ORIGINAL PAPER

Urinary apparatus tumours and asbestos: The Ramazzini Institute caseload

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Summary

Many studies have drawn attention to the possible association between occupational exposure to asbestos and tumours of the urinary apparatus. Besides the main etiological agents recognised today – such as smoking, obesity and hypertension – experimental and epidemiological evidence converges on the view that tumours of the kidney and bladder are largely due to occupational exposure to industrial agents: these and their transformation products linger in the body and are eventually eliminated by those organs. That one such agent targeting the urinary system is asbestos has found confirmation in the discovery of asbestos fibres in the urine of populations at risk. We here present 23 cases of work exposure to asbestos in a range of exposure scenarios where the workers developed tumours of the kidney and bladder. The cases came to the attention of the Ramazzini Institute casually.

KEY WORDS: Asbestos; Renal cancer; Occupational exposure.

Submitted 10 December 2012; Accepted 24 December 2012

TUMOURS OF THE URINARY APPARATUS IN WORKERS EXPOSED TO ASBESTOS

Renal excretion is one of the main elimination pathways for the toxic and carcinogenic chemical agents and metabolites to which man may be exposed. The urinary system is naturally often a target of such agents, the kidney being the filter in which they may be trapped, and the bladder a place where they may linger for a long time before being excreted.

The likelihood that asbestos has a carcinogenic effect on urinary tract tissues is supported by many studies which have shown the presence of asbestos fibre in the urine, caused by the occasional migration of such fibres from the gastro-intestinal wall to the bloodstream then into the urinary pathways (1-4). Asbestos formations have been detected in the kidneys and increased risk of kidney tumours was noted among miners from the Quebec asbestos mine (5). The presence of asbestos fibres in the urine both of occupationally exposed subjects (6-8) and of people who had drunk water contaminated with amphibolic asbestiform fibres (9, 10) has been documented on various occasions. Evidence of asbestos fibre lodging in the kidneys has come from experimental and epidemiological studies based on autopsy (11-14). It is thought by some researchers that asbestos formations start in the lungs and then migrate to the kidney. Once the asbestos fibres reach they form around asbestos fibres that had migrated to the kidneys in their own right. This is based on the demonstration that, once they reach the lungs by inhalation, they may pass the alveolar barrier, cross the interstitium and reach the lymph vessels and blood circulation; from there the fibres get distributed throughout the organs and tissues in concentrations that vary with local conditions (15). The highest concentration of asbestos fibres, outside the lungs, has been found in the kidney (high pressure and fast flow) and in the liver (high micro-vascular permeability); it is lower in the brain (owing to the blood-brain barrier) (16).

1. Renal tumours

➢ *Epidemiology*

Renal tumours occupy ninth place in the list of neoplasias commonly found in industrialised countries. They include carcinoma of the renal parenchyma (92%), carcinoma of the transition cells of the renal pelvis and ureter (7%) and Wilms' infancy tumour (1%) (17-19).

Although often were considered as renal tumours, renal pelvis and ureter tumours are urothelial neoplasms, therefore they are affected by the same risk factors of bladder cancer, the most frequent urothelial malignancy. Roughly 80% of renal parenchymal tumours are clear-cell (non-papilliferous) adenocarcinomas; the remainder are papilliferous/chromophilic (~ 15%) or chromophobic (~ 5%) tumours and carcinomas of the collector ducts (< 1%) (18).

It is estimated that some 273,500 new cases of renal carcinoma are diagnosed every year in the world, amounting to 2% of all tumours (20). The highest incidence is recorded in North America, the lowest in Asia and Africa. In Europe 86,000 new cases are observed every year, 8,200 of them in Italy which occupies nineteenth place among the European countries, the incidence being considerably higher in men (5,600) than in women (2,600) (17, 21). As well as differences between continents, there are considerable differences within one and the same continent or even the same nation. In Europe, for example, 15.2 cases per 100,000 inhabitants are found in the Czech Republic and 2.9 in Serbia (22). In Italy the incidence of renal tumour observed in the north-east (9.0/100,000 men and 3.9/100,000 women) is three times higher than in a southern province like Salerno (3.6/100,000 men and 1.6/100,000 women) (23).

From 1973 to 2000 the incidence of tumours to the kidney and renal pelvis increased by 47% in men and 65% in women, a rate of about 2% per year (24). In the subsequent decade (1999-2008) this increase rose to 3% (2.8% men and 3.1% women) with 20.4 cases per 100,000 in the age bracket 50-54 years, 43.5 cases per 100,000 in that between 60 and 64 years, and 70.0 per 100,000 for the population between 75 and 79 years of age (25).

➢ *Situations, risk factors and exogenous agents*

We here list the agents and general factors, as well as occupational situations, which are likely to increase the risk of renal carcinoma in man, going by the epidemiological evidence.

- Smoking: it doubles the risk of carcinoma of the renal parenchyma, triples the risk of tumours of the renal pelvis. An increased risk has been observed to correlate with the number of cigarettes: 1.3-1.6 for a 20-40 packets/year consumption, 9.3 for consumption over 40 packets/year (26, 27).
- Obesity: the risk is thought to grow by 24% in men and 34% in women with each 5 kg/m^2 increase in the body mass (28).
- Hypertension: an increased dose-response risk has been observed, correlating with high blood pressure values (23).
- Diet: diets rich in fruit and vegetables correlate inversely with increased risk of renal cancer (29).
- Occupational situations: as recognised to date, the risk factors and agents mentioned above seem to be causally involved in the onset of about half the renal tumours observed (18). This lends all the greater importance to epidemiological and experimental evidence connecting occupational exposure to the aetiology of renal cancer. The agents most frequently associated with renal tumours in the literature are: 1,3-butadiene, vinyl chloride, vinylidene chloride, trichloroethylene, tetrachloroethylene, aspartame and asbestos (23, 30-33).

