SOUTHEND
NATURAL MEDICINE

Dr. Laura M. Brown ND # 2886

southendguelph.ca

Bile and Bile Acids

Bile is made in the liver and chemically changed (conjugated) with taurine or glycine.

Bile is responsible for digestion and absorption of dietary fats, vitamins, and other nutrients and it aids in the elimination of excess cholesterol, bilirubin, waste, and toxins from the body.

50% of bile goes direct to the small intestine.

50% of bile is transported to the gallbladder. where it is concentrated 5–10 times

During a meal, cholecystokinin (CCK) from the upper part of the small intestine (duodenum) triggers contraction of the gallbladder and concentrated bile is released into the small intestine to aid in fat emulsification and absorption.

The small intestine and colon will reabsorb 95% the bile acids, send it back to the liver via the portal bloodstream and recycled into bile again. 5% will be excreted in stool. This cycle of release and reabsorption happens about 10x a day, or the equivalent of 20g a hour.

The primary Bile Acid pool in humans consists of:

1. Cholic acid (3α, 7α, 12α-trihydroxy-5β-cholan-24-oic acid, CA)
2. Chenodeoxycholic acid (3α, 7α-dihydroxy-5β-cholan-24-oic acid, CDCA)
3. Subsequent C24 taurine- or glycine-bound derivatives
4. Glycine and taurine bound bile acids are also referred to as bile salts

Components of bile:

- Bile acids
- Phospholipids
- Biliverdin/bilirubin
- Immunoglobulin A
- Mucus
- Endogenous products: lipo- vitamins, corticosteroids, progesterone, testosterone
- Trace metals
- Xenobiotics

Of the 5% bile acids not recirculated, enroute to excretion, while in the large intestine, they undergo chemical changes.

Gut microbes are involved in secondary bile acid formation and are also involved in regulating bile acids in the liver. When the microbiome is out of balance, so too will the primary and secondary bile acid synthesis.

- Higher levels of gram-negative LPS producing bacteria relate to lower levels of secondary bile acids
- Healthy levels of Firmicutes commensal gram-positive bacterium favour higher levels of secondary bile acids.
- Secondary bile acids affect composition and function of the microbiome and modulate fat digestion, cholesterol metabolism, vitamin absorption, liver function, and enterohepatic circulation through their combined signaling, detergent, and antimicrobial/immune mechanisms.
- Deficiency of secondary bile acids promotes intestinal inflammation.
- High levels of secondary bile acids -especially deoxycholic acid (DCA) -is associated with gut dysbiosis and disease
- Gut microbiota are also able to conjugate amino acids to make bile acids
- Alterations in the chemistry of these secondary bile acids have been linked to several diseases, such as cirrhosis, inflammatory bowel disease, and cancer.
- There is a significant association between microbial bile salt hydrolases (BSH) gene abundance and 10 human diseases, including gastrointestinal diseases, obesity, type 2 diabetes, advanced NAFLD and other liver diseases, IBD, colorectal cancer, cardiovascular diseases, and neurological diseases.

Microbes transform human bile acids in four distinct ways:

1.Deconjugation of the amino acids glycine or taurine via microbe derived bile salt hydrolases (BSH)

2.Dehydroxylation of the cholesterol core

3.Dehydrogenation of the cholesterol core

4.Epimerization of the cholesterol core.

Some secondary bile acids are recirculated and changed some more. This is the case with TUDCA (tauroursodeoxycholic acid).

Bile acids as a therapy:

1. TUDCA shows promise for therapeutic use as disease-modifier in neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's diseases, amyotrophic lateral sclerosis (ALS) and cerebral ischemia.
2. Chenodeoxycholic (CDCA) and/or ursodeoxycholic (UDCA) for dissolving cholesterol gallstones.
3. Used to correct a deficiency in bile acids because the liver isn't making it or the microbiome isn't transforming primary bile acids into secondary bile acids.
4. To reduce inflammation in IBD (ulcerative colitis and Crohn's disease)
5. To treat those with short bowel syndrome: Causes of short bowel syndrome include having parts of your small intestine removed during surgery, or being born with some of the small intestine missing or damaged. Conditions that may require surgical removal of portions of the small intestine include Crohn's disease, cancer, injuries and blood clots.

Gallstones, otherwise known as cholelithiasis is the result of excessive concentration of bile and bile stasis or delayed gallbladder emptying due to impaired motility (pregnancy, contraceptives, surgery, burns, diabetes, celiac). Complications may include infection, perforation, gangrene.

Symptoms of build-up in the gallbladder include indigestion, gas, periodic pain in the right side of the front rib cage, tension in the back of the shoulders near the neck (especially on the right side), bitter taste in the mouth and possible chest pain.
If you are female, overweight and over forty, *or* if you have permeable membranes (leaky gut), an imbalanced microbiome or gluten intolerance, you have an increased risk of gallbladder disease.

Early detection of the root cause of your gallbladder concerns could save you from gallbladder surgery.

If the small intestine is damaged from gluten, a poor microbiome, and /or leaky gut, then the cells that release cholecystokinin (CCK) may be unresponsive. CCK is normally released in the small intestine in response to a fatty meal and is needed to trigger the gallbladder to release its bile. If bile is not used, it hangs around and gets sludgy and with it, increased risk of gallstone formation and inflammation of the gallbladder tissue, called cholecystitis.

Additionally, without proper bile, the fat in the meal will be poorly digested, a condition called steatorrhea. In those with inflammatory bowel disease, this could be one reason for diarrhea after eating. Bile is like dish soap, breaking up the fat into tiny absorbable bubbles called micelles. In these fat droplets are essential fat-soluble nutrients you need to absorb like vitamins A, D, E, K and cholesterol.

Interesting also is the link of permeable membranes and gallbladder disease. Not only does the intestine have a selectively permeable membrane governed by tight junctions, hepatocytes (liver cells) and cholangiocytes (the cells that line the bile duct) are also held together by tight junctions.

Symptoms that indicate gallbladder needs attention:

- Heaviness in the upper abdomen

- Nausea
- Intolerance of alcohol and fats
- Headaches
- “Toxic” conditions associated with skin and autoimmune diseases
- Chronic constipation due to sluggish digestion

Modifiable risk factors for gallbladder dysfunction include:

- Obesity
- Rapid weight loss
- Metabolic syndrome (low high-density lipoprotein and high triglycerides)
- Consumption of refined sugars, saturated fat
- Gluten intolerance, celiac disease
- Crohn’s disease
- Low fibre intake
- Iron deficiency
- Low intake of Vitamin C
- Vitamin D suboptimal levels
- Medications
- Reduced physical activity
- Underlying disease: Crohn’s disease, cirrhosis, cystic fibrosis, celiac and non-celiac gluten sensitivity

Markers of impaired gallbladder function are possible, but not definitive. They can include different combinations of **elevated**:

- Aspartate transaminase (AST)
- Alanine aminotransferase (ALT)
- Bilirubin
- Alkaline phosphatase
- 5’-nucleotidase
- Lactate dehydrogenase (LDH)
- Gamma-glutamyl transferase (GGT)

What’s linked?

- Obesity
- High intake of refined sugar
- Lack of vegetables in the diet
- Lack of fibre in the diet
- Caffeine- consumption of coffee is protective
- Excessive weight loss (>3lbs/week)
- Intake of saturated fatty acids and or trans fats

- Food allergy/sensitivity
    - Wheat (undiagnosed celiac disease/ NCGS)
    - Egg
    - Pork
    - Onion
    - Other: poultry, milk, coffee, orange, corn, beans, nuts (although for some can be protective), apple, tomato

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