CEYLON COLLEGE OF PHYSICIANS

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1.1 Food allergies.

Many children with atopic dermatitis are inappropriately labeled as allergic to specific foods without undergoing oral food challenges. They are therefore placed unnecessarily with restricted diets with no evidence of food allergies. The common food allergens are Eggs, milk, pea nuts, fish, or wheat products. True allergies will be shown by large wheals on skin prick test. The commoner way of detection is to demonstrate an increased IGE level in the serum and thereafter by perform immuno assay for various allergens.

In a recent study, 93% of 103 children who were positive for either skin test or immune assays were found to be negative when challenged with the respective foods. The foods that were most likely to be associated with a positive food challenge were pea nuts, wheat and eggs. Milk was not among the foods most likely to be associated with a positive food challenge.

Comment: Children with atopic dermatitis should not be placed on restricted diets unless there is a positive food challenge test.

Ref: Fleischer D.M. et al J. Pediatr. 2011 Apr; 158: 578 e 1.

1.2 Esomeprazole (E) vs surgery (LARS) for chronic gastro –oesophageal reflux disease (GORD).

What is the best treatment for symptomatic GORD – is it surgical or medical?.

Surgery in this day and age is done laparoscopically by those with much surgical experience in the procedure. The efficacy of esomeprazole was compared with laparoscopic antireflux surgery (LARS).

554 patients with GORD were randomized to either 20mg/d, increased to 40mg/d of E or LARS. The primary outcome measure was the time to treatment failure(ie ; need for additional treatment in the E group or need for drug therapy or additional procedures in the last group). Secondary outcomes included various individual symptoms.

At 5 years, the remission rate was slightly higher in the E group (92% vs 85%; P = 0.048). There were no perioperative deaths and perioperative morbidity was only 3%. There were no serious adverse events in the E group. Acid regurgitation was more common in the E group (13% vs 2%; P = <0.001) but dysphagia, bloating and flatulence were less common in the E group. Residual heart burn, epigastric pain and diarrhea were equal.

Comment: The excellent results of LARS is due to the experience and expertise of the Surgeons. Less experienced Surgeons may not have the same results. However, even in this head to head comparison with the best surgical outcomes, medical therapy was still equivalent to or better than LARS for the primary outcome and most secondary outcomes. Long term medical therapy seems to be the best choice for patients who are willing to remain on daily acid reduction medication. Adverse effects on absorption of thyroxine, iron, calcium, and oral bisphosphonates, by long term PPIs need to be factored into the equation.

Ref: Galmische J.P. et al JAMA 2011 May 18; 305: 1969.

1.3 Is Vancomycin (V) the best drug for MRSA infections?.

V has poor tissue penetration and slow bactericidal activity. Further, emergence of both tolerant and resistant organisms compounds the problem.

In a study of 320 patients with MRSA infections, V failed in 52%. Independent predictors of failure included endocarditis, nosocomial infection and serum vancomycin trough levels < 15 mcg/ml. It has thus been suggested in recent guidelines (Clin. Infect. Dis. 2011; 52:285) that V trough levels be kept higher at 15 – 20 mcg/ml. For relatively resistant organisms, aggressive dosing regimens such as 2g every 12 hrs still has only a 60% chance of efficacy and a 30% chance of toxicity. Other antistaphylococcal drugs are **Linezolid** and **Tigecycline**. These may be used if a trial of V is not effective.

Ref: Kullar R. et al Clin. Infect. Dis. 2011 Apr 15; 52: 975.
Patel N. et al IBID: 969.

1.4 Is tobacco smoking a risk factor for Mycotuberculosis (MTB) infection?.

Researchers exposed mice to cigarette smoke for several months and then challenged them with low dose aerosol of MTB and compared them with control mice, not exposed previously to cigarette smoke. At one month, smoke exposed mice developed significantly greater MTB loads in the lungs and spleen and significantly larger lesions than in the control mice. Cigarette smoke was found to decrease TNF Alpha and IL 12, both of which protect against TB. Cigarette smoke also augmented the immunosuppressive IL 10 and macropharge control of MTB via both nicotine and acrolein , an aldehyde component of smoke.

Comment: These findings provide a mechanism for the enhanced severity of primary TB in smokers. The finding that smoking also raises the likelihood of reactivation of TB, awaits further research.

Ref: Shang S et al J.Infect. Dis. 2011 May 1; 203: 1240.

