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MEDICAL SUBJECT HEADINGS

HIGHLIGHTS-INDEX

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HIGHLIGHTS 2002

ACUTE CORONARY SYNDROMES

1-14 DIRECT THROMBIN INHIBITORS IN ACUTE CORONARY SYNDROMES

Direct thrombin inhibitors (eg, hirudin, derived from leeches) were superior to heparin in preventing MI and death in patients with acute coronary syndromes including those undergoing PTCA. But the NNT to benefit one patient was large, and equaled the NNT to harm.

The investigators recommend further development of DTIs for management of arterial thrombosis.

1-16 PLATELET GLYCOPROTEIN IIB/IIIA INHIBITORS IN ACUTE CORONARY SYNDROMES

Glycoprotein IIb/IIIa inhibitors reduced cardiac complications in patients with acute coronary syndromes not routinely scheduled for early revascularization. Treatment might be considered early after admission in high-risk patients and continued for 2 to 4 days until a decision about revascularization is made.

Benefit was evident only in those with an elevated troponin concentration. (Evidence of myocardial damage.)

The number needed to treat to benefit one patient = 100.

ALCOHOL

1-13 ALCOHOL CONSUMPTION AND RISK OF DEMENTIA: THE ROTTERDAM STUDY

Light-to-moderate alcohol consumption was associated with a reduced risk of dementia in elderly individuals over age 65. The effect seemed to be unchanged by the type of alcohol consumed. Benefits were modest.

3-11 PROSPECTIVE STUDY OF MODERATE ALCOHOL CONSUMPTION AND RISK OF HYPERTENSION IN YOUNG WOMEN

The association between alcohol consumption and risk of chronic hypertension in young women followed a J-shaped curve. Light drinkers demonstrated a modest decrease in risk. Regular, more heavy drinkers demonstrated increased risk.

5-10 EFFECTS OF MODERATE ALCOHOL INTAKE ON FASTING INSULIN AND GLUCOSE CONCENTRATIONS AND INSULIN SENSITIVITY IN POSTMENOPAUSAL WOMEN.

Consumption of 30 g/d of ethanol had beneficial effects on fasting insulin, insulin sensitivity, and triglyceride concentrations in non-diabetic postmenopausal women. This was independent of body mass index.

10-16 SCREENING AND BRIEF INTERVENTION OF EXCESSIVE ALCOHOL USE: Qualitative Interview Study Of Experiences Of General Practitioners.

Screening and brief intervention programs may fail to detect harmful drinkers, while requiring considerable resources for primary prevention in groups of hazardous drinkers. Screening-based brief interventions left the practitioners with a sense of failure in achieving rapport and compliance, and were not congruent with contemporary approaches to dealing with lifestyle issues.

Screening for excessive alcohol use created more problems than it solved.

ALZHEIMER'S DISEASE (See also DEMENTIA)

3- 6 PARTICIPATION IN COGNITIVELY STIMULATING ACTIVITIES AND RISK OF INCIDENT ALZHEIMER'S DISEASE

Frequent participation in cognitively stimulation activities was associated with reduced risk of cognitive decline and AD.

The benefit of cognitive activity was associated with a later onset of AD. The rate of cognitive decline even after first stages of AD are apparent may be slowed by continuing cognitive activity.

If cognitive activity is protective, reduced cognitive activity should be an early sign of disease. Practical point: Use it, or lose it!

11-9 EFFECTS OF COGNITIVE TRAINING INTERVENTIONS WITH OLDER ADULTS

Cognitive training interventions improved targeted cognitive abilities. Effects were of a magnitude equivalent to prevention of the usual amount of decline expected over 7- to 14-year intervals.

ANEURYSMS

5-14 IMMEDIATE REPAIR COMPARED WITH SURVEILLANCE OF SMALL ABDOMINAL AORTIC ANEURYSMS

Survival was not improved by elective repair of AAA smaller than 5.5 cm. The study supports a policy of reserving elective repair for those at least 5.5 cm in diameter.

11-14 THE MULTICENTER ANEURYSM SCREENING STUDY (MASS) INTO THE EFFECT OF ABDOMINAL ANEURYSM SCREENING OF MORTALITY IN MEN.

Substantial reductions in AAA-related mortality could be achieved by the implementation of a population-screening program for older men. Screening and following surgery was not associated with any decrease in quality-of-life.

ANGINA

7-15 THE VALUE OF INFLAMMATION FOR PREDICTING UNSTABLE ANGINA

Morphologically, atherosclerosis is an inflammatory disease.

“Active” coronary disease is clearly associated with evidence of inflammation, both systemically and at the level of the arterial wall. Elevated levels of fibrinogen (an acute-phase reactant) were independently associated with future coronary events. Increased levels of markers of inflammation (eg, cytokines, adhesion molecules, and C-reactive protein) predict future cardiovascular events.

Statin drugs, which reduce risk of coronary events, also reduce circulating inflammatory markers independently of their cholesterol-lowering effect.

Coronary angiography is not particularly useful in identifying the inflamed atherosclerotic plaques that are prone to produce clinical events. Acute myocardial infarction is often a consequence of coronary stenosis which is mild on angiography. Persons with an increased risk of acute coronary events are likely to have many vulnerable plaques throughout the coronary circulation. Plaque modification may be best modulated by systemic means (eg, statins; diet).

“The current challenge remains the identification of persons with vulnerable atherosclerotic plaques”

ANNUAL PHYSICAL EXAMINATIONS

5-7 PUBLIC EXPECTATIONS AND ATTITUDES FOR ANNUAL PHYSICAL EXAMINATIONS AND TESTING.

The public has high expectations for a comprehensive annual physical examination and extensive routine testing. The expectations are modified by costs.

Over the past 3 decades, most major medical organizations have changed recommendations for a scheduled complete physical examination to recommend selective preventive services in the context of visits for other reasons.

The public needs education about the value of periodic health examinations and current recommendations for specific preventive health services.

ANTIBIOTICS

1-6 REDUCING ANTIBIOTIC USE FOR ACUTE BRONCHITIS IN PRIMARY CARE

Most previously well adults who develop acute bronchitis were judged not to need antibiotics. Reassuring these patients and sharing uncertainty about the value of antibiotics in acute bronchitis is a safe strategy and reduces antibiotic use.

Primary care clinicians should use the "if" prescription more often.

12-11 ANTIBIOTICS FOR ACUTE PURULENT RHINITIS

Guidelines suggest that antibiotics are ineffective. This may not be true. However, the modest benefit for this condition, which is rarely life-threatening, may warrant constraint on their use because of side effects, cost, development of antibiotic resistance, and promotion of use of health services. Perhaps they should consider delayed prescriptions in an attempt to meet demand from patients while maintaining evidence based integrity.

ANTIBIOTIC-ASSOCIATED DIARRHEA

1-12 ANTIBIOTIC-ASSOCIATED DIARRHEA

C difficile infection should be considered in all patients with unexplained diarrhea who are receiving antibiotics or who have recently received antibiotics.

Enzyme assays to detect both toxins A and B are preferred. False negative results may occur if the only test is for toxin A.

Many patients will respond to withdrawal of the inducing antibiotic. If the patient's condition calls for continued antibiotic therapy, use an agent that is infrequently associated with AAD. (See list in abstract.)

If there is evidence of colitis or if discontinuation of the offending antibiotic does not result in resolution of the diarrhea, metronidazole is indicated. Lack of response to metronidazole is strong evidence against the C difficile colitis.

If assays for C difficile toxin are negative, and symptoms persist, repeat the test, expand the diagnostic evaluation to other causes (eg, look for staph and salmonella), or treat empirically. Practical point: Patients who are informed of this risk may be less likely to demand antibiotics.

ANTICOAGULATION

5-17 FONDAPARINUX: A New Synthetic Pentasaccharide For Thrombosis Prevention

A new anticoagulant (fondaparinux) is becoming available. This synthetic compound is almost identical to the natural pentasaccharide sequence of heparin. It inhibits factor Xa.

8-13 ORAL VITAMIN K LOWERS THE INTERNATIONAL NORMALIZED RATIO MORE READILY THAN SC VITAMIN K IN THE TREATMENT OF WARFARIN-ASSOCIATED COAGULOPATHY.

In asymptomatic patients with supra-therapeutic INR values (4.5 to 10) while receiving warfarin, 1 mg oral vitamin K lowered INR more rapidly to a therapeutic level than subcutaneous K.

The day after administration of oral K, the INRs remained within therapeutic range in many patients, allowing reinstitution of warfarin therapy.

9-18 FONDAPARINUX VS ENOXAPARIN FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM IN MAJOR ORTHOPEDIC SURGERY.

In patients undergoing orthopedic surgery, fondaparinux (a factor Xa inhibitor) once daily, starting 6 hours post surgery, showed major benefit over enoxaparin (a low-molecular weight heparin) in reducing DVT at the expense of a slightly increased risk of bleeding.

Fondaparinux may be a valuable addition to anticoagulant therapy.

10-20 XIMELAGATRAN VERSUS WARFARIN FOR PREVENTION OF VENOUS THROMBOEMBOLISM AFTER TOTAL KNEE ARTHROPLASTY

Ximelagatran is a novel oral anticoagulant which inhibits both free and clot-bound thrombin. If it pans out, its fixed dose, oral administration, absence of interactions with food and drugs, and the fact that it requires no anticoagulation monitoring will be great advantages. More confirmatory studies will be required before it can be entered into primary care practice. RTJ

10-14 HEPARIN PLUS ALTEPLASE COMPARED WITH HEPARIN ALONE IN PATIENTS WITH SUBMASSIVE PULMONARY EMBOLISM

Thrombolytic therapy with tissue plasminogen activator (t-PA; alteplase) plus heparin improved the clinical course of stable patients with acute submassive PE. It prevented further clinical and hemodynamic deterioration which would have required escalation of treatment.

ANTIPLATELET THERAPY

1-1 COLLABORATIVE META-ANALYSIS OF RANDOMIZED TRIALS OF ANTIPLATELET THERAPY FOR PREVENTION OF DEATH, MYOCARDIAL INFARCTION, AND STROKE IN HIGH RISK PATIENTS

Unless some definite contraindication exists, antiplatelet therapy (low-dose aspirin) should be considered routinely for all patients whose medical history implies a significant risk of occlusive vascular disease over the next few months or years (secondary prevention), and should generally be continued for as long as the risk remains high. Absolute benefits substantially outweigh the absolute risk of major extracranial bleeding.

Aspirin is protective in patients with a history of ischemic stroke, unstable and stable angina, previous myocardial infarction, previous stroke or cerebral ischemia, diabetes, peripheral vascular disease, or atrial fibrillation (when warfarin is not used).

Primary care clinicians should prescribe aspirin more often for secondary prevention of cardiovascular events.

AORTIC STENOSIS

2-10 AORTIC STENOSIS

When is the optimal time to intervene? What is the best intervention? In adults with calcified valves, balloon angioplasty may temporarily relieve symptoms but does not prolong survival. Replacement of the valve is required. Surgery is usually delayed until symptoms develop. Once angina, syncope, dyspnea or other symptoms of heart failure develop, the patient's life span is drastically shortened unless the valve is replaced.

The 10 year survival rates among those undergoing successful valve replacement approaches that of the normal population.

"There is overwhelming evidence that once patients with severe aortic stenosis become symptomatic, prompt valve replacement is indicated."

3-9 HMG COA REDUCTASE INHIBITOR (STATIN) AND AORTIC VALVE CALCIUM

Statin therapy may retard progression of calcific aortic valve disease.

APPENDICITIS

9-6 MANAGING ACUTE APPENDICITIS

The simple expedient of close observation and repeated re-evaluation has been shown to reduce the unnecessary exploration rate. The single greatest change in surgical practice has been the widespread introduction of laparoscopy. It has been quickly applied to the problem of acute appendicitis. A systematic review reported that laparoscopic appendectomy halves the number of wound infections, reduces pain, and shortens hospital stay and time to return to work. This is at a cost of a three-fold increase in the number of postoperative intra-abdominal abscesses.

ASPIRIN

1-1 COLLABORATIVE META-ANALYSIS OF RANDOMIZED TRIALS OF ANTIPLATELET THERAPY FOR PREVENTION OF DEATH, MYOCARDIAL INFARCTION, AND STROKE IN HIGH RISK PATIENTS

Unless some definite contraindication exists, antiplatelet therapy (*low-dose aspirin*) should be considered routinely for all patients whose medical history implies a significant risk of occlusive vascular disease over the next few months or years (*secondary prevention*), and should generally be continued for as long as the risk remains high. Absolute benefits substantially outweigh the absolute risk of major extracranial bleeding.

1-2 ASPIRIN FOR THE *PRIMARY* PREVENTION OF CARDIOVASCULAR EVENTS

Five trials have examined the effects of daily or every-other-day aspirin for primary prevention over 4 to 7 years. Most subjects were men over age 50. Meta-analysis of pooled data showed that aspirin reduced the risk of coronary heart disease by 28%. No effect on total mortality or stroke.

For patients at high risk of coronary heart disease (5% over 5 years) prophylactic aspirin would lead to avoidance of 6 to 20 CHD episodes over the 5 years.

Primary prevention is not recommended for those with a risk of 1% per year.

Primary care clinicians should prescribe aspirin more often for primary prevention of cardiovascular events. The clinician's challenge is to judge the degree of risk and to match the patient's concerns and wishes with the risk. Many individuals will benefit from primary prevention with aspirin.

5-13 SELECTIVE COX-2 INHIBITORS, NSAIDs, ASPIRIN, AND MYOCARDIAL INFARCTION

Use of naproxin was associated with a reduced rate of acute myocardial infarction. There is no evidence that use of COX-2 inhibitors increases (or decreases) the risk of myocardial infarction.

The effects noted are due to the anti-platelet, anti-thrombotic actions of naproxin, rather than a detrimental effect of COX-2 inhibitors.

The investigators concluded that there was no evidence for excess cardiovascular events in patients treated with rofecoxib compared with those treated with placebo or NSAIDs other than naproxin. The difference in outcomes was likely due to an antiplatelet effect of naproxin.

6-16 LANSOPRAZOLE FOR THE PREVENTION OF RECURRENCES OF ULCER COMPLICATIONS FROM LONG-TERM LOW-DOSE ASPIRIN

In patients with *H pylori* infection who had gastric or duodenal ulcer bleeding related to long-term use of low-dose aspirin, treatment with the proton-pump inhibitor, lansoprazole, in addition to eradication of the infection, reduced the rate of recurrence of bleeding despite continuation of aspirin.

ASTHMA

10-12 GLUCOCORTICOID AND BETA-RECEPTOR AGONIST INTERACTIONS IN ASTHMA

The preferred approach in asthma management combines a low-dose corticosteroid with an LABA. "It is notable that current management is based on pharmacological modification of two molecules that the adrenal glands produce in response to stress, namely adrenaline and hydrocortisone. It would make biological sense for these agents to potentiate each other's effects, therefore maximizing the benefits that can be obtained from smaller quantities of either agent alone."

ATRIAL FIBRILLATION

10-13 ELECTRODE POSITIONING FOR CARDIOVERSION OF ATRIAL FIBRILLATION

If control by cardioversion to sinus rhythm is chosen, positioning the electrodes anterior-posterior is more effective.

For management of AF, two alternative strategies have emerged: 1) attempts to cardiovert and maintain sinus rhythm, or 2) attempts to maintain ventricular rate control while AF continues and is treated with long-term anticoagulation.

Cumulatively, the data suggest that, compared with heart-rate control, maintaining sinus rhythm does *not* confer risk-benefits for mortality or thromboembolic events, or for major quality-of-life improvements.

12-2 A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

None of the presumed benefits of rhythm control by cardioversion were confirmed by this study.

The strategy of restoring and maintaining sinus rhythm by cardioversion had no clear advantage over the strategy of controlling ventricular rate, and allowing the AF to continue.

Patients in the cardioversion group were significantly more likely to be hospitalized and have adverse drug effects. This has some cost considerations.

Rate control (with drugs alone) should be considered a primary approach to therapy and rhythm control (by attempted cardioversion &/or drugs), may be abandoned early if it is not fully satisfactory.

BEREAVEMENT

6-19 SPIRITUAL BELIEFS MAY AFFECT OUTCOME OF BEREAVEMENT

Absence of spiritual belief may be a risk factor for delayed or complicated grief. People who profess stronger spiritual beliefs seem to resolve their grief more rapidly and completely after the death of a close person.

BETA-BLOCKERS

2-1 BETA-BLOCKERS IN HEART FAILURE: Clinical Applications

Beta-blockers should be initiated only in HF patients who are clinically euvolemic or receiving stable doses of diuretics without signs of fluid overload (pulmonary rales, jugular venous distention, or more than minimal peripheral edema).

Although there is currently insufficient evidence to recommend beta-blocker use in patients with asymptomatic LV dysfunction, guidelines suggest that they should be given because they reduce progression to HF.

Dosing should be guided by "start low" (about 1/10 the maximum dosage), "go slow" principle. This calls for doubling the dose every 2 to 4 weeks until the target is reached. When a dose is titrated upward, symptomatic hypotension can be expected to be greatest within 24 hours and improve within the next few doses.

There is some evidence for benefit from continuing very low doses of beta-blocker.

"All heart failure patients with left ventricular systolic dysfunction should be considered for beta-blockers to reduce morbidity and prevent mortality."

