PROCEEDINGS OF THE THIRD NCI/EPA/NIOSH COLLABORATIVE WORKSHOP: PROGRESS ON JOINT ENVIRONMENTAL AND OCCUPATIONAL CANCER STUDIES

PRESENTATION:

Study of the Dupont Chambers Works Plant Bladder Cancer Screening Program

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STUDY OF THE DUPONT CHAMBERS WORKS PLANT BLADDER CANCER SCREENING PROGRAM

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First of all, I would like to acknowledge the cooperation and support of Dr. Bruce W. Karrh, Vice President for Safety, Health and Environmental Affairs of the DuPont Company, who, facilitated the collaboration of Dr. Philip Prorok, who is now in the Division of Cancer Prevention and Control, and myself with Dr. William Neeld, who is the Medical Director of the DuPont Chambers Works, and William Vogler P.A., the Medical Administrator. We have been abstracting information from the medical records on a large group of individuals who have been screened by urinary cytologic methods for bladder cancer, as well as persons who developed their bladder cancer before the cytology program started.

Today I will present a progress report on our study. At present there are no completed analyses, but we do have some rather provocative preliminary tabulations which I will share with you.

In 1954 DuPont instituted a urinary cytologic screening program. We have been able to abstract information on all persons ever enrolled in the screening program, whether or not they went on to develop bladder cancer, as well as all historic bladder cancers for the entire history of this particular plant. Persons were enrolled in the cytology program if it was likely that they were exposed to either beta naphthylamine or benzidine.

There are 1,901 persons in our study, 316 of them have been diagnosed with bladder cancer. It is primarily a male work force, and almost all are white, although 6 bladder cancers have been identified among the black workers. We have information on 142 bladder cancer cases with cytology, and 174 bladder cancer cases without cytology.

What we have done over the past few years is develop an approach for abstracting information for all of these persons independent of whether or not they subsequently developed bladder cancer. From lifetime occupational histories we have, by job title/location on the plant and calendar time an independent assessment of the potential for exposure to beta naphthylamine and/or benzidine with some several hundred persons exposed only to benzidine. The potential exists within this particular data set to calculate a person months cumulative exposure score by job title and location through calendar time.

We have abstracted data from physical exams, on all persons by type of exam, whether it was pre-employment, annual, special, retirement, or post-retirement, for these persons are indeed entitled to a post-retirement physical examination.

Data have been abstracted from all urinalyses which were ever performed on all of these persons, with specific emphasis given to the notation of hematuria. The clinical contention is that hematuria is the better predictor of early

bladder disease, and that the cytology results may play a role in the complete workup of a particular individual. Cytologic readings were performed by one individual, and all readings have been abstracted.

Of specific interest to us are the early signs and symptoms of bladder disease. We utilized all of the nurses in the clinic at the DuPont Chambers Works and have successfully abstracted the entire lifetime clinical histories of all bladder cancer cases. Particular emphasis was given to genitourinary complaints such as frequency, burning, abdominal pain, coming to clinic because of blood in the urine, noting whatever procedures were followed and their findings as well as recommendations for follow-up. We will have the potential--and I will share some of that with you as I close--for looking at the timing of all of these clinical events.

The importance of this particular data set is that it is a very rich one. In addition to the above mentioned data we have pathologic confirmation on every case with specific emphasis given to type, location, grade, stage, multicentricity, evidence of metastatic spread, multiple primary tumors, and sites of secondary tumors.

What are some of the characteristics of this study population? If one looks at the number of hematurias found per person in the clinical histories, among our screened bladder cancer cases the median number of hematurias is 6 with an

extreme of 167 mentions for one person of discrete episodes of hematuria. Among our non-screened cases the median is 4 with an extreme of 61. Among our noncases the median is 2 with an extreme of 55.

What about timing? If hematuria is sentinel to early bladder disease and if time between subsequent hematurias is a reasonable clinical indicator, then one might a priori posit that among the nonscreened cases, because the potential exists for their having realized greater exposure, you might find a shorter time interval between subsequent hematurias.

Purposefully, I have considered the extremes. I have examined the times between the tenth and the eleventh mention of hematuria. These are persons who had at least 10 prior episodes. The median time between the tenth and the eleventh hematurias for the nonscreened case is 79 days, for the screened cases it is 115 days, and for the noncases 160 days.

What about the number of cytologies? The screened cases have a median of 10, the non-cases of 13. The non-cases have continued working, and we have a few additional cytologies per person.

What about the first cytology reading? Simply looking at the proportions of the first cytology readings, for which there was a finding of frankly malignant cells in the urine, the proportion among the persons who subsequently developed bladder cancer is ten times that of the persons who did not.

Now, where are we at present? We are finishing the editing of all of these data. By the end of April 1984 we will have in place programs which will allow calculation of a person months exposure score. Once that is done, we will have the ability to stratify our study population as a function of intensity of exposure and to utilize all of the clinical signs, whether they are hematuria or other GU signs, as well as the timing of the first diagnosis of bladder cancer, the extent of the disease and timing from first diagnosis to death.

All of you are cordially invited to hear me present the results of a number of these analyses at a meeting jointly sponsored by the NCI and NIOSH in Cincinnati in July. It is going to be called a Conference on Medical Screening and Biological Monitoring for Exposure in the Work Place.

At that time, hopefully we will be able to report that there is some indication, first of all, that the level of severity of cytology responds to increasing exposure to the two compounds in question and answer some fundamental questions concerning the time sequence of genitourinary signs and/or symptoms, related to exposure to beta naphthylamine and benzidine in the subsequent development of bladder cancer. We also will address some of the differences between persons who went on to develop bladder cancer and those who did not.

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