1.5 Is cancer attributable to alcohol consumption?

110,000 men and 255,000 women, age range 35 – 70, in 8 Western European countries who were cancer free were followed up for 5 – 13 years. Overall 10% of total cancers in men and 3% of total cancers in women were attributable to alcohol consumption. The alcohol attributable fractions in men and women were, respectively

Upper aero digestive tract	- 44 and 25%
Liver cancer	- 33 and 18%.
Colorectal cancer	- 17 and 4%.
Breast cancer in women	- 5%.

The recommended upper limit of alcohol - 2 drinks daily in men and one drink daily for women - accounted for much of the alcohol attributable cancers for all cancer categories.

Comment: Although only small proportions of total cancers in men (10%) and women (3%) in this study were attributable to alcohol consumption, higher proportions of specific cancers especially in the liver and aerodigestive tract were attributable to alcohol consumption. Much of the risk was associated with heavy consumption – more than 2 drinks daily for men and one drink daily for women. This finding should reassure light to moderate drinkers.

Ref: Schutze M. et al BMJ 2011 April 7; 342: d 1584.

1.6 Atrial fibrillation (AF) and mortality after MI.

3,220 patients with first MI were divided into 3 groups.

1. NO AF.
2. AF before MI.
3. AF within 2, 3-30 or > 30 days after MI.

AF during or after MI was associated with older age, hypertension, female sex, diabetes, chronic kidney disease, anterior MI and lower ejection fraction. AF after MI was associated with elevated risk for death during a mean follow up of 6.6 yrs (Hazard ratio 3.8). The highest risk was in those who developed AF after 30 days of MI.

Comment: AF was associated with elevated mortality after MI, particularly when AF occurred later during follow up. The presence of AF denotes a high risk subset of patients with MI. Such patients should be treated for both the coronary artery disease and the arrhythmia.

Ref: Jabre P et al Circulation 2011 May 17; 123: 2094.
Lubitz S.A. et al IBID : 2063.

1.7 Resistant hypertension (RH) – should it be diagnosed only after ambulatory BP monitoring?.

RH is diagnosed when there is persistent elevation of office measured BP, despite using three or more antihypertensive drugs (including a diuretic).

68,000 patients in a Spanish registry, 12% of whom exhibited RH were subjected to ambulatory BP monitoring. This revealed that only 62.5% had true RH while 37.5% had normal values and were considered to have " white coat hypertension". The true RH group had higher rates of cigarette smoking, diabetes, LV hypertrophy, microalbuminuria and previous cardiovascular disease. They were also younger, more likely to be male and had longer duration of hypertension.

Comment: In this large cohort of hypertensive patients, about 1 in 8 had RH of which 1/3rd turned out to have "white coat hypertension". Ambulatory BP monitoring is warranted in all hypertensive patients whose BP is not controlled on three or more drugs.

Ref: de la Sierra A. et al Hypertension 2011 May; 57: 898.

1.8 Should Aspirin or NSAIDs be prescribed for patients with colonic diverticulosis (CD)?.

47,000 male participants in the observational Health Professionals Follow Up Study (HPFUS) were followed up for 22 years. 939 of them reported diverticulitis of which 256 reported diverticular bleeding. In a multi – variate analysis, regular aspirin use was associated with significantly elevated risk for diverticulitis (HR = 1.25) and diverticular bleeding (HR 1.70). The same was true for regular NSAID use (HR 1.72 and 1.74 resp). These findings represent roughly 1 additional case of diverticular complications per 1,000 person years for either aspirin or NSAID use.

Comment: Because aspirin and NSAIDs inhibit mucosal protective mechanisms and promote bleeding, these findings are physiologically plausible. Even if the findings do reflect cause and effect, benefits of aspirin in secondary prevention of CV events or NSAIDs in pain relief will outweigh a small increase in

absolute risk for diverticular complications in many patients. However, for some patients with histories of diverticulitis or diverticular bleeding who have marginal indications for aspirin or NSAID use – this study provides reasons to avoid these drugs.

Ref: Strate L.L. et al Gastroenterology 2011 May; 140: 1427.

1.9 A new treatment for opioid detoxification - Extended release Naltrexone (N. er).

N.er is already FDA approved for treatment of alcohol dependence in 2006 and was approved in 2010 for prevention of relapse in opioid dependence.

