World J Urol (2004) 21: 382–391
DOI 10.1007/s00345-003-0377-5

TOPIC PAPER

Klaus Golka · Andreas Wiese · Giorgio Assennato
Hermann M. Bolt

Occupational exposure and urological cancer

Received: 21 October 2003 / Accepted: 21 October 2003 / Published online: 26 November 2003

Abstract Occupational exposure is definitely a major cause of cancer. In the field of urology, the urinary bladder is the most important target. A classical cause of bladder cancer is exposure to carcinogenic aromatic amines, especially benzidine and β-naphthylamine. Such exposures were related to work places in the chemical industry, implying production and processing of classical aromatic amines, and in the rubber industry. Occupational bladder cancer has also been observed in dyers, painters and hairdressers. Even some occupations with much lower exposures to carcinogenic aromatic amines, like coke oven workers or workers in the rubber industry after the ban on β-naphthylamine, are at risk. In these occupations, exposure to complex mixtures of substances containing combustion products (e.g. polycyclic aromatic hydrocarbons) or nitrosamines is common. Renal cell cancer has been observed as an occupational disease in cases of very high exposure to trichloroethylene having led to narcotic or prenarcotic symptoms. Occupationally related cancers of the prostate or the testes appear currently not relevant.

Keywords Transitional cell carcinoma · Renal cell carcinoma · Occupational exposure · Aromatic amines · Combustion products

Occupational exposure is a well-known cause of human malignancies. In the field of urology, one of the first descriptions of an occupationally related malignancy was presented by Sir Percival Pott [79]. He published observations on increased risk of squamous cell carcinoma of the scrotum in British chimneysweepers. Within the last decades, interesting observations on the relation of occupational exposure and urological malignancies have been made, especially regarding the urinary bladder and the kidneys. The present review highlights important occupational exposures, especially under aspects of improved safety measures.

K. Golka (✉) · A. Wiese · H. M. Bolt
Institute for Occupational Physiology at the University of Dortmund (IfADo), Ardeystr. 67, 44139 Dortmund, Germany
E-mail: golka@ifado.de
Tel.: +49-231-1084344
Fax: +49-231-1084308

G. Assennato
Dipartimento di Medicina Interna e Medicina Pubblica, Facolta di Medicina e Chirurgia, Universita di Bari, Policlinico, Italy

Bladder cancer

β-Naphthylamine and the rubber industry

In 1938, Hueper succeeded in inducing tumours of the urinary bladder in dogs by dosing β-naphthylamine (2-naphthylamine) [54]. As a result of this observation, β-naphthylamine has been banned in many countries. At that time, β-naphthylamine had been used as an antioxidant in the rubber industry on a large scale. With the introduction of these regulations, the health of workers in the rubber industries regarding professional diseases of the urinary bladder clearly improved, as shown by a number of authors investigating bladder cancer rates in rubber workers [23]. The extraordinary carcinogenic potential of β-naphthylamine in humans has been confirmed by Case et al. [22], reporting on a 200-fold elevated bladder cancer risk for British workers exposed to β-naphthylamine at that time.

Even nowadays, occupational bladder cancer in (former) rubber workers is still an issue. In 1993, Bolm-Audorff et al. reported on elevated bladder cancer risks, adjusted for smoking, for the profession of "rubber manufacturing and curing" with an odds ratio (OR) of 5.1 (95% CI 0.6–43.6) [13]. The results of this small study were subsequently confirmed by the largest study ever performed in the rubber industry [103]. In this cohort study on more than 11,000 workers in the rubber industry, elevated standardised mortality ratios (SMR) for bladder cancer were observed for "storage and shipment" (SMR 253; 95% CI 93–551) and for "general work" in this industry (SMR 159; 95% CI 92–279).

At the same time, the results of this study were also confirmed by a study in workers from a factory manufacturing chemicals for the rubber industry [96]. The standardised mortality ratio of workers exposed before 1955 was higher (SMR 560; 95% CI 225–1,154) than in the entire cohort (SMR 277; 95% CI 127–526). The authors suggested that this could be most easily explained by earlier exposures to phenyl-β-naphthylamine. It should be noted that β-naphthylamine had been gradually replaced by its derivative phenyl-β-naphthylamine, which was not considered to be carcinogenic. Later, it was recognised that phenyl-β-naphthylamine was partly metabolised to β-naphthylamine, demonstrating that also this substitute could present severe health effects [31]. Other substances used in the rubber industry might also contribute to an increased bladder cancer risk. For instance, different nitrosamines, which are highly carcinogenic in animal experiments, have been detected at typical work places in the rubber industry.

4-Aminobiphenyl

Another carcinogenic aromatic amine which also had been used in the rubber industry in the past was 4-aminobiphenyl. Melick et al. [67] had observed 19 cases in 171 workers in a 4-aminobiphenyl producing facility. It is notable that five of the 19 cases reported had occurred in subjects exposed only for less than 2 years. 4-Aminobiphenyl is now important as a carcinogenic component of tobacco smoke [97].

Benzidine and dye production

Toxicologically, benzidine has been the most important carcinogenic aromatic amine directed towards the human bladder. In contrast to β-naphthylamine, this aromatic amine has been produced on a very large scale. It has been used primarily in dye production and, to a much lesser extent, as a hardener in the rubber industry. In Europe, one of the most important industrial facilities has been in Leverkusen, Germany. As of 1991, 92 of 331 workers ever exposed to benzidine production at this facility before 1967 had eventually suffered from bladder cancer [62]; see also [42]. The medical experience in these cases has been of considerable importance for matters of compensation for the diseased workers [41, 58].

The production of benzidine in Leverkusen was discontinued in 1967, although benzidine was not officially banned in Germany until 1971. Historically, the production facility in Leverkusen was part of the large German chemical production trust, IG Farben, which had been dissected into different independent companies after World War II. Other main production sites were located in Frankfurt-Hoechst, Ludwigshafen and Wolfen.

Figures on bladder cancer cases related to benzidine production or its use have also been reported from the Peoples Republic of China. For instance, Bi et al. [8] reported on 30 bladder cancer cases among approximately 2,000 Chinese workers. This implied a 30-fold elevated bladder cancer risk due to occupation. Also, in another Chinese study [63, 111] the bladder cancer risk among a cohort of 784 benzidine-exposed workers was 35-fold increased and even increased up to 75-fold at work areas with exceptionally high exposures. The high carcinogenic potential of benzidine to the urinary bladder is also fundamental to elevations of bladder cancer risks in workers exposed to benzidine-based dyes and colourants with much lower exposures.

