

**Conclusion.** The use of aggressive multimodal therapy (surgery/chemotherapy) and evaluation of prognostic factors are necessary for successful treatment in patients with osteosarcoma relapse. Type of chemotherapy regimen should be assessed in randomized multicentric trials.

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POSTER

### Childhood cancer incidence in the Kyrgyz Republic 1985-1999

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**Background:** The study analyses geographical variations in cancer incidence, trends in survival, health status of long-term survivors of childhood cancer.

**Material and methods:** The incidence of cancer in children aged less than 15 years between 1985 and 1999. There were 1755 registered cases with new diagnoses of cancer. Male-female proportion 1.3. The study collected data from forms submitted along with histological or cytological findings, and deaths certificates. Histologically verified were 84.7% cases.

The population relative risk was estimated for main tumours in urban and rural areas. Detailed population figures from census have been available at the Kyrgyz National Centre of Statistics. The official estimates have been available for intercensal years. These are based on the census and data on natural population change. The population figures and cancer incidence rates for this report have been provided in for age-groups (0-4, 5-9, 10-14), ethnic groups, for each sex and calendar years of the study period. The crude and age-standardised rates per 1 million have been counted. The classification scheme was used according to the International Classification of Childhood Cancer.

**Results:** Total age-standardised (ASR) annual incidence rate was 74.8 per million. The most frequent diagnostic groups were leukaemias (ASR=20.8), brain and spinal tumours (7.3), lymphomas (5.4), sympathetic nervous system tumours (4.3), kidney tumours (5.0), soft-tissue sarcomas (4.4), retinoblastomas (3.9), germ cell tumours (3.3), hepatic tumours (1.2), carcinomas and non classified tumours (4.6).

Incidence was significantly higher in the Russians, with an ASR of 114.7 cases per million per year, compared with 77.6 for Uzbeks and 65.6 Kyrgyz children. Assigned risk was higher among Russians in lymphomas (RR=3.5), neuroblastomas (RR=2.5), than Kyrgyz. Kyrgyz and Uzbeks had an increased RR in tumours of eye and testis, but this was not statistically significant. Part of this apparent increase may have been due to the improved registration of cases in the 1980s, particularly of certain tumour types, and of tumours in older children who may have been treated outside the major paediatric treatment centres. Between the 2 periods, 5-year survival increased from 29% to 47%, with improvements in almost all tumour types. In some tumours (Wilms', soft tissue sarcoma, leukaemias, lymphomas and others) 5-year survival increased from 45% to 64%. There has been an evidence that with new treatment regimens introduced during the 1980s survival in the 1990s has shown the increased gains.

**Conclusions:** In Kyrgyzstan, the childhood cancer incidence is low and similar to those reported from Asian developing countries. The data could be used for a wide range of epidemiological and other studies.

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### Blood and bone marrow transcripts of tyrosine hydroxylase, dopa decarboxylase, and GD2 synthase in neuroblastoma

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**Background:** Neuroblastoma is the most common extra cranial tumor in childhood. In spite that multimodal therapy is used the outcome for children with severe neuroblastoma is still poor. The mRNA transcripts of tyrosine hydroxylase (TH) and GD2 synthase (GD2S) are two well-known candidates suitable for identification and monitoring neuroblastoma cells in blood and bone marrow. Dopa decarboxylase (DDC) mRNA also seems to be useful, but has not been systematically investigated. The utility of these transcripts for tracing minimal residual disease should therefore be compared in clinical material.

**Material and methods:** Real-time reverse transcription (RT)-polymerase chain reaction (PCR) methods were developed to quantify mRNA of TH, DDC and GD2S in blood and bone marrow in children with neuroblastoma. The calibrators used were obtained by amplification of segments of cDNA from the mRNAs of the enzymes, which included the targets.

A total of 229 blood samples from 47 patients and 106 bone marrow samples from 41 patients with neuroblastoma of different stages were analyzed. Cord blood from 52 babies and blood from 26 healthy children, 4 months to 16 years of age, were used as controls.

**Results:** Blood samples were obtained at diagnosis from 11 children with a stage 1-3 disease. Increased concentrations were found in 4 children regarding TH mRNA, 1 child regarding DDC mRNA and 3 children regarding GD2S mRNA.

Bone marrow samples were also received from 9 patients with stage 1-3 neuroblastoma. Two of them had TH mRNA values above cut off level, one had increased DDC mRNA and five had increased GD2S mRNA.

We received blood samples from 14 children with stage 4 disease at diagnosis. TH mRNA was increased in 13 of the cases, DDC mRNA in 7 cases, and GD2S mRNA was elevated in 10 of the cases.

