

Gilbert's Syndrome

A Look at a Common, Liver Enzyme Disorder

"I'm a 29 year old male from Melbourne, Australia. My symptoms tend to cycle up and down, for a few weeks I feel not so bad, then for a few weeks I feel terrible and my body feels like its falling apart. Sometimes my fatigue is so overwhelming that just lifting my arms feels like a big effort. In school I was a long distance runner. My stamina was my best athletic attribute. Now any intense athletic exertion wrecks me. Five minutes of basketball a few weeks back nearly had me throwing up. It was as if I'd run ten miles. I also got this weird metallic taste in the back of my mouth. When I'm going through a bad phase, I get almost constant colds and/or throat infections and I never fully recover before the next one starts. Sometimes I get mild hand tremors. My eyes are yellow except for a white ring around the iris. This is a blessing because the yellow isn't so obvious unless the eye is turned or rolled back. My skin has a general yellow tinge as well."

"I was diagnosed with GS when I was 16, which was when I started going downhill. Now my yellow eyes are something I hate, but really they are the least of my worries. It's the chronic fatigue and mental fogginess that depresses me. At my worst episodes, I feel like my blood is aching and that I'm being pulled down. I feel unreal, and after a week of that feeling, I start to lose it mentally, thinking I may not recover this time."

These are real accounts from people with Gilbert's Syndrome. Medical authorities today state that it is a common, asymptomatic, benign condition and that there is no treatment required. In the rare occasion that patients are given any treatment it will likely be the long-term use of Phenobarbital for the jaundice, which is an addictive barbiturate with sedating side-effects. Most folks are left to live with their conditions, struggling to find relief and perhaps severely compromising their quality of life.

WHAT IS IT?

Gilbert's Syndrome is an inherited, genetic mutation that causes only 20 to 30% of the liver enzyme UGT1A1 to be produced. Part of the glucuronidation pathway of phase two liver detoxification, this enzyme is the only one that detoxifies bilirubin, a product of the natural breakdown of red blood cells. This impaired function results in excess bilirubin, as well as other substances that are detoxified by this enzyme, to build up and circulate in the body for long periods of time. 94% of people with Gilbert's Syndrome also have genetic mutations in two other enzymes, UGT1A6 and UGT1A7, which act upon many carcinogens, drugs, hormones and other toxins and there is usually an overall slowing of liver function. The mutated gene must be passed to the individual by both parents for Gilbert's to manifest.

While frequency statistics vary widely (2% to 23%), the most commonly reported estimates by researchers are 5% to 10% of the population having GS, 65% to 85% of these people are male. Higher incidents are found in the populations of Africa and the Indian subcontinent and lower frequencies in the Pacific Islands and Southeast Asia.

THE ENZYMATIC MUTATIONS

UGT1A1 - Operating at 30% of Normal Capacity

Detoxifies bilirubin, phenols (a neurotoxin found in polycarobnates, epoxies, nylon, detergents, oral analgesics, hair dyes, sunscreens, drugs and herbicides), carcinogens (especially the ones found in well-cooked meats, tobacco smoke and wood smoke), oral synthetic estrogen pills, flavonoids, steroids, aspirin, coumarin (found in artificial vanilla and flavored tobaccos) and other substances.

UGT1A6 - Operating at 50% of Normal Capacity

Detoxifies serotonin, analgesic drugs such as aspirin and acetaminophen as well as other substances.

UGT1A7 - Operating at 17% of Normal Capacity

Expressed outside of the liver, mainly in the digestive tract and may be highly significant for colonic detoxification.

Detoxifies phenols (a neurotoxin found in polycarbonates, epoxies, nylon, detergents, drugs and herbicides, sunscreens, hair dyes, skin lightening products, oral analgesics like Chloraseptic and Carmex), coumarin (found in artificial vanilla), carcinogens (especially those found in tobacco smoke, charbroiled foods, wood smoke, auto exhaust) and other substances.

HISTORY

This syndrome was first described by French gastroenterologist, Augustin Nicolas Gilbert and his colleagues in 1901 as a syndrome of chronic, benign, intermittent jaundice in the absence of other liver disease. Along with jaundice, psychological symptoms were also described at that time as neurasthenia, a condition which includes fatigue, anxiety, headache, neuralgia and depressed mood.

