Bariatric Surgery: Techniques and Mechanisms of Action
Walter J. Pories, MD, FACS
Professor of Surgery
and Biochemistry
Brody School of Medicine
East Carolina University
Bariatric Surgery: Techniques and Mechanisms of Action
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Obesity trends among U.S. adults
BRFSS, 2005
(*BMI ≥ 30, or ~30 lbs overweight for 5’4” person)

Regions: percent obese
(body mass index: x ≥ 30.0)

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North Carolina 2001 to 2005: total population age-adjusted mortality due to diabetes mellitus

Regional convergence of social issues

Poverty rate

Percent of the population without health insurance

Premature mortality

1977: 1.2 million people; the nearest medical center 2½ hours away

The site of the new medical school
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Yes, obesity…

- Obesity is the most prevalent, fatal, chronic disease of the 21st century, increasing at a rate seen before only in infectious disease
- 64.5% of adult Americans are overweight or obese, even more in minorities

It's not just about weight!
The co-morbidities are even worse

<table>
<thead>
<tr>
<th>Diabetes</th>
<th>Heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep apnea</td>
<td>Stroke</td>
</tr>
<tr>
<td>Pulmonary failure</td>
<td>Hernias</td>
</tr>
<tr>
<td>Asthma</td>
<td>Pseudotumor cerebri</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Immune suppression</td>
</tr>
<tr>
<td>Infertility</td>
<td>Reflux</td>
</tr>
<tr>
<td>Depression</td>
<td>Stress incontinence</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Pulmonary embolism</td>
</tr>
</tbody>
</table>
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The intestinal bypass
1950's
12 motions/day
Hypo-proteinemia
Liver failure
Kidney stones
Mineral loss
Not a great answer

Mason gastric bypass
Greenville gastric bypass
1960's
1978 - 80

The platinum rules of clinical research
• Standardize: do not change the protocol
• Total integrity
• Follow forever
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The Greenville gastric bypass

10 - 20 ml gastric pouch
8 - 10 mm anastomosis
40 - 60 cm alimentary loop

Total group 1980-1998 = 831
16 year cohort = 147

Weight loss after bariatric surgery @ 16 years (95% followup)

<table>
<thead>
<tr>
<th>Mean weight</th>
<th>Mean % XS weight loss</th>
<th>Mean BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop</td>
<td>317</td>
<td>0</td>
</tr>
<tr>
<td>1 year</td>
<td>199</td>
<td>67</td>
</tr>
<tr>
<td>2 years</td>
<td>194</td>
<td>69</td>
</tr>
<tr>
<td>5 years</td>
<td>209</td>
<td>57</td>
</tr>
<tr>
<td>10 years</td>
<td>217</td>
<td>51</td>
</tr>
<tr>
<td>16 years</td>
<td>211</td>
<td>55</td>
</tr>
</tbody>
</table>

2003 Schauer U Pitt – 104 lb

The Greenville gastric bypass produces durable and safe weight loss
A morbidly obese woman who could not conceive...

The weight loss is sustained

Mean % weight change over 15 years
Swedish obesity study

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1980: the first diabetic patients

1. Normal glucose level after surgery?
2. Normal glucose level after surgery?
3. Normal glucose level after surgery?
   You don’t know how to work up patients!
4. Normal glucose level after surgery?
   Why isn’t the lab giving us reliable values?

Remission of diabetes after gastric bypass

<table>
<thead>
<tr>
<th>Date</th>
<th>Glucose</th>
<th>Insulin given</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 Nov '80</td>
<td>495</td>
<td>90</td>
</tr>
<tr>
<td>17 Nov</td>
<td>281</td>
<td>8</td>
</tr>
<tr>
<td>18 Nov</td>
<td>308</td>
<td>16</td>
</tr>
<tr>
<td>19 Nov</td>
<td>240</td>
<td>8</td>
</tr>
<tr>
<td>20 Nov</td>
<td>210</td>
<td>4</td>
</tr>
<tr>
<td>21 Nov</td>
<td>230</td>
<td>8</td>
</tr>
<tr>
<td>22 Nov</td>
<td>216</td>
<td>4</td>
</tr>
<tr>
<td>28 Nov</td>
<td>193</td>
<td>0</td>
</tr>
<tr>
<td>30 Nov</td>
<td>153</td>
<td>0</td>
</tr>
<tr>
<td>14 Dec</td>
<td>155</td>
<td>0</td>
</tr>
</tbody>
</table>

608 morbidly obese
165 Type 2 Diabetics
146 long enough followup
121/146 (83%) euglycemic

165 IGT “impaired”
152 long enough followup
150/152 (99%) euglycemic

Schauer: 1,160 pts. 83% remission
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232 morbidly obese diabetics

