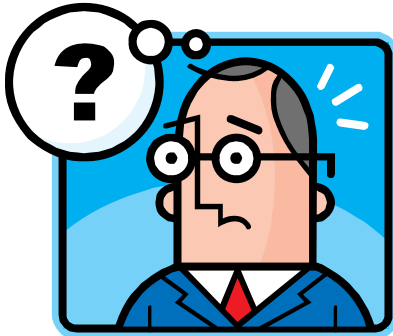




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Short vs. long-term androgen suppression therapy in prostate cancer.

Overall survival among patients with locally advanced prostate cancer has improved with use of external-beam radiotherapy (RT) combined with long-term androgen suppression therapy (AST) of ≥ 2 years. However, long-term AST can reduce the quality of life and increase the risk of fatal myocardial infarction, fractures and metabolic syndrome. A recent multinational study evaluated whether RT + 6 months' AST was as effective as RT + 3 years' AST in 970 men with locally advanced prostate cancer (*NEJM*

2009;360:2516-27). AST consisted of luteinising hormone-releasing hormone (LHRH) initiated on day one of RT, plus flutamide 750mg /day (initiated one week before LHRH). For those in the long-term AST arm, the flutamide was discontinued after 6 months and they were continued on LHRH alone. Results showed that after a median follow-up of 6.4 years, 132/483 of the 6 month group had died (47 due to prostate cancer, 31 due to CVD) compared with 98/487 in the 3 years group (28 due to prostate cancer, 25 due to CVD). This represents an overall 5-year mortality of 19% vs. 15.2% respectively. The main adverse effects were hot flashes, insomnia, reduced interest in sex and reduced sexual activity. Quality of Life questionnaires, completed every 6 months showed no overall difference in QoL between the groups although there were significant differences noted for hot flashes and sexual activity. The authors note that although the differences in mortality may appear modest in favour of long-term AST, they state that the advantage of 3 years' AST is likely to be maintained at 10 years while the beneficial effect of 6 months' therapy may be dissipated. An accompanying editorial (*NEJM 2009; 360: 2572-4*) notes that while this study has shown the overall survival benefit of longer term AST in males with advanced prostate cancer, the availability of repeat PSA testing has resulted in a large rise in prostate cancer diagnosis at an earlier lower-risk phase. Therefore, more studies are needed to look at optimum treatment for this patient group.



What is the best treatment for Bell's Palsy? Bell's Palsy is the most common cause of acute facial paralysis (annual incidence up to 45 cases per 100,000). The optimal treatment has not yet been established, with the therapeutic drug choices being corticosteroids (CS) and/or an antiviral agent (AV). CS are considered to be the most widely accepted treatment. A recent review sought to determine if there was a significant difference to recovery in patients with Bell's Palsy treated with CS compared to those who received combination treatment with CS and an AV (*Arch Otolaryngol Head Neck Surg. 2009;135: 558-564*). The review (n=738) analysed 5 randomised controlled trials (RCTs), with complete recovery of facial motor function 3 months after initiation of

therapy as the main outcome, of which 4 were included in a formal meta-analysis. The analysis of the studies suggest that combination treatment does not provide any additional benefit over CS alone (odds ratio 1.03 [95% CI 0.74-1.42]; p=0.88). The authors advise, that based on current evidence, the addition of an AV to CS for the treatment of Bell's palsy appears not to be justified. However they recommend that additional well-designed RCTs are required to assess the potential value of antiviral treatment in Bell's palsy.



British guideline on asthma updated (revised June 2009) The British Thoracic Society, in association with the Scottish Intercollegiate Guidelines Network (SIGN), has recently updated the 2008 guideline on the diagnosis and management of asthma. **The June 2009 revision includes updates to pharmacological management, the management of acute asthma and asthma in pregnancy.** Updates in relation to asthma in pregnancy include: advising pregnant women of the importance of maintaining good control of asthma and of the importance and safety of continuing their asthma medication. Short and long acting β_2 agonists can be used as normal during pregnancy. Women should be advised that the benefits of treatment with oral steroids outweigh the risks. Leukotriene antagonists may be continued in women who have demonstrated significant improvement in asthma control with these agents, not achievable with other medications, prior to pregnancy. Check out <http://www.brit-thoracic.org.uk/> or www.sign.ac.uk to get the full guidance document or a shortened Quick Reference Guide.