ONSET AND DIAGNOSIS

Gilbert syndrome is most commonly diagnosed after puberty, when alterations in sex hormone levels cause the blood bilirubin levels to rise. Situations that aggravate elevated blood bilirubin levels (such as fasting, destruction of red blood cells, or illnesses) may be the initial factors that cause the patient to seek medical attention.

Most people begin experiencing symptoms in their 20s-30s, and more commonly at the age of 25-30. For some, the condition comes on gradually, while others may experience a trigger which sets the condition off. Commonly reported triggers include the use of steroidal medications, antibiotics, viral infections, food poisoning, hepatitis vaccinations. People usually receive a diagnosis of Gilbert's during routine blood work that shows elevated bilirubin levels and the absence of other liver disease.

REPORTED SYMPTOMS

A survey of 283 people with Gilbert's Syndrome found the following symptoms were reported:

Frequently Reported: fatigue, tiredness, brain fog, headaches, poor memory, dizziness, depression, irritability, anxiety, nausea, loss of appetite, irritable bowel syndrome (IBS), stomach pain & cramping, liver/gallbladder pain, abdominal pain, tremors, itchiness, jaundice

Commonly Reported: insomnia, difficulty concentrating, panic attacks, hypoglycemic reaction to foods, intolerance to carbohydrates, food intolerances, alcohol intolerance, loose stools / diarrhea, abdominal bloating or swelling, breathlessness or labored breathing, heart palpitations, aching muscles / body ache, joint pain, numbness & tingling, weakness, chemical sensitivity, weight loss, lump in the throat, feeling constantly sick

Sometimes Reported: difficulty finding the right words, feeling drunk, vomiting, intolerance to fatty foods, strong hangovers, acid reflux, excessive thirst, chest pain, muscle twitches, cold hands and feet, environmental allergies, swollen lymph nodes, toxic feeling, bitter or metallic taste in the mouth, eye pain

Occasionally Reported: waking panic attack, mood swings, feeling antisocial, intolerance to drugs, constipation, pale stools, indigestion, back pain, dry skin, feeling cold, low body temperature, pale skin, low weight, night sweats, excessive sweating, poor immune system, sore or dry throat, light sensitivity, bloodshot eyes

RELATED CONDITIONS

People with GS are four times more likely to have chronic fatigue syndrome than others and hypothyroidism and candida infections are also common.

KNOWN EFFECTS

Reduced Liver Function and Swollen Liver - due to an overloaded phase two detoxification pathway, toxins can build up in the body, causing a toxic feeling, chemical sensitivities and intolerance to drugs among other symptoms. The liver is often swollen as well. Because there is a decrease in the breakdown of estrogens, conditions such as fibroids, premenstrual tension and other imbalances related to excess estrogen may be seen.

Increased levels of Bilirubin in the body - Higher than normal levels of unconjugated bilirubin circulate in the body and cause various conditions.

Jaundice - Yellowish pigmentation of the skin and whites of the eyes due to excess bilirubin in the blood. Jaundice often comes with intense itching. Some drugs and medications, especially antipsychotic drugs or drugs containing sex hormones (such as oral contraceptives), some antibiotics, salicylates, and drugs used during chemotherapy can raise bilirubin levels. Common drugs that can decrease bilirubin measurements include caffeine, barbiturates, some antibiotics, oral contraceptives and morphine.

Neurological Impact & Schizophrenia - there is a connection between moderate to high levels of unconjugated bilirubin in the blood and schizophrenia. This is because excess bilirubin may be deposited into the central nervous system and affects the brain cells. Astrocytes, the most abundant type of brain cell, stimulates an immune response when exposed to UCB. UCB disrupts several vital neural cellular functions, alters neural cell membranes, and decreases nerve cell viability. Individuals with Gilbert's Syndrome have an increased prevalence of schizophrenia. This may also be the cause of tremors in some people with GS.

Increased Risk of Gallstones - excess bilirubin acts as a trigger for gallstone formation.

Immune Suppression - elevated bilirubin levels have shown suppression of the immune response in mice and symptoms of immune suppression are frequently reported by those with GS.

Increased Hemolysis (Red Blood Cell Death) - Studies have found that those with Gilbert's Syndrome have increased breaking open of red blood cells and increased levels of carboxyhemoglobin (carbon monoxide in the red blood cells), which could be causing symptoms of fatigue in many patients. Increased hemolysis can also lead to jaundice, anemia and gall stones. Oxidative stress can contribute to hemolysis, which adds even more bilirubin to the blood as a byproduct.

