Recent advances

Geriatric medicine

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The primary aims of geriatric medicine are to relieve suffering in old people and to increase the number of years free of disability that they can enjoy. Here we focus on new evidence about the benefits of interventions commonly used in geriatric medicine.

We decided to focus on clinical interventions because of their importance to clinicians. We then selected the interventions that we judged (as editors of the *Journal of the American Geriatrics Society*) to be the more important ones dealt with in the English language medical journals in the past 18-24 months. We carried out thorough Medline searches on each intervention selected. In this article we have chosen a "lifetime" perspective; we have covered new studies whose subjects included middle aged people because the interventions are relevant to disorders related to aging.

Non-steroidal anti-inflammatory drugs

Their role in dementia and cancer

Non-steroidal anti-inflammatory drugs are used mainly to control pain and inflammation, but they may also protect from dementia and cancer. Two observational studies in cohorts of elderly subjects—the established populations for epidemiologic studies of the elderly and the Baltimore longitudinal study on aging—have shown that long term use of non-steroidal anti-inflammatory drugs is associated with improved cognitive function and a reduced risk of Alzheimer's disease.^{1,2} A case-control study found that the regular use of aspirin or other non-steroidal anti-inflammatory drugs such as ibuprofen, indomethacin, naproxen, and piroxicam was related to a reduced risk of breast cancer.³ However, a large cohort study found no such association with aspirin.⁴ Another case-control study in people of middle age and older showed an inverse association between the use of any non-steroidal anti-inflammatory drugs and the risk of colorectal cancer.⁵ Two small randomised, placebo controlled clinical trials showed that indomethacin suppositories and oral sulindac limited the growth of polyps in young and middle aged patients with familial rectal polyposis.^{6,7}

Cardiovascular disease

New data support the benefits of aspirin in cardiovascular disease, which is still the most common cause of death and disability in older people. The international stroke trial and the Chinese acute stroke trial showed that giving aspirin shortly after an ischaemic

Recent advances

Chronic inflammation has a key role in the abnormal processes related to aging, including changes in body composition, congestive heart failure, and possibly dementia

Increasing oxidative stress is a key aspect of aging. Studies suggest that vitamin E supplementation reduces coronary events associated with atherosclerosis and slows the processes underlying Alzheimer's disease

Control of high systolic blood pressure is important in preventing stroke

Targeted and coordinated home health care can improve the health of older people with chronic disease and reduce admissions to hospital

mic stroke reduced the risk of death or recurrent stroke for up to 4 weeks and 6 months of follow up respectively.^{8,9} These randomised trials have included more than 40 000 subjects; 84% in the international stroke trial and 68% in the Chinese acute stroke trial were aged 60 years or more. Aspirin was associated with a 12% reduction in risk in the international stroke trial and a 9% one in the Chinese trial.

Anti-inflammatory or antiplatelet effects

Until recently the beneficial effect of aspirin in coronary disease has been attributed mainly to its antiplatelet effects. Data are accumulating on the role of inflammation in atherosclerosis, and these suggest that aspirin may inhibit inflammation. In subjects aged 40-84 years enrolled in the physician's health study, the baseline concentration of plasma C reactive protein, a marker of systemic inflammation, predicted the occurrence of myocardial infarction or ischaemic stroke.¹⁰ The reduction in the risk of acute myocardial infarction associated with taking aspirin was greater in people with high concentrations of C reactive protein than in those with low values.

Importance of inflammation

In older people, the impact of inflammation may be widespread, and it may have important implications for

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their physical function and disability. Recent studies have highlighted the association of proinflammatory cytokines such as tumour necrosis factor α and interleukin 6 with a poor prognosis and increased severity of heart failure.^{11 12} Excess cytokine production is also associated with a loss of skeletal muscle and cachexia that accompanies heart failure.¹³ Whether generalised inflammation causes changes in body composition and accounts for the excess morbidity related to aging is being investigated in a long term cohort study of 3000 older people being conducted in the United States.

