Clippings

❑ Risk of developing cancer from exposure to radiation is well known. Diagnostic X-rays represent the largest man-made source of radiation exposure to the general population, contributing about 14% of the total annual exposure worldwide from all sources. An assessment of the risk of developing cancer from radiation exposure of diagnostic *X*-rays undertaken in UK and 13 other developed countries showed that 0.6-1.8% of the cumulative risk of cancer to age 75 years could be attributable to diagnostic *X*-rays, translating to roughly 700 cases of cancer per year. Since this data was based on several assumptions, it may have over-estimated the risk to some extent but it nevertheless points out that radiologic investigations should be undertaken with careful consideration of the long-term effects. (Lancet 2004; 363: 345-51).

❑ Children undergoing chemotherapy need long-term vascular access devices but infection and thrombosis in these devices are serious complications, which add to the overall morbidity. The efficacy of an every-2-week administration of urokinase versus standard heparin flushes was compared in a prospective, randomized phase III multicenter trial conducted by the Children's Cancer Group. All patients with implantable ports or tunneled catheters received either urokinase or heparin every 2 weeks for 12 months, with study end points being the time to first occlusion or the time to first device-related infection. Of the 577 patients enrolled from 29 institutions (51% with external catheters, 49% with ports), Urokinase administration resulted in fewer occlusive events than heparin (23% vs 31%; P = 0.02), a longer time to first occlusive event (log-rank analysis, P = 0.006), and a 1.6-fold difference in the rate of occlusive events (Poisson regression, P = 0.003), the results being similar for both ports and external catheters. However, they were significant only for tunneled catheters when comparing the overall rate of infection and the time to first infection. (J Clin Oncol 2004; 22: 2718-2723).

❑ Rasburicase (recombinant urate oxidase) is a novel therapy for prevention of hyperuricemia and acute tumour lysis syndrome following initiation of chemo-therapy in children. About 5-22% of pediatric patients with acute leukemia also have hyper-leukocytosis (WBC counts >100 × 109/L). Rasburi case was tried in patients with hyperleukocytosis at the initiation of induction chemotherapy and it was not associated with any metabolic abnormalities or the need for any other WBC reducing strategies. However, large-scale studies are needed in pediatric patients before it can become the standard of care. (Pediatr Nephrol 2004; 19: 924 - 927).

❑ The response to acute febrile illnesses may be hindered in children with acute lymphoblastic leukemia if they develop suppression of adrenal function after initial induction chemotherapy. A study evaluating the adrenal function in children with acute lymphoblastic leukemia after completion of the induction phase of chemotherapy found that 46% of patients had adrenal suppression two weeks after the discontinuation of prednisolone. It was found to persist longer in children more than 5 years of age with a total of 38%, 29% and 13% having continued adrenal suppression at 4, 8 and 12 weeks, respectively. During the study period, 4 children developed febrile neutropenia, all of them being from adrenal suppressed group and were found to have inability to mount an adequate response

to the stress of the infection. The utility of this finding for possible therapeutic intervention in these children will need further evaluation. (J Pediatr 2004 June; 144: 736-740).

❑ Gonadal dysfunction is a late effect of cancer chemotherapy that affects survivors of childhood cancer. Ovarian and testicular function was assessed in 67 long-term survivors (37 females, 30 males; aged 1-16 yrs, mean 5 yrs) of leukemia treated between 1973-1992. The majority received prophylactic cranial irradiation and 9 patients received treatment for relapse. Gonadal function was assessed by clinical examination and measurement of serum concentrations of estradiol, testosterone and those of LH and FSH (in basal state and after stimulation). Primary hypogonadism was found in 6 (9%) patients. Five (16.5%) males had primary hypogonadism with evidence of damage to the germinal epithelium, while 2 of them, treated with testicular RT, had evidence of damage to the Leydig cells and another 2 had evidence of dysfunction of Leydig cells as well. Five females also developed early puberty after cranial RT. The authors concluded that primary treatment for leukemia produces primary hypogonadism in boys but not in girls. Alkylating agents and gonadal RT are the most damaging factors and even Alkylating agents alone cause dysfunction of Leydig cells. (Leukemia Lymphoma 2004; 45: 1797- 1802).

❑ Cancer Chemotherapy leads to an increase in reactive oxygen species, which stresses the antioxidant defense system. A study was conducted to investigate the effect of cancer chemotherapy on antioxidant intakes in children with acute lymphoblastic leukemia, the relation between dietary antioxidant intakes and plasma antioxidant concentrations, and the relation between the incidence of side effects due to treatment and antioxidant intake. A 6-month observational study was carried out in 103 children with ALL and plasma micronutrient concentrations, dietary intakes, and incidence of side effects of chemotherapy were ascertained at diagnosis and after 3 and 6 mo of therapy. All patients ingested vitamin E, total carotenoid, ß-carotene, and vitamin A in amounts that were 66%, 30%, 59%, and 29%, respectively, of US RDA or of the 3rd NHANES. The authors found that a large percentage of children undergoing treatment have inadequate intakes of antioxidants and vitamin A. Lower intakes of antioxidants are associated with increases in the adverse effects of chemotherapy. In addition, greater vitamin C intakes at 6 months were associated with fewer therapy delays, less toxicity, and fewer days spent in the hospital. Greater vitamin E intakes at 3 months were associated with a lower incidence of infection. (Am J Clinical Nutrition 2004; 79: 1029 -1036).