2-2 BETA-BLOCKER THERAPY IN HEART FAILURE: Scientific Review

Acute treatment with beta-blockers decreases BP and cardiac index; long-term administration is associated with significant increases in ejection fraction and cardiac index, and a decrease in left ventricular diastolic pressure. A decrease in myocardial mass and LV volume improves hemodynamics. Beta-blockers have been evaluated in more than 10 000 patients with all grades of HF. Five meta-analyses have arrived at the same conclusion: beta-blockers are associated with a consistent 30% reduction in mortality and a 40% reduction in hospitalizations for HF. (NNT 1 year to prevent one death = 26.)

"The evidence suggests that virtually all patients with heart failure caused by LV systolic dysfunction benefit from beta-blockers."

3-5 BETA-BLOCKERS AND REDUCTION OF CARDIAC EVENTS IN NON-CARDIAC SURGERY

Use of beta blocker therapy perioperatively significantly reduces cardiac morbidity and mortality in patients at high risk.

This is an important clinical consideration for primary care clinicians whose patients are contemplating high risk surgery.

7-14 BETA-BLOCKER THERAPY AND SYMPTOMS OF DEPRESSION, FATIGUE, AND SEXUAL DYSFUNCTION

Beta-blocker therapy, compared with placebo, was *not* associated with substantial risk of depression, fatigue and sexual dysfunction. These small risks should be put in the context of the documented benefits of beta-blockers.

BODY MASS INDEX

10-1 BODY MASS INDEX, WAIST CIRCUMFERENCE, AND HEALTH RISK

Health risk is greater in individuals with high WC (> 40 inches in men and > 35 Inches in women) regardless of BMI category, including individuals with normal weight. A high WC independently predicts obesity-related disease.

BONE MINERAL DENSITY (See OSTEOPOROSIS)

BREAST CANCER

3-10 LONG-TERM EFFECTS OF MAMMOGRAPHY SCREENING: UPDATED OVERVIEW OF THE SWEDISH RANDOMISED TRIALS

The effect of BC screening in terms of BC mortality reduction persists after long-term follow up. The benefit is highest in women age 55-69 at randomization. The recent criticism against the Swedish trial is misleading and unfounded.

(*By my calculation, screening in the Swedish trial was associated with one death from BC prevented each year for every 1000 women screened. RTJ)*

Mammography is so engrained in our society, it would be difficult for primary care clinicians to deny it to their patients.

6-15 ORAL CONTRACEPTIVES AND THE RISK OF BREAST CANCER

Among women age 35-64, current or former use of OC was *not* associated with a significantly increased risk of BC.

Practical point: Primary care clinicians may reassure patients taking birth control pills.

11-8 USE OF POSTMENOPAUSAL HORMONES, ALCOHOL, AND RISK FOR INVASIVE BREAST CANCER

Women who use PMH and consume an average of *over* one alcoholic drink daily had a significantly increased risk of BC, independent of the risk of using PMH alone. “Women who are currently using PMH may wish to consider the added risks of regular alcohol consumption.”

BRONCHITIS

1-6 REDUCING ANTIBIOTIC USE FOR ACUTE BRONCHITIS IN PRIMARY CARE

Most previously well adults who develop acute bronchitis were judged not to need antibiotics. Reassuring these patients and sharing uncertainty about the value of antibiotics in acute bronchitis is a safe strategy and reduces antibiotic use.

Primary care clinicians should use the "if" prescription more often.

5-12 AZITHROMYCIN FOR ACUTE BRONCHITIS

Azithromycin was no more effective than low-dose vitamin C for treatment of acute bronchitis in adults.

CANCER (See organ cancers; eg, breast cancer; prostate cancer)

CANCER OF THE CERVIX (See HUMAN PAPILLOMA VIRUS)

CARDIOVASCULAR DISEASE

1-1 COLLABORATIVE META-ANALYSIS OF RANDOMIZED TRIALS OF ANTIPLATELET THERAPY FOR PREVENTION OF DEATH, MYOCARDIAL INFARCTION, AND STROKE IN HIGH RISK PATIENTS

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Primary care clinicians should prescribe aspirin more often for secondary prevention of cardiovascular events.

1-2 ASPIRIN FOR THE *PRIMARY* PREVENTION OF CARDIOVASCULAR EVENTS

Five trials have examined the effects of daily or every-other-day aspirin for primary prevention over 4 to 7 years. Most subjects were men over age 50. Meta-analysis of pooled data showed that aspirin reduced the risk of coronary heart disease by 28%. No effect on total mortality or stroke.

For patients at high risk of coronary heart disease (5% over 5 years) prophylactic aspirin would lead to avoidance of 6 to 20 CHD episodes over the 5 years.

Primary prevention is not recommended for those with a risk of 1% per year.

The clinician's challenge is to judge the degree of risk and to match the patient's concerns and wishes with the risk. Many individuals will benefit from primary prevention with aspirin.

2-15 ROLAXIFENE AND CARDIOVASCULAR EVENTS IN OSTEOPOROTIC POSTMENOPAUSAL WOMEN

There was no evidence that raloxifene (a selective estrogen receptor modulator) caused an early increase in risk of CV events in the group overall, or in the subset of women at high risk for CHD.

Raloxifene for 4 years significantly reduced the risk of CV events among the subgroup at high risk and among those with established CHD.

3-13 CARDIOVASCULAR MORBIDITY AND MORTALITY IN LOSARTAN INTERVENTION FOR ENDPOINT REDUCTION IN HYPERTENSION STUDY (LIFE): A Randomized Trial Against Atenolol

The angiotensin II blocker losartan prevented more combined cardiovascular morbidity and death and stroke than the beta-blocker atenolol for a similar reduction in BP. “Losartan seems to confer benefits (*in relation to stroke*) beyond reduction in BP.”

Another example of “spin” . The benefit of losartan applied to only one person out of 59 over 5 years. This may be “highly significant” statistically, but hardly significant clinically. Primary care clinicians should beware! I believe the conclusions of this study may mislead clinicians who do not have the time to judge the study in detail. Putting a favorable “spin” on conclusions of studies seems to be occurring more frequently.

3-5 BETA-BLOCKERS AND REDUCTION OF CARDIAC EVENTS IN NON-CARDIAC SURGERY

Use of beta blocker therapy perioperatively significantly reduces cardiac morbidity and mortality in patients at high risk.

This is an important clinical consideration for primary care clinicians whose patients are contemplating high risk surgery.

4-11 BLOOD LEVELS OF LONG CHAIN N-3 FATTY ACIDS AND THE RISK OF SUDDEN DEATH.

These prospective data suggest that long chain n-3FA found in fish may reduce the risk of sudden death from cardiac causes, even in men without a history of cardiovascular disease. More than 50% of all sudden deaths from cardiac causes occur in people with no history of cardiac disease. Fish are an important part of the healthy diet.

6-17 NUT CONSUMPTION AND DECREASED RISK OF SUDDEN CARDIAC DEATH IN THE PHYSICIAN’S HEALTH STUDY

This study suggests that the inverse association between nut consumption and total coronary heart disease death is primarily due to a reduction in risk of sudden cardiac death. Nuts are part of the healthy diet.

6-4 THERAPY WITH HYDROXYMETHYLGLUTARYL COENZYME-A REDUCTASE INHIBITORS (STATINS) AND ASSOCIATED RISK OF INCIDENT CARDIOVASCULAR EVENTS IN OLDER ADULTS

Use of statins was associated with decreased risk of incident cardiovascular events among elderly adults

Age per se in not a contraindication.

6-5 STATIN THERAPY IN OLDER PERSONS: Pertinent Issues

There is growing evidence that LDL-lowering therapy is effective in reducing risk for CHD in older persons. Statins are recommended for select elderly individuals.

7-2 MRC/BHF HEART PROTECTION STUDY OF CHOLESTEROL LOWERING WITH SIMVASTATIN IN 20 536 HIGH-RISK INDIVIDUALS.

Lowering LDL with simvastatin produced substantial benefits in reduction of cardiovascular events in a wide range of high-risk patients, irrespective of their initial cholesterol levels.

Benefits appeared to be largely independent of, and hence additional to, those of all other treatments being used by participants.

The benefits in reducing risk of stroke should resolve any uncertainty about the effects of statins on the risk of stroke.

It has been suggested that there might be a threshold of LDL below which lowering would not further reduce risk. This study demonstrated unequivocally that there is no threshold. Lowering LDL from 116 to 78 reduced vascular events over 5 years, similar to the reduction in events following lowering from 134 to 96. “If a threshold exists it is a LDL lower than 77 mg/dL and a total cholesterol below 135.”

9-7 WALKING COMPARED WITH VIGOROUS EXERCISE FOR THE PREVENTION OF CARDIOVASCULAR EVENTS IN WOMEN

Walking and vigorous exercise were associated with similar risk reductions.

Both walking and vigorous exercise were associated with substantial reductions in incidence of cardiovascular events among postmenopausal women, irrespective of race, ethnic group, age and body mass index. Prolonged sitting increased risk.

11-17 COMPARISON OF C-REACTIVE PROTEIN AND LOW-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS IN PREDICTION OF FIRST CARDIOVASCULAR EVENT.

CRP is a stronger predictor of cardiovascular risk than LDL-c. It adds to prognostic information to that conveyed by the Framingham risk score.

11-7 EXERCISE TO REDUCE CARDIOVASCULAR RISK – HOW MUCH IS ENOUGH?

Exercise is associated with a graded response in a number of different lipoprotein variables. The ensemble of changes is likely to be beneficial. The study documented an effect of exercise on lipoproteins with only minimal changes in body weight and provides a ray of hope for those who find it easier to exercise than lose weight.

12-10 EFFECTS OF SUBCLINICAL THYROID DYSFUNCTION ON THE HEART.

“Subclinical thyroid dysfunction is not a compensated biochemical state.” Timely treatment could help prevent cardiovascular involvement.” (Eg, judicious thyroxine replacement for high TSH states and beta-blockers for low TSH states.)

12-3 THE METABOLIC SYNDROME AND TOTAL AND CARDIOVASCULAR DISEASE MORTALITY IN MIDDLE-AGED MEN

Middle-aged men with the MET-S had an increased cardiovascular and overall mortality even in the absence of baseline diabetes and CVD. Early identification, treatment, and prevention of the MET-S presents a major challenge.

“The importance of the metabolic syndrome from a clinical and public health perspective may be greatest in it earliest stages, before development of CVD or diabetes.”

Modest lifestyle interventions can improve components of the MET-S.

CARPAL TUNNEL SYNDROME

9-8 SPLINTING VS SURGERY IN THE TREATMENT OF CARPAL TUNNEL SYNDROME

Treatment with open carpal tunnel release surgery resulted in better outcomes than treatment with wrist splinting for patients with CTS.

CERVICAL CANCER

4-10 MALE CIRCUMCISION, PENILE HUMAN PAPILLOMA VIRUS INFECTION, AND CERVICAL CANCER IN FEMALE PARTNERS.

Male circumcision was associated with a reduced risk of penile HPV.

In the case of men with a history of multiple sexual partners, a reduced risk of cervical cancer was evident in their current female partner.

A reasonable indication for circumcision**.**

11-3 A CONTROLLED TRIAL OF A HUMAN PAPILLOMA VIRUS TYPE 16 VIRUS

A HPV-16 vaccine given to young women reduced incidence of HPV-16 infection and cervical intraepithelial neoplasia. The vaccine may prevent cervical cancer.

CHRONIC FATIGUE SYNDROME

1-7 CHRONIC FATIGUE SYNDROME; A STEP TOWARD AGREEMENT

The Royal College of Physicians of the UK has issued a new report on the chronic fatigue syndrome (CFS) This editorial hopes it will mark a turning point in the history of the illness.

There was agreement that the illness "is a relatively common clinical condition which can cause profound illness and disability and can have a very substantial impact on the individual and family." It can affect both sexes, and a wide range of ages, even children. "It is no longer acceptable for clinicians to state that they do not 'believe' in CSF. Inaction . . .due to ignorance or denial of the condition is not excusable." A significant minority of patients who are very severely affected often receive the least attention. Patients need a positive and early diagnosis and appropriate management and advice. Patient organizations have an important role to play in this.

Primary care clinicians should accept the fact that CFS is "real" and support the patient.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

8-12 NEW STRAINS OF BACTERIA AND EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Isolation of new strains of bacteria are associated with acute exacerbations. This strengthens the use of antibiotics to treat.

12-8 CORTICOSTEROID THERAPY FOR PATIENTS WITH ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

Short courses of systemic corticosteroids in acute exacerbations of COPD improve spirometric and clinical outcomes.

COLONOSCOPY

6-18 RESULTS OF SCREENING COLONOSCOPY AMONG PERSONS 40 TO 49 YEARS OF AGE

Up to 1000 persons this age would have to be screened with colonoscopy to detect one cancer. Sigmoidoscopy would detect about 50% of these.

The current recommendations to begin screening at age 50 are unchanged.

COLORECTAL CANCER

4-9 SINGLE FLEXIBLE SIGMOIDOSCOPY SCREENING TO PREVENT COLORECTAL CANCER

This flex-sig screening regimen was acceptable, feasible, and safe. The prevalence of neoplasia detected was high.

Some patients who refuse colonoscopy may accept this less stressful procedure, even if they know it is incomplete screening.

CONGESTIVE HEART FAILURE (See HEART FAILURE)

CORONARY HEART DISEASE

2-16 OVERCOMING RESTENOSIS WITH SIROLIMUS

Preliminary studies using sirolimus coated stents have been quite promising and should reduce restenosis rate.

This will probably be another advance tilting patients with coronary disease toward PTCA and away from CABG.

4-3 LONG-TERM EFFECTIVENESS AND SAFETY OF PRAVASTATIN IN 9014 PATIENTS WITH CORONARY HEART DISEASE AND AVERAGE CHOLESTEROL CONCENTRATIONS: THE LIPID TRIAL FOLLOW-UP

Long-term therapy (8 years) yields benefits in addition to 6 years treatment. Benefits of therapy continued to accumulate after years of therapy. Older patients, women, and patients with cholesterol <210 mg/dL benefit. Incidence of stroke is reduced.

Almost all patients with established coronary atherosclerotic heart disease should be treated with long-term statins.

6-17 NUT CONSUMPTION AND DECREASED RISK OF SUDDEN CARDIAC DEATH IN THE PHYSICIAN'S HEALTH STUDY

This study suggests that the inverse association between nut consumption and total coronary heart disease death is primarily due to a reduction in risk of sudden cardiac death.

Nuts are part of the healthy diet.

6-12 TROPONIN T LEVELS IN PATIENTS WITH ACUTE CORONARY SYNDROMES, WITH AND WITHOUT RENAL DYSFUNCTION

Given that renal dysfunction is common in patients with coronary disease, the ability of cardiac troponin levels to predict outcomes irrespective of creatinine clearance expands their clinical usefulness. Practical point: cardiac troponin T predicted short-term prognosis in patients with ACS regardless of their level of creatinine clearance.

6-13 SIROLIMUS-ELUTING CORONARY STENTS

A sirolimus-eluting stent, as compared with a standard stent, shows considerable promise for prevention of neointimal restenosis.

The gradual elution occurs over a period of 30 days. Only a small quantity of the drug is required. This avoids systematic adverse effects. Primary care clinicians follow developments along with their cardiologist consultants.

COST EFFECTIVENESS

6-3 WHEN INCREASED THERAPEUTIC BENEFIT COMES AT INCREASED COST

A study in this issue of NEJM [1] compared cost effectiveness in reducing recurrent cardiovascular events using 1) aspirin alone, 2) clopidogrel alone, and 3) aspirin + clopidogrel. (A secondary prevention study)The investigators estimated cost effectiveness of the strategies. Given the extraordinarily low cost of aspirin, the estimated cost of each quality-adjusted year of life gained using aspirin alone was $11 000. Clopidogrel alone or in combination would cost $130 000 for each quality-adjusted year of life gained. (Present cost of one 75 mg tablet of clopidogrel [Plavix] is over $3) Is the benefit worth the harms and cost? Practical point: Primary care clinicians must increasingly consider the cost factor in the benefit/harm-cost ratio.

COX-2 INHIBITOR

1-15 EFFICACY OF ROFECOXIB, CELECOXIB, AND ACETAMINOPHEN IN OSTEOARTHRITIS OF THE KNEE

Rofecoxib 25 mg/d provided efficacy advantages over acetaminophen 4000 mg/d, and celecoxib 200 mg/d for symptomatic knee arthritis.

Despite this report, primary care clinicians will consider individual-patient response to various NSAIDs. Acetaminophen may be the best first-choice.

9-8 EFFICACY, TOLERABILITY AND UPPER GASTROINTESTINAL SAFETY OF CELECOXIB FOR TREATMENT OF OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS: Systematic Review

Celecoxib was as effective as other NSAIDS for relief of symptoms of arthritis, and had significantly improved gastrointestinal safety and tolerability even when aspirin was co-administered.

9-10 OBSERVATIONAL STUDY OF UPPER GASTROINTESTINAL HAEMORRHAGE IN ELDERLY PATIENTS GIVEN SELECTIVE CYCLO-OXYGENASE-2 INHIBITORS OR CONVENTIONAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS.

This population-based observational study found a lower short-term risk of upper gastrointestinal hemorrhage associated with selective COX-2 inhibitors compared with non-selective. But, risk of hemorrhage in those taking celecoxib was *not* increased compared with non-takers.

