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NEWS BRIEFS from the Aspirin Foundation

Aspirin Foundation conference on aspirin and cancer

The effectiveness and tolerability of aspirin in reducing the risk of cardiovascular disease is well established, but in recent years it has become clear that it may also lower the risk of developing certain cancers. Epidemiological studies show that aspirin is associated with a reduced risk of colorectal cancer and also possibly tumours of the breast, ovary, oesophagus and stomach. These findings are now being tested in prospective randomised trials.

The Aspirin Foundation therefore convened a conference at St Bartholomew's Hospital, London, to review the evidence on aspirin and cancer risk. Chaired by Professor Gordon McVie, former Director-General of Cancer Research UK, the conference also discussed possible mechanisms of action and policy initiatives that could promote wider use of aspirin.

Dr Richard Sullivan, Head of Clinical Programmes at Cancer Research UK, described the conference as a key opportunity to review progress in this exciting area. "Although individuals can reduce their risk of cancer by not smoking, controlling their weight and eating a balanced diet," he said, "vulnerability to the disease linked with ageing is beyond our control. Chemoprevention strategies may prove to be a very important tool in preventing cancer, and a number of studies have demonstrated aspirin's potential utility in preventing a range of cancers."

Full proceedings of the conference are available online at :-

www.aspirin-foundation.com

Aspirin - a new weapon against bacteria?

Aspirin and its active metabolite salicylic

acid could prove to be useful weapons in the war against bacteria.

Bacterial resistance to antibiotics is increasingly common, particularly among strains of *Staphylococcus aureus*. Some types of this common bacterium, known as methicillin-resistance staph aureus (MRSA), are resistant to virtually all antibiotics. *S aureus* causes serious infections such as endocarditis, which is becoming more frequent, and resistant strains are now spreading from hospitals into the community.

It has been known for some time that aspirin and salicylic acid can reduce the virulence of *S aureus*, lowering its ability to cause disease. Now, scientists in the United States have shown that salicylic acid exerts its effects at a fundamental level of bacterial development (*J Clin Invest* 2003;112:222-33). Using in vitro techniques and an experimental model of endocarditis, they found that salicylic acid inhibits gene activity in *S aureus* and down regulates the production of virulence factors that are essential for bacterial replication in the host tissues.

Aspirin and salicylic acid do not increase the bactericidal activity of antibiotics - instead, they reduce the ability of *S aureus* to initiate and spread infection. Provided a favourable safety profile can be established, the authors of the latest study conclude, aspirin may have potential as an adjunctive agent in treating serious staphylococcal infections in hospital and the community.

Future assured for 'fascinating' aspirin

Aspirin is unlikely to be supplanted as an inexpensive and effective agent for preventing thrombotic events and there is still more to learn about its effects, according to a recent editorial in the *British*

Medical Journal (2003;327:572-3).

Author Rod Flower, Professor of Biochemical Pharmacology at London's William Harvey Research Institute, notes recent epidemiological evidence showing that aspirin is associated with a reduced risk of several cancers. It has been suggested, he adds, that the link between diet and preventing colorectal cancer could be explained by the salicylic acid content of vegetable foodstuffs (salicylic acid is the active metabolite of aspirin). The other exciting observational finding is that long-term aspirin use is associated with a reduced risk of Alzheimer's disease and other forms of dementia.

Two important questions are still to be answered. First, the minimum effective dose of aspirin required to reduce the risk of cancer or Alzheimer's disease is not known. Second, it will be difficult to determine the balance of risk and benefit of taking aspirin to prevent these conditions because of the long duration and number of participants needed to produce statistically unambiguous results.

Nevertheless, aspirin's future is assured. It is by far the least expensive NSAID to be associated with these health benefits. Furthermore, research continues to develop better tolerated formulations and explore new mechanisms of action. For example, both efficacy and safety may be improved by modifying the molecule to include a functional group that releases nitric oxide; and a third form of cyclo-oxygenase has been discovered in the heart and central nervous system that is also inhibited by aspirin, providing yet another twist to the aspirin story.

Leukaemia risk halved in aspirin users

The risk of developing leukaemia among women taking aspirin regularly is less than half that reported by non-users, a new analysis of the Iowa Women's Health Study (IWHS) database shows (*Cancer Epidemiol Biomarkers Prev* 2003;12:534-7).

The study examined the incidence of leukaemia between 1993 and 2000 among 28,224 women participating in IWHS. Baseline use of aspirin and other NSAIDs was categorised by the number of times the

drug was taken per week (none, <1 - 1, 2 - 5 or 6 or more).

The relative risk of leukaemia among women taking aspirin at least twice weekly compared with those reporting no aspirin use was 0.45 (CI_{95%} 0.27, 0.75). Subgroup analysis revealed no difference by type of leukaemia (chronic myeloid or acute myelogenous) and adjustment for other risk factors did not alter the result. By contrast, there was non-significant increase in risk among women taking other NSAIDs (RR 1.31, CI_{95%} 0.77, 2.22).