4-Chloro-o-toluidine and chlordimeform production

Another highly carcinogenic aromatic amine is 4-chloro-o-toluidine, which was used for the production of chlordimeform in Frankfurt-Hoechst. Stasik [98] was the first to publish an increased bladder cancer risk. In different subsequent studies [78, 99] the increases in bladder cancer risks were quantified to be between 38 and 90 fold.

Aromatic amines and bladder cancer in workers applying azo dyes or colourants

Different experimental [80, 82] and clinical [30] studies have revealed that inert azo dyes can be cleaved to their toxicologically relevant amino components, which had been used to synthesise the respective azo dye. The underlying principle of the reductive cleavage of an azo dye is shown in Fig. 1. It is very important to emphasise that only bioavailable, i.e. water-soluble, azo dyes are cleaved in this way in the living organism [14, 15]. Therefore, non-bioavailable, i.e. non-water soluble, azo colourants (i.e. pigments) do not contribute to bladder cancer risk even if they contain carcinogenic aromatic amines as components.[1] This issue, confirmed in many studies, is also most important for the compensation of occupational bladder cancer cases. Comprehensive information on the chemical structure of dyes is available from the Colour Index [95]. For practical use in the medical context, the relevant information on structures of potentially carcinogenic azo dyes has been extracted from these files in a much smaller paperback by Myslak [70].

[1] According to the current technical and industrial nomenclature a *dye* is used in a dissolved state and must therefore be soluble. *Pigments* are non-soluble and are used in suspensions. Both dyes and pigments comprise the technical entity of *colourants*.

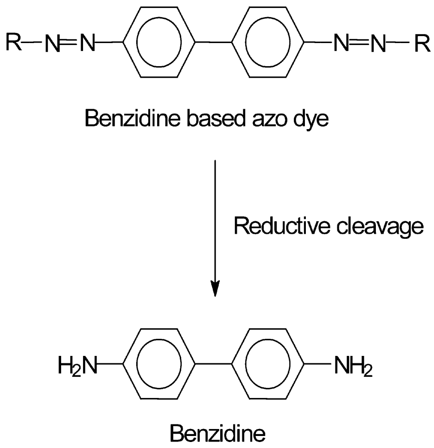

Fig. 1 Reductive biological cleavage of an azo dye

Dyers in textile and leather industries

Several professions in which azo dyes based on carcinogenic aromatic amines had been used have revealed increased bladder cancer risks in different studies. Among these, due to intensive dermal contact and inhalation exposure, have been dyers in the textile and leather industries [4, 37].

Painters and varnishers

Further professions with reports on an elevated risk for bladder cancer are painters and varnishers. Basic publications were those of Bethwaite et al. [7] based on the New Zealand cancer registry and of Myslak et al. [71] in the city of Dortmund (Table 1). Studies in other countries did not show such elevated bladder cancer risks for painters (see IARC, [55]). Nevertheless, the profession of a painter and varnisher was classified as an occupation associated with a considerable cancer risk [55]. Later, elevated smoking-adjusted risks of bladder cancer in German painters were confirmed by Golka et al. [44, 45] (Table 1). In a state-wide (state of Nordrhein-Westfalen, Germany) case-control study on after-care cancer patients approximately 10 years later, an elevated bladder cancer risk in painters and varnishers was again observed [40] (Table 1). These observations were supported by two other hospital-based case-control studies in Germany [13, 25] (Table 1).

The results of the German studies were later also confirmed by Steenland and Palu [100] investigating the mortality by bladder cancer in a cohort of more than 42,000 American painters, based on union records (SMR 1.23, 95% CI 1.05–1.43), compared with the US population. The standardised mortality ratio was as high as 1.77 (95% CI 1.13–2.77), when compared with a control of more than 14,000 organised non-painters. In a meta-analysis of 13 case-control studies, Chen and Seaton [24] found a standardised mortality ratio of painters in total, due to bladder cancer, of 1.3.

For painters and varnishers the bladder cancer risk is obviously dependent on the individual exposure, which is determined by a broad spectrum of working materials and techniques. This was different between countries. For example, painters who painted walls with materials based on titanium dioxide (white) or other mineral material pigments (coloured) do not present an increased bladder cancer risk. In contrast, painters who were regularly exposed in the 1940s and 1950s to dust of "aniline dyes" during preparation and application of the colourant mixtures, and who had frequently intensive dermal contact, presented an increased risk.

Due to the varying past exposure conditions between countries it is understandable that a number of studies did not show a significant bladder cancer risk for painters [55].

Table 1 Bladder cancer risk reported in German painters and varnishers

Authors	Study size cases/controls	Painters and varnishers cases/controls	OR	95% CI
Claude et al. [25]	531/531	0[1]–15[2]–12[3]	1.25*	0.59–2.67
		(3[1]–49[2]–17[3])[a]	(2.88*)	(1.70–4.88)
Myslak et al. [71]	403/426	21/8	2.76*	1.21–6.28
	21/76.298[4]	21/76.298	2.7*	1.8–4.1
	21/68.055[5]	21/68.055	2.8*	1.9–4.2
	21/2.759[6]	21/2.759	3.5*	2.4–5.2
Bolm-Audorff et al. [13]	219/219	10/5	1.56	0.51–4.78
		(6/2)[b]	(2.34)	(0.46–11.83)
Golka et al. [44]	412/414	20/8	2.4	1.05–5.57
Golka [40]	156/336	7/7	1.98	0.64–6.11

*not adjusted for smoking
[a]spray painting,
[b]house painters (included in painters and varnishers!)
[1]concordant pairs, ever exposed
[2]discordant pairs, only cases ever exposed
[3]discordant pairs, only controls ever exposed
[4]controls: census data 1956 in the state of Nordrhein-Westfalen for the occupation of a painter
[5]controls: census data 1976 in the state of Nordrhein-Westfalen for the occupation of a painter
[6]controls: census data 1976 in the city of Dortmund for the occupation of a painter

Hairdressers

The bladder cancer risk due to exposure to hair dyes is currently under discussion. A large population-based case-control study on incident bladder cases in Los Angeles [38] has recently claimed an elevated bladder cancer risk (OR 1.9; 95% CI 1.1–3.3) for subjects to which permanent hair dyes had been applied at least once a month, for 1 year or longer, compared with non-users. The risk increased to 3.3 (95% CI 1.3–8.4) for those to which permanent hair dyes had been applied at least once a month for 15 years or more. Hairdressers who had performed their jobs for more than 10 years showed a 5-fold increased risk (95% CI 1.3–19.2) compared with those who did not use hair dyes. This is in line with the view of Tola [104] who classically had postulated an increased bladder cancer risk for hairdressers.

