Risk Assessment of a Cohort Exposed to Aromatic Amines

Initial Results

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A cohort of 1,385 workers potentially exposed to carcinogenic amines was evaluated to determine the extent of its risk for bladder cancer. The cumulative incidence of bladder cancer was determined from death certificates, from interviews with community urologists, and from a screening program. A total of 13 confirmed cases of bladder cancer were identified at the conclusion of the first year of study. The entire cohort has approximately a fourfold excess risk of bladder cancer; however, black workers with more than 10 years of employment had a risk ratio of 111 (based on three cases). The onset of disease occurred, on the average, 15 years earlier in these black workers than in the general U.S. population. The cumulative incidence of bladder cancer increased with the duration of employment, ranging from 0.4% for workers with five or fewer years of employment to 36% for those with greater than 20 years. No significant differences were found between cases and noncases for cigarette smoking, coffee drinking, use of artificial sweeteners, or prior employment in high-risk occupations. More cases of bladder cancer are expected in this cohort because many members have not yet achieved the average latency found for the confirmed cases.

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Various aromatic amines, including β-naphthylamine (BNA) and benzidine, have been implicated since 1895 as occupational bladder carcinogens.[1] In 1981, the National Institute for Occupational Safety and Health (NIOSH) initiated a study to determine the risk of bladder cancer in a cohort of chemical workers exposed to aromatic amines, particularly BNA. This study was intended to support a pilot project for the notification of this cohort of its increased risk of bladder cancer. The study was performed to determine risk differences for bladder cancer within the cohort and then to provide a firm basis for future medical surveillance.

Methods and Materials

The cohort consisted of all 1,385 hourly employees who had worked at the Augusta Chemical Company (in Augusta, Ga.) between Jan. 1, 1940, and Dec. 31, 1972. During that interval, BNA and other aromatic amines were used and manufactured at the plant. The vital status of each member of the cohort was ascertained as of Dec. 31, 1980; addresses were updated, and in August, 1981, the 1,094 surviving members were sent individual letters informing them of their risk (details of this process have been described in the first article in this series[2]). The letter also indicated that a bladder cancer screening clinic was being

made available for their use without charge to the individual members of the cohort.

Determination of Incidence — The incidence rate of bladder cancer in the cohort was determined for the period Jan. 1, 1940, to Sept. 1, 1982. Cases were identified from three sources: (1) an ongoing NIOSH mortality study, (2) the above-mentioned bladder cancer screening clinic, (3) and a survey of local urologists. The incidence rate was based on all cases occurring in the cohort (not including recurrences) and was expressed as (1) an instantaneous rate of occurrence expressed in terms of "cases/person-years"[3] and (2) as a cumulative incidence expressed in the form of cases/population-at-risk/time period.

The criteria for inclusion as an incident case were the following:

1. The person had to have worked at the Augusta Chemical Company at any time during the period Jan. 1, 1940, to Dec. 31, 1972.

2. For deceased persons, either the death certificate or hospital record had to include a diagnosis of bladder cancer.

3. Pathological confirmation had to be obtained.

The date of first diagnosis of bladder cancer was ascertained for all cases based on hospital records and screening clinic results. Carcinoma in situ of the bladder, a noninvasive high-grade carcinoma, was included in the case definition as bladder cancer. This interpretation, as Utz et al (1980)[4] have reported, is consistent with what has become the prevailing opinion among urologists and pathologists since the 1970s.

Person-years at risk were calculated from the date of first employment until Sept. 1, 1982, the date of death, or the date of diagnosis, whichever occurred first. Person-years were calculated using a modified life-table technique developed by NIOSH based on five-year age groups, five-year calendar periods, and five-year work experience (exposure) periods.[5,6] Since the program for calculating person-years could not accept person-years accumulated after Dec. 31, 1980, these additional person-years had to be calculated manually. In this procedure, each person alive on Dec. 31, 1980, was considered to contribute 1.66 additional person-years, except those who were diagnosed with bladder cancer during that period; for those persons, additional person-years were accumulated only to their date of diagnosis. Person-years accumulated in each age category during the period 1980 to 1982 were allocated to the next older age category consistent with standard life-table technique. No cohort member was assumed to be lost to follow-up.