Balancing risks and benefits

The current evidence is insufficient to recommend the use of non-steroidal anti-inflammatory drugs in the prevention of dementia or cancer. Older people are more likely to have side effects such as acute renal failure, gastrointestinal perforation, and gastrointestinal bleeding.¹⁴⁻¹⁶ Recent data indicate that among individual non-steroidal anti-inflammatory agents, low dose ibuprofen is least likely to cause gastrointestinal complications; that buffering or enteric coating of aspirin does not protect against upper gastrointestinal bleeding; and that famotidine prevents gastric and duodenal ulcers caused by non-steroidal anti-inflammatory drugs.¹⁶⁻¹⁸

Oxidative stress

Vitamin E and dementing illnesses

Oxidative stress is one mechanism involved in aging. New findings show the effects of antioxidants on the health of people of various ages. In a two year randomised placebo controlled trial, 2000 IU of vitamin E per day given to patients with moderate Alzheimer's disease delayed by 50% the combined end point of death, admission to an institution, inability to perform the activities of daily living, or severe dementia.¹⁹ In the

Fig 1 Survival free of adverse events—death, admission to an institution, loss of the ability to perform activities of daily living, or severe dementia—in patients with Alzheimer's disease assigned to treatment with α tocopherol, selegiline, α tocopherol and selegiline, or placebo. Effects for all three active treatments were significant when compared with placebo ($P=0.012$, $P=0.001$, $P=0.049$, respectively). Reproduced with permission¹⁹

Fig 2 Kaplan-Meier curve of deaths from all forms of cancer in patients with skin cancer who were randomised to treatment with selenium or placebo ($P=0.001$). Reproduced with permission²⁴

same study a similar effect was obtained with selegiline alone or with selegiline and vitamin E combined (fig 1).

Antioxidant vitamins and heart disease

In the Cambridge heart antioxidant study, 2002 patients with coronary heart disease were randomised to receive vitamin E (400-800 IU per day) or placebo, and were followed up for a median time of 1.4 years.²⁰ The mean age of the study participants was 61.8 years. In the active treatment group, the combined end point of death from cardiovascular causes or non-fatal myocardial infarction was significantly reduced (relative risk 0.53; 95% confidence interval 0.34 to 0.83).

These favourable findings were not confirmed in a Finnish trial whose subjects were 1862 male smokers aged 50-69 years who had had a myocardial infarction.²¹ The men were randomised to receive vitamin E (50 mg/day), β carotene (20 mg/day), both vitamins, or placebo. After a median follow up of 5.3 years the four groups had similar rates of major coronary events. Use of low doses or different sources of vitamin E (synthetic compared with natural) might have accounted for the differences in results between this study and Cambridge heart antioxidant study. Participants randomised to receive β carotene had significantly higher rates of coronary deaths.

Vitamin E and the immune response

In a fourth trial, 88 healthy people aged 65 years or older were randomised to receive vitamin E (60 IU per day, 200 IU per day, or 800 IU per day) or placebo.²² After four months of follow up, those who had taken vitamin E supplements showed a significant improvement in the indices of immune response mediated by T cells. The benefits of vitamin E are not limited to pharmacological supplementation. One observational study followed 34 486 postmenopausal women (mean age 61.5 years) who had a high dietary intake of vitamin E. After seven years they showed a significantly reduced risk of death from coronary heart disease.²³ Intake of vitamins A and C was not associated with the risk of death from coronary heart disease.

Selenium

A randomised placebo controlled clinical trial (subjects' mean age 63.2 years, range 18-80 years) (fig 2) found that selenium, another antioxidant micronutri-

ent, may protect against all cancers, and a case-control study (subjects' mean age 53.1 years) found that it may protect against ovarian cancer.^{24 25} These findings need confirmation, however, since death from all forms of cancer was not the primary end point of the first trial and the association with several micronutrients was tested in the case-control study.

β Carotene and vitamin C

The results of supplementation with β carotene are less favourable. A randomised trial in 22 071 male doctors aged 40 to 84 years found that β carotene had no effect on the incidences of cancer and cardiovascular disease after 14 years of follow up.²⁶ In a trial in which 18 314 smokers (mean age 57.5 years) participated, the combination of β carotene and vitamin A increased the risk of death from lung cancer (relative risk 1.28; 1.04 to 1.57) and from all causes (1.17; 1.03 to 1.33) and tended to increase the risk of death from cardiovascular disease (1.26; 0.99 to 1.61). Another trial, the β carotene and retinol efficacy trial, in 18 314 men and women (mean age 58 years) has been stopped early because the incidence of and mortality from lung cancer was excessive.²⁷ A recent cohort study in Finnish men aged over 60 has shown that vitamin C deficiency, assessed by a low plasma ascorbate concentration, is a risk factor for coronary heart disease.²⁸ However, it is not known whether supplementation with vitamin C reduces the risk.

