Aspirin

a) Aspirin is a derivative of salicylic acid and was first marketed over 100 years ago. It is the forerunner of all of the NSAIDs that we know today and is still one of the world's most popular analgesic/antipyretics. Depending on the dose employed it can be used to reduce the risk of heart attack or stroke, to relieve pain and fever and, at higher doses, to relieve inflammation. Aspirin is available as solid or soluble tablets, in enteric-coated form or in slow release form. Studies have shown that soluble tablets allow very rapid plasma access of aspirin / *AQUAPRIN* solubilized aspirin formulations for instance enters the bloodstream within 5 minutes of dosing.

Foreword: *"PDR" Physician's Desk Reference* (Section: Miles Labs, Inc.) states:

"...Direct visualization with gastro camera shows that, as contrasted with acetylsalicylic acid (aspirin), the acetylsalicylic ion delivered IN SOLUTION [which is the case with "Aquaprin"), gastric damage and acute gastric mucosal lesions are NOT seen after administration."

b) The non-steroidal, anti-inflammatory, drug therapy arena abounds in household-name products ranging from Bayer's, Bufferin, Tylenol and Excedrin, to Anacin, Aleve and many others -- with total sales exceeding $5-billion annually. Regular aspirin, however, is still the most effective, economical and safe pain reliever available anywhere -- the "Gold Standard" of analgesia.

Effective in treating the common headache, and other aches and pains, aspirin is the only product proven to relieve the inflammation of arthritis and rheumatism, the cause of the severe pain of these diseases. For this same reason, aspirin has long been the drug of choice in combating inflammatory pain from exertion and sports activities;

Pain

Regardless of its origin, pain is the number one cause of disability in America and it costs us a great deal.

"Pain in itself probably costs the American population upwards of $120 billion each year," says Marc Hahn, DO, president of the American Academy of Pain Medicine. "That's not only in its medical treatment, but in its impact on society, in missed days, and decreased productivity at work."

Fifty million people in America are either partially or completely disabled by pain, says Hahn, and according to a recent survey of 1,000 people conducted by the Partners for Understanding Pain, one out of three are affected by it.

While many people might assume that chronic pain is a bigger problem for the elderly, the Partners for Understanding Pain survey found that 80% of those with chronic pain are between 24 and 64. says Penney Cowan, founder and executive director of the American Chronic Pain Association. Cowan -- whose organization, the American Chronic Pain Association, spearheaded the survey -- reports that sports injuries are among the most frequent causes of chronic pain for people in their 20s.

The good news about pain, Cowan and Hahn believe, is that attitudes are changing and doctors now better understand how to treat pain. The American Academy of Pain Medicine is also currently working on a medical education project that will help doctors and medical students learn more about diagnosing and easing pain.

Published Dec. 30, 2002. SOURCES: Penney Cowan, founder and executive director, American Chronic Pain Association • Marc Hahn, DO, president, American Academy of Pain Medicine • American Chronic Pain Association • American Academy of Pain Medicine • American Pain Foundation.

Emergency Use

There are two situations in which aspirin can be life saving: The first is "early" aspirin, when the drug is given on first contact with a patient with chest pain, who may be having a coronary thrombosis. An extension of this is "immediate" aspirin, i.e., the subject himself takes the drug as soon as the sudden onset of severe chest pain is experienced.

Patients who are judged, for any reason, to be at high risk of experiencing a thrombotic event should be instructed to chew and swallow an ordinary solubilized aspirin tablet, with water, at all times [far better would be ***Quik-Prin*** immediately when severe chest pain is experienced.

It would seem reasonable to give this advice to all patients at increased vascular risk, including those who take a small daily prophylactic dose of aspirin. The development of severe chest pain, despite daily exposure to aspirin, indicates that some "sensitive" platelets must have entered the circulation and a coronary thrombus may be forming. *Thus, an extra dose of 850 mg aspirin could well be life saving.*

Recommendations for aspirin use [PARA]* Patients who have had an MI, stroke or transient ischemic attack - give 75-100mg aspirin daily, indefinitely [PARA]* Patients with unstable angina - give 75-100mg aspirin daily, indefinitely [PARA]* Patients with stable angina (these patients are at high risk of a thrombotic event) - give 75-100mg aspirin daily, indefinitely [PARA]* Patients with intermittent claudication (these patients are at high risk of a thrombotic event) - give 75-100mg aspirin daily, indefinitely [PARA]* Patients with deep vein thrombosis - give 75-100mg aspirin daily until the condition is well stabilized. (Subjects likely to expose themselves to a situation where risk of DVT is high should be advised to take a single dose of 300mg).

Patients at high-risk of a cardiovascular event - low-dose aspirin should be considered in addition to whatever other drugs are judged appropriate.

In addition, patients at risk of a thrombotic event should be advised to carry a tablet of solubilized aspirin to be taken if sudden chest pain occurs

[Professor Elwood is honorary professor at the department of epidemiology and community medicine, University of Wales College of medicine, and Professor Stillings is honorary professor at the department of bioorganic chemistry, University of Hull, U.K.] ***Information about aspirin may be found on the web site for the European Aspirin Foundation (www.aspirin-foundation.com).***

The Pharmaceutical Journal, Vol 266 No 7138; pp 315-318; March 10, 2001

By Peter Elwood, M.D., F.R.C.PRCP, and Michael Stillings, Ph.D.

[Professor Elwood is honorary professor at The Department Of Epidemiology & Community Medicine, University of Wales College Of Medicine, and Professor Stillings is honorary professor at the Department Of Bio-organic Chemistry, University of Hull]

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Simple Headache

(Whinfield Surgery, Darlington, Durham, U.K. {whinfield.co.uk)

Headache is exceptionally common as a symptom. Very few of us escape them completely. There are, unfortunately serious causes but these are relatively uncommon.

Common causes are:

- Tension headaches. Stress, anxiety etc. cause muscle spasm in the scalp muscles, which in turn can cause headache "like a tight band around the head". If simple painkillers alone are insufficient then relaxation techniques can help.

- Musculo-skeletal headaches often come from the spine in the neck. They tend to cause headaches at the back of the head and around the side.

- Eyestrain. If you need glasses or if your glasses need updating then this puts a strain on the eye muscles and tends to give you a headache at the front of the head - especially after reading, watching TV or looking at the blackboard for any length of time.