Incidence rates in this cohort were compared with estimated incidence rates for bladder cancer in the United States, 1973 to 1977, derived by the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute.[7] These incidence rates were then expressed with a base of 100,000. Standardized incidence ratios were computed to express the incidence rates of bladder cancer in the cohort as percentages of the rates in the comparison U.S. population, adjusted for age; 95% confidence intervals were calculated by the method described by Breslow.[8] The risk ratio of observed to expected cases was calculated and evaluated by determining p values using the Poisson distribution[9] and the 95% confidence intervals calculated according to the method described by Breslow.[8]

Development of Screening Program: Prevalence Determination — A program for the screening of the cohort for bladder cancer was a key component of this pilot project. A special screening clinic was established in the Department of Family Medicine of the Medical College of Georgia (located in Augusta) for all members of the cohort who resided within 50 miles of Augusta, Ga. This screening program served as the focal point of the project for risk determination.

The screening program provided the data base for the following: (1) determination of the prevalence of malignant disease and abnormalities possibly related to bladder cancer, and also for the prevalence of known risk factors; (2) determination of participation rates; and (3) development of baseline information for ongoing surveillance. Data on the occurrence of bladder cancer in those cohort members living more than 50 miles from Augusta were determined by screening each person in his local community through contacts with local physicians. Arrangements with each local physician were made by a consulting urologist and were monitored by a NIOSH survey specialist.

The screening program consisted of an initial screen to identify all workers with abnormalities possibly related to bladder cancer and a diagnostic and follow-up program for those persons with suspicious or abnormal findings in the primary screen.

The major instrument for gathering information on the cohort was the history questionnaire, which was administered to each member of the cohort by interviewers at the time of screening. The following information was gathered by questionnaire administration: demographic information; occupational history with special reference to working in the BNA-grinding room, knowledge of BNA, work practices, and history of other jobs with potential bladder carcinogens; opinion about the NIOSH letter; alcohol, tobacco, coffee, and artificial sweetener use; familial and personal health history; and information on income and insurance.

The primary screening consisted of the following components: (1) medical history with emphasis on (*a*) history of hematuria, pyuria, or dysuria and (*b*) history of previously diagnosed urinary tract disease; (2) occupational history with two parts: (*a*) determination of whether the subject was on a list of workers who were believed to have had significant exposure to BNA (i.e., worked in the BON-Fusion or Naphthals departments) and (*b*) indication from questionnaire of whether the person had worked in the BNA-grinding room (reportedly a high-exposure area in the plant); (3) physical examination with emphasis on the urogenital system; (4) routine urinalysis with emphasis on hematuria and pyuria; and (5) urine cytology: (*a*) routine Papanicolaou staining of a pooled specimen consisting of two voided urine specimens using the semiautomated cytopreparation method of Bales[10] and (*b*) nuclear fluorescence spectrophotometry using the method of West.[11]

A person would be referred for a follow-up diagnostic urologic evaluation based on a "positive" finding on any

of the following primary screening criteria: (1) medical history — a "positive" was any "yes" answer to stipulated questionnaire items regarding urinary tract, kidney, or bladder problems since Jan. 1, 1979, or for hematuria in the last two years; (2) occupational history — a "positive" was anyone on the list of workers who, according to personnel records, was employed in apparently high-exposure jobs or who indicated that he had worked in the BNA-grinding room; (3) physical examination — evidence of bladder neoplasm such as a pelvic mass; (4) urinalysis — evidence of pyuria or hematuria constituted a "positive," more specifically: (*a*) on N-multi-stix, indication of positive for blood or nitrite (individuals with positive nitrite were referred for treatment); (*b*) centrifuged urine: more than four RBCs per high-power field or six WBCs per high-power field; positive for bacteria or *Trichomonas* (all urine clean catch, midstream for males, catheterized for females); and (5) urine cytology — a "positive" was any nonnegative (atypical, suspicious, or positive) by Papanicolaou cytology (read by a cytopathologist) or by nuclear fluorescence spectrophotometry.

