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Review

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A work-relatedness assessment in epidemiological case investigation of occupational cancers: II. Practice: an upper urinary tract cancer in a dyer

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Abbreviations
IARC: International Agency for Research on Cancer; MSDS: material safety data sheet; UUTC: upper urinary tract cancer.

Competing interests
The authors declare that they have no competing interests.

ABSTRACT

An epidemiological case investigation of occupational cancer is conducted to determine the causation between the cancer and the worker's job. This review describes the overall process of work-relatedness assessment of the epidemiological case investigation through a case of upper urinary tract cancer (UUTC) in benzidine exposed worker in dyeing industry. Medical referrals, occupational history, material safety data sheet, and working environment monitoring submitted by the Korea Workers' Compensation and Welfare Service were reviewed. We further investigated literatures about the cotton dyeing industry, the domestic law and working environment monitoring reports. Benzidine was listed as an International Agency for Research on Cancer risk factor only for bladder cancer among urinary tract cancers, requiring different logical grounds for establishing causation. A literature review was conducted on the metabolic pathways of benzidine to establish biological plausibility. In addition, several papers were investigated that UUTC and bladder cancer share risk factors to extrapolate the epidemiological studies of bladder cancer. Epidemiologic studies of benzidine and bladder cancer were investigated. The worker is a 71-year-old man and performed dyeing and transporting at several dyeing factories for 29 years. The worker was diagnosed with UUTC based on radiologic and histologic results. It was critical to consider that he worked as a dyer for 3 years. The cancer was diagnosed in 2018, with a latent period of approximately 35 years. The worker performed cotton dyeing, and benzidine-based dye was mainly used. The quantitative exposure level of benzidine was reported from non-detection to 397.4 μg/m^3. In biological metabolisms, N-acetylhydroxylamine changes DNA structure of urothelium. As a result of reviewing 4 epidemiological studies, the standardized incidence ratio and standardized mortality ratio were significantly high with 3 years of exposure. Work-relatedness was finally assessed as probable based on biological mechanisms and epidemiological evidence. This review will help solutions for work-relatedness assessment processes.

Keywords: Occupational exposure; Benzidine; Dyeing industry; Transitional cell carcinoma

Author Contributions
Conceptualization: Kim KH, Kim JW; Data curation: Kim KH, Oh HC; Investigation: Kim KH, Kim JW; Writing - original draft: Kim KH; Writing - review & editing: Oh HC, Kim JW.

BACKGROUND

In the field of occupational and environmental medicine, work-relatedness assessment is conducted to determine whether a worker's disease is caused by the works or occupational factors performed by skilled professionals. In occupational cancer, work-relatedness assessment is conducted to identify the causation between exposure to carcinogenic factors and disease in workers who are then able to receive industrial accident compensation if a reasonable causation is determined. Currently, epidemiological case investigation is used to determine the causation between cancer and the worker's job. A worker suspected with occupational cancer submits a medical benefit application and medical referrals to the Korea Workers' Compensation and Welfare Service. An epidemiological case investigation is conducted at Institute of Occupation and Environment or Occupational Safety & Health Research Institute. The overall process of the epidemiological case investigation comprises collection of worker's data, investigations of workers and related people, review of submitted data, and workplace investigation [1,2]. However, occupational cancer assessment is a difficult process even for professionals because of the absence or lack of past workplace data, loss of contact with colleagues, incorrect memories of the workers and their family, or exaggeration and concealment of facts. The International Agency for Research on Cancer (IARC) presents carcinogens for upper urinary tract cancers (UUTCs) as phenacetin and aristolochic acid [3]. In addition, several authors argue that carcinogens of bladder cancer could be those of UUTC [4-8]. In 2018, 3,922 patients were reported with renal pelvis cancer, and 45,846 patients were reported with bladder cancer [9]. From 2015 to 2018, there were 3 approved cases of bladder cancer [10]. But we couldn't find any case of renal pelvis cancer in respect to work-relatedness during the same period [10]. This review summarizes the progresses in work-relatedness assessment of the first case of UUTC in a dyeing worker domestically recognized. Additionally, the issues and logical grounds for assessment in the assessment processes are presented.

