Flow Cytometric Detection of Asparagine Synthetase Protein in Leukemia Cells; Indication for L-Asparaginase Therapy

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Background: During treatment for childhood ALL, patients are given L-asparaginase (ASNase). L-asparaginase therapy causes depletion of plasma asparagine followed by the loss of intracellular asparagine. Due to the lack of a rapid up-regulation of asparagine synthetase (ASNS) protein content in ALL cells, they are preferentially sensitive to ASNase. ASNS deficiency in leukemia cells is considered to confirm the effectiveness of ASNase. Elevated expression of ASNS within the leukemia cells causes decreased sensitivity to ASNase therapy.

Objective: Our aim was to test whether ASNS deficiency in leukemia cells can lead to sensitivity to ASNase.

Methods: ASNS expression in 3 leukemia cell lines and in eight sporadic leukemia cases was evaluated by flow cytometry with Z5808 McAb (Hybridoma 31: 325-332.2012) Fresh leukemia cases contained three ALLs, Ph1ALL, FABM1AML, M2AML, two M7AML cases. Leukemia cell lines were examined by MTT or WST1 cytotoxicity assay. ASNS expression was also compared with IC50 concentration to ASNase.

Results: K562 cells with the highest ASNS expression exhibited lower ASNase sensitivity than RS4;11 or Molt-4. RS4;11 exhibits the lowest ASNS expression and the lowest IC50, less than 0.02 IU/L, versus more than 10 IU/L for the K562 cells. ASNS Expression in ALL was almost near zero. ASNS expression in fresh AML was low in all cases except for M2. Indeed, at high ASNS expression, FABM2 was resistant in vitro to ASNase even in more than 10 IU/L.

Conclusion: We demonstrated here that many leukemia cells with low ASNS expression are more sensitive to ASNase than leukemia cells with high ASNS expression. Also, fresh leukemia cell with low ASNS expression are more sensitive to ASNase than with high ASNS expression. Plasma asparagine depletion by ASNase in selected patients having low or no ASNS may be a promising therapeutic approach even for AML.
Splenectomy for Children with Thalassemia: Total or Partial Splenectomy, Open or Laparoscopic Splenectomy

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Objectives: An analysis of our experience with 36 children with thalassemia who had splenectomy.

Patients and methods: 36 children (27 beta-thalassemia major, 3 Hb H disease, 6 thalassemia intermediate) who had total splenectomy (11 laparoscopic and 13 open) or partial splenectomy (12 patients) were reviewed.

Results: There were 17 M and 7 F in the total splenectomy (TS) group with a mean age of 7.6 years, and 4 M and 8 F in the partial splenectomy (PS) group with a mean age of 6.9 years. In the PS group, 2 with Hb H required no blood transfusions. The transfusions of the third decreased from 15 per year to 10 per year (1.2 g/week Hb drop preoperatively to 0.6 g/week Hb drop postoperatively) but subsequently his transfusions increased as a result of increase in the size of the splenic remnant, and underwent TS. For those with beta-thalassemia major who had PS (9 patients) there was a reduction in their transfusions from 15.2 per year (13–22 transfusions per year) to 8.2 per year (2–11 transfusions per year). Their Hb drop decreased from 1.6 g/week (0.8 –3.5 g/week) to 0.5 g/week (0.2–0.75 g/week). Subsequently and as a result of increase in the size of splenic remnant, their transfusion requirements increased, but none required TS. 24 had TS (13 open and 11 laparoscopic). Their transfusions decreased from 17.8 per year (12-23 transfusions per year) to 10 per year (8-12 transfusions per year) and their Hb drop decreased from 1.8 g/week (0.8-2.3 g/week) to 0.45 g/week (0.3-0.65 g/week).

Conclusions: TS is beneficial for children with beta-thalassemia major but LS is more advantageous. PS may be useful for those with Hb H disease, but for those with beta-thalassemia major it is beneficial as a temporary measure, and so it is recommended for children who are less than 5 years of age.
Mean Corpuscular Volume is a Predictor of Mortality in Extremely Low Birth Weight Infants

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Background: Mean corpuscular volume (MCV), or “mean cell volume” (MCV), is a measure of the average red blood cell volume that is reported as part of a standard complete blood count. The MCV diminished from 119 ± 7 fl (mean ±sd) in neonates ≤25 weeks gestation to 106 ± 4 fl at 40 weeks. MCV is an important predictor for anemia. MCV measurement allows classification as either a microcytic anemia (MCV below normal range), normocytic anemia (MCV within normal range) or macrocytic anemia (MCV above normal range). There are no data investigating the relationship between MCV and mortality of extremely low birth weight (ELBW) infants (1000 gr).

Aim: To assess the correlation between MCV and the mortality in a cohort of ELBW infants.

Subjects: We studied infants with a birth weight of 1000 g admitted to a third level Neonatal Intensive Care Unit. MCV was evaluated at sixth hour of life. MCV was categorized into quartiles as less than 111, 111 to 115, 115 to119 and greater than 119.