9-11 EFFICACY AND SAFETY OF COX-2 INHIBITORS

"At present, it is still difficult to give patients an honest, accurate, and understandable account of the balance between relief of pain and improved function on one hand and the likelihood of serious adverse effects on the other."

More information is required for prescribers to be able to make rational decisions about the use of these agents, particularly in older people in whom co-morbidity is common.

They may be safer, but they are not safe.

11-11 TREATING ACUTE GOUTY ARTHRITIS WITH SELECTIVE COX 2 INHIBITORS

Work just as well as other NSAIDs, but no better. Is the added cost worthwhile?

C-REACTIVE PROTEIN

11-17 COMPARISON OF C-REACTIVE PROTEIN AND LOW-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS IN PREDICTION OF FIRST CARDIOVASCULAR EVENT.

CRP is a stronger predictor of cardiovascular risk than LDL-c. It adds to prognostic information to that conveyed by the Framingham risk score.

DEATH AND DYING

4-4 TOO MUCH MEDICINE?

Death, pain, and sickness are part of being human. All cultures have developed means to help people cope with all three. Indeed good health care can even be defined as being successful in coping with these realities.

Modern medicine has launched an inhuman attempt to defeat death, pain, and sickness. It has sapped the will of the people to suffer reality. "People are conditioned to *get* things rather than to *do* them. They want to be taught, moved, treated, and guided rather than to learn, to heal, and to find their own way."

The more a society spends on health care, the more likely are its inhabitants to regard themselves as sick.

The concept of what is and what is not a "disease" is extremely slippery. It is easy to create new diseases and new treatments. Many of life's normal processes – birth, aging, sexuality, unhappiness, and death can be medicalized.

Primary care clinicians bear the responsibility of balancing medicalization with undertreatment. (Application of the "art" of medicine to the individual.)

4-5 UNDERSTANDING THE TREATMENT PREFERENCES OF SERIOUSLY ILL PEOPLE

The desirability of an intervention depends heavily on its outcome. Elicitation of patients' preferences should be based on outcomes rather than specific treatments

Planning should take into account patients' attitudes toward the burden of treatment, and the likelihood of adverse functional and cognitive outcomes. Discussions of advanced care planning should shift from whether patients would accept or reject specific treatments, to what they consider acceptable in terms of quality-of-life, the burdens of treatment, and the probability of successful outcome

"Clearly, treatment outcomes are a strong determinant of patients' preferences."

We should try to give terminally patients the best advice about possible outcomes and then let them choose the course.

4-6 BETWEEN HOPE AND ACCEPTANCE: The Medicalization of Dying

An active, rather than a passive approach to the care of dying people, is supplanting the fatalistic resignation of the doctor ("There is nothing more we can do"). We are challenged to find new and imaginative ways to continue caring up to the end of life.

The challenge for palliative physicians is no different from that facing their counterparts elsewhere in medicine: how to reconcile high expectations of technical expertise with calls for a humanistic and ethical orientation. Primary care clinicians should continue care and caring until the end of life.

DEMENTIA

1-13 ALCOHOL CONSUMPTION AND RISK OF DEMENTIA: THE ROTTERDAM STUDY

Light-to-moderate alcohol consumption was associated with a reduced risk of dementia in elderly individuals over age 65. The effect seemed to be unchanged by the type of alcohol consumed.

Although benefits in reducing incidence of dementia may be very modest, reports of low-dose alcohol consumption have been invariably favorable for a number of risks.

2-14 PLASMA HOMOCYSTEINE AS A RISK FACTOR FOR DEMENTIA AND ALZHEIMER'S DISEASE

An increased plasma homocysteine level was a strong, independent risk factor for the development of dementia and Alzheimer's disease.

The homocysteine connection lingers on in the literature. While not proven, the benefit/harm-cost of folate, B12, and B6 therapy may be high because harm and costs are low.

6-10 FOLIC ACID, AGEING, DEPRESSION, AND DEMENTIA

Folates are important for the nervous system at all ages. There is growing evidence of their involvement in the aging brain, especially in mood and cognitive function. Low folate concentrations in serum, red cells, and cerebrospinal fluid, and the associated rise in plasma homocysteine, are associated with depression and dementia. "Some of the deficiency may be related to ageing, some may be secondary to mental illness, and some primary. But, whether it is primary or secondary, open and controlled treatment studies confirm an aetological link with specific effects of the vitamin on mood, drive, initiative, alertness, concentration, psychomotor speed, and social activity." "Clearly, further clinical trials in precisely defined clinical categories are needed."

Daily multivitamin supplement contains RDA amount of folic acid.

6-6 WHAT WE NEED TO KNOW ABOUT AGE-RELATED MEMORY LOSS

Strategies for maintaining brain health.

Stress reduction

Physical activity

Healthy diet: (Include a daily multivitamin supplement).

Mental activity

Social involvement

Adopt lifestyle measures to reduce risk of atherosclerotic disease in order to protect the cerebrovascular circulation.

This includes moderate amounts of alcohol and smoking cessation.

Putative protective factors: NSAIDs, postmenopausal estrogen, statin drugs, and aerobic conditioning.

10-18 FISH, MEAT, AND RISK OF DEMENTIA: A Cohort Study

Regular consumption of fish was associated with a lower risk of future development of dementia.

10-17 PREVENTION OF DEMENTIA WITH ANTIHYPERTENSIVE TREATMENT

New Evidence from the Systolic Hypertension in Europe (Syst-Eur) Trial

A 4-year follow-up study extending antihypertension therapy reinforced the evidence that BP-lowering therapy initiated with a long-acting dihydropyridine calcium blocker (nitrendipine) protects against dementia in older patients with systolic hypertension.

DEPRESSION

5-2 SCREENING FOR DEPRESSION

Asking two simple questions about depressed mood detects a majority of depressed patients, and in some cases performs better than the original instruments from which they were derived:

1. "Over the past 2 weeks have you felt down, depressed, or hopeless?"
2. "Over the past 2 weeks have you felt little interest or pleasure in doing things?"

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“Clearly, further clinical trials in precisely defined clinical categories are needed.”

Daily multivitamin supplement contains RDA amount of folic acid.

11-15 META-ANALYSIS OF EFFECTS AND SIDE-EFFECTS OF LOW DOSAGE TRICYCLIC ANTIDEPRESSANTS IN DEPRESSION

Treatment of depression with low dose tricyclics is effective in many patients. Adverse effects and withdrawals are lees frequent than with “standard” doses. .

DIABETES

2-4 REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN

Lifestyle changes (physical activity, diet, weight loss) and metformin (*Glucophage*) both reduced incidence of diabetes in persons at high risk. Lifestyle changes were more effective.

This is one of several recent studies concluding that diabetes 2 can be prevented by improving lifestyle. Indeed, it might be possible to “cure” diabetes by lifestyle – ie, reduce glucose intolerance to a level below the WHO definition. Many people would rather take a pill to prevent diabetes than discipline themselves. I think this is misuse of an important drug.

2-5 DIETARY PATTERNS AND RISK OF TYPE 2 DIABETES MELLITUS IN MEN

Compared with the prudent diet (vegetables, fruit, fish, poultry, whole grains), the western type diet (red meat, processed meats, french fries, high-fat dairy, refined grains, sweets and deserts) was associated with an increased risk of DM-2. The more outrageous the intake of western type foods, the higher the risk. Combining a long history of intake of western type foods with obesity and a sedentary lifestyle greatly increased risk. However, the diet was independently related to these factors, and the western diet alone increased risk.

Another important benefit of a disciplined lifestyle.

5-10 EFFECTS OF MODERATE ALCOHOL INTAKE ON FASTING INSULIN AND GLUCOSE CONCENTRATIONS AND INSULIN SENSITIVITY IN POSTMENOPAUSAL WOMEN.

Consumption of 30 g/d of ethanol had beneficial effects on fasting insulin, insulin sensitivity, and triglyceride concentrations in non-diabetic postmenopausal women. This was independent of body mass index.

6-7 GLUCOSE METABOLISM IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND NO PREVIOUS DIAGNOSIS OF DIABETES MELLITUS.

Previously undiagnosed diabetes and impaired glucose tolerance are common in patients with AMI. These abnormalities can be detected early. They could be used as early markers of high-risk. Practical point: Surveillance and treatment of glucose intolerance may improve prognosis in patients with acute myocardial infarction.

6-8 ACARBOSE FOR PREVENTION OF TYPE 2 DIABETES MELLITUS

Acarbose, by reducing glycemic load, delays development of type 2 diabetes in patients with impaired glucose tolerance.
Practical point: Reduce glycemic load to lessen progression of glucose intolerance and risk of diabetes.

1-4 ORAL ANTIHYPERGLYCEMIC THERAPY FOR TYPE 2 DIABETES: SCIENTIFIC REVUE

Large trials in the UK compared metformin with placebo and intensive sulfonylurea-insulin therapy. With similar HbA1c reductions, metformin was associated with up to 40% fewer diabetic-related deaths, all cause mortality, risk of myocardial infarction, and all macrovascular endpoints.

Metformin is the only drug associated with weight loss, or at least weight neutrality. It has become the most widely prescribed single antihyperglycemic drug. It is generally regarded as the best first-line agent, at least in the obese patient. (Most patients with DM2 are overweight.) Its virtual lack of hypoglycemia makes it an attractive option.

There is no compelling reason in terms of antihyperglycemic effect alone, to favor one of the major class over another. However, the benefit of metformin demonstrated in the UK study (UKPDS) (which showed a lack of hypoglycemia and no weight gain) make it one of the most attractive options for obese — if not all— patients with DM2.

Combination therapy is a logical approach, given the multiple pathophysiological lesions in DM2. Indeed, most patients after a few years will require more than one drug for good control. A second drug may provide additive effect on lowering HbA1c. There is no evidence that one specific combination is any more effective than another in lowering glucose levels.

Only sulfonylureas and metformin have been shown to reduce microvascular complication. Metformin exhibits additional benefits on macrovascular risk. The popularity of metformin and thiazolidinediones is increasing since these agents avoid the risk of hypoglycemia and allow treatment of patients already near the euglycemic range.

"Most patients will require combination as their disease progresses."

Primary care clinicians consider selecting metformin as first-choice.

1-17 US RELAXES SUGAR BAN FOR PEOPLE WITH DIABETES

The American Diabetes Association has released new nutritional guidelines for diabetes control. It relaxes dietary restrictions on high sugar content foods. (*Diabetes Care 2002;25:148-98, 200-12*).

Now, someone with diabetes would be able to indulge in an occasional slice of sugary pie and drink moderate amounts of alcohol without violating their diet. A moderate amount of daily alcohol intake poses no threat and may be healthy.

Less than 10% of calorie intake should be derived from saturated fats and cholesterol intake should be no more than 300 mg/d.

The original may be worth accessing.

3-2 PREVALENCE OF IMPAIRED GLUCOSE TOLERANCE AMONG CHILDREN AND ADOLESCENTS WITH MARKED OBESITY

Impaired glucose tolerance is highly prevalent among children and adolescents with severe obesity. It is associated with insulin resistance while beta-cell function is still relatively preserved.

Overt DM2, which occurred in a few adolescents, was linked to beta-cell failure.

Impaired glucose tolerance (2 h pc glucose 126-200) is a more sensitive marker of risk of DM2 than elevated fasting glucose (110-125). This is an important clinical point.

Primary care clinicians should maximize efforts to reduce obesity in their adolescent patients.

5-8 TYPE 2 DIABETES IN PREGNANCY: A Growing Concern

The higher rates of type-2 diabetes in pregnancy bring with them higher rates of maternal and fetal morbidity, and might even contribute to the increasing incidence of type-2 diabetes. Better recognition of this growing entity by primary care physicians who see these patients before pregnancy, and a heightened awareness of the need for pre-pregnancy counseling about preconception glycemic control would lead to less morbidity and mortality from congenital anomalies.

Primary care clinicians have the responsibility and opportunity to reduce likelihood of development of type-2 diabetes in adolescents and young women. Those at risk should be screened by post-glucose challenge (glucose intolerance; post challenge blood glucose above 140). Education and reduction of risk may avert a tragedy.

5-1 THE GLYCEMIC INDEX

The rate of carbohydrate absorption after a meal, as quantified by the glycemic load (GL) has significant effects on postprandial hormonal and metabolic responses. High GL meals produce an initial period of high blood glucose and insulin levels. This may be followed by reactive hypoglycemia, counter-regulatory hormone secretion, and elevated free fatty acid concentrations. These events may promote excessive food intake, beta cell dysfunction, dyslipidemia, and endothelial dysfunction. As a result, the risk of obesity, type 2 diabetes, and heart disease increases – a hypothesis that derives considerable support from clinical trials and epidemiological analyses.

Despite controversy, clinical use of GL as a qualitative guide to food selection is prudent in view of the preponderance of evidence suggesting benefit and absence of adverse effects.

7-6 ASSOCIATION OF HEALTH LITERACY WITH DIABETES OUTCOMES.

Two thirds of patients in this sample who had a high school education or less, had inadequate health literacy.

Among primary care patients with type 2 diabetes, inadequate health literacy was independently associated with poorer glycemic control and higher rates of retinopathy. Inadequate health literacy contributes to the disproportionate burden of diabetes-related problems among

disadvantaged populations. (This large subset of patients is not included in randomized, controlled trials. Therefore primary care clinicians must treat these individuals empirically. RTJ)

7-7 METFORMIN: AN UPDATE

In treatment of type 2 diabetes, metformin has an excellent safety profile. It is effective as monotherapy and in combination with other drugs. It does not promote weight gain and may even cause weight reduction. It appears to have substantial benefit on lipid metabolism, clotting factors, and platelet function. It improves vascular relaxation and probably reduces BP. These cardio-protective benefits are in addition to its anti-hyperglycemic effect.

10-3 COMPLICATIONS OF DIABETES IN ELDERLY PEOPLE

As diabetes increasingly becomes a disease of elderly people, some of its unappreciated complication must be addressed. These include:

Cognitive disorders

Physical disability

Falls and fractures

Other geriatric syndromes

At least half of older diabetic adults will have a major physical or cognitive disability.

11-2 NUT AND PEANUT BUTTER CONSUMPTION AND RISK OF TYPE 2 DIABETES IN WOMEN

Higher nut and peanut butter intake was related to a reduced risk of DM-2

Regular nut consumption can be recommended as a replacement for consumption of refined grains and red or processed meats.

DIGOXIN

10-15 DIGOXIN – NEW PERSPECTIVE ON AN OLD DRUG.

Digoxin has a narrow therapeutic window. In patients with normal cardiac rhythm, the beneficial hemodynamic, neuro-hormonal, and clinical effects are found with a low concentration of approximately 0.7 ng/mL. Additional benefits are not seen with higher doses traditionally considered therapeutic (with serum concentrations of 1.0 to 1.5 ng/mL). These higher concentrations may predispose to arrhythmias.
Since digoxin may result in adrenergic stimulation at higher concentrations, or in patients with ischemia, the combination of digoxin with beta-blockade may have theoretical advantages

We should not abandon a therapy that may help patients with heart failure. Rather we should use a dose that will result in a serum concentration lower than 1.0 ng per milliliter.

DOCTOR-PATIENT RELATIONSHIP

9-12 SPONTANEOUS TALKING TIME AT START OF CONSULTATION IN OUTPATIENT CLINIC.

The average patient visiting a doctor in the USA gets 22 seconds for his initial statement, then the doctor takes the lead. Doctors may assume that patients will mess up the time schedule if allowed to talk as long as they wish.
This study asked – How long will patients actually talk, at least initially, if they are not interrupted? How long would it take outpatients to indicate they have completed their story?

Mean talking time was 92 seconds. About 3 out of 4 patients completed their statement within 2 minutes. Few patients talked more than 5 minutes

9-13 PATIENTS' PERCEPTIONS OF ENTITLEMENT TO TIME IN GENERAL PRACTICE FOR DEPRESSION.

Patients' self-impose restraint in taking up doctors' time. This has important consequences for the recognition and treatment of depression. Doctors need to have a greater awareness of patients' anxieties about time and should move to allay such anxieties by preemptive reassurance and reinforcing patients' sense of entitlement to time.

9-14 PATIENT'S VIEWS OF THE GOOD DOCTOR

"Technical skill, humaneness, competence, time for care, listening, involving patients in decisions, communication, trust, support, reassurance" Quite an order. Nevertheless, "Most doctors are good doctors in the eyes of most patients."

DRUG SAFETY

5-6 SAFETY OF NEWLY APPROVED DRUGS.

How reluctant should the primary care clinician be to prescribe a new drug? Certainly, by history, physicians have reason for concern about undiscovered toxicities. Even long-marketed drugs sometimes are shown to have unexpected toxicities. “There is no duration of use that allows a physician complete assurance that additional toxicity will not emerge.” But it is incorrect to describe the introduction of unsafe drugs as frequent.

Physicians contemplating prescribing a new drug should consider carefully the reason for the choice, particularly when an equally effective alternative is available. If there is sound reason to use a recently approved drug, there is no need to deny patients the treatment.

DYSPEPSIA

4-8 TREATING *HELICOBACTER PYLORI* INFECTION IN PRIMARY CARE PATIENTS WITH UNINVESTIGATED DYSPEPSIA

“Testing (with C-urea breath test) and treating” to eradicate *H pylori* in patients with uninvestigated dyspepsia provided long-term relief of symptoms and reduced health costs.

Patients in the USA with *H pylori* infection (with or without dyspepsia) should be treated.

