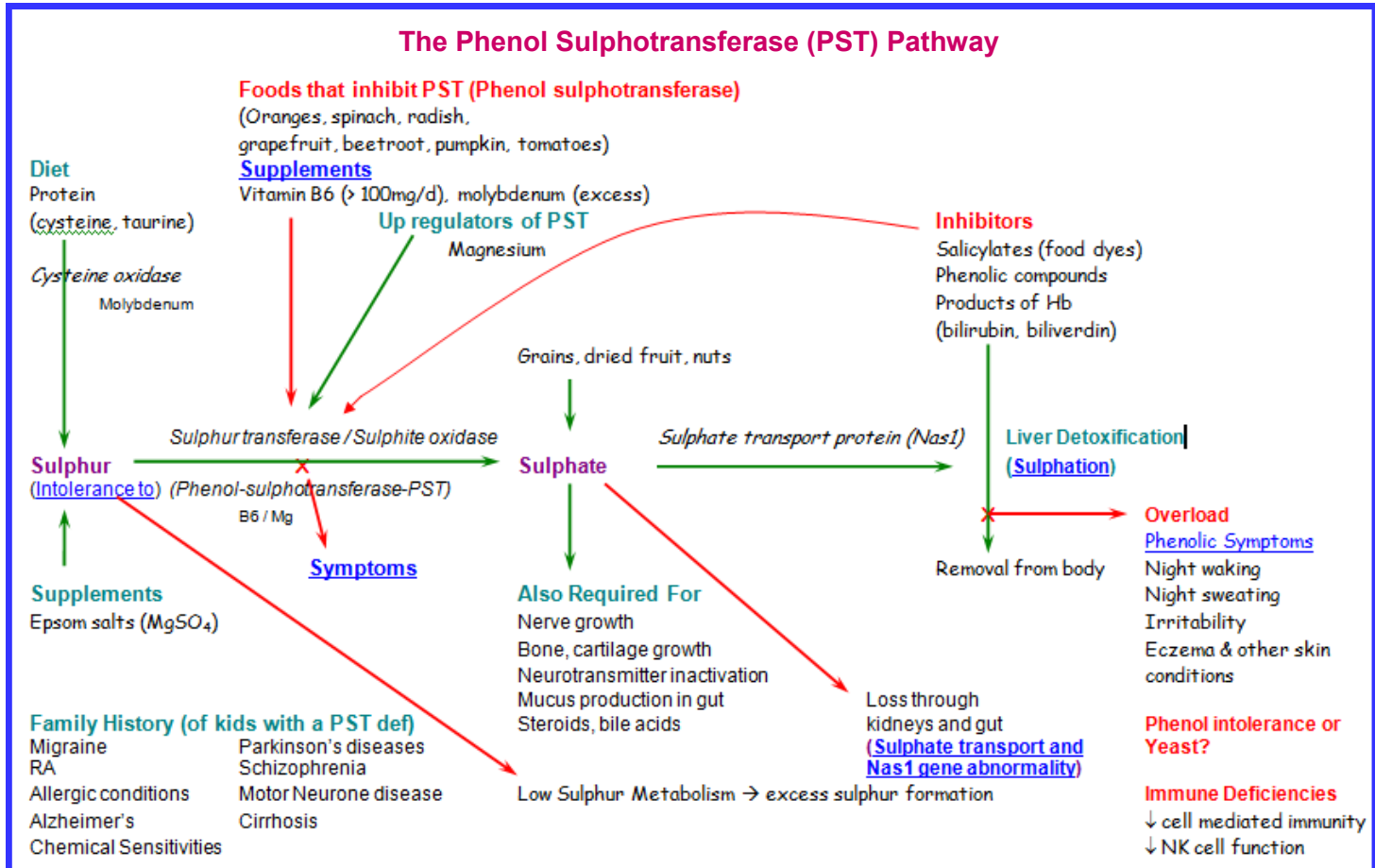


# Phenol Sulphotransferase (PST) Pathway

The phenol sulphotransferase (PST) sulfation pathway is necessary for the breakdown and removal of certain toxins in the body. The pathway is dependent on sulphur, sulphate, specific enzymes as well as co-factors to make it work. The diagram below is my understanding of how the pathway works.



