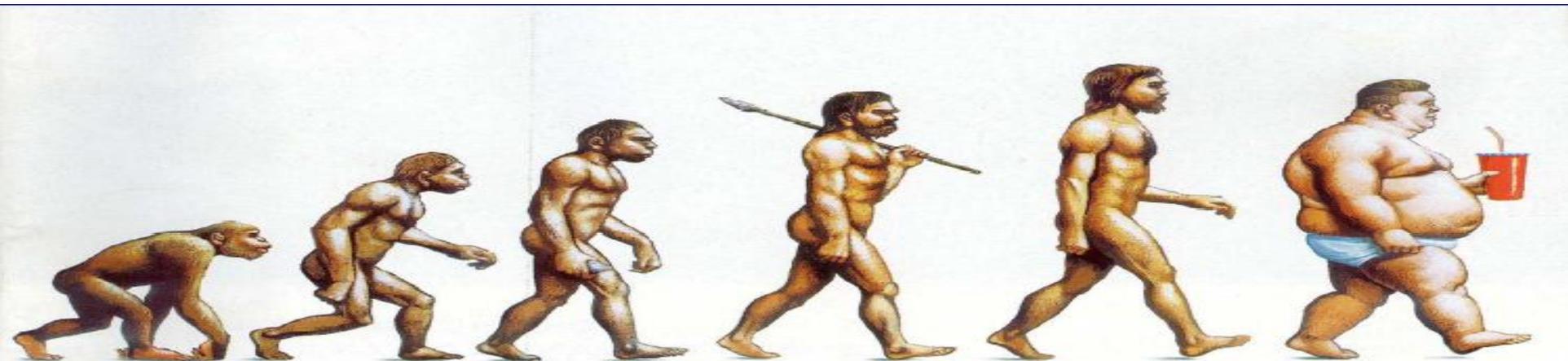


# Non-Alcoholic Fatty Liver Disease:

## Is Bariatric Surgery the Answer?

Dr. Mahler Ilanit  
Surgery B Department  
Rabin Medical Center



# Morbid obesity

- Obesity is a growing epidemic.
- Worldwide obesity has more than doubled since 1980.

<i>Weight</i>	<i>BMI values</i>
Healthy weight . . . . .	18.5–24.9
Overweight . . . . .	25.0–29.9
Obese . . . . .	30 and above

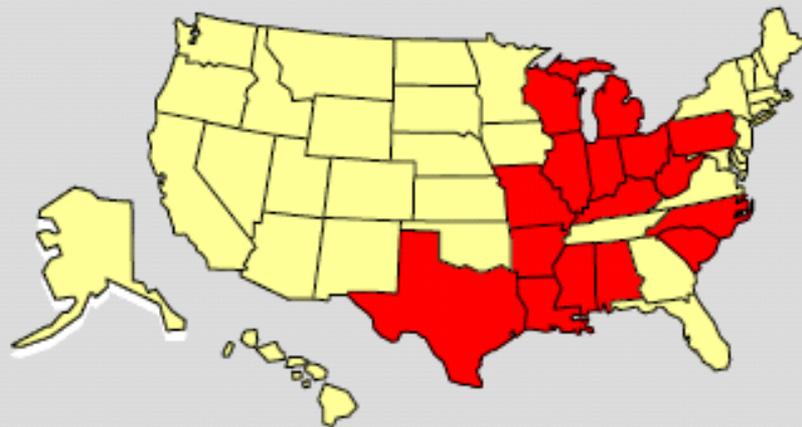
# World Health Organization:

- Globally there are more people who are obese than underweight.
- Overweight and obesity are linked to more deaths worldwide than underweight.



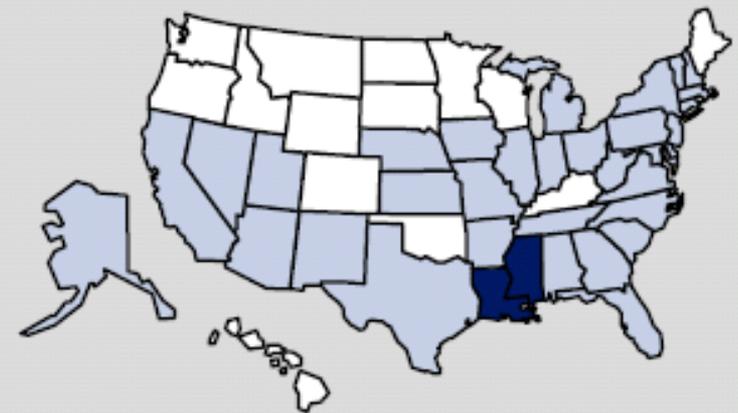
# Diabetes prevalence is tracking obesity

Obesity prevalence **1994**



Yellow <10-14% Red <15-19% Dark Red ≥20%

Diabetes prevalence **1994**

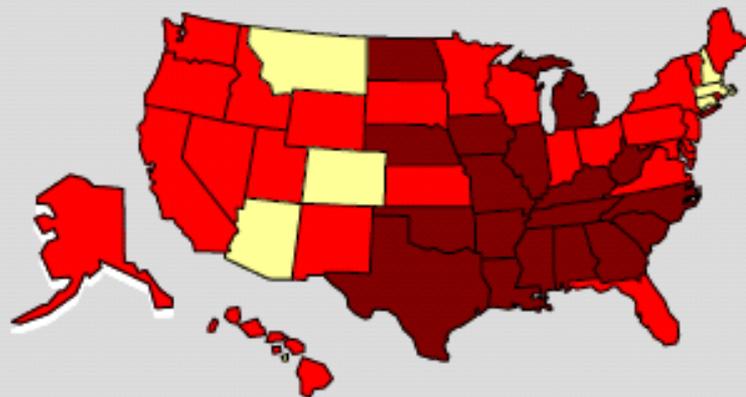


White <4% Light Blue <4-6% Dark Blue >6%

Notes: Rates reflect prevalence among adults. Obesity is defined as BMI  $\geq 30$ .  
Source: Centers for Disease Control and Prevention (CDC)

# Diabetes and obesity (cont'd)

Obesity prevalence **1999**



Legend for Obesity prevalence 1999:  
Light yellow: <10-14%  
Red: <15-19%  
Dark red:  $\geq 20\%$

Diabetes prevalence **1999**



Legend for Diabetes prevalence 1999:  
White: <4%  
Light blue: <4-6%  
Dark blue: >6%

Notes: Rates reflect prevalence among adults. Obesity is defined as BMI  $\geq 30$ .  
Source: Centers for Disease Control and Prevention (CDC)