Hypertension

Antihypertensive treatment and heart disease

The impact of medication for high blood pressure has been clarified with regard to intermediate major cardiovascular outcomes, such as stroke, coronary heart disease, and congestive heart failure. However, the effect of antihypertensive treatment on more long term degenerative disorders such as dementia and disability is less clear. Findings from the non-randomised Shanghai trial of nifedipine in the elderly²⁹ and the recent report of the Syst-Eur Trial³⁰ replicate and extend the findings of the systolic hypertension in the elderly program with regard to patients with isolated systolic hypertension or predominant systolic hypertension for the outcome of stroke. As was found for the regimen based on diuretic drugs in the systemic hypertension in the elderly program, both of these more recent trials show that giving a dihydropyridine calcium channel blocker to older people who have predominantly systolic hypertension decreases the rate of stroke when compared with placebo (relative risk in Shanghai trial 0.3 (0.24 to 0.77); in Syst-Eur trial 0.58, $P=0.003$).

Several studies indicate that lowering systolic blood pressure and maintaining control of blood pressure by any class of medication for hypertension is better than placebo for preventing stroke. In a recent meta-analysis, treatment with diuretics given in low doses to older adults was associated with reduced risks of stroke, coronary heart disease, congestive heart failure, and total mortality.³¹ Trials to determine which antihypertensive drugs are better at preventing major complications of hypertension continue in both the United States and Europe.

Data from the systolic hypertension in the elderly program show that diuretic drug treatment of isolated

Fig 3 Heart failure events in the systolic hypertension in the elderly program in relation to the following treatment groups: A=placebo with a baseline history of myocardial infarction (by personal history or electrocardiogram); B=active treatment with a baseline history of myocardial infarction; C=placebo without a baseline history of myocardial infarction; and D=active treatment without a baseline history of myocardial infarction. Reproduced with permission³³

systolic hypertension in patients with moderate type II diabetes was at least as effective as treatment with other types of antihypertensive drugs in reducing stroke (relative risk 0.78; 0.45 to 1.34), non-fatal myocardial infarction and coronary heart disease (0.46; 0.24 to 0.88), and all major cardiovascular events (0.66; 0.46 to 0.94).³² In addition, a recent publication from the same group has shown that treating isolated systolic hypertension with diuretic drugs can reduce the risk of heart failure over time (0.51; 0.37 to 0.71, $P<0.0001$). The reduction in congestive heart failure events is greatest in patients with a history of myocardial infarction or electrocardiac evidence of this (0.19; 0.06 to 0.53, $P=0.002$). Although smaller, the reduction was also seen in people without evidence of a previous myocardial infarction (fig 3).³³

Antihypertensive treatment and dementia

The effect of antihypertensive treatment in elderly people on another long term outcome—dementia—is less than certain. In the Medical Research Council's treatment trial of hypertension in older adults, treatment of moderate hypertension had no impact on cognitive function.³⁴ However, analyses of data from the Kungsholmen project, seem to show that Alzheimer's disease is associated with a decrease in both systolic and diastolic blood pressures.³⁵ Data available to date do not support the suggestion that lowering the systolic or diastolic blood pressure in older people has any effect on cognitive function or the subsequent development of dementia. In addition, the data from Kungsholmen are not definitive and a major study is still needed.

Exercise programmes

Various studies of exercise programmes have shown that some can improve balance.³⁶ Programmes which emphasise resistance exercises for the legs are particularly useful in helping older people rise from a chair and increase their walking speed.³⁷ The addition of upper body resistance exercises increases the range of activities of daily living (for example, carrying groceries) which older people can perform, and flexibility exercises may help protect against falls.³⁷

Home health care

Evidence continues to mount that home health care has a profound impact on older people who are frail and have chronic disease. Studies by Rich and colleagues have shown the benefit of home health care on patients with congestive heart failure.³⁸ A recent study has shown that home counselling of carers results in a lower rate of admission to nursing home in people with Alzheimer's disease.³⁹ In addition, a recent randomised controlled trial of the impact a psychogeriatric team had on elderly people living at home indicated that intervention in the home reduced the level of depression in this group (relative risk 0.33; 0.1 to 0.5).³⁹ Analyses indicate that the people who were given home care were more likely to start and continue treatment with antidepressant drugs, to have a review of social function with counselling, and to have professional support of interaction with family.⁴⁰ However, a randomised controlled trial of specialist nurse support at home for patients with stroke showed little benefit—a small improvement in social activities, and this only in patients who were moderately disabled.⁴¹ A long term follow up study of patients with urinary incontinence has shown that counselling by a nurse in primary care settings is effective: after four years, urinary incontinence was still improved in most study subjects.⁴²

Factors in disability

Little is known about the primary factors leading to disability in older people. Large cohort studies funded by the National Institute on Aging in the United States, such as the women's health and aging study and the health and body changes study, seek to identify risk factors of progressive and incident disability. The findings of these studies will help to target the interventions to be tested in older people in randomised clinical trials.

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