

# Salicylism in the Elderly: "A Little Aspirin Never Hurt Anybody!"

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Your patients may think that aspirin is completely safe.  
Do you?

BY NANCY FLEMING COURTS

Mrs. F. was an 85 year old who not only read widely but also prepared book reports and programs for a variety of local groups. Her only health problems were hypertension and severe osteoporosis with kyphosis. The previous summer she had broken her left hip, had a prosthesis inserted, and moved into the retirement home in her community. After 7 months, Mrs. F. arranged for daytime help and sitters for the night and moved back into her house. Four months later she had a lumbar compression fracture and began to self-treat the pain with 500 mg aspirin with calcium carbonate, magnesium oxide, and magnesium carbonate (Extra Strength Bufferin). She had had several fractures in the past that she had successfully treated with aspirin. This time, however, about 2 months after beginning the self-treatment, she began to have difficulty hearing, and this loss of hearing was interpreted as being the cause for her occasional confused responses. Her physician had a small amount of wax removed from her ears and substituted choline magnesium trisalicylate (Trilisate) tablets for the buffered aspirin. Mrs. F. did not consider the Trilisate tablets effective, so she began taking the buffered aspirin tablets again.

Over the next 7 days her condition deteriorated. Her mental confusion was now obvious, and she was experiencing hallucinations. Her physician insisted on an immediate computed axial tomographic (CAT) scan. Mrs. F. had to be transported by ambulance to a hospital in another town for the CAT scan. Her symptoms included confusion, rapid respirations and heart rate, diaphoresis, severe hand tremors, anorexia, and lethargy. It was at this point that salicylism was first suspected, and her use of the buffered aspirin was discontinued. Unfortunately, no blood work was done to test for salicylate intoxication.

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GERIATR NURS 1996;17:55-9.

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0197-6554/96/\$5.00 + 0 34/1/59596

Salicylates are not only the most frequently used over-the-counter (OTC) drug, they are also the most common OTC drug contributing to morbidity and mortality.<sup>1,2</sup> Common in older adults, chronic salicylate intoxication may occur even with therapeutic dosages.<sup>3</sup> Older adults are more susceptible to salicylism because they frequently take 3 to 7 prescription drugs (in addition to OTC drugs), have reduced liver and kidney function (which decreases the metabolism and excretion of salicylates), and have a variety of generalized aches and pains that they self-treat with salicylate-containing drugs.

**Since salicylate toxicity is often overlooked as a cause of confusion in elderly patients, it tends to be undiagnosed, leading to increased morbidity and even death.**

Salicylate toxicity in elders most often results from ingestion of salicylate products for physical problems.<sup>4</sup> Since salicylate toxicity is often overlooked as a cause of confusion in elderly patients, it tends to be undiagnosed, leading to increased morbidity and even death.<sup>1</sup> Salicylate toxicity increases health care costs by resulting in increased hospitalizations, numerous laboratory tests, and expensive diagnostic procedures, such as CAT scans.



This article presents information on (1) the pharmacodynamics of aspirin and salicylates: analgesic, antipyretic, antiinflammatory, and antiplatelet; (2) pharmacokinetics: absorption, metabolism, and excretion; (3) salicylate toxicity; (4) interventions for patients with salicylate toxicity; and (5) interventions to prevent salicylate toxicity.

### Pharmacodynamics of Aspirin and Salicylates

In the 1700s the bark of the willow tree was used for its analgesic and antipyretic effects. Later it was found that the bark contained a compound, salicylic acid.<sup>5</sup> By 1860, synthetic salicylates were being produced, and aspirin (acetylsalicylic acid) was introduced in 1899.<sup>6</sup> The two groups of salicylates are acetylsalicylic acid and salicylic acid-based drugs.<sup>7</sup>

Salicylic acid dissociates into salicylate at the normal blood pH, producing analgesic, antipyretic, and antiinflammatory actions.<sup>8</sup> Salicylates do not affect platelet aggregation. It is the acetyl group of aspirin (acetylsalicylic acid) that prevents platelet aggregation. Salicylates are the most commonly used analgesic compounds because they do not lead to addiction or tolerance.

