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# Diarrhoea Explained: Classification by Pathophysiology and Drug-Induced Mechanism

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**ABSTRACT**:
Diarrhoea is a more prevalent and multifaceted medical condition affecting individuals worldwide. This review aims to elucidate the diverse spectrum of diarrhoea, covering its myriad causes, underlying physiological mechanisms, and the role of drug-induced factors in its pathogenesis. Understanding the underlying mechanisms of diarrhoea, such as osmotic, secretory, inflammatory, and fatty diarrhoea, is crucial for effective management. Osmotic diarrhoea results from unabsorbable solutes, while secretory diarrhoea involves excessive fluid secretion by the bowel mucosa. Inflammatory diarrhoea involves damage to the intestinal lining, often triggered by infections or autoimmune reactions. Fatty diarrhoea, or steatorrhea, stems from malabsorption of fats. Additionally, numerous drugs can induce diarrhoea through various mechanisms, necessitating careful consideration in clinical practice. This review attempts to provide insights into the complicated terrain of diarrhea and attempts to enlighten the various paths of causative agents and mechanisms of induction of various diarrhoea.

**KEYWORDS:** Diarrhoea, Osmotic diarrhoea, Inflammatory Diarrhoea, Secretory Diarrhoea, Fatty diarrhoea/ steatorrhea.

## I. INTRODUCTION

Diarrhoea has been defined as the movement of loose watery stool more than the typical passage; however, the transit of completely formed stool is not classified as diarrhoea, nor are the soft and smooth stools of breastfeed newborns [1]. According to World Health Organisation (WHO) the diarrhoea is defined as the passage of 3 or more loose or liquid stools per day.[1]Diarrhoeal illness is the third largest cause of mortality in children aged 1 to 5 years. It is preventable and treated. Each year, diarrhoea kills nearly 443 832 children under the age of five, as well as 50,851 children aged five to nine. Safe drinking water, as well as proper sanitation and hygiene, can help to prevent a substantial amount of diarrhoeal sickness. Every year, over 1.7 billion instances of pediatric diarrhoea are reported worldwide [2].

**Common causes of diarrhoea:**

Diarrhoea can be caused by a variety of factors, including drugs, diet, intolerances (lactose intolerance) and allergies to foods, surgical procedures, various viral (Retrovirus, noroviruses), bacterial (Salmonella, E. coli, Clostridium), or parasitic (Cryptosporidium, giardia lamblia) infections, digestive abnormalities (Inflammatory Bowel Disease- IBD), and genetic causes [3].

Some of the drugs those induce the diarrhoea are the antibiotics, laxatives, antacids containing magnesium and calcium, chemotherapy, colchicine, proton pump inhibitors, Non Steroidal Anti-inflammatory Drugs (NSAIDs), Angiotensin-Coverting Enzyme (ACE) inhibitors, Cholesterol lowering medicines and more other [4,5].

The main physiological factors that cause diarrhoea are the decrease in absorption of electrolytes and water, increase in secretion from intestinal mucosa, increase in the luminal osmatic load, increase in Gastrointestinal (GI) motility and mucosal inflammation [6,7].

**Common symptoms of diarrhoea:**

The common diarrhoeal symptoms are loose motions, stomach pain due to intestinal contractions, high fever, blood in motion, bloating of stomach, weight loss, excessive thirst and weakness due to dehydration, dry cough and dark colored urine [8,9].

## II. GENERAL PHYSIOLOGY OF INTESTINAL ABSORPTION AND SECRETION

The human intestine manages significant quantities of water, electrolytes, and nutrients daily, primarily absorbed in the small intestine. Approximately 9 liters enter the small intestine

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daily, with only about 1.8 liters from oral intake [10]. Most absorption occurs in the jejunum, facilitated bysodium-coupled co-transport of organic substrates like glucose and amino acids. Water absorption relies on sodium movement, predominantly through the sodium-glucose transporter 1 (SGT1) and the sodium-hydrogen exchanger, driven by electrochemical gradients [11].

The ATPase sodium pump in the basolateral membrane aidsin active transport of nutrients and maintains the electrochemical gradient. In the ileum, specific electrolyteabsorption mechanisms, like sodium chloride transport, become more significant.Colon plays a role in fluidreabsorption, though less than the small intestine, and its function influences the occurrence of diarrhoea. Luminal bidirectional sodium/chloride channels in crypts regulate electrolyte and water movement; disruptions, like thosecaused by cholera toxin or Escherichia coli (E. Coli), lead to watery diarrhoea [12]. Overall, small intestine absorption and colonic function are crucial in maintaining fluid balance and preventing diarrhoea [13].

## III. TYPES OF DIARRHOEA BASED ON PHYSIOLOGY:

Diarrhoea results from an imbalance between absorption and secretion in the bowel.

### OSMOTIC DIARRHOEA:

It happens when there are too many osmotically active particles in the bowel, drawing in excess fluid. Causes of osmotic diarrhoea include ingestion of unabsorbable solutes and malabsorption conditions. Damage to the absorptive area of the mucosa can lead to osmotic diarrhoea. Motility disorders can also contribute to osmotic diarrhoea by reducing contact with the bowel lumen [14,15].