METHODS

Medical referrals, occupational history, material safety data sheet, and working environment monitoring submitted by the Korea Workers' Compensation and Welfare Service were reviewed. We further investigated literatures about the cotton dyeing industry, the domestic law and working environment monitoring reports. Benzidine was listed as an International Agency for Research on Cancer risk factor only for bladder cancer among urinary tract cancers, requiring different logical grounds for establishing causation. A literature review was conducted on the metabolic pathways of benzidine to establish biological plausibility. In addition, several papers were investigated that UUTC and bladder cancer share risk factors to extrapolate the epidemiological studies of bladder cancer. Epidemiologic studies of benzidine and bladder cancer were investigated.

RESULTS AND DISCUSSION

Cancer diagnosis

The worker is a 71-year-old man who performed several processes such as dyeing and transporting for 29 years at dyeing factories. The worker had a smoking history of 10 cigarettes per day for approximately 10 years from the age of 25 years and has quit smoking since age 35. The worker had no history of alcohol consumption. His younger brother had a history of colon cancer. Since March 2018, although the worker had undergone comprehensive tests for unexplained weight loss of 8 kg, no abnormality was observed. As of April 25, 2018, gross hematuria was observed, and abdominal computed tomography confirmed left upper renal pelvis carcinoma in the worker. Based on the result of a biopsy conducted on May 1, 2018, infiltrating urothelial carcinoma, grade III/III, with focal squamous differentiation was identified. Three neoadjuvant therapies were administered to reduce the size of the cancer, and left nephroureterectomy was performed on August 29, 2018. During the follow-up, recurrence in the bladder was diagnosed in the form of papillary urothelial carcinoma, and reoperation was performed on March 27, 2019. The worker is currently receiving medication for diabetes and hyperlipidemia. In summary, radiologic and histological results confirmed the final diagnosis of UUTC and suspected metastatic cancer in the bladder. Therefore, the work-relatedness assessment was conducted only for UUTC, which is the primary cancer.

Exposure assessment

Qualitative assessment: identification of carcinogens and exposure

1) Identification of carcinogens for the diagnosed cancer

Most occupational urinary tract cancers are known to occur in the urothelium, thus the risk factors of bladder cancer were considered as well [11]. According to the IARC, risk factors for UUTC include aristolochic acid and phenacetin, and risk factors for bladder cancer include painting, rubber industry, and aromatic amines such as benzidine and 2-naphthylamine [3].

2) Exposure identification

The worker's data submitted by the Korea Workers' Compensation and Welfare Service in October 2018 were reviewed comprehensively. Interviews with the worker reconfirmed the facts and supplemented the investigated data. The data were aggregated to assess exposure to carcinogens in a comprehensive manner and to determine whether further investigation was required accordingly.

(1) The worker's occupational history

Personal information, history of military service, occupational history, and exposure to hazards were identified based on statement of the worker and his colleagues, national health insurance records, and income records. There were insufficient data available on past workplaces because only the last workplace was in operation. The worker dropped out of high school and was engaged in agriculture before serving his 2-year military service; he had worked at a total of seven workplaces since then. Factory A produced plywood, and in this factory, the worker worked as a grinder worker for 6 years. Factory B performed cotton dyeing (mainly for knitwear), and in this factory, the worker had worked as a dyer for approximately 3 years, performing dye blending and dyeing. The average weekly working hours were estimated to be 66 hours. The working environment was dusty as he had to pour dye powders into a bowl for mixing, and it is estimated that the inside of the factory was filled with dyeing steam as people carried clothes from the dyeing machine. Although gas masks should be provided, only non-industrial disposable masks were worn. At factories C, D, and E, the worker outsourced cotton and polyester fabrics for approximately 9 years for dyeing and processing and then subsequently delivered the products to another workplace. From 1995 to 2018, factory F was a shoe fabric dyeing plant and the worker was responsible for the delivery of finished products to other factories. The occupational history of the worker is summarized in **Table 1**.