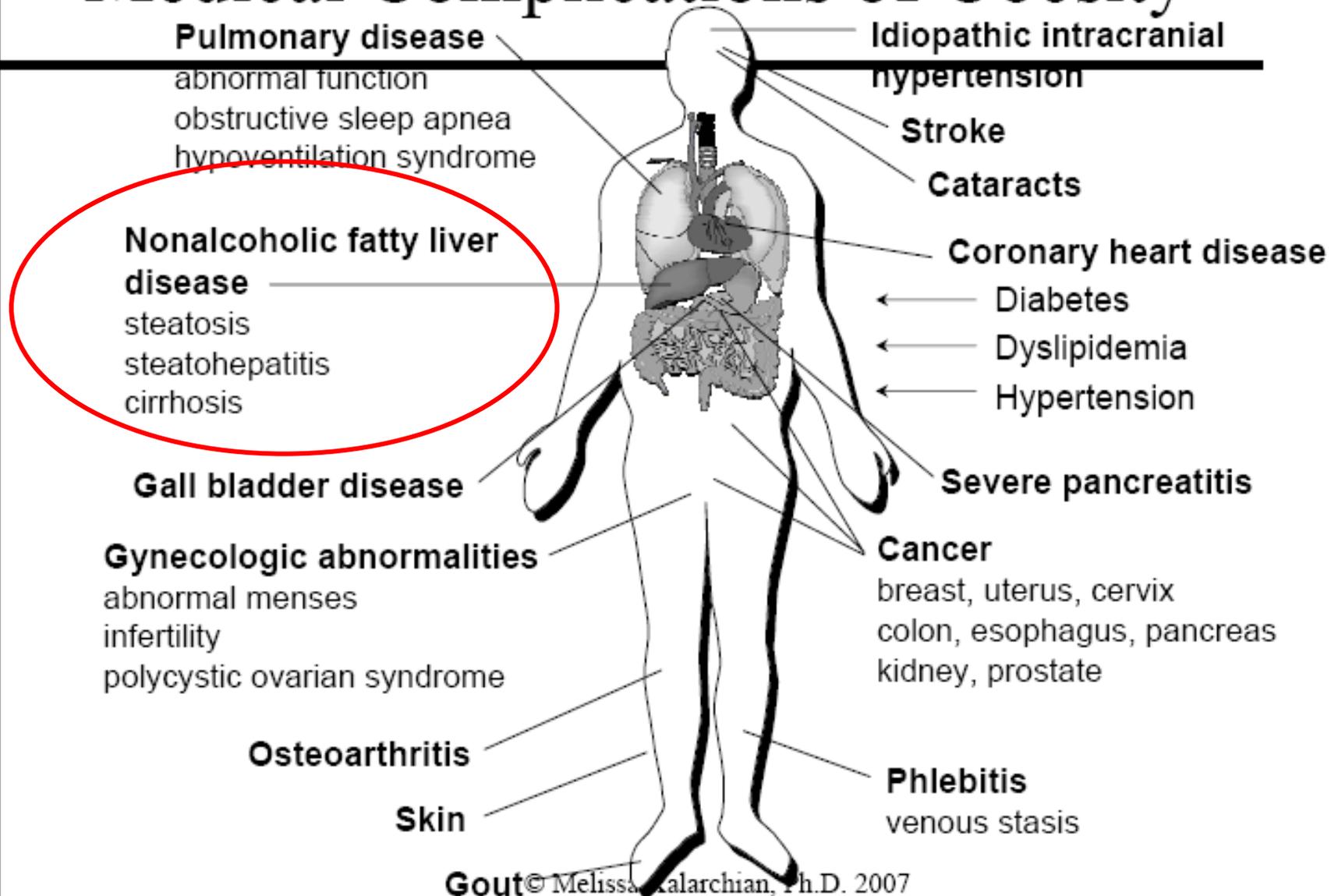
# United States

- 1/3 of adults are reported as being obese and by 2025 this number is expected to increase to 45%-50%.

Mid-life mortality:

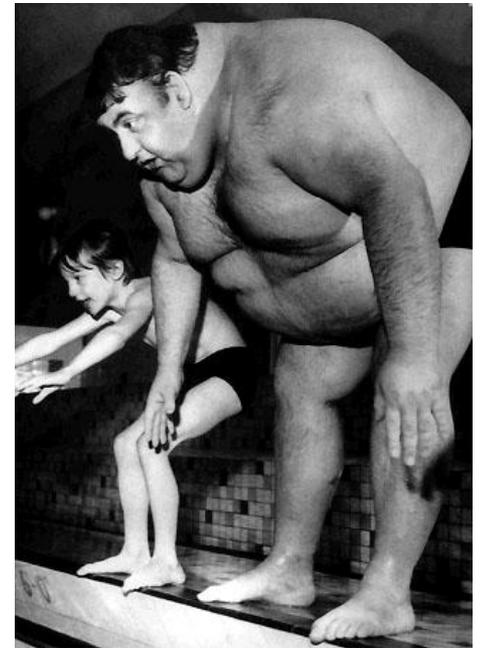
- **Overweight** patients had a 20%-40% increase.
- **Obese** individuals had 200%-300% increase in mortality.

# Medical Complications of Obesity



# National Institutes of Health guidelines for Bariatric surgery:

- BMI is greater than  $40 \text{ kg/m}^2$ .
- BMI  $35 \text{ kg/m}^2$  or over who have high-risk comorbidities such as heart disease, DM, hyperlipidemia, and OSA.



## הנדון: קווים מנחים לביצוע ניתוחים בריאטרים במבוגרים

### מטרות:

- הגדרת דרישות החובה מהמרכזים המבצעים ניתוחים בריאטרים;
- קביעת הנחיות לביצוע הערכה טרום ניתוחית ומעקב לאחר ניתוח;
- הגדרת אופן הדיווח על הפעילות הניתוחית הבריאטרית;
- קביעת התוויות לביצוע ניתוחים בריאטרים במבוגרים מעל גיל 18.

התוויות מומלצות לניתוחים בריאטרים במבוגרים מעל גיל 18 נכון ליום הפצת החוזר:

1. BMI < 40

2. BMI > 35 < 40 עם לפחות אחת מהמחלות הנלוות:

- סוכרת מסוג 2
- יתר לחץ דם
- מחלת לב איסכמית
- דיסליפידמיה
- דום נשימה בשינה.
- הפרעות בפוריות משניות להשמנה
- בעיות אורטופדיות משניות להשמנה ומגובות בתיעוד קליני של אורטופד
- אוסטיאוארטריטיס
- **כבד שומני**
- אירוע טרומבואמבולי

3. BMI > 30 < 35

- במנותחים שעברו ניתוח בריאטרי קודם ונכשלו בו
- בחולים עם סוכרת מסוג 2, כאשר הסוכרת אינה מאוזנת כהלכה באמצעות משטר טיפול תרופתי אופטימלי.