- 154 Gastric Bypass
- 78 Operation refused for personal or insurance reasons

Mortality
- 14/154 (9%)/9 yrs, 1%/yr
- 22/78 (28%)/6.2 yrs, 4.5%/yr

P<0.0003

Long-term survival Canada

Rel. Risk = 0.11 (.04-.27)
89% reduction in risk of death over 5 years

Unadjusted cumulative mortality
Swedish obesity study

Sjostrom: NEJM 2007; 357: 741-52

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Morbid obesity
Operative changes in abdominal pressure

Surgically induced weight loss effects on urinary diary parameters

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Pulmonary artery pressure before and after surgically induced weight loss for morbid obesity

PaO₂ and PaCO₂ before and after surgically weight loss for morbid obesity
Health problems associated with morbid obesity

- Diabetes
- Sleep apnea
- Pulmonary failure
- Asthma
- Hypertension
- Infertility
- Depression
- Arthritis
- Congestive heart failure
- Stroke
- Hernias
- Pseudotumor cerebri
- Immune suppression
- Reflux
- Stress incontinence
- Pulmonary embolism

Five year comorbidity comparison

- Cancer
- Infectious
- Musculoskeletal
- Endocrinological
- Cardiovascular

* p<0.001

What's going on here?

Let's go ask a medical student: "What is Diabetes Mellitus?"
Type 2 diabetes: “Patients don't make enough insulin…”

Insulin resistance

Look, type 2 diabetes is due to failure of the islets!

Are the islets the problem?
Oral glucose tolerance test

No, the islets may be sick, but they work; in fact, Type 2 diabetics are hyper-insulinemic
Type 2 diabetes: an islet of Langerhans demonstrates amorphous pink deposition of amyloid

Type 1 diabetes: an islet of Langerhans demonstrates insulitis with lymphocytic infiltrates in a patient developing type I diabetes mellitus

What if insulin resistance is a protective mechanism of the cell against the overproduction of insulin?
If the gut is overstimulating the islets, then bypassing the gut should make the insulin levels fall.

Response of insulin levels to the GGB

Too much gluconeogenesis

Overwhelmed mitochondria

Too much insulin
So, it's not just a matter of glucose levels…

CHO

incretins

Hormones from fat

Neuroendocrine

CCK
Ghrelin
oleylethanolamide
GLIP-1
GLIP-2
GIP
apo A-IV
PPY
Leptin
PYY
etc.

Muscle

Genetic leptin deficiency causes obesity in ob/ob mice

From Michael Swart

Leptin receptor mutation causes obesity in db/db mice

From Michael Swart
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**CHO**

- Incretins
  - CCK
  - Ghrelin
  - oleyethanolamide
  - GLIP-1
  - GLIP-2
  - GIP
  - apo A-IV
  - PYY

**Muscle**

- Leptin
- Insulin
- MC3R, PPARγ
- MC4R, PYY
- Neuropeptide Y
- Agouti-related prot
- Ciliary neutrophic factors, etc.

**Hormones from fat**

- Leptin
- Adiponectin
- Resistin
- Inflammatory cytokines
- etc.

**Hypothalamus**

- Neuroneurs one 
- Factors, etc.

**Insulin sensitivity in non-diabetic gastric bypass patients (post-surgery) and non-surgery control subjects**

- Lean BMI <25
- Weight-matched BMI = 25-35
- Morbidity obese BMI >35
- Post-surgery BMI = 28.5

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Muscle IRS1 serine phosphorylation in non-diabetic gastric bypass patients (post-surgery) and non-surgery control subjects

Lean
BMI <25

Weight-matched
BMI = 25-35

Morbidly obese
BMI >35

Post-surgery
BMI = 29.9

Lean Weight-matched Morbidly obese Post-surgery

IRS1-Phosp (arbitrary units)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Before surgery</th>
<th>Surgery week</th>
<th>3 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>120</td>
<td>140</td>
</tr>
<tr>
<td>60</td>
<td>80</td>
<td>100</td>
<td>120</td>
</tr>
<tr>
<td>120</td>
<td>60</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>180</td>
<td>40</td>
<td>60</td>
<td>80</td>
</tr>
<tr>
<td>240</td>
<td>20</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>300</td>
<td>0</td>
<td>20</td>
<td>40</td>
</tr>
</tbody>
</table>

