

## ASSIUT UNIVERSITY DRUG INFORMATION BULLETIN

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كليسة الصيدلسة

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# **Bariatric Surgery**

The term **bariatrics** was created around 1965, from the Greek root bar- ("weight," as in barometer), suffix -iatr ("treatment," as in pediatrics), and suffix -ic ("pertaining to").

Bariatric surgery is the surgical alteration of the stomach, intestine, or both to cause weight loss. Development of safer laparoscopic approaches has made this surgery more popular.

#### Indications

The generally accepted criteria for surgical treatment include

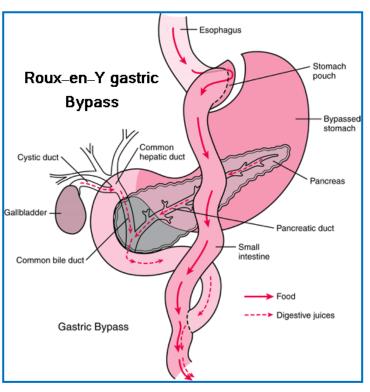
 Have a body mass index (BMI) of > 40 kg/m<sup>2</sup> or a BMI
35 kg/m<sup>2</sup> in combination with high-risk comorbid conditions (e.g., diabetes,

hypertension, obstructive sleep apnea, highrisk lipid profile).

- Have acceptable operative risk.
- Be well-informed and motivated.
- Have unsuccessfully tried all reasonable nonsurgical methods to lose weight and manage obesity-associated complications.

#### **Contraindications include**

- An uncontrolled psychiatric disorder such as major depression, untreated schizophrenia
- Current drug or alcohol abuse.
- Cancer that is not in remission.
- Another life-threatening disorder.
- Inability to comply with nutritional requirements, including life-long vitamin replacement (when indicated).



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#### Medical Therapy

A preoperative trial of weight loss is beneficial to ensure patient compliance with the postoperative diet protocol. Also, a preoperative liquid diet can shrink the liver, thus facilitating the surgical procedure.

#### **Surgical Procedures**

Types of bariatric surgery include the following:

- Restrictive procedures (eg, adjustable gastric banding, sleeve gastrectomy)
- Restrictive procedures with some malabsorption (eg, Roux-en-Y gastric bypass)
- Malabsorptive procedures with some restriction (eg, biliopancreatic diversion with duodenal switch)

Most procedures are done laparoscopically, resulting in less pain and a shorter healing time than open surgery.

#### Roux-en-Y gastric bypass surgery- RYGB

Accounts for about 80% of bariatric procedures in the US and is usually done laparoscopically. A small part of the proximal stomach is detached from the rest, creating a stomach pouch of < 30 mL. Also, food bypasses part of the stomach and small intestine, where it is normally absorbed, reducing the amount of food and calories absorbed. The pouch is connected to the proximal jejunum; the opening between them is narrow, limiting the rate of gastric emptying. The segment of small intestine. This arrangement allows bile acids and pancreatic enzymes to mix with GI contents, limiting malabsorption and nutritional deficiencies.

RYGB is particularly effective in treating diabetes; remission rates are up to 62% after 6 years. For many patients who have had RYGB, eating high-fat and high-sugar foods can cause **dumping syndrome**; symptoms can include light-headedness, diaphoresis, nausea, abdominal pain, and diarrhea. Dumping syndrome may inhibit the consumption of such foods by adverse conditioning.

#### Adjustable gastric banding-AGB

AGB is the 2nd most common bariatric procedure done in the US. A band is placed around the upper part of the stomach to divide the stomach into a small upper pouch and a larger lower pouch. Typically, the band is adjusted 4 to 6 times by injecting saline into the band via a port that is placed subcutaneously. When saline is injected, the band expands, restricting the upper pouch of the stomach. As a result, the pouch can hold much less food, patients eat more slowly, and satiety occurs earlier. This procedure is usually done laparoscopically. Saline can be removed from the band if a complication occurs or if the band is overly restrictive.

Weight loss with the band varies and is related to the frequency of follow-up; more frequent follow-ups result in greater weight loss. Although postoperative morbidity and mortality are less than those with RYGB, long-term **complications**, including repeat operations, are more likely, possibly occurring in up to 15% of patients.

