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## NEWS BRIEFS from the Aspirin Foundation

### Daily aspirin may prevent skin and ovarian skin cancers

Taking aspirin long-term may reduce your risk of cancers of the skin and ovary, according to two new studies.

#### **Skin cancer**

The first, from Australia (J Am Acad Dermatol 2005;53:966-72) compared 86 people with skin cancer – specifically ‘squamous cell’ cancer (one of the three common types of skin cancer) - and 187 ‘controls’ (similar in age and background) without cancer. Their past use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) (such as ibuprofen, naproxen or indomethacin) were compared. Fifty-nine per cent had preferred aspirin as their NSAID.

The longer and the more often the study subjects had taken aspirin, the less likely they were to develop squamous cell cancer. The people with skin cancers were much less likely than the controls to have used NSAIDs at any dose on 8 or more occasions a week for a year. They were also less likely to have taken 200mg of aspirin at least twice a week for 5 years. ‘Controls’ (ie non-cancer patients) who used NSAIDs regularly had half the numbers of actinic keratoses (sun-induced skin changes predisposing to squamous cell cancer) than controls who used no NSAIDs. This strongly suggests that the NSAIDs may prevent the early changes leading eventually to skin cancer.

#### **Ovarian cancer**

The second study, from America, compared the long-term use of painkillers before onset of ovarian cancer in 586 women with their use in 627 women without cancer (reference *Epidemiology* 2006;17:104-7). Women who had taken any NSAIDs (non-steroidal anti-

inflammatory drugs such as aspirin, ibuprofen, naproxen or indomethacin), even if they did so relatively infrequently and in small doses, had fewer cases, proportionately, of ovarian cancer than women who had taken no NSAIDs. Their risk was reduced by between 8 and 44 per cent, the best estimate of protection being 28 per cent. Specifically, any use of aspirin, no matter how small and how infrequently, was linked to a reduction of ovarian cancer risk of 37 per cent, with the range of possible change in ovarian cancer cases being between a reduction of 61 per cent and a tiny rise of 0.02 per cent. When the women had taken aspirin more often and for longer, (at least three times a month for three years or more) the risk of ovarian cancer was substantially lowered – by 50 per cent, the margins being between 16 and 70 percent. However, the trend to higher protection against cancer from more frequent and longer use of aspirin is strong.

### Taking ‘antiplatelet’ drugs beforehand makes a first stroke less severe initially, and leads to a better long-term recovery, than not taking them

American neurologists report that antiplatelet treatment reduces the severity of a first stroke and leads to better improvement in the patients’ physical and mental condition by the time they leave hospital (*Neurology* 2006;66:319-23).

Platelets, the smallest of the solid components (the others are the red and white blood cells) in the blood, are crucial to blood clotting. They initiate clotting in arteries by sticking together, forming ‘clumps’ in the circulation, and by sticking to artery walls, forming the focal point for the start of a blood clot, or ‘thrombosis’.

Thrombosis in an artery in the brain is the main cause (the other is bleeding from a blood vessel) of stroke. A stroke arising from a platelet-initiated thrombosis is described as 'ischaemic', because it prevents the blood (Latin name 'haem') from circulating beyond the point of blockage.

Antiplatelet drugs prevent this happening by reducing platelet 'stickiness', preventing them from clumping and from sticking to the artery walls. Thromboses do not form, and the impending stroke is prevented. Aspirin is the leading classical antiplatelet agent.

The American neurologists compared 92 patients admitted with acute ischaemic stroke who had been taking an antiplatelet agent with 92 similar patients who had not taken any drugs beforehand. Of those who had taken a regular NSAID beforehand, 74 percent had taken aspirin alone, and 18 percent had taken it along with other antiplatelet agents.

The research team used the National Institutes of Health (NIH) Stroke Scale, to measure the severity of each stroke within a day of the event. This is an internationally recognised and validated scale. The average score in those taking an antiplatelet agent (4.8) was significantly lower than in those who had not had an NSAID (8.0), but only when it was a first stroke or transient ischaemic attack (a temporary vascular event in the brain). There was no difference between the two groups of patients who had had previous strokes. However, antiplatelet treatment doubled the odds of a good outcome at discharge, based on tests of physical and mental function and deficits. No other drug treatment, including taking more than one antiplatelet agent or the anticoagulant warfarin, lessened the severity of strokes more than did simply taking aspirin alone.

This difference between the effect of previous antiplatelet therapy in patients with and without a history of stroke or transient ischaemic attack has not been reported before. The authors speculate that the brain may adapt in some way to the protective effect after a first event. They note that too few patients at increased risk of a first stroke are prescribed antiplatelet treatment such as aspirin. People at risk of a first stroke include people with high blood pressure, transient ischaemic attacks, diabetes, particularly when they are also smokers.