Obese

Diabetic

All patients – HOMA

Pre 1 Wk post 3 Mo post

HOMA

* p < 0.05
# p < 0.05
(n = 6)
Comparison of bariatric operations: the resolution of diabetes is “dose related”

n = 22,094 patients; 2738 citations 1990-2002

<table>
<thead>
<tr>
<th></th>
<th>Banding</th>
<th>Gastric</th>
<th>Duodenal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excess weight loss</td>
<td>47.5%</td>
<td>61.6%</td>
<td>70.1%</td>
</tr>
<tr>
<td>Operative mortality</td>
<td>0.1%</td>
<td>0.5%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Resolution of diabetes</td>
<td>47.8%</td>
<td>83.6%</td>
<td>97.9%</td>
</tr>
</tbody>
</table>

Buchwald, Avidor, Braunwald, Jensen, Pories, Farbach, Schoelles
JAMA 2004; 292: 1724-1737

Diabetologists maintain that the remission is due to weight loss alone; is that true?
Rubino: Goto-Kakizaki Rat (GK)
Animal model of type 2 diabetes
- The most-widely used lean model in type 2 diabetes research
  (Nature Genet 1996)
  - Non-obese
  - Normolipidemic
  - Hyperinsulinism
  - Insulin resistance

Rubino: duodenal-jejunal bypass (DJB) in the GK rat

Rubino: duodenal exclusion in the diabetic non-obese rat
OGTT

P<0.001
Rubino: OGTT after duodenal exclusion

Annals of Surgery 2006


Diabetic lean rats
Duodenal silastic tube; Diabetes clears
With perforations, the Diabetes returns

Insulin sensitivity in non-diabetic gastric bypass patients (>12 mo.) and non-surgery subjects
Interesting;
Have there been any studies
in non-obese diabetic patients?

**Duodenal-jejunal lap bypass**
in *lean* diabetic patients
Ramos A, Galvao Neto M, Galvao M.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Follow-up</th>
<th>Fasting Glycemia Pre-op</th>
<th>Fasting Glycemia Post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. RG</td>
<td>7m</td>
<td>216</td>
<td>98</td>
</tr>
<tr>
<td>2. CD</td>
<td>7m</td>
<td>168</td>
<td>110</td>
</tr>
<tr>
<td>3. MC</td>
<td>6m</td>
<td>157</td>
<td>79</td>
</tr>
<tr>
<td>4. MM</td>
<td>5m</td>
<td>148</td>
<td>82</td>
</tr>
<tr>
<td>5. RD</td>
<td>2m</td>
<td>225</td>
<td>94</td>
</tr>
<tr>
<td>6. JG</td>
<td>1m</td>
<td>173</td>
<td>92</td>
</tr>
</tbody>
</table>

**Duodenal-jejunal lap bypass**
in *lean* diabetic patients
Ramos A, Galvao Neto M, Galvao M.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Follow-up</th>
<th>HbA1c Pre-op</th>
<th>HbA1c Post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. RG</td>
<td>7m</td>
<td>8,6</td>
<td>6,2</td>
</tr>
<tr>
<td>2. CD</td>
<td>7m</td>
<td>7,5</td>
<td>6,0</td>
</tr>
<tr>
<td>3. MC</td>
<td>6m</td>
<td>8,2</td>
<td>5,8</td>
</tr>
<tr>
<td>4. MM</td>
<td>5m</td>
<td>7,8</td>
<td>6,3</td>
</tr>
<tr>
<td>5. RD</td>
<td>2m</td>
<td>8,2</td>
<td>7,6</td>
</tr>
<tr>
<td>6. JG</td>
<td>1m</td>
<td>8,7</td>
<td>7,9</td>
</tr>
</tbody>
</table>

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Dr M. Lakdawala M.S. India 6 months follow up
duodeno-jejunal bypass in lean diabetic patients

<table>
<thead>
<tr>
<th>Pre-surgery (N = 3)</th>
<th>Post surgery (6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI</strong></td>
<td></td>
</tr>
<tr>
<td>1. 27.5</td>
<td>27.5</td>
</tr>
<tr>
<td>2. 28</td>
<td>27</td>
</tr>
<tr>
<td>3. 29.5</td>
<td>29</td>
</tr>
<tr>
<td><strong>HbA1C</strong></td>
<td></td>
</tr>
<tr>
<td>1. 9</td>
<td>5.1</td>
</tr>
<tr>
<td>2. 10.4</td>
<td>6.3</td>
</tr>
<tr>
<td>3. 9.5</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>PP insulin</strong></td>
<td></td>
</tr>
<tr>
<td>1. 240</td>
<td>59.5</td>
</tr>
<tr>
<td>2. 232</td>
<td>56.5</td>
</tr>
<tr>
<td>3. 244</td>
<td>50.0</td>
</tr>
<tr>
<td><strong>FBS</strong></td>
<td></td>
</tr>
<tr>
<td>1. 128</td>
<td>95</td>
</tr>
<tr>
<td>2. 155</td>
<td>92</td>
</tr>
<tr>
<td>3. 162</td>
<td>90</td>
</tr>
<tr>
<td><strong>PPBS</strong></td>
<td></td>
</tr>
<tr>
<td>1. 245</td>
<td>104</td>
</tr>
<tr>
<td>2. 244</td>
<td>134</td>
</tr>
<tr>
<td>3. 275</td>
<td>124</td>
</tr>
</tbody>
</table>

