Medical Device Therapy for Obesity and Metabolic Disease – The Current Landscape

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Focus on Endoscopic Therapies for Primary Treatment

Devices will be mentioned to illustrate mechanisms
No endorsement intended for any devices or mechanisms
Not all devices will be reviewed
Obesity Trends (BMI ≥30) Among U.S. Adults

CDC.GOV
“Remember when we used to have to fatten the kids up first?”

Overweight boys
Percentage of 15-year-olds who are overweight 2001–02 selected countries

<table>
<thead>
<tr>
<th>Country</th>
<th>%</th>
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<tr>
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<td>7%</td>
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<td>France</td>
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<td>Italy</td>
<td>25%</td>
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<tr>
<td>Spain</td>
<td>34%</td>
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<tr>
<td>Canada</td>
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<td>USA</td>
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Overweight Girls
Percentage of 15-year-olds who are overweight 2001–02 selected countries

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<thead>
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<td>Canada</td>
<td>20%</td>
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<tr>
<td>USA</td>
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The Environment: Portion Size

1954
Burger King
2.8 oz
202 calories

2004

4.3 oz
310 calories

1955
McDonald's

1900
Hershey's
2 oz
297 calories
7 oz
1,000 calories

1916
Coca-Cola

6.5 fluid oz
79 calories
16 fluid oz
194 calories
Non-surgical Treatment for Obesity

Diet and exercise  (5 - 7% weight loss)

Behavioral therapy plus diet & exercise (10%)

Pharmacotherapy
- modest efficacy
- weight regain after stopping meds
- adverse effects
- uncertain long-term safety

After Stylopoulos, Aguirre GIE 2009; 70:1167-75
Surgery for Obesity
Restrictive Procedures

- Vertical Banded Gastroplasty (VBG)
- Adjustable Gastric Band (AGB)
- Sleeve Gastrectomy (SG)
- Gastric Imbrication (GI)

Surgery for Obesity
Restrictive and Malabsorptive Procedures

- Biliopancreatic diversion (BPD)
- Duodenal Switch (DS)
- Roux-en-Y Gastric Bypass (RYGB)
Weight Change after Surgery

**Figure 1.** Mean Percent Weight Change during a 15-Year Period in the Control Group and the Surgery Group, According to the Method of Bariatric Surgery. I bars denote 95% confidence intervals.

Rates of Remission of Diabetes

Adjustable Gastric Banding 38%
Roux-en-Y Gastric Bypass 84%
Biliopancreatic Diversion 98%

Buchwald H., JAMA 2004
RYGB: A Complex of 5 Operations
Gastric Bypass: Five Operations

1. Isolation of gastric cardia
Gastric Bypass: Five Operations

2. Exclusion of distal stomach
Gastric Bypass: Five Operations

3. Exclusion of duodenum and proximal jejunum
Gastric Bypass: Five Operations

4. Exposure of distal jejunum to undigested nutrients
Gastric Bypass: Five Operations

5. Partial vagotomy
Effects of Surgery on Diabetes

Potential Mechanisms

- Weight loss
- Decreased nutrient intake
- Changes in GI physiology or signaling
Weight and diabetes control after RYGB

« Distal mechanism – Hindgut theory »

Nutrients – fat, carbs, protein

L Cells

GLP-1, PYY, Oxyntomodulin

Hindgut theory – increased nutrients to distal gut

Effects on glucose homeostasis (incretins)
- ↑ Insulin secretion
- ↑ insulin sensing and sensitivity
- ↑ Beta cell mass
- ↓ Glucagon secretion

Effects on appetite and weight
- ↓ Gastric emptying
- ↓ Appetite
- ↓ Acid secretion

Weight and diabetes control after RYGB

« Proximal mechanism – Foregut theory »

Ghrelin

↓ Eaten

↑ Eating

Nutrients to the foregut

“Anti-incretins”

Foregut theory – bypass duodenal nutrient passage

Effects on glucose homeostasis
- ↓ Insulin secretion
- ↓ insulin sensing and sensitivity
- ↓ Beta cell mass

Effects on appetite and weight
- ↑ Gastric emptying
- ↑ Appetite
- ↑ Acid secretion

Rubino, F. Diabetes Care Feb 2008 Vol. 31 No. 2; S290-S296
Endoscopic Possibilities

- Bypass proximal duodenum and/or stomach
- Compartmentalize stomach/restrict volume
- Delay stomach emptying
- Mimic effects of surgery on weight and DM
EndoBarrier

- Alteration of gastric outlet
- Food goes down liner – duodenal exclusion
- Digestive juices go around liner
EndoBarrier System

- Anchor
  - Nitinol
  - Large proximal opening
  - Barbs in each direction
  - Retrieval drawstrings
- Sleeve
  - Impermeable fluoropolymer
  - 61 cm (2 ft) length
  - Radiopaque markers

Implant

Retrieval System

Co-axial Delivery Catheter
The present invention provides devices and methods for attachment of an implanted device, such as an artificial stoma device (202), a gastrointestinal sleeve device (200, 258, 278, 428, 458, 560) or an attachment cuff (214, 550, 570), within a patient's digestive tract for treatment of obesity. Special surgical fasteners (100, 130, 222, 240, 250, 276, 530, 542) provide a lasting and durable attachment to the gastrointestinal tissue without causing excessive pressure that could result in tissue erosion and detachment of the implanted device. Fastener delivery devices (150) that facilitate peroral placement and deployment of fasteners (100, 130, 222, 240, 250, 276, 530, 542) and secondary devices are also provided. Also described are implantable devices and attachment means (230, 234) that avoid causing excessive pressure within the tissue by having compliance that is compatible with the gastrointestinal tissues where it is attached.
Valentx Endo Bypass Sleeve