- Temperatures and infections. These often cause quite bad headaches. Obviously there is always a worry about meningitis but with a simple headache there is very little sensitivity to the light and the neck can be fully flexed forward - if there is any doubt ring to speak to the duty doctor for advice.

- Sinus infections can cause pain around the face and above the eyes. Inhaling steam and simple painkillers can be very helpful in this situation but antibiotics may be required.

- Migraine.

Migraines

30 million Americans a year suffer from migraines. Indeed, 8-10% of all men, and 18-20% of all women will experience migraines at some point in their lives. Migraines cost the nation $5-billion in lost productivity, with 270 lost workdays per 1,000 workers.

Regardless of its origin, pain is the number one cause of disability in America and it costs us a great deal. "Pain in itself probably costs the American population upwards of $120-billion each year," says Marc Hahn, DO, president of the American Academy of Pain Medicine. "That's not only in its medical treatment, but in its impact on society, in missed days, and decreased productivity at work."

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Published Dec. 30, 2002. SOURCES: Penney Cowan, Founder & Executive Director, American Chronic Pain Association • Marc Hahn, DO, President, American Academy of Pain Medicine • American Chronic Pain Association • American Academy of Pain Medicine • American Pain Foundation; WEBMDHEALTH http://my.webmd.com/content/Article/57/66051.htm?pagenumber=3]

Active Peptic Ulceration

Gastric upset

Aspirin was developed from salicylic acid primarily to reduce the associated gastric side effects. However, some damage to the gastric mucosae does occur with aspirin use. There are two main mechanisms that cause this damage:

- Local/systemic effects, due to aspirin inhibiting the production of gastro-protective prostaglandins

- Local irritant effects, due to the direct contact of aspirin particles with the gastric mucosae, causing local damage

While the damage resulting from the inhibition of gastro-protective prostaglandins is largely unavoidable, the local irritant effect can be minimized by reducing the physical size of aspirin particles in contact with the gastric mucosae and by ensuring that the aspirin is quickly and effectively absorbed.

Solubilized aspirin was formulated with these aims in mind, and have been shown to cause less local damage to the gastric mucosae than solid aspirin in several studies.

One investigation (Jaiswal et al IUPHAR 9th International Congress of Pharmacology, 1984) compared the effects of solubilized aspirin and solid aspirin on the gastric mucosae. This randomized, double blind, crossover study in 30 volunteers involved visual inspection by gastroscopy at various time intervals after drug administration. The results showed that the mean gastric damage score for solid aspirin was significantly higher than that for solubilized aspirin .

This study clearly shows that solubilized aspirin causes significantly less gastric damage than that which is seen with solid aspirin formulations.

Summary: Solubilized Aspirin: Gastric Tolerance

Aspirin has been shown to cause local damage to the gastric mucosae by two actions:

inhibition of gastro-protective prostaglandins
direct contact of particles of solid aspirin

Since the aspirin in **AQUAPRIN** is already dissolved, only solubilized aspirin is present in the stomach, and this is quickly absorbed, so...

- Solubilized aspirin is in contact with the gastric mucosae for only a short time, thus limiting the local damage caused.

- Whereas in solid [tablet] form, aspirin is present in the stomach in large particles for a longer time, which causes significantly more local damage.

- Solubilized aspirin formulations cause significantly less gastric damage than ordinary solid aspirin tablets

"...Direct visualization with gastrocamera shows that, as contrasted with acetylsalicylic acid (aspirin), the acetylsalicylic ion delivered IN SOLUTION [which is the case with **AQUAPRIN,**

QUIK-PRIN*], gastric damage and acute gastric mucosae lesions are NOT seen after administration."* [*"PDR" Physician's Desk Reference* (Section: Miles Labs, Inc.]

Aspirin has been shown to cause local damage to the gastric mucosae by two actions:

-- Inhibition of gastro-protective prostaglandins

-- Direct contact of particles of solid aspirin

Since the aspirin in **AQUAPRIN** is already dissolved, only solubilized aspirin is present in the stomach, and this is quickly absorbed

-- The aspirin from **AQUAPRIN** is in contact with the gastric mucosae for an extremely short time, thus virtually eliminating the local damage caused

-- Whereas, the aspirin from solid aspirin is present in the stomach in large particles for a longer time, which causes significantly more local damage.

-- **AQUAPRIN** solubilized aspirin derivative causes significantly less gastric damage than ordinary solid aspirin tablets.

Gastric Upset -- Discussion

Aspirin was developed from salicylic acid primarily to reduce the associated gastric side effects. However, some damage to the gastric mucosae does occur with aspirin use. There are two main mechanisms that cause this damage:
local/systemic effects, due to aspirin inhibiting the production of gastro-protective prostaglandins; local irritant effects, due to the direct contact of aspirin particles with the gastric mucosae, causing local damage.

While the damage resulting from the inhibition of gastro-protective prostaglandins is largely unavoidable, the local irritant effect can be minimized by reducing the physical size of aspirin particles in contact with the gastric mucosae and by ensuring that the aspirin is quickly and effectively absorbed.

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Arthritis / Anti-inflammation Dosage Threshold

Beside the gastro toxicity reported above, administering daily doses exceeding 5,000 mg requires swallowing over 10 tablets, a problem for the millions of elderly arthritics (and many others who prefer liquid medication) suffering from dysphasia (swallowing disorders).

Such large daily dosages of aspirin successfully control inflammation in over 70% of arthritics. When dosages are reduced by half, i.e. 2,500 mg, the success rate drops dramatically, to only about 10%.

There is thus a need for a new form of aspirin delivery, which would render administration of large, anti-inflammatory dosages of aspirin safe and well tolerated.

AQUAPRIN addresses this need: It is a crystalline composition readily soluble in water with formation of clear, palatable solutions. It conforms with FDA regulatory requirements, and is ready to be manufactured for drugstore shelves.

[Chart from "The Salicylates," Smith & Smith (John Wiley, 1966) to appear here:]

"This chart shows the effect of the solubility of various aspirin products on plasma salicylate levels "

Moreover, the "PDR" Physician's Desk Reference (Section: Miles, Inc.) states:

"...Direct visualization with gastrocamera shows that, as contrasted with acetylsalicylic acid (aspirin), the acetylsalicylic ion DELIVERED IN SOLUTION (which is the case with **QUELL**) gastric damage and acute gastric mucosal lesions are not seen after administration."