Results of the primary screening were reported in two parts. At the clinic the subjects were told of the results of their urinalysis and physical examination and of the evaluation of their occupational history. Subsequently, they were mailed letters with the results and interpretation of their entire evaluations.

Those persons satisfying the above-mentioned decision criteria were referred to the Urology Section of the Department of Surgery of the Medical College of Georgia for a diagnostic evaluation. This evaluation included (1) confirmation of urologic history, (2) repeated urinalysis and urine cytology, (3) radiologic evaluation of urinary tract, if appropriate, (4) cytologic analysis of bladder washings by Papanicolaou and nuclear fluorescence techniques, (5) cystoscopy for all subjects with a designated high-risk occupational history, history of hematuria, current hematuria, or nonnegative cytology unless there was a relevant contraindication due to a medical reason (people with pyuria were referred to their own physicians for treatment and reevaluated for bladder cancer when the pyuria was cured), and (6) random (within the bladder) biopsies for all people who underwent cystoscopy and who had a nonnegative cytology unless medically contraindicated.

Results from the diagnostic evaluation were conveyed orally to each cohort member at the urology clinic. Individuals with suspicious or positive findings on the nuclear fluorescence cytologic analysis were referred for aggressive follow-up.

Subjects who failed to appear for urologic evaluation were contacted by personnel from the Medical College of Georgia or by a field representative of the Richmond County Health Department and encouraged to attend. If the subject decided to see a private physician, an effort was made to secure a release of information from the private physician.

All of the data gathered both at the initial screening and at the urologic evaluation were recorded on precoded forms. These data included history questionnaire, physical examination form, urinalysis, and pathology forms. Special care was given to the pathology forms to allow for conformity with the standardized pathology nomenclature adopted by the National Bladder Cancer Project.[9]

Results

Incidence of Bladder Cancer — A total of 13 confirmed cases of bladder cancer were identified in the Augusta cohort through the end of 1982 (Table 1). To that date 28,918.10 person-years had been accrued by cohort members—19,264.48 by black workers and 9,653.62 by whites (Table 2). Three of the 13 cases were identified from death certificates identified through the mortality study. Physicians' reports confirmed another seven cases that had been detected and treated independently of this project. Three cases were found in the screening process and were confirmed from pathological reports. These 13 cases represent a cumulative incidence rate in the cohort of 1,385 workers of 0.9% for the period 1940 to 1982. All 13 cases occurred among the 1,313 males in the cohort.

Dates of onset of the bladder cancer extended over a period of 17 years from 1965 to 1982. Sixty-two percent of the cases occurred in black workers, and 38% in whites. The crude race-specific cumulative incidence rate for black males was 0.8% (7/871), and for white males, 1.4% (6/415).

When the incidence was examined by duration of employment, the following rates were found: for workers employed five or fewer years, 0.4% (5/1,320); those employed six to 10 years, 3% (1/38); 10 to 20 years, 18% (3/16); and more than 20 years, 36% (4/11) (Fig. 1). These data are not adjusted for age.

To examine incidence by age, race, and duration of em-

Table 1 — Method of Ascertainment and Histopathologic Findings for Cases Identified as of Aug. 1, 1982

Case No.	Method of Ascertainment	Date	Histopathologic Findings
1	Death certificate	1966*	Transitional cell carcinoma (grade II or III)
2	Community urologist	1971	Transitional papilloma, papillary carcinoma
3	Death certificate	1972	Infiltrating papillary transitional carcinoma
4	Community urologist	1973	Invasive carcinoma (grade III)
5	Community urologist	1973	Invasive carcinoma (grade II)
6	Death certificate	1976	Transitional cell carcinoma (grade IV)
7	Community urologist	1976	Carcinoma (grade I)
8	Community urologist	1976	Transitional cell carcinoma (grade III)
9	Community urologist	1977	Invasive carcinoma
10	Community urologist	1979	Papillary carcinoma (grade I)
11	Screening clinic	1982	Invasive urothelial carcinoma (grade II)
12	Screening clinic	1982	Carcinoma in situ
13	Screening clinic	1982	Carcinoma in situ

