Metabolic surgery

**Normal Hemoglobin (Hb)**

Hemoglobin contains four **HEME Groups** that bind Oxygen molecules to an Iron atom core.

**Glycated Hemoglobin (HbA1C)**

Glucose permanently binds to proteins like Hemoglobin after prolonged exposure to elevated blood sugar.
Natural History of Obesity Leading to Type 2 Diabetes
Fig. 7.1 Age-standardized prevalence of obesity in men aged 18 years and over (BMI ≥30 kg/m²), 2014
Figure 2: Diabetes Increase Accompanies Increase in Mean Body Weight

Estimated impact of the increasing trend in obesity by 2023:
- Stroke: +5%
- Angina: +12%
- Heart attack: +18%
- High Blood Pressure: +28%
- Type 2 Diabetes: +34%
Is Type II Diabetes Mellitus (NIDDM)
a Surgical Disease?

WALTER J. HORNER, M.D., KENNETH D. MAULDIN, J.A., M.D., EDWARD D. FUCHSBERG, M.D.,
G. L. RYNS DOMIN, R.P.H., S. MADDEN, S. S. POWELL, S. J. NEUMAN, M.D., R. E. HARRIS, M.D., H. W. MAY, M.D.,
FRANCISCO FRESNOPE, R.P.H., M. W. MILLER, W. J. SANDERS, R.P.H., ELIZABETH HERINGTON, R.P.H.,
R. J. OSBORNE, R.P.H., B. A., M. H. BROWN, M.D., J.

Since February 19, 1990, 515 morbidly obese patients have undergone the Gastric plicating type I (GBP) operation. Of these, 212 (41.2%) were male, 200 (39.4%) were either diabetic or had borderline diabetes, and 13 (2.5%) were unable to complete the procedure. The operation, which involves selective autonomic blockades in the esophageal and diaphragmatic regions and has resulted in significant improvements in diabetes control, is discussed in detail. The GBP has been shown to improve glycemic control, reduce body mass index, and increase lean body mass in patients with type II diabetes mellitus. The GBP also reduces the risk of diabetes-related complications, such as retinopathy, nephropathy, and neuropathy. In addition, there are broader systemic effects, such as the lowering of blood pressure. The economic impact of the disease is enormous. In 1995, it was estimated to be $35 billion and may well be twice that high given the inflation in health care costs. Although the exact prevalence is unknown, a rough estimate is that 10 million Americans have the disease and, of those, 1.25 million take insulin. 2 to 3 million are on oral antidiabetic agents, and another two to three million are being managed by diet alone. Many remain undiagnosed. The disease is generally classified into two groups: type I diabetes or insulin-dependent diabetes, which affects about 200,000 to 300,000, and the far more common type II diabetes or non-insulin-dependent diabetes mellitus (NIDDM), which accounts for more than 95% of the cases.

The benefits of the current treatment of NIDDM is the maintenance of normal and normal blood sugar levels. This "control of the disease" is considered the best approach to prevent the acute and chronic complications of diabetes and to alleviate those changes that are already present. Unfortunately, nephropathy cannot be
TABLE 3. The Control of NIDDM With the Gastric Bypass (n = 515)

<table>
<thead>
<tr>
<th>Category</th>
<th>Before Operation</th>
<th>After Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euglycemic</td>
<td>212 (41.2%)</td>
<td>457 (88.7%)</td>
</tr>
<tr>
<td>Hyperglycemic</td>
<td>288 (55.9%)</td>
<td>30 (5.8%)</td>
</tr>
<tr>
<td>Non-insulin-dependent diabetes mellitus</td>
<td>137 (26.6%)</td>
<td></td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>63 (12.2%)</td>
<td></td>
</tr>
<tr>
<td>Undefined, but abnormal</td>
<td>88 (17.1%)</td>
<td></td>
</tr>
<tr>
<td>Inadequate data</td>
<td>15 (2.9%)</td>
<td>28 (5.4%)</td>
</tr>
</tbody>
</table>