One investigation (Jaiswal et al IUPHAR 9th International Congress of Pharmacology, 1984) compared the effects of solubilized aspirin and solid aspirin on the gastric mucosae. This randomized, double blind, crossover study in 30 volunteers involved visual inspection by gastroscopy at various time intervals after

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Dose Effects of Aspirin on Gastric Prostaglandins and Stomach Mucosal Injury

Annals of Internal Medicine, 1 February 1994; 120: 184-189.

Makau Lee, MD, PhD; Byron Cryer, MD; and Mark Feldman, MD

Objective: To determine if a dose of aspirin exists that might inhibit thromboxane-dependent platelet function without causing gastric mucosal injury, we studied the effects of a wide range of doses of aspirin (3 mg/d to 2600 mg/d) on gastric juice prostaglandins (PGE_2 and PGF_{2a}), on serum thromboxane B_2, and on stomach mucosal injury as reflected by gastric juice hemoglobin and DNA concentrations.

Design: A randomized, placebo-controlled study.

Setting: Research laboratory at a Veterans Affairs medical center.

Participants: 16 healthy volunteers (5 men and 11 women).

Intervention: In the first part of the study, volunteers received placebo; aspirin, 324 mg/d; 1300 mg/d; or 2600 mg/d for 2 days. In the second part, volunteers received placebo; aspirin, 3 mg/d; 10 mg/d; 30 mg/d; or 81 mg/d for 8 days.

Measurements: Gastric juice PGE_2 and PGF_{2a}, hemoglobin and DNA concentrations; gastric juice volume and acidity; and serum salicylate and thromboxane B_2 concentrations.

Results: In the first part, significant and similar (approximately 50%) inhibition of gastric juice

prostaglandin output was observed with daily aspirin doses of 324 to 2600 mg. However, a significant increase in gastric juice hemoglobin output occurred only with 2600 mg/d. In the second part, significant inhibition (approximately 50%) of gastric PGE_2 output was noted at a daily aspirin dose of 30 mg. Lower aspirin doses did not reduce PGE_2 output significantly, although these doses did significantly reduce serum thromboxane B_2 in a dose-related manner.

Conclusions: Aspirin can significantly reduce serum thromboxane B_2 at doses of 3 mg/d or 10 mg/d, which are significantly below the threshold dose for significant gastric prostaglandin inhibition and acute stomach mucosal injury.

Ann Intern Med. 1994;120:184-189. *Annals of Internal Medicine* is published twice monthly and copyrighted © 1994 by the American College of Physicians.

From the University of Texas Southwestern Medical Center and the Veterans Affairs Medical Center, Dallas, Texas. For current author addresses, see end of text.

Aspirin is almost certainly the most widely used drug in the world. It is used both therapeutically (to reduce pain, inflammation, and fever) and prophylactically (to prevent thrombotic events). Although prophylactic, antithrombotic doses of aspirin are generally lower than therapeutic doses, epidemiologic studies suggest that such doses may still be associated with gastrointestinal damage (1-3).

In a long-term, placebo-controlled study evaluating aspirin for secondary prevention of myocardial infarction, a daily dose of 1000 mg increased the risk for hospitalization for gastric and duodenal ulcers by about eightfold (1). In another long-term, placebo- controlled study evaluating aspirin for stroke prevention in patients with transient ischemic attacks, the rate of hospitalization for serious gastrointestinal bleeding was increased approximately threefold with 1200 mg of aspirin per day and twofold with just 300 mg of aspirin per day (2). In another long-term study for primary prevention of cardiovascular diseases, an aspirin dose of 325 mg given

every other day was associated with a significantly greater risk for duodenal ulcer when compared with placebo (3).

Few experimental data exist on the risk for gastroduodenal mucosal injury as a function of aspirin dose, and it is not known whether any clinically used dose of aspirin is free of risk for gastroduodenal mucosal damage. In a recent endoscopic study of patients with coronary artery disease, most of whom were receiving only 100 mg of aspirin per day, the prevalence of gastric erosions was higher than the prevalence of erosions in a historical control group (4).

The literature contains little information on the relation between aspirin dosage and suppression of gastro duodenal mucosal prostaglandin synthesis in humans. Because suppression of gastro duodenal mucosal prostaglandin synthesis appears to be one of the important mechanisms for mucosal damage by aspirin (5, 6)…

Our goal was to determine the effects of a wide range of doses of aspirin (3 mg/d to 2600 mg/d) on gastric juice prostaglandins (PGE_2 and PGF_{2a}) and on stomach mucosal injury as reflected by gastric juice hemoglobin and DNA, both of which are sensitive indicators of mucosal injury (7, 8). Effects of various doses of aspirin were also related to their effects on gastric acid secretion and serum thromboxane B_2.

Discussion

We investigated the effect of a wide range of doses of aspirin on gastric prostaglandin production and on stomach mucosal injury in healthy adult volunteers. Other investigators have shown that a good correlation exists between gastric juice prostaglandin output and gastric mucosal prostaglandin generation in humans (5) and that gastric juice hemoglobin and DNA contents are sensitive indicators of stomach mucosal injury (7, 8).

In part 1 of our study, similar inhibition of gastric juice prostaglandin output was observed with daily aspirin doses ranging from 324 to 2600 mg, whereas significant stomach mucosal damage, as estimated by an increase in gastric juice hemoglobin output, occurred only with the highest aspirin dose (2600 mg/d). Our results indicate that higher

doses of aspirin may acutely damage the gastric mucosa by a prostaglandin-independent mechanism because daily aspirin doses of 324, 1300, or 2600 mg inhibited prostaglandin outputs by around 50%, yet only the last dose caused significant acute gastric mucosal injury as reflected by hemoglobin output.

Conclusions: because we have previously shown that sex has no significant effect on gastric mucosal prostaglandin concentrations (27) or on the severity of aspirin-induced acute gastric mucosal injury as documented endoscopically (9).

This work was presented in part at the 93rd and 94th annual meetings of the American Gastroenterological Association, 10 to 13 May 1992, in San Francisco, California, and 17 to 19 May 1993, in Boston, Massachusetts, and was published in abstract form (Gastroenterology. 1992; 102:A53; and 1993;104:A131).

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Drs. Cryer and Feldman: Medical Service (111), Dallas Veterans Affairs Medical Center, 4500 South Lancaster Road, Dallas, TX 75216.

