

Antidiarrheal Drugs

Diarrhea

Diarrhea is not a disease, but a symptom of some other problem characterized by either more frequent bowel movement and/or the consistency of the stool is softer and sometimes watery

Causes of Diarrhea	
Acute Diarrhea	Chronic Diarrhea
<ul style="list-style-type: none"> • Infections <ul style="list-style-type: none"> ○ Bacterial ○ Viral ○ Protozoal • Drug induced • Nutritional 	<ul style="list-style-type: none"> • Tumors • Diabetes • Addison's Disease • Hyperthyroidism • Irritable Bowel Syndrome

Fluid Replacement Therapy

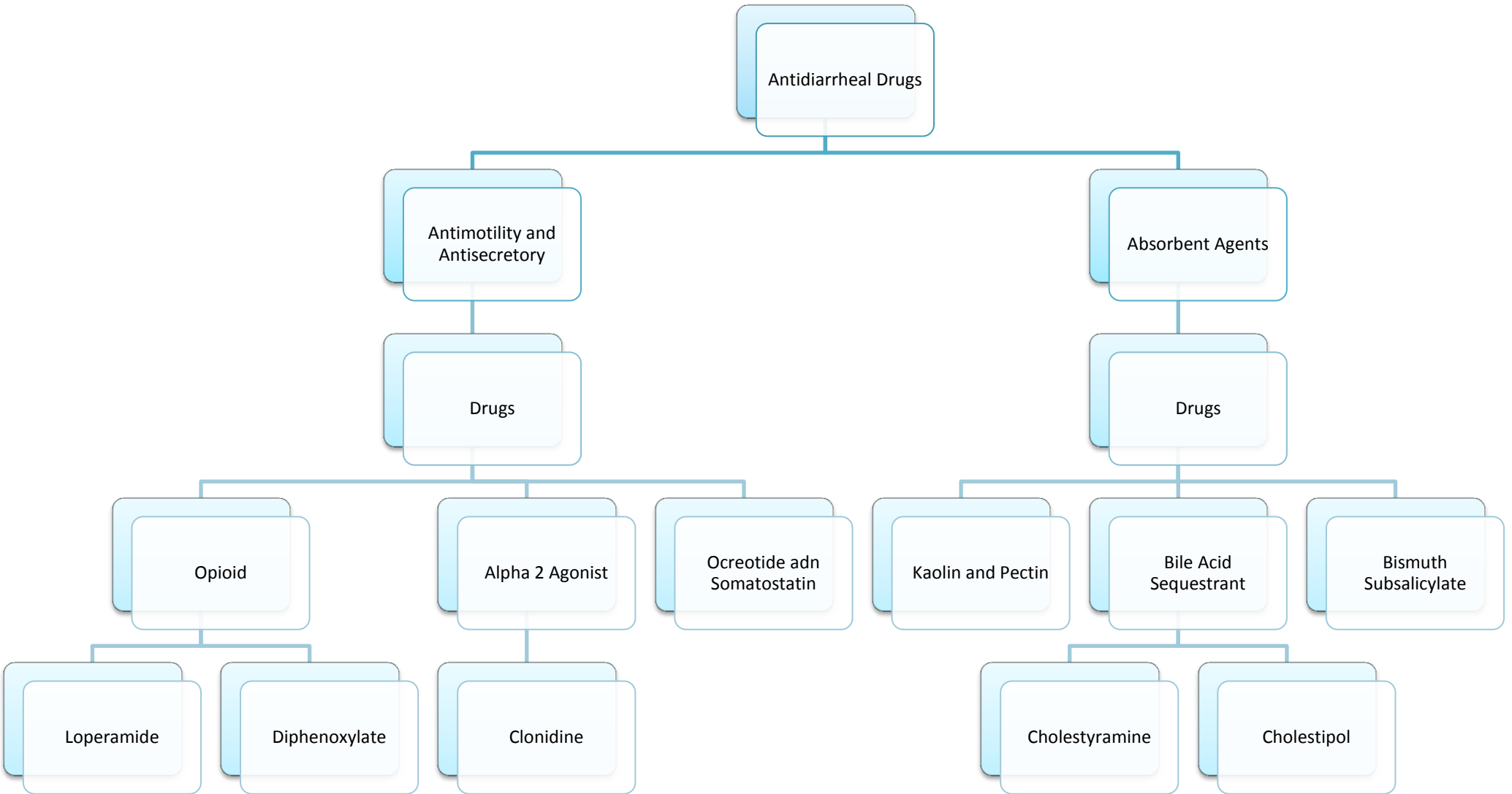
- Administration of either
 - Oral Rehydration Salt
 - Cereal Rehydration Slat
- Is given depending on the severity of dehydration, usually 4 hours of admin
- This treatment is not curing the underlying causes of the diarrhea but rather prevent any worsening condition secondary to excessive loss of fluid and electrolytes

