

**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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### 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.

**Patients and method:** This is a retrospective, unicentric study performed on a cohort of 189 consecutive patients with ALL, treated in our centre during 1983 until 1997. Their evolution portrayed by the OS and EFS at 3 and 5 years respectively was analysed related to the demographic data (age, gender), clinical (risk factors, initial CNS involvement), and biological data (leucocyte count, FAB classification, immunophenotype and cariotype). Special emphasis was given to the treatment: non-standardized therapy before 1990 (group I), ALL-BFM 90 during 1990-1995 and ALL-BFM 95 after 1995 (group II).

**Results:** Eligible for the study remained 75 of 97 patients from the first group and 88 of 92 from the second group. The rest of the patients either abandoned treatment or they did not follow strictly the standardized protocols. OS was for the first group 29% and 58% for the second group ( $p < 0,01$ ). EFS at 3 years was 32% for the first group and 69,3% for the second group, while EFS at 5 years was 24% in group I and 50% in group II ( $p < 0,01$ ). The parameters with negative prognostic value turned out to be the L3-FAB morphology and T-immunophenotype; but taking into account the small number of patients with L3 and T phenotype, the treatment remained with the highest predictive value.

**Conclusions:** Even not taking into account the great number of non-compliant patients of the first group, treatment remained definitely the main factor with impact on the overall prognosis of ALL in our study. The increased trust in the chances of survival as consequence of new therapeutical approaches, significantly improved also the compliance to treatment.

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### Psychological disorders in children with cancer

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**Objective:** The objective of this study is to evaluate the prevalence of psychological problems in children after the diagnosis of cancer and its therapy, especially neurosis, behavior problems and hyperactivity. When doctors and nurses are aware of the possible psychological problems children may have, they are able to recognize and treat them early.

**Material/Method:** We examined 132 children, who were hospitalized in our Department, during the first, third and sixth month after the diagnosis and compared them with 100 healthy children. The questionnaire of Rutter et al. for parents and teachers was used as an instrument for all the groups of children.

**Results:** Children with cancer had significantly more psychological problems in the third month after the diagnosis, than during the first and the sixth months. They had also more psychological problems than the control group. Specifically, they present with hyperactivity ( $P=0,003$ ), neurosis ( $P=0,045$ ) and behavior problems ( $P=0,38$ ). The disease, the treatment and the painful medical procedures mostly influence their psychological condition.

**Conclusion:** The prevalence of psychological problems ( $P=0,00001$ ) experienced by children treated for cancer is statistically significantly different than that found in healthy children. Future research should give greater attention to other aspects of life of children treated for cancer and their parents.

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### Space-time clustering analyses of childhood cancers supports a common infectious aetiology

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**Background.** In previous studies we demonstrated significant space-time clustering amongst cases of ALL, astrocytoma, soft tissue sarcoma and Wilms' tumour. We hypothesised that there may be a common aetiology particularly between some of these diagnostic groups. The aim of the present study was to test this hypothesis by analysing for cross-clustering between cases in different diagnostic groups.

**Materials and Methods.** Cases included in the Manchester Children's Tumour Registry during the period 1954-2001 were analysed. Knox tests for space-time interactions between cases were applied with fixed thresholds of close in space,  $<5\text{km}$  and close in time,  $<1$  year apart, to determine whether there are more pairs occurring in close proximity than expected by chance. Tests were repeated replacing geographical distance with distance to the Nth nearest neighbour [NN] to adjust for population density. N was chosen such that the mean distance was 5km. Data were also examined by a second order procedure based on K-functions to allow for multiple testing and boundary effects. Reference points in time and space were dates and addresses at birth and diagnosis respectively.

**Results.** All four methods showed statistically significant ( $p < 0.05$ ) cross-clustering between cases of HD and astrocytoma, ALL and astrocytoma, and ALL and NHL, based on time and place of birth; between cases of NHL and PNET's, and AML and peripheral neuroectodermal tumours, based on time and place of diagnosis; between cases of ALL and PNET's, and ALL and peripheral neuroectodermal tumours, based on time of diagnosis and place of birth; between cases of ALL and peripheral neuroectodermal tumours based on time of birth and place of diagnosis. There was little evidence of cross-clustering between Wilms' tumours, soft tissue sarcomas and other malignancies respectively.

**Conclusions.** These findings are consistent with a common infectious aetiology for certain haematological and neural malignancies in children.