* First diagnosis in 1965

Table 2 — Age- and Race-Specific Incidence Rates for Bladder Cancer per 100,000 Population and Standardized Incidence Ratios (SIR) for the Augusta Cohort (1940 to 1982) and the U.S. Population (1973-1977)

Age, yr (9/1/82)	White			Black		
	Cohort	U.S.*	SIR†	Cohort	U.S.	SIR
15-19	. . .	0.2	. . .	. . .	0.4	. . .
20-24	. . .	0.5	. . .	. . .	0.5	. . .
25-29	. . .	1.2	. . .	. . .	0.3	. . .
30-34	76.7	2.0	38.4	. . .	1.3	. . .
35-39	. . .	2.7	. . .	. . .	0.9	. . .
40-44	. . .	7.8	. . .	112.2	2.2	50.9
45-49	80.2	15.1	5.3	. . .	6.8	. . .
50-54	. . .	28.2	. . .	117.5	7.5	15.7
55-59	. . .	46.9	. . .	98.6	25.7	3.8
60-64	230.6	77.6	3.0	. . .	42.6	. . .
65-69	837.3	121.2	6.9	‡	62.6	. . .
70-74	. . .	167.9	. . .	. . .	92.9	. . .
75-79	. . .	230.0	. . .	. . .	127.3	. . .
80-84	. . .	251.8	. . .	. . .	140.4	. . .
85†	. . .	298.9	. . .	. . .	102.9	. . .
Total§	**51.7**	**2.4**	**21.5**	**41.8**	**1.2**	**34.8**

* Based on rated derived from the SEER Program (National Cancer Institute, 1981)

† SIR should be multiplied by 100 to express the incidence rate as a percentage of the rate in the U.S. population

‡ Two cases of carcinoma in situ occurred in this age group; this is an incidence rate of 708.8 per 100,000 compared with the U.S. rate of 1.4 per 100,000; the SIR is 517.5

§ Total rates are not age standardized

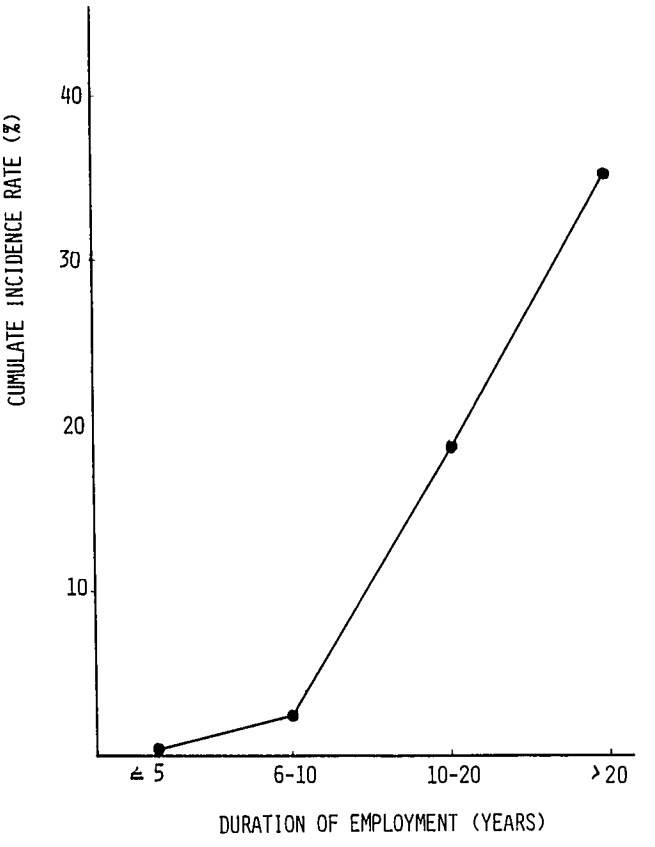

Fig. 1 — Relationship of bladder cancer incidence rate to duration of employment.