This is the first study to find that aspirin is associated with a reduced risk of leukaemia. The authors are unable to explain the absence of benefit associated with other NSAIDs and they have called for further studies to confirm their findings.

Update on primary prevention with aspirin

Current evidence now strongly supports prescribing aspirin as a primary preventive measure to reduce coronary events in people at increased risk, say US analysts (*Arch Intern Med* 2003;163:2006-10). Low-dose aspirin is currently recommended for secondary prevention but not, as yet, for primary prevention.

The new evidence comes from an updated meta-analysis of major clinical trials of aspirin to prevent myocardial infarction (MI) in people at increased risk (e.g. due to coronary heart disease) but who have not yet had an MI. They carried out a meta-analysis of five randomised studies involving a total of 55,580 people ranging in age from 40 to over 80 years. The average duration of follow-up was 3.6 - 6 years and the dose of aspirin ranged from 75 - 500 mg/day.

Compared with placebo, aspirin was associated with a 32% reduction in the risk of myocardial infarction (relative risk 0.68; CI_{95%} 0.59, 0.79) and a 15% reduction in the risk of any important vascular event (vascular death, nonfatal myocardial infarction and nonfatal stroke combined) (relative risk 0.85; CI_{95%} 0.79, 0.93); both reductions were statistically significant. In women, aspirin reduced the risk of first MI by an estimated 22% [*Note to editors: CI_{95%} not reported*]. Changes in the risk of

nonfatal stroke and types of stroke were not statistically significant and the possible effects of different doses was not investigated.

These benefits are comparable with the risk reductions observed with aspirin when it is prescribed as secondary prevention (i.e. in people who have had an MI already). The analysts conclude that their evidence supports aspirin as primary prevention in people whose risk of a first coronary event is at least 10 percent over 10 years. What remains unclear, they admit, is how to identify the people at risk.

Evidence 'insufficient' for advice on taking ibuprofen with aspirin

There is still insufficient evidence to formulate definitive advice about the use of ibuprofen by people taking low-dose aspirin, according to a *BMJ* editorial (2003;327:1298-9). The comment follows publication of another observational study showing that prescribed ibuprofen is not associated with an increased risk of myocardial infarction among older people taking aspirin prophylaxis (*Br Med J* 2003;327:1322-4).

The new study was carried out at Yale University in the United States. Investigators used a Medicare database to identify 66,739 patients aged 65 or older who had been prescribed low-dose aspirin alone, or with ibuprofen (844 patients) or another NSAID (2,733 patients), when they were discharged from hospital following a myocardial infarction. They then compared the number of patients in each group who had died during the following year.

Overall, 17.5% of patients prescribed only aspirin, 14% of those prescribed aspirin and ibuprofen, and 15.8% of those prescribed aspirin and another NSAID, died within a year. After adjustment for risk factors such as medical history, there was no statistically significant difference between the groups in the risk of death (hazard ratio for ibuprofen plus aspirin vs. aspirin alone 0.84; CI_{95%} 0.70, 1.01).

The *BMJ* commentary notes that two other observational studies have reported an increased risk among people taking both aspirin and regular (but not intermittent) ibuprofen, but points out that both suffer from a small sample size and other

methodological weaknesses. The latest study also has its problems - for example, it did not include use of over-the-counter drugs. With these misgivings, the authors say it is not yet possible to make a definitive recommendation about the use of ibuprofen by people taking prophylactic aspirin. Until firm evidence becomes available, they conclude, efficacy and the risk of bleeding should determine the choice of analgesic and anti-inflammatory medication.

Welsh Aspirin Group (WAG)

The Welsh Aspirin Group has recently been set up to bring together individuals with an interest in aspirin and to review the evidence and initiate discussions on the further promotion of aspirin prophylaxis in the community.

The Group are planning their first public meeting in the University Conference Centre, Penylan, Cardiff on 6th May 2004 – the conference title will be, 'The Public Health Potential of Aspirin in Wales' and will be chaired by Dame Dierdre Hine. Topics for discussion will include; evidence on aspirin prophylaxis in vascular disease; Alzheimer's disease and cancer; the current savings from aspirin prophylaxis and the possible further savings if aspirin was more actively promoted. Their major aim will be to stimulate discussion on the further promotion of aspirin and its possible future role in cancer prevention.

WAG plans to issue invitations widely to GPs and hospital physicians and members of the Welsh Assembly Government and public health practitioners and others in authority within the Local Health Boards throughout Wales.

If you would like more information on the Cardiff meeting please contact Peter Elwood on: pelwood@doctors.org.uk or Gareth Morgan on: Gareth.Morgan@nphs.wales.nhs.uk

Further information from:
G N Henderson, Executive Director, Aspirin Foundation
Tel: +(0)1305 871055
Fax: +(0)1305 871490 Email: aspirin@healthcom.eu.com
Website: www.aspirin-foundation.com