### *The risk of nephrotoxicity from aspirin is also increased in older adults.*

Salicylates produce their analgesic, antipyretic, and antiinflammatory actions by inhibiting production of prostaglandins. Prostaglandins, found in most body tissues and fluids, participate in most body functions. They are not stored in the body but are produced and released locally with cell damage. Some actions of prostaglandins include vasodilation, lysosome enzyme release, increased capillary permeability, and inhibition of platelet aggregation and gastric acid secretion.<sup>7</sup> By inhibiting prostaglandins, salicylate drugs have analgesic, antipyretic, and antiinflammatory actions.

Aspirin and salicylate-containing drugs are effective analgesics only when the pain is caused by the release of prostaglandins at sensitive nerve endings.<sup>9,10</sup> Prostaglandins alone do not cause pain, but they enhance algesic (pain-inducing) substances, like bradykinins, which stimulate pain-transmitting C fibers and smaller A fibers in the spinal cord.<sup>11</sup> Therefore aspirin is ineffective against visceral pain and the severe pain of trauma but effective against pain caused by tissue breakdown and inflammation. The analgesic action of aspirin occurs in a narrow therapeutic range and additional aspirin leads to toxicity but no increase in analgesia.<sup>9</sup> Two aspirin tablets have the analgesic equivalent of 60 mg of the opiate codeine,<sup>8</sup> although aspirin does not bind with

opiate receptors. Decreasing the synthesis and release of prostaglandins also contributes to the antipyretic effects of aspirin.

Salicylates affect neither normal temperature nor drug- or exercise-induced elevated temperature, but they can lead to a fall in elevated temperatures.<sup>10,11</sup> Aspirin is more effective than equal doses of salicylic acid-based drugs for lowering temperature.<sup>7</sup> One explanation for the antipyretic action is that endogenous pyrogens act on the hypothalamic thermoregulatory system to raise body temperature. Aspirin acts to reduce the effects of the pyrogen, but does not affect release of the pyrogen.<sup>11</sup> Some authors suggest pyrogens stimulate prostaglandin release in the central nervous system and most prostaglandins have a pyrogenic effect; therefore when prostaglandin production is blocked, the temperature is lowered.<sup>9</sup> In addition, hypothalamic stimulation leads to vasodilation and diaphoresis, which further reduce temperature elevations.<sup>10</sup>

Cell injury, releasing prostaglandins locally, both induces symptoms of inflammation and enhances bradykinin and histamine effects.<sup>11</sup> Vasodilation caused by the kinins, release of lysosomes, and increased permeability of vessels resulting from prostaglandins lead to the signs of inflammation—redness, edema, heat, and pain.<sup>7</sup> In addition, lysosomal membrane is damaged and several enzymes are released; as these enzymes clean up the debris, they also begin to break down connective tissue. This has a cyclic effect, leading to further release of prostaglandins and kinins and more inflammation.<sup>7</sup> Interference with prostaglandin release thus leads to a decrease in inflammation. Large doses of salicylates are needed to fight inflammation.<sup>11</sup>

Aspirin decreases the formation of thromboxane  $A_2$  and prostacyclin by acetylating the enzyme cyclooxygenase. Thromboxane  $A_2$ , synthesized by platelets, is a potent vasoconstrictor and increases platelet aggregation.<sup>8</sup> Prostacyclin has potent vasodilation properties and inhibits platelet aggregation.<sup>9</sup> Low doses of aspirin, but not other salicylates, selectively suppress the synthesis of platelet thromboxane  $A_2$  without inhibiting vascular prostacyclin. Suppression of thromboxane  $A_2$  inhibits platelet aggregation for the life of the platelets. Therefore physicians may prescribe one aspirin a day to decrease platelet aggregation. Because the inhibition of platelet aggregation lasts for the life of the platelets, aspirin should be avoided in patients with liver disease and bleeding disorders.