## Is an 'epidemic of fear' stopping low-dose aspirin use?

An epidemic of fear is discouraging people at increased risk of cardiovascular events from taking low-dose aspirin, according to Professor James F Fries, Professor of Medicine at Stanford University.

Professor Fries, author of important research papers on the stomach and gut of NSAIDs (e.g. *Arthritis Rheum* 2004;50:2433-40), says that misplaced concern about the effects of aspirin on the stomach may deter people from taking low-dose aspirin to prevent first and subsequent heart attacks. These fears arose in the days when aspirin was used in high doses (4.8 grams a day) in the long-term treatment of rheumatoid arthritis. The dose needed to prevent 'heart events' is tiny in comparison, at 75 milligrams a day.

He also points out that people taking low-dose aspirin can also take aspirin as an analgesic, saying in his experience the appropriate dose for acute pain is 1.2 g/day (one standard aspirin three times a day).

## Gender differences in aspirin's protective effect

Aspirin helps to prevent first heart attacks and strokes in both men and women, though in apparently different ways, according to a new analysis involving over 95,000 people. The report's authors do not recommend changes to current guidelines, advising instead that aspirin use depends on the balance in each person of possible benefit and harm.

The Women's Health Study showed that low-dose aspirin reduces the risk of stroke but not heart attack in women with no previous known heart or circulation disorders (cardiovascular disease). This was inconsistent with US guidelines at the time, which recommended the use of low-dose aspirin as primary prevention in women whose 10-year coronary risk was greater than 20%. US investigators have tried to resolve this contradiction by analysing the results for the two sexes separately in each primary prevention study with aspirin, then adding them together in a 'meta-analysis' (*J Am Med Assoc* 2006;295:306-13).

They identified six randomised placebo-controlled trials involving 51,342 women and 44,114 men (see Table). For women, low-dose aspirin was linked to a significant fall in the risks of major cardiovascular events and ischaemic stroke but not in myocardial infarction. Men taking aspirin had significantly fewer major cardiovascular events and myocardial infarctions but more haemorrhagic (bleeding) strokes. Aspirin did not reduce all-cause mortality in men or women and it increased the risk of a major bleeding episode by about 70 percent in both men and women. However, the actual numbers of such ill-effects were very low, being 7.6 per thousand on aspirin and 4.7 per thousand on placebo.

**Table. Summary of US meta-analysis of low-dose aspirin in men and women**

	Women	Men
Dose	100 mg on alternate days or 75 - 100 mg/day	325 mg on alternate days or 75 - 500 mg/day
	<b>odds ratios (CI<sub>95%</sub>)</b>	
major cardiovascular events	0.88 (0.79 - 0.99)	0.86 (0.78 - 0.94)
myocardial infarction	1.01 (0.84 - 1.21)	0.68 (0.54 - 0.86)
ischaemic stroke	0.76 (0.63 - 0.93)	1.00 (0.72 - 1.41)
haemorrhagic stroke	1.07 (0.42 - 2.69)	1.69 (1.04 - 2.73)
cardiovascular mortality	0.90 (.064 - 1.28)	0.99 (0.86 - 1.14)
all-cause mortality	0.94 (0.74 - 1.19)	0.93 (0.85 - 1.03)
major bleeding episodes	1.68 (1.13 - 2.52)	1.72 (1.35 - 2.20)

\*CI means confidence limits, a statistical assessment of the highest and lowest limits that could be inferred from the results. A figure below 1 denotes protection, and above 1 a higher risk. So 0.63 means a 37 percent reduction in risk and 1.07 a 7 per cent rise in risk.

The benefit of primary prevention with aspirin depends on the level of risk in the population being treated. In these primary prevention studies, the risk was relatively low and the authors estimate that 333 women and 270 men would have to be treated for a mean of 6.4 years to prevent one cardiovascular event. On the other hand, 400 women and 303 men

would have to be treated for the same period to cause one major bleeding episode.

Why should there be such differences between women and men? They may lie in differences between the sexes in the way they deal with (absorb, distribute, metabolise and excrete) the drugs; or in reduced drug effects in women. Stroke is relatively more common and myocardial infarction relatively less common in women than men; and aspirin resistance may be more common in women. The difference in dose was not believed to be important.

### Take your aspirin in the evening

If you wish to make the most of your aspirin treatment for preventing heart attacks and strokes, take it in the evening, not long before going to bed. That's the message of researchers at the University of Vigo in Spain, who found that taking aspirin before bed markedly reduces blood pressure. This may help to prevent strokes in the early hours before morning, when the blood pressure is known to rise.

### Aspirin will loom large in World Cup shindig

A giant aspirin weighing 25 tonnes has been erected in Berlin as part of an exhibition designed to show visitors to this year's World Cup football tournament how Germany has helped to make the world a better place. The metal aspirin, nearly 10m in diameter, fronts the "medical milestones" section of Berlin's new, government-funded outdoor display called Walk of Ideas. Aspirin was first produced by the German company Bayer in 1897.

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