NIDDM, non-insulin-dependent diabetes mellitus.
Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations


• « metabolic surgery »
• « diabetes surgery »
• « endocrine surgery »
• « bariatric surgery »
What happened?
Xavier Bichat
(1771-1802)

• Vitalisme !

la vie comme « l'ensemble des fonctions qui s'opposent à la mort »
Gout is a disorder of purine metabolism
Friedrich Wöhler
1800-1882

Synthèse de l’urée, 1928

Synthèse d’un composé organique à partir d’un composé inorganique (cyanate d’ammonium)

\[
\begin{align*}
\text{H}_4\text{N} \overset{\text{O}}{\text{O}} \overset{\Delta}{\rightarrow} \text{H}_2\text{N} \overset{\text{C}}{\text{C}} \overset{\text{NH}_2}{\text{N}}
\end{align*}
\]
Emil Theodor Kocher
1841-1917

• Une fois que la recherche du déterminisme des phénomènes est posée comme le principe fondamental de la méthode expérimentale, il n’y a plus ni matérialisme, ni spiritualisme, ni matière brute, ni matière vivante, il n’y a que des phénomènes dont il faut déterminer les conditions, c’est-à-dire les circonstances qui jouent par rapport à ce phénomène le rôle de cause prochaine.
Emil Theodor Kocher
1841-1917
The Nobel Prize in Physiology or Medicine 1909 was awarded to Theodor Kocher "for his work on the physiology, pathology and surgery of the thyroid gland".
Not only the *thyroid*, but also various other glands such as the *adrenals and the pancreas* play a characteristic part in the processes within the organism by elaborating a secretion peculiar to each gland, which is not excreted, but is diffused throughout the organism and is of the greatest importance to it.
• « metabolic surgery »
• « diabetes surgery »
• « endocrine surgery »
• « bariatric surgery »

**Hormone:**

• A chemical substance produced in the body
• that controls and regulates the activity of certain cells or organs.
THE MECHANISM OF PANCREATIC SECRETION.

By W. M. Bayliss and E. H. Starling. (Seventeen Figures in Text.)

(From the Physiological Laboratory of University College, London.)

CONTENTS.

1. Historical.
2. Experimental methods.
3. The effect of the injection of acid into the duodenum and pancreas.
4. The special experiment.
5. The secretion of secretin.
6. - Pancreatin.
7. The normal mechanism, chemical or nervous?
8. Fate of secretin in the stomach.
10. Action of secretin on the pancreas.
11. Action of other substances on the pancreatic secretion.
12. Inhibitory substances on specific chemical transmitters.

I. HISTORICAL.

It has long been known that the activity of the pancreas is normally called into play by events occurring in the alimentary canal. Börlard* found that the pancreatic secretion could be evoked by the introduction of ether into the stomach or duodenum, and Heidenhain* studied the relation of the time-course of the secretion to the processes of digestion going on in the stomach and intestines.

One exact knowledge of many of the factors determining pancreatic secretion we owe to the work of Pawlow and his pupils; who have shown that the flow of pancreatic juice begins with the entry of the chyme into the duodenum and is not excited directly by the presence of...
Ghrelin 1999

GLP-1
The New Biology of Gastrointestinal Hormones
Physiological Reviews vol 78, 1998 Jens F. Rehfeld
The New Biology of Gastrointestinal Hormones
Physiological Reviews vol 78, 1998 Jens F. Rehfeld
Incretin Effect Beta-cell Response to Iso-glycemic Glucose Challenge

As much as 50% of post-prandial insulin release dependent on Incretins

Diabetes & The “Incretin Effect”

Healthy Patients

Type 2 Diabetics


TRENDS in Endocrinology & Metabolism
Review

The gut as the largest endocrine organ in the body

H. Ahlman & O Nilsson

Department of Surgery and Pathology at the Lundberg Laboratory for Cancer Research, Glioblast University, Glioblast, Sweden