## Intolerance to Sulphur

Some people appear to be **intolerant to** many foods and supplements containing sulphur, including some B vitamins. This also includes glutathione shots and oral Lipocetual Glutathione. There are bacteria in the small and large intestine that convert (reduce) sulphate compounds from sulphur-containing foods and supplements to hydrogen sulphide gas (H<sub>2</sub>S). Excess hydrogen sulphide is a potent neurotoxin - affecting both the brain and nervous tissue. Candida yeast also produces some hydrogen sulphide gas when it ferments carbohydrates.

**If someone is having difficulty with all sulphur-containing substances except taurine and sulfate**, the problem may be at the **sulphite oxidase** step in the metabolism of sulphur. All the chemically reduced forms of sulphur except taurine must eventually pass through this step to get to sulphate, the most oxidized form of sulphur.

In some rare cases, the problem at the sulphite oxidase step is genetic, involving the formation of the active form of molybdenum (molybdopterin). People with this problem have severe disease. However, in many cases, just **taking more molybdenum will help**. Molybdenum is the cofactor for the enzyme sulphite oxidase. Molybdenum is also a cofactor for two other enzymes in the body, xanthine dehydrogenase and aldehyde oxidase. People with molybdenum deficiency therefore can have low urate (uric acid) levels as well as intolerance of alcohol.

### **Sulphate is required for:**

- **mucin proteins:** Mucin protein production is very important. **If there is a deficiency in sulphation there are known links with gut dysfunction and irritable bowel.** There must be enough sulphur attached to these proteins otherwise the gut wall will allow peptides through.
- production of steroids
- production of bile acids
- Phenol breakdown
- **cholecystokinin:** Cholecystokinin (cck-8) protein stimulates the secretion of enzymes, gastric acid and gall bladder contraction. It also controls food intake.
- **gastrin** must be sulphated to release active pepsin. **Pepsin activates secretin release and cholecystokinin, which when sulphated, stimulates the pancreas to release pancreatic enzymes.**
- catecholamine production
- formation of connective tissue

**The average plasma sulphate level is 4.9 in normal children but 0.49 in autistic children.**

### **Sulphation**

Sulphation is required for inactivation of some neurotransmitters in the brain. Low sulphation will lead to a build up of residual neurotransmitters. Mucins that make up the mucus within the intestines are sulphated, decreased sulphate leads to decreased mucin production, poor gut integrity predisposing to gut dysfunction and irritable bowel issues.

**Cholecystokinin (cck-8)** stimulates the secretion of enzymes, gastric acid and gall bladder contraction. It also controls food intake.

Sulphation must also be present for digestive hormones to function properly.

Gastrin must be sulphated to release active pepsin. Pepsin activates secretin release and cholecystokinin, which when sulphated, stimulates the pancreas to release pancreatic enzymes.

**Foods that inhibit these sulphation enzymes are:** oranges, spinach, radishes, grapefruit, beetroot, peppers, pumpkins and tomatoes. Other foods that inhibit sulphation are bananas, cheese and chocolate.

**Sulphation may also be reduced by excessive levels of molybdenum or vitamin B6 (> 100mg/ day).**

## PST Deficiency Symptoms

Some typical symptoms indicating your child may have a phenol problem are [not all of these need be present]:

- ⊗ Dark circles under the eyes,
- ⊗ Red face/ears,
- ⊗ Diarrhoea,
- ⊗ Hyperactivity,
- ⊗ Aggression,
- ⊗ Headache,
- ⊗ Head banging or other self-injury,
- ⊗ Inappropriate laughter,
- ⊗ Difficulty falling asleep at night
- ⊗ Night waking for several hours
- ⊗ Night sweats

**Testing:** A subjective test for PST efficiency is to **observe a reaction to Tylenol or acetaminophen** – either hyperactivity or lethargy. Therefore **Panadol** should be avoided for kids with a PST problem (One source suggested that one or two minutes after a dose of Tylenol™, the entire supply of sulphate in the liver is gone!)