In 15 children with stage 4 neuroblastoma there were increased bone marrow concentrations of TH mRNA in 14 cases, of DDC mRNA in 12 cases and of GD2S mRNA in 13 cases.

There was a high correlation between TH mRNA and DDC mRNA in blood taking all samples into account. This was not the case between GD2S and TH. The correlations were lower in bone marrow between DDC and TH but still higher than the correlation between GD2S and TH mRNA.

**Conclusions:** The data indicate that at diagnosis of neuroblastoma sensitivity for detection of stage 4 disease is higher with TH mRNA as compared with both DDC mRNA and GD2S mRNA. It also seems that GD2S is less discriminating of stage 4 from stage 1-3 in the bone marrow since 5 of 9 children with stage 1-3 disease had elevated levels in the bone marrow.

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POSTER

### Severe sepsis in children treated for leukemia in a single unit in Romania

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**Purpose:** This is a retrospective study aimed to determine the etiology and leading causes of death in severe sepsis related to leukemia in a country with limited financial resources.

**Patients and methods:** The records of 51 children treated for acute leukemia (ALL 44 pts and AML 7 pts) between 1991-2003 were retrospectively reviewed for severe sepsis. Data concerning clinical, microbiologic and other investigative documentation of infection and outcome were analyzed using the SPSS software programme.

**Results:** Forty five episodes of severe sepsis were documented in 27 patients. All were under chemotherapy: induction phase (6 episodes), consolidation (34 episodes) and maintenance (5 episodes). Etiology was precised in 58% of episodes: 77% bacterial and 11,5% viral and fungal, respectively. The commonest bacteria was *Pseudomonas aeruginosa* (23% episodes). Of three fungal infections, 2 were systemic aspergillosis and 1 candidiasis. Severe viral infections were varicella (2 pts) and CMV reactivation (1pt).

All severe septic episodes were determined by neutropenia and its degree of severity significantly correlated with mortality (p 0,05).

The addition of G-CSF in therapy had no significant contribution to reducing fatalities (p 0,58).

Mortality rate by sepsis was 19% and documented bacterial infections were 6: *Shigella* (2 cases) and *Pseudomonas*, *Acinetobacter*, *Haemophilus* and *Staphylococcus aureus* (1 case each).

**Conclusions:** Gram negative infection was the leading cause of morbidity and mortality during treatment of leukemia. Severity of neutropenia was the most important factor predicting fatality.

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POSTER

### Epidemiology of childhood cancer in Bihor and Timis counties during the years 1981-2000

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**Background:** the objective of this study was the epidemiologic study of childhood cancer in Bihor and Timis counties in order to describe the extend and nature of the cancer burden and to assess the effectiveness of cancer control activities in this part of the country.

**Materials and Methods:** incidence and survival analysis data of children diagnosed with cancer were determined using the routine data from hospital-based cancer and population-based cancer registries. Children aged 0 to 14 years old from Bihor and Timis counties diagnosed from the beginning of January 1981 to the end of December 2000 to whom the diagnosis was histologically or cytologically confirmed were included in the study. The basic statistic included: the absolute number of cases, the relative or percentual incidence, the age specific rates, cumulative and age-standardized rates. The direct method of standardization and the standard European population were used. Five years interval data from 1981 to 2000 are analysed and displayed. Estimation of survival by five years interval is presented then. Confidence interval was the statistical test used for specific incidence rates and for the difference of the rates.

**Results:** 702 children with cancer were diagnosed, the overall age-standardized rate of cancer in children varying between 12/100000 and 15,1/100000. About a third of all childhood cancers are leukaemias (31%), predominant acute lymphoblastic leukemia (26%); on the contrary to the international references lymphomas are the second most common diagnostic group (19%), and non-Hodgkin lymphoma has higher incidence (13,5%) than Hodgkin's disease; brain tumors account for 15% of registrations, neuroblastomas and Wilms tumors for 6% and 5% respectively, bone tumors for 6%, soft tissue tumors for 4% and retinoblastoma for 3% of all childhood cancers. Age standardized rates and cumulative rates by cancer type showed small differences among the incidence of the same cancer type over the time; there is no increasing or decreasing incidence tendency (time trends) by cancer type. International comparison: age standardized rates are increased for lymphomas and are decreased for brain tumours, neuroblastomas and soft tissue tumours over almost all periods of time. Survival analysis: very low survival probabilities at the beginning of the study; survival accounting over 60% during the years 1996-1998.

**Conclusions:** improvement of epidemiological research data quantification on pediatric oncologic patients is imperative; therefore to develop in many parts of our country strategies for uniform and systematic data collection and analysis is a very important objective.

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### Symptomatic avascular necrosis of the femoral head in children with ALL.