Antidiarrheal Drugs

- Administration of Antidiarrheal drugs for
 - Mild to moderate diarrhea
- This is also does not cure any of the underlying causes of diarrhea, instead providing symptomatic relief to the patients

Antimicrobial Therapy

- Administration of either Antimicrobial agents if
 - The Diarrhea is of severe presentation with known causative agents of Microbial
 - Diarrhea persists for more than 3 days
- This will provide definitive treatment to the diarrhea



Antimotility and Antisecretory Agents

Opioid Agonists

Drugs	Pharmacokinetics	Mechanism of Action	Clinical Uses	Adverse Effects
Loperamide	<p>Absorption</p> <ul style="list-style-type: none"> Poorly absorbed orally <p>Distribution</p> <ul style="list-style-type: none"> Does not cross the BBB unless in a very high dose, therefore doesn't lead to Opioid dependency 97% bound to plasma protein <p>Metabolism</p> <ul style="list-style-type: none"> Hepatic metabolism <p>Excretion</p> <ul style="list-style-type: none"> Urine Bile 	<ul style="list-style-type: none"> Opioid receptor agonist <ul style="list-style-type: none"> Bind to μ receptor on the Myenteric Plexus of GIT Stimulation of this receptor will lead to <ul style="list-style-type: none"> Decrease the tone of longitudinal smooth muscle cells <ul style="list-style-type: none"> Increase transit time Increase the tone of circular smooth muscle cells <ul style="list-style-type: none"> Increase the time for and capacity of intestine to absorb water Inhibition of Gastrocolic reflex All and all, it reduces GIT motility and increase transit time 	<ul style="list-style-type: none"> Travellers diarrhea Chronic diarrhea 	<ul style="list-style-type: none"> Abdominal pain Bloating Nausea Vomiting Constipation <p>Drug drug Reaction</p> <ul style="list-style-type: none"> If admin together with <ul style="list-style-type: none"> Quinidine Omeprazole Ritonavir These are all CYP450 inhibitors which may elevate the plasma level of Loperamide to as high as 3 folds These drugs enable Loperamide to pass the BBB and lead to sedative effects of Opioid agonists
			Contraindication	
Diphenoxylate	<p>Absorption</p> <ul style="list-style-type: none"> Good upon oral admin <p>Distribution</p> <ul style="list-style-type: none"> Active metabolite Difenoxin may pass the BBB <p>Metabolism</p> <ul style="list-style-type: none"> Hepatic <p>Excretion</p> <ul style="list-style-type: none"> Urine Bile 			