## Sulphate Transport and NaSi-1 Gene Mutation

**Sulphate** is ingested as a mineral in food such as grains, dried fruit and nuts, is absorbed in the small intestine and circulates in blood plasma where it is used by almost every cell in the body. For example it is required for nerve growth in the brain, detoxification processes in the liver and bone and cartilage growth. As sulphate is hydrophilic, it requires a transporter system to pass across plasma cell membranes. The kidney transporter proteins reabsorb sulphate to saturation point, and then sulphate is excreted in the urine. **Autistic individuals have lower serum sulphate levels compared to normal controls.** As sulphate transporter proteins control plasma sulphate levels, research is being undertaken to see if the transporter proteins are defective in autistic individuals. **Autistic individuals excrete large amounts of sulphate compared to non-autistic individuals.**

**Sulphate transporter genes, such as the NaSi-1 gene,** encode a sulphate transporter protein that is **expressed in the proximal tubule of the kidney.** When 20 autistic individuals were compared to controls, **two mutations were found in the gene that changes the function of the NaSi-1 protein.** One mutation caused complete loss of function of the protein, the other caused a partial loss of function.

In a mouse model where the NaSi-1 gene has been knocked out, the mice excrete large amounts of sulphate in their urine and exhibit some behavioural abnormalities and gastrointestinal disturbances, such as **soft stools**, which parallel symptoms of autistic individuals. Autistic individuals have 'leaky gut'. **Sulphate loss also occurs through the intestine and it is believed that autistic individuals are losing sulphate through both the kidneys and the intestine,** as the NaSi-1 gene is expressed in both organs. Autistic individuals usually have a five-fold lower level of serum sulphate compared to control individuals.

**Some neurotransmitters in the brain are inactivated by sulphation,** so sulphate plays a major role in maintaining the balance required for proper NS function. It is also suggested that **glutamate and serotonin** levels are altered in the brains of autistic individuals. If there is insufficient sulphate present to remove neurotransmitters this leads to residual neurotransmitters that cause problems. As sulphate is lower in autistics the brain may not be getting enough sulphate to get rid of those neurotransmitters that are no longer required.

**Mucins**, a group of glycoproteins that make up mucus in the small intestine, are lower in NaSi-1 knockout mice. **Mucins are sulphated**, a process that helps them in their function of forming a protective layer against infection in the gut. The under sulphation of mucins may also be present in autistic individuals, which would make them more prone to infection.

Ion transport may hold autism clues. Susan Williamson. Australian Life Scientist; Aug/ Sept, 2004.

### **Loss Through Kidneys and Gut**

Large amounts of sulphate are excreted via kidneys (defective sulphate transporter genes; *NaSi-1*) and intestines (leaky gut).

### **Foods & Supplements That Inhibit PST**

**B6 in the form of P5P (pyridoxal-5-phosphate) inhibits PST (phenol sulphur-transferase) activity.** (This could be why some children show adverse effects when supplements high in P5P are started) However the same study showed that increasing magnesium supplementation reverses this inhibition.

ARI got Rosemary Waring to do the research that showed that B6 can inhibit human sulfotransferases, but they are activated by magnesium so that **if you have at least a 1:1 mix of B6:Mg** there is no problem. This is why, if you have a problem with B6, try to see if taking magnesium will help.

**Foods that inhibit these sulphation enzymes are:** oranges, spinach, radishes, grapefruit, beetroot, peppers, pumpkins and tomatoes. Other foods that inhibit sulphation are bananas, cheese and chocolate.

**Sulphation is also reduced by excessive levels of molybdenum or vitamin B6 (> 100mg/ day).**