➢ *Renal tumours in workers exposed to asbestos*

One of the experimentally and epidemiologically identified carcinogens for the kidney is asbestos. More and more experimental and epidemiological studies are now confirming the causal link between cancer of the kidney and occupational exposure to asbestos, as discovered back in the 1970s (34). One experimental study performed in 1976 on Wistar rats orally treated with a suspension of chrysotile showed an increase in the incidence of renal carcinoma (35). Medium-length asbestos fibres (chrysotile) were administered to Fisher F344 rats in their food on its own and with 1,2- dimethylidrazine dichlorohydrate (DMH), a known carcinogen: among the females treated with asbestos a significant increase ($P < 0.05$) was noted in the incidence of mixed tumours of the kidney (34/175, 19%) as compared to DMH alone (13/125, 10%) (36). In a more recent study Wistar rats were treated with asbestos fibre (amosite) via intratracheal instillation. After six months' treatment no neoplastic lesions were found in the kidneys, but significant glomerulosclerosis and interstitial tubulo-fibrosis were found (37).

Increased incidence of renal carcinoma was observed in a cohort study on 17,800 insulation workers in the United States and Canada over the period from 1967 to 1986 (38, 39). Here 37 deaths by renal neoplasm were recorded, a relative risk (RR) of 1.96 which is statistically significant ($P< 0.001$) against expectation (Table 1). A second epidemiological study on 1,074 American workers employed in various sectors including textiles and asbestos-cement-based products, showed a statistically significant increase in renal tumour deaths: 7 cases observed versus 2.54 expected, with a Standardized Mortality Ratio (SMR) of 2.76 (Confidence Interval (CI) 95%: 1.29-5.18) (40). Another cohort study on 1,500 workers exposed to asbestos brought to light malignancies of the kidney that the authors considered correlated with asbestos exposure (41). Yet another case-control study based on 518 cases spread over 37 hospitals in Massachusetts, as identified between 1981 and 1984, showed increased incidence of renal adenocarcinoma induced by asbestos (42). *McCredie* and *Stewart's* case-control study in Australia evinced an RR of 1.62 (CI 95%: 1.04-2.53) for renal neoplasias, versus a sample of the general unexposed population (43). High incidence of kidney tumour was observed in workers with a cumulative exposure to asbestos of 300 mpcf.y (millions of particles per cubic foot per year) (44). In 1994 a high number of cases of renal tumour in Denmark were correlated with occupational exposure to asbestos (45). Another case-control study on workers exposed to asbestos and belonging to various job categories in vari-

Table 1.

Deaths among 17,800 insulation workers in the USA and Canada from 1/1/1967 to 31/12/1986 (1).

Causes of death	**Deaths expected** (2)	**Deaths observed**		**Observed/expected difference**		**SMR** (3)	
		Death certificate	**Cause ascertained** (4)	**Death certificate**	**Cause ascertained**	**Death certificate**	**Cause ascertained**
Total deaths, all causes	3.453,50	4.951	4.951	1.497,50	1.497,50	143***	143***
Total neoplasias, all locations	761,41	2.127	2.295	1.365.59	1.533,59	279***	301***
Pulmonary neoplasia	268,66	1.008	1.168	739,34	899,34	375***	435***
Pleural mesothelioma (5)	–	89	173	89,00	173,00	–	–
Peritoneal mesothelioma (5)	–	92	285	92,00	285,00	–	–
Neoplasia of the larynx	10,57	17	18	6,43	7,43	161	170*
Neoplasia of the oropharynx	22,02	38	48	15,98	25,98	173**	218***
Gastrointestinal neoplasia (6)	135,69	188	189	52,31	53,31	139***	139***
Digestive system neoplasia (7)	191,66	324	269	132,34	77,34	169***	140***
Renal neoplasia	**18,87**	**32**	**37**	**13,13**	**18,13**	**170****	**196****
Total non-infective lung diseases	144,82	465	507	320,18	362,18	321***	350***
Asbestosis (5)	–	201	427	201,00	427,00	–	–
Other causes	2.547,27	2.359	2.149	-188,27	-398,27	93***	84***

*1) From Selikoff & Seidman, 1991 (modified) (39); * p < 0.05; ** p < 0.01; *** p < 0.001.*
2) Expected deaths were calculated from age-specific death rates of white males produced by the U.S. National Center for Health Statistics, 1967-1986.
3) Standardised mortality ratio: deaths observed/deaths expected x 100.
4) Number of deaths recorded after acquisition and revision of clinical and/or surgical and/or autopsy documentation. Failing such documentation, we considered death certificates.
5) Mortality rates unavailable since considered rare causes of death.
6) Neoplasias of the oesophagus, stomach and colon-rectum.
7) Neoplasias of the oesophagus, stomach, colon-rectum, liver, gall bladder and bile ducts.

ous countries (*Australia, Denmark, Germany, Sweden and the USA*) confirmed the significant increase in renal neoplasias (RR = 1.4; CI 95%: 1.1-1.8) (46). In 2000 Gamble and Lewis published the results of two studies on deaths among three cohorts of American refinery and petrochemical industry workers. The studies showed that renal tumour decease increased in all three cohorts. The relative risk (RR = 1.86) in one cohort, especially, was of statistical significance (47, 48).

