Al-Maarif University	Clinical Pharmacy-I	4th Stage	College of Pharmacy

Diarrhoea and Constipation

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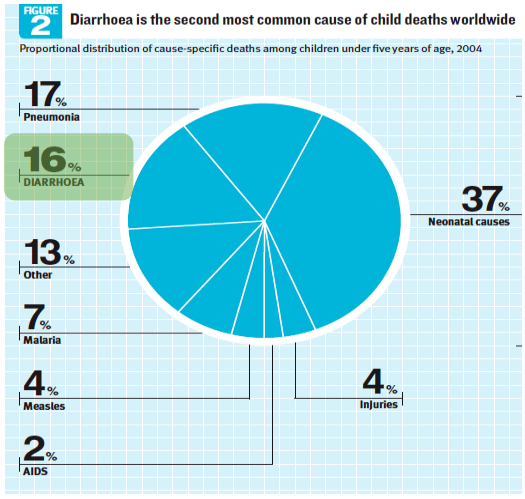
Lecture No. 5

Introductions

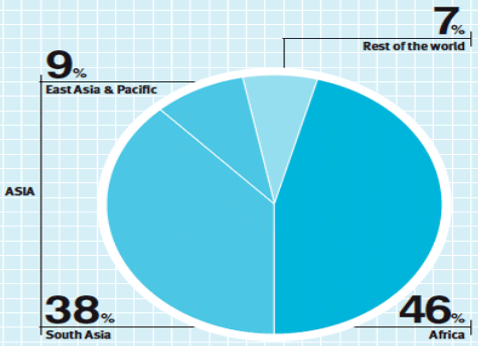
- Diarrhea is characterized by an **abnormal increase** in stool **frequency, liquidity, or weight**.
- Although normal bowel movement frequency varies among individuals, having **more than 3 bowel movements per day** is generally considered abnormal.
- **Global Impact**: Diarrhea is a **significant cause of morbidity** globally, with around **2.5 billion episodes** of **acute diarrhea** annually.
- It is particularly deadly for **children under 5 years old**, contributing to **1.9 million deaths each year**.



Introductions

FIGURE 3 More than 80 per cent of child deaths due to diarrhoea occur in Africa and South Asia

Proportional distribution of deaths due to diarrhoeal diseases among children under five years of age, by region, 2004



Source: World Health Organization, Global Burden of Disease estimates, 2004 update, with additional analyses to calculate UNICEF regions.

FIGURE 4 Nearly three quarters of child deaths due to diarrhoea occur in just 15 countries

RANK	COUNTRY	TOTAL NUMBER OF ANNUAL CHILD DEATHS DUE TO DIARRHOEA
1	India	386,600
2	Nigeria	151,700
3	Democratic Republic of the Congo	89,900
4	Afghanistan	82,100
5	Ethiopia	73,700
6	Pakistan	53,300
7	Bangladesh	50,800
8	China	40,000
9	Uganda	29,300
10	Kenya	27,400
11	Niger	26,400
12	Burkina Faso	24,300
13	United Republic of Tanzania	23,900
14	Mali	20,900
15	Angola	19,700

Source: World Health Organization, Global Burden of Disease estimates, 2004 update. The totals were calculated by applying the WHO cause of death estimates to the most recent estimates for the total number of under-five deaths (2007).

• Types of Diarrhea:

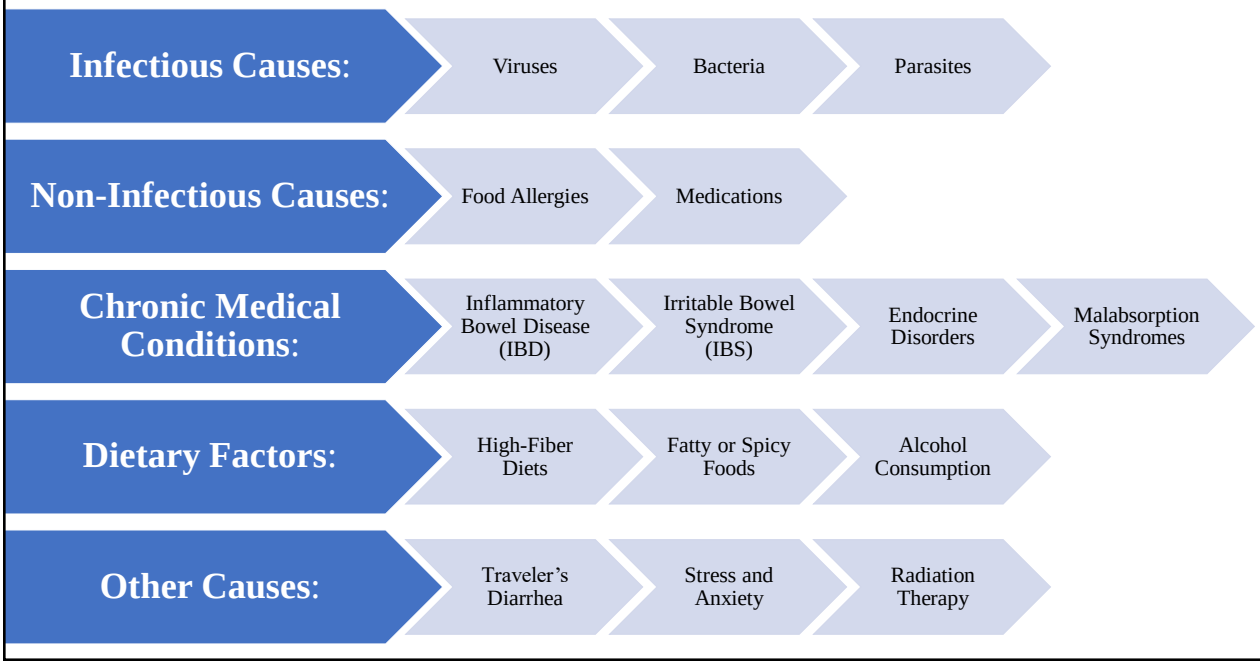
- **Defines** Diarrhea as **the passage of three or more loose or liquid stools per day**.
- It is **not a disease but a sign** of an underlying problem, such as an **infection** or **gastrointestinal disorder**.
- **It can be classified :**

By Duration:	• Acute Diarrhea • Persistent Diarrhea • Chronic Diarrhea
By Cause:	• Infectious Diarrhea • Non-Infectious Diarrhea • Traveler's Diarrhea
By Mechanism:	• Osmotic Diarrhea • Secretory Diarrhea • Inflammatory Diarrhea • Malabsorption/Maldigestion Diarrhea • Motility-Related Diarrhea

• Types of Diarrhea:

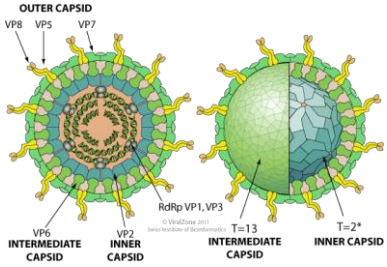
1. **Acute Diarrhea**: Lasts **less than 14 days**. It is typically managed with **fluid and electrolyte replacement**, **dietary changes**, and **nonprescription medications**.
2. **Persistent Diarrhea**: Lasts **14 days to 4 weeks**. It requires more thorough evaluation.
3. **Chronic Diarrhea**: Persists for **more than 4 weeks**. It is often due to underlying **chronic medical conditions** or treatments, and typically requires **medical care**. The focus here will be on **acute diarrhea**, as chronic and persistent types fall outside the scope of general management.

Etiology of Diarrhea



Etiology of Diarrhea

- **Acute gastroenteritis**, the most common cause of diarrhoea in all age groups, is usually viral in origin.
- Commonly implicated viruses are the **rotaviruses** (now vaccine available) and **noroviruses**.
- Viruses tend to cause diarrhoea by **blunting** the villi of the upper small intestine, decreasing the absorptive surface.