EATING DISORDERS

10-11 THE SCOFF QUESTIONNAIRE AND CLINICAL INTERVIEW FOR EATING DISORDERS IN GENERAL PRACTICE.

Do you ever make yourself SICK because you feel uncomfortably full?

Do you worry you have lost CONTROL over how much you eat?

Have you recently lost more than ONE stone (14 pounds)?

Do you believe yourself to be FAT?

Would you say that FOOD dominates your life?

The predictive value of a positive test was low; predictive value of a negative test was high. (Ie, if the test is positive, a definite diagnosis cannot be made – further observation is needed. If the test is negative, it is highly likely that the patient does not have A-B.

ELECTROCARDIOGRAPHY

10-13 ELECTRODE POSITIONING FOR CARDIOVERSION OF ATRIAL FIBRILLATION

If control by cardioversion to sinus rhythm is chosen, positioning the electrodes anterior-posterior is more effective.

For management of AF, two alternative strategies have emerged: 1) attempts to cardiovert and maintain sinus rhythm, or 2) attempts to maintain ventricular rate control while AF continues and is treated with long-term anticoagulation.

Cumulatively, the data suggest that, compared with heart-rate control, maintaining sinus rhythm does *not* confer risk-benefits for mortality or thromboembolic events, or for major quality-of-life improvements.

EMERGENCY CONTRACEPTION

8-11 EMERGENCY CONTRACEPTION

A review article. The public and patients should be educated about the difference between emergency contraception and abortion. Hormonal emergency contraception can substantially reduce the burden of unintended pregnancies. It does not interrupt a pregnancy. It prevents a pregnancy from starting.

12-12 LOW DOSE MIFEPRISTONE AND TWO REGIMENS OF LEVONORGESTREL FOR EMERGENCY CONTRACEPTION

Single-dose mifepristone, single-dose levonorgestrel and two-dose levonorgestrel were very efficacious and prevented a high percentage of pregnancies. There was no difference in efficacy.

A single dose of levonorgestrel can be substituted for the two-dose regimen. Efficacy extends, but diminishes, for up to 5 days.

ESOPHAGEAL CANCER

4-2 GASTROESOPHAGEAL REFLUX, BARRETT ESOPHAGUS, AND ESOPHAGEAL CANCER

Although strong evidence links GERD and adenocarcinoma, the risk in any given individual is low. Given the low incidence of cancer, and the lack of demonstrated efficacy of endoscopic screening, insufficient evidence exists to endorse routine endoscopy screening for patients with chronic symptoms.

Patients with chronic, severe symptoms of GERD may be given the results of this study, and then decide for themselves. Primary care clinicians should treat these patients with proton pump inhibitors. This will reduce the risk of erosion caused by the acid reflux.

ETHICS

8-7 WITHHOLDING ANTIBIOTIC TREATMENT IN PNEUMONIA PATIENTS WITH DEMENTIA

In the Netherlands, antibiotic treatment is commonly withheld in severely demented nursing home patients with pneumonia. Especially if they are very frail.

ESTROGEN (See HORMONE REPLACEMENT THERAPY)

EVIDENCE BASED MEDICINE

6-1 PHYSICIANS' AND PATIENTS' CHOICES IN EVIDENCE BASED MEDICINE

Clinical decisions must include consideration of: the patient's clinical and physical circumstances to establish what is wrong and what treatment options are available; 2) research evidence concerning the efficacy (as reported in systematic reviews); effectiveness (as applied in the real world of clinical practice) and efficiency (the benefit/harm-cost ratio) of the options; and 3) consideration of the patient's preferences and likely actions (in terms of what interventions she or he is ready and able to accept).

Finally, clinical expertise is needed to bring these considerations together and recommend the treatment that the patient is agreeable to accepting.

The term "evidence based medicine" was developed to encourage practitioners and patients to pay due respect – no more, no less – to current best evidence in making decisions.

Best research evidence does not apply to the great majority of individual patients presenting to primary care. Primary care clinicians must deal with a large group of patients as best they can without firm evidence on which to base decisions. The clinician will extrapolate from the evidence, and rely on best clinical judgment, expert doctor-patient communication, and patient preferences.

FATTY ACIDS

4-11 BLOOD LEVELS OF LONG CHAIN N-3 FATTY ACIDS AND THE RISK OF SUDDEN DEATH.

These prospective data suggest that long chain n-3FA found in fish may reduce the risk of sudden death from cardiac causes, even in men without a history of cardiovascular disease. More than 50% of all sudden deaths from cardiac causes occur in people with no history of cardiac disease. Fish are an important part of the healthy diet.

FATTY LIVER DISEASE

4-7 NONALCOHOLIC FATTY LIVER DISEASE

"NAFLD is the most common cause of abnormal liver-test results among adults in the USA. " Obesity, type 2 diabetes, and hyperlipidemia frequently coexist. NAFLD is histologically indistinguishable from liver damage due to alcohol abuse. A net retention of lipids within hepatocytes, mostly triglycerides, is a prerequisite for NAFLD.

Insulin resistance is the most reproducible factor. Insulin resistance and hyperinsulinism leads to fat accumulation in hepatocytes.

Although symptoms of liver disease rarely develop in patients with steatotic livers they may be vulnerable to further injury when challenged by additional insults. Another good reason to prevent and treat obesity, diabetes, and dyslipidemia.

FIBROMYALGIA

7-10 PRESCRIBED EXERCISE IN PEOPLE WITH FIBROMYALGIA

Prescribed, graded aerobic exercise was effective in improving symptoms of fibromyalgia. It is simple, cheap, and potentially widely available. Compliance with the protocol was poor.

FITNESS

3-3 EXERCISE CAPACITY AND MORTALITY AMONG MEN REFERRED FOR EXERCISE TESTING

Exercise capacity was a more powerful predictor of increased risk of death than established risk factors such as hypertension, smoking, and diabetes.

Poor fitness is a modifiable risk factor. Improvements in fitness over time have been demonstrated to improve prognosis.

Health professionals should incorporate into their practices strategies to promote physical activity at all stages of life. The greatest health benefits are achieved by increasing physical activity among the least fit, including persons without, as well as persons with, cardiovascular disease. Fitness will overcome some of the risks of established risk factors. If you can't stop smoking, at least get fit!

3-4 IMPROVED CARDIORESPIRATORY ENDURANCE FOLLOWING 6 MONTHS OF RESISTANCE EXERCISE IN ELDERLY MEN AND WOMEN

Resistance exercise led to significant improvements in muscle strength, aerobic capacity, and treadmill time in older adults. It is a clinically applicable means of improving fitness. The principal finding of the study was that peak O2 consumption and treadmill time increased in a low-intensity exercise group.

Almost all older, non-fit patients, even those with localized muscle weakness, could be instructed to perform some resistance exercises. A program could easily be designed with little equipment and applied at convenient times for variable duration. A formal machine-based program as described in the article would not be necessary. Problems would be motivation and consistency. A successful program would likely enhance balance, and reduce risk of falling.

9-7 WALKING COMPARED WITH VIGOROUS EXERCISE FOR THE PREVENTION OF CARDIOVASCULAR EVENTS IN WOMEN

Walking and vigorous exercise were associated with similar risk reductions.

Both walking and vigorous exercise were associated with substantial reductions in incidence of cardiovascular events among postmenopausal women, irrespective of race, ethnic group, age and body mass index. Prolonged sitting increased risk.

11-7 EXERCISE TO REDUCE CARDIOVASCULAR RISK – HOW MUCH IS ENOUGH?

Exercise is associated with a graded response in a number of different lipoprotein variables. The ensemble of changes is likely to be beneficial. The study documented an effect of exercise on lipoproteins with only minimal changes in body weight and provides a ray of hope for those who find it easier to exercise than lose weight.

11-16 WALKING AND LEISURE-TIME ACTIVITY AND RISK OF HIP FRACTURE IN POSTMENOPAUSAL WOMEN

More leisure-time activity was associated with a lower risk of hip fractures in postmenopausal women. Moderate levels of activity, including walking, were associated with substantially lower risk.

FOLIC ACID

6-10 FOLIC ACID, AGEING, DEPRESSION, AND DEMENTIA

Folates are important for the nervous system at all ages. There is growing evidence of their involvement in the aging brain, especially in mood and cognitive function. Low folate concentrations in serum, red cells, and cerebrospinal fluid, and the associated rise in plasma homocysteine, are associated with depression and dementia. "Some of the deficiency may be related to ageing, some may be secondary to mental illness, and some primary. But, whether it is primary or secondary, open and controlled treatment studies confirm an aetological link with specific effects of the vitamin on mood, drive, initiative, alertness, concentration, psychomotor speed, and social activity."

"Clearly, further clinical trials in precisely defined clinical categories are needed."

Daily multivitamin supplement contains RDA amount of folic acid.

FRACTURE

11-16 WALKING AND LEISURE-TIME ACTIVITY AND RISK OF HIP FRACTURE IN POSTMENOPAUSAL WOMEN

More leisure-time activity was associated with a lower risk of hip fractures in postmenopausal women. Moderate levels of activity, including walking, were associated with substantially lower risk.

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

4-2 GASTROESOPHAGEAL REFLUX, BARRETT ESOPHAGUS, AND ESOPHAGEAL CANCER

Although strong evidence links GERD and adenocarcinoma, the risk in any given individual is low. Given the low incidence of cancer, and the lack of demonstrated efficacy of endoscopic screening, insufficient evidence exists to endorse routine endoscopy screening for patients with chronic symptoms.

Patients with chronic, severe symptoms of GERD may be given the results of this study, and then decide for themselves. Primary care clinicians should treat these patients with proton pump inhibitors. This will reduce the risk of erosion caused by the acid reflux.

GASTROINTESTINAL ANGIODYSPLASIA

5-16 HORMONAL THERAPY FOR GASTROINTESTINAL ANGIODYSPLASIA

Results were uniformly negative for a beneficial effect of hormones. Interventional therapy is required.

GIANT-CELL ARTERITIS

7-13 POLYMYALGIA RHEUMATICA AND GIANT-CELL ARTERITIS

Recognizable and treatable. Devastating if neglected. A review of points of interest, both old and new.

GLYCEMIC INDEX

5-1 THE GLYCEMIC INDEX

The rate of carbohydrate absorption after a meal, as quantified by the glycemic load (GL) has significant effects on postprandial hormonal and metabolic responses. High GL meals produce an initial period of high blood glucose and insulin levels. This may be followed by reactive hypoglycemia, counter-regulatory hormone secretion, and elevated free fatty acid concentrations. These events may promote excessive food intake, beta cell dysfunction, dyslipidemia, and endothelial dysfunction. As a result, the risk of obesity, type 2 diabetes, and heart disease increases – a hypothesis that derives considerable support from clinical trials and epidemiological analyses.

Despite controversy, clinical use of GL as a qualitative guide to food selection is prudent in view of the preponderance of evidence suggesting benefit and absence of adverse effects.

GLYCOPROTEIN IIB/IIIA INHIBITORS

1-16 PLATELET GLYCOPROTEIN IIB/IIIA INHIBITORS IN ACUTE CORONARY SYNDROMES

Glycoprotein IIb/IIIa inhibitors reduced cardiac complications in patients with acute coronary syndromes not routinely scheduled for early revascularization. Treatment might be considered early after admission in high-risk patients and continued for 2 to 4 days until a decision about revascularization is made.

Benefit was evident only in those with a positive troponin.

The number needed to treat to benefit one patient = 100

GOUT

11-11 TREATING ACUTE GOUTY ARTHRITIS WITH SELECTIVE COX 2 INHIBITORS

Work just as well as other NSAIDs, but no better. Is the added cost worthwhile?

HANDWASHING

8-9 EFFICACY OF HANDRUBBING WITH ALCOHOL BASED SOLUTION VERSUS STANDARD HANDWASHING WITH ANTISEPTIC SOAP

The rapid efficacy of alcohol solutions and their availability at the bedside make them an ideal substitute for conventional handwashing. Compliance is increased.

8-10 HAND-RUBBING WITH AN AQUEOUS ALCOHOL SCRUBBING SOLUTION VS SURGICAL HAND-SCRUBBING AND 30-DAY SURGICAL SITE INFECTION RATES

Hand-rubbing with aqueous alcohol solution before surgical procedures was as effective as the traditional hand-scrubbing.

It was better tolerated and improved compliance..

"Hand rubbing with liquid aqueous alcoholic solutions can thus be safely used as an alternative to traditional hand-scrubbing."

HEAD LICE

5-9 HEAD LICE

Is exclusion from school necessary? Transmission does occur between pupils. Exclusion is almost universally practiced. However, because the infestation in a child has probably been present for weeks before detection, a few extra hours of exposure will probably make no difference in risk of transmission. "Exclusion from school based on the presence of lice or nits is *not* recommended by the American Public Health Association."

"Excluding children from school because of head lice results in anxiety, fear, social stigma, overtreatment, loss of education, and economic loss if parents miss work – a classic case of the cure being worse than the disease."

HEALTH LITERACY

7-6 ASSOCIATION OF HEALTH LITERACY WITH DIABETES OUTCOMES.

Two thirds of patients in this sample who had a high school education or less, had inadequate health literacy. Among primary care patients with type 2 diabetes, inadequate health literacy was independently associated with poorer glycemic control and higher rates of retinopathy. Inadequate health literacy contributes to the disproportionate burden of diabetes-related problems among disadvantaged populations. (*This large subset of patients is not included in randomized, controlled trials. Therefore primary care clinicians must treat these individuals empirically. RTJ*)

HEART FAILURE

2-1 BETA-BLOCKERS IN HEART FAILURE: Clinical Applications

Beta-blockers should be initiated only in HF patients who are clinically euvolemic or receiving stable doses of diuretics without signs of fluid overload (pulmonary rales, jugular venous distention, or more than minimal peripheral edema).

Although there is currently insufficient evidence to recommend beta-blocker use in patients with asymptomatic LV dysfunction, guidelines suggest that they should be given because they reduce progression to HF.

Dosing should be guided by "start low" (about 1/10 the maximum dosage), "go slow" principle. This calls for doubling the dose every 2 to 4 weeks until the target is reached. When a dose is titrated upward, symptomatic hypotension can be expected to be greatest within 24 hours and improve within the next few doses.

There is some evidence for benefit from continuing very low doses of beta-blocker.

"All heart failure patients with left ventricular systolic dysfunction should be considered for beta-blockers to reduce morbidity and prevent mortality."

2-2 BETA-BLOCKER THERAPY IN HEART FAILURE: Scientific Review

Acute treatment with beta-blockers decreases BP and cardiac index; long-term administration is associated with significant increases in ejection fraction and cardiac index, and a decrease in left ventricular diastolic pressure. A decrease in myocardial mass and LV volume improves hemodynamics. Beta-blockers have been evaluated in more than 10 000 patients with all grades of HF. Five meta-analyses have arrived at the

same conclusion: beta-blockers are associated with a consistent 30% reduction in mortality and a 40% reduction in hospitalizations for HF. (NNT 1 year to prevent one death = 26.)

2-8 ASSOCIATION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS WITH FIRST OCCURRENCE OF HEART FAILURE AND WITH RELAPSING HEART FAILURE

NSAID use was not associated with an increased risk of a first episode of HF.

In patients with past history of HF, current use of NSAIDs substantially increased risk of relapse.

Use NSAIDs with caution in persons with heart failure history. And in those with hypertension.

7-8 RAPID MEASUREMENT OF B-TYPE NATRIURETIC PEPTIDE IN THE EMERGENCY DIAGNOSIS OF HEART FAILURE.

B-TNP is included in the European guidelines for diagnosis of chronic HF. It offers valuable predictive information and assessment of severity of the disease. It will improve the ability of clinicians to differentiate patients with dyspnea due the HF from dyspnea due to other causes in the acute care setting. The diagnostic information can be immediately available.

7-9 B-TYPE NATRIURETIC PEPTIDE – A Window to the Heart

Measurement of B-type natriuretic peptide is valuable in the diagnosis of congestive heart failure. It parallels the severity of the congestive heart failure. It can be measured rapidly and accurately at the point of care. It can be used to confirm the diagnosis of congestive heart failure; to measure the severity of left ventricular compromise; to quantify the functional class; to estimate the prognosis and predict future cardiac events, including sudden death in patients with cardiomyopathy; and to evaluate efficacy of treatment.

8-2 OBESITY AND THE RISK OF HEART FAILURE

Elevated BMI was associated with an increased risk of HF without evidence of a threshold

Increased BMI was independently associated with an increased risk of HF. Given the high rates of obesity in the USA, strategies to promote optimal body weight may reduce the population burden of HF.

8-3 OBESITY AND HEART FAILURE – RISK FACTOR OR MECHANISM?

Overweight and obesity are associated with increased rates of hypertension, coronary heart disease, left ventricular hypertrophy, diabetes, and the "metabolic syndrome". All of these are important causes of HF. Nonetheless, BMI emerged as a significant *independent* and graded predictor of HF and remained so when other factors were analyzed together with BMI.

The editorialist suggests some drug treatment preferences for obese patients: renin-angiotensin inhibitors, metformin, statins, and aspirin.

10-15 DIGOXIN – NEW PERSPECTIVE ON AN OLD DRUG.

Digoxin has a narrow therapeutic window. In patients with normal cardiac rhythm, the beneficial hemodynamic, neuro-hormonal, and clinical effects are found with a low concentration of approximately 0.7 ng/mL. Additional benefits are not seen with higher doses traditionally considered therapeutic (with serum concentrations of 1.0 to 1.5 ng/mL). These higher concentrations may predispose to arrhythmias.