(2) Chemicals used (factory F)

All the workplaces except factory F were shutting down and related documents were

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Table 1. The occupational history of the worker

Period	Factory	Process	Job type
1977–1983	A	Plywood production	Grinder worker
1983–1986	B	Dye blending, dyeing	Dyer
1986–1988	C	Delivery dyed product	Driver
1988–1989	D	Delivery dyed product	Driver
1989–1992	C	Delivery dyed product	Driver
1992–1995	E	Delivery dyed product	Driver
1995–2018	F	Transporting, loading, and unloading dyed product in the factory	Porter

discarded, thus only available factory F information were reviewed. Material safety data sheet (MSDS) submitted from Korea Workers' Compensation and Welfare Service was reviewed to identify current and past material use. The worker used dyes, softeners, leveling agents, fiber aids, antistatic agents, fluorescent brighteners, and refinement penetrants. Depending on the workload, the amount of dyes, soft agents, and other chemicals used varied. The monthly usage of each chemical was 30–4,300 kg of dye, 100–250 kg of softener, 50–100 kg of leveling agent, 100–200 kg of fiber aid, 1,000–1,500 kg of antistatic agent, 10–20 kg of fluorescent brightener, and 50–100 kg of refinement penetrant. There was no working environment monitoring of shipment process because no chemicals were used. The MSDS for the materials used in the dyeing process were about the following substances: 2-butoxyethanol (1%–4.5%), formic acid (20%–30%), sodium hydroxide (2%–71%), silver (unknown), acetic acid (0.1%–100%), phenolic resin derivatives (0%–100%), and formaldehyde (0.5%). The materials contained several other ingredients, and they were not controlled materials. In the report on the working environment monitoring for the last 3 years, no hazardous substances were detected except formic acid (0.0206–0.029 mg/m^3).

(3) Legal changes in benzidine-based dye

The dyes used depends on the type of fabric (cotton, wool, viscose, polyester). Direct, disperse, reactive, acidic and basic, sulfur, and mordant dyes are some of the important types of dyes. The factory where the worker worked as a dyer performed cotton dyeing. Generally, for cotton dyeing, 1) direct dyes, 2) reactive dyes, 3) azoic dyes, 4) sulfide dyes, and 5) bat dyes are used [12].

Initially, several direct dyes with benzidine-based compounds were being used, but considering the carcinogenic effects of benzidine, the production of benzidine-based dyes gradually stopped. Kim [13] hypothesized that the benzidine-based dyes in Korea produced actively after the regulation of benzidine-based dyes in Japan in the 1970s. Since more than half of the direct dyes produced in Japan were benzidine-based, it was probable that several benzidine-based dyes were used after the 1970s [14]. Kim et al. [15] also noted that the peak use of benzidine was represented in 1980s.

According to an interview with long-term workers in the dyeing industry, reactive dyes are preferred more than direct dyes considering the safety and environmental issues of direct dyes. The use of reactive dyes increased after 1990, before which direct dyes were used considering that that were easy to use and cost-effective. In the 1980s, it was estimated that at least 70% of cotton dyers would have experience of using benzidine-based dye. In summary, the use of benzidine-based dyes was prominent from 1983 to 1986 during which the worker was a dyer. Currently, benzidine hydrochloride has been prohibited under the Occupational Safety and Health Act since 2000 [16]. It can be used only for research purposes.

(4) Overall assessment of exposure

The causation between carcinogen exposures and UUTC was assessed. The worker performed grinding work at the plywood production plant from 1977 to 1983, and the possible carcinogens could be formaldehyde contained in the adhesive. "IARC monograph 100F-29 formaldehyde" states that formaldehyde can cause nasopharyngeal cancer and leukemia, and formaldehyde is not listed IARC risk factors for urinary tract cancers [17]. From 1983 to 1986, the worker handled benzidine-based dyes while working as a dyer. There is a sufficient evidence for bladder cancer according to the "IARC monograph 99-11 dyes metabolized to benzidine" [18]. Since both bladder and renal pelvis cancers are mostly observed in the urothelium, further investigation of carcinogens for urothelial cancer is required. The possibility of carcinogen exposure was rare when the worker was performing delivery and shipment by car.