ployment in relation to national estimates of the incidence of bladder cancer, data for the Augusta cohort were compared with rates derived from the SEER Program[5] (Tables 3 and 4). The ratios (observed/expected ratio) of the number of cases of bladder cancer observed in each race and age group and in each duration category to the numbers expected in each of those groups from the national estimates were calculated. For the entire cohort, 13 cases of bladder cancer were observed compared with 3.3 expected. The overall risk ratio is 3.9 (p = .0001) (Table 5). Of the 13 cases, seven occurred in black workers; of these, six were invasive carcinomas and one was carcinoma in situ. Where the six invasive carcinomas were observed, 1.2 were expected, for a risk ratio of 5.0 (p = .0001). For those black workers with invasive carcinomas who had more than 10 years' employment at Augusta Chemical, three cases were observed and 0.027 were expected, for a risk ratio of 111.1 (p = .0001).

One black worker was diagnosed with carcinoma in situ compared with an expectation of 0.12, for a risk ratio of 8.3 (p = .001). This case was also in the category of "more than 10 years' employment," and compared with the expectation of 0.011 cases, yields a risk ratio of 91 (p = .01). The 95% confidence limits for all risk ratios are shown in Table 5 and all lower limits are greater than 1.0.

Five invasive carcinomas were observed in white workers against an expectation of 1.9, for a risk ratio of 2.6 (p = .01). Two of these occurred in men with more than 10 years' employment, compared with 0.25 expected, for a risk ratio in that group of 8.0 (p = .002). All lower 95%

Table 3 — Age- and Race-Specific Numbers of Person-Years at Risk of Bladder Cancer Accumulated by the Augusta Cohort (1940 to 1982)

Age, yr (9/1/82)	White	Black
15-19	70.35	233.61
20-24	626.40	1,536.01
25-29	1,148.95	2,793.76
30-34	1,303.46	3,114.08
35-39	1,341.20	2,973.59
40-44	1,328.29	2,674.66
45-49	1,247.04	2,241.02
50-54	1,029.78	1,702.30
55-59	707.74	1,013.92
60-64	433.68	540.77
65-69	238.86	282.16
70-74	116.48	115.83
75-79	39.42	31.91
80-84	14.43	7.37
85+	7.54	3.49
Total	**9,653.62**	**19,264.48**

Table 4 — Expected (E) and Observed (O) Numbers of Incident cases of Invasive* Bladder Cancer, by Age and Race (1940 to 1982)

	White			Black		
Age, yr	E	O	O/E	E	O	O/E
15-19	0.00014	0	. . .	0.00093	0	. . .
20-24	0.00313	0	. . .	0.00768	0	. . .
25-29	0.01378	0	. . .	0.00838	0	. . .
30-34	0.02606	1	38.36	0.04048	0	. . .
35-39	0.03621	0	. . .	0.02676	0	. . .
40-44	0.10360	0	. . .	0.05884	3	50.90
45-49	0.18830	1	5.31	0.15238	0	. . .
50-54	0.29038	0	. . .	0.12767	2	15.67
55-59	0.33193	0	. . .	0.26057	1	3.83
60-64	0.33653	1	2.97	0.23036	0	. . .
65-69	0.28949	2	6.90	0.17663	0	. . .
70-74	0.19556	0	. . .	0.10760	0	. . .
75-79	0.09066	0	. . .	0.04062	0	. . .
80-84	0.03720	0	. . .	0.01034	0	. . .
85+	0.02253	0	. . .	0.00359	0	. . .
Total†	**1.8619**	**5**	**2.68**	**1.2528**	**6**	**4.79**

* Does not include the two cases of carcinoma in situ

† Grand total: E = 3.1147, O = 11, O/E = 3.5

confidence limits were greater than 1.0. Ratios are generally higher in the younger age range (30 to 50 years) and lower thereafter. There was one case of carcinoma in situ in a white worker.

