Bile Acid Diarrhoea (BAD)

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Incidence

- Unknown but increasing evidence of up to 30% with IBS-D
- Can occur following Cholecystectomy, infection and pelvic chemoradiotherapy

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Bile Acids

- Vital to the digestion and absorption of fat
- Synthesized in the liver and excreted in bile (primary bile acids)
- Reabsorbed in the enterohepatic circulation
- Negative feedback through FXR and FGF19
- Disruption leads to diarrhoea

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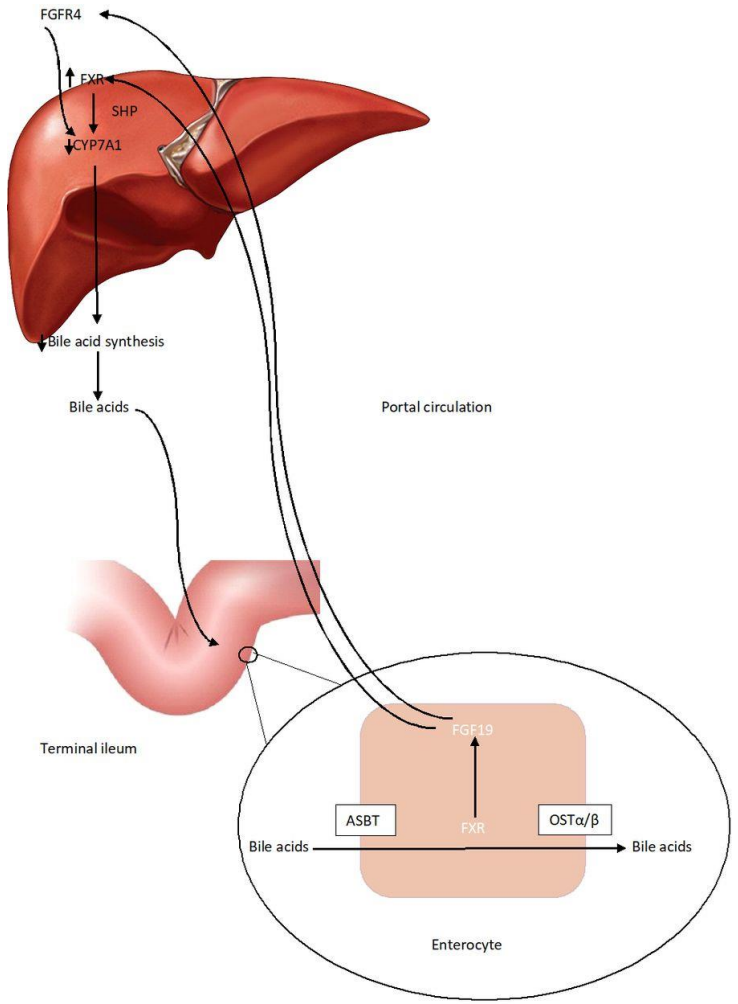
Enterohepatic circulation: Bile acids activate transcription of FGF19 which then acts on hepatic FXR to inhibit bile acid synthesis via CYP7A1.



Alexia Farrugia, and Ramesh Arasaradnam Frontline Gastroenterol 2021;12:500-507

Pathophysiology

- Hepatic Overproduction of bile acids or malabsorption in the terminal ileum
- Bile acid synthesis is regulated by negative feedback to the enterohepatic circulation – farnesoid X receptor and fibroblast growth factor 19
- Interruption of these feedback loops is thought to cause bile acid overproduction leading to BAD
- Idiopathic or a trigger
- Interplay with gut microbiota

Pathophysiology and Ddx

- Lower 75SeHCAT and higher C4 levels
- 50% respond to coletipol
- Terminal ileal disease
  - Crohn's with small bowel resection
  - Right Hemicolectomy
  - HIV enteropathy
- Cholecystectomy
- Post infectious diarrhoea
- Metformin
- Pancreatic insufficiency
- Rule out SIBO, Pancreatic insufficiency, Microscopic colitis, Cancer chemoradiotherapy

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Causes of BAD

Table 1
Causes of bile acid diarrhoea

Hepatic overproduction	True malabsorption
Idiopathic	Crohn's disease
Postcholecystectomy	Right hemicolectomy
Irritable bowel syndrome-diarrhoea predominant type	Enteropathy (such as HIV (human immunodeficiency syndrome)
Pancreatic insufficiency	Pelvic radiation
	Bariatric surgery
	Microscopic colitis
	Small bowel bacterial overgrowth

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Symptoms

- Bowel frequency
- Urgency
- Nocturnal defecation
- Excessive flatulence
- Stool incontinence

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Table 2

Comparison of diagnostic methods of bile acid diarrhoea (BAD)

Diagnostic method	Favourable points	Limitations
^{75}SeHCAT	Well established Predicts response to treatment	Involves radiation Limited availability in certain countries for example, unavailable in USA
C4	No radiation Simple	Diurnal variation Fasting sample Not widely available (in the UK as a research tool)
FGF19	No radiation Simple Commercial assay available	Diurnal variation Requires further validation
Faecal bile acids/faecal metabolomics	No radiation	Cumbersome 48 hours sample collection versus spot test Not widely available Poor patient compliance
Urine	Easy collection	Experimental Not widely available
Therapeutic trial	Easily available	Unreliable Poor response does not exclude diagnosis of BAD Not cost-effective Delays diagnosis and affects patients quality of life.

- **FGF19, fibroblast growth factor 19 .**

Management

- Bile acid sequestrants
  - Cholestyramine up to 80% response
  - Colestipol 50%
- Limited by taste
- Obeticholic acid (not available) –stimulates FGF19 reduces bile acid synthesis
- Low fat diet (reduces urgency, bloating, lack of control, bowel frequency, abdominal pain and nocturnal defecation)

Conclusions

- SeHCAT or C4 measurement
- Spot bile acid measurement

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Take home points

- Idiopathic bile acid diarrhoea (BAD) is due to overproduction of bile acids (rather than malabsorption).
- The negative feedback loops involved in bile acid synthesis are interrupted in BAD but there is lack of data regarding what causes the interruption.
- There is increasing evidence of an interplay between the gut microbiota, farnesoid X receptor and fibroblast growth factor 19 in BAD.
- Tests for BAD such as SeHCAT are not available worldwide but alternatives include plasma C4 testing and possibly faecal bile acid measurement.
- Idiopathic BAD is due to overproduction of bile acids (rather than malabsorption).