Management of Hepatitis C (Hep C) - Hep C is a major cause of significant liver disease. Its management was recently reviewed (*BMJ 2009;338:b2366*). In the UK it is estimated a GP with a list size of 1800 has 8-20 patients with chronic infection (of whom 50% are unaware they carry the virus). The prevalence varies between different groups (0.04% in blood donors to 50% in intravenous drug users). If such patients are identified and treated, the virus can be eradicated in up to half of them. The main mode of acquisition in the UK is through IV drug abuse. Acute infection is usually unrecognised; 60-85% of patients progress to chronic infection, the major complication of which is chronic hepatitis. This leads to advanced fibrosis and cirrhosis in 1 in 5 patients over 30 years and is a leading indication

for liver transplantation. Patients with cirrhosis have an increased risk of hepatocellular carcinoma, and Hep C infection is associated with an increased risk of insulin resistance and type 2 diabetes. **Assessment** - acute infection is not usually identified unless symptomatic hepatitis prompts investigation. Chronic infection (> 6months) is usually identified when investigating abnormal liver function tests, thrombocytopenia, and incidental imaging findings suggesting cirrhosis or decompensated liver disease. **General practice screening is recommended for at risk patient groups including: unexplained abnormal LFTs, history of IV drug abuse, blood transfusions before 1991 in the UK or any blood products before 1986, medical or dental treatment acquired under poor infection control (IC), children of infected mothers, sexual partners of infected people, exposure to blood where risk of transmission exists and tattoos, piercing or acupuncture with poor IC procedures.** Screening for specific antibodies identifies exposure to the virus (false negatives can occur in patients with acute infection, immunodeficiencies or end stage renal disease). Ongoing infection is confirmed in those with positive serology by testing for Hep C viral RNA; those with a positive result require referral. Patients who test positive for antibodies but negative for RNA should have repeat tests after 6 months. Liver biochemistry is insensitive at predicting disease severity and while ultrasound can identify focal lesions, normal findings do not exclude cirrhosis. Biopsy has its limitations including sampling error and patient reluctance. Non-invasive methods of assessing fibrosis are evolving. **Treatment** - while all patients with chronic infection are candidates for treatment, the risks and benefits should be considered on an individual basis. Treatment is considered successful when Hep C is undetectable 6 months after stopping treatment. Predictors of poor response to treatment include: advanced fibrosis, unfavourable genotype (1, 4 & 6) and insulin resistance. **The current treatment for chronic infection is the combination of:** peginterferon alfa and ribavirin, which achieves sustained virological responses in up to half of patients with genotype 1 and four fifths with genotypes 2 or 3. Failure to achieve an early virological response is a good predictor of non-response and treatment should be discontinued. Treatment is usually delayed in children until they reach adulthood and is poorly tolerated in patients with HIV, renal failure, haemophilia or viral recurrence after liver transplantation. Side effects are reported in greater than half of patients and range from mild, non-specific, influenza-like symptoms to major neuropsychiatric disturbance. Haematological adverse effects are common including: anaemia, thrombocytopenia and haemolytic anaemia. A multidisciplinary approach (often coordinated by nurse specialists) is important and includes regular clinical, laboratory assessment and patient education. Consideration should also be given to prevention of hepatitis A and B by vaccination. There are new approaches to treatment being evaluated including the use of specific Hep C enzyme inhibitors, including protease inhibitors (telaprevir and boceprevir - currently not authorised) and nucleoside and non-nucleoside polymerase inhibitors.



News from the NMIC - we are pleased to inform our readers that our website has recently been updated (www.nmic.ie). In addition to containing past issues of the Therapeutics Today newsletters and bulletins, it also contains an updated index which readers may find useful for locating past publications/topics of interest. [Editor's note: An updated index, to make our online documents more accessible was one of the requests from our readers, following our NMIC publication survey in 2008.]