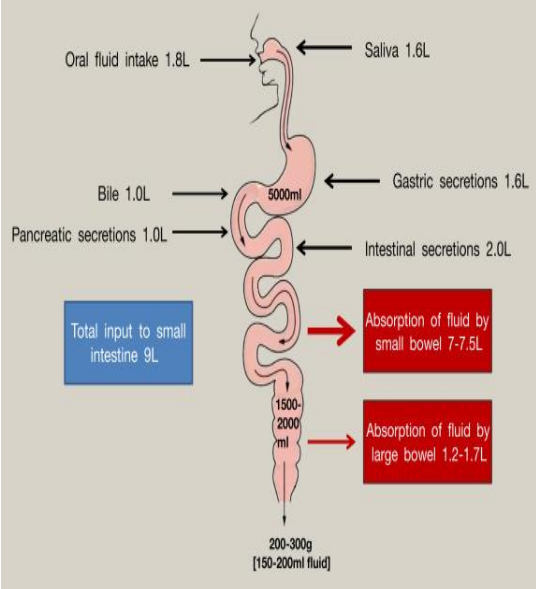
Etiology of Diarrhea

- **Bacterial** causes of diarrhoea are normally a result of **eating contaminated food** or **drink**, which cause diarrhoea by a number of mechanisms.
- For example,

1- Enterotoxigenic *Escherichia coli* (ETEC):	• Produces **enterotoxins** that cause secretion and **loss of fluids** in the intestines, leading to watery diarrhea.
2- Enteropathogenic *Escherichia coli* (EPEC):	• **Interferes with normal mucosal function**, disrupting the intestinal surface and leading to diarrhea.
3- Enteroinvasive *E. coli* (EIEC), Shigella, and **Salmonella spp.:**	• Cause **injury to the mucosa** of the small intestine and **deeper tissues**, often leading to bloody diarrhea and inflammation.

Pathophysiology

- **Fluid Intake and Production**:
- About **8 to 9 liters** of fluid enter the **small intestine** daily.
- This includes **1 to 2 liters** from **dietary intake**, with the remaining fluid coming from **salivary, gastric, biliary, pancreatic**, and **intestinal secretions**.
- **Absorption in the Small Intestine and colon**:
- The **small intestine absorbs** all but **1 to 2 liters** of this fluid, which then passes into the **colon**.
- The **colon absorbs most** of the remaining fluid, leaving less than **200 grams per day** of stool.
- **Mechanism of Diarrhea**:
- **Disruption** in the **absorption** of **ions, solutes, and water** or an **increase in electrolyte secretion** can lead to **water accumulation** in the intestinal lumen.
- This excess fluid in the intestinal lumen results in **diarrhea**.



key questions to ask patients with diarrhea

Nature of the Stools:	• Presence of **blood and mucus** (dysentery) suggests potential invasive infections • (e.g., *Shigella*, *Salmonella*, *Clostridium difficile*, *E. coli*). • Bloody stools can also indicate conditions like inflammatory bowel disease (IBD).
Periodicity:	• **Recurrent diarrhea** with no known cause should be **referred** for further investigation.
Duration:	• **Chronic** diarrhea warrants **referral**. Common causes include IBS, inflammatory disease, and colon cancer.
Onset of Symptoms:	• **Symptoms can appear within hours to days after consuming contaminated food**. It's important to assess recent food intake and if others were affected.
Timing of Diarrhea:	• Diarrhea **occurring first thing in the morning** could suggest underlying conditions like **IBS**.
Recent Change of Diet:	• Diet changes can affect bowel function, including travel-related causes like **giardiasis**.
Signs of Dehydration:	• **Mild dehydration** (<5% loss) includes symptoms like **tiredness** and **dry mouth**. • **Moderate dehydration** (5%-10%) is characterized **by dry mouth**, **sunken eyes**, **decreased urination**, and **reduced skin elasticity** (pinch test).

Clinical Features of Acute Diarrhea

- Symptoms typically develop rapidly, often in patients who were previously in good health.
- **Symptoms**:
  - **Nausea and vomiting** may occur before or during the diarrhea episode.
  - **Abdominal cramping, flatulence**, and **tenderness** are commonly present.
- If **rotavirus** is the cause, additional **viral prodromal symptoms** like **cough** and **cold** may be experienced.
- **Nature of Diarrhea**:
  - **Acute infective diarrhea** is typically **watery** without the presence of blood.
  - Symptoms usually **resolve within 2 to 4 days**.
  - Diarrhea lasting more than **10 days** is unlikely to have an **infective cause** and may indicate another underlying issue.

