# Oncology and haematology

## G14 FACTORS AFFECTING THE SUCCESS OR FAILURE OF SPERM BANKING IN ADOLESCENT MALE CANCER PATIENTS

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**Aims:** Advances in the treatment of childhood cancer have resulted in many patients becoming long term survivors. This has lead to an increased focus on the cost of cure. Male infertility is a major long-term effect of chemo- and/or radiotherapy. A wide range of commonly used chemotherapeutic agents are gonadotoxic, including elements of protocols for the treatment of all the common tumours of adolescence. Sperm banking is a widely available method of maintaining post-pubertal male fertility. However the adverse impact of a diagnosis of cancer, and the evolving nature of many of these patients' sexual identities, mean that this facility is not always used. This study was conducted to identify those factors contributing to this failure.

**Methods:** Patients aged between 12–20 years at diagnosis, diagnosed between 1997–2001 at RMCH or the Christie were identified. Questionnaires were administered to those who had been offered sperm banking.

**Results:** 45 of 55 questionnaires were completed. The mean age at diagnosis was 17.1 years, and the mean interval between diagnosis and interview was 2.1 years. 67% of patients had been able to successfully bank sperm. Those who had been unsuccessful were younger (mean age 15.3y compared to 17.8y). This group of patients had significantly higher levels of anxiety at diagnosis and significantly greater difficulty in talking about fertility than those who were successful. They also had less understanding of sperm banking at the time of diagnosis.

**Conclusion:** The majority of adolescent cancer patients are able to bank sperm. However young age, high anxiety, lack of understanding of the process, and a difficulty in discussing fertility are associated with a failure to store semen. The provision of expert information and counselling to such individuals may increase their chances of successful sperm banking.

## G15 STATISTICAL ANALYSES PROVIDE SUPPORT FOR THE ROLE OF ENVIRONMENTAL EXPOSURES IN THE AETIOLOGY OF CHILDHOOD SARCOMAS AND WILMS' TUMOURS

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**Aims:** (i) To use population-based childhood cancer registry data on childhood solid tumours (excluding brain tumours), 1954–1998, to test predictions of space-time clustering patterns which might arise as a result of environmental exposures. (ii) To distinguish between hypotheses relating to post-natal exposures or pre-natal events by using locations and dates of birth as well as at diagnosis.

**Methods**: Knox tests for space-time interactions between cases were applied with fixed thresholds of close in space, <5km and close in time <1 year apart. Both places and times of birth and diagnosis were utilised. Tests were repeated replacing geographical distance with distance to the Nth nearest neighbour (Nearest Neighbour [NN] threshold analysis). N was chosen such that the mean distance was 5km. Data were also examined by a second order procedure based on K-functions. Analyses were applied to 10 specific diagnostic groups of childhood solid tumours.

**Results:** There was statistically significant evidence of space-time clustering for the sarcomas (p=0.006 and p<0.001 using the geographical distance and NN versions of the K-function method) and for the Wilms' tumours, aged >32 months (p=0..002 and p=0.02 using the geographical distance and NN versions of the K-function method). These findings were based on time and location at birth, but not time and location at diagnosis. Additionally, clustering of Wilms' tumours was much more marked for space-time pairs involving males than for those involving females. There was one clustering pair for nasopharyngeal carcinoma based on time and location at birth (p=0.1 and p=0.07 using the geographical distance and NN threshold versions of the Knox method).

**Conclusions:** The striking and novel results, showing space-time clustering for childhood sarcomas and Wilms' tumours, provide support for the role of environmental factors in the aetiology, occurring around the time and place of birth. There is also a suggestion of an environmental aetiology for the very rare clustering pair of nasopharyngeal carcinomas.

## G16 SURVEILLANCE BLOOD COUNTS IN ASYMPTOMATIC CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) AFTER COMPLETION OF CHEMOTHERAPY—ARE THEY NECESSARY?

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**Background:** ALL is the commonest childhood cancer with a 70–80% cure rate and long term survival. Of these patients 1:5 relapse with no apparent difference between them and their successfully treated peers. Follow up of these patients is therefore important and they are generally closely reviewed for the first 5 years in outpatient clinics between the tertiary referral centres and the shared care district general hospitals. There is no consensus as yet to the value of the full blood count (FBC) analysis in the follow up of these patients.

**Aim:** To determine the role of FBC surveillance in the follow up of children with ALL after completion of chemotherapy

**Design:** Retrospective analysis of patient records: reviewing all cases of relapse ALL in a tertiary referral centre over a 10 year period 1990–end 1999.

**Main outcome measure:** Yield of detection of relapse using FBC surveillance alone.

**Results:** Only 2 FBC analyses out of an estimated 2237 blood counts done in patients off chemotherapy between 1990–end 1999 led to the detection of relapse in well asymptomatic patients. The majority of patients with relapse presented with symptoms with or without an abnormal FBC. Almost 50% (19/39) of the children who had clinical symptoms at relapse had normal full blood counts and relapse was confirmed either by bone marrow and/or CSF studies in these cases.