Gastrectomy and diabetes

THE AMELIORATION OF DIABETES MELLITUS FOLLOWING SUBTOTAL GASTRECTOMY
MERRILL B. FREEDMAN, M.D., F.A.C.S., ANTONIO J. SANCETTA, M.D., and
GEORGE J. RAGUENES, M.D., Brooklyn, New York

In 1953, Muslin noted the presence of a substance in extracts of the pancreas which
would raise the blood sugar. Subsequently, this hormone factor was demonstrated
and defined. Therefore, when subtotal gastrectomy for diabetes mellitus resulted in
marked amelioration of the diabetes, case was 2 cases at the Brooklyn Veterans Hospital.

Surgery. Gynecology & Obstetrics; February 1955

OK, you have my interest;
what are the indications for bariatric surgery today?

- BMI ≥ 40
- BMI ≥ 35 with significant co-morbidities
- ≥ 18 years of age
- Full understanding of surgery and its consequences
- Contract for life-long follow-up
- Supportive family
Which operation is best?

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Remission Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjustable gastric band</td>
<td>48%</td>
</tr>
<tr>
<td>Gastric bypass</td>
<td>84%</td>
</tr>
<tr>
<td>Gastric sleeve</td>
<td>75%</td>
</tr>
<tr>
<td>Duodenal switch</td>
<td>98%</td>
</tr>
<tr>
<td>Duodenal jejunal bypass</td>
<td>100%</td>
</tr>
</tbody>
</table>

Rates of remission of Type 2 diabetes

OK; but isn’t bariatric surgery dangerous?

 SRC data: 272 hospitals, 495 surgeons >110,000 patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital mortality</td>
<td>76</td>
</tr>
<tr>
<td>Operative mortality at 30 days</td>
<td>165</td>
</tr>
<tr>
<td>Operative mortality at 90 days</td>
<td>196</td>
</tr>
<tr>
<td>Re-admissions</td>
<td>1,956</td>
</tr>
<tr>
<td>Re-operations</td>
<td>887</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Value</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.14%</td>
<td>Hospital mortality</td>
</tr>
<tr>
<td>0.29%</td>
<td>Operative mortality at 30 days</td>
</tr>
<tr>
<td>0.35%</td>
<td>Operative mortality at 90 days</td>
</tr>
<tr>
<td>4.75%</td>
<td>Re-admissions</td>
</tr>
<tr>
<td>2.15%</td>
<td>Re-operations</td>
</tr>
</tbody>
</table>
### TABLE 2. Mortality rates following common operations in U.S. hospitals

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of hospitals performing operation</th>
<th>National average mortality rate(%)</th>
<th>Average hospital caseloads median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic Aneur</td>
<td>2485</td>
<td>3.9</td>
<td>30</td>
</tr>
<tr>
<td>CABG</td>
<td>1936</td>
<td>3.5</td>
<td>491</td>
</tr>
<tr>
<td>Craniot</td>
<td>1600</td>
<td>10.7</td>
<td>12</td>
</tr>
<tr>
<td>Esophag Resect</td>
<td>1717</td>
<td>9.1</td>
<td>5</td>
</tr>
<tr>
<td>Hip Replac</td>
<td>3445</td>
<td>6.3</td>
<td>24</td>
</tr>
<tr>
<td>Panc</td>
<td>1302</td>
<td>8.3</td>
<td>8</td>
</tr>
<tr>
<td>Ped. Heart Surgery</td>
<td>458</td>
<td>5.4</td>
<td>4</td>
</tr>
</tbody>
</table>

*Dimick JB, Welch WC, Birkmeyer JD; Surgical mortality as an indicator of hospital quality; JAMA 2004, 292, 847-851*

SRC: bariatric surgery mortality 0.3% (55,567 patients)

106 hospitals reporting average case load: 312 cases/year

---

### Conclusions

- Diabetes is no longer a hopeless disease
- Current medical therapies for diabetes are complex, expensive with little proof that the new medications are better
- Surgery for diabetes is effective and safe
- Surgery must be considered a therapeutic option
- Bariatric and metabolic surgery offers new research avenues toward the understanding of diabetes
- East Carolina University is a great place; come and visit us