The results of Gago-Dominguez et al. [38] were corroborated by the same authors [39] showing an over-representation of slow NAT2 acetylators among diseased female users. This genetic trait is a well-known additional risk factor for bladder cancer if exposure to aromatic amines has occurred [46, 108]. Bolm-Audorff et al. [13] reported an elevated smoking-adjusted odds ratio of 5.1 for hairdressers in a case-control study. In our own state-wide study on bladder cancer [40] the risk of bladder cancer also appeared elevated for hair dressers (OR, adjusted for smoking and age, 4.90; 95% CI 0.85–28.39). In 1993, IARC finally categorised the profession of hairdressers in group 2A ("limited evidence of carcinogenicity in humans") [56].

Other occupations with intensive contact to carcinogenic aromatic amines and/or azo dyes based on carcinogenic amines

Based on both the literature and our own medical experience with subjects claiming compensation of an occupational disease, it can clearly be stated that persons with intensive contact to aromatic amines or azo dyes, also in professions not explicitly listed above, may have an increased bladder cancer risk (for example, a teacher who had demonstrated the synthesis of benzidine-based azo dyes in chemistry school courses for years or a person who had weighed and sold powdery colourants without protective means (i.e. gloves and paper mask) for years).

High exposure to combustion products

For many years, combustion products have been suspected to cause bladder cancer. Exceptionally high industrial exposures to combustion products have occurred in coke oven workers and in workers in potrooms of the Söderberg electrolysis process in aluminium production plants. The exposure to combustion products in Söderberg potrooms has been extremely high, as 1,000 kg of a Söderberg electrode, which consists of 60% tar coke and 30% coal tar pitch, is used for the production of 500 kg aluminium. About 5–40% of the arising fumes may pass the potroom under former industrial conditions.

Benzo(a)pyrene concentrations from 500–116,000 ng/m^3 and 172–135,000 ng/m^3, respectively, at different working places in Söderberg electolysis facilities have been published [2, 3] (permissible value: 2,000 ng/m^3). The histories of our own cases observed in the Ruhr area of Germany displayed concentrations at this upper range, or even higher [16]. Several studies have shown elevated bladder cancer risks in this industry (for review, see Rönneberg and Langmark [85]) and are additionally supported by two recent studies of the aluminium industries: Romundstad et al. [84] reported a standardised incidence ratio (SIR) of 1.3 (95% CI 1.1–1.5) for all exposed and an SIR above 2 for higher exposed workers after a lag time of 30 years, and Moulin et al. [68] reported an elevated bladder cancer mortality in their whole cohort (seven cases; SMR 1.77; 95% CI 0.71–3.64).

Coke oven workers are also exposed to extremely high concentrations of combustion products. For instance, Manz [66] reported an elevated bladder cancer risk for coke oven workers in Hamburg based on death certificates. Bladder cancer was noticed as the cause of death on six death certificates of 134 coke oven workers, three death certificates of 108 pipeline network workers, two death certificates of 236 workmen and on only one death certificate of 205 office workers. Doll et al. [32] reported an elevated bladder cancer mortality for coke oven workers in a prospective study, that was significantly higher than the national rate ($p = 0.003$). For the time period of 1961–1965, the death incidence rate from bladder cancer was described as 2.5 times higher than the national incidence.

Intermediate types of exposure to combustion products such as tar pitch or similar products

Numerous studies have been performed on different workplaces with exposures to tar and/or tar products. These workplaces are characterised by much lower concentrations of combustion products than those occurring at coke ovens and in potrooms of the Söderberg electrolysis process. Nevertheless, elevated bladder cancer risks were reported.

Hammond et al. [51] reported an elevated bladder cancer mortality for those having worked as roofers in the USA for more than 20 years (O/E 13/7.72, ratio 1.68), probably due to considerable exposure to the tar products used for flat roofs. This is in line with a more recent study [102] on the mortality of more than 11,000 roofers and waterproofers (PMR 138; 95% CI 111–170). Tar and related materials contain polycyclic aromatic hydrocarbons (PAH) and at least certain tar-related products also contain small amounts of carcinogenic aromatic amines [48].

The release of carcinogenic compounds causing bladder cancer seems to be dependent both on the temperature of the tar products used and on the duration of exposure. Thus, an increased bladder cancer risk in road construction workers has been controversially discussed. Risch et al. [81] reported an odds ratio of 3.11 ($p = 0.019$) for those occupationally exposed to tars or asphalt. For road construction it must be considered that the use of carcinogenic substances has definitely decreased over the years. Due to regulatory measures, even processes of recycling of old asphalt surfaces have to be controlled for PAH release to prevent using contaminated asphalt for building new roads. The change from tar to bitumen, the latter considered to be less problematic with regard to the workers' health, took many years and varied between different countries. In Germany, tar-bitumen mixtures were commonly used until the middle of the 1960s. Nevertheless, even at the end of the 1970s, tar-bitumen mixtures could be observed in Germany [59, 60]. Regarding the carcinogenicity of tar and related materials to the human bladder, a study performed in the largest European tar processing chemical facility in Castrop-Rauxel is of particular interest [61]. In a total cohort of 568 male workers with tar-related skin changes, 13 cases of bladder cancer and seven cases of papilloma of the bladder (according to the former classification of papilloma of the bladder) had been noted.

Low exposure to combustion products

Professional drivers, mechanics, and other professions are exposed to elevated levels of emissions from combustion engines. Some authors found rather small bladder cancer risks for subjects exposed to exhausts of combustion engines [6, 25, 88, 93, 94]. By contrast, others did not find elevated risks [27, 28, 101, 107]. Olsen and Jensen [77] observed an elevated risk only after exposures for more than 20 years.

In total, it appears doubtful that exposures to combustion exhausts are nowadays a significant risk of human bladder cancer.

Chlorinated hydrocarbons

Three large studies on bladder cancer in US dry cleaners have revealed elevated risk. Blair et al. [11] reported a 1.7-fold increased bladder cancer mortality in more than 5,300 members of the union of the dry cleaners. Katz and Jowett [57] observed a 1.9-fold mortality in 671 passed-away dry cleaners, and Brown and Kaplan [18] observed a 3.0-fold mortality for bladder cancer in 1,690 dry cleaners exposed to the dry-cleaning solvent perchloroethylene (tetrachloroethylene) for at least 1 year. This is in line with a population-based case-control study by Silverman et al. [93] on 300 white male bladder cancer cases, the results of which showed a 2.4-fold increased relative bladder cancer risk for dry cleaners and for laundry service personal.

In a very recent review on the carcinogenicity of perchloroethylene it has been noticed that both cohort studies and case-control studies pointed to an excess of bladder cancer in the study populations, which mostly included laundry and dry cleaning workers [69].