Comparison of the age-specific incidence rates of bladder cancer in the Augusta cohort with the age patterns seen nationally shows that, for blacks in the Augusta cohort, the age of onset of bladder cancer is shifted toward the younger age groups. For blacks, the most frequent age at onset in the Augusta cohort was in the 40- to 44-year range; while for the U.S. population it was in the 55- to 59-year range. For whites the most frequent age of onset in the Augusta cohort was in the 65- to 69-year range, which was the same as for the U.S. population. However, for whites there was also a general shift of age incidence toward the younger age groups (Figs. 2 and 3).

The average age at onset (first diagnosis) of bladder cancer in the Augusta cohort is 52.5 ± 10.7 years. The average age at onset of disease for the seven black workers was 48.6 ± 6.0 years (Fig. 4), and for the six white workers 57.2 ± 12.9 years (Fig. 5). The mean latent period (defined as the date of detection minus the date of first employment) for the whole series of cases was 21.4 ± 7.9 years (range, four to 32 years). For black workers the latent period was 22.3 ± 6.1 years, and for white workers it was 20.3 ± 8.3 years.

The mean duration of employment for all cases was 12.3 ± 11.0 years. All nine cancer patients for whom there was detailed occupational history reported working in the grinding room, whereas, of the entire screened cohort (in-town), only 49% said they had worked in the grinding room (p = .006).

Cases were also compared with noncases for the prevalence of other known or suspected risk factors for bladder cancer. No statistically significant differences were observed between the groups for cigarette smoking, coffee drinking, use of artificial sweeteners, source of drinking water, or other employment in high-risk occupations.

Discussion

The data obtained in this study indicate an incidence of at least 13 cases of bladder cancer in a cohort of 1,385 persons exposed to aromatic amines and, thus, confirm the presumed existence of an excess risk in this population. The incidence rate increased sharply with duration of employment, and so exhibited a clear dose-response relationship.

The risk is greatest in workers who reported having worked in the grinding room and especially for those who worked there for more than 10 years. The risk is also in excess for workers who were assigned to the BON-Fusion or Naphthals departments. The risk of bladder cancers in "particularly exposed" workers was seven times greater than that in "nonexposed" workers. Although work in the grinding room appeared to be a significant risk factor, there is a possibility that some of this effect may be the result of a recall or "litigation" bias.

The racial differential, indicated by a risk ratio of 5.0 for black workers and 2.6 for white workers, occurred despite

Table 5 — Risk Ratios for the Augusta Cohort

	Observed Cases	Expected Cases	Risk Ratio	p	95% Confidence Limits
All bladder cancers	13	3.3	3.9	.0001	2.2 - 6.8
Invasive cancer					
White	5	1.9	2.6	.01	1.1 - 6.4
Black	6	1.2	5.0	.0001	2.2 - 11.3
> 10 yr employment					
White	2	0.25	8.0	.002	1.9 - 32.9
Black	3	0.027	111.1	.0001	35.0 - 352.5
Carcinoma in situ					
Black	2	0.12	16.7	.001	4.1 - 68.7
> 10 yr employment	2	0.012	166.7	.0001	40.6 - 686.9

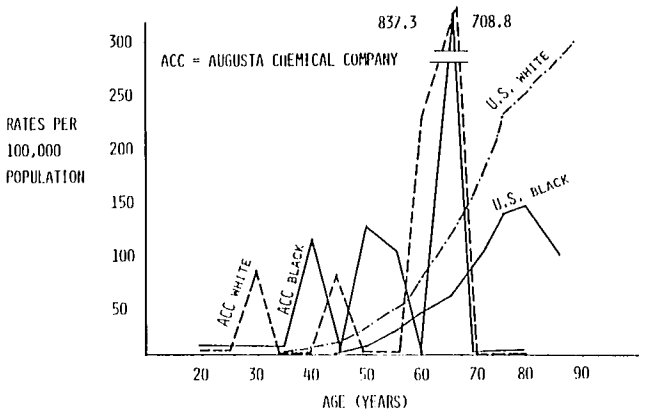

Fig. 2 — Age- and race-specific bladder cancer incidence rates for males in Augusta cohort (1940 to Sept. 1, 1982).

