INTRODUCTION

Investigation of the epidemiology of cancers of childhood provides some unique challenges, and offers the prospect of deeper understanding of the process of carcinogenesis as it applies to both adults and children. It can also be a frustrating and unrewarding pursuit. The question of the effect of paternal exposure on risk of cancer in an offspring illustrates both the fascination of this field, and its limitations.

A key issue, of relevance to this meeting, is the relative contributions of environmental and genetic factors in the pathogenesis of cancers of childhood. In adults, it is widely accepted that the environment we inhabit is much more important than the genes we inherit, although this perception may be biased by the fact that we have, in the past, been better able to observe the environment than the genetic inheritance of an individual. However, adult and childhood cancers are very different—for example, in their histological spectrum—and the roles of environmental and genetic factors for most childhood cancers has yet to be clearly established. Some cancers, most notably retinoblastoma, have an unequivocal heritable component, but the evidence from studies of twins, siblings and offspring of affected children indicates that overall the genetic contribution is modest at best.

On the other hand, there is little compelling evidence for environmental risk factors. Geographic variation in incidence is substantially less than for adult cancers, suggesting that environmental factors may be correspondingly less important. Furthermore, the short average interval between conception to cancer diagnosis should greatly assist those looking for an environmental cause: the fact that so few reproducible findings have come from a fairly substantial research effort in this field can’t help but call into question the role of the child’s environment.

That is not to say that case-control studies of childhood cancer have been completely unproductive. While attempts to implicate environmental exposures to the
child have not yielded many useful leads, most studies have also included questions on parental exposures and there have been numerous reports of significant associations between parental occupation and cancer risk. Parental exposures could be transferred to the child on work clothes or skin, or passed on from mother to a child transplacentally, or via breast milk. Alternatively, and more controversially, the exposure could damage sperm or ova leading to a constitutional genetic defect that manifested as a malignancy. In this paper, I will present some of the data linking parental exposures to risk of cancer in an offspring, consider the relevant methodological questions and caveats, touch on the issues of imprinting and preferential allele loss and consider possible mechanisms.

DATA

The literature concerning parental occupation and childhood cancer risk has been comprehensively reviewed in two recent publications (Leary et al., 1991; Savitz and Chen, 1990). There is so much between-study variation with respect to case population, control group, data collection method and analysis and interpretation of the data that it is very difficult to compare study findings directly. Some broad generalizations are possible however:

1) Most studies that look for increased risks associated with parental occupational exposures report some statistically significant associations;
2) Although the nature of these associations vary widely, some exposures appear to recur. Specifically, occupational exposures to solvents, petroleum products, paints/pigments, pesticides, radiation and metals have been repeatedly linked to cancers in children; and
3) Paternal occupational exposures are more commonly reported to be significant than are maternal.

Assessment of job-related exposures is problematic. Three different approaches are possible. The first is to classify jobs into broad categories with, presumably, a similar spectrum of exposures: an example can be seen in the study by Fabia and Thuy which showed an association of cancer of all types and hydrocarbon-related occupations. The second approach is to use a job-exposure matrix to infer specific exposures from the reported occupational titles. This method has the advantage of minimizing recall biases (since the respondent need only remember the job title), and can make use of information that has been routinely recorded, such as on birth or death certificates. The disadvantage is that the quality of the exposure measure is directly related to the accuracy and appropriateness of the job-exposure matrix used, and most would agree that currently available matrices have many limitations. Even a perfect matrix can only provide an estimate of the probability that a person in a given job had a given exposure, not whether or not he did. To learn that, there is no alternative to asking the parent (or perhaps his employer) about the specific chemical and physical agents that he was exposed to at work. This might seem to be the ideal approach, provided the parent is available for interview, but is susceptible to recall bias and presumes that the person knows what he is exposed to. The studies by Lowengart et al. and Buckley et al. relied on self-reported exposures.

Tables 1-3 provide a summary of the data for some of the more commonly reported associations. Table 1 concerns a loosely defined group of chemicals--solvents, petroleum products and paints. There is obviously overlap amongst these categories in that solvents may be petroleum products, and paints or pesticides may contain chemical solvents, etc. As can be seen, associations with this group of chemicals have been reported on many occasions for a range of malignancies.