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The Risks of Bismuth Subsalicylate Accumulation Associated with the Pepto Treatment

by Wayne Persky

Long-term, or excessive use of oral bismuth subsalicylate treatments can sometimes result in serious neurological symptoms in some patients. Although this is a rather rare issue, it's worrisome enough that the gastroenterologist who developed the Pepto Treatment, Dr. Kenneth Fine, no longer recommends the Pepto Treatment for treating microscopic colitis (MC). Instead, he recommends the gluten-free diet as a first-line treatment. The New York Times recently published an article that vividly described how an active, otherwise healthy, 70-year-old man who normally walked 10 to 15 miles per day, suddenly developed debilitating neurological issues that almost turned him into an invalid (Sanders, 2024, March 7)[1].

The doctor who correctly diagnosed the cause of the man's problems, discovered that he had been taking 4 Pepto-Bismol tablets per day for 8 months. When the doctor ordered a test to measure the bismuth levels in his body, the level was found to be 28 times the normal amount (which, of course, is in the toxic range).

Long-term Pepto use can result in slow buildup of bismuth.

Impaired kidney function can increase bismuth buildup.

How is bismuth subsalicylate metabolized?

According to a Drug Bank webpage, bismuth subsalicylate is hydrolyzed in the stomach at pH levels below 3, to become bismuth oxychloride and salicylic acid (DrugBank, 2024, March 8)[2]. Any bismuth subsalicylate that is unchanged by the stomach, reacts with other anions such as bicarbonate and phosphate, when it reaches the small intestine, to form insoluble bismuth salts. And any unchanged bismuth subsalicylate reaching the colon, along with other bismuth salts, react with hydrogen sulfide (that's available due to the action of anaerobic bacteria), to create bismuth sulfide, which is the insoluble black salt that's responsible for turning stools black. Salicylates are excreted in the urine, and bismuth is eliminated primarily by urinary and biliary (via the bile duct leading to the duodenum) routes.

But it turns out that the elimination process has certain limits.

1. The elimination rate is limited by the half-life of the substances, which means that prompt complete elimination does not occur. Although most of the substance may be eliminated within a matter of hours, complete elimination is a time-dependent process. Therefore, if the dose is continued on a regular basis

complete elimination is a time-dependent process. Therefore, if the dose is continued on a regular basis, it's likely that a slow buildup of the substance will occur.

2. The elimination rate has an upper limit, which means that a high dose may exceed the elimination rate of which the body is capable. After that point is reached (if doses exceed a certain limit), elimination proceeds at a fixed (steady) rate. Obviously, this results in a buildup of the substance, if the ingestion of that substance continues at that rate.

In the New York Times example, the patient had been taking 4 tablets per day for 8 months, so long-term treatment can obviously be a problem, even at lower dosage rates, for some patients. During that time his body was slowly accumulating residual amounts, and although his body had been eliminating the bismuth subsalicylate, it hadn't been eliminating enough of it, fast enough to prevent an overdose accumulation by the time he had been taking it for 8 months. It's likely that he had compromised kidney function, although that's strictly speculation, as that wasn't specified in the article.

> **Elimination of bismuth is through the kidneys and liver.**

> **Impaired kidney or liver function reduces the rate of elimination.**

So how much bismuth subsalicylate is toxic?

According to the Drug Bank website, the lowest lethal dose (LDLo) for humans is 700 mg per kilogram. For an individual weighing approximately 70 kg, (approximately 154 pounds) this amounts to 49,000 mg of bismuth subsalicylate, which amounts to 187 Pepto-Bismol tablets. In other words, if we were to take 187 Pepto-Bismol tablets at one time, that dose might be fatal. But, of course, as MC patients, we don't take 187 Pepto-Bismol tablets at one time, although we do exceed that total amount before we complete the Pepto Treatment. So obviously, it's necessary for our bodies to eliminate bismuth salicylate and its metabolites as promptly as it possibly can. And as long as our liver and kidneys are functioning normally, safe elimination will occur.

The Pepto treatment consists of 8 Pepto-Bismol tablets per

day, for 8 weeks. And as noted in Travel Medicine (2nd Edition), the recommended treatment for traveler's diarrhea is 2 Pepto-Bismol tablets, chewed 4 times per day, so this is a commonly accepted treatment, and not considered to be a

particularly high dose (Ericsson, 2008)[3].