Axelson et al. [5] did not observe an elevated standardised morbidity ratio of bladder cancer in a large study in Sweden comprising more than 1,400 male and more than 200 female subjects exposed only for short periods and/or to low concentrations of the solvent trichloroethylene (which differs from perchloroethylene by one chlorine atom).

Coal miners

Several case-control studies have reported an elevated bladder cancer risk in coal miners treated in hospitals of New York City [110], in the Belgian Charleroi and Liège areas [87], the adjacent French mining area [28] and in the Ruhr area [44] (Table 2).

The results of these studies are in line with a large multicentre study in Germany [47] (smoking-adjusted OR for bladder cancer in miners: 8.8). The pathomechanism of the bladder cancer risks for hard coal miners is still unknown. A study on enzyme polymorphisms made a hidden source of aromatic amines unlikely, based on an inconspicuous percentage of the slow acetylation state, but pointed to substrates of the GSTM1 to be involved, e.g. to polymorphic aromatic hydrocarbons [43].

Miscellaneous

Some additional exposures/occupations have been considered to be related with an increased risk of occupational bladder cancer. Thus, several studies

Table 2 Bladder cancer risk in European and North American coal miners

Author	Study size cases/controls	Coal miners cases/controls	OR	95% CI
Wynder et al. [110]	300/300	7/1	7.14*	0.87–58.42
Schifflers et al. [87]	74/203	13/22	1.87	0.87–4.02
Cordier et al. [28]	658/658	36/14	2.4	1.25–4.67
Golka et al. [40]	412/414	88/37	2.5	1.64–3.93

*not adjusted for smoking

including one on 632 Danish foundry workers (O/E 6/0.67) [52], a further study on 6,144 Danish foundry workers (O/E 63/50.93) [92] and a French study on 658 cases and 658 controls (21 cases, 13 controls) [26] claimed elevated bladder cancer risks in foundry workers.

Workers exposed to the explosive dinitrotoluene have also been reported to have an elevated risk, although the data base is quite limited [20, 83].

Gustavsson et al. [50] reported a risk (SIR) of more than 2 for bladder cancer (23 observed vs. 9.8 expected cases) based on a cancer incidence study on 5,266 Swedish chimneysweepers employed between 1918 and 1980, which was confirmed later in a follow-up (SIR 2.47; 95% CI 1.31–4.22) [36]. Two studies have claimed relevant bladder cancer risks for retired firefighters who had started their careers at least 40 years before [49, 106].

Bladder cancer risks in subjects from oil and related industries have been investigated in different studies (review: Delzell et al. [29]). Until now, the results of the studies have been inconclusive.

Renal cell carcinoma

Trichloroethylene

A most relevant occupational carcinogen regarding the kidneys is the organic solvent trichloroethylene. This has been shown to cause kidney cancer in laboratory animals, with [72] and without [65, 75, 76] the mutagenic stabilisers epichlorhydrin and epoxybutane, which had been used in the past. Chlorothioketene is believed to be the ultimately carcinogenic metabolite, arising from trichloroethylene locally in the kidney [19, 53]. In 1995, a cohort study showed for the first time an elevated renal cell cancer risk (SIR 7.97; 95% CI 2.59–8.59) in workers highly exposed in a cardboard factory [53], who showed frequent symptoms of repetitive acute trichloroethylene intoxications like unconsciousness or prenarcotic symptoms such as drunkenness or vertigo. Two subsequent case-control studies [21, 105] confirmed this observation. Recommendations for matters of compensation of the diseased workers from the urologist's point of view have been published by Schöps et al. [89].

In contrast, no elevated risks due to trichloroethylene were observed in renal cell cancer cases in Sweden [5]. These had been exposed only to low levels of trichloroethylene which had been controlled by periodical biomonitoring of the main metabolite trichloroacetic acid, indicating that 81% of the cases were exposed to concentrations only ≤ 20 ppm (below current Occupational Exposure Limits). Typical carcinogenic trichloroethylene exposures had been greasing and degreasing of metal, especially cleaning of hot devices or using hot trichloroethylene [19].

Perchloroethylene

Perchloroethylene (tetrachloroethylene) has caused elevated rates of kidney carcinomas in rats [74]. In different studies in highly exposed dry cleaners in the USA an elevated risk has also been claimed. Blair et al. [10] reported a PMR of 200 ($\chi^2 = 0.215$) based on death certificates of 279 former dry cleaners issued from 1957 to 1970. In a follow-up, Blair et al. [11] observed a PMR of 1.7 (equivalent to a PMR of 170 of the former study). In a recently published follow-up study [12] bladder cancer mortality was not significantly elevated in white persons. These findings correspond to studies on the mortality among dry cleaners by Duh and Nabih [33] (SMOR 3.8; 95% CI 1.9–7.6), Brown and Kaplan [18] (SMR 200; 95% CI 55–517), and Katz and Jowett [57] (PMR 257, $p < 0.05$). In a very recently published review it was noticed that due to limitations and inconsistencies in the published literature, it is not possible to draw a definite conclusion regarding the relationship between perchloroethylene and renal cell (or kidney) cancer [69].

Asbestos

A large prospective study on more than 12,000 asbestos-exposed insulators in the USA and in Canada was closed in 1976 [91]; it demonstrated an elevated mortality for tumours located in the kidneys (no further histopathologic diagnosis given) of 2.29 or 2.14 (best available information or death certificate, respectively). It should be noted that exposure conditions at these earlier times were not comparable to exposure conditions later.

Enterline et al. [35] investigated more than 1,000 white Americans with professional asbestos exposure having retired between 1941 and 1967. Standardised mortality ratio (SMR) of kidney cancer was 2.58 ($p < 0.05$). In a case-control study in New South Wales, Australia, comprising 489 renal cell carcinoma cases and 523 controls [64], age and sex-adjusted odds ratio for formerly asbestos-exposed cases was 1.58 (95% CI 1.02–2.44). In contrast, in a large mortality study on 4,000 employees with exposure to asbestos in Germany, no increased number of deaths due to renal cell carcinoma could be observed among 609 males and 64 females who had passed away [86]. Due to such differences of results, the risk of renal cell cancer, with regard to exposure to asbestos, is presently not clear and still under discussion.

Miscellaneous

In a group of 500 underground copper miners in the former German Democratic Republic, 14 renal cell carcinoma cases were observed to be connected with high exposures to the explosive dinitrotoluene [20]. Several studies performed on workers exposed to crude oil and its products revealed conflicting results (review: Delzell et al. [29]).

Prostate cancer

Some older studies have claimed an elevated risk for prostate cancer with exposure to cadmium, whereas others have not (review: Elinder et al. [34]).