Quantitative assessment: estimation of the exposure level

For quantitative assessment, we did walk-through factory F with an experienced industrial hygienist, and checked the working processes, MSDS, and working environment monitoring on April 15, 2019. Exposure to suspected carcinogens at present is unlikely as mentioned in "Legal changes in benzidine-based law" paragraph, hence, additional working environment monitoring was not performed. The benzidine exposure assessment at the domestic dye manufacturing factories was carried out in 4 papers [15,19-21]. In the papers, the exposure levels of benzidine were reported from non-detection to 649.6 μg/m^3. The exposure level of benzidine in foreign countries were reported from non-detection to 17.6 mg/m^3 [18].

Considerations for work-relatedness assessment

Minimum induction period and maximum latent period

Studies assessing the minimum induction period and maximum latent period for benzidine exposure have not been conducted yet. Schulte et al. [22] and Wallace [23] reported that exposure to aromatic amines increases the risk of bladder cancer, averaging approximately 22 years of exposure leading to cancer. Miyakawa et al. [24] reported that average latent period of bladder cancer patients who handled benzidine or beta-naphthylamine was 29.6 years. Kim et al. [15] reported that generally the latent period was 20 years or more, and the latent period varies depending on the level of exposure and the duration of exposure. The latent period of the worker was approximately 35 years. It is mentioned that the latent period of bladder cancer induced by aromatic amines is longer than that of general occupational cancer [24].

Biological mechanisms to cause cancers

Benzidine was not listed as an IARC risk factor for UUTC. In order to establish biological plausibility, literatures on biological mechanisms were investigated. Aromatic amines including benzidine are absorbed into the body through inhalation or skin exposure and undergo metabolic processes. They are transformed to hydroxylamine in the liver, and transported to the kidneys through the blood. Hydroxylamine is *O*-acetylated by *N*-acetyltransferase1 which is highly expressed in the urothelium to form N-acetylhydroxylamine. N-acetylhydroxylamine is carcinogenic as it changes DNA structure [25]. Histological and cytogenetic changes in the urothelium during aromatic amine exposure have been reported to be similar across the urinary system [26-28].

Review on epidemiological studies

We searched for papers and reports based on PubMed, and found 4 epidemiological studies that identified the causation between benzidine exposure and UUTC [29-32]. It was difficult to apply the epidemiological studies to the worker owing to multiple exposures of other carcinogens and uncertainties in the exposure period. Urothelial carcinoma occurs 90%–95% in bladder and only 5%–10% in upper urinary tract [33]. Benzidine was not included in the IARC risk factor for UUTC because the relevant evidences might not be sufficiently supported mainly from few researches of very rare diseases.

It was necessary to establish causation through different logical grounds. Benzidine changes DNA structure by its metabolites contained in urine acting on urothelium [34]. Since urothelium forms the epidermis of renal pelvis as well as the bladder, we hypothesized that benzidine would have a similar effect on the urothelium of renal pelvis. Based on literature review, non-bladder urinary tract cancer was found to have risk factors of similar to those of bladder cancer [4-8]. In particular, Wilson et al. [6] noted that both cancers share occupational risk factors. Therefore, it was assumed that UUTC shares risk factors with bladder cancer. As per the National Toxicology Program, dyes are metabolized to benzidine; therefore, benzidine-based dyes and benzidine have similar levels of exposure [35]. Thus, we considered the published reports on both benzidine and benzidine-based dyes.

Epidemiological studies conducted on benzidine were not found in domestic literature. In foreign literature, 4 epidemiological studies reported on the exposure period for benzidine as shown in **Table 2** [36-39]. Except the study by Montanaro et al. [36], the studies were conducted at benzidine-based dye manufacturing factories. Thus, to apply the epidemiological studies conducted at the benzidine-based dye manufacturing factories to workers, the differences of exposure intensity between the dyeing industry and dye production industry should be compared. Golka et al. [40] reported that workers exposed to benzidine-based dyes may be exposed to lower levels of benzidine than those exposed to benzidine directly. As workers in the dye manufacturing factory directly handle benzidine in the process of producing benzidine-based dyes, the dyeing factory was evaluated to have lower exposure intensity than the dye manufacturing factory.

