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ASSOCIATION OF CONGENITAL MALFORMATIONS AND MINOR ANOMALIES IN CHILDREN WITH MALIGNANCIES

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1./A retrospective analysis of 211 children with leukaemia was performed.Association of major congenital malformations and the mean survival times were recorded.17 major anomalies/13 in children with acute lymphoblastic leukaemia/ALL/ and 4 with acute myeloblastic leukaemia/AML/were found: 5 of them were diagnosed as Down's syndrome.The association of malformations with ALL was more frequent in girls/11.4 per cent/ than in boys/5.4 per cent/.When compared with age,- and sex-matched control children treated by the same approach,no difference in prognosis, complete remission and mean survival time could be found.Remission rate in the cases with Down's syndrome was 5o per cent, while it was loo per cent in the other patients with malformations.
2./ 55 minor anomalies in loo children with malignancies/51 with leukaemia and 49 with different solid tumours/were analyzed. The frequency of minor anomalies in the patients'group/2.12 anomalies/person/ was significantly higher than in healthy controls/o.94 anomalies/person/. Although some types of minor anomalies occurred more frequently in children with malignancies, no tumour-specific association could be demonstrated.

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LOSS OF HETEROZYGOSITY OF CHROMOSOME 13 IN OSTEOSARCOMA

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Development of tumour as a result of mutation of a gene followed by loss of the remaining normal allele has been suggested to be a general mechanism in childhood cancers occuring in both hereditary and sporadic forms. The best known example is retinoblastoma. A gene at a locus in band q14 of chromosome 13 appears to be involved in its development. Since survivors of the hereditary form of this tumour are at an increased risk for the development of osteosarcoma, the same gene may be responsible for this second malignancy. Using chromosome 13-specific polymorphic DNA probes we studied a possible loss of heterozygosity of chromosome 13 in osteosarcomas from patients that had not developed retinoblastoma before. Out of four cases where heterozygosity for the probes used was present in constitutional DNA, two appeared with homozygosity in the tumour DNA at the loci tested. Our results support the idea that a mutant allele in 13q14 is involved in the development of osteosarcoma.

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DIFFERENCE IN PLOIDY BETWEEN INFANTILE ORCHIDOBLASTOMA AND TESTICULAR GERM CELL TUMORS OF ADULTS.

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Among the germ cell tumors of the testis, the infantile orchidoblastoma is a separate entity. Histologically it is a pure yolk sac tumor, whereas pure yolk sac tumors are exceptionally rare in adult males. Contrary to testicular germ cell tumors in adults, orchidoblastoma can usually be cured with orchidectomy alone. We speculated that the DNA contents of orchidoblastoma and germ cell tumors of the testis of adult males might be different.

DNA-flow cytometry was performed on suspensions of fresh and paraffin embedded tissue. Histological components in the samples used for DNA measurement were morphologically checked.

Infantile orchidoblastoma (n=9), seminoma (n=17) and non-seminoma (n=22) showed statistically significant differences in DNA-index (i.e. tumor G1 : normal G1 ratio): 1.93, 1.67 and 1.37 respectively. The difference between the DNA-index in orchidoblastoma and germ cell tumors of the adult testis may relate to the absence of spermatogenesis in the former.

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NEW TUMOR MARKERS IN CHILDHOOD CANCER

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Urinary cathecolamines and NSE are generally used tumor markers in children with neuroblastoma, AFP in those with hepatoblastoma, and AFP and hCG in patients with yolk sac tumor (YST). Virtually nothing is known about the new generation of markers, based on monoclonal antibodies, in these patients. We have explored the combined use of marker analysis 1) in patients with YST, and 2) in those with solid tumors and leukemias. We have compared previously documented tumor markers with the new ones in different patient groups.
Sera from 11 patients with malignant YST were serially determined for AFP, hCG, SP1, CA 19-9 and CA 125. At diagnosis, AFP was elevated in 8/11 and placental protein (hCG/SP1) in 4/7 patients.The concentrations normalized after successful treatment. In two cases, a benign sacrococcygeal teratoma was operated in a newborn and the AFP level decreased; these patients later developed a malignant pelvic YST, and an elevation of the AFP level (and SP1 in one case) was noted. The CA 19-9 and/or CA 125 were elevated in 1/1 patient with malignant ovarian YST, and also in 2/2 patients with benign ovarian teratomas. Occasionally, elevated levels of the CA 19-9, CA 125, AFP and/or SP1 were seen in patients with leukemia (8/32), MDS (0/2), solid tumors (11/52) and various benign tumors (1/7). The clinical significance of these results remains to be evaluated.

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ISOLATED REGIONAL PERFUSION USING CISPLATIN IN THE TREATMENT OF OSTEOSARCOMA OF THE EXTREMITIES (IN DOGS)

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Treatment results of osteosarcoma improved significantly with systemic chemotherapy. Local tumor response could be higher with regional chemotherapy. This study was designed to investigate the role of isolated regional perfusion (IRP) with cisplatin in the (local) treatment of osteosarcoma in the extremities (in dogs). Cisplatin is active for osteosarcoma and IRP prevents general toxicity. In a feasibility study using mongrel dogs (n=10) our standardized technique of IRP was used with cisplatin. Toxicity studies revealed that the highest possible dosage of cisplatin is 30 mg/liter extremity volume. Plasma levels are 10-20 fold higher compared to systemic application. Dogs from veterinary practice with extremity osteosarcoma were used to evaluate tumor response after IRP with cisplatin. Parameters: Clinical - Radiological - Histological. Seven dogs underwent perfusion, two died immediately after perfusion. Evaluable dogs (n=5) demonstrated a marked clinical improvement and good response on X-rays. Histologically responses were graded 2-4 according to Huvos, after a single perfusion with cisplatin (biopsy: 2 and 6 weeks after perfusion). Follow-up: 1-11 months. One dog had a relapse 4 months after perfusion.
It is concluded that IRP with cisplatin can be very effective in the (temporary) local control of extremity osteosarcoma (in dogs). This kind of regional preoperative chemotherapy can be a contribution to limb salvage. Further study aims for optimal conditions of perfusion and evaluation of platin analogs.

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INTRAOPERATIVE RADIOTHERAPY. A NEW COMBINED MODALITY THERAPY IN PEDIATRIC ONCOLOGY?

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One of the more challenging problems in pediatric oncology is the management of children with inoperable, non-metastatic intraabdominal, retroperitoneal or pelvic malignancies. The conventional treatment of these children is the delivery of tumorincidal dose with external beam radiotherapy (EBRT) following surgery which is accompanied by significant short and long-term toxicity to normal tissues. Intraoperative radiotherapy (IORT) has the potential to overcome the limitations of conventional EBRT by limiting radiation exposure of normal tissues and therefore limiting radiation toxicity. Twenty-two age and weight matched adult female Beagles were subjected to laparotomy and IORT of the retroperitoneum with 6 MeV 0, 30 and 40 Gy (90% isodose line) to establish a range of normal tissue tolerance of the retroperitoneal structures to IORT. Up to two years no abnormal changes have been observed on histological examination of the aorta, vena cava, retroperitoneal soft tissue, except uretral fibrosis and stenosis and nephritis. IORT may be a new useful combined treatment modality in pediatric oncology.