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INCREASED LEPTIN LEVELS IN CHILDREN WITH INFECTIONS

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Leptin is an adipocyte-derived hormone/cytokine that links nutritional status with neuroendocrine and immune functions. As a hormone, leptin regulates food intake and basal metabolism, and is sexually dimorphic that is, its serum concentration is higher in females than in males with a similar body fat mass. As a cytokine, leptin can affect thymic homeostasis and the secretion of acute-phase reactants such as interleukin-1 and tumour-necrosis factor. Similar to other pro-inflammatory cytokines, leptin promotes Thelper1 (TH1)-cell differentiation and can modulate the onset and progression of autoimmune responses in several animal models. Many studies in animals have demonstrated that leptin levels increase acutely during infection and inflammation. We studied the leptin response to infections in 27 children with bacterial infections mainly respiratory and urinary tract. Serum Amyloid A protein (SAA) and C-reactive protein (CRP) in serum were measured by particle-enhanced immunonephelometric assays (BNProSpec Dade Behring), procalcitonin (PCT) levels were determined by chemiluminescence (Brahms), while leptin levels were measured by an enzymatically amplified two-step sandwich-type immunoassay (DSL). The main results of the study are summarized in the table:

	CRP (mg/L)	SAA (mg/L)	PCT (ug/L)	Leptin (ug/L)
Day 0	121.9±18.3	428.7±83.9	7.2±1.7	11.7±1.8
Day 3	43.1±6.8	148.1±32.3	2.1±0.5	6.2±0.8
Difference	p=0.00004	p=0.0003	p=0.0008	p=0.00002

Leptin levels increased in all patients independently of their BMI, at diagnosis of the infection and returned to normal levels after treatment. This is an indication of normal expression of leptin genes and leptin receptor and this suggests that leptin is also an inflammatory marker. Similar results have been described in patients with sepsis, whereas the non-increase of leptin levels was associated with increased mortality. The secretion of leptin in the first hours of inflammation in children is stimulated by the endotoxins of bacteria as it has been shown in animal models. Leptin seems to play an important role being part of the cytokine network and modulating the inflammatory-immune response and the host defense mechanisms.

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MORTALITY OF VERY PRETERM BIRTHS: ASSOCIATIONS WITH TERMINATIONS OF PREGNANCY AND CONGENITAL ANOMALIES IN THE MOSAIC COHORT.

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Context: Practices related to screening and termination of pregnancy (TOP) for congenital anomalies (CA) vary within Europe countries and could explain some of the variability in mortality among very preterm births.

Methods: The MOSAIC study (1) collected data on all stillbirths and live births between 22 and 31 weeks of gestation in 10 European regions in 2003. Babies transferred to NICU were followed to discharge from hospital. Data were extracted from medical records in the maternity and neonatal wards, including information on reasons for TOP and the presence of a lethal congenital anomaly for stillbirths and live births.

Results: There were significant differences in the proportion of termination of pregnancies among stillbirths, ranging from about 50% in the regions in France and Italy to lows in the regions in Poland (9%) and in Germany (17%). In most regions, 80% or more TOP were for CA, with some exceptions such as in Poland, where only one third of TOP were for CA. The proportion of CA among stillbirths, after exclusion of TOP, varied by region, with high rates in Portugal and the Netherlands and low rates in Hesse, Denmark, Ile de France and Lazio. The rates of neonatal death associated with a congenital anomaly among live born infants 22/31 weeks also differed: in Poland and Portugal rates were higher in comparison with Ile de France and Lazio.

Conclusion: Practices related to pregnancy termination appear to have an impact on fetal and neonatal mortality due to CA in the very preterm population. These differences could be explained by the legal context, policies of systematic screening and the gestational age at screening. 1. Eur J Obstet Gynecol reprod biol 2005;118:272–4

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TREATMENT WITH ENZYMATIC REPLACEMENT THERAPY (ERT) IN PATIENTS WITH MUCOPOLYSACCHARIDOSIS TYPE I. THIRTY MONTHS EXPERIENCE

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Aims: Evaluation of the effects of alfa-L iduronidase in 6 Italian MPS I patients. Patients and

Methods: 6 pts (2 MPS IH/S and 4 MPS IS) mean age 24 yrs (range 11–38 yrs) received ERT 100 U/kg/week for 18.7 month mean (range 4–33 ms). We tested urinary glycosaminoglycans (GAGs), heart function, splenomegaly, joint function and quality of life (QoL).

