Statins versus Aspirin

By Edward J. Petrus, M.D.

Statins have become the pill for all reasons. Originally used to reduce cholesterol production in the liver, they are now prescribed for persons with normal cholesterol levels, to act as an anti-inflammatory agent. Statins are now the most widely used drugs for the treatment and prevention of cardiovascular disease (CVD), but half of all CV events occur with normal cholesterol or low LDL levels (Circ 2003;108:2292-2297). While statins have been used for over 20 years, the heart attack death rate has not dramatically declined during that time.

Industry estimates put total annual spending on statins at more than $22 billion. The fundamental flaw in focusing on cholesterol and statin agents is the perception that cholesterol identifies hidden heart disease and that lowering cholesterol is the way to a future free of heart attacks. While statins lower total cholesterol and low-density lipoprotein (LDL) by 30-50%, they do not identify or cure coronary heart disease. Statin therapy for high cholesterol is just one piece of the puzzle. High cholesterol is among the risk factors for heart disease, but is not the leading risk factor. In the Scandinavian Simvastatin Survival Study (Circulation 1998, 21;97(15):1453-60) nine heart attacks were prevented, reducing the number of heart attacks from 28 to 19. Nevertheless, 19 heart attacks still occurred. Why does lowering LDL with statin drugs result in such limited success?

A recent Cochrane review concluded that there is not enough evidence to recommend the widespread use of statins in the primary prevention of heart disease (Cochrane Database Syst Rev 2011;1(CD004816)). The authors reviewed 14 trials involving 34,272 patients, and concluded that none of the individual trials showed strong evidence of a reduction in total mortality, in a high risk primary prevention population.

**Statin Problems**


Statin use has no effect in preventing dementia or Alzheimer’s disease (Cochrane Stst. Rev.2009 (CD007514)) and contraindicated in persons with a history of hemorrhagic stroke (Arch Nervoul Jan 10, 2011).
Aspirin

Advocates call the statin drugs the “new aspirin” but they don’t compare to the benefits of aspirin. Published studies have shown that: low dose aspirin reduced the risk of cardiovascular death by 44% at 3.6 years follow up (Lancet 2001;357:89-95), a five year study of 22,071 physicians showed that alternate day aspirin conferred a 44% reduction in risk of the first myocardial infarction (Circulation 2003;108:1191-1195), regular aspirin use was linked to a 28% reduction in cardiac events (Ann Int Med 2002;136:157-172), there was a 25% reduction in the incidence of subsequent myocardial infarction, stroke and death from cardiovascular disease (Postgraduate Medicine 1996;99(2):109-120, those on aspirin had 42% fewer strokes (Lancet 1997;349:1563-1565, 1569-1581).

The primary complication of deep vein thrombosis (DVT) is pulmonary embolism (PE), of which 300,000 people die each year, more than die from breast cancer and AIDS combined (Drug Topics September 17, 2007, pgs 38-42). Published studies have also shown that: among the 13,356 patients with hip fracture, aspirin produced an overall 43% reduction in pulmonary embolism and a 29% reduction in deep vein thrombosis (Lancet 2000;355:1295-302). There is a three-fold increase in DVT in travelers, rising 18% every two hours for any type of travel and 26% for every two hours of air travel (Annals of Int. Med, August 4, 2009). Aspirin and clopidogrel are currently the only recommended antiplatelet therapy for use in the prevention of cardiovascular events in patients with peripheral artery disease (JNMA, 2009;101:999-1007).

The prevalence of Alzheimer’s disease is six times greater in the general population than among patients with rheumatoid arthritis, who are taking NSAIDs or steroids. Patients taking NSAIDs for more than two years were spared Alzheimer’s disease. (Neurology Reviews 1997;5(9):1-26). If the process that damages neurons in Alzheimer’s disease is at least in part inflammatory, then it is reasonable to defend these brain cell with anti-inflammatory agents (Neurology 1996 ;43:425-432)(Brain Res Rev, 1995;21:195-218). Daily aspirin use decreases the risk of Alzheimer’s disease by 50% (Alzheimer’s Disease, 1998;1(1):8-11)(Daily Mail, 9/24/2002, pg 10).

Periodontal disease has been associated with peripheral vascular disease and may increase the risk of heart attack and stroke by 20% (Crit Rev Oral Biol Med, 2004;15(6):403-13). Dental disease may play a role in the formation of carotid atheromas (J Dent Res, 2003,82(2):82-90). Bacteria and toxins in the periodontal pockets are linked to an inflammatory response that elevates white blood cells and c-reactive protein (J Am Coll Cardiol 2011;57:971-6). Low dose aspirin taken for at least 2 years reduced the rate of periodontal attachment loss (J Clin Periodontal, 2001;28(1):38-45). Aspirin reduce inflammation by inhibiting prostaglandin formation and released lipoxins that control inflammation. Studies suggest that individuals over 50 years, particularly ex-smokers, may benefit by taking low-dose aspirin to reduce the risk of periodontal disease (J Clin Periodontol, 2001;28(2):38-45).