### Pathophysiology Of Osmotic Dirrhoea:

Different physiological reactions happen when a lactase-deficient person consumes a lactose test meal, or when a physiologically normal person consumes a nonabsorbable solute like Mg2+ or polyethylene glycol (PEG). In the case of the lactase-deficient subject, ingestion of lactose leads to an inability to reabsorb fluid in the duodenum due to the unabsorbable nature of lactose, which remains unmetabolized to absorbable glucose and galactose [16].

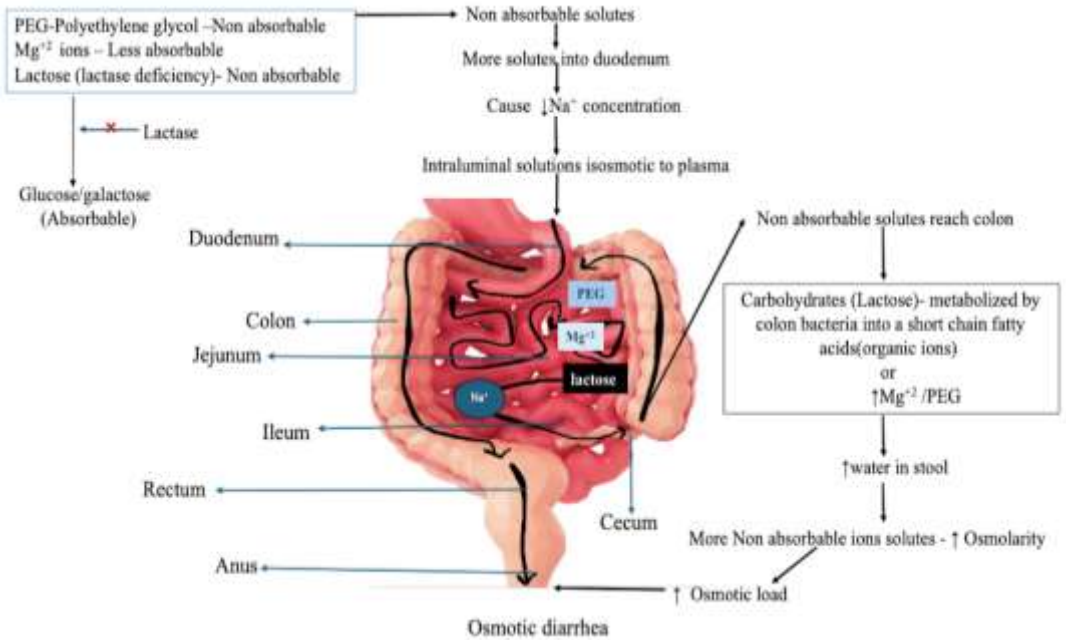


**Figure 1:** The diagrammatic representation of the pathophysiology of Osmotic diarrhoea.

Similarly, ingesting nonabsorbable solutes like PEG or Mg2+ results in the entry of fluid into the small bowel due to their osmotic activity, rendering intralumenal solutions isosmotic with plasma [17].

These mechanisms induce a considerable decline in intralumenal Na+ concentrations, which

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makes it difficult for the permeable the jejunum to absorb Na+ in opposition to the high lumen-to-plasma gradient. Depending on the type of unabsorbed solute, the chyme's destiny in the colon changes [17].

PEG and Mg2+ are examples of nonmetabolizable solutes that may permit the colon to absorb some Na+ and water, but not all of the excess water in the stool, which results in a rise in stool weight proportionate to the ingest osmotic load of PEG as we see in fig.1. [18].

However, if the not absorbed solute is a digestible carbohydrate like lactose or lactulose, it ferments in the colon by bacteria to produce organic anions, or short-chain fatty acids [19]. amount of osmotically active particles in the colon is greatly increased by these organic anions, which force the retention of inorganic cations. This encourages more fluid to enter the colon as a result. The unabsorbed carbohydrate is eventually eliminated in the stool together with the organic anions and fluid, even if some may be absorbed while passing through the colon [20].

In both scenarios involving ingestion of unabsorbable solutes or unabsorbed carbohydrates, there is a considerable gap between stool osmolality and the sum of electrolytes in the stool, reflecting the contribution of Non absorbed solutes to stool osmolality as seen in fig 1. These osmotic solutes contributing to osmotic diarrhoeas can arise from exogenous (ingested) or endogenous sources and may be associated with congenital or acquired malabsorptive diseases , the types and causes are shown in Fig.2. [21].