Conditions to Eliminate in Cases of Diarrhea

Medicine-Induced Diarrhea:	• Such as Antibiotics, Chemotherapy, NSAIDs, and Mg containing drugs. If suspected, the patient's doctor should be contacted for alternatives.
Irritable Bowel Syndrome:	• A functional **gastrointestinal disorder**.
Giardiasis:	• A **protozoan infection** contracted through drinking **contaminated** water.
Fecal Impaction:	• Often seen in **older adults** or those with **limited mobility**.
Ulcerative Colitis and Crohn's Disease:	• Both can affect any age group, with bloody diarrhea as a major symptom in mild cases. Patients may experience left lower quadrant pain, urgency, nocturnal diarrhea, and early morning rushes.
Colorectal Cancer:	• Strongly related to age, with 75% of cases in individuals aged > 65 . Signs such as anemia, change in bowel habits, and weight loss (typically in later stages) require further invistigations.
Malabsorption Syndromes:	• **Lactose Intolerance**: Commonly diagnosed in infants < 1 yr, presenting with loose stools, fever, vomiting, and weight gain failure. • **Celiac Disease**: Has a bimodal incidence (early infancy and ages 40-50) when cereals become a major constituent of the diet. Symptoms include steatorrhea, bloating, abdominal pain, fatigue, and weight loss.

Evidence Base for Over-the-Counter Medication in Acute Diarrhea

Acute infectious diarrhea remains a leading cause of death in developing countries, despite treatment advancements.

Goals of OTC Treatment:	• The primary focus is on **symptom relief** for patients. • Most causes of diarrhea resolve within **24 to 48 hours**; therefore, treatment aims to manage symptoms during this period.
Hydration Focus:	• The main treatment objective is to **prevent dehydration** resulting from fluid loss.
Motility-Reducing Agents:	• Medications that alter gut motility, such as **loperamide**, should be used cautiously and reserved for situations where **it is impractical for the patient to stay at home and rest.**

Options for Diarrhea Treatment

Oral Rehydration Solutions (ORS):	• Used to prevent and treat dehydration by replenishing lost fluids and electrolytes.
Antidiarrheal Medications:	• **Loperamide (Imodium)**: Slows gut motility, effective for non-infectious diarrhea. • **Bismuth Subsalicylate (Pepto-Bismol)**: Provides symptomatic relief and has antimicrobial properties.
Probiotics:	• Supplements that can help restore gut flora and may reduce the duration of diarrhea.
Dietary Modifications:	• **BRAT Diet**: Bananas, Rice, Apple sauce, Toast – recommended for mild cases. • Avoiding dairy, fatty foods, and high-fiber foods during recovery.
Medications for Specific Causes:	• **Antibiotics**: Indicated for bacterial infections (e.g., **Ciprofloxacin** for travelers' diarrhea) based on specific pathogens identified. • **Antiparasitics**: For protozoal infections like giardiasis (e.g., **Metronidazole**).
Fluid Replacement:	• Intravenous (IV) fluids may be necessary for severe dehydration or inability to take ORS orally.
Symptomatic Relief:	• Antiemetics for nausea and vomiting (e.g., **Ondansetron**).
Referral	• Essential for persistent, severe, or bloody diarrhea, or if accompanied by high fever or severe abdominal pain

Oral Rehydration Solution (ORS)

ORS is a simple and highly effective treatment that significantly reduces mortality and morbidity associated with dehydration. ORS is first-line treatment for all age groups, especially children and frail older adults.

WHO Recommended Formula:	• The formula contains:
	  • **Glucose**: 75 mmol/L
	  • **Sodium**: 75 mmol/L
	  • **Potassium**: 20 mmol/L
	  • **Chloride**: 65 mmol/L
	  • **Citrate**: 10 mmol/L
	• The solution is formulated to be almost isotonic.