Results: only one patient had an adverse reaction (severe urticaria) and it was necessary to reduce the dosage to 80 U/Kg/week. Results in the 3 MPS IS and 2 MPS I HS treated with a mean follow-up of 19,2 ms (range 12–30 ms) are the following: reduction in urinary GAGs excretion (-78 % mean; range -50%-91%), in bipolar diameter of the spleen (mean 1.2 cm, range 0 - 4 cm); cardiac parameters stabilised. Improvement of joint mobility with a maximum of 30 for shoulder abduction. Improvement of QoL in one MPS IS (30 ms treatment), especially in dressing herself and in the daily care; no improvement in QoL in the other two MPS IS after one year, although their joint mobility became better. Parents of the two pts affected by MPS HIS noted a stabilisation in one case and an improvement in the other in the daily care. Conclusions: ERT led, as expected, to a reduction of urinary GAGs excretion, splenomegaly, and improvement of joint mobility. The improvement of the QoL was clear in only 1/5 pts. Probably, for the less severe forms of MPS IS a longer follow up is needed to appreciate an improvement, while, on the other side in MPS I HS pts, severe disability could heavily influence the quality of life and the autonomy, hiding the benefits of an increased joint mobility.

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LONG-TERM OUTCOME AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT) IN PATIENTS AFFECTED BY MUCOPOLYSACCHARIDOSIS I HURLER (MPS IH)

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Aims: To evaluate the long-term effect of HCT in MPS IH pts. Patients and methods: 6 MPS IH (median age at diagnosis 1.2 yrs, 0.5–1.5) pts underwent 8 B- and T-depleted HCTs (after autologous reconstitution 2 pts received a second HCT) at a median age of 1.7 yrs (1.2–2.5). Heart, pulmonary, eye, ear, bone and neurological involvement was periodically evaluated.

Results: At a median follow-up of 4.2 yrs (2.8–5.3), 5 out of 6 pts (mean age 6.3 yrs, 5.3–6.9) are alive (one pt died 1 yr after HCT), 4 complete and 1 partial chimeras, all with normal enzymatic activity and a reduction in the excretion of urinary glycosaminoglicans. Patients showed a reduction in hepatosplenomegaly and in respiratory infection and stabilisation of corneal cloudings. Joint mobility clearly improved. Hearing was normal in one patient, the other 4 had hearing loss which stabilised in 1 and improved in 3 pts. Cardiac involvement was stable in 2 and slight improved in 3 cases. X-ray showed a stability in genu-valgum in 4/4 and in kyphosis in 2/2 cases. The cerebral MRI was stable in 2 and improved in 2 pts. The basal median developmental quotient (Griffiths scale) of 89 (70–93) decreased during the first year after HCT and then stabilised reaching a median of 74 (53–82) after a median of 3.0 yrs (1.5–3.3).

Conclusions: HCT represent a good therapeutic option for selected MPS IH patients and could determine an improvement in the natural history of the disease influencing the cardiac, joint and pulmonary function but also bone and the central nervous system involvement. Acknowledgement: Comitato Maria Letizia Verga, Fondazione Pierfranco e Luisa Mariani and MPS Italian Association.

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DO NOT RESUSCITATE ORDERS AND WITHDRAWAL OF LIFE SUPPORT IN DYING PEDIATRIC PATIENTS

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Purpose: For some critically ill children, resuscitation is not attempted when further therapy is judged inappropriate. Most pediatric deaths involve withdrawal of life support (WDS). Do not resuscitate (DNR) orders remain infrequent in children.

Methods: From a sample of 120 in-patient pediatric deaths at an academic children's hospital, we abstracted demographics, end-of-life care conferences, DNRs, WDS, and time intervals between conferences and death from hospital charts.

Results: Of 63 charts reviewed to date, median age at death was 29 days. Median duration of terminal hospitalization was 10 days. Median time from first care conference to death was 2 days. 95% of deaths occurred in intensive care settings. 11 patients neither WDS nor DNR. 24 patients had written DNRs, while 43 patients had WDS. Of 19 with both DNR and WDS, 16 DNRs were written within 48 hours of WDS. DNRs were more common when patients died $>= 2$ days versus < 2 days ($p=0.01$) after the first parent conference. DNR orders did not differ by age at death, length of stay, race, or unit at death, although sample size is still small. Primary diagnoses (oncologic, infectious, prematurity, non-cardiac anomalies, cardiac, respiratory, and CNS conditions) were not correlated with DNR status.

Conclusions: Most pediatric deaths occur in intensive care settings and many patients die receiving maximal care. Almost 50% of patients undergoing WDS have no DNR. DNRs seem an uncommon first step in limiting treatment, written with the expectation of WDS and imminent death. Finally, earlier patient care conferences significantly increased the probability of having DNRs. Given the short interval from poor prognosis to death, we may need to tailor palliative care practices to fit the realities of how and where children die.