### Pharmacokinetics: Absorption, Metabolism, and Excretion

Aspirin is absorbed in the stomach and upper small intestine within 30 minutes of ingestion.<sup>10</sup> Although pure and buffered aspirin forms are readily absorbed, the absorption rate is slowed with sustained-release and enteric coated aspirin, food and



antacids in the stomach, high gastric and intestinal pH, and delayed gastric emptying time. Once absorbed, 50% to 90% of the drug is bound to plasma albumin.<sup>8</sup> In patients with poor nutritional status and low albumin levels, salicylate toxicity may develop more quickly because there is more free drug.

Aspirin is hydrolyzed in the liver into salicylic acid. Normal aging changes in the liver include a reduction in size and in blood flow and a reduced ability to synthesize proteins and metabolize drugs.<sup>12</sup> Thus older adults are more susceptible to drug toxicities of any type, and especially to those drugs that are metabolized in the liver. It has been suggested that frequent drug blood levels be drawn if an older adult is taking three or more drugs that are metabolized in the liver.<sup>12</sup> **The liver inactivation system is saturated with a single 325 mg aspirin tablet, so the liver cannot metabolize aspirin in large doses.**<sup>8</sup>

The kidneys excrete the salicylate metabolites and some drug unchanged.<sup>10</sup> Elevated plasma levels of salicylic acid are found with kidney dysfunction.<sup>9</sup> Furthermore, older adults have a decrease in the number of functional units of the kidney with a concomitant decrease in function. Because the serum creatinine may remain within normal range, creatinine clearance rates are needed when dosage is critical.<sup>12</sup> The risk of nephrotoxicity from aspirin is also increased in older adults.<sup>3</sup> When the renal pathway is saturated, large plasma increases result from small increases of aspirin.<sup>7</sup> **When the urine is acidic, less salicylates are excreted; therefore large doses of vitamin C or large amounts of cranberry juice may increase serum levels of salicylates.** Conversely, when patients are taking buffered aspirin or taking an antacid with the aspirin, the pH of the urine is raised and increased amounts of the drug are excreted.<sup>8</sup>

### Salicylate Toxicity

Chronic salicylate use among elderly persons is common, with the development of salicylate toxicity from unintentional overdose.<sup>2,3</sup> This chronic use, coupled with the normal physiologic changes of aging and polypharmacy, places this population at greater risk for salicylate toxicity. Although salicylism usually occurs with aspirin, it may also occur with increased levels of other **nonsteroid antiinflammatory drugs with salicylic acid.** Mild salicylism occurs when the serum salicylate levels are 45 to 65 mg/dl.<sup>8</sup>

Signs and symptoms of mild salicylate toxicity include tinnitus (ringing in the ears), dizziness, headache, and changes in mentation.<sup>7,11</sup> Severe salicylate toxicity manifests, with plasma levels above 90 mg/dl,<sup>8</sup> with hyperpnea, acid-base problems, nausea and vomiting, petechial hemorrhage, delirium, hyperthermia, convulsions, and coma.<sup>11</sup> Other signs and symptoms include drowsiness, headache, hyperventilation, diaphoresis, thirst, nausea, vomiting, and diarrhea.<sup>9</sup>

Gastric ulceration and gastritis are the most

common adverse reactions to salicylates.<sup>7,11</sup> Prostaglandins inhibit gastric acid secretion; therefore the inhibition of prostaglandins by aspirin increases the presence of gastric acid, which is responsible for gastritis and gastric ulcer formation. The acetylation of the cyclooxygenase with the concomitant antiplatelet action leads to a prolonged bleeding time, which may double with 650 mg of aspirin.<sup>9</sup> In addition, large doses of aspirin decrease prothrombin production, which further aggravates gastric bleeding tendencies.<sup>4,9</sup>