2. Tumours of the bladder

➢ *Epidemiology*

Malignant tumours of the bladder (MTB) are the fourth neoplasia in order of frequency, above all in men where the ratio vis-à-vis women is 3.5:1. There are estimated to be around 200,000 new cases per year worldwide (49). The elderly are at greater risk than the young: after the age of 70, the risk is about 30 times higher than in more youthful age brackets (21, 50).

According to recent data, MTB represents 4.8% of all tumours in the two sexes (6.9% in men and 2.5% in women) with a mortality rate of 3.4% and 1.5% in men and women respectively (50). In the United States the incidence tended to rise until 1990 in both sexes, but mortality is now diminishing especially among men (51). Over the period 2002-2006 the incidence among males in the United States was 37.1 per 100,000 inhabitants and 9.3 per 100,000 women. Over the same period mortality was 7.5 and 2.2 per 100,000 among men and women respectively (52). The highest rates were recorded in North America, North Africa, the Middle East and Europe - particularly Italy, Spain and French Switzerland with incidences higher than 30 per 100,000 men. The highest death rates were recorded in Denmark, Spain, Poland, Malta and Ireland. In Europe mortality increased up to the Eighties, above all in the South and East, and then tapered between 1988 and 2000 (53). In women the highest death rate found is around 2-3 per 100,000 in Denmark and Great Britain (54).

MTBs also reflect racial differences. For example, in the USA the Filipinos' and Afro-Americans' risk of developing a vesical carcinoma is respectively one-fifth and half that of whites. This finding with MTBs runs counter to the trend with other kinds of tumour where the incidence and mortality of Afro-Americans is always higher than among whites (55). In developed countries the incidence is twice as high in urban and industrialised areas as it is in the countryside. The differences are more marked among men than women. In the United States between 80 and 95% of MTBs are transition-cell carcinomas (56). The remaining malignant tumours are basically squamocellular carcinomas and adenocarcinomas. Some authors think the percentage of squamocellular carcinomas is growing steeply among blacks as compared to whites (12% vs 2%) and again, more in women than in men (18.3% vs 7.6%) (57). The latency period of MTBs (the interval between start of exposure and onset of neoplasia pathology) varies according to type and intensity of exposure to factors and agents responsible. The latency period for cancer of the bladder ranges between 6 and 20 years, with a maximum of 45 years. The most commonly reported mean time is 20 years (58).

➢ *Situations, risk factors and exogenous agents*

Clinical-pathology findings from a hundred years ago (i.e. the historical dawn of bladder carcinogenesis) down to today's epidemiological surveys and experimental research

enable us to identify the exogenous carcinogen risks for the bladder.

We here list the agents and general factors, as well as occupational situations, which entail an adequately proven risk of bladder cancer in man, according to epidemiology (51, 59):

- Smoking: a relation has been found between the number of cigarettes smoked and the risk run.
- Schistosoma haematobium: the high incidence of vesical carcinoma among patients with schistosomiasis is a problem for some areas of Africa and the Middle East, especially Egypt.
- Occupational situations: colouring industry (aromatic amines and related agents), aluminium industry, coal distillation, combustion products from engines, shoe, furniture, rubber and textile industries.

➢ *Tumours of the bladder in workers exposed to asbestos*

It is thought that a sizable part of MTBs (5-25%) can be put down to occupational origin (56). There is mounting evidence of a causal link between tumours of the urinary apparatus, including bladder cancer, and occupational exposure to asbestos. This is hardly surprising if one thinks that many carcinogens, and especially their active biotransformation products, are excreted in the urine. The literature shows a heightened risk of MTB in at least 40 different job categories, including paint-sprayers, truck drivers, electricians, mechanics, turners, barmen and waiters. A case-control study carried out in Spain between 1978 and 1982 examined 406 patients of the La Paz Hospital, Madrid, whose diagnosis of bladder cancer was associated with occupational exposure to asbestos (60). An increase in urinary tract tumours was observed in a German case-control study for 1977-1985 focusing on asbestos-exposed workers (Odds Ratio (OR) = 1.3, IC 95% = 0.7-2.5) from various categories, including foundries where the environment was heavily contaminated with asbestos (OR = 1.6, IC 95% = 0.8-2.9) (61). An epidemiological study performed in Finland on 33 patients from a surgical clinic over the period October-December 1988, revealed that out of 28 MTB sufferers, as many as 17 (61%) had been occupationally exposed to asbestos, and in 94% the exposure was certain (OR = 2.4, IC 95% = 0.9-8.4) (62). A cohort study on worker deaths at a shipyard in Genoa demonstrated an increase in MTB in relation to asbestos fibre associated with aromatic polycyclic hydrocarbons, industrial oils and welding fumes. One notes especially that the bladder cancer latency among the workers involved proved to be about 25 years of continuous exposure, an important fact for follow-ups on people exposed (63). Another case-control study in four Canadian provinces evidenced a further confirmation of an association between MTB and exposure to certain chemical agents such as: asbestos (OR = 1.69, IC 95% = 1.07-2.65), mineral lubricant oils (OR = 1.64, IC 95% = 1.06-2.55), benzidine (OR = 2.20, IC 95% = 1.00-4.87) (64). The cohort study on workers at the Porto Torres petrochemical works in Sardinia (5,350 males were included in the follow-up) showed an increased risk of MTB (RR = 1.46; 95% IC 1.09-1.96) in the sub-cohort of workers potentially exposed to asbestos (65).