Aspirin reduces vision loss in the elderly (Am J Ophthal, 2004;137:615-624) and prevents gall stone formation (Gut 1992;33(8):1113-7). Regular aspirin use was associated with a reduced risk of Parkinson Disease (Arch Neurol, 2003;60:1059-1064).
Cancer is believed by researchers to be caused by prolonged inflammation. Colorectal cancer represents the third most common type of cancer in both sexes (after lung and breast cancer) and is the second leading cause of cancer-related deaths in the United States. More than 80% of colorectal cancers arise from adenomatous polyps. Between 1-10% of these polyps will progress to cancer in 5-10 years. 30-50% of Americans older than age 50 will develop polyps. Regular use of low-dose aspirin for 5 years was associated with significant reductions in colorectal cancers (Lancet 2010;376:1741). Deaths due to esophageal, pancreatic, brain and lung cancer were reduced with low-dose aspirin (Lancet, 2011;377:31-41). Aspirin use was associated with decreased risk of breast cancer death after diagnosis of breast cancer (J Clin Oncol, 2010;28(9):1467-1472). Regular aspirin users were 40% less likely to have Hodgkin’s disease (J Natl Can Inst 2004;96:305-315). Regular aspirin use is associated with a lower incidence of prostate cancer (Mayo Clin Proc 2002;77:217-225). Aspirin use is associated with a 28% reduction of breast cancer (JAMA 2004;291(20):2433-2489). Aspirin use reduced esophageal cancer by 43%, esophageal adenocarcinoma by 33% and esophageal squamous cell carcinoma by 42% (Gastroenterology 2003;124:37-56, 246-248).

Cholesterol itself is not the cause of atherosclerosis, but the oxidation of fats during food preparation triggers the inflammation that leads to atherosclerosis. Oxidized cholesterol from a single meal persists in the blood for over three days. High-fat meals increase plasma triglycerides and have an immediate prothrombotic effect that may contribute to acute clot formation resulting in a heart attack or stroke (Arterioscler Thromb Vasc Biol 1997;17). Diabetic patients on aspirin therapy showed decreases in hepatic glucose production (22%), fasting plasma glucose (24%), fatty acids (50%) and triglycerides (48%) and a 19% increase in peripheral glucose disposal (J Clin Invest 2002;109:1321-1326). Breast cancer increased 74% in women who ate flame-broiled foods more than twice a month, but the heterocyclic amines (HCAs) believed responsible for cancer were neutralized with aspirin. Perhaps aspirin should become the new after dinner mint?

**Aspirin Problems**

The annual incidence of aspirin-induced ulcer complications was 0.8% in patients with no risk factors, but increases with; advanced age, history of previous peptic ulcer, steroid use, anticoagulant use, high doses of aspirin, *Helicobacter pylori* infection and taking two or more NSAIDs (NEJM 1999;340(24):1888-1899. Over 60% of persons with GI bleeding are the result of an *H pylori* infection. Treat the infection, and prevent the bleeding. Low-dose aspirin (81mg) has less incidence of ulcer complication, or perhaps no risk at all if the tablet dissolves in the mouth.

Aspirin inactivates the platelets to reduce blood clotting which prevents heart attacks or strokes. In a study comparing coated versus uncoated aspirin, 65% of patients taking coated aspirin – no matter what the strength – had no reduced clotting, while 75% of patients taking uncoated aspirin had reduced clotting (Stroke, 2004;35:175-178). About half the patients who have a heart attack or stroke are taking aspirin at the time, and has been called “aspirin resistance” when in fact this should be labeled as “treatment failure” either because the dose is too low, the coating never
opens up to release the aspirin, or NSAIDs, such as ibuprofen and naproxen compete with aspirin-binding sites on platelets and interfere with the aspirin response

A new study reported the incidence of small bowel complications induced by enteric coated low-dose (100mg) aspirin with and without a proton pump inhibitor (rebamipide) (World J of Gastroenterology, 2011;17(2):226-230). After two weeks, capsule endoscopy, showed a decrease in small bowel blood flow, and increased small bowel inflammation and injury. The proton pump inhibitor is useful for upper GI tract protection, but was not effective for the lower GI tract because of a lack of acid secretion. Coated low-dose aspirin avoids mucosal injury to the stomach, which may cause dyspepsia or GI bleeding, but appears to cause injury to the small intestine, where the absorption of nutrients occurs. The long term effect of coated aspirin or other NSAIDs may have a more significant deleterious effect.

The safer form of low-dose aspirin is in the form of an orally disintegrating tablet (ODT). The oral mucosa offers several advantages; it is well supplied with both vascular and lymphatic drainage, bypasses metabolism in the liver, avoids GI side effects, and is rapidly absorbed into the bloodstream. A recent study (International J of Medical and Clinical Research, 2011;2(2):72-77) demonstrated that Fasprin® a low-dose (81mg) aspirin that dissolves in the mouth was absorbed by the blood stream in 5 minutes. Fasprin® showed a 78% bioavailability (the amount of aspirin available) compared to 40-50% of an ingested aspirin tablet. About 40% of the population have difficulty swallowing tablets, making Fasprin® an easier choice.

**Conclusion**

Aspirin is less costly and more effective for preventing coronary heart disease (CHD) events in middle-aged men whose 10-year risk for CHD is 7.5% or higher (Ann Intern Med 2006;144:326-336). The benefits of statins begin to appear only 1 year or more after initiation of therapy, in contrast, aspirin has an immediate antiplatelet effect (Arch Intern Med 2004;164:40-44).

Aspirin is more underused than statins despite its more favorable cost-effectiveness. Statins are newer and more intensely advertised than aspirin, which may partly explain the preferential use of these drugs (PLos Medicine 2005;2(12):1292-1298). Considering the many advantages of aspirin, and the history of benefits for over a hundred years, this Golden Pill should be at the top of the list for maintaining optimal health.

Print out this article but before starting any aspirin therapy consult your physician or healthcare provider.

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