A Russian study randomized 250 patients to i.m. N.er 380mg every 4 weeks or placebo for 24 weeks. The patients had been opioid dependent for an average 10 years and had completed up to 30 days of inpatient detoxification and were opioid free for at least for 7 days. 53% of N.er and 38% of placebo recipients completed the trial. The median proportion of confirmed abstinence weeks was significantly greater with N.er (90%) than with placebo 35%. One N.er patient and 17 placebo patients relapsed.

Comment: Monthly N.er after opioid detoxification might be a useful alternative to long term opioid maintenance. However N.er can re sensitise opioid receptors, thereby raising the risk for opioid overdose in patients who relapse. The criticism of this trial centres around the fact that it lacked post termination safety data and because N.er was compared with placebo, rather than to the best available treatments viz Methadone or Buprenorphine.

Ref: Krupitsky E. et al Lancet 2011 Apr 30; 377: 1506.
Wolfe D. et al IBID: 1468.

1.10 Is Niacin effective in patients with cardiovascular disease who are being treated with statins?.

Niacin is often prescribed for statin treated patients, to raise HDLC or to manipulate lipid subfractions. The clinical effects of this practice is unclear.

In the NIH sponsored AIM – HIGH study, 3,414 patients with established CVD were randomized to receive Simvastatin + either extended release Niacin or placebo. Enrollment criteria included HDLC levels < 40mg/dl for men and <50mg/dl for women and TG levels between 150 – 400 mg/dl. The dose of Niacin was high – 1,500 to 2,000 mg daily. The dose of Simvastatin was between 40 and 80mg daily. The LDLC target level was < 80mg/dl. Most patients also received Aspirin, Beta blockers and ACEIs. The randomized phase was preceded by an open label run in phase to determine whether they could tolerate the high Niacin doses.

Compared with placebo, Niacin therapy induced significant changes in LDLC, HDLC and TG levels. However, the trial was stopped after an average follow up of 3 years, when no hint of CV benefits and a trend toward more strokes with Niacin were reported. The primary outcome of a composite of adverse coronary events, strokes and revascularization occurred in 16% in each group. The incidence of stroke was 1.7% with Niacin and 1.1% with placebo (P= 0.09).

Comment: These results indicate that extended release Niacin does not benefit patients with known CV disease who achieve low LDLC levels with statin monotherapy. This study was a purely secondary prevention trial and there is no evidence that Niacin improves outcomes when given for primary prevention.

Ref: The AIM – High Investigators NEJM 2011Nov 15; e pub.

1.11 Which is better for preschool children with recurrent asthma - low dose daily inhaled Budesonide or intermittent high dose Budesonide?.

278 children – age range 12 – 53 months who had recurrent wheezing and at least one episode requiring oral gluco corticoid therapy, emergency admission or hospitalization were randomized to either daily low dose inhaled Budesonide 0.5mg nightly or intermittent high dose Budesonide 1mg b.d for 7 days. After 12 months, no significant differences were noted between groups in frequency of exacerbations requiring oral steroid rescue, time to first exacerbation of asthma and frequency of treatment failure. No significant differences were also observed in quality of life, height, weight or head circumference.

Comment: Intermittent high dose inhaled Budesonide was as effective as currently recommended daily inhaled low dose steroids in this carefully selected group of preschool children with recurrent wheezing. The average Budesonide exposure over the 12 months was 180mg for the low dose group and 104mg for the high dose intermittent group. Lesser steroid exposure of the high dose intermittent group is highly desirable.

Ref: Zeiger R.S. et al NEJMed 2011 Nov24; 365: 1990.

1.12 Vitamin E and Prostate cancer.

Early results from a large control trial of Vitamin E supplementation showed no fewer cases - but possibly an excess risk for prostate cancer after 3 years of supplementation. The trial was therefore halted (JAMA 2009; 301: 39). A new report includes data from 3 additional years of follow up.

Originally, the 35,533 men were randomized daily Selenium (200 mcg) + Vitamin E placebo, Vitamin E (400 iu) + Selenium placebo, both Selenium and Vitamin E or double placebo. Participants had normal PSA levels below 4 ng /ml and normal digital rectal exams. The overall risk for prostate cancer was significantly elevated by 17% in the Vitamin E group with no significant difference in the other treatment groups.

Comment: These results confirm what was suspected in the first analysis viz Vitamin E raised risk for prostate cancer and that risk was mitigated by Selenium supplementation. Vitamin E should not be taken by older men for unsubstantiated benefits.