This isn't just a Pepto-Bismol problem, it's a problem with all salicylates.

The same problem can occur in anyone taking aspirin in large doses, or for an extended period of time. According to a Drugs.com webpage, 500 mg per kilogram of body weight is considered to be a lethal dose of aspirin (Drugs.com, 2022, August 23)[4]. This works out to 35,000 mg for someone who weighs approximately 70 kg (approximately 154 pounds). Since the average aspirin contains 325 mg of active ingredient, this amounts to 108 aspirins, and if we're taking 4 aspirin tablets per day, for example, we could reach this limit in less than a month, if our liver and kidneys are not functioning properly.

Compromised kidney function is the primary cause of the most serious risks.

As pointed out in the Travel Medicine (2nd Edition) article (and other sources), patients who have compromised kidney function tend to be unable to eliminate salicylates at normal rates, imposing significant risks of a salicylate build up when taking bismuth salicylate or any other source of salicylates, such as aspirin. And hot weather, or dehydration from any cause, tends to reduce the salicylate elimination rate, thereby increasing the risk of a chronic overdose.

Neurological problems develop as salicylate buildups reach toxic levels.

Toxic levels are obviously below lethal levels and anywhere from 150 to 300 mg per kilogram of body weight is considered to be a toxic dose. This works out to approximately 10,500 mg to 21,000 mg for a 70 kg (154 pound) person. At 8 tablets per day, someone using the Pepto Treatment would reach even the maximum level in 10 days, if their body was not capable of eliminating any of the bismuth subsalicylate. Someone taking a maximum dose aspirin of 650 mg every 6 hours would reach the limit in 8 days (if their body was not capable of eliminating any of the salicylate). So obviously, anyone who has kidney or liver problems should be very cautious if they use any salicylates.

Many foods are high in salicylates.

And the problem doesn't end there, unfortunately, because many foods contain high levels of salicylates, naturally. Certain foods, such as legumes, including lentils, beans, peanuts, and peas; vegetables, such as broccoli, cauliflower, cucumbers, radishes, spinach, zucchini, and mushrooms; fruits, including apples, oranges, cranberries, avocados, berries, plums, watermelons, pineapples, cherries, grapes, and peaches; some cereal grains, such as buckwheat, oats, and corn; and many herbs and spices, and even almonds and honey, for example, contain relatively high levels of salicylates. And this is not a comprehensive list. Overdose symptoms can include fatigue, mood changes, decreased cognition, tremors, lethargy, insomnia,

delirium, tinnitus, seizures, depression, and possibly other neurological symptoms

> **Salicylate buildup is also a problem.**

> **Aspirin and certain foods can add to the Pepto salicylate buildup.**

What Should We Conclude from All This?

Anyone who intends to try the Pepto treatment to put their MC into remission, or for any other reason, should be very sure that their liver and kidneys are functioning normally, and they don't allow themselves to become dehydrated. The same advice applies to anyone who intends to use aspirin, or any other medication based on salicylates, as a long-term treatment. And always remember that nonsteroidal anti-inflammatory medications (NSAIDs), in general, are contraindicated for MC patients.

Presumably, the elevated salicylate levels in foods won't create any problems for any of us, unless we have major liver or kidney issues for which we're being treated. However, it's certainly not impossible that salicylates from food might add to the problems experienced by anyone taking high doses of Pepto, or any other medication based on salicylates, for an extended treatment. Labeled doses are generally safe — it's when we exceed those label recommendations that we're risking an overdose, especially if our liver function, or kidney function is compromised.

Despite caveats regarding NSAID use, the Pepto treatment is generally safe and effective for MC patients. At least it's generally safe for anyone who has normal kidney function and normal liver function. Extended, or repeat treatments may not be safe, even if kidney function and liver function appear to be normal, and the risks increase as the treatment time increases. Anyone who is taking high doses of salicylates, especially for an extended length of time, should be aware of these risks, and these limitations. And if while taking Pepto-Bismol, you should begin to experience any of the neurological symptoms associated with salicylate overdose, please proceed to a hospital emergency ward, immediately, and advise the staff that you suspect you are experiencing a salicylate overdose.

> **The Pepto treatment is mostly safe if kidney and liver function is normal.**

> **Extended or repeated Pepto treatment might not be safe.**

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