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New Uses For Old Drugs Aspirin – The First 'Miracle Drug'

(By Peter Elwood, M.D., FRCP, and Michael Stillings, Ph.D.)

Aspirin has justifiably been called the first miracle drug. In this article, a summary is given of the history of aspirin and its use in cardiovascular disease. A brief account of possible new uses is also included.

Over 100 years ago, aspirin became the first drug to be made synthetically, and its marketing laid the foundation of the modern pharmaceutical industry. It is still the benchmark against which other analgesics are measured. In the mid-1970s, aspirin use entered a new phase when it was shown to reduce substantially the risk of coronary thrombosis. Overviews of more than 145 randomized, controlled trials have confirmed its value in the reduction of risk of vascular thrombosis.[PARA]The aspirin story is not over, and possible new uses to reduce cognitive decline and dementia, Alzheimer's disease, cataract and intestinal cancer are currently under investigatioCardiovascular Disease

Aspirin has a remarkable feature that the other non-steroidal anti-inflammatory drugs (NSAIDs) do not have - by virtue of its labile acetyl group, it irreversibly inhibits cyclo-oxygenase (COX), the main mediating enzyme in the synthesis of prostaglandins. It is this feature, which explains aspirin's action on platelets and, ultimately, its cardiovascular protection. Other NSAIDs also inhibit COX, but the effect declines as the drug is metabolized and excreted.

Platelet activity Al Donné, a French physiologist, seems to have been the first researcher to describe platelets, in 1842.1 however, they were largely ignored until the late 1950s when there was general agreement about their role in coronary and other thrombotic processes. [PARA] Once the relevance of platelets to thrombosis came to be generally accepted, the search for drugs

that affected platelet aggregation began. Numerous drugs were tested and, in 1967, the effect of aspirin on platelet aggregation was first shown.2

Another thrombotic condition in which aspirin has been shown to be of benefit is deep vein thrombosis. Patients recovering from surgery are at risk of deep vein thrombosis and, recently, its occasional occurrence, possibly as a result of long-distance flights, has received much media attention. Low-dose aspirin gives the same relative protection against deep vein thrombosis as it does in other conditions of vascular risk.10 [PARA] Primary prevention when assessing the risks and benefits of primary prevention, it is important to distinguish between "relative" reduction and "absolute" reduction in risk. [PARA] The relative reduction in vascular risk achieved by aspirin is around one-third. A risk reduction of one-third indicates that about 30 patients have to be treated for one year to prevent one event. Men who have recently had a stroke or an MI are at high risk, and about 10% will have a further event within the following year.

The absolute reduction depends on how "at risk" the subjects under consideration are. Trials in healthy British doctors11 and US physicians12 have confirmed that taking aspirin reduces the relative risk of suffering a vascular event in healthy subjects to the same degree as in post-MI patients. However, the absolute saving in terms of the number of events is trivial because healthy subjects are at low risk of a vascular event. The absolute risk reduction calculated in these trials showed that 500 to 1,000 healthy subjects have to be given aspirin for one year, for one event to be prevented. Although the cost of treatment would be low, the number of subjects within that group of 500 who would experience side effects is relatively large, and one or two might have a serious bleed.

Conclusions

Numerous trials have established that a small daily dose of aspirin (75 to 150mg) reduces the risk of a vascular event by about one-third. If a patient is on any treatment for cardiovascular disease (eg, a cholesterol-lowering or anti-hypertensive drug), then it could be judged clinically irresponsible if a patient at increased risk of thrombosis is not receiving aspirin.

Aspirin, used in cardiovascular prophylaxis, is undoubtedly the most thoroughly tested and the most highly cost-effective drug available.

Aspirin Cuts First Heart Attack Risk

A study by Mount Sinai Medical Center and the Miami Heart Institute shows a daily aspirin regimen reduces the risk of a first heart attack by 32 percent. An analysis of the five major randomized clinical trials done on aspirin as a preventive treatment also shows it reduces the combined risk of heart attack, stroke and vascular death by 15 percent. The study supports guidelines from the American Heart Association that aspirin should be recommended for men and women whose 10-year risks of a first coronary event are 10 percent or greater. The U.S. Preventive Services Task Force took a similar position, urging aspirin therapy for patients who have a 6 percent or greater 10-year risk of a coronary event.

Cardio-Protective Anti-Thrombotic: Analysis Supports Aspirin Use

A new study suggests aspirin's life-saving benefits outweigh its risks. The paper, published in the journal Archives of Internal Medicine, highlights the benefits of aspirin in preventing a second heart attack or stroke. Patient and physician concerns about potential gastrointestinal side effects have prevented some eligible men and women from getting aspirin's benefits, the authors said. "It is likely that confusion over the relative benefits and risks of treatment has been in part responsible for under-use of this highly effective, inexpensive therapy among the large group of patients at risk for cardiovascular disease," said pharmacologist Steven Weisman, who co-authored the study. The American College of Cardiology and the American Heart Association recommend daily aspirin therapy at doses of 75 to 325 mg be considered for patients at increased risk of a heart attack.

Study Shows Aspirin Reduces Heart Attack Risk

Aspirin reduces the risk of suffering a first heart attack by one-third, researchers have found. The investigators at Mount Sinai Medical Center and Miami Heart Institute in Chicago said their analysis of five trials evaluating aspirin shows the drug reduces the risk of a first heart attack by 32 percent and the combined risk of heart attack, stroke and vascular death by 15 percent. The findings support the American Heart Association guidelines recommending that all men and women with elevated cardiovascular risk take aspirin as a preventive measure. The U.S. Preventive Services Task Force earlier this year urged doctors to speak about aspirin therapy with patients who have a 6 percent or greater 10-year risk of a coronary malfunction. "The individual trials and their meta-analysis strongly support the recent AHA recommendation," said Dr. Charles Hennekens, co-director of cardiovascular research. "The more widespread and appropriate use of aspirin in primary prevention could avoid more than 180,000 heart attacks and many other vascular events each year."