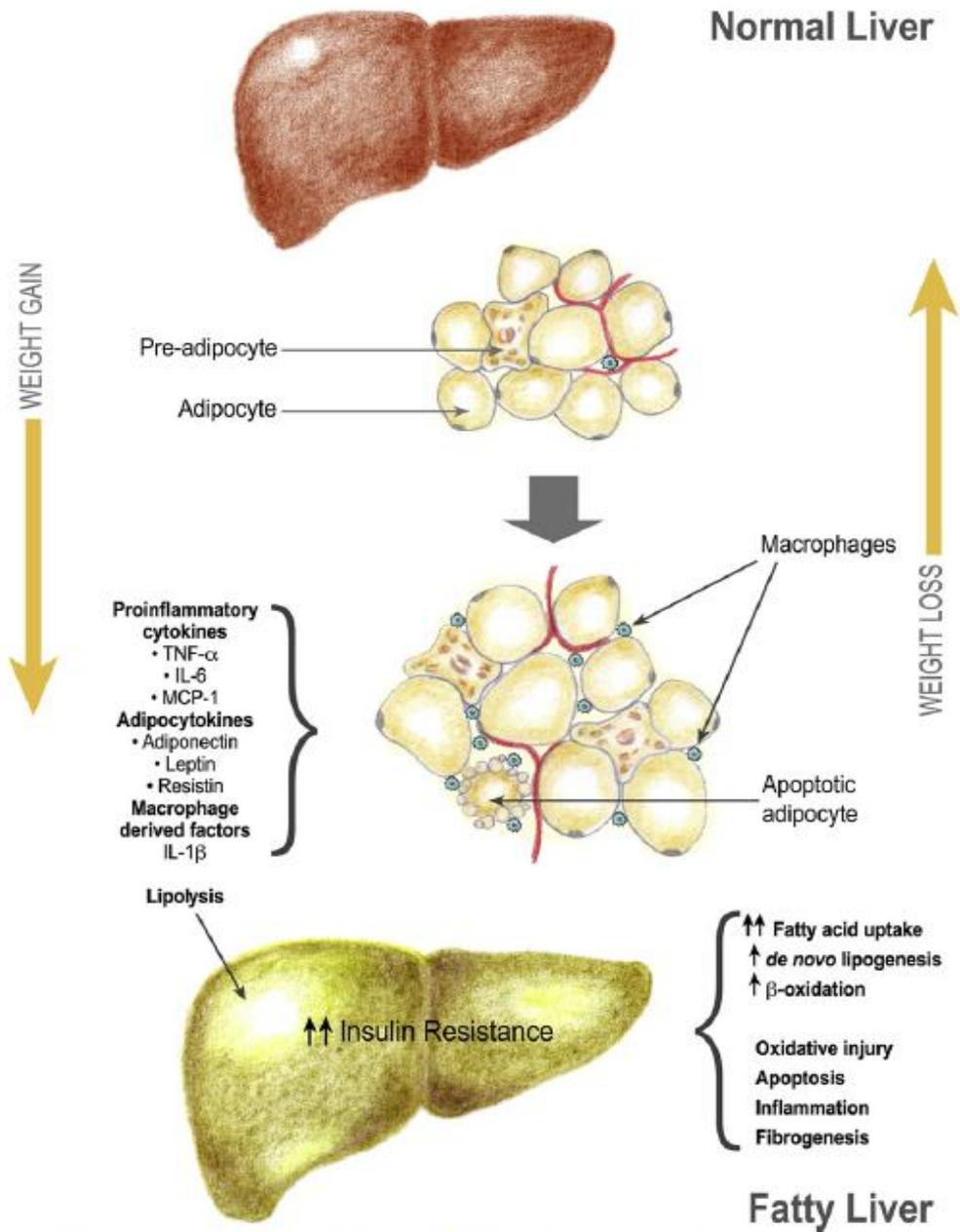


Fig. 1. Alterations in adipose and hepatic tissue related to weight change.

# The effect of liposuction on metabolic parameters:

- Visceral adipose - more metabolic activity than subcutaneous adipose tissue.
- Liposuction: no changes were observed in obesity-related metabolic derangements or proinflammatory cytokines.

Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease.  
N Engl J Med 2004.

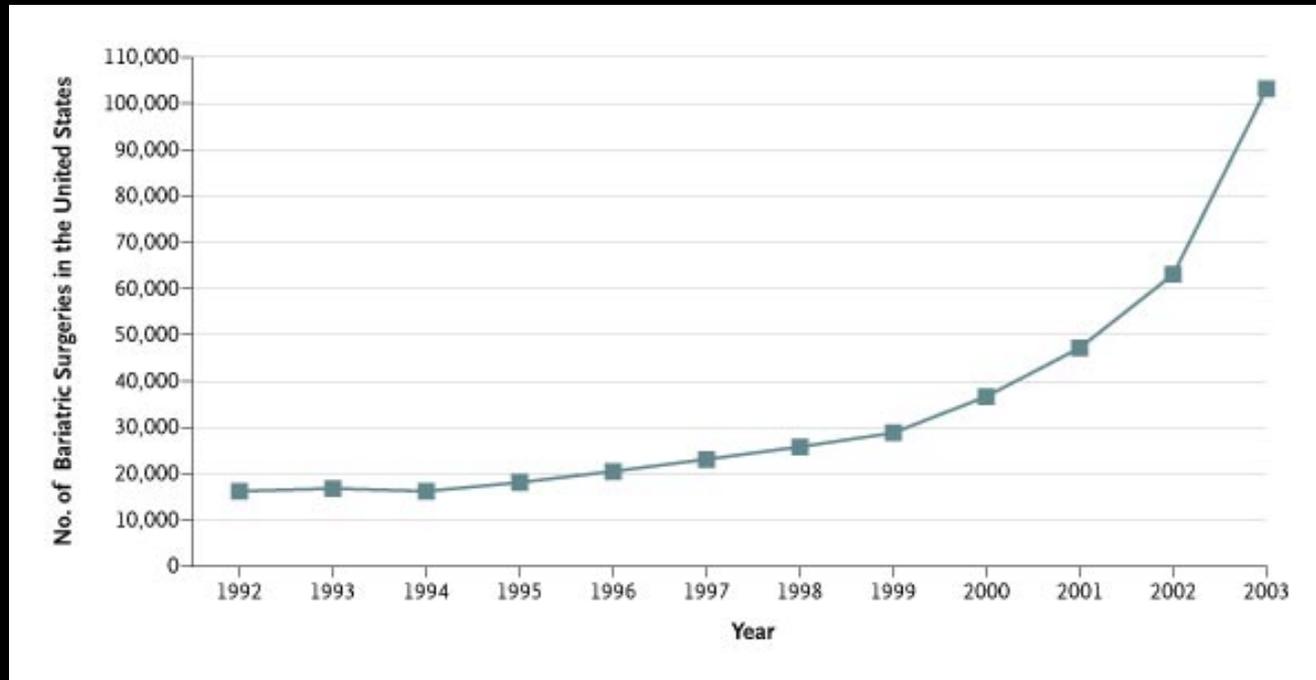
# Success Rate of Weight Loss Treatments for Morbid Obesity

