







Coventina's Column

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 Post menopausal women with breast cancer positive for hormonal receptors are currently treated with tamoxifen post operatively. A recent study (The Lancet, Dec 19, 2009-Jan 1, 2010. Vol. 374, Iss. 9707; pg. 2055) has investigated whether adding chemotherapy to adjuvant tamoxifen increased disease-free survival compared with tamoxifen alone in hormonal receptor- positive, node-positive post-menopausal women with breast cancer, and also whether there was a difference if the tamoxifen was given concurrently with the chemotherapy compared with its administration after the chemotherapy. The chemotherapy consisted of six cycles of cyclophosphamide, doxorubicin, and fluorouracil (CAF) given four weekly, and the tamoxifen was given for five years, either starting at the same time as the chemotherapy (CAFT) or starting after the chemotherapy (CAF-T). The results showed that treatment with tamoxifen plus chemotherapy significantly prolonged disease-free survival compared with tamoxifen alone, whether the tamoxifen was given with (CAFT) or after (CAF-T) the chemotherapy, although overall survival was only minimally increased. When the CAFT and CAF-T groups were compared, both disease-free survival and overall survival were better in the CAF-T group (where the tamoxifen was started after the chemotherapy) than in the CAFT group (where the two were given concurrently), but the difference was not statistically significant. Therefore, chemotherapy with CAF followed by tamoxifen seems to be more effective adjuvant treatment for post-menopausal women with hormone receptor-positive, node-positive breast cancer than tamoxifen alone. In view of the debilitating side effects of chemotherapy, further investigation is warranted to ascertain whether certain subgroups of patients are more responsive to this therapy than others.

 Post-operative wound infection is a cause of much morbidity and, more rarely, mortality, so surgeons may be interested to hear that a recent study (New England Journal of Medicine. Vol 362 January 7, 2010; pages 18 – 26) demonstrates a significantly lower incidence of infection of surgical incisions in patients in whom the pre-operative skin antisepsis is carried out with chlorhexidine-alcohol than with povidone-iodine. A total of 849 patients were included in the trial, and those in whom chlorhexidine-alcohol was used had a significantly lower incidence of wound infection than those cleansed with povidone-iodine. This significance held for both superficial and deep infections of the incision, but not for infections of the organ spaces, which did not reach significance. The partial instant tan of the post-operative patient may be a thing of the past – hospital laundrettes will rejoice.

 Women of *un age certain* have long been aware that the description 'grey and interesting' seems to apply to one gender only. The attractiveness or otherwise of crinkles round the eyes and a well lived-in face are themes for another day but it has always been easy to disguise grey hair because of the vast range of permanent hair dyes on offer. Manufacturers have always stressed the safety of their products. However, a recent animal study (British Journal of Dermatology January 2010; pages 102 - 107) suggests that these products may cause more immune stimulation than previously believed. Mice were exposed to two hair dye products containing p-Phenylenediamine (PPD) and its related substances, which are constituents of more than two thirds of permanent hair dyes. Application of the product caused major allergic immune activation, inducing skin production of interleukins 1 and 6 and tumour necrosis factor as well as systemic production of interleukin 6. The draining lymph nodes were infiltrated with B and T cells. The immune reaction was more than 50% greater when the two constituents of the hair dyes – colour gel and developer – were combined than with the constituents on their own, demonstrating a problem with safety testing of these products which are based on testing the individual constituents alone, despite the fact that the products are combined in use. Whether repeated immune activation of this sort plays a role in the development of subsequent auto immune problems also requires investigation.

 There are a large number of considerations for individuals contemplating the selfless act of live kidney organ donation and a not insignificant one is the wound pain associated with open nephrectomy. Laparoscopic nephrectomy may markedly reduce pain, but would the recipient's transplant be compromised? A recent randomized controlled trial of eighty four live kidney donors (British Journal of Surgery, Volume 97, Jan 2010, pages 21 – 28) compared the safety of nephrectomy and the viability of the subsequent transplants in short-incision open nephrectomy not involving rib resection compared with laparoscopic nephrectomy. Although the warm ischaemic time and duration of operation were longer in the laparoscopic group there were no differences in renal function or survival of the grafted organ in the recipient at the median follow-up time of 74 months. The laparoscopic group experienced less pain, fewer wound infections, less respiratory compromise, a shorter duration in hospital and a quicker return to work than the open nephrectomy group.



Multiple sclerosis (MS) is more common in the highlands and islands of Scotland than anywhere else in the world but the reasons for this remain uncertain. Recent research from Glasgow's Southern General Hospital (European Journal of Neurology Jan 2010. Vol 63, pages 36 - 40) examines whether MS patients show any pattern in the month of their birth. The researchers examined data for 1309 MS patients and found that there were 22% more spring births than expected, with the peak month for birth of MS patients being in April. There were fewer MS patients born in autumn than would be expected. This seasonal association requires further investigation. It is possible that pregnancy during the winter months and/or birth in the early spring may lead to vitamin D deficiency through lack of sunlight in either the pregnant mothers of babies who go on to develop MS or in the babies themselves in the early months of life when the central nervous system continues to develop, or both. Implication of a lack of sunlight and/or vitamin D may also explain why MS is more common in Scotland than in sunnier climes.



Another area of research in MS is the specific immune mechanisms involved in the pathogenesis of the disease. It is known that certain immune responses are very different in the patient with MS than in healthy patients. A recent issue of Neurology (Neurology. Volume 74, Jan 5 2010) has devoted much space to this disease and immune mechanisms in MS patients. Therapies targeting the CD4 T cells thought to be active in the demyelination process have been disappointing for the most part. More recent research into the experimental model of MS has highlighted other immune idiosyncrasies in these patients. As well as an informative article comparing the normal immune system to that in MS patients, there is a review of emerging oral drugs for MS. These medicines, which are currently undergoing evaluation in phase 11/111 clinical trials, include Fingolimod, an immunosuppressant which caused a significant reduction in the number of relapses in phase 11/111 trials, Laquinimod, an immunomodulator which lowered the number of active lesions, Cladribine, another immunomodulator which more than halved the number of relapses and decreased certain lesions by more than 70%, oral fumarate which reduced the number of lesions in a phase 11 study, and the immunomodulator teriflunomide, which reduced annual relapses and MRI lesions. These are promising signs - effective therapies for MS have so far been restricted to intravenous drugs such as the beta interferons, so oral therapies may significantly improve both compliance and the quality of life of MS patients.