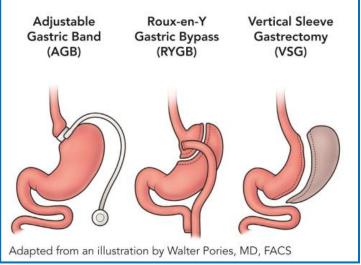
#### Sleeve gastrectomy-SG

Traditionally, SG has been done only when patients are considered too high risk for procedures such as RYGB and biliopancreatic diversion (eg, patients with a BMI > 60); typically before one of these procedures or another similar procedure is done. However, because SG causes substantial and sustained weight loss, it is being used increasingly in the US as definitive treatment for severe obesity. Part of the stomach is removed, creating a tubular stomach passage. The procedure does not involve anatomic changes to the small intestine.

Mean excess weight loss tends to be higher than with that with AGB. Although traditionally classified as a restrictive procedure, weight loss is probably also related to neurohormonal changes. The most serious **complication** is gastric leak at the suture line; it accounts for 1 to 3% of complications.

#### Biliopancreatic diversion with a duodenal switch

This procedure accounts for < 5%of bariatric procedures done in the US. Part of the stomach is removed, causing restriction. The remaining part empties into the duodenum. The duodenum is cut and attached to the ileum. bypassing much of the small intestine, including the sphincter of (where bile acids Oddi and pancreatic enzymes enter); as a result, food absorption decreases. procedure is technically This demanding but can sometimes be laparoscopically. done



Malabsorption and nutritional deficiencies often develop.

#### What are the endocrine-related benefits of bariatric surgery?

- Improve or eliminate type 2 diabetes. RYGB can improve diabetes within days, even without weight loss.
- Help bring blood fat levels back to normal—lowering LDL and triglycerides, and raising HDL.
- Improve fertility in women who are obese, especially women with polycystic ovary syndrome (PCOS). PCOS is a common condition in women of reproductive age. It can result in diabetes, high blood pressure, and unhealthy blood fat levels
- Increase testosterone levels in men who are very obese
- Improve or eliminate high blood pressure

#### What are the endocrine-related risks of bariatric surgery?

Perioperative risks are lowest when bariatric surgery is done in an accredited center.

Complications include gastric and/or anastomotic leaks, pulmonary complications (eg, ventilator dependence, pneumonia, pulmonary embolism), MI, wound infection, incisional hernia, small-bowel obstruction, GI bleeding, ventral hernia, and deep venous thrombosis. These complications can cause significant morbidity, prolong

hospitalization, and increase costs. Tachycardia may be the only early sign of anastomotic leak.

Later problems may include prolonged nausea and vomiting secondary to small-bowel obstruction and anastomotic stenosis. Nutritional deficiencies (eg, protein-energy undernutrition, vitamin B<sub>12</sub> deficiency, iron deficiency) may result from inadequate intake, inadequate supplementation, or malabsorption. Malodorous flatulence, diarrhea, or both may develop, particularly after malabsorptive procedures. Ca and vitamin D absorption may be impaired, causing deficiencies and sometimes hypocalcemia and secondary hyperparathyroidism. With prolonged vomiting, thiamin deficiency may occur. Patients may have symptoms of reflux, especially after SG. During rapid weight loss, cholelithiasis (often symptomatic), gout, and nephrolithiasis may develop.

Eating habits may be disordered. Adjusting to new eating habits can be difficult.

#### Prognosis

Overall 30-day mortality in hospitals accredited by the American Society of Bariatric Surgery as centers of excellence is 0.2 to 0.3%. Mortality is higher with RYGB than laparoscopic AGB and higher with open procedures (2.1%) than laparoscopic procedures (0.2%). Factors that predict higher risk of mortality include a history of deep venous thrombosis or pulmonary embolism, obstructive sleep apnea, and poor functional status. Other factors such as severe obesity (BMI > 50), older age, and male sex have also been associated with higher risk but the evidence is inconsistent.

Average excess weight loss depends on the procedure.

For *laparoscopic AGB*, weight loss is 45 to 72% at 3 to 6 yr and 14 to 60% at 7 to 10 yr. Percentage of weight loss is related to the frequency of follow-ups and number of band adjustments. Patients with a lower BMI tend to lose more weight than those with a higher BMI. For *SG*, weight loss is 33 to 58% at 2 yr and 58 to 72% at 3 to 6 yr; longer-term data are not available. For *RYGB*, weight loss is 50 to 65%.

Comorbid conditions that tend to recede or resolve after bariatric surgery include cardiovascular risk factors (eg, dyslipidemia, hypertension, diabetes), cardiovascular disorders, diabetes, obstructive sleep apnea, osteoarthritis, and depression. Diabetes is particularly likely to remit (eg, with RYGB, up to 62% of patients at 6 yr). All-cause mortality decreases by 25%, primarily because cardiovascular and cancer mortality is reduced.