Blair and Zahm [9] found a limited increased risk for people having worked in agriculture. This finding is in line with the results of a very large prospective cohort study on pesticide applicators that revealed a prostate cancer standardised incidence ratio of 1.14 (95% CI 1.05–1.24), which was higher in several subgroups, especially among exposed subjects with a family history of prostate cancer [1].

The great majority of studies, however, did not find clear associations between occupational factors and prostate cancer. In general, the prostate cancer risk due to occupational exposure factors appears negligible.

Testicular cancer

No relevant studies on occupationally related testicular cancer have been published.

Discussion

Bladder cancer is by far the most important occupationally caused malignancy among urological patients. In Germany, although the industrial production of the two most important carcinogenic aromatic amines, β-naphthylamine and benzidine, was terminated in 1949 and 1967, respectively, bladder cancer due to aromatic amines is still an issue. This is in part due to the very long latency time of bladder cancer, which is often longer than 20 years [73]. This is important because bladder cancer due to smoking shows decreasing risks if the person has stopped smoking [17], although cigarette smoke contains small amounts of carcinogenic aromatic amines like 4-aminobiphenyl, β-naphthylamine and o-anisidine [97].

Interestingly, an increased bladder cancer risk due to aromatic amines is also seen when the occupational exposure ended decades ago. The differential mechanisms underlying bladder cancer, either after smoking or after occupational exposure to aromatic amines, remain unclear. It seems likely that in cigarette smoke, carcinogens other than aromatic amines such as polycyclic aromatic hydrocarbons are also involved.

Besides, interactions between occupational bladder carcinogens and smoking might become more important. Thus, even exposures to low levels of carcinogens could contribute substantially to transitional cell carcinoma risk.

For questions of compensation, it seems relevant that odds ratios for bladder cancer adjusted for smoking are mostly not distinctly different from non-adjusted odds ratios, suggesting that former occupational exposures would remain important, also if a person has smoked.

For the urologists, it is important that, when taking the patient's history, all professions ever performed for 6 months or longer should be asked for, at least in all patients with transitional cell carcinoma. In general, it is easy to identify an occupational cancer case if the urologist is familiar with the occupations and/or exposures at risk. A challenge remains to identify elevated cancer risks connected with unusual exposures.

Recently, low levels of aromatic amines and/or metabolites thereof have been reported in urine samples from non-exposed general populations [90, 109]. Origin and possible health impact of these background levels remain unclear.

It should be noted that, compared with other malignancies, the urological malignancies covered in this review have favourable prognoses. Thus, studies based on mortality clearly underestimate occupational risks, compared with studies on cancer incidence rates or hospital-based studies.

In the first decades of the last century, macrohematuria due to exposure to toxic chemicals at the workplace was a common clinical picture for occupational physicians and urologists close to certain chemical production sites. Due to decrease of exposure, this has disappeared, while elevated bladder cancer risks are still a relevant issue.

References

1. Alavanja MC, Samanic C, Dosemeci M, Lubin J, Tarone R, Lynch CF et al (2003) Use of agricultural pesticides and prostate cancer risk in the Agricultural Health Study cohort. Am J Epidemiol 157:800–814
2. Anonymous (1979) Benzo(a)pyren am Arbeitsplatz. Staubforschungsinstitut und Institut für Lärmbekämpfung des Hauptverbandes der gewerblichen Berufsgenossenschaften eV, Bonn (STF/IFL Information Nr 8/79)
3. Anonymous (1983) Polyzyklische aromatische Kohlenwasserstoffe (PAH) am Arbeitsplatz. Berufsgenossenschaftliches Institut für Arbeitssicherheit, St Augustin (BIA-Report 3/83)
4. Anthony HM (1974) Industrial exposure in patients with carcinoma of the bladder. J Soc Occup Med 24:110–116
5. Axelson O, Seldén A, Andersson K, Hogstedt C (1994) Updated and expanded Swedish cohort study on trichloroethylene and cancer risk. J Occup Med 36:556–562
6. Baxter PJ, McDowall ME (1986) Occupation and cancer in London: an investigation into nasal and bladder cancer using the Cancer Atlas. Br J Ind Med 43:44–49
7. Bethwaite P, Pearce N, Fraser J (1990) Cancer risks in painters: study based on the New Zealand Cancer Registry. Br J Ind Med 47:742–746
8. Bi W, Hayes RB, Feng P, Qi Y, You X, Zhen J, et al (1992) Mortality and incidence of bladder cancer in benzidine-exposed workers in China. Am J Ind Med 21:481–489
9. Blair A, Zahm SH (1991) Cancer among farmers. Occup Med State of the Art Reviews 6:335–354
10. Blair A, Decoufle P, Grauman D (1979) Causes of death among laundry and dry cleaning workers. Am J Public Health 69:508–511
11. Blair A, Stewart PA, Tolbert PE, Grauman D, Moran FX, Vaught J, et al (1990) Cancer and other causes of death among a cohort of dry cleaners. Br J Ind Med 47:162–168
12. Blair A, Petralia SA, Stewart PA (2003) Extended mortality follow-up of a cohort of dry cleaners. Ann Epidemiol 13:50–56

