

in statistical analyses when indicated. Criteria used to diagnose BP included: (a) a total WBC count $<4000 (\times 10^6 \text{ L}^{-1})$, or WBC count $4000\text{--}5000 (\times 10^6 \text{ L}^{-1})$ and a platelet count $<80,000 (\times 10^6 \text{ L}^{-1})$, or an absolute neutrophil count $<2000 (\times 10^6 \text{ L}^{-1})$, (b) employment in a factory with documented benzene exposure for at least 6 months and (c) exclusion of other causes for abnormal blood counts. Hospital-based cases of MDS and BID were diagnosed in our laboratory based on evaluation of peripheral blood and bone marrow using morphologic, immunohistochemical, flow cytometric, cytogenetic, and molecular genetic techniques as previously described [1,24]. Workplace controls were also required to have at least 6 months employment in a factory using benzene in order to maintain comparability with cases. Patients with a history or symptoms associated with the following conditions were excluded from both case and control groups: infectious disease, concomitant chronic disorders (e.g. renal failure, arteritis, autoimmune disease, diabetes or cancer) or hematological abnormalities due to nutritional deficiencies or other causes. In addition, subjects were excluded if they had been treated for tuberculosis or used any of the following medications within the previous 5 years: chloramphenicol, sulfonamides, meprobamate, phenytoin, colchicine, cyclophosphamide, propylthiouracil, tolbutamid, primaquine and Chinese traditional herbs (e.g. Bezoar, Angelica, arsenic or Thunder cloud vine).

2.2. Benzene exposure assessment

The exposure assessment employed several approaches according to how the subjects were recruited to the study and available work history details. Hospital based MDS subjects had a work history questionnaire administered by trained interviewers. Expert review of questionnaires suggested low

to no benzene exposure potential and further evaluation was not warranted. Many of the BP and BID subjects and benzene exposed worker controls worked in the same facilities. Therefore, exposure assessment for these groups used the same approach. Occupational exposure to benzene was evaluated by review of factory industrial hygiene monitoring records, review of the Chinese literature on benzene exposed industries and jobs, Chinese regulatory authority benzene exposure databases and by current quantitative industrial hygiene surveys, including personal benzene exposure samples and breathing zone/area sample analyses. Based on current measurements, 210 subjects had recent full-shift time weighted air concentration exposures ranging from 0.26 mg/m^3 (0.08 parts per million (ppm)) to 353.5 mg/m^3 (110 ppm). The exposures summarized in Table 1 include retrospective as well as current exposure. The retrospective exposure estimates are based on current data, historic data, and consideration of ventilation, material composition and other exposure modifying changes in the factories. Expert judgment was used more extensively with available historic data to assess exposures for three of the BID subjects. A total of 193 subjects had ongoing exposure during our evaluation, while the majority of BID subjects were removed from exposure an average of 2.7 years prior to diagnosis and exposure evaluation. Since many of the BID and BP/worker control subjects worked in the same facilities, differences in the mean exposures between BID and BP/worker controls largely reflect changes in the working environment over the past 3–5 years. The varying exposure periods of time for all subjects ranged from 2 to 37 years.

Cumulative exposure and long term average exposure was usually treated as a continuous variable, but was also categorized. Categories of cumulative exposure (in $\text{mg/m}^3 \text{ year}$) were: <175 , 175 to <500 , 500 to <1183 , 1183 to <4330 , and

Table 1
Distribution of demographic, lifestyle, exposure and polymorphisms among study groups

Characteristic	MDS, <i>N</i> = 95	BID, <i>N</i> = 23	BP, <i>N</i> = 46	Worker controls, <i>N</i> = 141	Hospital controls, <i>N</i> = 89
Gender					
Male	51 (53.7%)	8 (35%)	24 (52%)	84 (60%)	53 (60%)
Female	44 (46.3%)	15 (65%)	22 (48%)	57 (40%)	36 (40%)
Smoking ^a (% ever smoked)	73 (81%)	17 (74%)	40 (87%)	91 (65%)	57 (64%)
Alcohol (% current use)	72 (81%)	21 (91%)	37 (80%)	94 (67%)	74 (83%)
Age	54.9 ± 17	45.5 ± 7.8	42.7 ± 6.3	43.4 ± 7.4	44.5 ± 18.7
(year, mean $\pm$ S.D.) (range)	19–87	34–59	29–53	25–59	17–90
Benzene: long term average exposure (mg/m^3)	NA	977 (49–1436) [305]	395 (2.5–1675)	207 (1.7–1280)	NA
(mean, range) [mean ppm]			[123]	[65]	
Benzene cumulative exposure ($\text{mg/m}^3 \text{ year}$)	NA	14,300 (728–28,600)	5826 (10.8–44,400)	2870 (2.3–30,700)	NA
(mean, range) [mean ppm year]		[4469]	[1821]	[897]	
Cumulative exposure category 3+ (%) (see text)	NA	100%	48%	43%	NA
Long-term average category 3+ (%) (see text)	NA	100%	65%	50%	NA
–238 N (% AG + AA)	2 (2.1%)	5 (21.7%)	3 (6.5%)	6 (4.3%)	5 (5.6%) (1 ND)
–308	10 (10.5%)	3 (13.0%)	10 (21.7%)	20 (14.2%)	14 (15.7%)
N (% AG+AA)					(2 ND)
–857 N (% CT + TT)	ND	3 (13.0%) (3 ND)	6 (13.0%)	24 (17.0%) (9 ND)	20 (22.5%) (1 ND)
–863 N (% AC + AA)	ND	7 (30.4%) (3 ND)	6 (13.0%) (9 ND)	34 (24.1%)	25 (28.1%)

^a MDS: five unknowns; BID: two unknowns; BP: two unknowns; ND: not determined