Arteriosclerosis – Another Reason To Take A Daily Aspirin

Another discovery about the benefits of daily aspirin, according to a study in the journal Circulation, of the American Heart Association, is that it can prevent heart attacks and stroke by reducing inflammation associated with arteriosclerosis. It also stabilizes atherosclerotic plaque. University of Pennsylvania researchers say arteriosclerosis -- hardening of the arteries -- is a main cause of heart attacks and strokes, two leading causes of death. Many factors, including genetics and diet, spur the disease, which occurs as cholesterol-rich cells of the immune system accumulate inside blood vessels, causing them to narrow so blood cannot flow properly. The Penn researchers say low-dose aspirin leads to a change in the composition of the plaque, turning it from a soft foamy material to a harder material that is less likely to rupture and cause a blockage.

Low Potassium May Lead To Stroke

A study of 5,600 men and women past their 65th birthday shows those with the lowest amount of potassium in their diet -- 2.4 grams a day -- were 1.5 times more likely to suffer a stroke than were those with the highest amount -- more than 4 grams. More studies are needed to confirm the results and determine whether increasing potassium in the diet can prevent strokes, the researchers said. Studies have linked low amounts of potassium in the diet with a greater risk of death from stroke.

The new study also looked at people taking diuretics, common medications for high blood pressure, congestive heart failure and kidney disease, which can reduce the amount of water and potassium in the body. "Diuretics clearly help prevent stroke by controlling high blood pressure, but we wanted to see whether their effect on potassium levels would affect the risk of stroke," said study author Dr. Deborah Green of the Neuroscience Institute at The Queen's Medical Center in Honolulu. Of people taking diuretics, those with the lowest level of potassium in their blood were 2.5 times more likely to have a stroke than those with the highest level, the study showed. The results do not imply that diuretics increase stroke risk, Green said. "The question is whether diuretics would be even more effective with adequate potassium intake," she said.

New Guidelines For Preventing Hypertension

The National High Blood Pressure Education Program has issued new recommendations for preventing hypertension that include dietary guidelines for eating potassium-rich foods. The experts recommend a diet plentiful in fruits, vegetables and low-fat dairy products and low in saturated and total fat. The advisory also reinforces earlier recommendations to limit consumption of sodium and alcohol, reduce excess body weight and increase levels of physical activity. Published in The Journal of the American Medical Association, the report also cautions that some widely publicized approaches have unproven or uncertain effectiveness. Fish oil (omega-3 polyunsaturated fatty acids) and calcium supplements lower blood pressure only slightly in individuals with hypertension, the scientists found. In addition, the ability of herbal and botanical supplements to safely lower blood pressure is unproven, and these unregulated products can interact adversely with medications, researchers said. "The United States has made substantial gains over the past several decades in preventing high blood pressure and in detecting and controlling high blood pressure when it does develop," said Dr. Claude Lenfant, director of the National Heart, Lung and Blood Institute, which coordinates the NHBPEP. "However, Americans continue to be at high risk for hypertension and related complications. These revised recommendations can help us do better."

ARCA/MAX: Health Tips for [NL]Friday December 27, 2002

Diuretics Better For Hypertension (Need For Potassium)

Blood pressure medications called diuretics, used for decades, are less expensive and more effective than the newer hypertension medications. That's the conclusion of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial or ALLHAT clinical trial from 1994 to 2002. "The preferred drug is the diuretic for three reasons. It provides better control of hypertension; it reduces complications from hypertension -- particularly heart failure -- more effectively; and it is 10 to 20 times less expensive than the other drugs used in the trial," says Dr. Curt Furberg of Wake Forest University Baptist Medical Center, study chairman.

ALLHAT is the largest study ever to compare different types of hypertension drugs and it included more than 33,000 participants age 55 years or older at 623 clinical sites in North America. The diuretics were compared with a calcium channel blocker sold under the name Norvasc or lisinopril; an angiotensin-converting enzyme inhibitor sold under the names Prinivil and Zestril.

Low Potassium May Lead To Stroke

AQUAPRIN'S essential POTASSIUM ingredient has unexpected benefits in its own right (unlike many other formulations based on SODIUM, which is contra-indicated in many conditions):

"A study of 5,600 men and women past their 65th birthday shows those with the lowest amount of POTASSIUM in their diet -- 2.4 grams a day -- were 1.5 times more likely to suffer a stroke than were those with the highest amount -- more than 4 grams," said study author Dr. Deborah Green of the Neuroscience Institute at The Queen's Medical Center in Honolulu.

Gastric Upset, Dyspepsia, Chronic Aspirin Gastropathy

Aspirin and its relatives are thought to cause as many as 16,500 deaths a year from stomach and intestinal problems

Aspirin was developed from salicylic acid primarily to reduce the associated gastric side effects. However, some damage to the gastric mucosae does occur with aspirin use. There are two main mechanisms that cause this damage:

-- Local/systemic effects, due to aspirin inhibiting the production of gastro-protective prostaglandins;

-- Local irritant effects, due to the direct contact of aspirin particles with the gastric mucosae , causing local damage.

While the damage resulting from the inhibition of gastro-protective prostaglandins is largely unavoidable, the local irritant effect can be minimized by reducing the physical size of aspirin particles in contact with the gastric mucosae and by ensuring that the aspirin is quickly and effectively absorbed.

Reckitt Bensicker (liquid aspirin mixtures and gastric damage)

The other ingredients that go with the aspirin have to be selected with care, as it is prone to hydrolysis breaking down into acetic acid and salicylic acid (try smelling some very old tablets - they may smell of vinegar due to the release of acetic acid). This hydrolysis reaction occurs more quickly in the presence of water and so materials with low moisture content may be selected - this is why you never see an aspirin liquid mixture! The hydrolysis reaction can also be promoted by the presence of alkali materials and so effervescent agents and lubricants need to be selected carefully.

It's important to consider what happens to the tablet when the patient takes them. Early tablets were simple swallow tablets - which were swallowed whole and gradually disintegrated in the stomach. Because this led to local high concentrations of aspirin that could cause damage to the stomach lining in many patients new formulations were produced to avoid this.

(Competition) COX-2 Inhibitors Delay Bone Healing

Stanford University Medical Center research shows selective COX-2 inhibitors -- a class of medications to treat inflammatory conditions such arthritis -- interfere with healing after a bone fracture or cement-less joint implant surgery. Researchers say patients who regularly take COX-2 inhibitors should switch to a different medication following such events.