13. Bolm-Audorff U, Jöckel KH, Kilguss B, Pohlabeln H, Siepenkothen T (1993) Bösartige Tumoren der ableitenden Harnwege und Risiken am Arbeitsplatz. Wirtschaftsverlag NW, Bremerhaven (Schriftenreihe der Bundesanstalt für Arbeitsschutz, Dortmund, Forschung; Fb 697)
14. Bolt HM (1995) Special points in the toxicity assessment of colourants (dyes and pigments) In: Thomas H, Hess R, Waechter F (eds) Toxicology of industrial compounds. Taylor & Francis, London, pp 303–310
15. Bolt HM, Golka K (1993a) Zur früheren Exposition von Malern gegenüber Azofarbmitteln. Arbeitsmed Sozialmed Umweltmed 28:417–421
16. Bolt HM, Golka K (1993b) Cases of lung cancer and tar-related skin changes in an aluminium reduction plant. Med Lav 84:178–181
17. Brennan P, Bogillot O, Cordier S, Greiser E, Schill W, Vineis P, et al (2000) Cigarette smoking and bladder cancer in men: a pooled analysis of 11 case-control studies. Int J Cancer 86:289–294
18. Brown DP, Kaplan SD (1987) Retrospective cohort mortality study of dry cleaner workers using perchloroethylene. J Occup Med 29:535–541
19. Brüning T, Bolt HM (2000) Renal toxicity and carcinogenicity of trichloroethylene: key results, mechanisms, and controversies. Crit Rev Toxicol 2000 30:253–285
20. Brüning T, Chronz C, Thier R, Havelka J, Ko Y, Bolt HM (1999) Occurrence of urinary tract tumors in miners highly exposed to dinitrotoluene. J Occup Environ Med 41:144–149
21. Brüning T, Pesch B, Wiesenhütter B, Rabstein S, Lammert M, Baumüller A, et al (2003) Renal cell cancer risk and occupational exposure to trichloroethylene: results of a consecutive case-control study in Arnsberg, Germany. Am J Ind Med. 43:274–285
22. Case RAM, Hosker ME (1954) Tumours of the urinary bladder as an occupational disease in the rubber industry in England and Wales. Br J Prev Soc Med 8:39–50
23. Checkoway H, Smith A, McMichael A, Jones F, Monson R, Tyroler H (1981) A case-control study of bladder cancer in the United States rubber and tyre industry. Br J Ind Med 38:240–246
24. Chen R, Seaton A (1998) A meta-analysis of painting exposure and cancer mortality. Cancer Detect Prev 22:533–539
25. Claude J, Kunze E, Frentzel-Beyme R (1988) Occupation and risk of cancer of the lower urinary tract among men: a case-control study. Int J Cancer 41:271–279
26. Clavel J, Mandereau L, Limasset JC, Hemond D, Cordier S (1994) Occupational exposure to polycyclic aromatic hydrocarbons and the risk of bladder cancer: a French case-control study. Int J Epidemiol 23:1145–1153
27. Coggon D, Pannett B, Acheson ED (1984) Use of job-exposure matrix in an occupational analysis of lung and bladder cancers on the basis of death certificates. J Natl Cancer Inst 72:61–65
28. Cordier S, Clavel J, Limasset JC, Boccon-Gibod L, Le Moual L, Mandereau L, et al (1993) Occupational risks of bladder cancer in France: a multicentre case-control study. Int J Epidemiol 22:403–411
29. Delzell E, Austin H, Cole P (1988) Epidemiologic studies of the petroleum industry. Occup Med State of the Art Reviews 3:455–474
30. Dewan A, Jani JP, Patel JS, Gandhi DN, Variya MR, Ghodasara NB (1988) Benzidine and its acetylated metabolites in the urine of workers exposed to Direkt Black 38. Arch Environ Health 43:269–272
31. DFG (1977) Phenyl-2-naphthylamin. In: Gesundheitschädliche Arbeitsstoffe. Toxikologisch-Arbeitsmedizinische Begründungen von MAK-Werten. Senatskommission zur Prüfung gesundheitschädlicher Arbeitstoffe. Greim H (Hrsg). Wiley-VCH, Weinheim
32. Doll R, Vessey MP, Beasley RWR, Buckley AR, Fear EC, Fisher REW, et al (1972) Mortality of gasworkers—final report of a prospective study. Br J Ind Med 29:394–406
33. Duh RW, Nabih RA (1984) Mortality among laundry and dry cleaning workers in Oklahoma. Am J Publ Health 74:1278–1280
34. Elinder CG, Kjellstrom T, Hogstedt C, Andersson K, Spang G (1985) Cancer mortality of cadmium workers. Br J Ind Med 42:651–655
35. Enterline PE, Hartley J, Henderson V (1987) Asbestos and cancer: a cohort followed up to death. Br J Ind Med 44:396–401
36. Evanoff BA, Gustavsson P, Hogstedt C (1993) Mortality and incidence of cancer in a cohort of Swedish chimney sweeps: an extended follow up study. Br J Ind Med 50:450–459
37. Frumin E, Velez H, Bingham E, Gillen M, Brathwaite M, LaBarck R (1990) Occupational bladder cancer in textile dyeing and printing workers: six cases and their significance for screening programs. J Occup Med 32:887–890
38. Gago-Dominguez M, Castelao JE, Yuan JM, Yu MC, Ross RK (2001) Use of permanent hair dyes and bladder-cancer risk. Int J Cancer 91:575–579
39. Gago-Dominguez M, Bell DA, Watson MA, Yuan JM, Castelao JE, Hein DW, et al (2003) Permanent hair dyes and bladder cancer: risk modification by cytochrome P450 1A2 and N-acetyltransferases 1 and 2. Carcinogenesis 24:483–489
40. Golka K (1999) Untersuchungen zur beruflichen Exposition bei Patienten mit Harnblasenkarzinom. Habilitationsschrift zur Erlangung der Venia legendi für das Fach "Arbeitsmedizin". Medizinische Fakultät der Ruhr-Universität Bochum
41. Golka K, Schöps W, Kierfeld G, Bolt HM (1994) Urothelial diseases as an occupational disease. Versicherungsmedizin 46:158–161 (in German)
42. Golka K, Prior V, Blaszkewicz M, Cascorbi I, Schöps W, Kierfeld G, et al (1996) Occupational history aspects and genetic N-acetyltransferase (NAT2) polymorphism in urothelial cancer patients in Leverkusen, Germany. Scand J Work Environ Health 22:332–338
43. Golka K, Reckwitz T, Kempkes M, Cascorbi I, Blaszkewicz M, Reich SE, et al (1997) N-Acetyltransferase 2 (NAT2) and glutathione S-transferase μ (GSTM1) in bladder cancer patients in a highly industrialized area. Int J Occup Environ Health 3:105–110
44. Golka K, Bandel T, Schlaefke S, Reich SE, Reckwitz T, Urfer W, et al (1998) Urothelial cancer of the bladder in an area of former coal, iron, and steel industries in Germany: a case-control study. Int J Occup Environ Health 4:79–84
45. Golka K, Bandel T, Reckwitz T, Urfer W, Bolt HM, Bremicker KD, et al (1999) Occupational risk factors for bladder carcinoma. A case control study. Urologe [A] 38:358–363 (in German)
46. Golka K, Prior V, Blaszkewicz M, Bolt HM (2002) The enhanced bladder cancer susceptibility of NAT2 slow acetylators towards aromatic amines: a review considering ethnic differences. Toxicol Lett 128:229–241
47. Greiser E, Mohlzahn M (1997) Multizentrische Nieren- und Urothel-Carcinom-Studie Wirtschaftsverl NW, Bremerhaven (Schriftenreihe der Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Dortmund/Berlin, Forschung; Fb 780)
48. Grimmer G, Naujack KW, Dettbarn G (1987) Beitrag zur Ursachenforschung exogen bedingter Blasencarcinome. Profilanalyse aromatischer Amine am Arbeitsplatz. Schriftenreihe der Bundesanstalt für Arbeitsschutz, Wirtschaftverlag NW, Bremerhaven (Schriftenreihe der Bundesanstalt für Arbeitsschutz, Dortmund, Forschung; Fb 511)
49. Guidotti TL (1993) Mortality of urban firefighters in Alberta, 1927–1987. Am J Ind Med 23:921–940
50. Gustavsson P, Gustavsson A, Hogstedt C (1988) Excess of cancer in Swedish chimney sweeps. Br J Ind Med 45:777–781
51. Hammond EC, Selikoff IJ, Lawther PL, Seidman H (1976) Inhalation of benzpyrene and cancer in man. Ann N Y Acad Sci 271:116–124
52. Hansen ES (1991) Cancer mortality among Danish molders. Am J Ind Med 20:401–409