To the best of our knowledge, the first study pointing to increased risk of MTB dates from 1965, a survey on electrical industry workers which is a sector much polluted by asbestos – see the specific exposure scenario that follows – given the almost ubiquitous use of asbestos in electriccables (66). This observation of electrical workers at increased risk of MTB was subsequently confirmed by many papers (67-69), including one that shows the combined results of 11 case-control studies (OR = 3.99, IC 95% = 1.10-14.51) (70). One Spanish study covering from 1998-2000 on 1,219 bladder cancer patients and 1,271 control patients found a statistically significant affect, all the more marked in exposures of ten years and more: the workers involved were from the medical gas-electricity sector (OR = 3.94, IC 95% = 1.49-10.44) and the electrical sector (OR = 1.31, IC 95% = 0.62-2.77) (71). The risk of MTB appears significantly greater when the exposure is a lasting one (over 10 years): this is confirmed by the study published by *Cassidy et al.* in 2009 (OR = 4.37, IC 95% = 1.62-11.77) and that by *Colt et al.* in 2011 which points to statistically significant increased risks run by car electricians (OR = 1.5, IC 95% = 1.02-2.3) and an increase among other electricians as well (OR = 1.1, IC 95% = 0.6-2.1) (72,73).

Several studies in the literature point to an increased risk of MTB in foundry workers, another category heavily exposed to asbestos, as described in Case 1 below. *Claude et al.* published a case-control study on 531 urinary tract patients from a range of different jobs including foundries (OR = 1.56, IC 95% = 0.84-2.91) as well as thermo-electric power stations and kilns (OR = 2.17, IC 95% = 0.84-5.57) (69).

The Ramazzini Institute caseload on urinary apparatus tumours and asbestos

In 1995 Professor Cesare Maltoni and his group at the Ramazzini Institute first encountered a renal tumour in a worker occupationally exposed to asbestos. In a quite random way since then our attention has been drawn to another 22 cases, all men (the most gender exposed in the past) who had tumours of the urinary apparatus. The 23 cases include 18 kidney cancers, 2 of the ureter, and 3 of the bladder, traceable to asbestos exposure at work in various exposure scenarios recounted at first hand. In what follows we present an account of these cases in the order of presentation. The data are summarised in Table 2.

Discussion and conclusions

Tumours of the urinary apparatus are on the increase in the most industrialised countries and regions. The many epidemiological and experimental studies show that many agents can cause such tumours, and asbestos is emerging as one of them.

Asbestos is the generic name for a series of natural fibrous silicates which are widespread in nature and were extensively used in the last century in a range of manufacturing sectors: building, railways, shipyards, textile firms, the ceramics industry, brickworks, foundries and sugar refineries. Its main uses are as: 1) asbestos-cement for building materials (roofing, walls, panels, ceilings, floors,

Table 2.

Asbestos-related tumours of the urinary system: the Ramazzini Institute caseload.

Case N.	Patient initials	Place of work	Exposure scenario: exposure to asbestos	Period of exposure (length)	Diagnosis	Year of diagnosis	Age at diagnosis	Latency
1	MZ	BO, MO	Foundry: thermal and electrical insulation of kilns, protective gear	1964-1991 (27)	Renal carcinoma	1990	46	26
2	PN	PD	Officine Stanga (Firema): lining and insulation of railway carriages	1969-1998 (29)	Renal oncocytoma asbestosis)	1999 (48)	51	30
3	CT	BO	State railways: lining and insulation of railway carriages	1972-1989 (17)	Renal adenocarcinoma	1989	37	17
4	MM	BO	State railways: lining and insulation of railway carriages	1941-1974 (33)	Renal carcinoma	1994	70	53
5	GS	BO	State railways: lining and insulation of railway carriages	-	Renal carcinoma	1988	72	-
6	GP	BO	Casaralta Componenti (Firema): lining and insulation of railway carriages	1977-1987 (10)	Renal carcinoma	-	-	-
7	SE	NA	Metalworking firm: lining and insulation of railway carriages	-	Renal neoplasia	1985	79	-
8	CN	BO	Sugar refinery (home exposure): lining and insulation	1938-1960 (22)	Renal carcinoma	1995	59	57
9	CV	GE	Shipyard: thermal and electric-cable insulation, lining	1962-1999 (37)	Carcinoma of the ureter	1997	58	35
10	PC	BR, SA, VE, TA, FG, LE	Petrochemical: thermal and electric-cable insulation, insulation and gaskets	1969-1975 1977-1992 (21)	Renal carcinoma	2001	53	32
11	TL	RA	Compagnia Portuale: movement flows, transport and storage bags of asbestos, insulation and lining	1962-1981 (19)	Renal adenocarcinoma	1980	43	18
12	ED	RA	Compagnia Portuale: movement flows, transport and storage bags of asbestos, insulation and lining	1960-1984 (24)	Renal carcinoma	1995	69	35
13	GG	RA	Compagnia Portuale: movement flows, transporting and storing bags of asbestos, insulation and lining	1972-1992 (20)	Renal carcinoma	2004	55	32
14	VM	MO	Car coachworks: electric-cable insulation protective tubing for engines	1963-1991 (28)	Renal carcinoma	2007	66	44
15	IB	RE	Carpentry: insulating railway carriages	1975-1987 (12)	Renal neoplasia	2006	76	31
16	FM	RM	State railways: lining and insulating railway carriages	1954-1992 (38)	Bladder carcinoma	2009	75	55
17	LC	BO	Magneti Marelli: thermal and electric-cable insulation for kilns, protective gear	1974-1990 (16)	Renal carcinoma	1990	53	16
18	BG	BO	Magneti Marelli: thermal and electric-cable insulation for kilns, protective gear	1976-1983 (7)	Renal carcinoma	2004	77	28
19	MM	BO	Magneti Marelli: thermal and electric-cable insulation for kilns, protective gear	1970-2002 (32)	Ureteral carcinoma	2001	52	31
20	EB	MO	Magneti Marelli: thermal and electric-cable insulation for kilns, protective gear	1974-2012 (38)	Renal carcinoma	2001	49	27
21	EM	BO	Sugar refinery-Magneti Marelli: lining, insulation, thermal and electric-cable insulation for kilns, protective gear	1962-1991 (29)	Bladder carcinoma	1993	57	31
22	OS	MO	Car coachworks: electric-cable insulation protective tubing for engines	1974-1998 (24)	Renal carcinoma	2009	62	35
23	DG	FE	Magneti Marelli: lining, insulation, thermal and electric-cable insulation for kilns, protective gear	1980-present (32)	Bladder carcinoma	2008	52	28

