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Commentary On Wilms' Tumour

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WILMS' TUMOUR is one of the success stories of modern oncology, as clearly discussed in Dr Green's Update in this issue of the European Journal of Cancer (pages 409–418). However, these achievements in the treatment of Wilms' tumour should not detract from the sometimes very malignant course of the disease. As such, it is still very important that prognostic factors of the disease are better defined. Adaptation of treatment according to these factors will contribute to improved survival rates for the high risk patients, and a better quality of life from less therapy for those with intermediate and low risk disease.

Early detection could also improve the outcome of children with Wilms' tumour. Since Wilms' tumour is associated with some well known congenital syndromes, screening for Wilms' tumour has been considered in these high-risk children [1]. Thus far, there is no real evidence to support screening in this population, but since the screening method is easy to apply and tolerable for the patients, it could be recommended that high-risk children are followed up to their seventh or eighth year by sonography, initially every 3-4 months, extending this to every 6 months later on. In some of these children, early detection may make partial nephrectomy possible.

Dr Green's Update succinctly describes current methods of pretherapy staging of patients with Wilms' tumour, particularly in the U.S.A. In Continental Europe, staging procedures are somewhat different, with clinical staging carried out at diagnosis, followed by 4 weeks of pre-operative chemotherapy. Surgical and pathological stages are determined after the neo-adjuvant chemotherapy. Another major difference is the fact that contrast enhanced computed tomography (CT) of the abdomen is not part of the routine clinical examination in SIOP protocols. The very low number of incorrect diagnoses reported in recent SIOP studies (1.5%), as well as some other points raised in the Update, justifies this policy. Furthermore, in a climate where cost-effectiveness has to be considered, CT scanning is an expensive procedure, which may limit its use in some institutions.

Because it is important that protocols for Wilms' tumour from large study groups should be applicable in centres all over the world, sonography is a preferred technique for the diagnosis of Wilms' tumour, since there tends to be more extensive experience of this technique, with cheaper improved equipment. Wilms' tumour is an outstanding example of how cost-effective medicine can be applied, not only in diagnostic procedures but also in therapeutic strategies.

There is international agreement on staging in Wilms' tumour, and the few remaining discrepancies will be resolved in the near future. However, for patients with lower stage tumours, there is now a drive towards minimal necessary therapy, as exemplified by the so-called 'low-grade' histology. This defines a subgroup of patients, among those with favourable histology, who have a 100% recurrence-free survival. The prognostic value of this subgroup has been prospectively tested in stage I patients in the SIOP study. These patients need no further therapy after pre-operative chemotherapy and surgery. It is of interest that among these patients are those with a completely necrotic tumour indicating that pre-operative chemotherapy, far from obscuring important staging information as suggested by Dr Green, seems to contribute to the selection of those patients for whom only minimal therapy is necessary. The strategy of pre-operative chemotherapy, as used in nearly all other childhood solid tumours, increased the number of stage I tumours from 22% in the surgery first arm of SIOP-I to 53% in SIOP-IV and 65% in SIOP-IX, and less than 15% of the patients needed postoperative radiotherapy. In addition, the number of surgical complications compared favourably with the number in a group of patients who had no chemotherapy prior to surgery, with a total surgical complication rate in SIOP-IX patients of 6.7%. The reported surgical complication rate in NWTS-III in which small bowel obstruction alone was reported was 6.9% [4]. As a consequence of these results, partial nephrectomy is now more often being considered as a radical operation. In stage IV patients, pre-operative chemotherapy also seems to be of use. It has been known for many years that the outcome of these patients is related to the stage of the abdominal tumour. Pre-operative chemotherapy can down-stage the primary tumour and result in regression of pulmonary...
metastasis to such an extent that postoperative radiotherapy can be avoided in a large number of patients [5].

Currently, the treatment of Wilms' tumour has been refined so that chemotherapy has been minimised by using a selected number of drugs and reducing the duration of the postoperative and maintenance phase of the treatment; the dose of radiotherapy has been reduced, organ sparing surgery is now more often considered and pre-operative criteria are defined. The pathologists have determined categories of patients with an exceptionally low risk of recurrence. What more can be done to improve the treatment of Wilms' tumour? Can we reduce therapy still further? In the days when surgery was the only treatment modality, 30% of patients were cured. We have not yet identified the characteristics of this subgroup, although patients scheduled for surgery only in the NWTS study and the low risk stage I patients of the SIOP 93-01 study are serious attempts to do this. There is evidence from studies in the U.K. that surgery and vincristine alone can cure some patients [6]. The use of anthracyclines, especially in 'pulse intensive' schedules, is still a matter of concern in the long term. These issues and others still need to be clarified, but as clearly discussed by Dr Green, the advances in the treatment of Wilms' tumour have made optimal therapy available for patients all over the world, with treatment schemes adaptable for different circumstances, especially for those countries with minimal resources.