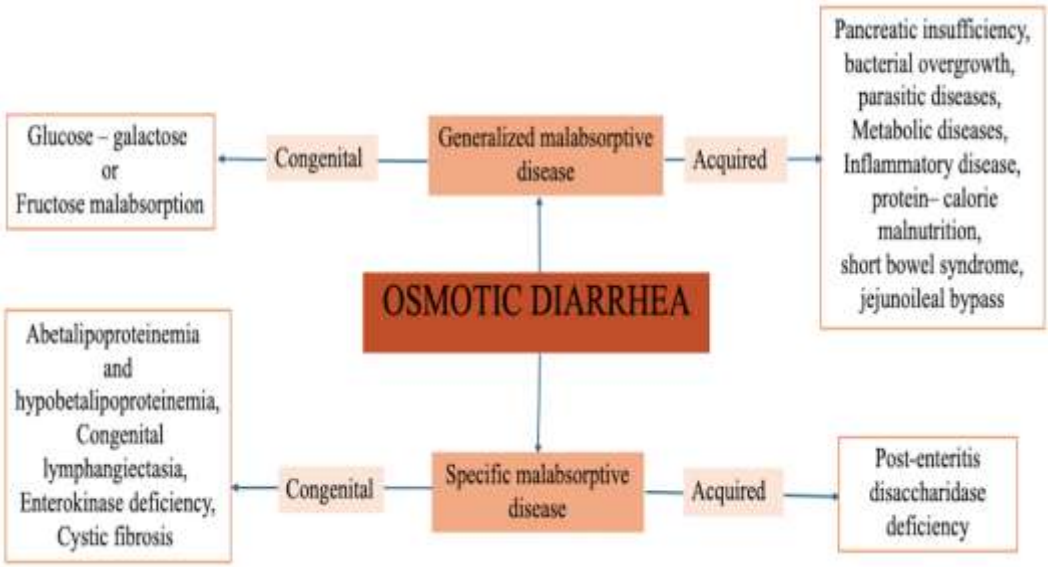


**Figure 2:** The types and causes of the osmotic diarrhoea both the acquired and congenital.

**SECRETORY DIARRHOEA:**

It occurs when the bowel mucosa excessively secretes fluid due to various factors. In secretory diarrhoea, absorptive mechanisms may be overwhelmed. Secretory diarrhoea persists even when the individual is not eating [22]. Sodium transport in the gut involves reabsorption in the villi via ATPase sodium channels and sodium-glucose channels. Active secretion occurs in the crypts of the small intestine.

leading to net secretion of fluid, seen in conditions like cholera and congenital chloride diarrhoea [23]. There are various physiological and pathological causes for diarrhoea are as shown in Fig.4.

**Pathopysiology Of Secretory Diarrhoea**

**Na+ k+ ATPase:**

Fluid secretion relies on osmotic gradients established by active transmembrane electrolyte transport, primarily driven by $Na^+$ -$K^+$ -ATPase pumps on the basolateral membrane. These pumps expend energy to extrude $Na^+$ ions from the cell while importing $K^+$ ions as shown in Fig 2. This process, fueled by ATP hydrolysis, maintains low intracellular $Na^+$ concentrations, crucial for driving secondary active transport pathways. $Na^+$ -$K^+$ -ATPase pumps consist of a, b, and Phe-Xaa-Tyr-Asp proteins (FXYD) subunits, with multiple isoforms [24]. The catalytically active subunit, phosphorylated during transport cycles, alternates its affinity between $Na^+$ and $K^+$ ions [25]. The b

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subunit acts as a chaperone for proper folding and membrane insertion of a subunit. FXYD proteins, tissue-specific and diverse, modulate pump properties, including ion affinity. Together, these components orchestrate electrolyte transport essential for fluid secretion [26,27,28].

**NKCC1: ($Na^+$ / $k^+$ / $Cl^-$ symporter)**

130-kDa protein facilitates $Na^+$ , $K^+$ , and 2 $Cl^-$ ion uptake into intestinal epithelial cells. Its basolateral membrane location allows it to capitalize on the low intracellular $Na^+$ levels maintained by $Na^+$ -$K^+$ -ATPase pumps (as in fig 3)

[29]. Being electroneutral, it imports ions without net charge transfer. Key domains include KCNE subunits [32,33].