conduits), pipelines (aqueducts, oil lines), basins and tanks; 2) insulating material (heat, electricity, sound) in various types of building (factories, public buildings, homes) and in pipes, boilers, vehicles, rolling stock, ships, etc.; 3) friction parts (brakes); 4) paper and board; 5) textiles; 6) plastics; 7) gaskets; 8) filters. Apart from these main uses, asbestos has been employed in innumerable ways. One recent estimate is that about 3,000 uses have been listed (4).

In Italy about 75% of asbestos went into asbestos-cement. The remaining 25% was almost entirely used in the textile sector, gaskets, paper and board. Asbestos spread more or

less everywhere because of its multiple properties: resistance, non-flammability, insulation, durability, low cost. Such qualities make it non-degradable. It lingers indefinitely in the environment; once it penetrates the organism, it is partly retained by tissues along its route. Its carcinogenic effects on the human organism are irreversible, all the evidence suggests. Again, nowadays asbestos, though ubiquitous, is at its highest and most dangerous concentration in certain work and living conditions. It is difficult to list all the work conditions at risk. Exposure to asbestos occurs to: those who extract it, those who make asbestos-based products, those who handle such materials, repairers and demolishers of asbestos-containing materials, port stevedores, transporters and all whose work environment is polluted by asbestos. One occupational category thought to be most exposed and at the greatest carcinogenic risk from asbestos are the technicians making, checking, cleaning and demolishing rolling stock containing asbestos. In Italy asbestos was extensively used by the railways from the 1930s to the 1970s in the form of panels and lagging strips for various parts of locomotives, infrastructure, and also making asbestos-cement sleepers for rail-track. From the places where it is employed, movement, wear and tear and vibration spread it inside rolling stock, in depots and in outdoor and indoor repair workshops, in and around railway stations, and also in workers' homes, since they carry asbestos fibre on their hair and work clothes. Another work category at high risk of asbestos-related cancer is that of dockers heavily and permanently exposed as large quantities of the material are shifted, loaded, unloaded and stored. At least until the late-Eighties, the lack of collective or individual protection measures, as well as lack of information about the risk of inhaling the fibres, further increased the degree of environmental exposure.

The IARC has classified asbestos as a carcinogen for man (Group 1) and states that it gives rise to mesothelioma, lung, larynx and ovary tumour and – somewhat less proven – tumours of the pharynx, stomach and colon-rectum (74). INAIL sees neoplasias of the lung, pleura, peritoneum, pericardium and the tunica vaginalis testis as highly attributable to asbestos exposure, and (to a lesser degree of probability) neoplasias of the larynx and gastrointestinal tract.

Greater controversy still surrounds the aetiological role of asbestos in tumours of the urinary apparatus, despite the existence of wide scientific documentation of a causal link (not least, the finding of asbestos fibres in exposed workers' urine and kidneys). The 23 cases from the RI caseload here published give grounds for thought on various counts. First, they comprise workers whose asbestos exposure was certain and recognised: many of them worked directly or indirectly on the railways, or were dockers, shipyard workers, foundry workers or from sugar refineries where the massive asbestos pollution is proven. Among them are cases recognised by INAIL as heavily and continuously exposed to asbestos, or suffering from asbestosis which is a specific marker for asbestos exposure. The second reason is the length of exposure and time of latency (the period from when exposure starts to when the neoplasia sets in): respectively 26.2 years (range 7-57) and 33.1 years (range 16-57). Such time-frames are most frequently observed in occupational tumours and may be seen as expressing the high environmental oncogenic potential to which the workers were exposed. Again, the early mean age at onset (59.6 years: range 37-79) points to an occupational origin. The 43.5% of these tumours set in below 55 years of age, 10 years earlier than the incidence rates observed in men over the period 2006-2008 (20). Lastly, the RI caseload came to our notice quite randomly and is not the result of a systematic epidemiological survey detailing the exposure scenario of the worker categories involved: if anything, it underestimates the situation. Let us not forget that it took decades before official recognition was given to pleural mesothelioma – nowadays considered the most specific asbestos-related tumour. Bearing in mind the wide range of risk categories and the picture painted by the scientific literature, we urgently need to implement measures to protect workers and their families, as well as the population at large. Nationwide and internationally, it is to be hoped that new epidemiological efforts will be made to quantify the global cancer risk from asbestos – especially in view of all the "unexpected" malignancies that have occurred – and improve prevention strategies as well as obtaining legislative recognition of the occupational origin behind these neoplasias. Greater light might be shed on this if the categories exposed to asbestos were regularly monitored by oncologists – a project the Ramazzini Institute has in mind to undertake, responding to pressure from workers and as a way of standing by them in this difficult phase.