Treatment	Average Weight Loss (% Total)	% Excess Weight Loss at Five Years
Placebo	4–6%	0%
Diet/Behavior Modification	8–12%	1.6% (10 Years)
Drug Therapy	< 10%	10%
Gastric Bypass Surgery	65–85%	Up to 100%
Laparoscopic Adjustable Gastric Banding	45–50%	56%

Surgical treatments for patients who are morbidly obese were pioneered as early as the 1950s



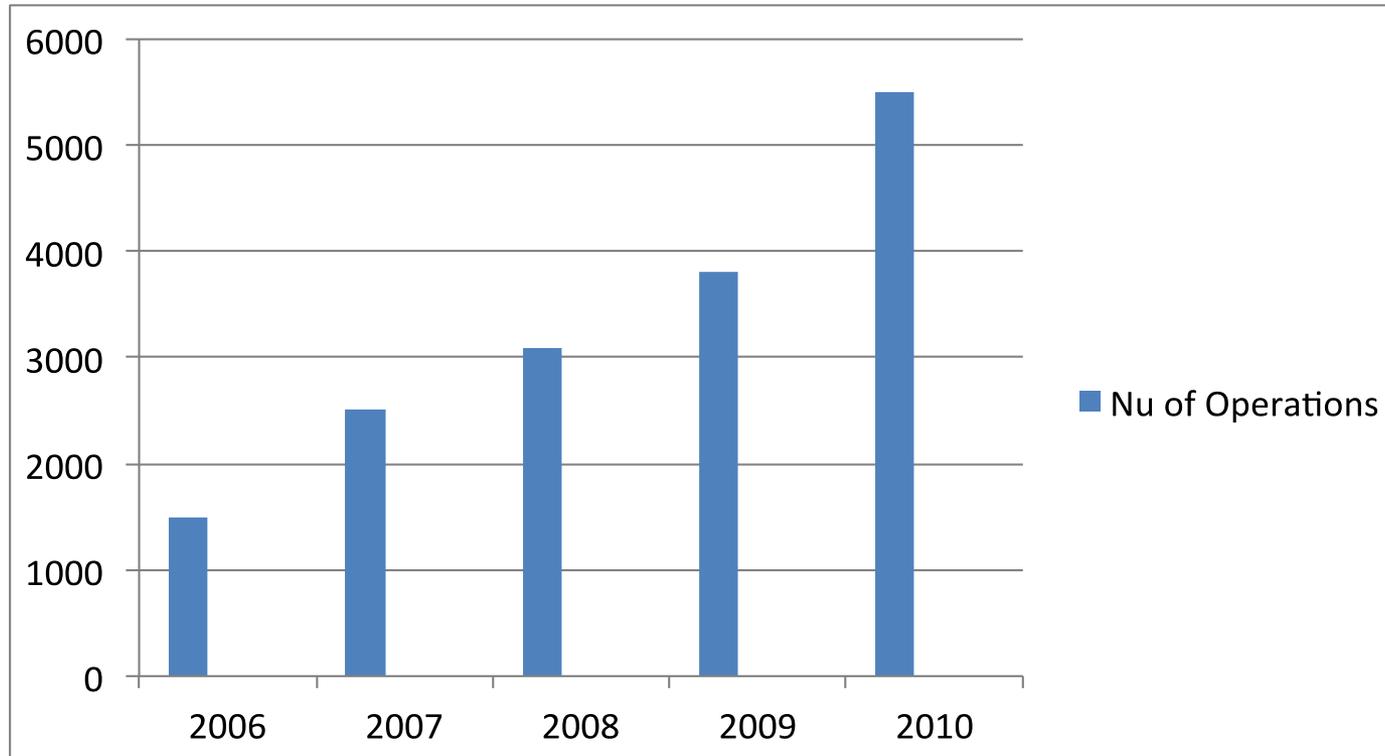
## Estimated Number of Bariatric Operations Performed in the United States, 1992-2003



Steinbrook, R. N Engl J Med 2004;350:1075-1079



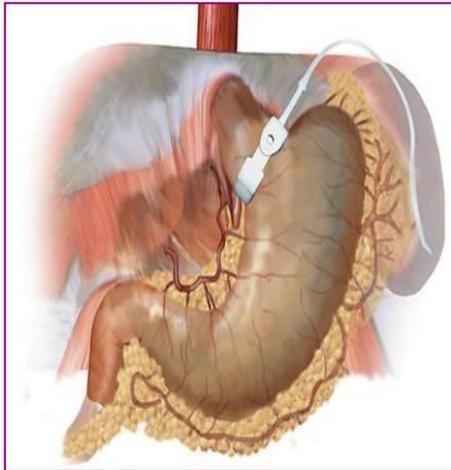
# Bariatric operations in Israel:



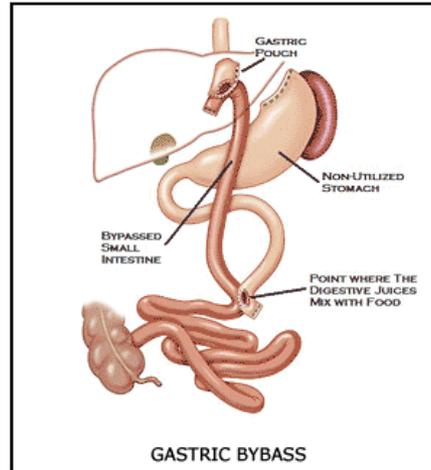
2006 – 1,600 Surgeries  
2010 – 5,500 Surgeries  
**2016 - 10,000 Surgeries**

# Bariatric Procedures

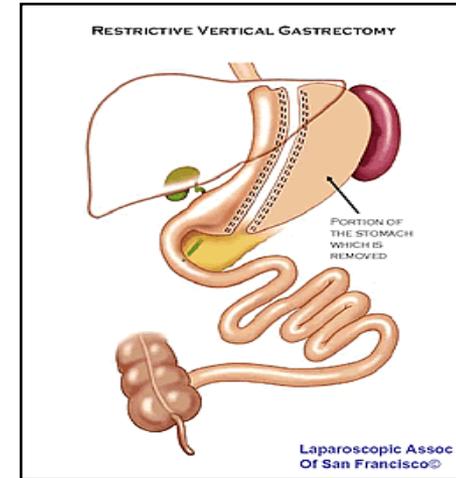
## Adjustable Gastric Banding



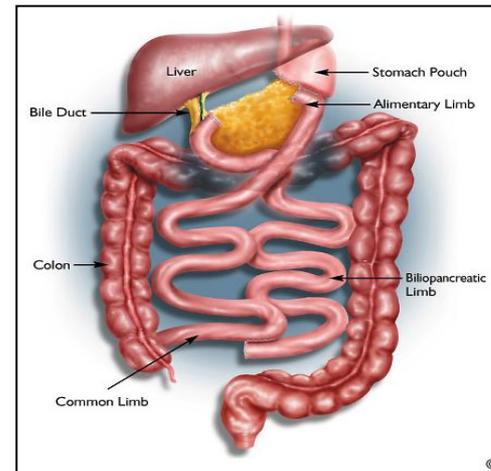
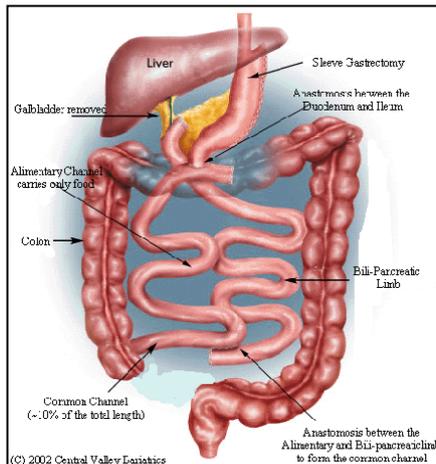
## Rou-X-En-Y Gastric Bypass