Gastroparesis (Delayed Gastric Emptying) - Gastric emptying is delayed significantly in Gilbert's Syndrome. This could result in nausea, vomiting, early satiety, abdominal bloating, heartburn or gastric reflux, changes in blood sugar levels, lack of appetite and weight loss. Gastroparesis is often misdiagnosed as Irritable Bowel Syndrome in subjects with GS.

THERAPEUTIC RECOMMENDATIONS

General Recommendations

Reducing bilirubin levels is critical. No therapy will work for very long if this issue is not addressed. Avoidance of known triggers for hyperbilirubinemia, such as dehydration, fasting, antibiotics, stress and illness is very important. General support of the body are also necessary, specifically, the use of adaptogens and nervines to help the body/mind/spirit deal with the stress of the condition and to keep homeostasis within the body, the use of alteratives and therapies to support the detoxification process, including building and supporting the blood, which carries all of the nutrients into the body and wastes out of the body, removing strains to the liver by limiting exposure to environmental toxins and eating a diet that is liver-friendly, supporting and protecting the liver and liver function, enhancing liver enzyme production, boosting and supporting the immune system, and supporting the digestive process to ease

symptoms and allow easier absorption as well as moving the bile through the system.

Detoxification of Bilirubin and Jaundice

Bilirubin is light sensitive and decomposes in the light so **phototherapy** may be helpful, either through therapeutic sun exposure or the use of artificial light. Light changes the shape of the bilirubin molecules and allows it to be excreted without the usual liver conjugation process. The use of barley water, which is made by simmering one cup of barley in three liters of water for three hours may also be helpful in clearing bilirubin from the body. The UGT enzyme that breaks bilirubin down requires glucose to operate, so **ensuring that blood sugar levels stay stable** will assist the enzyme in its functions. Blood levels of bilirubin may be high and symptoms experienced in the lack of visible yellow discoloration.

The use of **antipruritics** will help ease the intense itching that may occur with elevated levels of bilirubin in the blood. Consider chickweed, balmony, plantain, yellow dock, witch hazel or comfrey.

Herbs for non-obstructive **jaundice**: fringe tree, barberry, blessed thistle, celandine, asafetida, goldenseal, Queen Anne's lace, St. Johns Wort, yellow dock, balmony, Oregon grape.

Stress response

Full body support is especially beneficial and can be achieved through the use of adaptogens and nervines.

Specific recommendations for **adaptogens** are: codonopsis (immune tonic and digestive protectant), shatavari, schisandra, reishi, goji berries, licorice, guduchi, ginseng, amla, astragalus, ashwagandha.

Herbs for **nervous system support**: St. Johns Wort, skullcap, oats, lemon balm, black cohosh, cramp bark, motherwort.

General Detoxification Support

The use of **alteratives** and **other therapies** is critical since the liver is not fully functional. The detoxification processes can be supported by avoiding alcohol, excess saturated fat, artificial flavorings and preservatives, exposure to environmental toxins, smoking, charred foods, caffeine, sugar and pesticides/herbicides. Practices which may be helpful include: dry skin brushing, castor oil packs over the abdomen, Yoga, Tai Chi, Qi Gong and other deep-breathing practices, infrared saunas, hot & cold showers, coffee enemas, Epsom salt baths and salt scrubs.

Alteratives and Blood Building

"Worry accelerates aging because it weakens the blood, which carries nutrients necessary for cell regeneration." ~Paul Pitchford

Alterative (blood cleansing) herbs include: dandelion root, goldenseal root, chaparral, echinacea, yellow dock, red clover, horehound, poke root and burdock.

Herbal tonics for general blood building include: dong quai, jujube dates, goji berries, rehmannia, peony root, hawthorn, figwort, amla, American ginseng, astragalus, prickly ash and fo-ti.

Foods to build blood are: blackstrap molasses, figs, raisins, bone marrow soup, red meat, beets, dark grapes, cooked onions, blackberries, raspberries, bilberries (huckleberries), black currants, mulberries, cherries and gelatin. Additionally, eating a variety of foods in their unrefined state, especially vegetables, legumes, grains, nuts and seeds will be helpful.

Nutrients needed to build blood include: iron (requires adequate copper and B & C vitamins for absorption), folic acid (sources are micro algae, sprouts, leafy greens and chlorophyll-rich foods), Vitamin B12, adequate protein and royal jelly.

