The NIEHS Uterine Fibroid Study: Epidemiologic Findings

Research on the epidemiology of uterine fibroids is in its infancy. A decade ago, when we began planning our study, there had only been three studies that had focused on identifying risk factors for fibroids. Only one was conducted in the United States, and all three had studied only fibroid surgery cases. These studies found that menopause is strongly protective, while increasing age up to menopause is associated with increased risk. Parity and smoking appeared protective. It was also suspected that African Americans were at higher risk than whites based on US hospital discharge data.

The major new data on risk factors for fibroids in the last decade have come from the Nurses Health Study and the Black Women's Health Study. In these large cohort studies, the definition of fibroid cases was broadened to include women who had been diagnosed with fibroids, not just those having surgery for fibroids.

The NIEHS Uterine Fibroid Study was designed to expand the definition of fibroid cases even further. We screened randomly sampled women for fibroids so women with fibroids that had not yet been clinically diagnosed would also be identified as fibroid cases. We collaborated with researchers at George Washington University Medical Center to assess fibroid status and collect data on potential risk factors for a sample of nearly 1500 25-49 year old women.

Based on ultrasound screening we estimated the age-specific cumulative incidence of fibroids for African American and white participants. Estimates indicate that over 80% of black women and ~70% of white women will develop fibroids by the time they reach menopause (Baird et al., 2003).

We examine risk factors for fibroids with logistic regression, considering both the prevalence of tumors and the size of the tumors (categorized by diameter of largest tumor: <2 cm, 2-4 cm, 4+ cm). Each group is compared with those who were found to have no visible tumors. We also use Bayesian methods to supplement the logistic regression analyses. The Bayesian method uses the age data with data on previous diagnosis of fibroids in a quasi-longitudinal approach that allows us to investigate whether a risk factor in question is more strongly associated with tumor onset or tumor progression.

Given that fibroids are hormonally dependent, we first examined hormonal and reproductive factors. Preliminary results indicate that prenatal exposure to DES is a risk for fibroids, though number of exposed was small (Baird and Newbold, in press). Late age of menarche was protective (adjusted odds ratios (aOR) and 95% confidence intervals were 0.8 (0.7, 1.0) for both African Americans and whites. The association with parity may be nonlinear depending on age at pregnancy and previous pregnancy history (Baird et al., 2003), so we considered births after age 24. Adjusted ORs associated with increased parity (considering only births after age 24) were 0.8 (0.7, 1.0) for African Americans and 0.7 (06, 0.9) for whites. Infertility, age at first birth, breastfeeding, oral contraceptive use, and short menstrual cycle length were not significantly related to fibroids. Given the reports of LH receptors in myometrium and fibroid tissue, we hypothesized that increased circulating LH would be associated with increased tumor

development, and this was substantiated in our data (high vs low tertile of urinary LH showed aOR of 1.8 (1.0, 3.0).

Inflammatory factors have also been hypothesized to increase risk of uterine fibroids, but when we examined associations with data related to risk of sexually transmitted diseases, IUD use, or talc use, none were significantly related to fibroids. Nor were we able to find evidence of viral DNA or intracellular Chlamydia within tumor tissue selected from women who reported prior STD risk.

Metabolism-related factors such as hyperinsulinemia have also been hypothesized to increase risk for fibroids. BMI was related to increased risk among African Americans but not whites (respective aORs 1.5 (1.0, 2.2) and 1.0 (0.6, 1.5) for overweight or obese relative to normal weight). Circulating insulin-like-growth-factor levels or the major binding protein, BP-3, were not related to risk, while insulin tended to be protective, though not significantly so. However, exercise was protective, and this was confirmed by the Bayesian analysis.

Life-style factors and occupational exposures have also been examined. Alcohol intake was found to be a significant risk (see D'Aloisio poster), but smoking and caffeine were not related to fibroids.

Our analyses are in progress, so the unpublished findings presented here must be considered preliminary. The risk factors we have identified to date do not explain the black/white differences in risk of uterine fibroids.

Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High incidence of uterine liomyoma: Ultrasound evidence. Am J Obstet. Gynecol 188:100-107, 2003.

Baird DD, Newbold RN. Prenatal diethylstilbestrol (DES) exposure is associated with uterine leiomyoma development. Reprod Tox, in press.

Baird DD, Dunson DB. Why is parity protective for uterine fibroids? Epidemiology, 14:247-250, 2003.