## Sleeve Gastrectomy



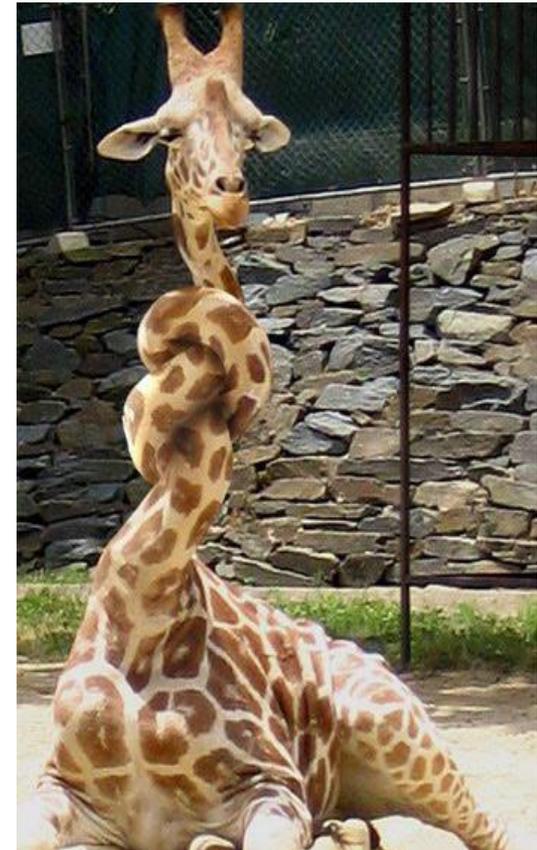
## Biliopancreatic Diversion and Duodenal Switch (BPD+DS)



## Biliopancreatic Diversion BPD (Scopinaro)

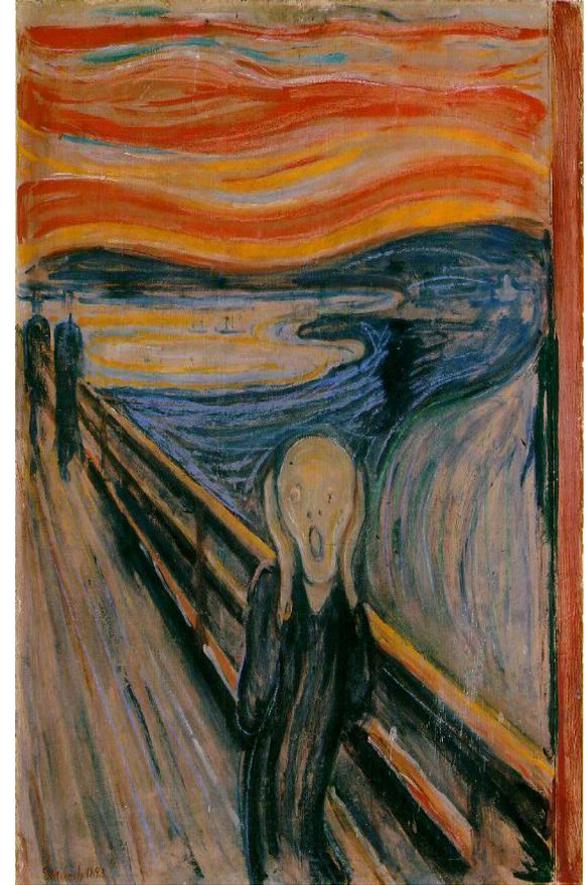
# Surgical Procedures - Current Bariatric

- **Restrictive**
  - Vertical Banded Gastroplasty -VBG, SRVG
  - Laparoscopic Adjustable Gastric Banding
  - Sleeve gastrectomy
- **Malabsorptive**
  - Laparoscopic Duodenal Switch
  - Biliopancreatic Diversion
- **Restrictive and Malabsorptive**
  - Laparoscopic Roux-en-Y Gastric Bypass
  - Omega loop gastric bypass (mini ?)



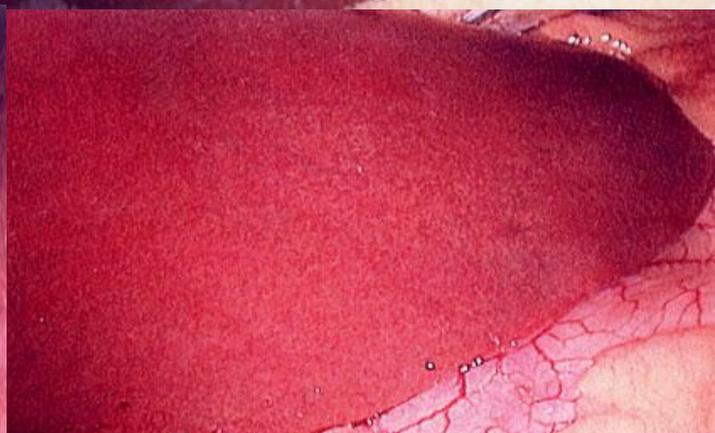
# Changes in Bariatric surgery

- Increasing weight of candidates
- Lower morbidity mortality and postoperative hospital stay
- Laparoscopy
- Operations in extreme ages
- Change in the indications for operations



# The bariatric population:

- Most patients undergoing bariatric surgery have some degree of hepatic steatosis:
- 85% - 95% of morbidly obese populations seem to have NAFLD.
- 25%-33% have NASH
- 1%-3% will have cirrhosis incidentally found in the operating room.