Ref: Klein E.A. et al JAMA 2011 Oct 12; 306: 1549.

1.13 What is the short term risk of Transient Ischaemic Attacks (TIA).

TIA is defined as a neurological deficit that lasts less than 24 hours. Some patients with TIAs have ischaemic changes on MRI diffusion weighted images (DWI). These patients have worse short term prognosis than those with normal DWI studies.

The ABCD2 (Age, Blood pressure, Clinical features, Duration, Diabetes) score uses clinical information for short term prediction of stroke risk in patients with TIA. In this International multicentre study, researchers examined whether DWI added to ABCD2 scoring predicts more accurately which patients with TIA will have subsequent strokes.

Of 3,200 TIA patients, 28% exhibited acute infarction on DWI. The 7 day stroke rate was 7% in DWI positive patients but only 0.4% in DWI negative patients. In DWI positive patients, the ABCD2 score added prognostic information and added little when it was DWI negative. The ABCD2 score of 0 – 3 gave a 7 day stroke rate of 1.8% and when the score rate was 6-7 a stroke rate of 12.5%.

Comment: For prediction of short term stroke risk after a TIA the combined ABCD2 score and MRI DWI complemented each other. ABCD2 scores range from 0 – 7. Age > 60 (1 point) , Systolic BP > 140 or Diastolic BP > 90 (1 point), unilateral weakness with or without impaired speech (2 points) or speech disturbance without weakness (1 point) , Symptom duration, 10 – 59 mts (1 point) or more than 60 mts (2 points), Diabetes (1 point).

Ref: Giles M.F. et al Neurology 2011 Sept 27; 77: 1222.

1.14 Can MRI studies be performed safely in patients with implantable cardiac devices?.

MRI is usually avoided in patients with implantable cardiac devices because of safety concerns. A prospective study was conducted in one US center and One Israeli center to determine whether MRI could be performed safely at the commonly used magnetic strength of 1.5T in patients with implantable cardiac devices who had clinical indications for MRI. Overall 438 patients with either pace makers or implantable cardioverter defibrillators underwent MRI. In 3 patients (0.7%) implantable devices reverted to a back up mode that allows the devices to function after loss of programmable memory. None of these patients experienced long term device dysfunction. Minor short term and long term changes were observed which did not require revision or reprogramming.

Comment: MRI procedures were performed safely in patients with implantable cardiac devices in this study using a defined protocol. The editorialistsuggest that the presence of an implantable cardiac device "should no longer be considered as an absolute contraindication to MRI". However, these results should not be extrapolated to MRI scanners with field strengths lower or higher than 1.5T. The FDA has recently approved a pace maker designed to function safely in the MRI environment under certain conditions and that defined MRI magnet strengths.

Ref: Nazarian S et al Ann.Intern.Med 2011 Oct 4; 155: 415.
Reynolds M.R. et al IBID: 470.

1.15 Colchicine for recurrent pericarditis.

10 – 30 % of patients with acute pericarditis not due to neoplastic or bacterial causes experience recurrence and half of these patients experience further recurrences. Observational studies suggest that Colchicine can prevent recurrence of pericarditis. To study this effect further, researchers randomized 120 patients with the first recurrence of pericarditis (not due to neoplastic or bacterial causes) to either colchicines or placebo for 6 months. The dose of colchicines was 1.0 – 2.0 mg on the first day, then 0.5 – 1.0 mg daily for 6 months. All patients also received anti inflammatory treatment such as Aspirin or Ibuprofen. Mean follow up was for more than 20 months. The recurrence rate was 24% in the Colchicine arm and 55% in the placebo arm. The remission rate at 1 week was also greater among the Colchicine recipients (82% vs 48%). The rates of withdrawal and adverse effects were similar in both groups.

Comment: This is the first prospective randomized trial to evaluate the efficacy of Colchicine for secondary prevention of recurrent pericarditis. These findings strongly support using low dose Colchicine in this setting, given that the number needed to treat for benefit was approximately 3.

Ref: Imazio M. et al Ann. Intern. Med 2011 Oct 4; 155: 409.