Summary

Secretory, gastrin and cholecystokinin were the first discovered gut hormones. Today we recognize more than 30 gut hormones genes and a multitude of bioactive peptides, which make the gut the largest endocrine organ in the body. Due to structural homologues gut peptide hormones, growth factors have been divided into separate families. It has been emphasized that these peptides are widely distributed, but have a specific expression in different cell types. The intestine can also be regarded as a sensory organ operating via neurons, endocrine cells or hormone cells with gut peptides as signalling substances. Expression studies of peptide receptors in gut neuroendocrine tumors in combination with isolated peptide analogues have been helpful in developing new diagnostic and therapeutic strategies. New fields of research will refer to gut peptides associated with deficiency disorders and its potential growth factors in malignancies. Enterochromaffine cells, scattered throughout the entire gastrointestinal mucosa, form the largest endocrine cell system. The physiological role of gastrointestinal messenger, peptide receptors and amino transporters is currently under investigation as well as their potential involvement in disease, e.g. the parathyroid disease associated with malnutrition and tumors.

Key words: gastrointestinal tract, mucocytes, neuroendocrine tumors, peptide hormones
Biochemistry of adipose tissue: an endocrine organ

Mónica Coelho, Tânia Oliveira, Ruben Fernandes

Abstract
Adipose tissue is no longer considered to be an inert tissue that stores fat. This tissue is capable of expelling an increased production through hyperactivity of existing adipocytes and by inducing differentiation of pre-adipocytes. Adipose tissue metabolism exerts an impact on whole body metabolism. As an endocrine organ, adipose tissue is responsible for the synthesis and release of several hormones. These are active in a range of processes, such as control of nutritional intake (insulin, angiotensin), control of sensitivity to insulin and inflammatory processes (interleukin-6 (IL-6), retinol, visfatin, adiponectin, among others) and pathways (hypoxia-inducible factor-1 (HIF-1), interleukin-6 (IL-6), retinol, visfatin, adiponectin, among others) and pathways (hypoxia-inducible factor-1 (HIF-1), interleukin-6 (IL-6), retinol, visfatin, adiponectin, among others).

Keywords: adipose tissue, adipocytes, adipokines.
The New Biology of Gastrointestinal Hormones
Physiological Reviews vol 78, 1998 Jens F. Rehfeld

Ghrelin
1999
Getting Your Leptin & Ghrelin in Balance
Metabolic syndrome

- insulin resistance
- obesity
- atherogenic dyslipidemia
- Hypertension

- « metabolic surgery »
- « diabetes surgery »
- (endocrine surgery)
- (bariatric surgery > BMI 35)
Metabolic surgery
How could it work?
Restriction calorique
Foregut vs. Hindgut

- Foregut hypothesis suggests exclusion of duodenum and proximal jejunum from the transit of nutrients may interrupt signals that lead to insulin resistance and Type 2 DM

- Hindgut hypothesis suggests enhanced delivery of nutrients to distal ileum alters secretion of hormones & improves glucose metabolism

*** GLP-1 may be a major mediator of this effect

*Rubino F. Bariatric Surgery: effects on glucose homeostasis. Curr Opin Clin Nutr Metab Care 9:497-507*
Anti-Incretins

Rubino & Gagner
Ann Surg 2002

- Cells producing incretins
  (ileum, duodenum, jejunum)
- Cells producing the unknown factor with anti-incretin effect
Anti-Incretins: The Effect of Duodenal Exclusion

Possible mechanisms of action:
1. Avoidance of stimulation of cells producing the unknown factor with anti-incretin effect
2. Earlier and/or increased GLP-1 production

GLP-1 and other hormones

Improved insulin response and action

Anti-incretin factor

Normalization of plasma insulin and glucose

Rubino & Gagner
Ann Surg 2002
75 % = restriction

25 % =
fore gut theory
glucagon / CCK / biliopancreatic enzymes
hind gut theory
(GLP-1 / PYY)
Bariatric–metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial

Gaitreude Mingrone, Simona Piacentini, Andrea de Gaetano, Caterina Guidone, Amerigo Lencioni, Giuseppe Nannini, Marco Castegnato, Stefan Bohnlein, Francesca Rubino

Lancet 2015; 386: 964-73
Lancet 2015; 386: 964–73
Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations

Francesco Rubino1, David M. Nathan2, Robert H. Eckel3, Philip R. Schauer, K. George M.M. Alberti5, Paul Z. Zimmet6, Stefano Del Prato7, Linong Ji8, Shaukat M. Sadikot9, William H. Herman10, Stephanie A. Amiel1, Lee M. Kaplan2, Gaspar Taroncher-Oldenburg11 and David E. Cummings12 on behalf of the Delegates of the 2nd Diabetes Surgery Summit*
Questions for evidence assessment included the following

• 1) long-term effects of surgery on glycemic control in patients with T2D;

• 2) effectiveness of surgery compared with medical/lifestyle interventions on glycemic control;

• 3) comparative effectiveness of different procedures on T2D;

• 4) effects of surgery on microvascular complications of diabetes, CVD risk, CVD events, and mortality;

• 5) short- and long-term surgical safety;

• 6) comparative safety profile of different operations.
## A

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<th>Study Description</th>
<th>Surgery</th>
<th>N</th>
<th>Mean</th>
<th>SEM</th>
<th>95% CI</th>
<th>P Value</th>
<th>Study Details</th>
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## B

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### Footnotes
- Footnote 1: [Details]
- Footnote 2: [Details]
- Footnote 3: [Details]
# ABCD SCORE (RANGE 0 TO 10)

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<th>&lt;2</th>
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<th>3-4.9</th>
<th>&gt;5</th>
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<td>C-peptide (mmol/L)</td>
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<td>2-2.9</td>
<td>3-4.9</td>
<td>&gt;5</td>
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<td>DURATION T2DM</td>
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<td>4-8</td>
<td>1-3.9</td>
<td>&lt;1</td>
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<tr>
<td>BMI</td>
<td>&lt;27</td>
<td>27-34.9</td>
<td>35-41.9</td>
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<td>BMI</td>
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<td>C-peptide (mmol/L)</td>
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<tr>
<td>DURATION T2DM</td>
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4th May, 2017
Remission rate of T2DM according to ABCD score

<table>
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<tr>
<th>ABCD SCORE</th>
<th>HbA1C &lt; 6%</th>
<th>HbA1C&lt;6.5%</th>
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<tbody>
<tr>
<td>0</td>
<td>5.9 %</td>
<td>5.9 %</td>
</tr>
<tr>
<td>1</td>
<td>5 %</td>
<td>20 %</td>
</tr>
<tr>
<td>2</td>
<td>26.3 %</td>
<td>38.6 %</td>
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<tr>
<td>3</td>
<td>31.9 %</td>
<td>42 %</td>
</tr>
<tr>
<td>4</td>
<td>52.5 %</td>
<td>67.8 %</td>
</tr>
<tr>
<td>5</td>
<td>55.4 %</td>
<td>75 %</td>
</tr>
<tr>
<td>6</td>
<td>61.7 %</td>
<td>78.3 %</td>
</tr>
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<td>7</td>
<td>77 %</td>
<td>92.3 %</td>
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<tr>
<td>8</td>
<td>85.2 %</td>
<td>96.3 %</td>
</tr>
<tr>
<td>9</td>
<td>87.1 %</td>
<td>87.1 %</td>
</tr>
<tr>
<td>10</td>
<td>93.3 %</td>
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</tr>
<tr>
<td>Overall</td>
<td>52.2 %</td>
<td>64.7 %</td>
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According to the analysis of 510 cases of Asian Diabetes Surgery Study (ADSS)
Bariatric surgery

Metabolic surgery