The study, which was done in rabbits, also suggests physicians should consider changing prescribing patterns since many doctors commonly prescribe anti-inflammatory drugs such as COX-2 inhibitors under the very circumstances in which they should be avoided. "It's very common. You break a bone and go to the ER. The doctor sets it in a splint and prescribes one of these anti-inflammatory drugs (including COX-2 inhibitors) for pain," said Dr. Stuart Goodman, a Stanford professor of orthopedic surgery. "We now know that could actually delay healing."

(Competition) Painkillers Can Hinder Healing

Certain popular drugs used to relieve pain can retard or even prevent the healing of bone fractures. Of primary concern are the newer non-steroidal anti-inflammatory drugs sold under the brand names Vioxx (which now has been taken off of the market), and Celebrex. When University of New Jersey researchers gave these painkillers to rats, their broken bones did not fully heal. Yet both drugs are often used to ease the pain of broken bones. For more than 20 years there have been occasional reports of impaired bone healing in patients taking this type of painkillers, an article in the latest issue of New Scientists magazine reports. The issue may have escaped attention because the older generation of these drugs, including ibuprofen and indomethacin, only appear to delay healing by a few weeks instead of blocking it, the article states. Aspirin is one of the few non-steroidal anti-inflammatories that appear to kill pain without this side effect.

(Competition) Tylenol: “Pain Killers Linked To Hypertension”

Acetaminophen and nonsteroidal anti-inflammatory drugs called NSAIDS are being linked to high blood pressure in younger women. Harvard Medical School researchers, writing in this week's Archives of Internal Medicine, expand on studies that show NSAIDs cause a small increase in blood pressure and increases the risk of hypertension but aspirin and acetaminophen do not. The Harvard team looked at the frequency of use of three classes of commonly used analgesics and the risk of hypertension among 80,020 women, ages 31 to 50, participating in the Nurses' Health Study II. After adjusting for differences in age, the use of all three classes of analgesics was associated with

(Tylenol) Clearer Liver Warning Required For Painkillers

The makers of Tylenol say they already plan to add one to the label, a day after an FDA panel has urged that warnings become mandatory. By Adam Marcus -- Experts are urging the federal government to mandate clearer and more consistent warning labels for acetaminophen, and the nation's leading maker of the pain and fever remedy has announced it is ready to do so.

Concerned that many Americans accidentally take toxic doses of acetaminophen, a Food and Drug Administration advisory panel yesterday overwhelmingly recommended that the agency force manufacturers to state boldly that misuse of the ubiquitous product can be deadly.

The panel said the risk of liver damage associated with acetaminophen, the active ingredient in Tylenol and its knockoffs, was great enough to warrant the change. Overdoses of acetaminophen, both intentional and accidental, are among the most common causes of adverse drug reactions in the world, experts said. The makers of Tylenol, the best-selling acetaminophen product, plan to add a message on the warning label saying the drug can damage the liver.

The FDA has determined that acetaminophen overdoses lead to more than 56,000 emergency room visits a year in the United States, many involving infants and young children. Of those, about a quarter are unintended, and 100 are deadly. "The fear is that people don't realize how many products contain acetaminophen," said Laura Bradbard, an FDA spokeswoman.

Those with a history of alcohol abuse or other liver trouble may suffer harm at lower amounts. Fasting, such as loss of appetite from a viral illness, also appears to be factor in overdoses and liver harm, experts said. Dr. Susan Farrell, a toxicologist at Brigham and Women's Hospital in Boston, said high doses of acetaminophen are broken down by the liver into a toxic form that can harm the organ. However, the damage is reversible if it isn't deadly. Farrell agreed with the panel that "probably there needs to be better" labeling to reflect the hazard. Dr. Anthony R. Temple, vice president of medical and regulatory science for McNeil Consumer & Specialty Pharmaceuticals, which makes Tylenol, said the company would soon change its packaging to say the medication "may cause liver damage. That makes it more specific to the type of health problems that may occur," said. In particular, the agency is looking at the risks of gastric bleeding and kidney failure linked to the compounds. Aspirin and its relatives are thought to cause as many as 16,500 deaths a year from stomach and intestinal problems.

For more on the health risks of acetaminophen, SOURCES: Laura Bradbard, spokeswoman, Food and Drug Administration, Rockville, Md.; Susan Farrell, M.D., medical toxicologist, Brigham and Women's Hospital, Boston; Anthony R. Temple, M.D., vice president of regulatory and medical sciences, McNeil Consumer & Specialty Pharmaceuticals, Philadelphia;

Arthritis/ Anti-inflammation Dosage Threshold

Beside the gastrotoxicity reported above, administering daily doses exceeding 5,000 mg requires swallowing over 10 tablets, a problem for the millions of elderly arthritics (and many others who prefer liquid medication) suffering from dysphagia (swallowing disorders).

Such large daily dosages of aspirin successfully control inflammation in over 70% of arthritics. When dosages are reduced by half, i.e. 2,500 mg, the success rate drops dramatically, to only about 10%.

Geriatric Clinical Study

(a) The antipyretic and analgesic properties of salicylates have resulted in widespread usage in herbal preparations since the time of Hippocrates in 400 B.C. and probably much earlier. Aspirin is the drug of choice and mainstay of arthritis therapy.

In small doses, 325-500 mg, aspirin relieves the minor aches and pains of arthritis, while in large daily doses of 5,000 mg and over; it is a potent anti-inflammatory agent, attacking the very cause of arthritis--inflammation.

(b) In many arthritics, aspirin causes a number of adverse-reactions: Irritation of the gastrointestinal tract, gastroduodenal bleeding, ulceration, pain, nausea and heartburn.

As mentioned, the chief drawback of regular aspirin tablets is its insolubility, that is, its inability to completely dissolve in water or in body fluid (saliva and gastric fluid). The resulting un-dissolved particles cling to and imbed themselves onto the stomach and intestinal lining in 5% to 25% of all aspirin users, causing such often severe adverse-reactions as gastritis, active peptic ulceration, heartburn, indigestion, nausea, and stomach bleeding.

While certain of these side-effects are systemic and common to all anti-inflammatory drugs, most are topical and caused by aspirin's insoluble nature: Direct gastroscopy graphically reveals the erosion, inflammation and irritation occurring just beneath undissolved aspirin particles adhering to the stomach lining. Clinical studies show that solubilized aspirin produces no maximal lesions (superficial or deep

erosions). These studies conclude with the statement that **`...We reiterate our belief that solubilized aspirin preparations should be used routinely in place of insoluble standard varieties.'**

These side effects have prevented the use aspirin to its fullest medical potential, namely, the anti-inflammatory treatment of arthritis.