1.16 Should Clopidogrel be stopped before vascular surgery?.

Many Surgeons believe that Clopidogrel raises risk for perioperative bleeding complications and withdraw Clopidogrel 6 days before surgery. Researchers analysed data from a US multicenter registry representing 10,000 vascular surgery cases from 66 Surgeons. The vascular surgery undertaken consisted of carotid endarterectomy, lower extremity bypass, endovascular repair of abdominal aortic aneurysm and open abdominal aortic aneurysm repair.

Within 48 hours before surgery, 69% of patients were taking Aspirin alone, 2% clopidogrel alone, 10 % were taking both and 19% were taking neither drug. The incidence of post operative bleeding was almost similar among all 4 groups (about 1%). In addition, no significant difference between groups were observed in the need for blood transfusion or average number of units given among those who received transfusion.

Comment: Although only 12% of this group were taking Clopidogrel with or without Aspirin, the absolute number of Clopidogrel users were substantial. The results suggest that patients with valid indications for Clopidogrel can continue the drug preoperatively when they undergo vascular surgery.

Ref: Stone D.H. et al J.Vasc. Surg. 2011 Sept; 54: 779.

1.17 Are dietary supplements in older women associated with increased mortality?.

Dietary supplements, particularly Iron, Calcium and several Vitamins are used and sometimes even demanded by atleast 50% of adults, despite little evidence of benefit and some suggestion of harm. In a study, researchers assessed the use of 15 supplements in 38,772 women (mean age 62, nearly all white), in Iowa USA, in 1986, 1997 and 2004.

During a mean follow up of 19 years 40% died. The most commonly used supplements were Calcium, Multivitamins, Vitamin C and E. In adjusted analyses, use of multivitamins, folic acid, Iron or Magnesium was associated with a 6-15% increase in risk for death. Copper supplementation was associated with a 45% increased risk. Calcium use was associated with a 9% lower risk.

Comment: At the very least, routine dietary supplements seem to provide no benefit in older women. They should not be given unless a specific deficiency is detected.

Ref: Mursu J. et al Arch. Intern. Med 2011 Oct 10; 171: 1625.

1.18 Should we screen all irritable bowel syndrome (IBS) patients for coeliac disease?.

An expert panel recently recommended screening for celiac disease in patients with diarrhoea predominant or mixed IBS (Am. J.Gastroenterol. 2009; 104(Suppl1): S1). Now a prospective multicenter study was performed to determine the prevalence of celiac disease among 492 non constipation predominant IBS and compared with 458 healthy controls who underwent screening colonoscopy. Each patient and control was tested for 4 coeliac antibodies. Those with one or more positive results underwent small bowel biopsy.

The prevalence of at least one abnormal celiac antibody test was not significantly higher in IBS patients than in controls (7% vs 5%). The prevalence of HLA Haplotypes associated with celiac disease (HLA-DQ2 or DQ8) was not higher in IBS patients than in controls.

Comment: This US study failed to document an elevated prevalence of celiac disease in patients with a diagnosis of diarrhoea predominant IBS.

Ref: Cash B.D. et al Gastroenterology 2011 Oct; 141: 1187.

1.19 Is the risk for recurrent venous thromboembolism (RVTE) associated with sex of the patient?.

A meta analysis of 2,554 patients with a first VTE were followed up for a mean 27 months. The one year incidence of RVTE was 5.3% in women and 9.5% in men. The 3 year incidence of RVTE was 9.1% in women and 19.7% in men. The hazard ratio for men was 2.2. In patients with provoked (as opposed to unprovoked) VTE, was the same for men and women. Women with VTE due to hormone induced causes had less RVTE than women without hormonal causes.

Comment: Men with unprovoked VTE have a 2.2 fold higher risk for RVTE than women. In patients with a first provoked VTE the risk between the sexes does not differ. Indefinite or prolonged anticoagulation should be given consideration in men rather than women after a first VTE.

Ref: Douketis J. et al BMJ 2011; 342: d 813. Contributed by Prof. P. L. Ariyananda

1.20 Is there an increased risk for stroke after a hip fracture?.

Stroke may result in weakness and incordination and thus result in an increased risk for hip fracture. What about the converse?

2,101 patients with hip fracture were followed up for one year and compared with a control group. 4.1% of those with prior hip fracture and 2.7% in the comparison group had stroke in the first year of follow up giving a hazard ratio of 1.55 for those with prior hip fracture.

Comment: Hip fracture is associated with increased risk of stroke in the first year.

Ref: Kang. J.H.et al STROKE 2011; 42: 336 – 341.
Dr. PLA.