Volume of Solution:	• The amount of ORS given depends on the volume of fluid lost.
Dosage for Adults:	• Administer **2 liters** of ORS in the first **24 hours**. • Afterward, allow **unrestricted normal fluids**. • Provide an additional **200 mL** of rehydration solution for each loose stool.
Administration Method:	• The solution should be sipped every **5 to 10 minutes** rather than consumed in large quantities at once.
Dosage for Infants:	• Administer **1 to 1.5 times** the usual feeding volume of ORS.

Loperamide Overview

- Loperamide is a **synthetic opioid analogue**. It is a useful adjunct in reducing the number of bowel movements.
- **Mechanism of Action**:
  - It works by binding to **opiate receptors** in the gut, leading to a reduction in intestinal motility and increasing the water absorption capacity of the intestines.
  - Loperamide has **minimal CNS side effects**, making it safer for most patients.
- Dosage:
  - **Initial Dose**: Two tablets taken immediately.
  - **Subsequent Doses**: One tablet after each additional bout of diarrhea.
  - The maximum **over-the-counter (OTC) dosage** is **16 mg/day**.
  - **Not recommended for children** under 12 years of age.

Rotavirus Vaccine

- The **rotavirus vaccine** was added to the **UK childhood vaccination schedule** in **2013**.

- **Administration**:
  - The vaccine is **oral** and given in **two doses**:
    - **First Dose**: At **2 months** of age.
    - **Second Dose**: At **3 months** of age.
  - It is administered alongside other routine childhood vaccinations.
- **Impact**:
  - Since the introduction of the vaccine, **rotavirus cases** have decreased by more than **80%**, significantly reducing the burden of the disease.

Introduction: Constipation

- Constipation is characterized by the **infrequent passage of hard stools**.
- Patients may have symptoms such as **straining**, **a sensation of incomplete evacuation**, and **discomfort on abdomen**.
- It is considered a symptom rather than an independent condition, similar to diarrhea.
- **Types**:
  - **Acute Constipation**: Lasts less than 1 week.
  - **Chronic Constipation**: Persists for more than 4 weeks.

Prevalence and Epidemiology of Constipation

❑Constipation is a common issue that **affects individuals across all age groups**.

- It is particularly prevalent among older adults.
- Many maintain a normal frequency of bowel movements but experience **straining** due to factors like a **sedentary lifestyle**, **decreased fluid intake**, **poor nutrition**, **avoidance of fibrous foods**, and **chronic illnesses**.

❑**Gender Differences**

- Women are 2 to 3 times more likely to suffer from constipation compared to men.
- **Pregnancy**: Around 40% of women experience constipation during late pregnancy.

Aetiology of Constipation

Decreased Intestinal Transit Time	• The primary cause of constipation is **a decreased transit time** through the intestinal tract. This allows more water to be absorbed from the large bowel, resulting in harder, more difficult-to-pass stools.
Dietary Fibre Deficiency	• A low intake of dietary fiber is a significant contributor to constipation, as fiber helps in bowel movements.
Lifestyle and Environmental Changes	• Changes in daily routine, **reduced physical activity**, or **shifts in environment can contribute to constipation**.
Medication	• Opioids, Ca Channel Blocker, Diuretics and Aluminum containing antacids.

Differential Diagnosis for Constipation

Establish the Patient's Normal Bowel Habit:	• Compare current symptoms with what is typical for the patient.
Assess for serious Pathology:	• While constipation is often not due to a serious condition, any significant changes should be evaluated.
Identify Primary Causes:	• **Dietary Intake**: Low in fiber. • **Lifestyle Factors**: Lack of physical activity. • **Disorders of Rectal Evacuation**.
Consider Secondary Causes:	• **Medications**: Such as opioids. • **Neurological Disorders**: e.g., multiple sclerosis, Parkinson's disease. • **Metabolic and Endocrine Conditions**: e.g., diabetes, hypothyroidism. • **Psychological Factors**: e.g., depression, eating disorders.

