385

CARCINOMA IN SITU OF THE BREAST: TRUE PRECURSOR OR MARKER OF INCREASED RISK? *A Trentham-Dietz (University of Wisconsin-Madison, WI)

Incidence of breast carcinoma in situ (BCIS) has increased 12-fold since the early 1980s, currently constituting 20% of all breast cancer diagnoses (up from 1 to 5% before 1980). Most BCIS diagnoses are not palpable but instead detected through mammography. Many women diagnosed with BCIS receive aggressive treatment with mastectomy and tamoxifen even though over 95% long-term survival is expected without such intervention. Some experts argue that avoidance of an invasive breast cancer ''recurrence'' provides a legitimate rationale for this approach in women with noninvasive tumors, even in the absence of an overall survival benefit. The handful of available studies exploring the etiology of BCIS suggests that many risk factors for in situ and invasive breast cancer are shared. Other evidence including patterns of gene expression supports the notion that invasive breast cancer arises from in situ. However, the malignant potential of the majority of in situ tumors is most likely limited and there is disagreement regarding whether in situ breast cancer is a true precursor or a marker of increased risk of invasive breast cancer. Controversy also surrounds whether BCIS (or even early invasive breast cancer) can regress. However, there is universal agreement that a critical need exists to define which cases of BCIS are likely to lead to a second, invasive breast cancer diagnosis and, conversely, which women can receive less aggressive therapy since their BCIS lesions are unlikely to anticipate an invasive diagnosis. This presentation will focus on risk factors for in situ and invasive breast cancer to explore potentially important differences in etiology. Challenges to evaluating risk factors for BCIS incidence as well as risk factors for second breast events among BCIS cases will be highlighted.

386

OVERCOMING METHODOLOGICAL CHALLENGES IN IDENTIFYING CAUSES OF BIRTH DEFECTS. *M A Honein, M M Werler, C C Lawson, A F Olshan, M J Strickland (Centers for Disease Control and Prevention, Atlanta, GA, 30333)

Identifying modifiable risk factors for major birth defects can have a substantial public health impact because of the morbidity and mortality associated with these disorders. However, there are challenges in birth defects research related to exposure misclassification and selection bias. Specific methods can improve the ascertainment of medication exposures that occurred during pregnancy, particularly for retrospective maternal report of medication use. Occupational exposures are important because they might represent the highest level of certain exposures, but accurate assessment of exposure levels retrospectively is also difficult. Because each type of birth defect has unique causal factors and ''birth defects'' as a group do not share one etiology, epidemiologists typically assess the association between particular exposures and each type of birth defect. The resulting assessment of multiple exposures (e.g. several specific medications or occupational exposures) and multiple outcome groups requires consideration of the impact of multiple comparisons on the findings observed. Finally, the likely levels of exposure misclassification and selection bias can be modeled to determine the possible impact on effect measure estimates.

Speakers:

1. Martha Werler, ScD(Slone Epidemiology Center, Boston University)—*Improving retrospective ascertainment of medication exposures during pregnancy*
2. Christina Lawson, PhD (NIOSH)—*Assessing occupational exposures in studies of major birth defects*
3. Matthew Strickland (Battelle)—*Adjustment for multiple results in a hypothesis-generating study of maternal antihistamine use and birth defects*
4. Andrew Olshan, PhD (University of North Carolina, Chapel Hill)—*An assessment of exposure misclassification and selection bias in the National Birth Defects Prevention Study*

387

IMPROVING RETROSPECTIVE ASCERTAINMENT OF MEDICATION EXPOSURES DURING PREGNANCY. *M Werler (Slone Epidemiology Center at Boston University, Boston MA)

Certain medication exposures in pregnancy have been associated with adverse birth outcomes, but the safety or risks of many drugs remain under-studied, due in part to methodological challenges. Use of prescription medications can be ascertained or partially validated with pharmacy, billing, or medical records, but documentation of use of over-the-counter products relies on individual recall, making validation difficult. Evidence shows that accuracy improves with duration of use, but the majority of medications are taken for short duration, regardless of whether they are available over-the-counter or by prescription. Further, over-the-counter brand names often refer to a line of products, the contents of which can vary. For example, the Robitussin brand includes over 15 products with an expectorant alone or in combination with five or more other active ingredients. To improve retrospective ascertainment of medication use, several approaches can be utilized. One such approach is to limit the duration of time between pregnancy and data collection. Other approaches involve questionnaire design. To prompt memory, questions should be specific and cover illnesses for which medications might be taken (e.g., kidney, bladder, or urinary tract infection), groups or types of medications (e.g., antibiotics), and specific medications (e.g., amoxicillin, macrobid, zithromax). If the study subject can locate the package of the medication, the label can help identify exact exposures. For complicated over-the-counter product lines, a medication identification booklet may help the study subject identify which specific product was taken, which can then be linked to actual ingredients for a more accurate assignment of exposures.

388

ASSESSING OCCUPATIONAL EXPOSURES IN STUDIES OF MAJOR BIRTH DEFECTS. *C C Lawson, M A Waters, P A Stewart (National Institute for Occupational Safety and Health, Cincinnati, OH, 45226)

Over half of U.S. children are born to working women, and 65% of employed men and women are of reproductive age. Most chemicals used in the workplace, however, have not been evaluated for reproductive toxicity. Studying workers exposed to these chemicals is important for establishing safe limits to protect workers and their offspring. Because workers are often among the most highly exposed, such research can also lead to recommendations for lower exposures in the general public. Characteristics of occupational exposure assessment in birth defects research include a relatively short time between exposure and effect and specific critical exposure windows during development. The combination of rare outcomes and low exposures inherent in population-based studies results in the need for the most accurate available methods for retrospective exposure assessment in order to detect significant risk factors. Issues in occupational exposure assessment will be discussed, and improvements in methods will be highlighted.