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NEUROBLASTOMA CELL DETECTION IN PERIPHERAL BLOOD BY REVERSE TRANSCRIPTASE-POLYMERASE CHAIN REACTION (RT-PCR).

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In neuroblastoma disseminating disease is associated with a poor prognosis. Early detection and treatment may improve the outcome for the patient. In the present study we have used RT-PCR to detect neuroblastoma cells in peripheral blood, using tyrosine hydroxylase (TH) as the tissue specific target gene. From isolated RNA cDNA is synthesised using RT; cDNA is amplified for the TH gene by PCR and the products analysed by electrophoresis. This method is sensitive (detecting 10 neuroblastoma cells in 1ml of whole blood) and specific (no TH mRNA was detected in control bloods). 4/6 patient bloods were positive at the time of diagnosis or relapse; 2 from newly diagnosed patients with stage IV disease, 1 from a relapsed stage III and 1 from a relapsed stage IV. Both relapsed patients subsequently died from neuroblastoma. The 2 negative samples were from newly diagnosed stage II and stage IV patients. 16/17 blood samples from patients disease free on follow up were negative. The 1 positive blood in this group was found in a patient successfully treated for stage IV neuroblastoma; whether this is an indication of early metastasis is very intriguing. Early results are encouraging, suggesting that RT-PCR using TH as the target gene may be useful for the detection of circulating neuroblastoma cells. We hope analysis of more patient samples will define the role of this technique in both staging and peripheral stem cell harvesting and increase understanding of neuroblastoma as a disease process.

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GROWTH HORMONE DEFICIT INDUCED BY CHEMOTHERAPY (CT) IN CHILDREN WITH CANCER.

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In an attempt to investigate the effects of CT on GH secretion, we have studied a group of 25 patients (11 males and 14 females) affected of osteosarcoma, mean age 13.3 yr (6.3-19.8 yr) who received CT and surgery as only treatment. Patients with adult bone age were excluded from growth evaluation. None of them was given cranial radiotherapy. GH reserve was assessed by two different stimuli (Clonidine and L-Dopa). Mean time between completion of treatment and GH evaluation was 18.56 months (range 2-34). At that time all patients were in complete remission. At diagnosis time, height was 0.2 ± 1.3 SDS and growth rate 0.1 ± 1.5 SDS in the GH deficient group; and in the non-deficient GH (n-GHD) group 0.1 ± 1.2 SDS and 0.2 ± 1.7 SDS. GH deficiency (GHD) was diagnosed by classical criteria in 11 out of 25 patients (44%). Results were reported as Score Deviation Standard (SDS) to allow comparison of different sex and age. At the end of therapy the mean height in the GHD group was -0.3 ± 1.2 SDS, in the n-GHD group the mean height at the end of CT was -0.17 ± 1.4 SDS differing from the former group ($p=0.06$). For a mean follow-up of 30 months, the mean height was -0.49 ± 1.0 SDS for the GHD group and -0.26 ± 1.3 SDS for the n-GHD group. Growth rate at the end of treatment was different between GHD group and n-GHD group (-0.32 ± 2.6 SDS vs -0.21 ± 2.0 SDS, $p=0.06$). Although growth impairment in children treated because of malignant diseases has a multifactorial etiology, GH deficit caused by CT has to be considered. An endocrine follow-up should be programmed in order to detect and treat hormonal deficiencies as early as possible.

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PROGRESS IN THE TREATMENT OF 155 CHILDREN WITH RHABDOMYOSARCOMA IN ONE CENTER DURING 28 YEARS

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Treatment results of 155 children with rhabdomyosarcoma/RMS/changing through years from 1962-90 according to progress of chemotherapy /CHT/, introduction of megavoltage radiotherapy /RTX/ and conservative surgery with attempts to preserve life-important organs are presented.

In consecutive periods 1962-80, 1981-85 and 1986-90 the overall survival elevated respectively from 27% /20/74/, through 41,3% /19/46/ to 60% /27/35/.