The following study is typical in its report of aspirin gastropathy and erosive gastritis:

Journal of the Hong Kong Geriatrics Society • Vol. 11 No.1 Jan. 2002

"Tolerability Of Aspirin And Predictors For Withdrawal In Elderly Patients"

SUMMARY

Aspirin has been proven to reduce risk of thrombotic cardiovascular events such as ischemic stroke and myocardial infarction. However, side effects are not uncommon with gastrointestinal side-effects and hemorrhagic complications being the commonest causes of its withdrawal of soluble aspirin al*. A retrospective review was performed to study the tolerability of aspirin in elderly patients and predictors for drug withdrawal. Between 1995 and 1999, 285 consecutive patients aged over 60 who were started on aspirin and followed up in the Geriatrics outpatient clinic of Tuen Mun Hospital were recruited for study.*

INTRODUCTION

Aspirin (acetylsalicylic acid) is the commonest anti-platelet agent used in clinical practice. Aspirin has proven benefit in the secondary prevention of a number of occlusive vascular disorders such as unstable angina, myocardial infarction, transient ischemic attack (TIA) and stroke

1. In the first report of the Antiplatelet Trialists' Collaboration (ATC) 1, it was concluded that antiplatelet therapy, particularly with aspirin, reduced the risk of death from cardiovascular causes by about one-sixth and the risk of nonfatal myocardial infarction and stroke by approximately one-third in patients with unstable angina or a history of myocardial infarction, TIA or stroke. Moreover, there is evidence from recent studies that aspirin is also beneficial in the primary prevent ion of thromboembolism in patients at risk.

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J HK Geriatr Soc 2002; 11:11-15

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Because of the well-proven efficacy of aspirin in the secondary prevention of cardiovascular and cerebrovascular disorders, this antiplatelet agent is routinely prescribed for all patients who are admitted to our hospital because of vascular events, unless definite contraindications are evident. As a substantial proportion of acute admissions to the medical and geriatric wards are patients with cerebrovascular accident (CVA), transient ischemic attack (TIA) and ischemic heart disease (IHD), aspirin is one of the most commonly prescribed drugs in our unit. A previous small local study reported that the withdrawal rate of aspirin, administered at a dosage of 300mg/day, in elderly patients with cerebrovascular accident was 42% at 12 months and the chief reason for drug withdrawal was gastrointestinal toxicities6

Discussion

This study examined the tolerability and withdrawal rate of aspirin in a cohort of elderly patients and the clinical predictors for aspirin withdrawal. The commonest reason for aspirin discontinuation in our cohort of patients was GI side effects and it was noteworthy that a significant proportion of patients with aspirin induced GI complications did not have preceding symptoms of GI upset.

Among the various side effects of aspirin, GI toxicity deserves most concern because it is associated with significant morbidity and mortality. The relative risks (RR) for the occurrence of gastric and duodenal ulcers in chronic aspirin users were estimated to be 4.7 and 1.2, respectively and the relative risk for GI bleeding was 3.3 for aspirin

users9. In the Thrombosis Prevention Trial (TPT) 3 and the Hypertension Optimal Treatment (HOT)study10, the incidence of major GI bleeding was reported to be 0.74 and 2.16 per 1000 patient-years, respectively. In both trials, non-fatal major GI bleeding was shown to be significantly more common in aspirin users than placebo. The risk of aspirin-induced GI bleeding appears to be dose dependent. Weil et al11 demonstrated that the odd

References: Hawkey CJ. Non-steroidal anti-inflammatory drugs and peptic ulcers: facts and figures multiply, but do they add up? *Br Med J* 1990; **300:278**-284

Hansson L, Zanchetti A, Carruthers S et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomized trial. HOT Study Group. *Lancet* 1998; **351:1755**-1762

Weil J, Colin-Jones D, Langman M, et al. Prophylactic aspirin and risk of peptic ulcer bleeding. *Br Med J* 1995; **310:827**-830

McCarthy D. Nonsteroidal anti-inflammatory drug-related gastrointestinal toxicity: definitions and epidemiology. *Am J Med* 1998; **105(5A)**:3S-9S

LEARNING POINTS:

…. The main reason for aspirin withdraw was peptic ulceration with or without gastrointestinal bleeding.

Study: Aspirin May Delay, Prevent Alzheimer's

Aspirin keeps earning its keep as the world's wonder drug. Researchers from the Veterans Administration Puget Sound Health Care System in Seattle report aside from its many cardiac benefits, aspirin -- and other NSAIDs -- may reduce dementia in the elderly. The key is, researchers say, taking the drug for at least two years before onset of dementia or Alzheimer's disease. This new study looked at more than 5,000 elderly residents of Cache County in Utah. It found long-term use of NSAIDs was associated with a dementia incidence rate only 45 percent of that seen in non-users. Common NSAIDs include aspirin compounds and non-aspirin drugs such as ibuprofen, naproxen, diclofenac, nabumetone, sulindac and oxaprozin, as well as histamine H2 receptor antagonists. Other medicines, including acetaminophen, allopurinol, propoxyphene and other opioids, as well as antacids and anti-flatulants and other stomach remedies, were tested but had no effect.

Aspirin and Dementia

A reduction in cognitive decline and dementia in patients who take aspirin has been suggested. If confirmed, this will be of enormous importance to public health. It seems likely that aspirin might have some effect, because a high proportion of cases of dementia are caused either by damage following a stroke, or repeated, small, sub-clinical cerebral infarcts - multi-infarct dementia. Lesser degrees of damage from vascular lesions may also be prevented by low-dose aspirin. Evidence from a number of trials is urgently needed but results from one trial have already suggested benefit.20

Another form of dementia is Alzheimer's disease. The causes of this disease are not thoroughly understood but it is thought that some of the damage occurs through inflammatory processes around the so-called tangles that develop within the substance of the brain. Aspirin, even at low doses, has an anti-inflammatory action. It is not surprising, therefore, that a large number of observational studies have shown a reduced incidence of Alzheimer's disease in patients taking aspirin or other anti-inflammatory drugs.21,22

Aspirin May Fight Pancreatic Cancer

Researchers at the University of Minnesota have found aspirin use may decrease the incidence of pancreatic cancer, possibly through its anti-inflammatory effects. The researchers followed a group of post-menopausal women for 7 years. They asked the women how often they took aspirin or aspirin-containing products, as well as other non-steroidal anti-inflammatory drugs.