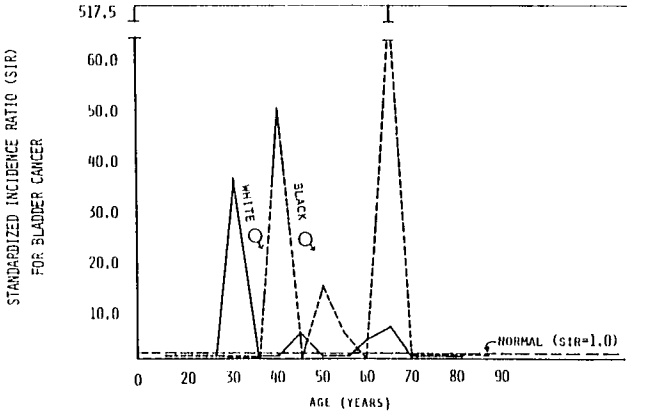

Fig. 3 — Age- and race-specific standardized incidence ratios for Augusta cohort.

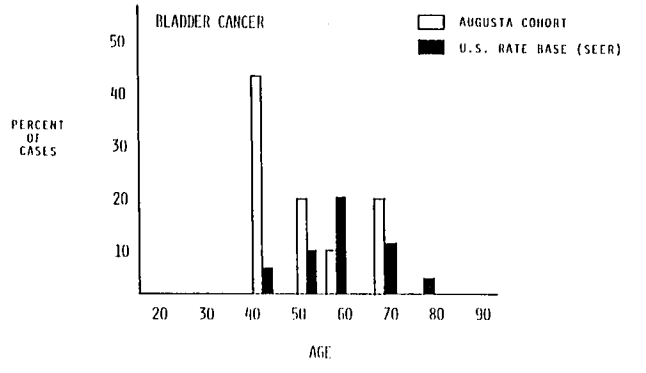

Fig. 4 — Age at onset of bladder cancer cases (black males) in Augusta cohort and of expected cases based on U.S. incidence rates.

the fact that the age-adjusted incidence rate for U.S. white males is approximately twice the rate for black males (27 *v* 13.6 per 100,000; National Cancer Institute, 1981). Moreover, the ratio of expected cases showed that there should have been 2.55 times more cases in whites than in blacks

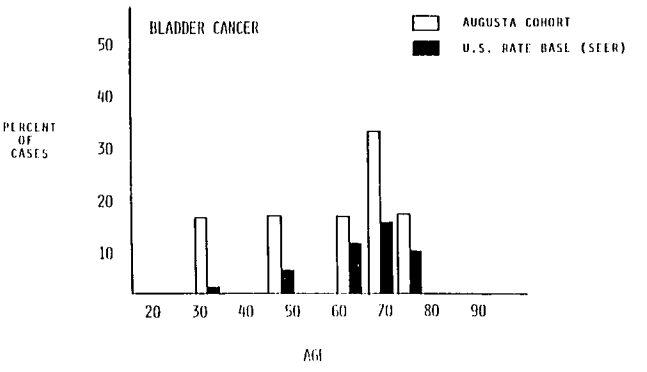

Fig. 5 — Age at onset of bladder cancer cases (white males) in Augusta cohort and of expected cases based on U.S. incidence rates.

in the cohort. It is likely that the main reason for the deviation of the Augusta cohort from the national pattern is that, in general, black workers had jobs involving greater exposure to BNA. These risk ratios are based on small numbers and thus have fairly wide confidence intervals. Despite this limitation, the data are consistent internally and with the literature on aromatic amine exposure.

