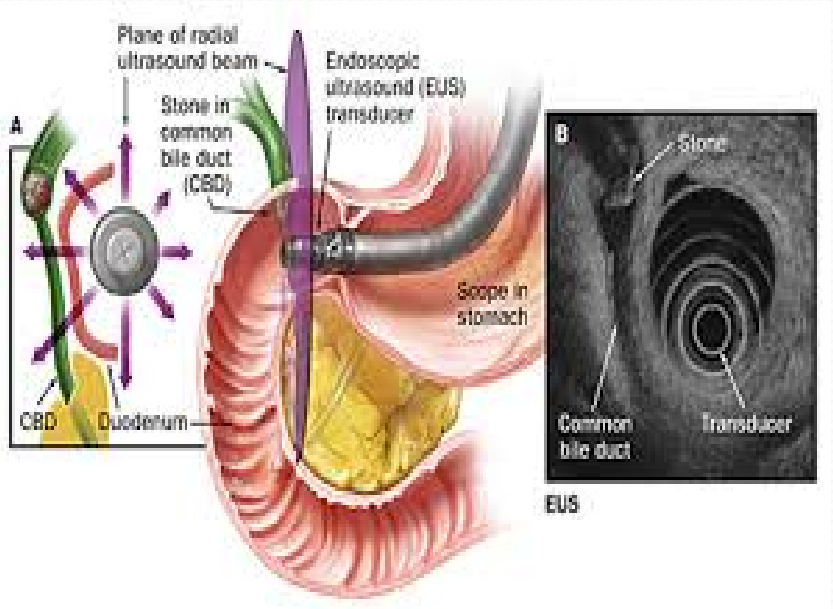
- Increase in risk of pancreatitis likely explained from increase in cholesterol stones and subsequent cholelithiasis
- Acute pancreatitis is more severe in overweight and obese subjects
- Increase in infectious complications and longer hospital stay in obese patients

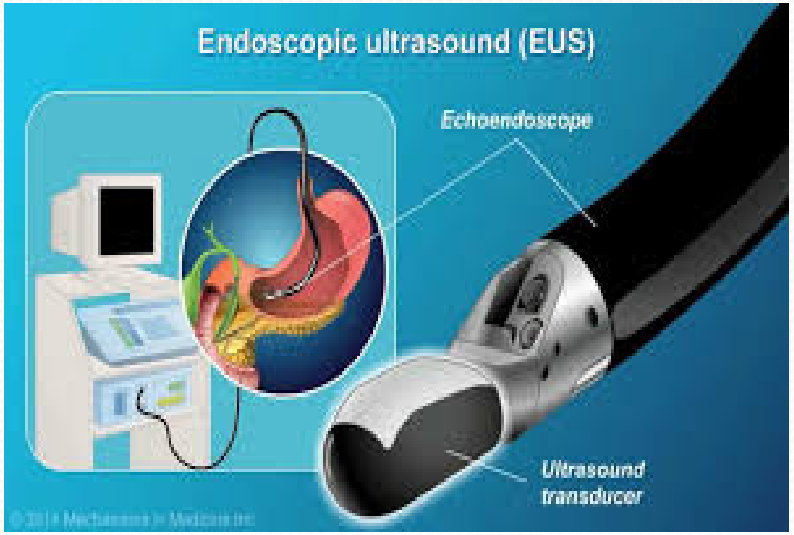
PANCREATIC DISEASE

- Obesity is associated with pancreatic cancer – It is uncertain whether this association is direct association or secondary to the relationship of obesity with diabetes
- Diabetes is an established risk factor for pancreatic cancer
- A meta-analysis estimated that obese subjects have a 20% increase in the risk of developing pancreatic cancer when compared to subjects with a normal body weight

Br J Cancer 2003

Endoscopic Untrasonogram





LIVER DISEASE

- There is an increase in prevalence of NAFLD with BMI increase in both genders and in all races
- Liver biopsies from morbidly obese individuals performed at the time of bariatric surgeries demonstrated NAFLD in over 80% of cases Obesity Surgery 2002
- NAFLD is the hepatic consequence of insulin resistance and the associated metabolic syndrome that leads to an overproduction of pro-inflammatory mediators

LIVER DISEASE

- ~20 % NAFLD can progress to nonalcoholic steatohepatitis (NASH)
- NASH is characterized by hepatocyte injury and death accompanied by infiltration of acute and chronic inflammatory cells
- ~20% NASH can progress to fibrosis with subsequent cirrhosis and death
- Hyperleptinemia plays a role in the occurrence of fibrosis by activating hepatic stellate cells (collagen formation)

LIVER DISEASE

- Transaminases and γ-glutamyl transferase are usually increased less than fourfold and do not correlate with the severity of disease
- Goal of therapy in subjects with NAFLD is to improve insulin sensitivity Dietary modifications – Pharmacological treatment – A gradual weight loss of 10% or more of body weight can correct abnormal liver chemistries and decrease hepatomegaly, fat content and histological features of steatohepatitis

LIVER DISEASE

- Obesity shortens survival in patients undergoing orthotopic liver transplant
- University of Maryland – 285 patients with liver transplants 2000-2008 –
- 2-yr and 5-yr survival among obese at 67% and 54%, respectively compared to 79% and 63% survival rates in non-obese

GI & Hepatology News 2011

Fibroscan

CAP
NEW
FibroScan touch 502
INNOVATION
in liver disease management

Fibroscan

Comparative Scoring Systems for Histologic Stage (Fibrosis)			
Score	**IASL**	**Batts-Ludwig**	**Metavir**
0	No Fibrosis	No Fibrosis	No Fibrosis
1	Mild fibrosis	Fibrous portal expansion	Periportal fibrotic expansion
2	Moderate fibrosis	Rare bridges or septae	Periportal septae (> 1 septum)
3	Severe fibrosis	Numerous bridges or septae	Portal-central septae
4	Cirrhosis	Cirrhosis	Cirrhosis

Table 2. FibroScan results

Variable	Degree of fibrosis		
	≥F2	≥F3	F4
Sensitivity	67%	73%	87%
Specificity	89%	91%	91%
PPV	95%	87%	77%
NPV	48%	81%	95%

PPV=positive predictive value; NPV=negative predictive value.

COLON DISEASE

- The risk of adenomatous colon polyps is also increased about two fold in obese individuals
- Higher in men than in women Gastroenterol Clin North Am 2005
- Several cohort and case–control studies demonstrate a positive association between obesity and colorectal cancer
- Men have an increased risk of ~ 1.5- to 3-fold Int J Obes Relat Metab Disord 2004 – Women have a weaker yet still positive association

Gut 2002