Pancreatic cancer occurred 43 percent less frequently among those women who reported aspirin use compared to those who did not. "There is strong evidence to suggest that using aspirin may help in preventing pancreatic cancer, and what's most encouraging is that we've seen these benefits in women who've taken aspirin two to five times per week," researchers said. They added further studies are needed to learn more about other factors such as dose, duration, and types of non-steroidal drugs that may help prevent the disease. Researchers said it is important to consult physicians before starting an aspirin regimen.

Aspirin and Aids

AIDS TREATMENT NEWS No. 109 - August 17, 1990
John S. James

http://www.aegis.com/pubs/atn/1990/ATN10901.html

Since early in the AIDS epidemic, some research has suggested that ordinary aspirin (or certain aspirin substitutes) might have a role in treating the disease, other than the relief of minor symptoms. Aspirin could not be the whole answer, of course. But laboratory studies have suggested that reducing certain inflammatory reactions, as aspirin does, may affect the pathogenesis of the disease, improving some immune functions, and possibly slowing the replication of HIV by reducing the levels of certain chemical messengers, which may trigger the growth of the virus. Some anecdotal reports which have come to our attention also support the possibility that aspirin may have a role in the treatment of AIDS or HIV.

For several years a number of physicians have used aspirin or other anti-inflammatory drugs to help patients with AIDS feel better -- especially to relieve fever or diarrhea when these symptoms are unexplained, and in some other cases such as fevers caused by MAI. While aspirin works for these purposes, until recently the treatment of choice was usually indomethacin, a nonsteroidal anti-inflammatory drug (NSAID); the reason for preferring indomethacin is that published information was available, since most of the early research was done with that drug. But new research is now suggesting that aspirin might be better than indomethacin or other NSAIDs. Both provide symptomatic relief from fever and diarrhea, and both reduce synthesis of a certain prostaglandin (see explanation below ?h?), which appears to be excessive in persons with AIDS and may make the disease worse. But aspirin might also have an anti-HIV effect which indomethacin does not.

Cataracts

An association between regular aspirin taking and reduced development of cataract has been reported. If real, this may be due to the inhibition of an enzyme within the lens tissues. Although the benefit from regular aspirin is likely to be modest, there seems to be a potentially important reduction in posterior subcapsular caratact, a particularly disabling subtype.23 [PARA] Colorectal cancer. Of great interest is a marked reduction in colorectal cancer in habitual aspirin takers. This has been reported in a number of studies.24,25 when diseased, a number of plants secrete salicylates in order to kill the affected parts and to limit the spread of the disease. This may give a clue as to the mechanism of aspirin in cancer and it has, therefore, been suggested that within human subjects the drug may enhance apoptosis of the cells involved in early cancer. [PARA] A number of trials have been set up in patients with familial polyposis and in other high-risk groups to find out whether this is the case.

Low-dose aspirin in cardiovascular disease [PARA] Aspirin reduces the risk of a cardiovascular event, such as heart attack, stroke or deep vein thrombosis, by about 30 per cent. [NL][NL]If a thrombosis does occur in patients on low-dose aspirin the infarct is likely to be less serious.[NL][NL]The absolute reduction in risk is dependent on the patient group:[PARA]* Three events per hundred per year in patients at high risk [PARA]* Three events per thousand per year in healthy subjects at low risk [PARA]The reduction in risk is dependent upon compliance. Benefit obtained from erratic doses is substantially less than that from a regular daily dose.

Aspirin May Prevent Diabetic Retinopathy

The RetinaSource.com (July 2001)

Can An Aspirin A Day Keep Diabetic Retinopathy Away?

New Research Suggests Aspirin Could Slow The Progress of Vision Loss Related to Diabetic Retinopathy

http://www.theretinasource.com/news/articles/AspirinDiabetic_0717.htm

Researchers at the Schepens Eye Research Institute, Harvard Medical School in Boston, have discovered that people with diabetes have blood clots in the tiny blood vessels that nourish the retina. There is research that suggests aspirin, a drug known to dissolve blood clots, could help to prevent this eye damaging complication of diabetes.

Diabetic retinopathy, a disease that affects half of all Americans diagnosed with diabetes, often has no early warning signs. When small capillaries are damaged, they leak fluid into the retina causing macular edema. Macula edema or swelling of the central retina can cause blurry vision and permanent loss of vision.

It has always been suspected that capillary blood clots were part of the reason for background diabetic retinopathy progressing to the more severe stage known as proliferative diabetic retinopathy.

Dr. Dan Montzka, a vitreo-retinal surgeon at St. Luke's Retina Institute, points out that "the first line of defense against diabetic retinopathy is good blood sugar control and regular screening exams." Aspirin should only be used after consulting your physician.

Ref: Diabetes 2001; National Eye Institute

Deep-Vein Thrombosis – Reducing the Risk

Avoid prolonged bed rest if possible. If medical conditions related to pregnancy require you to be confined to bed, or keep you relatively immobile, be sure to keep your lower limbs moving on a regular basis. Stopping smoking is important for everyone, but particularly for people at risk of developing deep vein thrombosis. Regular exercise is important too. Ask your doctor which type of exercise is best for you.

Your chances of developing DVT from a long flight or other journey are small but, significantly high enough to warrant everyone being vigilant and taking all precautions known to reduce the risk. Take 75mg solubilized aspirin 2 hours before you board the plane followed by a further 75mg 4 hours into your flight and a further 75mg 6 hours later. Continue to take the solubilized aspirin but at longer intervals thereafter of 12 hours until the day after you have completed your journey. WARNING If you suffer from gastric disorders or intestinal bleeding consult your doctor before taking aspirin, your doctor may prefer you to take an alternative anti coagulant.

This helps to thin the blood. However, do not take aspirin if you have stomach ulcers or suffer from acute indigestion, as aspirin can induce in bleeding in your stomach (it is generally safe). The normal aspirin tablet is 300mg but the smaller 75mmg are available. Alternatively break evenly into 4 pieces a 300mg tablet. Wear loose clothing and move around before boarding. Most important of all, do not just sit still in your seat during the flight.

http://www.50plushealth.co.uk/index.cfm?articleid=505&ArticleAction=print