Work-relatedness assessment

Overall, the worker could have been exposed to benzidine-based dyes for 3 years from 1983 to 1986. Exposure to benzidine-based dye, a risk factor for bladder cancer, is also a risk factor for cancer of the renal pelvis urothelium. The mechanism of cancer and the characteristics of renal urothelial carcinoma were found to be similar to those of bladder cancer. Most epidemiological studies conducted on benzidine have focused on the benzidine or benzidine-based dye manufacturing factories. The intensity of exposure in a dyeing factory is relatively lower than that in a dye manufacturing factory [40]. However, despite short-term exposure to benzidine, the standardized incidence ratio or standardized mortality ratio is significantly high as noted in **Table 2**. Considering 66 hours of work per week and poor working conditions, work-relatedness was assessed to be probable even with 3 years of exposure as a dyer. The latent period of the worker was approximately 35 years, consistent with the literature reviews on latent period. Urinary stones, infections, and viruses which are common

Table 2. Epidemiological studies on casual association between benzidine/benzidine-based dyes and bladder cancer according to exposure period

Paper	Exposure group	Standardized incidence ratio	Standardized mortality ratio
Montanaro et al. [36]	Tannery worker exposed to benzidine-based dyes for less than 5 years	4.4 (0.9–12.8)	
Bulbulyan et al. [37]	Aniline dye manufacturing workers exposed to benzidine for less than 3 years	17.7 (3.6–51.8)	
Meigs et al. [38]	Benzidine manufacturing male workers exposed to benzidine more than 2 years	13.0 (4.8–28.4)	
You et al. [39]	Benzidine manufacturing male workers exposed to benzidine average 8 years	19.2 ($p < 0.01$)	14.7 ($p < 0.01$)

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causes of UUTC are not identified. Smoking history can increase the likelihood of cancer by interacting with benzidine-based dye exposure. McLaughlin et al. [41] reported a significant increase in the hazard ratio of UUTC to 2.0 (1.2–3.2) for 1–20 pack-year smokers. In the same study, the hazard ratio of UUTC for quit-smokers over 25 years was significantly decreased to 0.3 (0.2–0.5) compared to current smokers [41]. The smoking history of the worker is 5 pack-years and the smoking cessation period is 35 years. Therefore, the carcinogenic effects of smoking may be less likely.

CONCLUSIONS

Finally, the work-relatedness of UUTC in benzidine exposed worker was first approved at the meeting of integrated committee. The work-relatedness recognition of bladder cancer in a benzidine exposed worker was first reported in 1999 [42]. As mentioned above, UUTC has a relatively very lower incidence than bladder cancer and is not listed in the IARC risk factor [3,34]. These reasons might have contributed to the difficulty in recognizing the work-relatedness of UUTC patients. There were several issues to consider in drawing the final conclusion. A literature review was conducted on the metabolic pathways of benzidine to establish biological plausibility. Based on literature evidences that UUTC and bladder cancer share risk factors, a logical ground for extrapolating the epidemiological studies performed on bladder cancer to UUTC was established. Foreign epidemiological studies were considered because there was no epidemiological study conducted on benzidine exposure in Korea. Since the majority of epidemiological studies were conducted at dye manufacturing factories, a logical ground was needed to extrapolate to dyeing factory. Based on the literature comparing the exposure intensity of two factories, epidemiological studies conducted at dye manufacturing factories were extrapolated to this case. This review will help us understand the process of work-relatedness assessment of occupational cancer and help determine solutions for issues involved in the evaluation process.