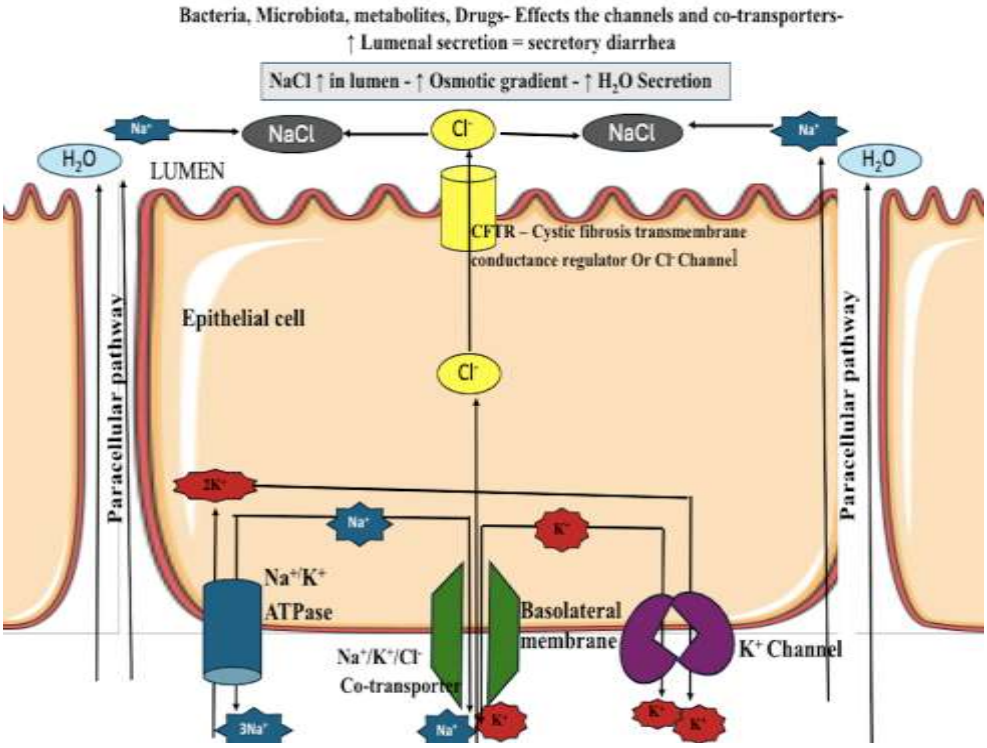


**Figure 3:** The diagrammatic representation of pathophysiology of the secretory diarrhoea

KCNN4, regulated by intracellular $Ca^{2+}$ , is a tetrameric $K^+$ channel with six transmembrane domains, sensitive to intracellular $Ca^{2+}$ levels due to a calmodulin binding domain [34,35,36].

**$Cl^-$ channel:**

Basolateral $Na^+$ -$K^+$ -ATPase pumps, NKCC1, and $K^+$ channels work together to accumulate $Cl^-$ intracellularly, establishing an electrochemical gradient (fig 2).Apical chloride channels, primarily CFTR, facilitate $Cl^-$ exit into the lumen. CFTR, an ABC transporter, comprises two TMDs, two NBDs, and an R domain [37,38], requiring ATP binding and R domain phosphorylation for channel opening [39-41]. PKA is the main regulator, but PKG, PKC, and phosphatases also modulate CFTR activity. Additionally, other $Cl^-$ channels like CaCC and TMEM16A (anoctamin 1) exist, with TMEM16A potentially significant in neonatal mice but minor in human intestine [42-44].

**$K^+$ channel:**

In the $Cl^-$ secretory pathway, $K^+$ channels play a crucial role in maintaining the electrochemical gradient. $K^+$ exitsepithelial cells through basolateral channels after entering via NKCC1 or $Na^+$ -$K^+$ -ATPase. KCNQ1 and KCNN4 (SK4) are vital $K^+$ channels in this process. KCNQ1 forms a voltage-gated, low-conductance $K^+$ channel, regulated by

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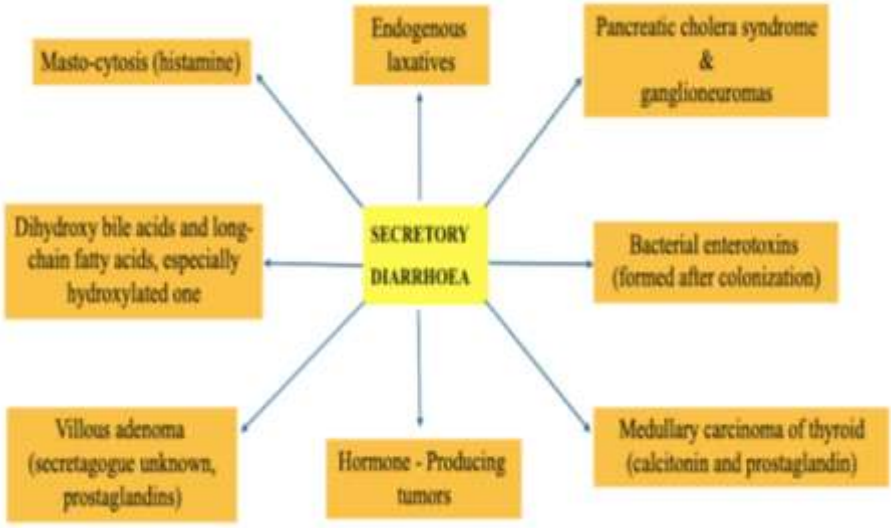


**Figure 4:** The different causes of the secretory diarrhoea

Apical chloride channels, primarily CFTR, facilitate $Cl^-$ exit into the lumen. CFTR, an ABC transporter, comprises two TMDs, two NBDs, and an R domain [37,38], requiring ATP binding and R domain phosphorylation for channel opening [39-41]. PKA is the main regulator, but PKG, PKC, and phosphatases also modulate CFTR activity. Additionally, other $Cl^-$ channels like CaCC and TMEM16A (anoctamin 1) exist, with TMEM16A potentially significant in neonatal mice but minor in human intestine [42-44].