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Avascular necrosis of the femoral head (AVNFH) in childhood ALL is reported in 1-17% of children. In an attempt to evaluate the incidence of symptomatic AVNFH in children with ALL treated aggressively in our department from 2/89 to 12/01, we retrospectively studied 245 children given at least one course of Reinduction which included Dexamethasone. Of the 245 children, 134 were boys and 111 were girls, age 6 months to 15 years, and among them in 6 (4 girls and 2 boys) age > 12 in 3/6 symptomatic AVNFH was documented in first remission after the Reinduction course and while in maintenance therapy (0.025%). Only 1 of 6 had received prophylactic CNS irradiation. The lesion was seen in plain films and in MRI and was unilateral in 4 and bilateral in 2. All 6 children were approached conservatively with avoidance of weight bearing and physical therapy and in all 4 with unilateral involvement the disease subsided whereas in the bilateral disease in one there is progression and in the other clinical and radiological steady state.

**Conclusions:** Symptomatic AVNFH is a rare complication in our group of patients with ALL more common in adolescent girls and it may be attributed to prolonged therapy with steroids (Prednisone, Dexamethasone). Early diagnosis will lead to conservative care and avoidance of serious dysfunction of the extremity.

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### Dental abnormalities in long-term survivors of childhood cancer

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**Purpose:** To determine the frequency and type of dental abnormalities

among children diagnosed of cancer and treated with chemotherapy and/or radiotherapy in a sole institution.

**Patients and Methods:** Fifty-two patients diagnosed of cancer in our hospital between 1980 and 1993 were included. They were younger than 10 years of age when chemotherapy and/or radiotherapy was administered and remained in continuous remission. All patients were evaluated with oral examination at least 5 years after diagnosis. Panoramic radiographs were done looking for dental abnormalities. We recorded the following findings: hypodontia, microdontia, enamel defects, root stunting and excessive number of caries.

**Results:** Dental abnormalities were found in 53.8% of the patients. The main findings were hypodontia in 48%, root stunting in 15.3%, microdontia in 15.3%, enamel defects in 3.8% and total absence of the root in 1.9%. The dmf index (decayed missed and filled deciduous teeth) was 3.3. An interventional program was applied when anomalies suitable to be repaired were detected.

**Comments:** Children treated with chemotherapy and/or radiotherapy were at high risk for abnormal dental development. Due to the abnormalities found in these patients, a special surveillance is required with an appropriate odontologic care. A protocol for improving the dental health of children with cancer has been designed in order to be applied during and after treatment

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### Gonadal toxicity following treatment of lymphoma in childhood

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**Objective:** To evaluate late effects of treatment on gonadal function in children with Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL).

**Methods:** Gonadal function was assessed in 26 patients with HD and 32 patients with NHL. Twenty one boys and 5 girls with HD were treated with three cycles (stage I-II) or six cycles (stage III-IV) of combination chemotherapy (COPP/ABVD) and involved field low dose radiotherapy (20-25 Gy). Patients with NHL (25 boys, 7 girls) were treated with modified BFM-90 and LMT-89 protocols. Median age at diagnosis were 8.5 years (range; 3-14) in the HD group and 7.7 years (range; 3.3-16) in the NHL group. Gonadal function was evaluated at a median of 6.4 years and 5.7 years after treatment respectively.

**Results:** Of 21 male patients with HD four had elevated FSH, one had elevated LH and 9 had low testosterone levels. Three patients had small testes. Out of 7 patients in whom semen analysis was performed two had azoospermia, four had oligospermia and one had normospermia. All female patients had normal estradiol and LH levels. One had raised FSH. Of 25 patients with NHL 6 had elevated FSH, 7 had elevated LH levels and 16 had low testosterone levels. Three patients had small testes. Out of 8 NHL patients in whom semen analysis was performed two had azoospermia, 5 had oligospermia and one had normospermia. All female patients had normal FSH, LH and estradiol levels.

**Conclusion:** There is a high incidence of germinal epithelium damage and a lesser degree of Leydig cell dysfunction in male patients treated for HD and NHL in childhood. Ovarian function appears to be less severely affected.

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POSTER

### The therapeutic approach - a main prognostic factor in paediatric acute lymphoblastic leukemia

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**Background:** Acute lymphoblastic leukemia (ALL) is a heterogeneous haematological disorder with a multifactorial dependent evolution. The quality of the therapeutic approach is without any doubt, accepted to have a definite prognostic impact on the overall survival (OS) of patients with ALL. Our objective was the analysis of the results obtained through medical assistance in paediatric ALL, while attempting to define the factors with prognostic value on the OS, with a special emphasis on the treatment as a prognostic factor.