❑ Neutropenia is one of the grave consequences of cancer chemotherapy, and the treatment of febrile neutropenic patients with intravenous (IV) antibiotics reduces mortality but oral therapy could be an alternative approach for selected patients. In a systematic review of published literature comparing the efficacy of oral antibiotics versus IV antibiotic therapy in febrile neutropenic cancer patients, the mortality rate was similar among oral and IV antibiotic treatment groups (RR 0.83, 95% CI 0.49-1.41, 2224 patients). Treatment failure rates were also similar (RR 0.94, 95% CI 0.84-1.05, 15 trials) and no significant heterogeneity was shown for the primary outcomes. Quinolones alone or combined with other antibiotics were used with comparable results and adverse reactions, mostly gastrointestinal, were more common with oral antibiotics. It concluded that oral antibiotics might be safely offered to neutropenic patients with fever who are at low risk for mortality. (J Antimicrob Chemother 2004; 54: 29-37).

❑ Doxorubicin chemotherapy is very effective in children with acute lymphoblastic leukemia (ALL) but causes significant cardiac toxicity Dexrazoxane, a free-radical scavenger, may protect the heart from Doxorubicin-associated damage. In a study, 101 children with ALL were randomly assigned to receive Doxorubicin alone (30 mg per m2 every 3 weeks for 10 doses) and another 105 to receive Dexrazoxane (300 mg per m^2) followed immediately by Doxorubicin. Serial measurements of serum cardiac troponin T were obtained in 76 of 101 patients in the Doxorubicin group and 82 of 105 patients in the group given Dexrazoxane and Doxorubicin. The results showed that patients treated with Doxorubicin alone were more likely than those who received Dexrazoxane and Doxorubicin to have elevated troponin T levels (50% vs. 21%, P <0.001) and extremely elevated troponin T levels (32% vs. 10%, P <0.001). The median follow-up was 2.7 years and the rate of event-free survival at 2.5 years was 83% in both groups (P = 0.87 by the log-rank test). Although Dexrazoxane reduces cardiac injury, without compromising the antileukemic efficacy of Doxorubicin, longer follow-up will be necessary to determine the influence on echocardiographic findings and on event-free survival. (NEJM 2004; 351: 145-153).

❑ Immunocompromised patients are prone to Parvovirus B_{19} infections and it may result in pure red cell aplasia and chronic anemia. The contribution of Parvovirus B_{19} infection to anemia in children with acute lymphoblastic leukemia (ALL) receiving maintenance chemotherapy was assessed and two groups were formed, comprising of 50 patients with persistent anemia (*i.e.*, extending for >2 weeks) and 34 patients without anemia (controls). Parvovirus B_{19} DNA was detected (in bone marrow by nested PCR) in 11 of the 50 (22%). All children with anemia, 4 of whom were also IgM positive. In addition, IgM positivity was observed in 9 (18%) other children who were negative for Parvovirus B_{19} DNA and IgG was found to be positive in a total of 19 (38%) cases, with B_{19} DNA present in 6 of them. The authors suggest that it is important to consider Parvovirus B_{19} infections as a cause of anemia and suppressed erythropoiesis in children with ALL who are receiving ongoing treatment. (J Pediatr Hemat Oncol 2004; 26: 403-406).

❑ Imatinib Mesylate is a novel therapy for leukemias and its use has been validated in adults in several studies. A phase I study was carried out in children with refractory or recurrent Philadelphia chromosome-positive (Ph^+) leukemias by the Children's Oncology Group to determine the optimal dose, dose-limiting toxicities, and pharmacokinetics of imatinib mesylate. Oral imatinib mesylate was administered daily at dose levels ranging from 260-570 mg/m^2 in consecutive 28-day courses of therapy. Serial blood samples for plasma pharmacokinetic studies were collected on days 1 and 8 of course 1. The most common toxicities associated with imatinib administration, which occurred in < 5% of courses, were nausea, vomiting, fatigue, diarrhea and reversible increases in serum transaminases. Among twelve CML patients evaluable for cytogenetic response, 10 had a complete response and 1 had a partial response. Pharmacokinetic analyses revealed that there was marked interpatient variability. The study concluded that daily oral imatinib mesylate is well tolerated in children with Ph^+ leukemias but needs further large scale studies to define its role in therapy for childhood leukemias. (Blood 2004 Jul 1 [Epub ahead of print]).

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