**INFLAMMATORY DIARRHOEA:**

Conditions leading to inflammatory diarrhoea often entail damage to the intestinal epithelial lining, triggered by various noxious stimuli. White blood cells release inflammatory mediators, including proteases, oxygen radicals, and cytokines, which contribute to intestinal secretion and epithelial damage, leading to ulcerations [45]. This cascade of events can result in secretory diarrhoea, protein-losing enteropathy, bleeding, and malabsorption. Despite its detrimental effects, this response serves as a protective mechanism by expelling antigens and microorganisms from the gut. Infections, notably, are a prevalent cause of inflammatory diarrhoea. T-lymphocyte activation has been implicated in villus atrophy and crypt hyperplasia, commonly observed in various small intestinal infections [46]. Other causes include autoimmune disorders, hypersensitivity reactions, chemotherapeutic agents, radiation therapy, and idiopathic inflammatory conditions like Crohn's disease and ulcerative colitis as shown in Fig.5. Clinically, these disorders exhibit mucosal damage detectable via endoscopy and are characterized by the presence of fecal leukocytes, persisting even after fasting [47].

**Pathophysiology Of Inflammatory Diarrhoea:**

Our understanding of inflammatory diarrhoea has significantly advanced with increased knowledge of mucosal immunology and neuro-immunophysiology. These concepts elucidate the mechanisms during gut inflammation, including deranged epithelial electrolyte transport, influx and activation of mucosal inflammatory cells, and epithelial damage leading to ulceration [48,49].

The first concept involves the secretion of various mediatorsby activated mast cells, phagocytes, myofibroblasts, and T cells in the lamina propria [50-53]. These mediators inhibit NaCl absorption or stimulate $Cl^-$ secretion by intestinal epithelial cells, leading to diarrhoea. Additionally, they damage enterocytes and secrete proinflammatory cytokines and chemokines, further promoting inflammation [50,51,53,49].

The second concept highlights the activation of lamina propria inflammatory cells and epithelial cells by innate immunity [54]. Cell surface Toll-like receptors (TLRs) and cytoplasmic receptors recognize microbial ligands, transmitting activating signals to inflammatory or mesenchymal cells [55, 56]. Subsequent antigen presentation to T-lymphocytes augments and sustains the inflammatory response.

The third concept involves pathological microorganisms, such as Salmonella, invading the cell membrane [57], or crossing the epithelial barrier between cells [58]. Certain diseases may increase

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junctional permeability, allowing antigens to contribute to clinical disease [58-62]. The fourth concept focuses on certain bacteria possessing molecular protein secretion systems capable of injecting toxins into epithelial cells, altering electrolyte transport and permeability [63-64].

Inflammatory diarrhoeas can be induced by microorganisms capable of invading epithelial cells or adhering to them and secreting toxins. Immune cell activation, both innate and adaptive, contributes to tissue damage and altered electrolyte transport.

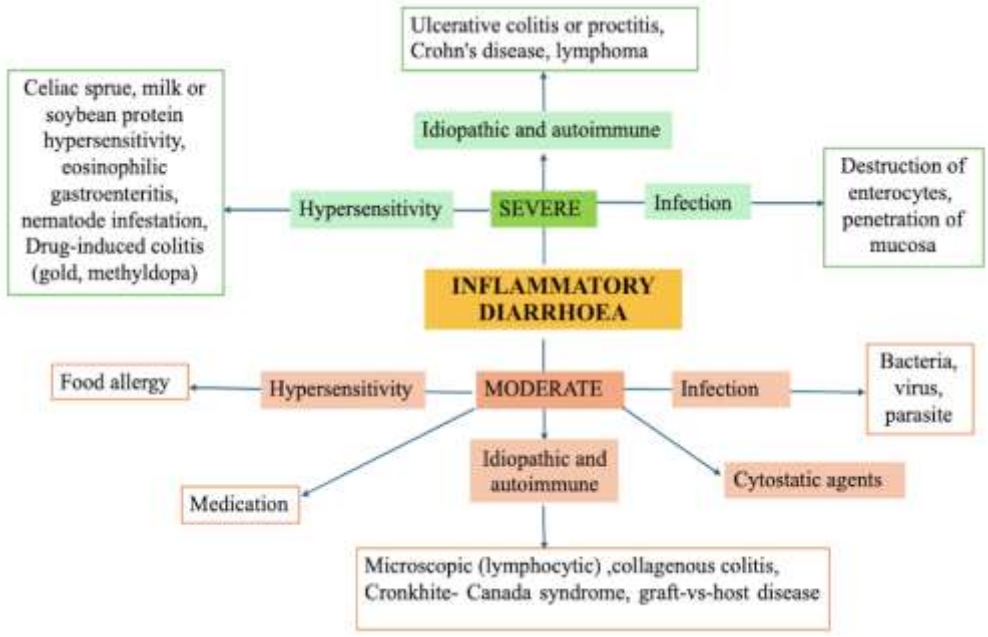


**Figure 5:** Types and causes of the inflammatory

Autoimmune inflammatory diarrhoeas may involve increased epithelial barrier permeabilitycoupled with other genetic or acquired defects [65]. Inflammatory diarrhoea encompasses four general categories: infection, hypersensitivity, cytostatic agents, and idiopathic diseases as shown in Fig.5[66].