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Appendix

Individual case descriptions

Case 1

MZ, born in the province of Ferrara on 20/4/1944 and resident in Bologna. Smoker.

Work anamnesis

- 1964-1977: worked for the Caster Foundry, Bologna, in charge of liquid chemical testing, technology checks on moulding earths and sand-resin mixes, trials on molten metals, metallographic tests.
- 1977-1979: worked for the Casting House Foundry, Mirandola (near Modena), as metallurgy foreman for fusion processes, checks and trials.
- 1979-1984: worked for the Fonderia Bolognese at Zola Predosa (near Bologna), as metallurgy foreman for fusion processes, checks and trials.
- 1984-1991: worked for the Cadriano Foundry (near Bologna), as metallurgy foreman for fusion processes, checks (on raw materials and finished products) and trials.

Exposure scenario

Work exposure to many carcinogenic compounds, including asbestos, contained in thermal and electric insulation for kilns and the workplace. Specialised metal carpentry as a forge operator, boiler-maker and welder entailed high exposure to asbestos, linked to the widespread and constant use of asbestos products like cords and boards, and to powdered asbestos, used as it stands for insertion in certain plants. During forging operations, for example, pieces would be brought to extremely high temperature inside kilns and then hot-pressed or hammered into other shapes. During these operations the worker used asbestos-based protective covering against the heat of the deforming process. Add to this the standard technical or protective gear, such as gloves and wraps to protect pieces for forging being carried at very high temperatures. The asbestos underwent thermal stress and was hence easily inhaled since it lingered in the environment, the sheds being provided with extractors sited high up in the air.

Clinical anamnesis

Neoplasia of the left kidney was detected in 1990. Histological examination of the portion excised under eradication surgery revealed the presence of: nephrocarcinoma of clear-cell (50%) and eosinophile (50%) type.

Years of exposure: 27; latency: 26 years; age at diagnosis: 46.

Case 2

PN, born in the province of Padua on 22/3/1948 and resident there. Non-smoker

Work anamnesis

- 15/12/1969-30/10/1998: worked as a paint-sprayer until 1978 and then as a warehouseman at Officine Meccaniche Stanga, Padua, belonging to the Firema Consortium, a metal-working company designing, building and repairing locomotives, carriages, underground rolling stock and trams.
- 31/10/1998: retired.

Exposure scenario

Exposed to solvents (paints and catalysts) until 1978 and to asbestos throughout his career. The scenario is similar to case 3. In 1997 asbestos corpuscles were detected in his sputum.

Clinical anamnesis

In 1996 a diagnosis of pleural asbestosis was made and confirmed in 1997 when the certificate read: presents a considerable number of asbestos corpuscles in the sputum and broncholavage liquid. Together with the presence of pleural plaques, these are an expression of exposure to dust containing asbestos fibres over a prolonged period (years). Left-kidney neoplasia was discovered in 1999. Histological examination of the portion excised under eradication surgery revealed the presence of: renal oncocytoma.

Years of exposure: 29; latency: 30 years; age at diagnosis: 51.

Case 3

CT, born in Bologna on 19/5/1952, resident in the province of Bologna, died there on 19/9/1989. Non-smoker.

Work anamnesis

- 1972-1989: worked at the Santa Viola electric sub-station belonging to the State Railways, Bologna Department, technician in charge of electric control-boards.

Exposure scenario

From employees' statements taken at the inquest, the asbestos exposure conditions regarded ordinary and extraordinary maintenance of rolling stock. Ordinary rolling stock maintenance involved servicing electric meters and coachwork. Maintenance of electric meters entailed preliminary cleaning with compressed air, followed by sanding down and scraping panels insulated by asbestos-cement. The panels were situated in arc-extinguishing chimneys fitted to extra-rapid switches that were subject to friction and combustion. When the restraining magnetic flow failed during operations and the switch clicked over, an arc would form between the two poles and gradually increase as the current built up; it would be