Recipe for building blood (Candis Cantin)

Make a strong decoction of equal parts rehmannia, yellow dock and dong quai, remove from heat, add an equal part of nettles and cover. Let the nettles infuse into the covered decoction for 20-30 minutes. Strain and add an equal amount of molasses.

Dosage for moderate blood building is 1 tsp, three times per day with meals.

Liver Support and Protection

Cruciferous vegetables increase the activity of the UGT1A1 enzyme and protect the liver. Seeds and nuts build the liver and fruits such as citrus are cleansing. Also, eating a variety of yellow, orange, purple and red fruits and vegetables is very beneficial. Asparagus, watermelon and broccoli are helpful in liver detoxification processes. Bitter foods such as dandelion greens and mustard greens are cleansing. Drinking lots of water, especially with the inclusion of lemon, will be helpful in the eliminative processes and will keep the body well hydrated. Cilantro and parsley are especially effective at pulling toxins out of the body and evening primrose oil is healing to the liver. The use of probiotics will assist in keeping the glucuronidation pathway of the liver functioning as well as possible, since they compete with the pathological bacteria Beta-glucuronidase found in the gut, which can reverse this pathway. The nutrient, Calcium d-glucurate inhibits Beta-glucuronidase and can be found in stone fruit, cruciferous vegetables, squash and melons.

Hepatic herbs that provide general support to the liver include: turmeric, black root, barberry, burdock, fennel, artichoke, boldo, rehmannia, milk thistle, dandelion, prickly ash, schisandra, gentian, fringe tree, bupleurum, white peony, yellow dock.

Other herbs to consider using are specifics for:

Swollen Liver: celandine, chicory, fumitory, Oregon grape, red root.

Depressed Enzymes: celandine, licorice, schisandra, cabbage (as a food).

Bile Movers: boldo, bupleurum, cornsilk, dandelion, devil's claw, gentian, hops, oregano, St. Johns Wort, artichoke leaf, fumitory.

Gastroparesis (Delayed Gastric Emptying)

Eating 4 to 6 small meals per day rather than 2 to 3 large ones can be helpful. Avoidance of foods high in fat and the use of high nutrient liquids such as miso, nettle infusion and bone broths may be helpful since nutrient absorption may be low. Other practices that may help are the use of blended or blended or easy-to-digest foods such as soups and smoothies, apple cider vinegar in water before meals and the application of abdominal massage to relieve stress and tension.

Ginger accelerates gastric emptying and bitters such as artichoke leaf may be helpful. Other herbs and herbal preparations that may be used include: shatavari, Triphala, magnolia bark, fennel, rosemary, cardamom, chamomile, valerian and mugwort.

Since the vagus nerve controls the muscles of the stomach, **herbs that support the nervous system** may also be helpful. Consider oats, St. Johns Wort, skullcap, red sage, schisandra, lemon balm, elecampane, ginseng and damiana.

Immune Support

"The single most important principle for strengthening immunity is an attitude of non-separation in one's personal life. Courage may be required, along with sincere forgiveness and unconditional gratitude for everything that happens and has happened. According to traditional Chinese physiology, getting rid of old resentments clears the liver of obstructions, which in turn permits the smooth and vigorous circulation of protective and other qi energies." ~Paul Pitchford

Herbs to support the immune system's function include the following immunomodulators: astragalus, codonopsis, reishi, shiitake, schisandra, rehmannia.

During active illnesses, use herbs appropriate to the acute condition. Herbs to consider are: Echinacea, garlic, usnea, thuja, boneset and elder.

The immune system also requires the **nutrients** zinc, selenium and vitamins A, C, E & B complex to function optimally.

CONCLUSION

It is entirely possible that one in ten clients we see as clinicians could have GS. Some gastroenterologists have placed estimates even higher. Given its prevalence in the population and the fact that medical authorities currently dismiss it almost entirely, as well as the intense suffering and greatly diminished quality of life many people report, we as herbal practitioners, would do a great service to our clients to watch for the tell-tale symptoms of extreme fatigue, abdominal distress, psychological symptoms such as anxiety, depression and mind fog, along with possible yellow discoloration of the skin or eyes and employ effective therapies tailored to the individual. This syndrome is often missed among the myriad of related conditions it can cause and putting all of the pieces together to form an integrated therapeutic approach can greatly benefit people and help them to live a vastly improved quality of life.