Specific questions to ask patients presenting with constipation:

Change of Diet or Routine:	• Constipation often has social or behavioral causes, and it's important to determine if any recent changes have precipitated the symptoms.
Pain on Defecation:	• Pain during bowel movements may indicate a **local anorectal issue**, often leading to the suppression of defecation due to pain. A physical examination may be required.
Presence of Blood:	• **Bright red blood** could indicate **hemorrhoids** or an anal fissure. Blood mixed with the stool (**melaena**) or black, tarry stools suggest a more serious issue, like an **upper gastrointestinal bleed**, necessitating **referral**.
Duration (Chronic or Recent):	• **Chronic cases** without improvement or of **more than 14 days**' duration may need **further investigation**.
Lifestyle Changes:	• Life events like changes in job can trigger physiological symptoms, highlighting the need to explore recent changes in the patient's life.

The clinical features of constipation

- **Difficulty in defecation**
- **Abdominal discomfort and bloating**
- **Children**: parents may observe
  - Increased irritability,
  - Reduced appetite, and
  - Discomfort in their child.
- **Blood in stools**
- **Onset and duration**:
- **Neonatal onset**: may suggest a congenital condition affecting bowel movements.
- A sudden alteration in bowel habits in adults may point to more serious underlying conditions, such as colonic carcinoma, and requires further investigation.

Conditions to Eliminate in Cases of Constipation

Medicine-Induced Constipation:	• Opioids, can reduce intestinal motility, increase sphincter tone and reduce sensitivity to rectal distension.
Irritable Bowel Syndrome (IBS):	• It is characterized by **abdominal pain** and **altered bowel habits**, which may not be linked to any organic disease.
Functional Causes in Children:	• **Dietary issues** or **traumatic experiences** associated with defecation, such as prior pain during bowel movements, rather than organic disease.
Pregnancy:	• Constipation in the third trimester. • Factors contributing to this include **increased levels of progestogen**, pressure on the colon, decreased physical activity, and iron supplementation. • **Bulk-forming laxatives are generally recommended if treatment is needed.**
Colorectal Cancer:	• Any patient **over the age of 40** presenting with a significant change in bowel habits for the first time should be evaluated for colorectal cancer

Conditions to Eliminate in Cases of Constipation

Depression:	• Depression is associated with gastrointestinal complaints. Key symptoms to note include persistent low mood and loss of interest in most activities. • These indicators prompt a **referral**.
Hypothyroidism:	• Constipation can occur. • Other symptoms such as lethargy and cold intolerance. • Thyroid function tests should be conducted.

Evidence Base for Over-the-Counter Medication for Constipation

First-Line Treatment:	• For uncomplicated constipation, **non-drug treatments** are recommended as the first-line approach for all patient groups. These treatments primarily involve simple **dietary and lifestyle modifications**.

Dietary Modifications:	• **Fiber Intake**: Increasing dietary fiber intake is crucial. It is recommended to aim for approximately **30 g of fiber per day**. This can be achieved through:
	  • **Fruits**: such as apples, pears, and berries.
	  • **Vegetables**: including broccoli, carrots, and leafy greens.
	  • **Cereals and Grain Foods**: like oats, brown rice, and whole-grain bread.

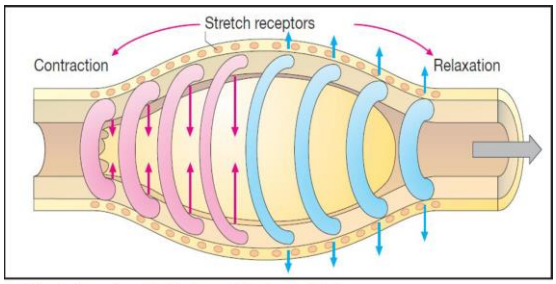
Hydration:	• It is essential to ensure **adequate fluid intake**, typically around **2 liters per day**. • This is particularly important when consuming a high-fiber diet, as sufficient hydration helps facilitate bowel movements and prevents exacerbating constipation.
Lifestyle Changes:	• Encouraging patients to **increase physical activity** can also contribute significantly to alleviating constipation symptoms. Regular exercise **promotes intestinal motility** and **overall gastrointestinal health**.