**FATTY DIARRHOEA/ STEATORRHEA:**

Clinical symptoms usually result from malabsorption of either fat or carbohydrate, though malabsorption of all three primary nutrients—protein, fat, and carbohydrate—can occur [67]. Although protein or amino acid malabsorption (azotorrhea) can happen, it is usually not observed unless the condition is severe enough to result in malnourishment or if certain anomalies in the transport of amino acids induce a congenital illness. Furthermore, the physiological cause of malabsorptive diarrhoeas is influenced by the malabsorption of water and electrolytes [68].If significant amounts of divalent ions, including MgSO4 and MgPO4, are consumed in excess, the gut's limited ability to absorb these ions might cause clinically noticeable diarrhea. But steatorrhea is a common symptom of broad malabsorptive disorders, which emphasizes how crucial it is to appreciate fat absorption in order to understand malabsorptive conditions [69].

According to the normal physiology of the absorption of fats, there are three main forms of fat malabsorption: post mucosal malabsorption associated to lymphatic blockage, mucosal malabsorption, and intralumenal maldigestion. Malabsorptive disease can arise as a result of various mechanisms, each of which is represented by a category. These pathways may limit fat absorption [70–72].

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**Table 1:** Types and causes of the fatty diarrhoea / steatorrhea

| | |
|---|---|
| Intralumenal maldigestion | Cirrhosis & bile duct obstruction |
| | Pancreatic exocrine insufficiency |
| Mucosal malabsorption | Drug |
| | Infectious disease |
| | Autoimmune enteropathies |
| | Mastocytosis&eosinophilic gastroenteritis |
| | Celiac sprue |
| | Dermatitis herpetiformis |
| | Whipple disease |
| | Lipoproteinemia |
| Post mucosal obstruction | Intestinal lymphangiectasia (whipple disease, trauma, lymphoma, carcinoma) |
| | Lymphangiectasis |
| | Protein losing enteropathy |
| Mixed causes | Bacterial overgrowth |
| | Short bowel syndrome |
| | Metabolic disease |

## IV. TYPES OF DIARRHOEA BASED ON DURATION

### ACUTE DIARRHOEA

Acute diarrhoea, typically lasting less than four weeks, is a general reaction of the intestine to various conditions such as infections, drug reactions, inflammatory bowel disease, and ischemia. While infections are the primary cause, identifying specific organisms is often challenging. Patients usually seek medical attention for severe or prolonged diarrhoea, or if they experience concerning symptoms like fever, weakness, or rectal bleeding [73]. Infections causing acute diarrhoea are mainly acquired through fecal-oral transmission, typically via contaminated water or food. Upon ingestion, these microorganisms must overcome host defense mechanisms, including gastric acid, local and systemic immune responses, and gastrointestinal motility, which hinders their ability to adhere to the intestinal mucosa [74].

### CHRONIC DIARRHOEA

Chronic diarrhoea is characterized by frequent passage of loose or liquid stools, urgency to evacuate, or discomfort in the abdomen, lasting over four weeks. Stool consistency is typically determined by the balance between fecal water and the water-holding capacity of solid components. Since stools contain mostly water, quantifying consistency is challenging, with stool weight used as an indirect measure [75]. Diarrhoea is often defined by stool weight or volume over 24-72 hours (about 3 days), with over 200g/24h considered objectively indicative. However, this definition may exclude up to 20% of patients with liquid diarrhoea but lower stool weight. A practical definition includes frequent passage of loose or liquid stools more than three times daily and/or an output exceeding 200g/day [76]. The causes are detailed in Table.2.

**Table 2:** The causes of the acute and chronic diarrhoea

| | | | |
|---|---|---|---|
| Acute diarrhoea | Traveller's diarrhoea | | |
| | Virus | Bacteria | parasite |
| | Noroviruses,<br>Adenoviruses,<br>Enteroviruses,<br>Rotaviruses,<br>Astroviruses | Campylobacter jejuni,<br>Salmonella.<br>E. coli,<br>Clostridium difficile,<br>Shigella. | Cryptosporidium,<br>Giardia lamblia,<br>Entamoeba histiolytica |
| Chronic diarrhoea | Coeliac disease, giardiasis, tropical sprue, collagenous sprue, refractory coeliac disease, whipple disease, amyloidosis, pancreatic insufficiency, tumors, bile acids and STDs. | | |

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**DRUG INDUCED DIARRHOEA:**

More than 700 drugs have been identified as potential causes of diarrhoea, accounting for roughly 7% of all reported adverse drug effects. However, the specific mechanisms by which certain drugs induce diarrhoea are not well understood. Often, drug-induced diarrhoea is suspected when it occurs shortly after initiating a new medication, though evidence supporting this link is typically circumstantial. In such cases, the medication is usually discontinued, and if the diarrhoea resolves, the side effect is attributed to the drug without further investigation into the underlying mechanisms. Consequently, our understanding of drug-induced diarrhoea ranges from solid comprehension to reasonable hypotheses to considerable speculation. The gastrointestinal tract is regulated by a complex interplay of paracrine, immune, neural, and endocrine systems that coordinate changes in mucosal and muscular function to adapt to varying conditions. Medications can influence this regulatory system through various pathways, potentially contributing to diarrhoea [77,78].So here we summarize various drugs the induce diarrhoea as asideeffect and mechanism of action with its type detailed in Table 3.