REFERENCES

1. Lim JH. A guideline for evaluating work-relatedness of occupational cancer. Ulsan: Korea Occupational Safety and Health Agency; 2011.
2. Park DW. The protocol for work-relatedness of worker diseases. Ulsan: Korea Occupational Safety and Health Agency; 2013.
3. International Agency for Research on Cancer. List of classifications by cancer sites with sufficient or limited evidence in humans, volumes 1 to 123. Lyon: International Agency for Research on Cancer; 2018.
4. Charbotel B, Fervers B, Droz JP. Occupational exposures in rare cancers: a critical review of the literature. Crit Rev Oncol Hematol 2014;90(2):99-134.
PUBMED | CROSSREF
5. Pukkala E, Martinsen JI, Lynge E, Gunnarsdottir HK, Sparén P, Tryggvadottir L, et al. Occupation and cancer - follow-up of 15 million people in five Nordic countries. Acta Oncol 2009;48(5):646-790.
PUBMED | CROSSREF
6. Wilson RT, Donahue M, Gridley G, Adami J, El Ghormli L, Dosemeci M. Shared occupational risks for transitional cell cancer of the bladder and renal pelvis among men and women in Sweden. Am J Ind Med 2008;51(2):83-99.
PUBMED | CROSSREF
7. Jensen OM, Knudsen JB, McLaughlin JK, Sørensen BL. The Copenhagen case-control study of renal pelvis and ureter cancer: role of smoking and occupational exposures. Int J Cancer 1988;41(4):557-61.
PUBMED | CROSSREF

8. Soria F, Shariat SF, Lerner SP, Fritsche HM, Rink M, Kassouf W, et al. Epidemiology, diagnosis, preoperative evaluation and prognostic assessment of upper-tract urothelial carcinoma (UTUC). World J Urol 2017;35(3):379-87.
PUBMED | CROSSREF
9. Health Insurance Review & Assessment Service. 2018 National health insurance statistical yearbook. Wonju: Health Insurance Review & Assessment Service; 2019.
10. Kim KH. A case study and case analysis of occupational cancer convalescence decision. Ulsan: Korea Workers' Compensation and Welfare Service; 2019.
11. Korean Society of Occupational and Environmental Medicine. Occupational and Environmental Medicine. Seoul, Korea: Gyechuk Press; 2014.
12. Korea Textile Inspection & Testing Institute. Dye chemistry for dyeing technician: cellulose fiber dye (1). Seongnam: Korea Textile Inspection & Testing Institute; 2011.
13. Kim EA. Benzidine and occupational bladder cancer. Seoul: Korea Industrial Health Association; 2010.
14. Kim TG. History of the synthetic dye industry. Daegu: Textile Material Solution Center; 2012.
15. Kim Y, Park J, Shin YC. Dye-manufacturing workers and bladder cancer in South Korea. Arch Toxicol 2007;81(5):381-4.
PUBMED | CROSSREF
16. Ministry of Employment and Labor. Occupational safety and health act. Enforcement ordinance: article 29. A presidential decree. Sejong: Ministry of Employment and Labor; 2000.
17. International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans 100F-formaldehyde. Lyon: International Agency for Research on Cancer; 2006.
18. International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 99. Some aromatic amines, organic dyes, and related exposures. Lyon: International Agency for Research on Cancer; 2010.
19. Oh SM, Park DW, Shin YC, Park SH, Lee NR, Lee GY. A study on the exposure concentration and countermeasures of workers handling benzidine hydrochloride. Ulsan: Korea Occupational Safety and Health Agency; 1994.
20. Roh JH, Ahn YS, Kim KS, Kim CN, Kim HS. Benzidine exposure among benzidine-based dye manufacturing workers. Korean J Occup Environ Med 1995;7(2):347-53.
21. Yeom HK, Song JS, Kim CN, Won JU, Roh J. Evaluation of dermal measurement for workers in benzidine dihydrochloride and benzidine based dye manufacturing factory. Korean J Occup Environ Med 1998;10(1):83-93.
22. Schulte PA, Ringen K, Hemstreet GP, Ward E. Occupational cancer of the urinary tract. Occup Med 1987;2(1):85-107.
PUBMED
23. Wallace DM. Occupational urothelial cancer. Br J Urol 1988;61(3):175-82.
PUBMED | CROSSREF
24. Miyakawa M, Tachibana M, Miyakawa A, Yoshida K, Shimada N, Murai M, et al. Re-evaluation of the latent period of bladder cancer in dyestuff-plant workers in Japan. Int J Urol 2001;8(8):423-30.
PUBMED | CROSSREF
25. Jung I, Messing E. Molecular mechanisms and pathways in bladder cancer development and progression. Cancer Contr 2000;7(4):325-34.
PUBMED | CROSSREF
26. Kirkali Z, Tuzel E. Transitional cell carcinoma of the ureter and renal pelvis. Crit Rev Oncol Hematol 2003;47(2):155-69.
PUBMED | CROSSREF
27. Fadl-Elmula I, Gorunova L, Mandahl N, Elfving P, Lundgren R, Rademark C, et al. Cytogenetic analysis of upper urinary tract transitional cell carcinomas. Cancer Genet Cytogenet 1999;115(2):123-7.
PUBMED | CROSSREF
28. Rigola MA, Fuster C, Casadevall C, Bernués M, Caballín MR, Gelabert A, et al. Comparative genomic hybridization analysis of transitional cell carcinomas of the renal pelvis. Cancer Genet Cytogenet 2001;127(1):59-63.
PUBMED | CROSSREF
29. Mazeman E. Tumors of the upper excretory urinary tract, calices, renal pelvis and ureter. J Urol Nephrol (Paris) 1972;78:1-219.
PUBMED