channelled into a sheet-metal conduit (called a chimney) so that it could be fractioned and interrupted by an upward jet of air from beneath. This reaction caused a detonation which would release fragments, fumes and exhalations. When the asbestos-cement panels were found to be worn, they were replaced with new ones obtained by cutting down larger panels using a jig-saw or stone-grinder. Maintenance to coachwork entailed removing (part of) panels insulated with asbestos-cement. Cleaning operations were by broom, generally once a week and by hand, which left dust and asbestos residue on the floor for a number of days. Extraordinary maintenance consisted in complete removal of panels, furnishings and plant. Removing panels from rolling stock laid bare the asbestos which had become friable and hence dispersed into the workplace following operations involving close contact with the insulating material. In some cases overhauling plant would entail removing the asbestos by hand or by scraper. Asbestos powder dispersed into the environment would later be swept into normal rubbish bins. From the late-Forties on, asbestos began to be employed in the form of insulating board surrounding electric heating units. From the mid-Fifties on, new rolling stock began to be "*spray-insulated*" with asbestos as a form of maintenance, an operation that was performed in the ordinary work environment, massively polluting the workplace and involving a large number of workers, regardless of their specific duties. At the beginning of the Sixties it was decided to extend this kind of insulation to all current rolling stock, the overall number of which amounted to about 8,000.
The first preventive measures began to be mooted in the early-Eighties, but operators were only equipped with aspirators from the Nineties onwards.

Clinical anamnesis
A right-kidney neoplasia was discovered in 1989. Histological examination of the portion excised under eradication surgery revealed the presence of: nephrocarcinoma of clear-cell (80%) and dark-cell type with a high degree of malignancy, subsequently metastasising to other locations: lungs, liver, intestine, bones.

Years of exposure:17; latency: 17 years; age at diagnosis: 37.

Case 4

MM, born on 30/6/1924 in the province of Ravenna and resident in Bologna. Non-smoker.

Work anamnesis
- 1934-1941: worked for the State Railways as an errand-boy in summer months (exposure at such time not considered in the general exposure calculation).
- 1941-1974: worked for the State Railways on track repairs until 1956 when he became an electrician for safety devices.
- 1974: retired.

Exposure scenario
In his career he was exposed to asbestos contained as insulation in the workplace and as insulation for electric cables. The scenario is similar to case 3.

Clinical anamnesis
A left-kidney neoplasia was discovered in 1994. Histological examination of the portion excised under eradication surgery revealed the presence of: nephrocarcinoma of clear-cell type, with subsequent liver metastasis.

Years of exposure: 33; latency: 53 years; age at diagnosis: 70.

Case 5

GS, born on 1/7/1916. Smoker. No further documentation acquired (NFDA).

Work anamnesis
Worked for the State Railways at Bologna (period and duties unknown).

Clinical anamnesis
Right- and left-kidney neoplasias were discovered in 1988. Histological examination of the portion excised under eradication surgery revealed the presence of: clear-cell carcinoma left and cystic-papillary carcinoma right, later metastasising to the liver and pancreas.

Years of exposure: -; latency: -; age at diagnosis: 72.

Case 6

GP. NFDA

Work anamnesis
1977-1987: worked as a plasterer, insulator and painter for the firm of Casaralta Componenti, Bologna, belonging to the Firema Consortium, a metal and mechanical engineering company that designed, built and repaired locomotives trains, underground railways and trams.

Exposure scenario
Similar to case 3.

Clinical anamnesis
Renal carcinoma.

Years of exposure: 10; latency: -; age at diagnosis: -.

Case 7

SE, born in 1906 and died in 1997. NFDA

Work anamnesis
Worked for Sofer, Pozzuoli (near Naples), a metal and mechanical engineering company involved in making and repairing rolling stock and buses.

Exposure scenario
The patient described the heavy environmental pollution, especially during asbestos spray insulation which he performed until 1978. The scenario is similar to case 3.

Clinical anamnesis
A renal neoplasia (Not Otherwise Specified) was discovered in 1985. NFDA.

Years of exposure: -; latency: -; age at diagnosis: 79.

Case 8

CN, born on 24/3/1936 in the province of Bologna and resident there. One-time occasional cigar-smoker

Work anamnesis
- 1955-1985: representative for various articles: detergent (1 year), confectionary (a few years) and toys for early childhood (25 years). The patient was only involved in customer relations and orders, not transport or deliveries.
- 1985-1995: partner in a company manufacturing cushions in sheds roofed in Eternit for the second half of the period 1990.

Exposure scenario
In his job CN was exposed to substances that had no bearing on the aetiology of the neoplasia he incurred. What was relevant was his domestic family exposure to asbestos since his father worked at a sugar refinery from 1938 to 1960 as a foreman in charge of maintaining and repairing water-heating plant, and hence subject to massive asbestos exposure. More information on sugar refineries is given in the exposure scenario to case 21. CN lived with his father for 22 years and was hence exposed to asbestos fibres at home via his father's work clothes and hair.

Clinical anamnesis
A right-kidney neoplasia was discovered in 1995. Histological examination of the portion excised under eradication surgery revealed the presence of: renal carcinoma.

Years of exposure: 57; latency: 57 years; age at diagnosis: 59.

Case 9
CV, born on 12/11/1939, in the province of Ferrara, lived in Genoa and died there on 15/4/1999 at the age of 59. Smoker.

Work anamnesis
- 1960-1962: did his military service in the Italian Navy as a radar operator (this period of exposure not considered in the overall calculation).
- 1962-1999: worked at the Genoa shipyards as an electrician installing and maintaining electric plant. CV worked on board ships being built or repaired or restyled; mainly in the engine-rooms.

Exposure scenario
CV was heavily exposed to asbestos since this was widely used to insulate ships, especially in the post-war period. Over the 37 years he spent working for the firms that successively ran the Genoa shipyards, CV installed and repaired vessels' electrical plant; when insulation panels were mounted or removed, asbestos dust would be released. Since shifts were not synchronised among the various work squads, the pollution to the work environment was generalised so that all working on board a ship were exposed to inhalation of fibres.