**References:**1)www.merckmanuals.com/professional/nutritional\_disorders/obesity\_and\_the\_metabolic\_syndrome/bar iatric\_surgery.html

2) http://emedicine.medscape.com/article/197081-overview 3) http://www.hormone.org



## Terminology March Haemoglobinuria

A complication of walking and running over long distances (marathon running). It is due to damage to red blood cells in the blood vessels of the soles of the feet. This results in haemoglobin being released into the bloodstream, which is then voided in the urine causing redness of the urine – the condition known as HAEMOGLOBINURIA. No treatment is required but can be minimized by decreasing walking/running on hard surfaces or wearing more appropriate footwear and padded shoes.

**Reference:**1) Marcovitch H. 2005. Black's Medical Dictionary. 41<sup>th</sup> ed. London: A&C Black Publishers Limited. p 432. 2) http://www.oxfordreference.com/view/10.1093/oi/authority.20110803100133231

# FDA Approval FDA Approval: Dapagliflozin for Type 2 Diabetes

The US FDA has approved dapagliflozin (Farxiga) for the treatment of type 2 diabetes.

It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus as monotherapy, as initial therapy with metformin, or as an add-on to other oral glucose-lowering agents, including metformin, pioglitazone, glimepiride, sitagliptin (*Januvia*), and insulin.

Dapagliflozin works by inhibiting SGLT2 (sodium/glucose cotransporter) and blocking resorption of glucose in the kidney, leading to an increase in urinary glucose excretion and lowering of both plasma glucose levels and body weight.



Dapagliflozin is the second SGLT2 inhibitor to be licensed in the

United States. The FDA cleared the first, canagliflozin (*Invokana*), for marketing in March 2013. The agency is expected to announce a decision on a third SGLT-2 inhibitor, empagliflozin, by the end of March 2014.

Dapagliflozin is already approved in the 28 member states of the European Union, where it is known by the brand name *Forxiga*, and in Argentina, Australia, Brazil, Iceland, Mexico, Norway, and New Zealand.

#### FDA Requiring Several Postmarketing Studies

The safety and effectiveness of dapagliflozin were evaluated in 16 clinical trials involving more than 9400 patients with type 2 diabetes, showing improvement in hemoglobin A1c (HbA1c) levels. The most common adverse effects among those treated with dapagliflozin were genital fungal infections and urinary tract infections.

Because a numeric increase in bladder cancer was seen with dapagliflozin in one of these trials, dapagliflozin is not recommended for patients with active bladder cancer or moderate to severe renal impairment.

The FDA is requiring the companies to perform several postmarketing studies, including one already underway called DECLARE-TIMI 58 (Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events) in which more than 17,000 patients will be observed for 4 to 5 years to ascertain whether dapagliflozin is associated with increased risks for cardiovascular events, liver problems, or malignancies.

Other required postmarketing trials will further assess bladder cancer and the drug's effect in a pediatric population. The FDA is also requiring an enhanced pharmacovigilance program to monitor reports of liver problems and pregnancy outcomes.

The FDA had previously rejected dapagliflozin in January 2012, in part because of the breast- and bladder-cancer concerns. New data provided at a December 2013 advisory committee hearing allayed those concerns in large part.

Source: www.medscape.org/viewarticle/818575?src=cmemp

# **Test Your Knowledge**

- 1. Patients with phenylketonuria (PKU) should avoid food products containing
- (A) unsaturated fats
- (D) sodium chloride

- (C) soy protein (E) aspartame
- 2. A patient with an abnormally elevated number of erythrocytes
- is said to have
- (A) macrocytic anemia
- (C) sickle cell anemia
- (B) polycythemia (D) aplastic anemia

(B) ethacrynic acid

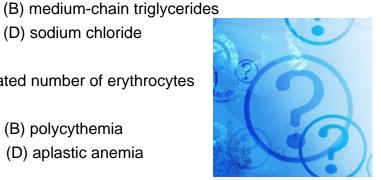
- (E) microcytic anemia
- 3. The agent most likely to precipitate when added to DsW or NS is
- (A) tetracycline HCI
- (C) tobramycin sulfate (D) phenytoin sodium
- (E) ascorbic acid
- 4. A tine test is employed in identifying patients who have been exposed to
- (A) acquired immunodeficiency syndrome(AIDS)
- (B) influenza
- (D) hepatitis virus

(C) herpes simplex (E) tuberculosis



At the "Drug Information Center", we respond to enquiries from the professional health team as well as from others. Here's one of the enquiries received at the center! Enquiry received from Ph. Sara Emad - Pediatrics' Hospital, Assiut Uni. **Enquiry:** How is Phenytoin withdrawn? Summary of Answer:

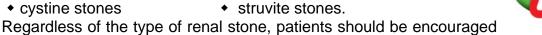
- Carefully and slowly adjust dosage according to individual requirements and response.
- When a patient is transferred from phenytoin to another anticonvulsant, gradually reduce the phenytoin dosage over a period of about 1 week while at the same time therapy is instituted with a low dose of the replacement drug.
- When phenytoin replaces phenobarbital or any other barbiturate anticonvulsant, reduce the dose of the barbiturate gradually over a period of 1 week to prevent withdrawal symptoms.
- Withdraw phenytoin slowly to avoid precipitating seizures or status epilepticus



## Ask the expert- Clinical Nutrition Should patients with renal stones follow a special diet?

Renal stones are generally generated when the concentration of components in the urine is above the level that allows crystallization. According to their chemical constituents, they are classified as:

- calcium stones
- uric acid stones
- cystine stones



to increase their fluid intake in order to produce at least two liters of urine per day. Moreover, sodium restriction seems to be beneficial for patients with renal stones, as urinary sodium excretion is correlated with calcium, uric acid and cystine excretion. In the past, patients with calcium stones were advised to reduce calcium intake. However, calcium restriction (<400mg/day) does not positively affect calcium stone formation. On the contrary, the reduction of dietary oxalate is advised, as the majority of urinary calculi contain oxalate. The principal dietary sources of oxalate are spinach, beetroots, strawberries, chocolate, peanuts, tea and rhubarb. Moreover, as vitamin C is important for the formation of oxalic acid in the human body, the supplemental intake of this vitamin should be avoided [reference nutrient intake (RNI) = 60mg/day, recommended dietary allowance (RDA) = 60-95mg/dav].

Regarding uric acid stones, patients should be advised to decrease their protein intake, especially from sources with high purine content. In addition to that, other dietary sources of purine should be avoided. (Examples high-purine of sources include: sweetbreads, anchovies, sardines, liver, beef kidneys, brains, meat extracts, herring, mackerel, scallops, game meats, beer and gravy).

References : 1) Katsilambrose .N. , 2010, Clinical Nutrition In Practice. A John Wiley & Sons, Ltd., Publication, p. 128 2) www.webmd.com

## **Complementary medicine** Arnica montana L.

#### Part Used: Flower head

Sesquiterpene Constituents: lactones (arnifolin, arnicolides, helenalin); flavonoids (such as eupafolin, patuletin, and spinacetin); volatile oil, containing thymol and various ethers of thymol; miscellaneous: phenolic acids, coumarins, resins, bitters (arnicin), tannins, carotenes.

#### Actions: Anti-inflammatory, vulnerary

**Indications:** This herb should not be taken internally, as it is potentially toxic. However, arnica provides us with



one of the best external remedies for local healing, and may be considered a specific when it comes to the treatment of bruises and sprains.

The homeopathic preparation is entirely safe to take internally, especially when used according to homeopathic directions. The herb itself, used externally, will help relieve pain and inflammation of phlebitis, rheumatism, and similar conditions. In fact, it may be used on the skin in all cases of pain or inflammation, as long as the skin is not broken. Arnica has been shown to be an immunostimulant, as both the sesquiterpene lactone

helenalin and the polysaccharide fraction stimulate phagocytosis. Sesquiterpene lactones are known to have anti-inflammatory activity, and their biological effects appear to be mediated through immunological processes. The fact that helenalin is an anti-inflammatory sesquiterpene lactone might help account for the value of arnica for pain and inflammation.

**Safety Considerations:** Due to the toxicity of the sesquiterpene lactones it contains, oral use of arnica must be avoided altogether. Topical applications of arnica may cause an allergy in the form of painful, itchy, inflammatory changes to the skin in some people.

**Preparations and Dosage:** For topical use, a simple folk tincture will suffice. Pour  $\frac{1}{2}$  liter (1 pint) of 70% alcohol over 50 g (2 ounces) of freshly picked flowers in a clear glass container. Seal and let stand for at least a week in the sun or a warm place. Filter and store in a sealed container; keep out of direct sunlight. Use as needed.

Reference: Hoffmann. D. 2003, MEDICAL HERBALISM- The Science and Practice of Herbal Medicine p.529.

Answers:

- Q1: (E) aspartame
- **Q2:** (B) polycythemia
- Q3: (D) phenytoin sodium
- **Q4:** (E) tuberculosis

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