Renal prostaglandins, produced by the medulla of the kidney, are potent vasodilators that regulate renal blood flow to the kidney, renin release, and sodium reabsorption.<sup>7</sup> Blocking the synthesis of renal prostaglandins contributes to lower renal blood flow with decreased renin production. Chronic salicylate therapy may lead to the development of renal insufficiency in vulnerable patients.<sup>3</sup> Metabolic problems from salicylate toxicity include inhibition of amino acids and carbohydrates and disruption of glucose homeostasis, leading to hypoglycemia or hyperglycemia.<sup>1</sup>

High doses of salicylates lead to central nervous system stimulation of the medullary ventilatory center, producing hyperventilation,<sup>4,9</sup> and this results in respiratory alkalosis. As carbon dioxide (CO<sub>2</sub>) is blown off, respiratory alkalosis develops. To compensate, bicarbonate, sodium, potassium, and water are excreted to maintain normal blood pH levels.<sup>3,9</sup> This leads to metabolic acidosis, hypokalemia, and dehydration. In addition, salicylic acid affects metabolism of carbohydrates, proteins, and lipids, fur-

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ther increasing the metabolic acidosis.<sup>3</sup> Therefore patients may initially be seen with respiratory alkalosis and metabolic acidosis.<sup>1</sup>

**Additional central nervous system signs and symptoms of salicylate toxicity include irritability and disorientation, which progress to lethargy and hallucinations, and end with seizures and coma.**<sup>7</sup> Stimulation of medullary chemoreceptor trigger zones by large doses of salicylates produces nausea and vomiting. Mortality from salicylate toxicity is usually caused by central nervous system dysfunction.

### Interventions

Chronic salicylate toxicity should be suspected



when an elderly patient has rapid unexplained confusion or delirium or unexplained hyperventilation with fever and vomiting.<sup>3,4</sup> Physical assessment includes thorough respiratory and neurologic assessments. It is important to note the following:

- Hyperventilation associated with salicylate toxicity is manifested by hyperpnea (increased depth of respirations), rather than by tachypnea (increased rate of respirations).<sup>4</sup>
- Common neurologic problems range from confusion, delirium, and agitation to hyperactivity and restlessness with movement disorders.<sup>3</sup>
- Tinnitus, the most common side effect of mild salicylate toxicity, may be associated with some hearing loss.<sup>8</sup>
- Additional problems may include arrhythmias caused by the hypokalemia and dehydration. The definitive diagnosis is made with serum salicylate levels.

To differentiate the confusion of delirium and depression from dementia, it is imperative that one determine the patient's previous level of cognitive functioning from family and friends who accompany the patient to the hospital or clinic. Mrs. F.'s confusion is best labelled as delirium, in that she experienced the following: rapid onset of symptoms (days), hallucinations, disorientation, incoherent speech, impaired memory, and some disordered reasoning.<sup>13</sup> In contrast, symptoms of depression include an onset of weeks to months; disorientation; sad or depressed affect, with excessive sleeping or insomnia; slow recall, with short-term memory deficits; negative or paranoid thoughts; and fre-

***The cause of confusion with a recent rapid onset must be identified before appropriate treatment may begin.***

quent responses of "I don't know" to questions.<sup>13</sup> Dementia has a gradual onset over years, with a slow and progressive decline.

The cause of confusion with a recent rapid onset must be identified before appropriate treatment may begin. A thorough nursing history, with emphasis on current medications, prescribed and OTC, is essential and may speed the diagnostic process. Specific questions about the medicines bought at the drug store or grocery are needed to obtain this information, since these drugs are often not considered important by the patient. Accurate medication information may be difficult to obtain because patients with a rapid onset of confusion have probably

been administering their own medications, and, at this point, they are poor historians. Ask family, friends, or caregivers to identify when the aspirin was purchased and to count the number of pills left. With salicylate toxicity, patients may be unaware how frequently they are taking the drug.

