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TABOOS AND PITFALLS IN PEDIATRIC SURGICAL ONCOLOGY

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Success in the treatment of malignant solid tumours in children depends to a large extent on a multidisciplinary approach.

The role of surgery in this context is very important, but to perform the correct operation at the right time requires an exact tissue diagnosis, knowledge: of extent of disease (stage), of all prognostic factors, e.g. site, age, natural history, biological parameters, of response to chemotherapy.

In many, but not all situations, pre-operative chemotherapy has made surgery easier (better?) and reduced the severity of late sequela as well as improved survival. Guidelines and protocols are available and should be used for most pediatric tumours and applying these sensibly can prevent many complications.

Nevertheless, the ultimate decisions in surgery, e.g. operability, resectability, margins, etc. are a matter for the surgeon.

In this lecture I will, rather than giving these guidelines, concentrate on specific situations and tumours where inappropriate surgery can compromise the result (taboos).

In general these "errors" can be categorised as those of ommision - those of commition.

Tumours particularly susceptible to errors of judgement or controversial decisions are:

- lymphomas
- mediastinal tumours
- soft tissue tumours
- tumours in the newborn
- adult type of tumours
- rare tumours
- unusual sites

These and other specific examples will be discussed in detail.

The surgical treatment begins with the biopsy and even this "small" procedure has its pitfalls.

Otherwise routine surgical procedures in children under massive chemotherapy and/or radiotherapy present their own specific problems and these will also be discussed.

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ADJUVANT SYSTEMIC THERAPY IN BREAST CANCER.

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Systemic adjuvant therapy has improved the prognosis of patients with primary breast cancer. Meta-analyses have demonstrated that approximately 1/4 of deaths can be avoided among younger women treated with multiple cytotoxic drug regimens and among older women treated with tamoxifen. However, with the treatments available today, many aspects related to the optimal therapy, taking into account the physical, psycological and socio-economic consequences are still open.

As concerns endocrine therapy some of the major questions relate to the duration of tamoxifen and to the role of castration. According to the meta-analyses indirect comparisons indicate 2 or more years of tamoxifen to be superior to shorter treatment duration, however, this remains to be analyzed in randomized trials. The meta-analyses have demonstrated that castration reduces the mortality by approximately 25% in premenopausal patients and trials are now ongoing to compare the efficacy of endocrine therapy (castration, tamoxifen, LH-RH-analogs) with chemotherapy in premenopausal patients.

Major open questions related to chemotherapy include the use of anthracyclines and the dose/response relationship. Major trials have been initiated to define the role of anthracyclines as adjuvant therapy but no firm conclusions can yet be drawn. As far as dose is concerned randomized trials are now in progress, some of which use different ways to protect the bone marrow to allow significant dose escalation (growth factors, bone marrow rescus).

The optimal timing of the systemic therapy in relation to the primary operation (pre-, per- or postoperatively) is now the subject of randomized trials. So far a high responsiveness of the primary tumor has been demonstrated, but the impact upon survival remains to be defined.

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FACTORS INFLUENCING THE RADIATION TOLERANCE OF SLOWLY DIVIDING NORMAL TISSUES

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The radiation tolerance dose of normal tissues differs widely for different tissues. Under standard radiation conditions large differences in sensitivity are observed, which may only be partly explained by differences in sensitivity of target cells, but more likely by differences in tissue structure and cellular organization. With changes in radiation schedules, such as the total number of fractions, multiple daily fractions, dose-rate, overall time, and irradiated volume, the tolerance dose changes which is again tissue or organ-specific. As the time to response of a tissue is largely determined by its rate of cell renewal, slowly dividing tissues are characterized by a late development of reactions after irradiation. These so-called "late effect" tissues are often the most critical organs in radiotherapy, e.g. the central nervous system, kidney, and lung. In this lecture the influence of the following radiobiological variables on the tolerance of these late reacting critical normal tissues will be reviewed.

1. Dose per fraction. This is probably the most important variable influencing late normal tissue tolerance, showing large changes in tolerance with changes in dose per fraction. In the linear-quadratic model the fractionation sensitivity is denoted by the $\alpha/\beta$ ratio, with the lowest values for late responding tissues.
2. Overall time. Lengthening the time of a standard schedule generally shows an increase in acute normal tissue tolerance due to proliferation, but in late responding tissues variation in overall time has a negligible influence on tissue tolerance.
3. Repair kinetics. Shortening the overall time by administration of more than one fraction per day introduces the rate of repair between subsequent fractions as an important variable. For several late responding tissues (CNS, lung) fast and slow repair components have been described, which has an impact on overall tolerance in short schedules.
4. Dose-rate. This variable basically represents a mixture of repair kinetics, fractionation sensitivity, and overall time, but it is not settled whether data on high dose-rate fractionated irradiations are directly applicable to conditions of low dose-rate continuous irradiation.
5. Volume. A reduction in treatment volume with an associated rise in tissue tolerance is considered as the main advantage of conformal therapy. The volume-dependence of different organs will be briefly reviewed.