53. Henschler D, Vamvakas S, Lammert M, Dekant W, Kraus B, Thomas MB, et al (1995) Increased incidence of renal cell tumors in a cohort of cardboard workers exposed to trichloroethene. Arch Toxicol 69:291–299
54. Hueper WC, Wiley FH, Wolfe HD (1938) Experimental production of bladder tumors in dogs by administration of beta-naphthylamine. Ind Hyg Toxicol 20:46–84
55. IARC International Agency for Research on Cancer (1989) IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans: Some organic solvents, resin monomers and related compounds, pigments, and occupational exposures in paint manufacture and painting. World Health Organization, Lyon (IARC monographs on the evaluation of carcinogenic risks to humans, vol. 47)
56. IARC International Agency for Research on Cancer (1993) IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans: Occupational exposures of hairdressers and barbers and personal use of hair colourants, some hair dyes, cosmetic colourants, industrial dyestuffs and aromatic amines. World Health Organization, Lyon (IARC monographs on the evaluation of carcinogenic risks to humans, vol. 57)
57. Katz RM, Jowett D (1981) Female laundry and dry cleaning workers in Wisconsin: a mortality analysis. Am J Public Health 71:305–307
58. Kierfeld G, Schöps W (1994) MdE und "Heilungsbewährung", insbesondere bei Krebserkrankungen—in der Begutachtung für die gesetzliche Unfallversicherung. Med Sach 90:43–46
59. Knecht U, Woitowitz HJ (1989) Risk of cancer from the use of tar bitumen in road works. Br J Ind Med 46:24–30
60. Knecht U, Woitowitz HJ (1990) Krebsgefährdung bei Verwendung von Pechbitumen im Straßenbau (PT-AT). Wirtschaftsverlag NW, Bremerhaven (Schriftenreihe der Bundesanstalt für Arbeitsschutz, Dortmund, Forschung; Fb 612)
61. Letzel S, Letzel H, Blümner E, Hendrichs A, Sommerburg C (1992) Haut-, Bronchial-, Kehlkopf-, und Harnwegskarzinommorbidität bei Patienten mit berufsbedingter Teerhaut. Schriftenreihe des Hauptverbandes der gewerblichen Berufsgenossenschaften, Sankt Augustin
62. Lewalter J, Miksche LW (1992) Empfehlungen zur arbeitsmedizinischen Prävention expositions- und dispositionsbedingter Arbeitsstoff-Beanspruchungen. Verh Dt Ges Arbeitsmed 31:135–139
63. Ma QW, Lin GF, Qin YQ, Lu DR, Golka K, Geller F, et al (2003) *GSTP1* $A^{1578}G$ ($Ile^{105}Val$) polymorphism in benzidine-exposed workers: an association with cytological grading of exfoliated urothelial cells. Pharmacogenetics 13:409–415
64. MacCredie M, Stewart JH (1993) Risk factors for kidney cancer in New South Wales. IV. Occupation. Br J Ind Med 50:349–354
65. Maltoni C, Lefemine G, Cotti G, Perino G (1988) Long-term carcinogenicity bioassays on trichloroethylene administered by inhalation to Sprague-Dawley rats and Swiss and $B6C3F_1$ mice. Ann N Y Acad Sci 53:316–342
66. Manz A (1976) Harnwegskarzinome bei Beschäftigten der Gasindustrie. Münch Med Wschr 118:65–68
67. Melick WF, Escue HM, Naryka JJ, Mezera RA, Wheeler EP (1955) The first reported cases of human bladder tumors due to a new carcinogen—Xenylamine. J Urol 74:760–766
68. Moulin JJ, Clavel T, Buclez B, Laffitte-Rigaud G (2000) A mortality study among workers in a French aluminium reduction plant. Int Arch Occup Environ Health 73:323–330
69. Mundt KA, Birk T, Burch MT (2003) Critical review of the epidemiological literature on occupational exposure to perchloroethylene and cancer. Int Arch Occup Environ Health 76:473–491
70. Myslak ZW (1990) Azofarbmittel auf der Basis krebserzeugender und -verdächtiger aromatischer Amine Identifikation, Verwendungsbereiche, Herstellungszeiträume Wirtschaftsverlag NW, Bremerhaven (Schriftenreihe der Bundesanstalt für Arbeitsschutz, Dortmund, Gefährliche Arbeitsstoffe—GA 35)
71. Myslak ZW, Bolt HM, Brockmann W (1991) Tumors of the urinary bladder in painters: a case-control study. Am J Ind Med 19:705–713
72. NCI Carcinogenesis bioassay of trichloroethylene (1976) CAS No 79-01-6 National Cancer Institute Technical Report Series No 2, Feb 1976 US Dept Health Education, and Welfare, Washington, DC. http://ntp-server.niehs.nih.gov/htdocs/LT_rtps/tr002.pdf
73. Norpoth K, Woitowitz HJ (1991) Beruflich verursachte Tumoren. Grundlagen der Entscheidung zur BK-Verdachtsanzeige. Deutscher Ärzteverlag, Köln, pp 25–31
74. NTP Technical report on the toxicology and carcinogenesis studies on tetrachloroethylene (perchloroethylene) (CAS No. 127-18-4) in F344/N rats and $B6C3F_1$ mice (inhalation studies) NTP TR 311 NIH Publication No. 86-2567 (1986) U.S. Department of Health and Human Services. http://ntp-server.niehs.nih.gov/htdocs/LT_rtps/tr311.pdf
75. NTP Technical report on the toxicology and carcinogenesis studies of trichloroethylene (CAS No. 79-01-6) in four strains of rats (gavage studies) NTP TR 273 NIH Publication No. 88-2529 (1988) U.S. Department of Health and Human Services. http://ntp-server.niehs.nih.gov/htdocs/LT_rtps/tr273.pdf
76. NTP Technical report on the carcinogenesis studies of trichloroethylene (without epichlorohydrin) (CAS No. 79-01-6) in F344/N rats and $B6C3F_1$ mice (gavage studies) NTP TR 243 NIH Publication No. 90-1779 (1990) U.S. Department of Health and Human Services. http://ntp-server.niehs.nih.gov/htdocs/LT_rtps/tr243.pdf
77. Olsen JH, Jensen OM (1987) Occupation and risk of cancer in Denmark. An analysis of 93810 cancer cases, 1970–1979. Scand J Work Environ Health 13[Suppl 1]: 1–91
78. Popp W, Schmieding W, Speck M, Vahrenholz C, Norpoth K (1992) Incidence of bladder cancer in a cohort of workers exposed to 4-chloro-o-toluidine while synthesising chlordimeform. Br J Ind Med 49:529–531
79. Pott P (1775) Chirurgical observations relative to the cataract, the polypus of the nose, the cancer of the scrotum, the different kind of ruptures and the mortification of the toes and feet. London
80. Rinde E, Troll W (1975) Metabolic reduction of benzidine azo dyes to benzidine in the Rhesus monkey. J Natl Cancer Inst 55:181–182
81. Risch HA, Burch JD, Miller AB, Hill GB, Steele R, Howe GR (1988) Occupational factors and the incidence of cancer of the bladder in Canada. Br J Ind Med 45:361–367
82. Robens JF, Dill GS, Ward JM, Joiner JR, Griesemer RA, Douglas JF (1980) Thirteen-week subchronic studies of Direct Blue 6, Direct Black 38 and Direct Brown 95 dyes. Toxicol Appl Pharmacol 54:431–442
83. Roemer HC, Golka K, Schulze H, Loehlein D (2002) Two extrapulmonary neoplasms in a uranium miner. J Roy Soc Med 95:302
84. Romundstad P, Andersen A, Haldorsen T (2000) Cancer incidence among workers in six Norwegian aluminum plants. Scand J Work Environ Health 26:461–469
85. Rönneberg A, Langmark F (1992) Epidemiologic evidence of cancer in aluminium reduction plant workers. Am J Ind Med 22:573–590
86. Rösler JA, Woitowitz HJ, Woitowitz RH, Rödelsperger K (1994) Tumorrisiken durch Asbest in Deutschland im internationalen Vergleich. Arbeitsmed Sozialmed Umweltmed 29:458–462
87. Schifflers E, Jamart J, Renard V (1987) Tobacco and occupation as risk factors in bladder cancer: a case-control study in southern Belgium. Int J Cancer 39:287–292
88. Schoenberg JB, Stemhagen A, Mogielnicki AP, Altman R, Abe T, Mason TJ (1984) Case-control study of bladder cancer in New Jersey. I. Occupational exposures in white males. J Natl Cancer Inst 72:973–981