Medications

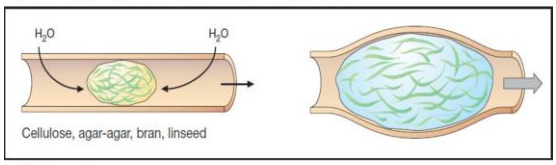
1. Bulk-forming Laxatives:	• Psyllium (Metamucil) • Methylcellulose (Citrucel) • Polycarbophil (FiberCon)
2. Osmotic Laxatives:	• Polyethylene glycol (MiraLAX) • Lactulose • Magnesium hydroxide (Milk of Magnesia)
3. Stimulant Laxatives:	• Bisacodyl (Dulcolax) • Senna (Senokot)
4. Stool Softeners (Emollients):	• Docusate sodium (Colace) • Docusate calcium (Surfak)
5. Lubricant Laxatives:	• Mineral oil

Bulk-forming laxatives

- Bulk-forming laxatives exert their effect by mimicking increased fibre consumption, **swelling in the bowel** and **increasing faecal mass.**
- In addition, they **encourage the proliferation of colonic bacteria**, and this helps further **increase faecal bulk** and stool softness.
- Patients should be **advised to increase their fluid intake** while taking bulk-forming medicines.



A. Stimulation of peristalsis by an intraluminal bolus



B. Bulk laxatives

Bulk-forming laxatives

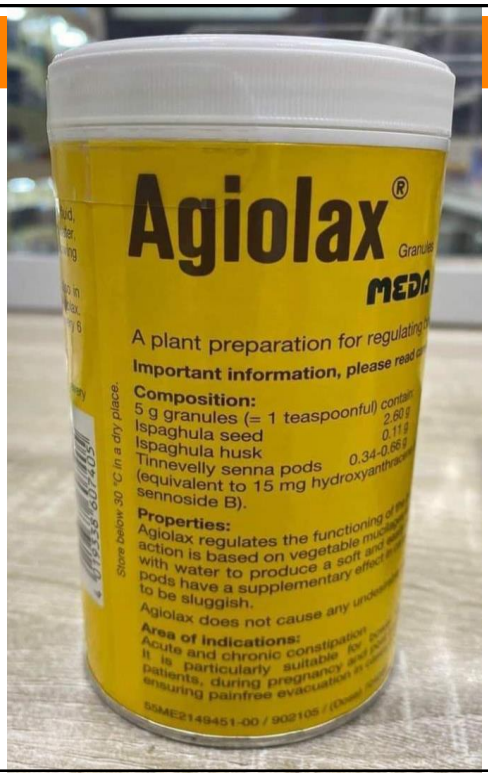
- The effect is usually seen in **12 to 36 hours** but can take as long as 72 hours.

❑**Side effects**

- commonly experienced include **flatulence** and **abdominal distension**.
- They are well tolerated in pregnancy and breastfeeding and have no teratogenic effects.
- They appear to have no drug interactions of any note.

Bulk-forming laxatives

- **Ispaghula husk (Fybogel®)**
- Ispaghula husk has to be reconstituted with water before taking.
- Adults should take one or two sachet, 5-mL spoonsful twice daily;
- For children between 6 and 12 years, ½ to one sachet, 5-mL spoonful twice daily.



Stimulant Laxatives

- Stimulant laxatives have a specific mechanism and some notable risks:
- **Mechanism**: They increase gastrointestinal (GI) motility by **directly stimulating the nerves in the colon**, which **leads to stronger and more frequent muscle contractions**. This helps propel stool through the bowel more quickly.
- **Main Side Effect**: This stimulation can cause abdominal cramping or pain, which is one of the most common side effects of these laxatives.

Stimulant Laxatives

- **Risks with Long-term Use**:
  - **Nerve Damage**: Prolonged use can potentially lead to damage of the colonic nerves, reducing the bowel's natural ability to function without the aid of laxatives.
  - **Laxative Abuse**: They are also among the most commonly abused, especially in **cases of eating disorders** or attempts **at rapid weight loss**, leading to **dependency** and further complications like **electrolyte imbalances.**

Stimulant Laxatives

- **Onset of Action**:
  - relatively **quickly** compared to other laxatives, typically producing a bowel movement within **6 to 12 hours** when taken orally.
- **Suitability for Different Patient Groups**:
  - They can be used by most patient groups and are not known to have significant drug interactions.
- **Safety in Pregnancy and Breastfeeding**:
  - Generally considered safe, their use should be **cautious**. Due to their ability to **stimulate muscle contractions**, it's recommended to **avoid them in pregnancy if possible**, as there is a theoretical risk of inducing uterine contractions.