Antimotility and Antisecretory Agents

Drugs	Pharmacokinetics	Mechanism of Action	Clinical Uses	Adverse Effects
<p>Alpha 2 Agonists</p> <ul style="list-style-type: none"> • Clonidine 	<p>Absorption</p> <ul style="list-style-type: none"> • Good upon oral admin <p>Distribution</p> <ul style="list-style-type: none"> • Plasma protein bound <p>Metabolism</p> <ul style="list-style-type: none"> • Hepatic <p>Excretion</p> <ul style="list-style-type: none"> • Urine 	<ul style="list-style-type: none"> • Binds to presynaptic Alpha 2 Adrenergic receptor • It leads to reduction in the release of Neurotransmitters by inhibition of Adenylate Cyclase • Exerts its antidiarrheal effects through <ul style="list-style-type: none"> ○ Reducing GIT motility by <ul style="list-style-type: none"> ▪ Increasing transit time ▪ Increase GIT capacity ○ Absorption of electrolytes and fluid ○ Reducing secretion of fluid 	<ul style="list-style-type: none"> • Diarrhea in Diabetic patient • Diarrhea due to withdrawal of Opioid 	<ul style="list-style-type: none"> • Rebound hypertension • Depression
<p>Octreotide and Somatostatin</p> <ul style="list-style-type: none"> • Octreotide is a synthetic analogue for Somatostatin • Octerotide has 400-500 more potency compared to Somatostatin 	<p>Absorption</p> <ul style="list-style-type: none"> • Complete absorption after S/C admin <p>Distribution</p> <ul style="list-style-type: none"> • Distributed across body compartment <p>Metabolism</p> <ul style="list-style-type: none"> • Unknown <p>Excretion</p> <ul style="list-style-type: none"> • Urine 	<ul style="list-style-type: none"> • Resembles the activity of Somatostatin <ul style="list-style-type: none"> ○ Inhibits the release of various hormones <ul style="list-style-type: none"> ▪ GIT hormones <ul style="list-style-type: none"> • Gastrin • CCK-PZ • Secretin • Pancreatic Polypeptide • Vasoactive Intestinal Peptide ▪ Other Hormones <ul style="list-style-type: none"> • Insulin • Glucagon • TSH • Growth Hormone ○ Reduces fluid and electrolyte secretion from the Intestine ○ Reduces GIT motility ○ Vasoconstriction in the blood vessels 	<ul style="list-style-type: none"> • Secretory diarrhea due to <ul style="list-style-type: none"> ○ Hormone secreting tumor of Pancreas or Intestine • Chemotherapy • HIV • Diabetes Mellitus 	<ul style="list-style-type: none"> • Hypothyroidism • Hypo/hyperglycaemia • Reduce Insulin release • QT prolongation • Gallstones formation • Bradycardia

Absorbent Agents

Drugs	Mechanism of Action	Clinical Uses	Adverse Effects
<p style="text-align: center;">Bulk-Forming and Hydroscopic Agents</p> <ul style="list-style-type: none"> • Kaolin <ul style="list-style-type: none"> ○ Naturally occurring hydrated Magnesium Aluminum Silicate • Pectin <ul style="list-style-type: none"> ○ Indigestible carbohydrate derived from apples. 	<ul style="list-style-type: none"> • May work as gels to modify stool texture and viscosity • Produce a perception of decreased stool fluidity • May bind bacterial toxins especially Enterotoxin • May bind to bile salts 	<ul style="list-style-type: none"> • Symptomatic relieve of <ul style="list-style-type: none"> ○ Acute diarrhea ○ Chronic diarrhea 	<ul style="list-style-type: none"> • Interfere with many oral drugs absorption in the GIT
<p style="text-align: center;">Bile Acids Sequestrants</p> <ul style="list-style-type: none"> • Cholestyramine • Cholestipol 	<ul style="list-style-type: none"> • Bile salt binding in the intestine • Leading to increase in bulk of the stool • Make the stools less watery 	<ul style="list-style-type: none"> • Bile salt-induced diarrhea <ul style="list-style-type: none"> ○ In patients with resection of the distal ileum 	<ul style="list-style-type: none"> • Hypertriglyceridaemia • Constipation • Bloating • Flatulence • Heartburn • Diarrhea • Steatorrhea • Malabsorption of Vitamin K <ul style="list-style-type: none"> ○ Hypoprothrombinaemia • Gallstones formation
<p style="text-align: center;">Bismuth Subsalicylate</p>	<ul style="list-style-type: none"> • Retarding the expulsion of fluids into the digestive system by irritated tissues, by "coating" them. • Stimulation of absorption of fluids and electrolytes by the intestinal wall (antisecretory action) • Reducing inflammation/irritation of stomach and intestinal lining through inhibition of prostaglandin G/H Synthase 1/2 • Reduction in hypermotility of the stomach • Binding of toxins produced by E. coli • Bactericidal action 	<ul style="list-style-type: none"> • Prophylaxis for Traveller's diarrhea • Treatment of H. pylori infection 	<ul style="list-style-type: none"> • Dark stools (sometimes mistaken for melena) • Black staining of the tongue