Since digoxin may result in adrenergic stimulation at higher concentrations, or in patients with ischemia, the combination of digoxin with beta-blockade may have theoretical advantages

We should not abandon a therapy that may help patients with heart failure. Rather we should use a dose that will result in a serum concentration lower than 1.0 ng per milliliter**.**

HELICOBACTER PYLORI

1-11 ERADICATION OF *HELICOBACTER PYLORI* AND RISK OF PEPTIC ULCERS IN PATIENTS STARTING LONG-TERM TREATMENT WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS.

Screening and treatment of *H pylori* infection reduced the risk of development of peptic ulcer in patients starting long-term NSAID treatment.

Consider screening and treatment of *H pylori* in select patients.

4-8 TREATING *HELICOBACTER PYLORI* INFECTION IN PRIMARY CARE PATIENTS WITH UNINVESTIGATED DYSPEPSIA

"Testing (with C-urea breath test) and treating" to eradicate *H pylori* in patients with uninvestigated dyspepsia provided long-term relief of symptoms and reduced health costs.

Patients in the USA with *H pylori* infection (with or without dyspepsia) should be treated.

HEPATITIS

4-14 SMOKING AND ALANINE AMINOTRANSFERASE LEVELS IN HEPATITIS C VIRUS INFECTION

Alcohol and cigarette consumption were independently associated with elevated ALT levels among persons with HCV infection, but not among those infected with hepatitis B. "Smoking, like alcohol, is an independent promoting factor for hepatic necroinflammation."

The liver is a target organ for the chemicals in tobacco and alcohol. Abstinence from both would probably slow the progression of hepatitis. Patients with HCV infection are strongly advised not to smoke as well as to abstain from alcohol.

9-17 PEGINTERFERON ALFA-2a PLUS RIBAVIRIN FOR CHRONIC HEPATITIS C VIRUS INFECTION

In patients with chronic hepatitis C, peginterferon alfa-2a once weekly + ribavirin daily offered significantly enhanced sustained virologic responses in all patients regardless of HCV genotype and viral load. The combination was tolerated as well as other regimens.

HERPES ZOSTER

7-16 CONTACTS WITH VARICELLA OR WITH CHILDREN AND PROTECTION AGAINST HERPES ZOSTER IN ADULTS

Re-exposure to varicella-zoster virus via contact with children seemed to protect latently infected adults against HZ.

This suggests that vaccination of the elderly might protect against HZ.

8-8 HERPES ZOSTER: Clinical Review

Treatment of pain in the *acute* phase: Pain can be very severe and should not be underestimated. Sympathetic blockade can provide rapid, temporary relief. Scheduled short-acting narcotics should be prescribed. For acute pain which persists, long-acting controlled release opioids (oral or transdermal) are preferred. Early attenuation of the pain may prevent initiation of central mechanisms of chronic pain, thereby reducing severity of post-herpetic neuralgia.

Prevention of post-herpetic neuralgia: Antiviral therapy does not reliably prevent it. Hypothetically, combining antivirals with analgesics, tricyclic antidepressants, or anticonvulsants at onset of HZ could reduce the risk.

Suggestions for treatment of post-herpetic neuralgia.

HOMOCYSTEINE

2-14 PLASMA HOMOCYSTEINE AS A RISK FACTOR FOR DEMENTIA AND ALZHEIMER'S DISEASE

An increased plasma homocysteine level was a strong, independent risk factor for the development of dementia and Alzheimer's disease.

The homocysteine connection lingers on in the literature. While not proven, the benefit/harm-cost of folate, B12, and B6 therapy may be high because harm and costs are low.

8-5 EFFECT OF HOMOCYSTEINE-LOWERING THERAPY WITH FOLIC ACID, VITAMIN B12, AND VITAMIN B6 ON CLINICAL OUTCOME AFTER PERCUTANEOUS CORONARY INTERVENTION.

Homocysteine-lowering therapy with folic acid, vitamin B12, and vitamin B6 significantly reduced incidence of major adverse events after percutaneous coronary intervention. This strengthens the evidence linking the beneficial effects of folic acid, B12, and B6 in lowering homocysteine and the risk of atherosclerotic disease. 11-1 HOMOCYSTEINE AND CARDIOVASCULAR DISEASE

"A raised serum homocysteine concentration is a cause of cardiovascular disease." Risk can be reduced by folic acid supplementation.

HORMONE REPLACEMENT THERAPY

2-6 QUALITY-OF-LIFE AND DEPRESSIVE SYMPTOMS IN POSTMENOPAUSAL WOMEN AFTER RECEIVING HORMONE THERAPY: Results from the Heart and Estrogen/Progestin Replacement Study (HERS) Trial

HRT may have either positive or negative effects on quality of life depending on the presence or absence of menopausal symptoms. Women with menopausal symptoms have improvement in emotional dimensions of quality of life when given HRT.

For women without menopausal symptoms, HRT was associated with net *negative* effects on physical dimensions of quality of life.

Menopausal symptoms are the only reason to prescribe HRT. And the only effective treatment. Other drugs are more effective in preventing osteoporosis and cardiovascular disease.

2-7 POSTMENOPAUSAL HORMONE THERAPY AND QUALITY OF LIFE

All women in the study were well past the age of onset of menopausal symptoms. All had a history of cardiovascular events in the past which, along with their age, placed them at high risk for recurrence. The decline in quality of life in this cohort therefore may have been due to the increased rates of cardiovascular events associated with HRT in the first year of replacement therapy. (*Presumably due to a combination of high risk and a pro-thrombotic effect of HRT. RTJ*) Thus, in women with established cardiovascular disease, HRT may cause more harm than benefit.

The risk of cardiovascular events and other outcomes among younger women and for those without cardiovascular disease are less clear.

For prevention of osteoporosis and lipid disorders, more effective drugs are available.

6-14 ALVEOLAR AND POSTCRANIAL BONE DENSITY IN POSTMENOPAUSAL WOMEN RECEIVING HORMONE/ESTROGEN REPLACEMENT THERAPY

HRT combined with supplemental calcium and vitamin D, produced significant improvement in oral bone mass.

Practical point: Informing postmenopausal women of this risk may increase compliance with anti-osteoporotic therapy.

7-3 RISKS AND BENEFITS OF ESTROGEN PLUS PROGESTIN IN HEALTHY POSTMENOPAUSAL WOMEN

Among a large cohort of healthy postmenopausal women, overall health risks slightly exceeded benefits from use of combined estrogen/progestin for an average of 5 years. (Overall, 19 more adverse effects per 10 000 persons per year.)

Combined HRT should not be used for primary prevention of chronic diseases.

7-4 CARDIOVASCULAR DISEASE OUTCOMES DURING 6.8 YEARS OF HORMONE THERAPY (Heart and Estrogen/progestin Replacement Study Follow-up (HERS II)

HRT did not reduce risk of cardiovascular events in a group of women with established coronary heart disease. Neither was there an *increase* in risk.

7-5 NON-CARDIAC OUTCOMES DURING 6.8 YEARS OF HORMONE THERAPY (The HERS II Follow-up Study)

Treatment with estrogen plus progestin in older women with coronary disease was associated with an increase in rates of venous thromboembolism and biliary tract surgery.

9-1 EVIDENCE FROM RANDOMIZED TRIALS ON THE LONG-TERM EFFECTS OF HORMONE REPLACEMENT THERAPY

Over 5 years of use by 1000 healthy post-menopausal women HRT was estimated to cause:

In women age 50-59: 6 extra strokes, 6 breast cancers, and 6 extra pulmonary emboli.

Prevent 2 colorectal cancers and 2 fractured femurs.

In women age 60-69: 12 extra strokes, breast cancers, and pulmonary emboli.

Prevent 5 colorectal cancers and 5 fractured femurs.

The increased risk of harms is greater than the benefits. Excess risk over 5 years:

Women age 50-59: 1 per 230 users

Women age 60-69: 1 per 150 users

9-2 HORMONE REPLACEMENT THERAPY AND ASSOCIATED RISK OF STROKE IN POSTMENOPAUSAL WOMEN.

Cardiovascular risks may be greater in the first year of HRT use.

Lower doses of estrogen may be safer.

11-8 USE OF POSTMENOPAUSAL HORMONES, ALCOHOL, AND RISK FOR INVASIVE BREAST CANCER

Women who use PMH and consume an average of *over* one alcoholic drink daily had a significantly increased risk of BC, independent of the risk of using PMH alone. “Women who are currently using PMH may wish to consider the added risks of regular alcohol consumption.”

11-10 HORMONE REPLACEMENT THERAPY AND INCIDENCE OF ALZHEIMER DISEASE IN OLDER WOMEN.

Prior HRT use was associated with reduced risk of AD. There was no apparent benefit with current use unless such use exceeded 10 years.

11-6 OSTEOPOROSIS AND FRACTURES IN POSTMENOPAUSAL WOMEN USING ESTROGEN

Estrogen replacement increases bone density and lowers probability of fractures. However, risk of osteoporosis and fractures is still high in older women even if they use estrogens for years after menopause.

Other interventions are required to prevent osteoporosis.

12-5 SIGNIFICANT DIFFERENTIAL EFFECTS OF ALENDRONATE, ESTROGEN, OR COMBINATION THERAPY ON THE RATE OF BONE LOSS AFTER DISCONTINUATION OF TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS.

At one year, accelerated bone loss was seen after withdrawal of estrogen., but not after withdrawal of alendronate or combined estrogen/alendronate therapy.

Combined alendronate/HRT is likely more beneficial than either alone.

Therapy to preserve BMD must be continued indefinitely.

HOT FLASHES

12-4 HOT FLUSHES

Hormone replacement therapy remains the most effective therapy by far. But some women are now reluctant to take them.

Selective serotonin reuptake inhibitors (SSRIs) are somewhat effective, but a poor second choice.

HUMAN PAPILLOMA VIRUS

4-10 MALE CIRCUMCISION, PENILE HUMAN PAPILLOMA VIRUS INFECTION, AND CERVICAL CANCER IN FEMALE PARTNERS.

Male circumcision was associated with a reduced risk of penile HPV.

In the case of men with a history of multiple sexual partners, a reduced risk of cervical cancer was evident in their current female partner.

Practical point: A reasonable indication for circumcision.

11-3 A CONTROLLED TRIAL OF A HUMAN PAPILLOMA VIRUS TYPE 16 VIRUS

A HPV-16 vaccine given to young women reduced incidence of HPV-16 infection and cervical intraepithelial neoplasia. The vaccine may prevent cervical cancer.

HYPERCALCIURIA

1-8 COMPARISON OF TWO DIETS FOR THE PREVENTION OF RECURRENT STONES IN IDIOPATHIC HYPERCALCIURIA

A diet containing normal amounts of calcium and low animal protein and salt was more effective than a low calcium diet for prevention of recurrent calcium oxalate stones in men with idiopathic hypercalciuria.

Aim to reduce concentration of oxalate in the urine, thus lowering saturation of Ca-oxalate, the chief stone former.

Practical point: This diet should be standard therapy for recurrent calcium-oxalate stones.

1-9 RECURRENT HYPERCALCIURIC NEPHROLITHIASIS — DOES DIET HELP?

Practical point: "Physicians should no longer prescribe a low-calcium diet to prevent recurrent nephrolithiasis in patients with idiopathic hypercalciuria."

HYPERTENSION

2-11 PHYSICIAN-RELATED BARRIERS TO THE EFFECTIVE MANAGEMENT OF UNCONTROLLED HYPERTENSION

“Our findings suggest that an important reason why physicians do not treat hypertension more aggressively is that they are willing to accept an elevated systolic BP in their patients.”

Practical point: I believe primary care clinicians have good reason to accept a higher BP in some individual patients.

2-9 RESIDUAL LIFETIME RISK OF DEVELOPING HYPERTENSION IN MIDDLE-AGE WOMEN AND MEN.

In persons with normal BP (<140/90) at ages 55 and 65, the likelihood of development of hypertension as they grow older approaches 90%. Efforts should be directed at primary prevention. Lifestyle management is essential. "The approach of waiting for hypertension to develop and only then treating the elevated blood pressure is injudicious."

Drug therapy is not indicated in many older persons with BP > 140/90. Primary care clinicians use their clinical judgment. They resist rigid applications of "evidence-based medicine" because they know EBM inclusion and exclusion criteria simply do not apply to many of their individual patients.

3-13 CARDIOVASCULAR MORBIDITY AND MORTALITY IN LOSARTAN INTERVENTION FOR ENDPOINT REDUCTION IN HYPERTENSION STUDY (LIFE): A Randomized Trial Against Atenolol

The angiotensin II blocker losartan prevented more combined cardiovascular morbidity and death and stroke than the beta-blocker atenolol for a similar reduction in BP. "Losartan seems to confer benefits (*in relation to stroke*) beyond reduction in BP."

Practical point: Another example of "spin" . The benefit of losartan applied to only one person out of 59 over 5 years. This may be "highly significant" statistically, but hardly significant clinically. Primary care clinicians should beware! I believe the conclusions of this study may mislead clinicians who do not have the time to judge the study in detail. Putting a favorable "spin" on conclusions of studies seems to be occurring more frequently.

3-11 PROSPECTIVE STUDY OF MODERATE ALCOHOL CONSUMPTION AND RISK OF HYPERTENSION IN YOUNG WOMEN

The association between alcohol consumption and risk of chronic hypertension in young women followed a J-shaped curve. Light drinkers demonstrated a modest decrease in risk. Regular, more heavy drinkers demonstrated increased risk.

The epidemiological evidence for benefits of light drinking is strong and consistent.

8-1 COMPARISON OF AGREEMENT BETWEEN DIFFERENT MEASURES OF BLOOD PRESSURE IN PRIMARY CARE AND DAYTIME AMBULATORY BLOOD PRESSURE.

The white coat effect is important in diagnosing and assessing control of hypertension. If ambulatory machine measurement is not available, repeated measurement by nurses or by patients themselves will result in fewer patients receiving unnecessary treatment or change in treatment.

"It is time to stop using high blood pressure readings documented by general practitioners to make treatment decisions."

9-15 EFFECTS OF LOSARTAN ON CARDIOVASCULAR MORBIDITY AND MORTALITY IN PATIENTS WITH ISOLATED SYSTOLIC HYPERTENSION AND LEFT VENTRICULAR HYPERTROPHY

Therapy based on the angiotensin II blocker, losartan, was more effective than a beta-blocker-based therapy with atenolol in preventing CV morbidity and mortality (especially stroke) in patients with isolated systolic BP and left ventricular hypertrophy.

However, the NNT for one year is over 100. Additional cost is over $400 a year.

10-17 PREVENTION OF DEMENTIA WITH ANTIHYPERTENSIVE TREATMENT

New Evidence from the Systolic Hypertension in Europe (Syst-Eur) Trial

A 4-year follow-up study extending antihypertension therapy reinforced the evidence that BP-lowering therapy initiated with a long-acting dihydropyridine calcium blocker (nitrendipine) protects against dementia in older patients with systolic hypertension.

10-10 PRIMARY PREVENTION OF HYPERTENSION

Current recommendations for primary prevention involve a population-based approach and an intensive strategy targeted on individuals at high risk for hypertension. The 2 strategies are complementary. They emphasize 6 approaches with proven efficacy for prevention:

Engage in moderate physical activity

Maintain normal body weight

Limit alcohol consumption

Reduce sodium intake

Maintain adequate intake of potassium

Consume a diet rich in fruits, vegetables, and low-fat dairy products with reduced saturated and total fat.

12-1 MAJOR OUTCOMES IN HIGH-RISK HYPERTENSIVE PATIENTS RANDOMIZED TO ANGIOTENSIN-CONVERTING ENZYME INHIBITOR OR CALCIUM CHANNEL BLOCKER VS DIURETIC

"Thiazide-type diuretics should be considered *first* for pharmacologic therapy in patients with hypertension." They are unsurpassed in lowering BP, in reducing clinical events, and in tolerability. They are much less costly.

Since a large proportion of participants required more than one drug to control their BP, it is reasonable to infer that a diuretic should be included in all multidrug regimens.

INSECT REPELLENTS

7-17 COMPARATIVE EFFICACY OF INSECT REPELLENTS AGAINST MOSQUITO BITES

Only DEET products offered long-lasting protection after a single application. Currently available non-DEET repellants cannot be relied on to provide prolonged protection in environments where mosquito-borne diseases are a substantial threat. DEET has a remarkable safety record.

KIDNEY STONES

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”Physicians should no longer prescribe a low-calcium diet to prevent recurrent nephrolithiasis in patients with idiopathic hypercalciuria."

LEG ULCERS

5-15 PENTOXIFYLLINE FOR TREATMENT OF VENOUS LEG ULCERS

These results suggest that pentoxifylline gives benefits in addition to compression for venous leg ulcers. It is possibly beneficial when used alone.

LIPIDS

4-3 LONG-TERM EFFECTIVENESS AND SAFETY OF PRAVASTATIN IN 9014 PATIENTS WITH CORONARY HEART DISEASE AND AVERAGE CHOLESTEROL CONCENTRATIONS: THE LIPID TRIAL FOLLOW-UP

Long-term therapy (8 years) yields benefits in addition to 6 years treatment. Benefits of therapy continued to accumulate after years of therapy. Older patients, women, and patients with cholesterol <210 mg/dL benefit. Incidence of stroke is reduced.