**Table 3:** The detail notes on things that induce diarrhoea, its indication, the type of diarrhoea drugs induced with their mechanism

| Type of diarrhoea | Drug that induced | Drug used for/ indication | Mechanism of causing diarrhoea | Reference |
|---|---|---|---|---|
| Osmotic diarrhoea | Magnesium containing salts | Antiacid, Constipation, Laxatives. | Osmotically mediated water retention, which triggers peristalsis, is the cause of cathartic action resulting from inadequate absorption in the GIT. | 79, |
| | Polyethylene glycols | | | 80 |
| | Sodium phosphates | | | 81 |
| | Carbohydrates: lactulose | Hepatic encephalopathy, constipation, | The primary cause of diarrhoea is fluid entry into the gut caused by improper absorption, digestion, or passage through the small intestinal tract. | 80, 82, 83 |
| | Digoxin | CHF | Digoxin targets the heart $Na^+/K^+$ ATPase as an area of therapy. However, diarrhoea could result from blockage of the colonic intestinal $Na^+$ pumps. | 80 |
| | Auranofin | Rheumatoid arthritis | By blocking channels of calcium and lowering $K^+$ conductivity, | 80 |
| | Quinidine and Propafenone | Antiarrhythmic drugs | Impair the water and $Na^+$ absorption through the epithelium, resulting in diarrhoea | 84 |

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| | | | | |
|---|---|---|---|---|
| | Lubiprostone | Constipation | Increases the production of intestinal fluid by specifically activating intestinal ClC-2 chloride channels. | 85 |
| | Olsalazine | Ulcerative colitis | The ileum's promotion of sodium chloride and bicarbonate secretion | 77, 86 |
| | Sulfasalazine and mesalazine | Azo compounds | Although the exact mechanism is unknown, it might work directly on anion transporters as opposed to having an anti-inflammatory impact. | 87 |
| Secretory Diarrhoea | Phosphodiesterase inhibitor, theophylline, | Lung disease | Changing intracellular signaling pathways, or raising the levels of calcium, cGMP, or AMP. Increases secretion, opens chloride channels, and increases cyclic AMP, which causes diarrhoea. | 88 |
| | Coffee | Stimulant | Causes diarrhoea by increasing cyclic AMP, opening chloride channels, and increasing secretion | 88 |
| | Prostaglandin analogues | Glaucoma | The peptides that induce secretion, as well as through changes in permeability, mobility, and electrolytes transport | 88 |
| | Mioprostol | Antiulcer treating when ulcer caused by nsaids | Causes diarrhoea and intraluminal fluid buildup by stimulating epithelium Cl- secretion through camp. | 80 |
| | Chenodeoxycholic acid, dihydroxy bile acid, ursodiol | A bile acid initially used to dissolve cholesterol gallstones, | The -OH groups' arrangement in relation to chenodeoxycholic | 89, 90 |

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| | | | | |
|---|---|---|---|---|
| | | | acid | |
| | Chenodeoxycholic acid | Gall stone treatment | Increase in GMP and intracellular cAMP levels; | 89, 90 |
| | Castor oil | Laxative | Converted by lipases into glycerol and the active ingredient, ricinoleic acid, in the small intestine. This drug mainly operates in the colon to promote fluid and electrolyte output by raising cyclic amp and accelerating intestinal transit. | 90-92 |
| | Calcitonin | Medullary carcinoma | Intravenous infusions caused a rapid and noticeable rise in water, sodium, chloride, and potassium secretion from the jejunum as well as a decrease in bicarbonate absorption. These effects were rapidly reversed when the infusion was stopped. | 93-95 |
| | Omeprazole | Anti-ulcer | Mechanism of bacterial overgrowth, which causes the colon to secrete net fluid and electrolytes as a result of the bacteria's deconjugation of primary bile salts to dihydroxy bile acids. | 80 |
| | Diphenylmethane derivatives and anthraquinones | Stimulant laxatives | They work by causing a small- to large-intestinal restricted low-grade inflammation, which encourages the absorption of water and electrolytes and increases intestinal motility. This is accomplished by producing platelet-activating factor, activating the prostaglandin-cyclic | 79 |