The usual treatment of chronic salicylate toxicity is drug withdrawal with supportive therapy.<sup>3</sup> With enteric-coated aspirin or gastric outlet obstruction, treatment may include gastric lavage, induction of emesis, or administration of activated charcoal.<sup>14</sup> Intravenous therapy is initiated to correct electrolyte and fluid disturbances. Sodium bicarbonate solutions may be given to maintain a urine pH of 8 or greater, which increases salicylate excretion, and to correct the acidosis to prevent salicylates from readily entering the brain.<sup>3,11</sup> Hyperthermia is treated with tepid water sponges or a cooling blanket.<sup>11</sup>

Mrs. F. became aware of her confusion when she responded to questions and observed the facial expressions of people to whom she was talking. This was quite frightening. She remembered some events but had difficulty understanding or remembering others. It is important to explain to patients who were previously cognitively intact what is happening to them. It is also important to explain to patients and their families that the confusion is not dementia, will not be progressive, is caused by too much medication, and will clear up as the salicylate is metabolized and excreted. Furthermore, explain to patients' families that the patient will soon seem coherent and oriented but may not remember recent details and decisions. Therefore, if possible, important decisions should be postponed for several weeks.

The elderly patient has been taking aspirin in large amounts for pain and will probably need another pain medication. If the aspirin was taken for its antiinflammatory effects, it may be necessary to give another type of nonsteroid antiinflammatory drug (NSAID), because acetaminophen will not be effective. The type and severity of pain determine the patient's level of activity. Mrs. F. was quite content to stay in bed and needed encouragement to move and get out of bed. Because they are confused, other patients may require close supervision to prevent wandering and falls.

If diaphoresis is present, frequent skin care is needed to prevent breakdown and an increase in fluid intake is needed to prevent dehydration and support elimination of the salicylate. Patients may require a supplement to meet nutritional requirements, especially if they have nausea and vomiting. Avoid foods containing salicylin, such as bananas, oranges, and apples; drugs and processed foods with tartrazine dye or sodium benzoate; and other salicylate-containing NSAIDs.<sup>8</sup>

**Interventions to Prevent Salicylate Toxicity**

Salicylates, in both prescription and OTC preparations, are widely used by elderly persons. Preventive



interventions with long-term use of salicylate preparations include the following:

- Avoid concomitant use of several salicylate preparations.
- Monitor kidney function to detect nephrotoxicity.
- Screen for gastrointestinal bleeding.
- Monitor blood levels.
- Use misoprostol in patients with a history of gastrointestinal problems.<sup>3</sup>

Because salicylates are commonly used by elderly persons and because long-term use predisposes them to salicylism, it is important to determine their use as a routine assessment. It is further recommended that nurses teach people that:

- OTC drugs, and especially aspirin, often have significant side effects, especially when combined with other medications.
- Older adults frequently need lower doses of medications to obtain therapeutic levels.
- The polypharmacy of older adults increases their risk of drug interactions and toxicities.
- All drugs should be reported to each of their physicians at each visit.

Many people do not know that OTC drugs such as Pepto-Bismol, Doan's Pills, Goody, Alka-Seltzer, Anacin, Excedrin Extra Strength, Goody's Headache Powder, and BC Headache Powder contain aspirin. Since aspirin is the most used, most effective, and most toxic of the salicylates,<sup>7,9</sup> elderly patients, their families, and caregivers may need a reminder of the importance of following the directions on the container. An OTC drug should never be taken longer

than recommended because it is vital that older adults see their physician if symptoms persist.

In addition, nurses are in a position to lobby drug companies to include signs and symptoms of toxicity on bottle labels in letters large enough and in language simple enough to be read and understood by older adults. There need to be special directions for older adults since they metabolize and excrete drugs at different rates from younger people. **Constant vigilance to slight mental status changes in older patients may reduce or eliminate salicylate toxicity, decrease morbidity and mortality, and control health care costs.** ■

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