30. Hamasaki T, Aramaki K, Hida T, Inatomi H, Fujimoto N, Okamura T, et al. Clinical study of occupational uroepithelial cancer. J UOEH 1996;18(4):247-59.
PUBMED | CROSSREF

31. Naito S, Tanaka K, Koga H, Kotoh S, Hirohata T, Kumazawa J. Cancer occurrence among dyestuff workers exposed to aromatic amines. A long term follow-up study. Cancer 1995;76(8):1445-52.
PUBMED | CROSSREF

32. Shinka T, Miyai M, Sawada Y, Inagaki T, Okawa T. Factors affecting the occurrence of urothelial tumors in dye workers exposed to aromatic amines. Int J Urol 1995;2(4):243-8.
PUBMED | CROSSREF

33. Rouprêt M, Babjuk M, Compérat E, Zigeuner R, Sylvester RJ, Burger M, et al. European association of urology guidelines on upper urinary tract urothelial carcinoma: 2017 update. Eur Urol 2018;73(1):111-22.
PUBMED | CROSSREF

34. International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans 100F-benzidine. Lyon: International Agency for Research on Cancer; 2008.

35. National Toxicology Program. Benzidine and dyes metabolized to benzidine, report on carcinogens, fourteenth edition. Triangle Park, NC: National Institute of Environmental Health and Safety; 2016.

36. Montanaro F, Ceppi M, Demers PA, Puntoni R, Bonassi S. Mortality in a cohort of tannery workers. Occup Environ Med 1997;54(8):588-91.
PUBMED | CROSSREF

37. Bulbulyan MA, Figgs LW, Zahm SH, Savitskaya T, Goldfarb A, Astashevsky S, et al. Cancer incidence and mortality among beta-naphthylamine and benzidine dye workers in Moscow. Int J Epidemiol 1995;24(2):266-75.
PUBMED | CROSSREF

38. Meigs JW, Marrett LD, Ulrich FU, Flannery JT. Bladder tumor incidence among workers exposed to benzidine: a thirty-year follow-up. J Natl Cancer Inst 1986;76(1):1-8.
PUBMED

39. You XY, Chen JG, Hu YN. Studies on the relation between bladder cancer and benzidine or its derived dyes in Shanghai. Br J Ind Med 1990;47(8):544-52.
PUBMED | CROSSREF

40. Golka K, Wiese A, Assennato G, Bolt HM. Occupational exposure and urological cancer. World J Urol 2004;21(6):382-91.
PUBMED | CROSSREF

41. McLaughlin JK, Silverman DT, Hsing AW, Ross RK, Schoenberg JB, Yu MC, et al. Cigarette smoking and cancers of the renal pelvis and ureter. Cancer Res 1992;52(2):254-7.
PUBMED

42. Kim SA, Lee JW, Kim BW, Shin YC. Bladder cancer with exposure to benzidine-based dyes of dyer. Korean J Occup Environ Med 1999;11(2):304-12.
CROSSREF