THIRD ANNUAL GEORGE C. CHALLIS LECTURESHIP

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University of Washington, Seattle
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HSC, Communicore, C1-3

Title: THE VALUE OF LONG TERM FOLLOW-UP:

LESSONS FROM THE NATIONAL WILMS TUMOR STUDY

Abstract:
Wilms tumor (WT) is an embryonal tumor of the kidney that affects approximately one child in every 10,000. During the 20th century, cure rates increased from 10% to 90% as first radiation and then chemotherapy joined surgical removal of the diseased kidney as standard treatment. The National Wilms Tumor Study Group (NWTSG) conducted five protocol studies and registered nearly 10,000 patients during 1969-2002. For the past 15-20 years the study enrolled 70-80% of the 550 cases estimated to occur annually in North America. Its focus has been the identification of patient subgroups at high and low risk of relapse, and the substitution of combination chemotherapy for radiation therapy, with a primary goal to reduce long term complications while producing the maximum number of cures.

The NWTSG Data and Statistical Center, located in Seattle for the 33 year duration of the study, played a major role in this effort. Systematic follow-up of surviving patients documented the long term "costs of cure" and the wisdom of reserving the most toxic treatments for those who actually needed them. Secondary cancers, for example, which once affected 1.6% of Wilms tumor survivors by 15 years from diagnosis, have been much reduced since 60% of patients no longer receive radiation therapy.

Statistical study of the NWTSG database has challenged prevailing theories for the genetic origins of WT and led to new hypotheses for investigation by molecular biologists. This talk considers three issues: (1) whether all bilateral and multicentric WT are hereditary; (2) whether Asians lack WT caused by loss of imprinting of the insulin growth factor gene IGF2; and (3) whether constitutional deletion of the WT gene WT1 in patients with the WT-aniridia (WAGR) syndrome has a less severe effect on renal function than a point mutation in WT1 in patients with the Denys-Drash syndome. Key factors that facilitated these statistical contributions include a compulsive effort to maintain continuity in data collection and follow-up and a constant search for ways to use the clinical and epidemiologic data to answer questions of basic biological significance.