RYGB

Endo Bypass Sleeve

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Techniques for Reduction of Gastric Volume

- Balloons and bezoars
- Sewing
- Stapling
- Implants
Balloons and Devices to Fill Gastric Space
ReShape Duo
Delivery System
Spatz Balloon

- Adjustable
- Retrievable
- Prevents migration of balloon
- Visible on imaging
Full Sense Device
Full Sense™ Device - Evolution

First Generation Device with barbs

Second Generation Device without barbs

Initial Trial Device

Current Device
Some Sewing Tools

- NDO
- EndoCinch
- SafeStitch
- OverStitch
- StomaPhyx
- Spiderman
- G-Prox
- Eagle Claw
- TAS
Gastric restriction and Compartmentalization

EndoCinch concept (Swain 2002)

EndoCinch attempt

The TOGa System (Satiety)

**TOGa Sleeve Stapler**
- 54F (18mm) diameter
- Designed to use an 8.6 mm OD endoscope
- Direct visualization
- Creates stapled sleeve along lesser curve

**TOGa Restrictor**
- 45F (15mm) diameter
- Delivered alongside endoscope
- Creates stapled “pleats” at distal end of sleeve, restricting outflow
Sleeve Stapler inserted over guidewire, positioned on lesser curve.

Sail / septum deployed to spread tissue.

Vacuum applied to capture anterior and posterior tissue.

Stapler jaws closed and fired.

Result is stapled sleeve. Repeat to create longer sleeve, then use restrictor.
BaroSense Transoral Platform

- **TERIS (Transoral Endoscopic Restrictive Implant System)**

  Creates a Small proximal Pouch distal to the GE junction

  - Full thickness plication anchor points
  - Food Outlet
HourGlass Technologies developed an incision-free weight-loss procedure for morbidly obese patients. The left figure represents a stomach after the HourGlass procedure has been performed, featuring the same restrictive anatomy that is present with surgical gastric banding, as seen on the right.
Alteration of Gastric Motility

- BOTOX
- Neuromodulation
- Pyloroduodenal obstructing devices
BOTOX Injection

- In animal studies - delayed gastric emptying from antral injections

- Human studies showed variable results for antral injections

- Adding fundic injection in RCT:
  - wt loss 11 vs 5 kg; \( p<0.001 \)
  - BMI reduction 4 vs 2; \( p<0.001 \)
  - Delayed stomach emptying

Electrical Neuro-modulation

- Enteromedics
- Leptos Biomedical
- IntraPace
- MetaCure
- Medtronic (Transneuronix)

**Mechanisms:**
- increase satiety
- reduce appetite and food intake
- alter neuro-endocrine responses
- affect gastric and intestinal motility

Current surgical placement could evolve to endoscopic
Transpyloric Shuttle TPS™

Intermittent sealing of pylorus in concert with peristalsis may:

• Delay gastric emptying
• Induce early satiety
Entirely endoscopic ... Self-placing...
Non-anchored...Multi-year dwell
Endocore Pyloric Valve

ABSTRACT

A pyloric valve is provided for inhibiting the flow of chyme through the pyloric region of the gastrointestinal tract. The pyloric valve includes a blocking portion having a plurality of disc-shaped flanges connected in series. The blocking portion may be disposed in a contractual position whereas the plurality of disc-shaped flanges is disposed in a stacked configuration and a resting position wherein the plurality of disc-shaped flanges is disposed in a linear configuration. The pyloric valve may further include a sleeve that may have a beveled distal end. The pyloric valve may be constructed of silicon. Also provided are methods of inserting and removing the pyloric valve, which each include a step of manipulating the support between its resting and contracted positions. Insertion and removal systems are also provided for use with the pyloric valve.
Aspire Bariatrics

- Divert ingested nutrient flow out of the body
- BariAssist G-Shunt
Future Developments

- NOTES
- Capsules
Role of NOTES

• Compartmentalization
• Gastrojejunostomy
• Sleeve Gastrectomy

“Human transvaginal sleeve gastrectomy: initial experience”

Ramos AC, Zundel N, Neto MG, Maalouf M
Gastrojejunostomy

- The endoscope advanced into the peritoneal cavity
- A loop of jejunum identified and pulled into the stomach
The loop of jejunum is secured with sutures to the stomach
Incision made into the jejunal loop using a needle-knife
The open ends of the incision are secured to the gastric incision with a second line of sutures completing the gastrojejunostomy.
Bariatron Gastric Bypass Device
Currently Lap-Endo Hybrid Approach

Schurr MO, HO C, Rieber F et al.
Capsular Intragastric Balloon

(a) Deflated balloon

(b) Inflated balloon
Endolumenal Treatment for Obesity

More Expensive

Less Expensive

Surgery

Endoscopic Procedures

Medication

Diet and Exercise

More Effective

Less Effective
We anticipate the development of endoscopic treatments that will help manage our most recent human evolution...