Comparative analysis of two last periods pointed out the significant progress of treatment results in III clinical group /IRS classification/, /20,7% vs 62,9% and parameningeal RMS /70% vs 58%.

The main prognostic factors and treatment failures of last years are presented in respective tables.

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HIGH DOSE IFOSFAMIDE (IFOS) AND MESNA (M) IN REFRACTORY PEDIATRIC SOLID TUMORS AFTER PREVIOUS EXPOSURE TO "CONVENTIONAL" IFOS.

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Responses to conventional doses (CD) of IFOS ($1.8 \text{ g/M}^2/\text{day} \times 5 \text{ days}$) are well documented. In an effort to enhance its activity, higher doses were investigated. IFOS was administered as $3 \text{ g/m}^2/\text{day} \times 5 \text{ days}$ by continuous infusion (CI) mixed with M in equal doses. To date, 19 patients (pts) with refractory tumors and measurable disease have been enrolled. Fifteen had had IFOS at CD. After 2 cycles: 4 pts showed a complete response (CR) and 8 partial responses (PR). Toxicity was analyzed after 37 cycles: the major was pancytopenia in all cycles, 30 required antibiotics. Reversible neurotoxicity was found in 1 pt; no hematuria was noted. Conclusions: (1) This protocol is effective: 63% (CR+PR). (2) The most effective dose of IFOS remains to be determined. (3) Until a more effective dose is discovered, we recommend investigating this approach in high risk newly diagnosed solid tumors in children and adolescents.

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LATE CARDIAC EFFECTS AFTER MODERATE DOSES OF ANTHRACYCLINES

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Cardiac toxicity after high doses of anthracyclines is well documented. However some recent publications suggest late cardiac involvement at lower anthracycline doses. Stress test seems a logical approach to determine subclinical cardiac lesions.

We studied 55 subjects (11 controls, 25 patients who completed chemotherapy with anthracyclines (<550 mg/m²) at least 5 years before the test (group 1), 19 patients who completed chemotherapy without anthracyclines at least 5 years before the test (group 2), age 11-26 years). Standard echocardiography (M-mode) and Doppler of aorta (Ao) and mitral valve (MV) and a standard effort ECG were performed in each subject. A stress test on a supine bicycle with a 3 minute incremental protocol and with Doppler study of Aortic (Vmax Ao) and mitral velocities (VE) during effort was performed in the 11 controls, 10 group 1 patients and 6 group 2 patients.

No significant differences could be found between the 3 populations for rest values (M-mode and Doppler) and for standard effort ECG. However, the increase in Vmax Ao and VE during supine exercise showed a significant difference between controls and group 1 ($P<0,005$) as there was also a difference in VE increase between controls and respectively group 1 and 2 ($p<0,05$).

In conclusion: supine bicycle stress echocardiography shows systolic and diastolic cardiac dysfunction even after moderate doses of anthracyclines. But treatment regimens without anthracyclines don't seem free of cardiac toxicity either.

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PARENTERAL NUTRITION INFLUENCE ON TOLERANCE AND EFFECT OF ANTICANCER CHEMOTHERAPY IN CHILDREN

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The analysis of 21 episodes of parenteral nutrition/PN/lasting 10-45 days/mean 22 days/in 20 patients /pts/ with cancer /80% of them with advanced disease/ and 3 consecutive chemotherapy /CHT/ courses, correlated with early and final treatment results was performed.

The increase of nutritional parameters was obtained in 80% of pts. Delayed CHT of mean 6 days concerned 21,3% of all 61 courses. 34,7% of drugs doses were decreased to mean 80%. Myelosuppression lasting about 6 days appeared after 50% of CHT courses. Infections complicated 23% of CHT courses, beginning by mean 8-th day after CHT. 28,6% of them were of unknown origin. Complete and partial remissions were obtained in 60% of pts, the same being the final survival. We assume that PN is life-saving method in severe CHT complications, allows to perform intensive CHT in malnourished pts and can improve indirectly the final results of treatment.