Results: One hundred and eighty five infants were studied. Median gestational week was 26 weeks (21-31 w), median birth weight was 820 grams (min 440- max 1000 g). Eighty one (43%) infants were died in this period. Sixty nine (37%) were died in first seven days. After the effect of gestational week and birth weight were controlled, MCV was significantly correlated with mortality (r=0.21 p= 0.04) and CRIB scores (r=0.30 p= 0.001). And this correlation is significant in blood groups other than O blood group.

Conclusions: High MCV in the first hours of life may reflect the presence of a risk factor for the mortality in extremely low birth weight infants. This might be associated with reactivation of bone marrow, inflammatory and oxidative process, hypoxia, trace element deficiency, perinatal factors, and cellular mechanisms. Higher MCV values are associated with the mortality and also CRIB score in this study population.
Recent studies suggest conflicting findings regarding association between obesity and adolescent bone mineral content (BMC) and bone mineral density (BMD).

Aim: to explore the impact of being obese on whole body (WB) BMC and BMD in a group of Egyptian adolescent girls.

Methods: Study included 35 obese adolescent girls (13.5±1.8 years) with body mass index (BMI) 95th percentile and 35 maturation-matched (14.2±1.4 years) controls with BMI 15th - 85th percentile for age and gender. Bone mineral areas (BMA), BMC, BMD at the WB and body composition (lean mass, fat mass and fat %) were assessed by dual-energy X-ray absorpiometry (DXA). Calculations of the BMC/height ratio and bone mineral apparent density (BMAD) were computed for the WB.

Results: BMD, BMC, BMAD and BMC/height ratio were highly significant higher in obese adolescent girls compared to controls. Body weight, height, BMI, lean mass, fat mass and fat% had highly significant positive correlations with BMD, BMC, BMAD and BMC/height ratio. BMA had highly significant positive correlations only with weight, height, lean and fat mass. After adjusting for either body weight or total fat mass, BMD, BMC, BMAD, BMC/height and even BMA became highly significant higher in control than obese girls. After adjusting for total lean mass, the same was observed but the differences were only highly significant between the two groups in BMC and BMA.

Conclusion: This study suggests that there is positive effect of obesity on BMC, BMD, BMAD and BMC/height ratio due to body weight, while obesity has no effect on BMA.
Mindfulness is a practice of kindness. With sustained practice, the ability to cultivate calm, conscious, compassionate choices for the self, others and life becomes possible.

It is estimated that over 2,000 schools globally are running Mindfulness Programs. It is also being widely embraced in therapeutic practices. Preliminary research indicates a wealth of benefits for children; including effective stress management, impulse control, enhanced performance and academic achievement, increased empathy and optimism.

This workshop is a hands/hearts/minds-on opportunity to learn simple, practical ways to engage children in a variety of fun, simple and creative mindful skills. These skills have been trialed with thousands of students.

Mindfulness programs can be effectively tailored to suit children from 4-18 years of age. A wide range of activities, games, stories, quotes and relevant Mindful focus points offer scope for personal discovery and engagement. Programs can be structured sequentially to develop the general tenets of self-awareness, culminating in specific practices to enhance subtle focus skills.

They can easily be integrated into the clinic, classroom and life: with techniques ranging from 60 seconds to 5-10 minute practices.

Content includes:

- Body Awareness
- Understanding stress
- Tuning in to emotions and thoughts
- Connecting to the senses
- Be-friending the self and others

As well as being a catalyst for personal growth, Mindfulness practices engender empathy and compassion. Opportunities to shift from hearing to listening and judging to understanding. Mindful discussions bridge differences and build relationships. Time spent together in Mindful Meditation deepen bonds and a sense of trust between children, their therapists, teachers and parents.
Depression in Survivors of Childhood Cancer

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Aims: Five year survival from childhood cancer is 82%. This population may be at greater risk of developing major depressive disorder (MDD) in later life. The purpose of this study was to investigate the effect of childhood cancer and its treatment on self-reported mental health in adult survivors of childhood cancer in Britain.

Methods: Responses of a postal questionnaire of 10,488 survivors from the British Childhood Cancer Survivor Study (BCCSS) were analysed. Self-reported anti-depressant use and three Medical Short Form Questionnaire 36 (SF-36) scores were calculated which best measures the mental component of health status - 1) Role limitation due to emotional problems; 2) social functioning; 3) mental health. This was compared between the survivors using a multivariable logistic regression.

Results: Anti-depressant use in survivors of childhood cancer was strongly associated with gender, diagnostic group and attained age but not age at diagnosis or treatment modality.

Females were twice as likely to take antidepressant medication compared to men and performed worse in all three SF-36 scores (p<0.0001). Survivors of Non-Hodgkins Lymphoma (NHL) and bone tumours scored significantly lower SF-36 scores (for all three scores for NHL and bone tumours p<0.0001).

A linear correlation was found between age at questionnaire completion and all three SF-36 scores. The likelihood of anti-depressant use also increased with age at questionnaire completion in a non-linear fashion.

Conclusions: This study has highlighted sub-groups within the survivor cohort at particular risk for mental health morbidity, notably depression. Identification of subgroups within the survivor cohort that are at increased risk for mental health conditions in later life will enable rapid engagement with mental health services and subsequently earlier commencement of appropriate therapy. Identification of these at-risk subgroups enables more targeted preventative interventions against mental health morbidity.