**Conclusions:** FBC analysis in well asymptomatic children off treatment should be discontinued as it does not aid in detection of relapse in these cases. The importance of clinical review and examination should be emphasised and it should be noted that a normal FBC in a symptomatic child may be falsely reassuring. This evidence is important to all paediatric healthcare personnel to enable re-education of patients and their families and allow for a change in practice that is more effective and beneficial.

## G17 PREDICTORS OF NOCTURNAL HYPOXAEMIA IN CHILDREN WITH SICKLE CELL DISEASE

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Nocturnal hypoxaemia (NH, mean saturation <96% on overnight pulse oximetry) appears to be a predictor of central nervous system events and frequent pain in children with sickle cell disease (SCD). Obstructive sleep apnoea (OSA) is also common and may be treated with adenotonsillectomy. The risk factors for hypoxaemia are poorly understood, but might include increasing age, genotype, haematocrit, recurrent chest crisis or upper airway infection.

Of an unselected hospital cohort of children, 69 (median age 7.8 (range 1–16.5) years; 39 male) had overnight pulse oximetry at home between 1990 and 1995. Clinical details, including Casualty attendances and hospital admissions, were obtained from the hospital notes for the period preceding the overnight study. Logistic regression was used to look at predictors of NH.

25 children (36%) had NH. 13 had dips in saturation suggesting OSA, of whom 10 also had mean saturation <96%. There was no evidence that NH was associated with concurrent snoring (Fisher's exact test, p=0.8) in the 36 patients for whom the data were available. Of 11 children with abnormal overnight studies who had repeat overnight pulse oximetry after adenotonsillectomy, 8 were still abnormal. In univariate logistic regression, haematocrit at the time of the study (p=0.004), and age at first Casualty attendance for an upper airways infection (p=0.02) were associated with NH and there were trends for genotype (p=0.1) and white cell count at the time of the study (p=0.06). There was no effect of age at sleep study, number of admissions with chest infection or any other measure of complication

rate. Both haematocrit at the time of the study (p=0.01) and age at first upper airway infection (p=0.03) remained in the multiple logistic regression model.

NH in SCD is difficult to predict clinically and may not improve with adenotonsillectomy. Prospective studies should look at the role of infection.

## G18 ACUTE CHEST SYNDROME AND BRONCHIAL HYPERREACTIVITY IN CHILDREN WITH SICKLE CELL DISEASE

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**Background:** Episodes of acute chest syndrome (ACS) and pulmonary vascular occlusion during vaso-occlusive episodes in children with sickle cell disease (SCD) result in damage to the airway epithelium. The resulting increase in epithelial permeability and loss of intact epithelium might lead to bronchial hyperreactivity (BHR).

**Aim:** To test the hypothesis that amongst SCD children those who had had ACS compared to similarly aged SCD who never had an ACS would have an increased incidence of BHR.

**Patients:** Thirty-five SCD children (17 male) who had had ACS (ACS children), mean age 8.6 years (range 0.3–14.9years) and thirty-five SCD children without ACS (non ACS), mean age 8.5 years (range 0.3–14.9years).

**Methods:** SCD children were recruited from two specialist clinics in South Thames. Respiratory function was measured before and after BD. Functional residual capacity was assessed by helium gas dilution technique ($FRC_{He}$) and whole body plethysmography ($FRC_{pleth}$). FVC, FEV1 and PEFR were determined by spirometry. The magnitude of change in the respiratory function test results in response to BD was compared between the two groups.

**Results:** The ACS compared to the non ACS children had a greater fall in $FRC_{He}$ (mean change 9.9% ACS versus 0.1% non ACS ($p<0.01$)). In addition, there was a trend towards a greater change in PEFR following BD administration in the ACS group (mean change 15% ACS versus 9% non ACS).

**Conclusions:** These results suggest SCD children who have had an ACS are more likely to have BHR, whether this is a cause or consequence of ACS requires testing.

## G19 INITIAL RESULTS FORM THE SECOND INTERNATIONAL STUDY (1996–2001) OF THERAPY FOR LANGERHANS CELL HISTIOCYTOSIS (LCH II)