Almost all patients with established coronary atherosclerotic heart disease should be treated with long-term statins.

7-2 MRC/BHF HEART PROTECTION STUDY OF CHOLESTEROL LOWERING WITH SIMVASTATIN IN 20 536 HIGH-RISK INDIVIDUALS.

Lowering LDL with simvastatin produced substantial benefits in reduction of cardiovascular events in a wide range of high-risk patients, irrespective of their initial cholesterol levels.

Benefits appeared to be largely independent of, and hence additional to, all other treatments being used by participants.

The benefits in reducing risk of stroke should resolve any uncertainty about the effects of statins on the risk of stroke.

It has been suggested that there might be a threshold of LDL below which lowering would not further reduce risk. This study demonstrated unequivocally that there is no threshold. Lowering LDL from 116 to 78 reduced vascular events over 5 years, similar to the reduction in events following lowering from 134 to 96. “If a threshold exists it is a LDL lower than 77 mg/dL and a total cholesterol below 135.”

10-2 THE NEW NATIONAL CHOLESTEROL EDUCATION PROGRAM GUIDELINES

The new NCEP-III guidelines present new clinical challenges to health care providers and their patients. They recommend stricter target lipid levels as well as a broader approach to risk assessment.

11-17 COMPARISON OF C-REACTIVE PROTEIN AND LOW-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS IN PREDICTION OF FIRST CARDIOVASCULAR EVENT.

CRP is a stronger predictor of cardiovascular risk than LDL-c. It adds to prognostic information to that conveyed by the Framingham risk score.

LOSARTAN

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Another example of "spin" . The benefit of losartan applied to only one person out of 59 over 5 years. This may be "highly significant" statistically, but hardly significant clinically. Primary care clinicians should beware! I believe the conclusions of this study may mislead clinicians who do not have the time to judge the study in detail. Putting a favorable "spin" on conclusions of studies seems to be occurring more frequently.

MAMMOGRAPHY

3-10 LONG-TERM EFFECTS OF MAMMOGRAPHY SCREENING: UPDATED OVERVIEW OF THE SWEDISH RANDOMISED TRIALS

The effect of BC screening in terms of BC mortality reduction persists after long-term follow up. The benefit is highest in women age 55-69 at randomization. The recent criticism against the Swedish trial is misleading and unfounded.

(*By my calculation, screening in the Swedish trial was associated with one death from BC prevented each year for every 1000 women screened. RTJ)*

Mammography is so engrained in our society, it would be difficult for primary care clinicians to deny it to their patients.

MEDICAL ETHICS

7-12 IS PLACEBO SURGERY UNETHICAL?

The editorialist states that we should not confound the ethics of clinical research with the ethics of clinical care. The randomized, controlled trial is not a form of individualized medical therapy. It is a scientific tool for evaluating treatments in groups of research participants with the aim of improving the care of patients in the future. Clinical trials are not designed to promote the medical best interests of enrolled patients. Indeed, they often expose them to risks that are not outweighed by known potential medical benefits. "The use of placebo surgery must be evaluated in terms of the ethical principles appropriate to clinical research, which are not identical to the ethical principles of clinical practice."

MENOPAUSE

2-6 QUALITY-OF-LIFE AND DEPRESSIVE SYMPTOMS IN POSTMENOPAUSAL WOMEN AFTER RECEIVING HORMONE THERAPY: Results from the Heart and Estrogen/Progestin Replacement Study (HERS) Trial

HRT may have either positive or negative effects on quality of life depending on the presence or absence of menopausal symptoms. Women with menopausal symptoms have improvement in emotional dimensions of quality of life when given HRT.

For women without menopausal symptoms, HRT was associated with net *negative* effects on physical dimensions of quality of life.

Menopausal symptoms are the only reason to prescribe HRT. And the only effective treatment. Other drugs are more effective in preventing osteoporosis and cardiovascular disease.

2-7 POSTMENOPAUSAL HORMONE THERAPY AND QUALITY OF LIFE

All women in the study were well past the age of onset of menopausal symptoms. All had a history of cardiovascular events in the past which, along with their age, placed them at high risk for recurrence. The decline in quality of life in this cohort therefore may have been due to the increased rates of cardiovascular events associated with HRT in the first year of replacement therapy. (*Presumably due to a combination of high risk and a pro-thrombotic effect of HRT. RTJ*) Thus, in women with established cardiovascular disease, HRT may cause more harm than benefit.

The risk of cardiovascular events and other outcomes among younger women and for those without cardiovascular disease are less clear.

For prevention of osteoporosis and lipid disorders, more effective drugs are available.

Menopausal symptoms make some women miserable. HRT is the most effective treatment. Despite the possible risk in women with many risk factors for heart disease, or with past history of cardiovascular disease, benefits may outweigh possible harms. Prophylactic aspirin and statin drugs may be given to lessen harms of HRT.

MENINGITIS

11-12 DEXAMETHASONE IN ADULTS WITH BACTERIAL MENINGITIS

In adults with acute bacterial meningitis, dexamethasone given before initiation of antibiotic therapy improved outcomes and reduced rate of death. Dexamethasone should be given before the first dose of antibiotic.

METABOLIC SYNDROME

1-3 PREVALENCE OF THE METABOLIC SYNDROME AMONG US ADULTS

About 22% of Americans have the metabolic syndrome. (47 million) Implications for health care are critical. Correction and prevention of the syndrome is a national health-care priority.

Correction and prevention of the syndrome in individual patients is a health-care priority.

12-3 THE METABOLIC SYNDROME AND TOTAL AND CARDIOVASCULAR DISEASE MORTALITY IN MIDDLE-AGED MEN

Middle-aged men with the MET-S had an increased cardiovascular and overall mortality even in the absence of baseline diabetes and CVD. Early identification, treatment, and prevention of the MET-S presents a major challenge.

"The importance of the metabolic syndrome from a clinical and public health perspective may be greatest in it earliest stages, before development of CVD or diabetes." Modest lifestyle interventions can improve components of the MET-S.

METFORMIN

7-7 METFORMIN: AN UPDATE

In treatment of type 2 diabetes, metformin has an excellent safety profile. It is effective as monotherapy and in combination with other drugs. It does not promote weight gain and may even cause weight reduction. It appears to have substantial benefit on lipid metabolism, clotting factors, and platelet function. It improves vascular relaxation and probably reduces BP. These cardio-protective benefits are in addition to its anti-hyperglycemic effect.

MYOCARDIAL INFARCTION

4-13 THROMBOLYTIC THERAPY VS PRIMARY PERCUTANEOUS CORONARY INTERVENTION FOR MYOCARDIAL INFARCTION IN PATIENTS PRESENTING TO HOSPITALS WITHOUT ON-SITE CARDIAC SURGERY.

After an extensive development program, primary PCI can be performed safely, promptly, and effectively in the community hospitals without an elective PCI or cardiac surgery program.

Compared with thrombolysis, the availability of primary PCI resulted in a reduction in deaths, recurrent MI, and stroke.

In this study, the absolute reduction in mortality in patients with acute ST-elevation MI was 5.5% with primary PCI vs 7.6% for thrombolysis. (NNT to prevent one death = 43). Intracranial hemorrhage was essentially eliminated.

"Primary PCI is considered a superior strategy both for efficacy and safety." It should be made more available in the community.

5-13 SELECTIVE COX-2 INHIBITORS, NSAIDs, ASPIRIN, AND MYOCARDIAL INFARCTION

Use of naproxin was associated with a reduced rate of acute myocardial infarction. There is no evidence that use of COX-2 inhibitors increases (or decreases) the risk of myocardial infarction.

The effects noted are due to the anti-platelet, anti-thrombotic actions of naproxin, rather than a detrimental effect of COX-2 inhibitors.

The investigators concluded that there was no evidence for excess cardiovascular events in patients treated with rofecoxib compared with those treated with placebo or NSAIDs other than naproxin. The difference in outcomes was likely due to an antiplatelet effect of naproxin.

6-11 DECISION MAKING WITH CARDIAC TROPONIN TESTS

"Cardiac troponin assays offer clinicians a valuable tool for diagnosing myocardial infarction even at the level of microinfarction."

Cardiac-specific troponins come close to fulfilling many of the criteria for an ideal biologic marker. They convey prognostic information useful in making therapeutic decisions regarding patients with acute coronary syndromes.

Microinfarction can produce elevations of cardiac troponins. Levels can increase without any elevation of creatine kinase MB fraction (CK-MB). Troponins are much more sensitive to damage to small areas of myocardium. Given the nearly absolute specificity of cardiac troponins, they are now considered the preferred biologic markers for diagnosing myocardial infarction

Measurement may be useful for distinguishing unstable angina from MI without ST elevation. About 30% of patients previously considered to have unstable angina on the basis of CK-MB levels are now given a diagnosis of MI without ST elevation on the basis of troponin levels. Troponins also help to establish prognosis, select therapy, and diagnose reinfarction.

Patients with an acute coronary syndrome who are troponin-positive are more likely to have coronary thrombi, to have intermittent showers of emboli in the coronary microvasculature, and to have depressed ventricular function. The benefits of glycoprotein IIb/IIIa inhibitors, low molecular weight heparin, and an early invasive strategy are far greater in troponin-positive patients.

Cardiac troponin screening by primary care clinicians may aid diagnosis, triage, and treatment of patients with symptoms suggesting unstable angina and acute myocardial infarction.

6-7 GLUCOSE METABOLISM IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND NO PREVIOUS DIAGNOSIS OF DIABETES MELLITUS.

Previously undiagnosed diabetes and impaired glucose tolerance are common in patients with AMI. These abnormalities can be detected early. They could be used as early markers of high-risk.

Surveillance and treatment of glucose intolerance may improve prognosis in patients with acute myocardial infarction.

7-1 THE NEW DEFINITION OF MYOCARDIAL INFARCTION

In 2000, the European and American Cardiology Societies published a new definition of AMI which for the first time included troponins. According to the definition, 1) elevated levels of enzymes (CK-MB or troponin I or T), with 2) either symptoms or ECG changes suggestive of ischemia constitute an AMI.

Application of new criteria for diagnosis of AMI resulted in a substantial increase in the number of patients diagnosed with AMI.

NATRIURETIC PEPTIDES

7-8 RAPID MEASUREMENT OF B-TYPE NATRIURETIC PEPTIDE IN THE EMERGENCY DIAGNOSIS OF HEART FAILURE.

B-TNP is included in the European guidelines for diagnosis of chronic HF. It offers valuable predictive information and assessment of severity of the disease. It will improve the ability of clinicians to differentiate patients with dyspnea due the HF from dyspnea due to other causes in the acute care setting. The diagnostic information can be immediately available.

7-9 B-TYPE NATRIURETIC PEPTIDE – A Window to the Heart

Measurement of B-type natriuretic peptide is valuable in the diagnosis of congestive heart failure. It parallels the severity of the congestive heart failure. It can be measured rapidly and accurately at the point of care. It can be used to confirm the diagnosis of congestive heart failure; to

measure the severity of left ventricular compromise; to quantify the functional class; to estimate the prognosis and predict future cardiac events, including sudden death in patients with cardiomyopathy; and to evaluate efficacy of treatment.

9-16 PLASMA NATRIURETIC PEPTIDES FOR COMMUNITY SCREENING FOR LEFT VENTRICULAR HYPERTROPHY AND SYSTOLIC DYSFUNCTION: The Framingham Heart Study

In a large community-based sample, the performance of BNP and ANP for detection of elevated LV mass and LVSD was suboptimal. Natriuretic peptides are of limited usefulness as mass screening tests.

NOCEBO PHENONEMON

3-15 NONSPECIFIC MEDICATION SIDE EFFECTS AND THE NOCEBO PHENONEMON

This article used the nocebo phenomenon to explore the occurrence of adverse, nonspecific effects in patients taking active medications and suggest ways in which clinicians can deal more effectively with them.

Nocebo and placebo effects accompany all medical interventions. Primary care clinicians accept them even if they do not understand them.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

1-11 ERADICATION OF HELICOBACTER PYLORI AND RISK OF PEPTIC ULCERS IN PATIENTS STARTING LONG-TERM TREATMENT WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS.

Screening and treatment of H pylori infection reduced the risk of development of peptic ulcer in patients starting long-term NSAID treatment.

Consider screening and treatment of H pylori in select patients.

2-8 ASSOCIATION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS WITH FIRST OCCURRENCE OF HEART FAILURE AND WITH RELAPSING HEART FAILURE

NSAID use was not associated with an increased risk of a first episode of HF.

In patients with past history of HF, current use of NSAIDs substantially increased risk of relapse.

Use NSAIDs with caution in persons with heart failure history. And in those with hypertension.

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The investigators concluded that there was no evidence for excess cardiovascular events in patients treated with rofecoxib compared with those treated with placebo or NSAIDs other than naproxin. The difference in outcomes was likely due to an antiplatelet effect of naproxin.

NUTS

6-17 NUT CONSUMPTION AND DECREASED RISK OF SUDDEN CARDIAC DEATH IN THE PHYSICIAN'S HEALTH STUDY

This study suggests that the inverse association between nut consumption and total coronary heart disease death is primarily due to a reduction in risk of sudden cardiac death.

Nuts are part of the healthy diet.

11-2 NUT AND PEANUT BUTTER CONSUMPTION AND RISK OF TYPE 2 DIABETES IN WOMEN

Higher nut and peanut butter intake was related to a reduced risk of DM-2

Regular nut consumption can be recommended as a replacement for consumption of refined grains and red or processed meats.

OBESITY

3-2 PREVALENCE OF IMPAIRED GLUCOSE TOLERANCE AMONG CHILDREN AND ADOLESCENTS WITH MARKED OBESITY

Impaired glucose tolerance is highly prevalent among children and adolescents with severe obesity. It is associated with insulin resistance while beta-cell function is still relatively preserved.

Overt DM2, which occurred in a few adolescents, was linked to beta-cell failure.

Impaired glucose tolerance (2 h pc glucose 126-200) is a more sensitive marker of risk of DM2 than elevated fasting glucose (110-125). This is an important clinical point.

Primary care clinicians should maximize efforts to reduce obesity in their adolescent patients.

8-2 OBESITY AND THE RISK OF HEART FAILURE

Elevated BMI was associated with an increased risk of HF without evidence of a threshold

Increased BMI was independently associated with an increased risk of HF. Given the high rates of obesity in the USA, strategies to promote optimal body weight may reduce the population burden of HF.

8-3 OBESITY AND HEART FAILURE – RISK FACTOR OR MECHANISM?

Overweight and obesity are associated with increased rates of hypertension, coronary heart disease, left ventricular hypertrophy, diabetes, and the "metabolic syndrome". All of these are important causes of HF. Nonetheless, BMI emerged as a significant independent and graded predictor of HF and remained so when other factors were analyzed together with BMI.

The editorialist suggests some drug treatment preferences for obese patients: renin-angiotensin inhibitors, metformin, statins, and aspirin.

12-6 BODY MASS INDEX AND THE RISK OF STROKE IN MEN

Overweight and obese men were at increasing risk of stroke. The risk appeared to be independent of hypertension, diabetes, and cholesterol levels.

Increased risk of stroke is another hazard of obesity.

OSTEOARTHRITIS

1-15 EFFICACY OF ROFECOXIB, CELECOXIB, AND ACETAMINOPHEN IN OSTEOARTHRITIS OF THE KNEE

Rofecoxib 25 mg/d provided efficacy advantages over acetaminophen 4000 mg/d, and celecoxib 200 mg/d for symptomatic knee arthritis.

Despite this report, primary care **clinicians will consider individual-patient response to various NSAIDs. Acetaminophen may be the best first-choice.**

2-12 EFFECTS OF HYALURONATE SODIUM ON PAIN AND PHYSICAL FUNCTIONING IN OSTEOARTHRITIS OF THE KNEE

For resting pain relief, HS seems to be as effective as NSAIDs. HS may be superior to placebo or NSAIDs for improving functional performance and relieving pain with physical activity.

Based on adequate informed consent, some patients will accept HS injections and will report benefit.

2-13 HYALURONATE SODIUM INJECTIONS FOR OSTEOARTHRITIS *Hope, Hype, And Hard Truths*

This editorial presents a contrary view. It concludes that the present data fails to demonstrate and benefit beyond the placebo effect.

Primary care clinicians frequently face divergent opinions such as this. They then depend on the individual patient's acceptance and outcomes from the treatment

7-11 DEBRIDEMENT AND LAVAGE FOR OSTEOARTHRITIS OF THE KNEE

"Numerous uncontrolled, retrospective case series have reported substantial pain relief after arthroscopic lavage or arthroscopic debridement for osteoarthritis of the knee." "This study provides strong evidence that arthroscopic lavage with and without debridement is not better than, and appears to be equivalent to a placebo procedure in improving knee pain and self-reported function." The study has also shown the great potential for a placebo effect of surgery.

10-7 HOME BASED EXERCISE PROGRAMME FOR KNEE PAIN AND KNEE OSTEOARTHRITIS

A simple home-based exercise program can produce significant reductions in knee pain and stiffness, and improvement in physical functioning over 2 years.

10-9 GLUCOSAMINE SULFATE USE AND DELAY OF PROGRESSION OF KNEE OSTEOARTHRITIS.

Long-term treatment with glucosamine sulfate retarded the progression of knee OA.