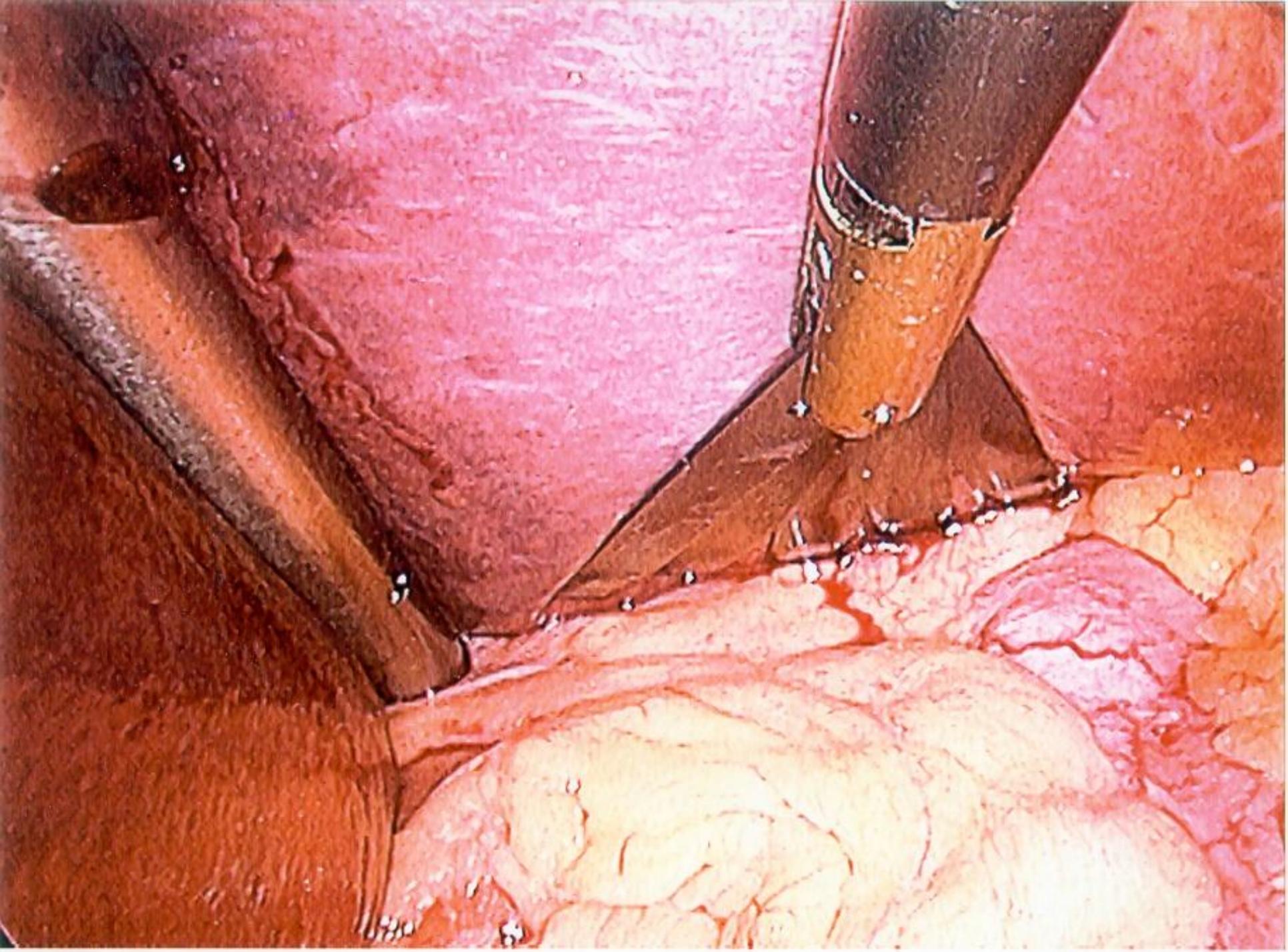


# Cirrhosis:



**Lose weight before surgery**





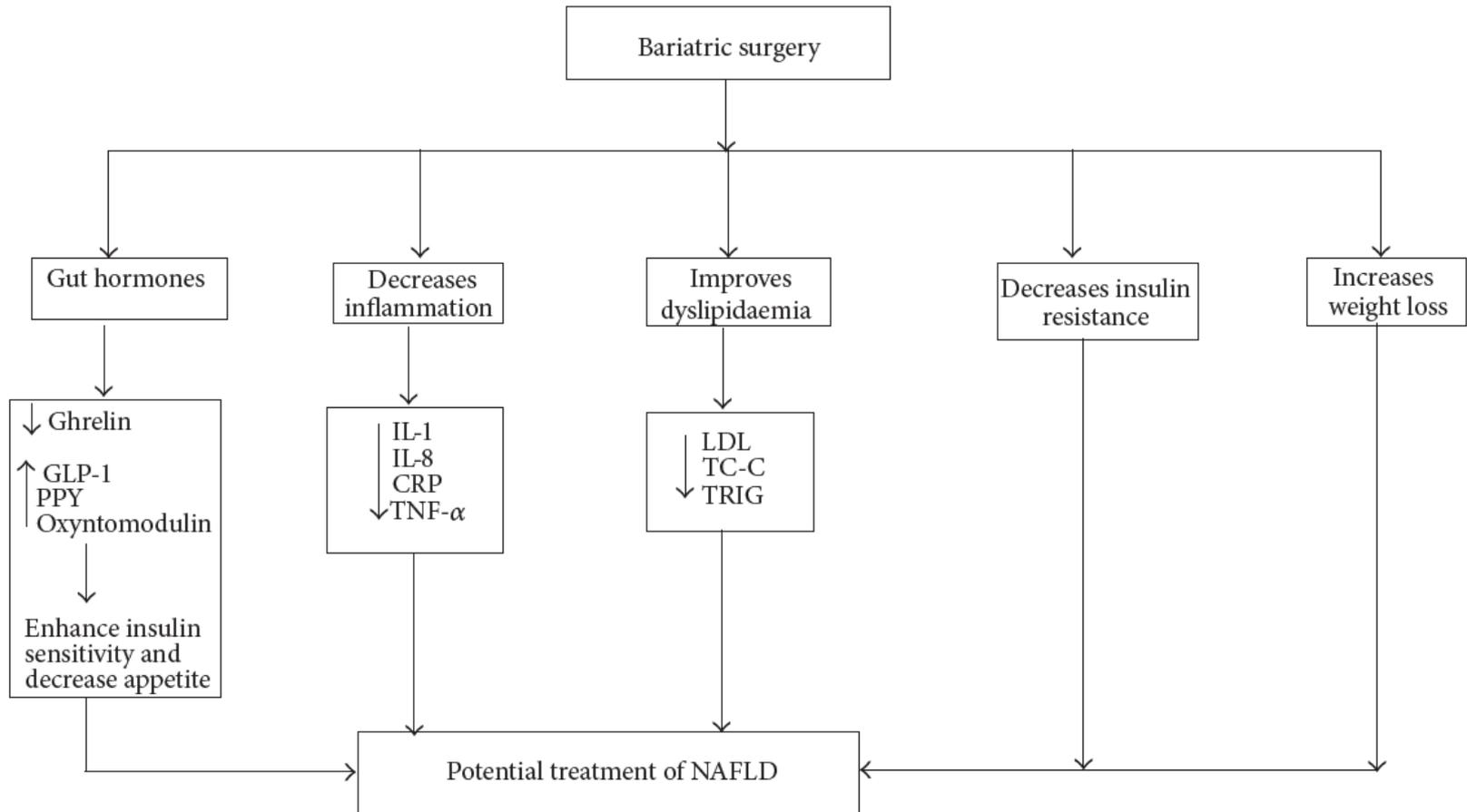
# Gut peptides:

		<p>GASTRIC BYPASS</p>	<p>RESTRICTIVE VERTICAL GASTRECTOMY</p>		
<p>↑</p>	<p>↑</p>	<p>or ↑ ↓</p>	<p>↓ ↓</p>	<p>or ↑ ↔</p>	<p><b>Ghrelin</b></p>
<p>↔</p>	<p>↑</p>	<p>↑ ↑</p>	<p>?</p>	<p>↔</p>	<p><b>GLP-1</b></p>
<p>↓</p>	<p>↑</p>	<p>↑</p>	<p>↑</p>	<p>↔</p>	<p><b>PYY</b></p>

# Gut Peptides:

- Patients who undergo RYGB have shown a marked reduction in hepatic lipid content and improved hepatic insulin sensitivity well before significant weight loss occurs.
- These benefits to the liver are directly related to gut peptides (GLP-1 and PYY).

# Bariatric surgery- mechanisms:



# The effects of bariatric surgery on NAFLD

Table 2

The effects of bariatric surgery on liver histology in NAFLD patients

Study	Surgery	Total/NASH, N	Cirrhosis, N	Mean Initial BMI	Mean Interval to Second Biopsy (months)	Mean Excess Weight Loss	Histology					NASH Resolution
							Steatosis	Ballooning	Inflammation	Fibrosis		
Dixon, 2004 <sup>73</sup>	AGB	36/23	1	47 (±10.6)	25.6	52%	↓	↓	↓	↓		82%
Dixon et al, 2006 <sup>65</sup>	AGB	60/30		45.9 (±7.4)	29.5	32%	↓	Not reported	↓		↓	80%
Mattar et al, 2005 <sup>61</sup>	RYGB (41) SG (23) AGB (6)	70	2	56 (±11)	15	59%	↓	Not reported	↓		↓	Not reported
Mathurin et al, 2006 <sup>62</sup>	BIB (71) AGB (100)	121/24		49 (±8)	12	19%	↓	Not reported	Not reported		↑	75%
Kral et al, 2004 <sup>74</sup>	BPD	104	11	31 (±8)	41	34%	↓	Not reported	↓		↓/↑	Not reported
Mottin et al, 2005 <sup>59</sup>	RYGB	90		46.7 (±0.88)	12	81.4%	↓	Not reported	Not reported		Not reported	Not reported
Clark et al, 2005 <sup>60</sup>	RYGB	16		51.1 (±6.1)	10	35.4%	↓	↓	↓		↓	Not reported
Csendes et al, 2006 <sup>63</sup>	RYGB	16/4	1	44.3	17.5	72%	↓	↓	↓		↑	100%
de Almeida et al, 2006 <sup>64</sup>	RYGB	16		53.4 (±8.8)	23.5	42%	↓	↓	↓		↓/↑	Not reported
Barker et al, 2006 <sup>66</sup>	RYGB	19/19	1	47 (±4.4)	21.4	52.4%	↓	↓	↓		↓/↑	89%
Liu et al, 2007 <sup>67</sup>	RYGB	39/23		47.7 (±6.2)	18	Not reported	↓	↓	↓		↓/↑	100%
Furuya et al, 2007 <sup>68</sup>	RYGB	18/12	1	51.7 (±7.4)	24	60%	↓	↓		Not reported	↓	Not reported

# Fibrosis

- Interestingly, in the study of Kral *et al*, bariatric surgery seemed to have differential effects, depending on the degree of baseline fibrosis.
- Patients with minimal fibrosis (stage  $\leq 2$ ) showed progressive fibrosis postoperatively, whereas those with advanced fibrosis (stage  $2 \leq$ , including cirrhosis) showed marked regression of fibrosis after surgery.

# CLINICAL ADVANCES IN LIVER, PANCREAS, AND BILIARY TRACT

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## Prospective Study of the Long-Term Effects of Bariatric Surgery on Liver Injury in Patients Without Advanced Disease

PHILIPPE MATHURIN,<sup>\*,‡</sup> ANTOINE HOLLEBECQUE,<sup>\*,‡</sup> LAURENT ARNALSTEEN,<sup>§,||</sup> DAVID BUOB,<sup>¶</sup>  
EMMANUELLE LETEURTRE,<sup>¶</sup> ROBERT CAIAZZO,<sup>§,||</sup> MARIE PIGEYRE,<sup>#</sup> HÉLÈNE VERKINDT,<sup>||</sup> SÉBASTIEN DHARANCY,<sup>\*,‡</sup>  
ALEXANDRE LOUVET,<sup>\*,‡</sup> MONIQUE ROMON,<sup>#</sup> and FRANÇOIS PATTOU<sup>§,||</sup>

*\*Service d'Hépatogastroentérologie, ‡Unité Inserm U 795, §Unité Inserm U 859, Services de, ||Chirurgie Endocrinienne, ¶d'Anatomie Pathologique, #de Nutrition, CHRU de Lille, Université Lille 2, France*

## GASTROENTEROLOGY 2009

- Prospective study - clinical, metabolic and liver histology at baseline, Yr 1 and Yr 5 after bariatric surgery in 381 adult patients with severe obesity (56% Gastric Band, 21% Gastric bypass, Bilio-intestinal bypass 23%).

# Conclusions

- Improvement in steatosis and ballooning occurred mainly within the first year and persisted up to 5 years.
- Fibrosis worsened at 5 years, although 95% of patients had a fibrosis score  $F1 \geq$  at 5 years.) .

- Patients with persistent severe steatosis after surgery were found to have more insulin resistance.
- **Insulin resistance as the hallmark of NAFLD**  
and if insulin resistance is still present postoperatively, it is likely that liver disease will persist as well.

# **Effect of Bariatric Surgery on Nonalcoholic Fatty Liver Disease: Systematic Review and Meta-Analysis**

RAJASEKHARA R. MUMMADI,\* KRISHNA S. KASTURI,\* SWAPNA CHENNAREDDYGARI,\* and GAGAN K. SOOD<sup>‡</sup>

*\*Internal Medicine, <sup>‡</sup>Gastroenterology and Hepatology, University of Texas Medical Branch, Galveston, Texas*

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2008;6:1396–1402

# Results:

- An improvement of histopathologic features of NAFLD in more than three fourths of the patients.
- The majority of patients experience complete resolution of NAFLD after bariatric surgery, and the risk of progression of inflammatory changes and fibrosis seems to be minimal.