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From 1991–95 the Histiocyte Society organised LCH I, which revealed no difference in the efficacy of Vinblastine (VBL) and Etoposide (VP16) in the treatment of LCH. LCH II was designed to study whether improvement could be obtained in children with putative poor prognostic features by combining these drugs (VBL & VP16 vs VBL alone). Children were assigned to a "RISK" group if they had multisystem disease under the age of two years or at any age if it involved a risk organ—liver, spleen, marrow, or lung. Children who had less serious "LOW RISK" disease, and were treated with VBL alone, were also followed. 697 patients from 9 countries were registered on study. 321 patients had multi-system disease. 87 (27%) of these were stratified as LOW RISK and 233 (73%) were classified as RISK patients. 176 (76%) of the RISK patients were randomised. 66 (37%) of the RISK patients were under 2 years of age without involvement of RISK organs and, of these, 41 (62%) were randomised. Among 170 randomised RISK patients, in whom the response at wk 6 was available, 113 (66%) were judged as responders. The overall probability of survival of the multi-system patients did not differ significantly between the 2 arms and was around 80%. Thus there is a "HIGH RISK" population of 20% of multi-system patients which cannot be rescued with either treatment. Among the 118 randomised patients with risk organ involvement (any age) 22% showed progressive disease at week 6 and 35% of the remaining patients did not achieve a further improvement within the next 6 weeks of treatment. This meant that by week 12, about 50% of the patients with RISK organ involvement had not shown a response to treatment, but still had intermediate active or progressive disease. For these patients the probability of mortality after 12 weeks of treatment is about 75%. In the overall analysis, age < 2yr did not constitute an independently significant risk factor. In the LOW RISK group there were 89% responders, only 1 non-responder at week 6, and no fatalities.

## G20 SALVAGE OF CENTRAL VENOUS CATHETERS IN PAEDIATRIC ONCOLOGY PATIENTS WITH GRAM-NEGATIVE STAPHYLOCOCCAL-AUREUS BACTEREMIA

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**Aim:** It has been suggested that bacteremia with staphylococcal-aureus (*S.aureus*) and gram-negative organisms in the presence of central venous catheters (CVC) is optimally managed by removal of the CVC. The aim of this study was to document the outcome of gram-negative and *S.aureus* catheter-related bacteremia in paediatric oncology patients with particular reference to the salvage of CVCs.

**Methods:** A retrospective analysis of all paediatric oncology patients with positive blood cultures over a 5-year period was undertaken. Episodes of gram-negative and *S.aureus* bacteremia in patients with CVCs were analysed in detail. Time from insertion of CVC, clinical course, need for supportive care and outcome including removal/retention of CVC were determined from case notes. Recurrence of bacteremia with the same organism within 4 weeks was recorded.

**Results:** A total of 199 episodes of bacteremia in 102 patients were identified. Of these 56 episodes were due to gram-negative organisms (including *Pseudomonas aeruginosa*-10) and *S.aureus*. These 56 episodes in 40 patients were analysed in detail. The CVC was a Hickman line in 49 episodes and a Portacath in 7. Six episodes were within 2 weeks of insertion of the catheter (of these *S.aureus* was the pathogen in 5). Neutropenia was documented in 32 (57%) of these episodes and concurrent mucositis in 12 (22%) episodes. Only 1 patient needed admission to ITU. The CVC was removed in 16 (28%) episodes and retained in the rest. In 75% of these the CVC was retained for >50 days following the episode. In the patients in whom the CVC was retained, 5 had recurrence of bacteremia within 4 weeks but the CVC was salvaged again in all 5. All patients made a complete recovery.

**Conclusion:** It appears that gram-negative and *S.aureus* bacteremia can be successfully managed without catheter removal in majority of paediatric oncology patients. However in some patients catheter removal may be necessary on clinical grounds.

## G21 ECONOMIC IMPACT OF NOVOSEVEN IN THE TREATMENT OF MINOR BLEEDS IN CHILDREN WITH INHIBITORS TO COAGULATION FACTORS VIII AND IX

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**Aims:** To estimate the costs and consequences of managing a minor (i.e. mild to moderate) bleeding episode in children with high titre, high responding inhibitors (>IOBU), with NovoSeven (recombinant activated Factor VII) compared to FEIBA (activated prothrombin-complex concentrate) from the perspective of the UK's National Health Service (NHS).

**Methods:** Clinical outcomes and resource utilisation attributable to managing a minor bleed were obtained from the published literature and a panel of consultant haematologists (n=22) experienced in managing inhibitor patients. Using this information, two decision trees were constructed. One modelled the management of a minor bleed, initially at home, and the other at a hospital treatment centre (Comprehensive Care Centre (CCC)). Consensus on the probabilities and resource utilisation estimates in the models were reached at a meeting comprising seven of the haematologists.

**Results:** The expected mean NHS cost of managing a minor bleeding episode among children initially treated with NovoSeven or FEIBA at home (at a CCC) was estimated to be £5,680 (£5,351) and £5,301 (£5,835) respectively. The expected mean time to resolving a minor bleeding episode when initially treated with NovoSeven or FEIBA was estimated to be 31-34 hours and 56-62 hours respectively.

**Conclusions**: The costs of managing a minor bleed in children either at home or at a CCC using NovoSeven or FEIBA are comparable. However, using NovoSeven instead of FEIBA is expected to resolve a minor bleeding episode in about half the time. Consequently, the decision to use either NovoSeven or FEIBA for managing a minor bleed should be based on efficacy, safety and patient preferences and not drug acquisition costs.