Stimulant Laxatives

- **Bisacodyl (Dulcolax®)**
  - **Forms**: Available as tablets or suppositories.
  - **Indications**: Suitable for patients older than 4 years.
  - **Dosage**:
    - **Children (4-10 years)**: 5 mg (one pediatric suppository).
    - **Adults and Children (over 10 years)**: 5 to 10 mg (one or two tablets, or one 10-mg suppository).

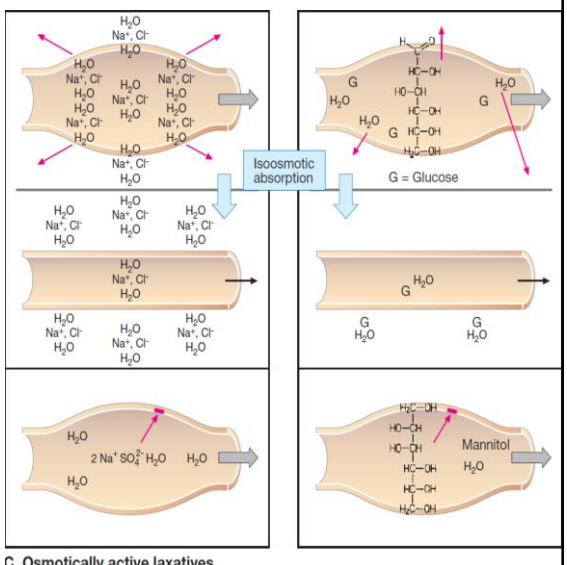
Stimulant Laxatives

❑Senna (e.g., Senokot®, Ex-Lax Senna®)

- **Forms**: Available as **syrup, tablets,** or **granules**.
- **Dosage for Adults and Children (over 12 years)**:
  - **15 mg daily** (typically two tablets or 10 mL of syrup).
  - It is recommended to take the dose **at bedtime** for overnight relief, with effects usually seen in the morning.

Osmotic Laxatives

- Lactulose, Macrogol (Polyethylene Glycol), Magnesium Salts.
- **Mechanism of Action**:
  - These laxatives work by **retaining fluid in the bowel** through osmosis or by altering the water distribution in the stool, which helps to soften the stool and promote bowel movements.
- **Common Side Effects**:
  - Flatulence, abdominal pain, and colic are frequently reported.
- **Suitable for All Patient Groups**: Can be used by most patients, including children and the elderly.
- **No Significant Drug Interactions**.
- **Safe in Pregnancy and Breastfeeding**.



C. Osmotically active laxatives

Osmotic Laxatives

- **Glycerol Suppositories**
  - **Indications**: Used for rapid relief when a quick bowel movement is needed.
  - **Onset of Action**: Typically produces a bowel movement in **15 to 30 minutes**.
  - **Dosage**:
    - **Infants**: 1-g suppositories.
    - **Children**: 2-g suppositories.
    - **Adults**: 4-g suppositories.

Osmotic Laxatives and stool softener

- **Lactulose** (Osmotic Laxative)
- **Dosing**: Administered **twice daily** for all ages.
  - **Adults**: Start with **15 mL**, adjusting upwards based on response.
- **Side Effects**: Up to **20% of patients** may experience flatulence and cramps, though these side effects often diminish after a few days.
- **Onset of Action**: May take **48 hours or longer** to produce an effect.

Osmotic Laxatives and stool softener

- **Docusate Sodium** (Stool Softener)
- **Mechanism**: Acts as a **nonionic surfactant** with stool-softening properties, allowing fluids to penetrate the stool. It also has **weak stimulant** properties.
- **Suitability**: Can be used in children aged **6 months and older**.