# Summery:

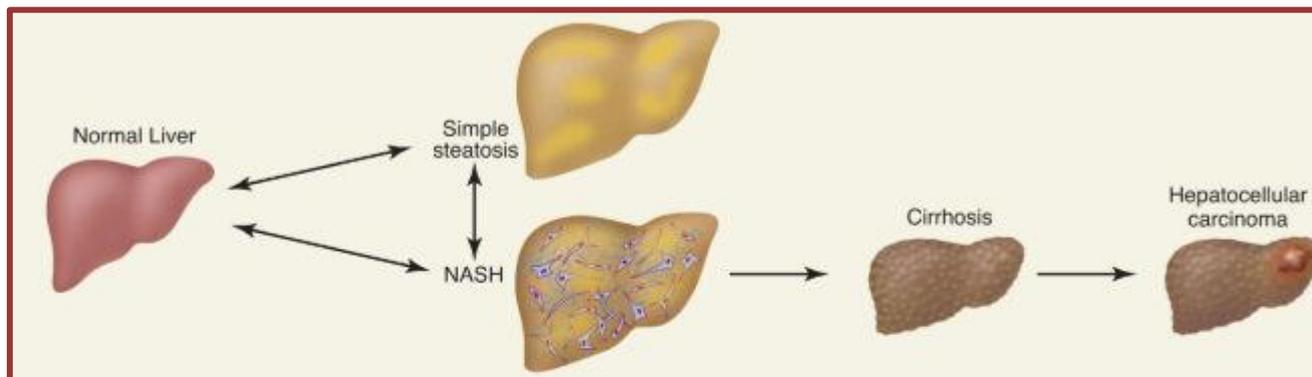
- Explosive growth in obesity →

NAFLD ↑

- NAFLD not only contributes to the development of liver-related morbidity and mortality, it is a predisposing factor for cardiovascular disease and malignancy.

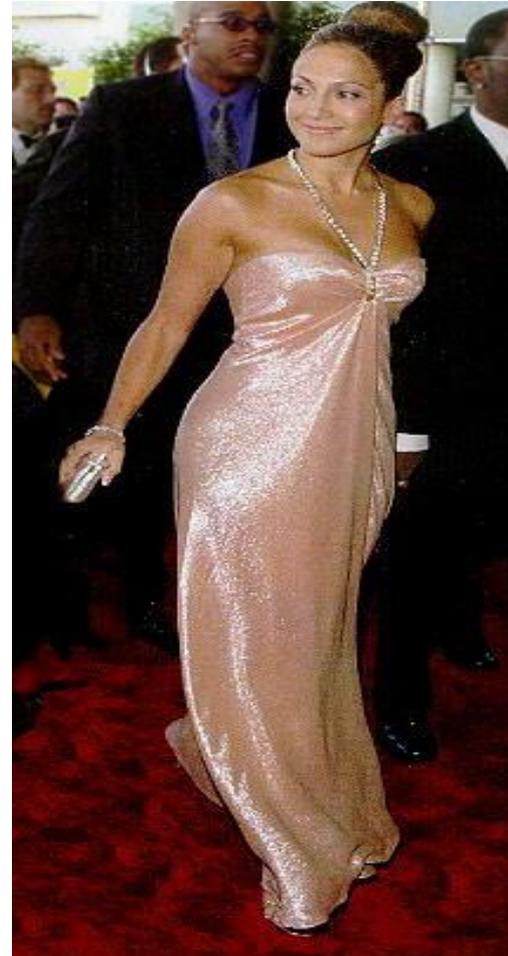
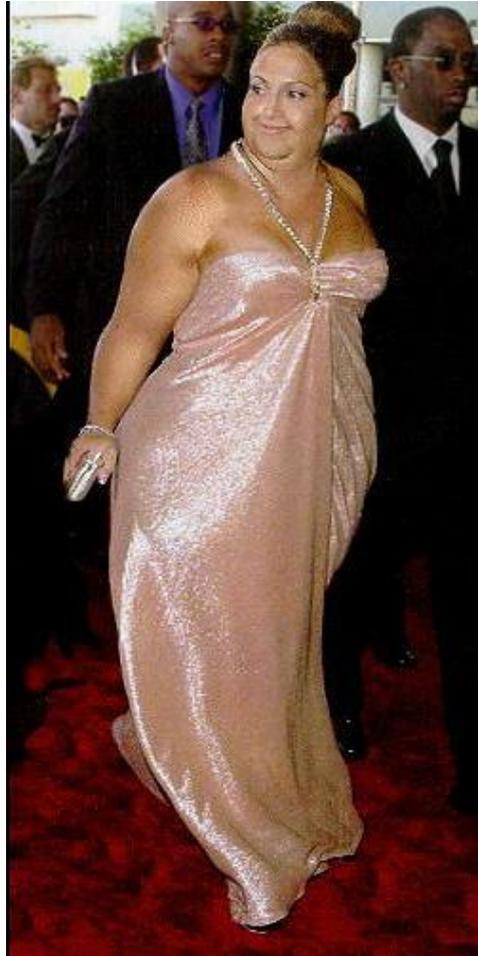
# Improvement in the liver histology:

- Steatosis, steatohepatitis, and fibrosis appear to improve or completely resolve in the majority of patients after bariatric surgery results in significant weight loss.



- The only effective treatment for NAFLD is weight loss.
- Sustained weight loss can be beneficial in preventing and even reversing NAFLD.
- The only effective treatment for morbid obesity is bariatric surgery.

*The end....*



# RYGB

TABLE 1: Considerable studies showed that RYGB is associated with marked improvement in NAFLD.

Study	Ref	Main outcomes	Type of study	Sample size	Followup
Silverman et al., 1995	[20]	Improved steatosis and fibrosis	Retrospective cohort	91	18.4 months
Clark et al., 2005	[21]	Improved steatosis, fibrosis, and inflammation	Prospective cohort	16	305 ± 131 days
Mattar et al., 2005	[22]	Improved metabolic syndrome, steatosis, and fibrosis	Prospective cohort	70	15 ± 9 months
Mottin et al., 2005	[23]	82% improvement in liver steatosis and fibrosis not measured	Retrospective cohort	90	12 months
Klein et al., 2006	[24]	Decreased factors lead to liver fibrosis and inflammation	Prospective cohort	7	12 months
Barker et al., 2006	[25]	Improved histology of NAFLD	Prospective cohort	19	21.4 months
Csendes et al., 2006	[26]	Improved histology in 80%	Prospective cohort	16	22 months
de Almeida et al., 2006	[27]	Improved steatosis, fibrosis, and inflammation	Prospective cohort	16	23.5 ± 8.4 months
Furuya et al., 2007	[28]	Improved steatosis and fibrosis	Prospective cohort	18	24 months
Liu et al., 2007	[29]	Resolved NASH in 60%	Retrospective cohort	39	18 months
Weiner 2010	[30]	Complete regression of NAFLD in 83%	Retrospective cohort	116	18.6 ± 8.3 months
Moretto et al., 2012	[31]	Resolved fibrosis in 50%	Retrospective cohort	78	Unavailable