OSTEOPOROSIS

2-17 RECOMBINANT HUMAN PARATHYROID HORMONE

A recent FDA panel recommended approval of an N-terminal fragment of parathyroid hormone for treatment of osteoporosis (teriparatide; *Forsteo*). The application for approval was based on evidence from a randomized trial in women with osteoporosis demonstrating large increases in cancellous (trabecular) bone formation in the vertebral bodies and a greatly reduced risk of spine fracture.

PTH expands the bony envelope in the hip. Thus, its biggest impact may be in prevention of fractures of the hip. "From being one of medicine's most untreatable disorders, osteoporosis is following the footsteps of hypertension and proving amenable to treatment through several targets: estrogen receptors; osteoclasts (by targeting them with bisphosphonates) and now parathyroid hormone receptors."

A potential advance in prevention and treatment of osteoporosis. Watch for developments.

2-18 INTRAVENOUS ZOLEDRONIC ACID IN POSTMENOPAUSAL WOMEN WITH LOW BONE MINERAL DENSITY

Zoledronic acid infusions given at intervals for up to 1 year produced effects on BMD and bone turnover as great as those achieved by oral bisphosphonates.

One annual infusion might be an effective treatment. A potential advance in prevention and treatment of osteoporosis. Watch for developments. See who wins.

2-15 ROLAXIFENE AND CARDIOVASCULAR EVENTS IN OSTEOPOROTIC POSTMENOPAUSAL WOMEN

There was no evidence that raloxifene (a selective estrogen receptor modulator) caused an early increase in risk of CV events in the group overall, or in the subset of women at high risk for CHD

Raloxifene for 4 years significantly reduced the risk of CV events among the subgroup at high risk and among those with established CHD.

3-8 STATIN USE, BONE MINERAL DENSITY, AND FRACTURE RISK

Over 2 years, statin use was associated with a 4% absolute reduction in fracture risk . (NNT to benefit one over 2 y = 26)

The protective effect was greater than would be expected from increases in BMD. The mechanism of action is not clear.

Many elderly persons will be taking statins for lipid control. Is this an added bonus? Watch for developments.

5-4 ALENDRONATE IMPROVES BONE MINERAL DENSITY IN ELDERLY WOMEN WITH OSTEOPOROSIS RESIDING IN LONG-TERM CARE FACILITIES

Alendronate increased BMD in women past age 79.

5-5 THERAPEUTIC EQUIVALENCE OF ALENDRONATE 70 MG ONCE-WEEKLY AND ALENDRONATE 10 MG DAILY IN THE TREATMENT OF OSTEOPOROSIS

Alendronate once weekly will provide patients with a more convenient, therapeutically equivalent alternative dosing schedule. Periodic, instead of daily administration, will likely become the norm.

6-14 ALVEOLAR AND POSTCRANIAL BONE DENSITY IN POSTMENOPAUSAL WOMEN RECEIVING HORMONE/ESTROGEN REPLACEMENT THERAPY

HRT combined with supplemental calcium and vitamin D, produced significant improvement in oral bone mass.

Informing postmenopausal women of this risk may increase compliance with anti-osteoporotic therapy

10-8 UNDERTREATMENT OF OSTEOPOROSIS IN MEN WITH HIP FRACTURE

The burden of hip fracture is high in old men as well as women. Few men receive antiresorptive therapy. Men should be tested for osteoporosis before fracture closes the door of effective therapy.

11-16 WALKING AND LEISURE-TIME ACTIVITY AND RISK OF HIP FRACTURE IN POSTMENOPAUSAL WOMEN

More leisure-time activity was associated with a lower risk of hip fractures in postmenopausal women. Moderate levels of activity, including walking, were associated with substantially lower risk.

11-13 PARATHYROID HORMONE FOR TREATMENT OF OSTEOPOROSIS

PTH increases BMD in the spine in a dose-dependent manner. But fracture reduction data are not robust, especially at non-vertebral sites. PTH may have detrimental effects on the radius BMD.

It protects against vertebral fractures, regardless of time since menopause. Approximately the same degree of fracture reduction resulted from PTH as from the bisphosphonate, alendronate (Fosamax), and the selective estrogen receptor modulator raloxifene (*Evista*)

11-6 OSTEOPOROSIS AND FRACTURES IN POSTMENOPAUSAL WOMEN USING ESTROGEN

Estrogen replacement increases bone density and lowers probability of fractures. However, risk of osteoporosis and fractures is still high in older women even if they use estrogens for years after menopause.

Other interventions are required to prevent osteoporosis.

12-5 SIGNIFICANT DIFFERENTIAL EFFECTS OF ALENDRONATE, ESTROGEN, OR COMBINATION THERAPY ON THE RATE OF BONE LOSS AFTER DISCONTINUATION OF TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS.

At one year, accelerated bone loss was seen after withdrawal of estrogen., but not after withdrawal of alendronate or combined estrogen/alendronate therapy. Combined alendronate/HRT is likely more beneficial than either alone. Therapy to preserve BMD must be continued indefinitely.

PAIN CONTROL

8-15 EFFECTIVE PAIN TREATMENT PROMOTES ACTIVITIES

"Pain is whatever the patient says it is, and exists whenever the patients says it does."

"The patient's self-report is the single most reliable indicator of pain and its intensity."

Physical dependence and tolerance are expected responses to prolonged treatment. Some patients show reluctance about using pain medication, fearing addiction or uncontrollable adverse effects. Some think use of medication will hide other aspects of the disease, or that they should reserve medications until the pain is unbearable. Patient education aimed at these concerns is integral to therapy.

When prescribing opioids, individualized dosage is the key. There is no way to know in advance what a patient will require. Medication should be taken around the clock, rather than as needed.

Tricyclic antidepressants raise levels of serotonin and norepinephrine, particularly at the level of the spinal cord, thereby shutting off nocioceptive signals from the periphery. Nortriptyline (generic) and desipramine (Norpramin; generic) are preferred because they have fewer adverse effects.

"Physicians can promote use of cognitive-behavioral techniques by educating patients about mind/body interactions and reassuring them that the pain is real and that psychologic therapies complement other medical care."

Multidisciplinary pain treatment centers don't see pain cessation as their primary goal. Instead, they seek to help people return to normal activities and improve quality of life.

The article pertains mainly to pain-specialists. Primary care clinicians may help their patients with chronic pain to understand the approaches to treatment**.**

PARATHYROID HORMONE

2-17 RECOMBINANT HUMAN PARATHYROID HORMONE

A recent FDA panel recommended approval of an N-terminal fragment of parathyroid hormone for treatment of osteoporosis (teriparatide; *Forteo*). The application for approval was based on evidence from a randomized trial in women with osteoporosis demonstrating large increases in cancellous (trabecular) bone formation in the vertebral bodies and a greatly reduced risk of spine fracture.

PTH expands the bony envelope in the hip. Thus, its biggest impact may be in prevention of fractures of the hip.

"From being one of medicine's most untreatable disorders, osteoporosis is following the footsteps of hypertension and proving amenable to treatment through several targets: estrogen receptors; osteoclasts (by targeting them with bisphosphonates) and now parathyroid hormone receptors."

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PATIENT PREFERENCES

5-3 "WHAT SHOULD I DO, DOC?" Helping Patients Decide.

Patients often ask their physician – "What would you do if you had my condition?".

Physicians may reply – "This is your decision to make. The right choice depends on your preferences."

Getting patients involved in their medical decisions can often be challenging. Decisions are almost never value neutral.

PATIENT SAFETY

6-2 PUTTING THE PATIENT IN PATIENT-SAFETY

Medical error has been addressed primarily through malpractice litigation. When in courts, patients rarely speak. They are spoken for.

A study in this issue of JAMA invites physicians to take a step away from the "community of experts" approach to patient safety and move a step closer to the patient. It categorizes complaints as relating to communication, humaneness, care and treatment access and availability, or billing. It finds no category of complaint more likely than any other to predict litigation.

Health care organizations need to elicit patients' stories, capture information relevant to safety, and feed that information back to the professionals who organize and deliver care.

Medical practice can be improved by providing earlier and more reliable warning of problems rather than waiting for suits to be filed. Hospitals must be enabled to learn about valid claims from patients whether or not the rarer and more chilling event of formal litigation ensues. "Uncaring medicine is itself bad medicine, something that tends to be overlooked in the rush to achieve technical perfection."

"A small number of physicians experience a disproportionate share of malpractice claims. If malpractice risk is related to factors such as patient dissatisfaction with interpersonal behaviors, care and treatment, and access, it might be possible to monitor physicians' risk of being sued."

Establish rapport, provide access, administer care consistent with expectations, and communicate effectively.

PENTOXIFYLLINE

5-15 PENTOXIFYLLINE FOR TREATMENT OF VENOUS LEG ULCERS

These results suggest that pentoxifylline gives benefits in addition to compression for venous leg ulcers. It is possibly beneficial when used alone.

PEPTIC ULCER

1-11 ERADICATION OF HELICOBACTER PYLORI AND RISK OF PEPTIC ULCERS IN PATIENTS STARTING LONG-TERM TREATMENT WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS.

Screening and treatment of H pylori infection reduced the risk of development of peptic ulcer in patients starting long-term NSAID treatment.

Consider screening and treatment of H pylori in select patients.

6-16 LANSOPRAZOLE FOR THE PREVENTION OF RECURRENCES OF ULCER COMPLICATIONS FROM LONG-TERM LOW-DOSE ASPIRIN USE

In patients with H pylori infection who had gastric or duodenal ulcer bleeding related to long-term use of low-dose aspirin, treatment with the proton-pump inhibitor, lansoprazole, in addition to eradication of the infection, reduced the rate of recurrence of bleeding despite continuation of aspirin.

Proton pump inhibitors protect against NSAID-induced ulcers.

9-19 PEPTIC-ULCER DISEASE

A review of the remarkable progress in our understanding over the past 20 years.

Many questions answered; more questions arise.

PLACEBO EFFECT

3-14 DECONSTRUCTING THE PLACEBO EFFECT

The authors of this article present a new perspective to what has been known as the "placebo effect". The most recent serious attempt to try logically to define the placebo effect failed utterly. One definition: "A placebo is a substance or procedure without specific activity for the condition being treated. The placebo effect is the therapeutic effect produced by a placebo." This makes no sense whatsoever. It flies in the face of the obvious. "The one thing of which we can be absolutely certain is that placebos do not cause placebo effects. Placebos are inert and don't cause anything."

The editorialists suggest thinking about this issue in a new way. "Although placebos clearly cannot do anything themselves, their meaning can."

PNEUMONIA

2-3 GUIDELINES FOR MANAGING COMMUNITY ACQUIRED PNEUMONIA

Streptococcus pneumoniae remains the most common bacterial pathogen. Mycoplasma and chlamydia each cause about 10% of all pneumonias. Primary care clinicians make most of their management decisions without access to chest X-ray. Diagnosing pneumonia clinically is inaccurate and the etiological agent cannot be reliably predicted from clinical features.

The respiratory rate is a most important indicator of disease severity. In the elderly, assessment of the mental state is especially important. Guidelines identify four core adverse prognostic features: confusion; elevated blood urea; respiratory rate above 30; and BP less than 90 systolic or 60 diastolic. If available, pulse oximetry (saturation less than 92%) indicates severe disease.

Patients under age 50 years without comorbidity and lacking any of the core features, do not usually require hospitalization.

See the abstract for suggested oral antibiotics for outpatients.

3-1 RAPID ANTIBIOTIC DELIVERY AND APPROPRIATE ANTIBIOTIC SELECTION REDUCE LENGTH OF HOSPITAL STAY IN PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA

Rapid delivery of the appropriate antibiotic in the ED was associated with a shorter length of stay in hospitalized patients with community-acquired pneumonia.

Primary care clinicians who see very ill patients with infectious disease should administer a full dose of the reasonably appropriate antibiotic immediately in the home, office or emergency department. Do not wait for delivery from the pharmacy or the long door- to-antibiotic time in the hospital. This will improve prognosis.

POLYMYALGIA RHEUMATICA

7-13 POLYMYALGIA RHEUMATICA AND GIANT-CELL ARTERITIS

Recognizable and treatable. Devastating if neglected. A review of points of interest, both old and new**.**

PRIMARY CARE

8-6 A PRIMARY CARE HOME FOR AMERICANS

"It is clear that primary care in the United States is not designed to deliver the accessible, comprehensive, longitudinal and coordinated care required by a 21st century health care system."

"It is time for primary care to get its house in order. New ideas are needed"

Suggestions for improvement are made. Economic factors constrain application.

PROSTATE CANCER

4-1 ERADICATION OF A DISEASE: How We Cured Symptomless Prostate Cancer

"Certainly SPC was common. And now, in the new millennium, what is the frequency of this disease? Perhaps we haven't progressed quite as far as with smallpox, but we are getting close. Symptomless prostate cancer is no longer a very rare disease."

What key discovery led to this remarkable reduction in frequency of SPC? The key was an inexpensive blood test called prostate specific antigen (**PSA**) which provided patients and their doctors with evidence of the presence of PC cells. An avalanche of studies in the past 15 years

assured the end of peaceful co-existence between microscopic deposits of PC cells and their symptom-free hosts. "No longer do patients arrive for yearly checkups, enjoying their lives in blissful ignorance of their cancer. They now arrive monthly, flustered and anxious, some of them with graphs in hand. They no longer have *symptomless* PC, but *symptomatic* PC."

Patients should be informed about the potential harms as well as the potential benefits of PCA testing before the test is performed.

9-3 A RANDOMIZED TRIAL COMPARING RADICAL PROSTATECTOMY WITH WATCHFUL WAITING IN EARLY PROSTATE CANCER

In a select group of generally healthy men mean age 65 with moderately-well, or well-differentiated PC, the study found a statistically significant difference in the risk of death over 6 years due to PC after radical prostatectomy as compared with watchful waiting (surgery – 5%; waiting – 9%).

Local progression and distant metastases were much less common in the surgery group.

No difference in overall mortality.

9-4 QUALITY OF LIFE AFTER RADICAL PROSTATECTOMY OR WATCHFUL WAITING

Assignment of patients to watchful waiting or radical prostatectomy entails different risks, but on average, the choice has little if any influence on well-being and or subjective quality of life after 4 years.

9-5 SURGERY AND THE REDUCTION OF MORTALITY FROM PROSTATE CANCER.

Should all undergo radical prostatectomy? The answer is a categorical "no".

Should no one be followed by watchful waiting? The answer is a categorical "no".

In a young man with localized mild- to moderate-PC who is otherwise in good health, surgery performed by an experienced surgeon, is an excellent option. And his subsequent quality of life should be more satisfactory.

10-4 WHY MEN WITH PROSTATE CANCER WANT WIDER ACCESS TO PROSTATE SPECIFIC ANTIGEN TESTING: Qualitative Study

Most men with established or suspected PC received little information about risks and benefits of screening beforehand. Most thought that universal screening should be available.

Many men are ill prepared for test results, and for the possible iatrogenic effects of treatment.

10-5 NATURAL EXPERIMENT EXAMINING IMPACT OF AGGRESSIVE SCREENING AND TREATMENT ON PROSTATE CANCER MORTALITY IN TWO FIXED COHORTS FROM SEATTLE AREA AND CONNECTICUT

More intensive screening and treatment for PC was not associated with a lower PC-specific mortality over 11 years.

10-6 PROSTATE SPECIFIC ANTIGEN TESTING FOR PROSTATE CANCER

"If a patient asks a medical practitioner for help, the doctor does the best possible. The doctor is not responsible for defects in medical knowledge. If, however, the practitioner initiates screening procedures, the doctor is in a very different situation. The doctor should, in our view, have conclusive evidence that screening can alter the natural history of disease in a significant proportion of those screened."

The difficulty remains – who and when to screen, or not to screen at all. All men who choose screening should be adequately informed about risks and benefits beforehand.

12-7 SCREENING FOR PROSTATE CANCER: AN UPDATE OF THE EVIDENCE FOR THE U.S. PREVENTIVE SERVICES TASK FORCE

Screening can detect PC earlier. A major problem is the heterogeneity of PC. The large discrepancy between PC diagnosis and deaths indicates that some, and probably most, PC detected by screening is clinically unimportant. Because precise evidence regarding the prognosis of various types of PC is lacking, the types of PC that will cause clinical symptoms and death, and that can be treated better if detected early, are not defined. The most appropriate targets of screening are not known. "Since research has not yet clearly defined the characteristics of clinically important prostate cancer, we do not know what the specific target of screening should be."

"The efficacy of screening for prostate cancer remains uncertain."

"The USPTF concludes that evidence is insufficient to determine whether the benefits outweigh the harms for a screened population."

PROSTATECTOMY

5-11 SEXUAL DYSFUNCTION IN MEN AFTER TREATMENT FOR LOWER URINARY TRACT SYMPTOMS

Assertions that minimally invasive treatment such as laser therapy may have less impact on sexual function seem to be unjustified. Compared with laser, TURP had a beneficial effect on aspects of sexual function – particularly in improving erectile dysfunction and reducing pain on ejaculation.

Older men who need treatment for troublesome lower urinary tract symptoms and who wish to retain (or even improve) sexual function may consider TURP.

PROSTATE SPECIFIC ANTIGEN (PSA) see PROSTATE CANCER

PULMONARY EMBOLISM

10-14 HEPARIN PLUS ALTEPLASE COMPARED WITH HEPARIN ALONE IN PATIENTS WITH SUBMASSIVE PULMONARY EMBOLISM

Treatment with alteplase + heparin improved the clinical course of stable patients with acute submassive PE. It prevented further clinical and hemodynamic deterioration which would have required escalation of treatment.