The results of this study differ from the findings suggested by Hoover and Cole,[11] that risk of bladder cancer does not increase beyond two years of exposure. The clear dose-response relationship found for the Augusta cohort indicates that risk does increase as exposure increases. Similarly, Monson and Nakano[14] found that for bladder cancer in the rubber industry there was an increasing risk with increasing employment beyond two years. The different findings of Hoover and Cole may reflect the fact that their study involved broad industrial and occupational categories rather than the single industrial plants evaluated in these studies.

The confirmed bladder cancer cases show characteristics similar to the cases seen by Case and colleagues[15] in their studies of British BNA manufacturers. As in Great Britain, the Augusta cases show a latency of about 20 years, an earlier age at onset than normal, mean employment greater than a decade, and a dose-response relationship with employment. The range of latency (four to 32 years) found in the Augusta cohort is similar to that found by Scott (1952),[16] four to 33 years; Case et al (1954),[15] two to 45 years; and Goldblatt (1947),[17] four to 48 years.

It is difficult to evalute the three cases who had employment for less than 0.08 years (29 days), although Case et al[15] and Scott[16] each reported one case with less than six months of exposure. Other researchers have also indicated that very small exposures to BNA may be sufficient to cause an increased risk of bladder cancer.[1] Foulger[18] claimed that "a daily exposure to 0.3 — 0.6 mg of beta-naphthylamine for one month represents an effective human contact."[1] One of three cases with brief exposure had worked only after BNA production had ceased. However, the extent of residual contamination of the plant is not known and exposure cannot be ruled out. Heuper[1] indicated that workers employed in a building formerly used for the production of BNA sustained a bladder cancer hazard because of their exposure to volatilized BNA that had

impregnated wood and bricks. The other two Augusta cases were employed only in 1946 or 1947. BNA may not have been handled during this time, although no clear record of the earliest handling has been found. Benzidine, however, was handled as early as 1945. Even if those three cases are deleted from consideration, the risk in the Augusta cohort would still be elevated in the group with 10 years or more of employment.

There is no evidence that significant detection bias for invasive cancer exists in this study. In fact, it is likely that there has been an underreporting of cases, owing to the failure to locate and follow at least 20% of the cohort. The characteristics of those persons lost to follow-up are not known; therefore, it is difficult to estimate whether their risk is any different from that of those located. These lost cases are considered in the analysis as negatives. In contrast, it is likely that there is a possible detection bias for carcinoma in situ. The cases of carcinoma in situ in this study were confirmed by a consultant pathologist who evaluated the screening results of asymptomatic subjects. The detection of carcinoma in situ in the general U.S. population was more likely the result of follow-up symptomatic patients. Since the Augusta cases were asymptomatic, it is not likely that they would have been biopsied had they not been included in this study. Therefore, it is possible that the rate of in situ cancer may be artificially inflated.

The number of cases of bladder cancer expected in the Augusta cohort was estimated using rates from the SEER Program. There are few other sources of incidence data. For example, a commonly used source is the Connecticut Tumor Registry, which is a part of the SEER Program. It was, however, not utilized because more stable age-specific bladder cancer incidence rates for blacks could be obtained from data for the entire SEER Program, which included almost 10% of the U.S. population.

The focus of this article has been on the assessment of bladder cancer risk in a cohort exposed to aromatic amines. However, in the overall evaluation of the Augusta cohort, the effects of other risk factors for bladder cancer, particularly cigarette smoking, were also evaluated.[19] These effects and their possible interactions with occupational exposures will be discussed in subsequent publications. In those evaluations, occupational exposure was still the most significant variable in a multivariate model that included smoking.

The full extent of the bladder cancer risk in this cohort can not yet be determined. The majority of the cohort has not yet achieved the average latency period of 21 years observed for the cases detected thus far. Consequently, more cases might be expected to occur in the future. An additional 36 workers identified by various historic, cytologic, histologic, and urologic criteria may represent a subset of the cohort at elevated risk of bladder cancer from which the earliest future cases would appear. Also, the number of cases may increase when the additional data are included. The study is still in progress.

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