these decisions become somewhat easier once genetic testing becomes available.

As far as interventions that might be employed prophylactic mastectomy would only be considered for these extreme cases and even this intervention cannot guarantee 100% protection. Mammographic screening for the pre-menopausal women where the familial predisposition tends to express itself is of unproven value.

Finally a good prospect for intervention for familial predisposition to breast cancer would be chemoprophylaxis. Trials of tamoxifen are currently under way but these may be more appropriate to post-menopausal women. For the pre-menopausal women I am of the opinion that we will one day be able to develop a safe and effective contraceptive regimen that will incidentally reduce the risk of breast cancer.

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NEW STRATEGIES FOR PREVENTION OF COLON CANCER—PARADIGM: FAMILIAR POLYPOSIS COLI, HEREDITARY NONPOLYPOID COLON CANCER (HNPCC) AND ULCERATIVE COLITIS

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Familial colorectal cancer can be divided into two distinct classes, familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC). Identification of gene loci assigned to FAP (APC gene) and HNPCC (mismatch repair genes) has allowed molecular analyses of affected patients as well as individuals at risk within those families. We established a presymptomatic molecular diagnosis for FAP families registered at our hospital. Since the majority of mutations identified to date lead to truncated proteins we used a non-radio-active protein truncation test (PTT) as a screening method. According to this assay five overlapping segments of the APC coding sequence were amplified by PCR and subsequently transcribed and translated *in vitro* in a rabbit reticulocyte lysate using biotinylated t-RNA Lys. Labelled proteins were separated by PAGE, transferred to nylon membranes, and detected by streptavidin-alkaline phosphatase complex in a colour reaction.

We have started analyzing HNPCC patients at the molecular level. Selection of patients was not based on strict Amsterdam criteria but rather on early age of onset of disease (<50 years) or anamnestic criteria. Seven colorectal cancer patients—three of them matching the Amsterdam criteria—were analyzed for mutations within the complete coding sequence of the hMutS2 mismatch repair gene by PTT and direct sequencing. No mutations were found although microsatellite instabilities could be demonstrated in three patients. Since microsatellite instabilities are indicative of replication error caused by a defective mismatch repair system our future sequence analyses will be extended to the other known mismatch repair genes.

While in the 80's we still considered the subtotal colectomy and ileorectal anastomosis in FAP as a good alternative to a restorative proctocolectomy in cases of few rectal polyps, we nowadays almost exclusively perform a mucosal proctectomy and ileal pouch-anal anastomosis with equal functional results. Even singular polyps in the rectum are for us a reason to go for this far more radical and safe procedure from the oncological point of view. And we are reinforced by our longterm experience with subtotal colectomies requiring secondary surgery or even developing metachronous rectal cancer despite close follow-up of the rectum.

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CHOICE OF TREATMENT IN MEN SYNDROMES

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Multiple Endocrine Neoplasia syndromes are genetic diseases with autosomal dominant inheritance. There are three such syndromes. The MEN type 1 syndrome is characterized by hyperparathyroidism, pancreatic islets tumors, and pituitary adenomas. The genetic defect has been mapped to chromosome 11. The MEN type 2A syndrome includes hyperparathyroidism, medullary thyroid carcinoma and pheochromocytoma(s). The MEN type 2B syndrome includes medullary thyroid carcinoma and pheochromocytoma(s) but also ganglio-neuromas of the gastrointestinal tract. The inherited defects responsible for the MEN2 syndromes map to the pericentromeric region of chromosome 10. Hormonal screening of members of MEN families have led to earlier diagnosis and treatment. This has improved the quality of life and the survival. In our experience the patients with MEN 2A syndromes have the same survival as the normal population. The introduction of genetic diagnosis will further improve the outcome of treatment for these patients.

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APPROACHES TO LOCAL RECURRENCES AND METASTATIC CANCER

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Surgery of Local Recurrences is conditioned by the "radicality of previous surgery, the likelihood of total ressection, the histological type, the response to chemotherapy, prognoses, sensitivity to radiotherapy and absence of metastatic lesions (unless those are amenable to surgical ressection). Surgery for metastatic cancer implies that all metastatic lesions can be excised and the primitive tumour is or can be controlled.

In both cases a good general health of the patient is a prerequisite for surgery of recurrence or metastases. The most difficult decision is option between "radical" treatment or just paliation, in order not to jeopardize the quality of life of the patient during his remaining life span. Several examples are presented, from abstention to radical surgery. Treatment must be individualized and take into account previous treatments, probability of response to alternative treatment methods and overall prognoses. If the above criteria are respected, surgery remains an essential step for the cure of recurrent or metastatic solid tumours in children.

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THERAPEUTICAL PHILOSOPHY OF SECUNDARITIES IN CHILDREN WITH SOLID TUMOURS

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After years of experience, every responsible oncologist has to create a personal oncologic philosophy/and therefore a personal philosophy of his or her professional and moral accomplishment/which allows orientation in problems of the field. Using the professional philosophy it is possible to search for and find the principles, structure and form of scientific knowledge. This way it is also possible to analyse techniques and methods of the field, to derive and justify scientific findings linked to their development, and to establish strategies of scientific and research programmes. Without such a personal philosophy one cannot make decisions about therapy of life-threatening childhood diseases recidives and metastates of tumours being good examples of this. A wise equilibrium among all substantial circumstances—i.e., study of the disease, complex medical status of the patient, the physician's attitude and abilities, scientifically approved therapeutic choices, their limits and ethical principles—is the only possible alternative now as well as a ground for the future. The lecture indicates the aforementioned direction.

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SURGERY OF LUNG METASTASES

A. Vos

Background: A retrospective analysis was performed of the results of surgical excision of lung metastases in children to identify prognostic factors.

Methods: From 1970 to 1992 139 thoracotomies were performed in 91 patients aged between 1 and 19 years with metastases of osteogenic sarcoma (40), nephroblastoma (24), Ewing sarcoma (12) and various other tumours (15).

Results: There were no perioperative deaths, and only one serious complication: chylothorax necessitating re-operation. Twenty-three patients are currently alive (26%), two with residual disease. Twelve patients (50%) with nephroblastoma aler alive; 7 patients with osteogenic sarcoma (18%) and 4 with other tumours (27%). Negative prognostic factors were: incomplete excision, primary tumour not controlled, or metastases developing during treatment. Not of significant influence on