RALOXIFENE

2-15 ROLAXIFENE AND CARDIOVASCULAR EVENTS IN OSTEOPOROTIC POSTMENOPAUSAL WOMEN

There was no evidence that raloxifene (a selective estrogen receptor modulator) caused an early increase in risk of CV events in the group overall, or in the subset of women at high risk for CHD

Raloxifene for 4 years significantly reduced the risk of CV events among the subgroup at high risk and among those with established CHD.

RHEUMATOID ARTHRITIS

1-10 LOW-DOSE PREDNISONE THERAPY FOR PATIENTS WITH EARLY ACTIVE RHEUMATOID ARTHRITIS

Prednisone 10 mg/d provided clinical benefit, particularly in the first 6 months, and substantially inhibited progression of radiologic joint damage in patients with early RA who had no previous treatment with DMARDs. Because of the limited disease-modifying effects of prednisone, DMARDs should be added to prednisone. Practical point:

Primary care clinicians may consider low-dose prednisone as a first-line treatment in early RA.

RHINITIS

12-11 ANTIBIOTICS FOR ACUTE PURULENT RHINITIS

Guidelines suggest that antibiotics are ineffective. This may not be true. However, the modest benefit for this condition, which is rarely life-threatening, may warrant constraint on their use because of side effects, cost, development of antibiotic resistance, and promotion of use of heath services. Perhaps they should consider delayed prescriptions in an attempt to meet demand from patients while maintaining evidence based integrity.

SEXUAL DYSFUNCTION

5-11 SEXUAL DYSFUNCTION IN MEN AFTER TREATMENT FOR LOWER URINARY TRACT SYMPTOMS

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Older men who need treatment for troublesome lower urinary tract symptoms and who wish to retain (or even improve) sexual function may consider TURP.

SEXUALLY TRANSMITTED DISEASES

8-4 U.S CENTERS FOR DISEASE CONTROL AND PREVENTION GUIDELINES FOR THE TREATMENT OF SEXUALLY TRANSMITTED DISEASES: 2002 Guidelines

Primary care clinicians may wish to file and consult this article to obtain the latest information. A table of selected recommendations for treatment of STDs appears on page 257. The authors include several new guidelines.

SIGMOIDOSCOPY

4-9 SINGLE FLEXIBLE SIGMOIDOSCOPY SCREENING TO PREVENT COLORECTAL CANCER

This flex-sig screening regimen was acceptable, feasible, and safe. The prevalence of neoplasia detected was high.

Some patients who refuse colonoscopy may accept this less stressful procedure, even if they know it is incomplete screening.

SIROLIMUS

2-16 OVERCOMING RESTENOSIS WITH SIROLIMUS

Preliminary studies using sirolimus coated stents have been quite promising and should reduce restenosis rate.

This will probably be another advance tilting patients with coronary disease toward PTCA and away from CABG.

SMOKING

1-5 EFFECT OF PREOPERATIVE SMOKING INTERVENTION ON POSTOPERATIVE COMPLICATIONS

An effective smoking cessation program applied for at least 6 weeks prior to hip and knee surgery more than halved the frequency of postoperative complications.

Primary care clinicians should stress this benefit.

4-14 SMOKING AND ALANINE AMINOTRANSFERASE LEVELS IN HEPATITIS C VIRUS INFECTION

Alcohol and cigarette consumption were independently associated with elevated ALT levels among persons with HCV infection, but not among those infected with hepatitis B. "Smoking, like alcohol, is an independent promoting factor for hepatic necroinflammation."

The liver is a target organ for the chemicals in tobacco and alcohol. Abstinence from both would probably slow the progression of hepatitis.

Patients with HCV infection are strongly advised not to smoke as well as to abstain from alcohol.

STATIN DRUGS (See also OSTEOPOROSIS; LIPIDS; DEMENTIA)

3-8 STATIN USE, BONE MINERAL DENSITY, AND FRACTURE RIS

Over 2 years, statin use was associated with a 4% absolute reduction in fracture risk . (NNT to benefit one over 2 y = 26)

The protective effect was greater than would be expected from increases in BMD. The mechanism of action is not clear.

Many elderly persons will be taking statins for lipid control. Is this an added bonus? Watch for developments.

3-9 HMG COA REDUCTASE INHIBITOR (STATIN) AND AORTIC VALVE CALCIUM

Statin therapy may retard progression of calcific aortic valve disease. Another added bonus?

6-4 THERAPY WITH HYDROXYMETHYLGLUTARYL COENZYME-A REDUCTASE INHIBITORS (STATINS) AND ASSOCIATED RISK OF INCIDENT CARDIOVASCULAR EVENTS IN OLDER ADULTS

Use of statins was associated with decreased risk of incident cardiovascular events among elderly adults Age per se in not a contraindication.

6-5 STATIN THERAPY IN OLDER PERSONS: Pertinent Issues

There is growing evidence that LDL-lowering therapy is effective in reducing risk for CHD in older persons. Statins are recommended for select elderly individuals.

7-2 MRC/BHF HEART PROTECTION STUDY OF CHOLESTEROL LOWERING WITH SIMVASTATIN IN 20 536 HIGH-RISK INDIVIDUALS

Lowering LDL with simvastatin produced substantial benefits in reduction of cardiovascular events in a wide range of high-risk patients, irrespective of their initial cholesterol levels.

Benefits appeared to be largely independent of, and hence additional to, all other treatments being used by participants.

The benefits in reducing risk of stroke should resolve any uncertainty about the effects of statins on the risk of stroke.

It has been suggested that there might be a threshold of LDL below which lowering would not further reduce risk. This study demonstrated unequivocally that there is no threshold. Lowering LDL from 116 to 78 reduced vascular events over 5 years, similar to the reduction in events following lowering from 134 to 96. "If a threshold exists it is a LDL lower than 77 mg/dL and a total cholesterol below 135."

10-19 STATIN-ASSOCIATED MYOPATHY WITH NORMAL CREATININE LEVELS

"Some patients who develop muscle symptoms while receiving statin therapy have demonstrable weakness and histopathologic findings of myopathy despite normal serum creatinine kinase levels." Symptoms and histologic features reverted to normal on withdrawal of the drug.

STENTS

6-13 SIROLIMUS-ELUTING CORONARY STENTS

A sirolimus-eluting stent, as compared with a standard stent, shows considerable promise for prevention of neointimal restenosis. The gradual elution occurs over a period of 30 days. Only a small quantity of the drug is required. This avoids systematic adverse effects.

Primary care clinicians follow developments along with their cardiologist consultants.

STREPTOCOCCI

4-12 ERYTHROMYCIN-RESISTANT GROUP A STREPTOCOCCI IN SCHOOLCHILDREN IN PITTSBURGH

A longitudinal study of schoolchildren detected the emergence of erythromycin resistance in pharyngeal isolates of group A streptococci. The clonal outbreak also affected the wider community.

"We recommend that macrolide antibiotics not be used for the routine treatment of pharyngitis due to group A streptococci until more epidemiological information is available.

STROKE

3-12 USE OF RAMIPRIL IN PREVENTING STROKE

The ACE inhibitor, ramipril, was associated with a reduced incidence of stroke despite a modest reduction in BP.

This is a good example of the "spin" investigators sometimes place on their studies. Their abstract states the relative risk of fatal stroke was reduced by 61%. (In absolute terms this actually amounted to 0.6%; NNT = 166 for 4.5 years to prevent one fatal stroke)

9-2 HORMONE REPLACEMENT THERAPY AND ASSOCIATED RISK OF STROKE IN POSTMENOPAUSAL WOMEN.

Cardiovascular risks may be greater in the first year of HRT use.Lower doses of estrogen may be safer.

11-5 TRANSIENT ISCHEMIC ATTACK: Review Article

The high short-term risk of stroke after a TIA supports an approach involving rapid evaluation and initiation of treatment. Initial evaluation should include electrocardiography, imaging studies of the head, and Doppler ultrasonography of the carotids. Brain imaging may reveal a non-ischemic cause – eg, brain tumor or subdural hematoma.

12-6 BODY MASS INDEX AND THE RISK OF STROKE IN MEN

Overweight and obese men were at increasing risk of stroke. The risk appeared to be independent of hypertension, diabetes, and cholesterol levels. Increased risk of stroke is another hazard of obesity.

TECHNOLOGY AND MEDICINE

3-7 MODERN WORRIES, NEW TECHNOLOGY, AND MEDICINE

Historically, the introduction of new technologies has frequently been accompanied by new complaints, fears, and illness. Currently, the adoption of new technologies is accelerating and is occurring in a climate of suspicion and mistrust in medical evidence. Distrust of experts is now commonplace. At its extreme it can merge into the conspirational thinking that is part of a modern paranoid style. Well publicized crises have clearly dented confidence. Mismanaged environmental incidents and examples of the fallibility of experts are easily recalled.

"It is difficult to feel optimistic." Despite all the evidence of the extraordinary improvements in public health during the past century, surveys show that we experience more symptoms and feel worse than our ancestors." The rapid introduction of new technologies, while improving quality of life, has been accompanied by important adverse effects in the way people make sense of illness and present with health complaints.

Controversy in "scientific" medicine itself compounds the public confusion. Expressions of differences in opinions and conflicting studies published in medical journals quickly reach the media. Is mammography really effective in reducing breast cancer death? Is PCA screening helpful or harmful? What about all the confusion about benefits and harms of hormone replacement therapy? How common are the harms associated with drug therapy and hospitalization?

Do you agree? If so, what is to be done?

THROMBOLYSIS (See also MYOCARDIAL IFARCTION)

10-14 HEPARIN PLUS ALTEPLASE COMPARED WITH HEPARIN ALONE IN PATIENTS WITH SUBMASSIVE PULMONARY EMBOLISM

Treatment with alteplase + heparin improved the clinical course of stable patients with acute submassive PE. It prevented further clinical and hemodynamic deterioration which would have required escalation of treatment.

THYROID DISEASE

12-9 THYROID-HORMONE SUPPRESSIVE THERAPY IN BENIGN THYROID NODULES –IS IT EFFECTIVE?

Despite the wide use of thyroid hormones in the treatment of thyroid nodules, there is still lack of evidence to generally justify thyroid suppression as a therapy. "It is not known If thyroid-hormone treatment is effective in controlling the size of thyroid nodules, or safe, particularly if suppression of thyroid-stimulating hormone is long-term."

12-10 EFFECTS OF SUBCLINICAL THYROID DYSFUNCTION ON THE HEART.

"Subclinical thyroid dysfunction is not a compensated biochemical state." Timely treatment could help prevent cardiovascular involvement." (Eg, judicious thyroxine replacement for high TSH states and beta-blockers for low TSH states.)

TRANSIENT ISCHEMIC ATTACK (See also STROKE)

11-5 TRANSIENT ISCHEMIC ATTACK: Review Article

The high short-term risk of stroke after a TIA supports an approach involving rapid evaluation and initiation of treatment. Initial evaluation should include electrocardiography, imaging studies of the head, and Doppler ultrasonography of the carotids. Brain imaging may reveal a non-ischemic cause – eg, brain tumor or subdural hematoma.

11-4 TRANSIENT ISCHEMIC ATTACK – PROPOSAL FOR A NEW DEFINITION

A TIA is a brief episode of neurological dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction.

With the new definition, the difference between a TIA and a stroke becomes similar to the distinction between an episode of angina pectoris and a myocardial infarction. Angina is a symptom of ischemia, which is usually brief, but can be prolonged, without myocardial infarction. If there is evidence of myocardial damage, myocardial infarction is diagnosed.

TROPONIN

6-12 TROPONIN T LEVELS IN PATIENTS WITH ACUTE CORONARY SYNDROMES, WITH AND WITHOUT RENAL DYSFUNCTION

Given that renal dysfunction is common in patients with coronary disease, the ability of cardiac troponin levels to predict outcomes irrespective of creatinine clearance expands their clinical usefulness.

Cardiac troponin T predicted short-term prognosis in patients with ACS regardless of their level of creatinine clearance.

6-11 DECISION MAKING WITH CARDIAC TROPONIN TESTS

"Cardiac troponin assays offer clinicians a valuable tool for diagnosing myocardial infarction even at the level of microinfarction."

Cardiac-specific troponins come close to fulfilling many of the criteria for an ideal biologic marker. They convey prognostic information useful in making therapeutic decisions regarding patients with acute coronary syndromes.

Microinfarction can produce elevations of cardiac troponins. Levels can increase without any elevation of creatine kinase MB fraction (CK-MB). Troponins are much more sensitive to damage to small areas of myocardium. Given the nearly absolute specificity of cardiac troponins, they are now considered the preferred biologic markers for diagnosing myocardial infarction.

Measurement may be useful for distinguishing unstable angina from MI without ST elevation. About 30% of patients previously considered to have unstable angina on the basis of CK-MB levels are now given a diagnosis of MI without ST elevation on the basis of troponin levels. Troponins also help to establish prognosis, select therapy, and diagnose reinfarction.

Patients with an acute coronary syndrome who are troponin-positive are more likely to have coronary thrombi, to have intermittent showers of emboli in the coronary microvasculature, and to have depressed ventricular function. The benefits of glycoprotein IIb/IIIa inhibitors, low molecular weight heparin, and an early invasive strategy are far greater in troponin-positive patients.

Cardiac troponin screening by primary care clinicians may aid diagnosis, triage, and treatment of patients with symptoms suggesting unstable angina and acute myocardial infarction.

UNSTABLE ANGINA (See ANGINA)

VENOUS CANNULAS.

8-16 LOCAL WARMING AND INSERTION OF PERIPHERAL VENOUS CANNULAS.

Local warming of the hand facilitated the insertion of cannulas, reducing both the time and number of attempts required. This application may help primary care clinicians more easily start routine i.v. fluids in patients with difficult veins.

VENOUS THROMBOEMBOLISM

9-18 FONDAPARINUX VS ENOXAPARIN FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM IN MAJOR ORTHOPEDIC SURGERY.

In patients undergoing orthopedic surgery, fondaparinux (a factor Xa inhibitor) once daily, starting 6 hours post surgery, showed major benefit over enoxaparin (a low-molecular weight heparin) in reducing DVT at the expense of a slightly increased risk of bleeding.

Fondaparinux may be a valuable addition to anticoagulant therapy.

VITAMINS

6-9 VITAMINS FOR CHRONIC DISEASE PREVENTION IN ADULTS

"Most people do not consume an optimal amount of vitamins by diet alone. Pending strong evidence of effectiveness from randomized trials, it appears prudent for all adults to take vitamin supplements." It is reasonable to consider a dose of two ordinary multivitamins daily for the elderly, especially since there is a high prevalence of suboptimal vitamin D and B12 intake.

"We recommend that all adults take one multivitamin daily." They are safe and inexpensive. "We recommend multivitamins, rather than individual vitamins, because they are cheaper and simpler to take, and because a large proportion of the population needs supplementation of more than one."

6-10 FOLIC ACID, AGEING, DEPRESSION, AND DEMENTIA

Folates are important for the nervous system at all ages. There is growing evidence of their involvement in the aging brain, especially in mood and cognitive function. Low folate concentrations in serum, red cells, and cerebrospinal fluid, and the associated rise in plasma homocysteine, are associated with depression and dementia. “Some of the deficiency may be related to ageing, some may be secondary to mental illness, and some primary. But, whether it is primary or secondary, open and controlled treatment studies confirm an aetological link with specific effects of the vitamin on mood, drive, initiative, alertness, concentration, psychomotor speed, and social activity.”

“Clearly, further clinical trials in precisely defined clinical categories are needed.” Practical point: Daily multivitamin supplement contains RDA amount of folic acid.

8-5 EFFECT OF HOMOCYSTEINE-LOWERING THERAPY WITH FOLIC ACID, VITAMIN B12, AND VITAMIN B6 ON CLINICAL OUTCOME AFTER PERCUTANEOUS CORONARY INTERVENTION.

Homocysteine-lowering therapy with folic acid, vitamin B12, and vitamin B6 significantly reduced incidence of major adverse events after percutaneous coronary intervention. This strengthens the evidence linking the beneficial effects of folic acid, B12, and B6 in lowering homocysteine and the risk of atherosclerotic disease.

11-1 HOMOCYSTEINE AND CARDIOVASCULAR DISEASE

“A raised serum homocysteine concentration is a cause of cardiovascular disease.” Risk can be reduced by folic acid supplementation.

VITAMIN K

8-13 ORAL VITAMIN K LOWERS THE INTERNATIONAL NORMALIZED RATIO MORE READILY THAN SC VITAMIN K IN THE TREATMENT OF WARFARIN-ASSOCIATED COAGULOPATHY.

In asymptomatic patients with supra-therapeutic INR values (4.5 to 10) while receiving warfarin, 1 mg oral vitamin K lowered INR more rapidly to a therapeutic level than subcutaneous K.

The day after administration of oral K, the INRs remained within therapeutic range in many patients, allowing reinstitution of warfarin therapy.

WAIST CIRCUMFERENCE

10-1 BODY MASS INDEX, WAIST CIRCUMFERENCE, AND HEALTH RISK

Health risk is greater in individuals with high WC (> 40 inches in men and > 35 Inches in women) regardless of BMI category, including individuals with normal weight. A high WC independently predicts obesity-related disease.

WARFARIN

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WARTS

8-14 LOCAL TREATMENTS FOR CUTANEOUS WARTS

Compared with other topicals, salicylic acid has a more favorable therapeutic effect