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| | | | | |
|---|---|---|---|---|
| | | | AMP and NO-cyclic GMP pathways, and perhaps inhibiting $Na^+/K^+$ ATPase. | |
| | Diacerein | Osteoarthritis | Create massive intestinal contractions that migrate and secrete water and electrolytes. | 96 |
| | Bethanecol | Urinary retention and neurogenic bladder | Two types of G protein-coupled muscarinic receptors in the gastrointestinal tract, M2 and M3, mediate the impact of acetylcholine on smooth muscle. Through the Gq-PLC-IP3 pathway, the M3 receptor's activation raises intracellular $Ca^{2+}$. As a result, there is an increase in the peristalsis and gastrointestinal and secretions from the pancreas. | 79 |
| | Acetylcholinesterase inhibitors | Alzheimer's disease | Permit acetylcholine to build up in neuromuscular and synaptic connections. These medications intensify contractile effects, resulting in diarrhoea. | 77, 80 |
| | Neostigmine | Ogilvie's syndrome and paralytic ileus | Severe diarrhoea caused by acetylcholinesterase inhibition in cholinergic-like syndrome | 79 |
| | Colchicine | Gout | a microtubule inhibitor that acts by obstructing the migration of epithelial cells from the crypt to the villus, perhaps causing diarrhoea. It might also obstruct certain transport proteins intracellular | 88 |

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|---|---|---|---|---|
| | | | trafficking. | |
| | Ticlopidine | inhibitor of platelet function | Increase motility is thought to be the principal mechanism | 97 |
| | Irinotecan | chemotherapeutic agent | Severe diarrhoea caused by acetylcholinesterase inhibition in cholinergic-like syndrome | 77 |
| Inflammatory Diarrhoea | Simvastatin, lovastatin, and pravastatin | Anti-hyperlipidemia | Acute mucosal localized superficial inflammatory infiltration. | 77 |
| | Isotretinoid | Acne | | |
| | NSAIDs | Anti inflammatory | While NSAIDs promote in vitro absorption (increased Na+ absorption and decreased Cl- secretion), diarrhoea must also result from other mechanisms, such as direct mucosal injury. | 98-100 |
| | clindamycin, amoxicillin, and ampicillin,cephalosporins | Antibiotics | Enterotoxin A, which sticks to the brush-border membranes of the enterocytes and triggers a response of inflammation, and cytotoxin B, which directly damages mucosae, are the two substances secreted by C. difficile germs that cause diarrhoea. | 77-79,101 |
| | Lansoprazole | acid-reducing agents | carrying of an infection caused by C. difficile, raising the possibility of colitis that is pseudomembranous. | 80,102 |
| | 5-fluorouracil, irinotecan, methotrexate, and cisplatin | chemotherapeutic agents | A shift in the ratio of mature villus to immature crypt cells may upset the equilibrium between secretion and absorption. The | 102,96 |
| | Mycophenol mofetil | immunosuppressive | | 102 |

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| | | | | |
|---|---|---|---|---|
| | | | breakdown of gastrointestinal epithelial homeostasis accompanied by some superficial necrosis disrupts the gut's secretory, motility, and absorptive processes, which in turn contributes to diarrhoea. | |
| Fatty diarrhoea/ steatorrhea | neomycin, polymyxin, and bacitracin | oral antibacterial agents | The small-intestinal mucosa is harmed by malabsorption, which lowers enterocytes' enzyme activity. They might also lessen the absorption of fats by binding bile acids in the gastrointestinal lumen. | 80, 100,103 |
| | Levo-thyroxine | hypothyroidism | aberrant SeHCAT values have been linked to bile acid malabsorption. Nonetheless, the enhanced motility might take precedence over this effect. | 80 |
| | Biguanide, metformin. | type 2 diabetes | reduces disaccharidase activities and causes malabsorptive diarrhoea on the brush boundary. | 104 |
| | Octreotide | Antidiarrhoeal agent | Paradoxical action that results in steatorrhea at larger dosages. | 77, 105 |
| | L-dopa, | Parkinson disease | Can result in steatorrhea by altering the jejunal mucosa. | 101, 102 |
| | Allopurinol | Lower uric acid levels | | |
| | Didanosine , Abacavir, Lopinavir | Antiretroviral therapy | Hypersensitivity reaction | 106 |
| | Orlistat | Gastrointestinal lipase inhibitor | Malabsorptive diarrhoea | 107 |
| | Colchicine | Gout | Cause malabsorption in large doses by | 80 |

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| | | | | |
|---|---|---|---|---|
| | | | villous atrophy | |
| | Irinotecan | Chemotherapeutic agent | Severe diarrhoea caused by acetylcholinesterase inhibition in cholinergic-like syndrome | 80 |
| | Mefanamic acid | Anti inflammatory | Can result in steatorrhea by altering the jejunal mucosa. | 101,98 |

## V. CONCLUSION

Diarrhoea represents a significant global health concern, particularly among children under five years old, with millions of deaths annually. Understanding the diverse causes and physiological mechanisms behind diarrhoea is crucial for effective prevention and treatment strategies. Nowadays, research has progressed towards exploring probiotics, prebiotics, and alternative drugs, which offer more effective options for the treatment and prevention of diarrhoea. Comprehensive management always continues to require addressing underlying causes whether infectious, inflammatory, or pharmacological to effectively mitigate the burden of diarrhoeal illness.

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