89. Schöps W, Golka K, Bolt HM, Kierfeld G (1997) Das Nierenzellkarzinom als Berufserkrankung. Med Sach 93:146–148
90. Seidel A, Grimmer G, Dettbarn G, Jacob J (2001) Urinary excretion of carcinogenic aromatic amines by nonsmokers. Umweltmed Forsch Prax 6:213–220 (in German)
91. Selikoff IJ, Hammond EC, Seidman H (1979) Mortality experience of insulation workers in the United States and Canada, 1943–1976. Ann N Y Acad Sci 330:91–116
92. Sherson D, Svane O, Lyng E (1991) Cancer incidence among foundry workers in Denmark. Arch Environ Health 46:75–81
93. Silverman DT, Hoover RH, Albert S, Graff KM (1983) Occupation and cancer of the lower urinary tract in Detroit. J Natl Cancer Inst 70:237–245
94. Smith AH, Pearce NE, Callas PW (1988) Cancer case-control studies with other cancers as controls. Int J Epidemiol 17:298–306
95. Society of Dyers and Colourists and American Association of Textile Chemists and Colorists (2002) Colour Index, 4th electronical edition www.colour-index.org
96. Sorahan T, Hamilton L, Jackson JR (2000) A further cohort study of workers employed at a factory manufacturing chemicals for the rubber industry, with special reference to the chemicals 2-mercaptobenzothiazole (MBT), aniline, phenyl-beta-naphthylamine and o-toluidine. Occup Environ Med 57:106–115
97. Stabbert R, Schafer KH, Biefel C, Rustemeier K (2003) Analysis of aromatic amines in cigarette smoke. Rapid Commun Mass Spectrom 17:2125–2132
98. Stasik MJ (1988) Carcinomas of the urinary bladder in a 4-chloro-o-toluidine cohort. Int Arch Occup Environ Health 60:21–24
99. Stasik MJ, Konietzko J, Godlewski A, Fortak W (2000) Current studies of 4-chloro-o-toluidine and chlordimeform carcinogenicity. 26th International Congress on Occupational Health, August 27–September 1, 2000, Singapore. Scientific Programme and Abstracts, p 311
100. Steenland K, Palu S (1999) Cohort mortality study of 57,000 painters and other union members: a 15 year update. Occup Environ Med 56:315–321
101. Steineck G, Plato N, Norell SE, Hogstedt C (1990) Urothelial cancer and some industry-related chemicals: An evaluation on the epidemiologic literature. Am J Ind Med 17:371–391
102. Stern FB, Ruder AM, Chen G (2000) Proportionate mortality among unionized roofers and waterproofers. Am J Ind Med 37:478–492
103. Straif K, Weiland SK, Werner B, Chambless L, Mundt KA, Keil U (1998) Workplace risk factors for cancer in the German rubber industry: Part 2 Mortality from non-respiratory cancers. Occup Environ Med 55:325–332
104. Tola S (1980) Occupational cancer of the urinary bladder. J Toxicol Environ Health 6:1253–1260
105. Vamvakas S, Brüning T, Thomasson B, Lammert M, Baumüller A, Bolt HM, et al (1998) Renal cell cancer correlated with occupational exposure to trichloroethene. J Cancer Res Clin Oncol 124:374–382
106. Vena JE, Fiedler RC (1987) Mortality of a municipal-worker cohort: IV fire fighters. Am J Ind Med 11:671–684
107. Vineis P, Magnani C (1985) Occupation and bladder cancer in males: a case-control study. Int J Cancer 35:599–606
108. Vineis P (2003) This issue
109. Weiss T, Ewers U, Flieger A, Angerer J (2000) Innere Belastung der Allgemeinbevölkerung mit Amino- und Nitroaromatischen Verbindungen. Umweltmed Forsch Prax 5:101–106
110. Wynder EL, Onderdonk J, Mantel N (1963) An epidemiological investigation of cancer of the bladder. Cancer 16:1388–1407
111. You XY, Chen JG, Yao YF (1983) A retrospective prospective investigation on bladder cancer in the workers exposed to benzidine in Shanghai dyestuff industry. Tumor 3:197–201 (in Chinese)