Clinical anamnesis
Neoplasia of the left ureter was discovered in 1997. Histological examination of the portion excised under eradication surgery revealed the presence of: excrescent and invasive transitional carcinoma.

Years of exposure: 37; latency: 35 years; age at diagnosis: 58.

Case 10
PC, born on 16/1/1948 in the province of Brindisi and resident there. Smoker.

Work anamnesis
- 1969-1970: worked for the Brindisi company SOIMI S.p.A. a subcontractor to Petrolchimico at Brindisi; metal-worker, assistant pipe operator.
- 1970-1975: worked for the company Fratelli Grandis Impianti Industriali at Albissola del Capo (Savona), another sub-contractor to: 1970-1971: Petrolchimico of Brindisi, as full pipe operator. 1971-1972: Petrolchimico at Marghera (near Venice), as a qualified pipe operator. 1972-1975: Italsider at Taranto.
- 1975-1977: worked as a dealer in domestic appliances, gas bottles, etc.
- 1978-1985: worked for the Compagnia Generale Montaggi Industriali (CoGeMI) S.p.A. at Brindisi, a contractor to the Montedison petrolchemical works there, again as a pipe operator.
- 1985-1987: worked for the Cooperativa Mucafer S.c.r.l. at Manfredonia (near Foggia), as a pipe operator.
- 1987-2001: worked for the Cooperativa Tecnosic S.c.r.l. at Lecce, as a pipe operator.

Exposure scenario
PC was exposed to a number of chemical and physical agents when mounting and lagging pipes with asbestos fibre, using tools like blow torches and grinders. Asbestos sheeting would be used to avoid fire risk. Inspection by INAIL (National Institute for Insurance against Accident at Work) found that in working on petrochemical industrial plants PC was continuously exposed to asbestos from 1969 to 1992, except for a gap of two years (1975-1977) when he worked in a different sector.

Clinical anamnesis
A left-kidney neoplasia was discovered in 2001. Histological examination of the portion excised under eradication surgery revealed the presence of: renal carcinoma of clear-cell type.

Years of exposure: 21; latency: 32 years; age at diagnosis: 53.

Case 11
TL, born on 22/2/1937 in the province of Ravenna, where he lived and died on 29/11/1997, at the age of 60. Non-smoker.

Work anamnesis
- Until 1961: worked on his parents' farm.
- 1962-1981: worked for the Ravenna Compagnia Portuale as a porter/crane operator moving goods and cleaning out ship holds; he breathed in the dust which was continuously contaminated by asbestos, large quantities of which were stored loose in warehouses, dumped against walls as late as 1981.
- 1982: retired.

Exposure scenario
The Ravenna Port Company handled loading/unloading of ships and stored goods in its warehouses. Among the materials was asbestos which was unloaded from ships

there from the Seventies on. Dock workers did daily shifts on board ships, on wharfs and in yards and warehouses in the port of Ravenna. Among other jobs, they would prepare piles of asbestos-containing canvas sacks in the hold ready for hoisting by crane onto the quayside, from where they would be loaded onto railway trucks or stored in warehouses. Sacks would occasionally burst and their contents pollute the surrounding environment. In time canvas was replaced by tougher plastic. Another source of pollution to wares in transit was the asbestos insulation on board ships which included the hold. Small quantities of asbestos were also stored loose in ships' holds.

Clinical anamnesis
A right-kidney neoplasia was discovered in 1980. Histological examination of the portion excised under eradication surgery revealed the presence of: eosinophilic, tubulo-papillary renal adenocarcinoma.

Years of exposure: 19; latency: 18 years; age at diagnosis: 43.

Case 12

ED, born on 2/11/1926 at Ravenna and resident there. Light smoker as a young man.

Work anamnesis
– 1937-1959: worked on the land.
– 1960-1984: worked for the Ravenna Compagnia Portuale as a navy/crane operator handling goods.
– 1984: retired.

Exposure scenario
Similar to case 11.

Clinical anamnesis
A right-kidney neoplasia was discovered in 1995. Histological examination of the portion excised under eradication surgery revealed the presence of: carcinoma of clear-cell type.

Years of exposure: 24; latency: 35 years; age at diagnosis: 69.

Case 13

GG, born on 18/2/1949 in the province of Ravenna and lived in Ravenna. Moderate smoker.

Work anamnesis
– 1972-1992: worked for the Ravenna Compagnia Portuale as a navy/crane operator handling goods.
– 1992: retired.

Exposure scenario
Similar to case 11.

Clinical anamnesis
A left-kidney neoplasia was discovered in 2004. Histological examination of the portion excised under eradication surgery revealed the presence of: tubulo-papillary renal carcinoma.

Years of exposure: 20; latency: 32 years; age at diagnosis: 55.

Case 14

VM, born at Modena on 24/1/1941 and resident there. Non-smoker.

Work anamnesis
– 1963-1966: worked for the Modena firm of Carrozzeria Emiliana making, installing and repairing electric cable on the work-bench and on board buses (electrician).
– 1966-1991: worked for the Modena firm of Officine Padane SpA making, installing and repairing electric cable on the work-bench and on board buses (electrician).
– 1992: retired.

Exposure scenario
Handling asbestos-board panels used as a thermal barrier between electric control-boards and engines; also asbestos-cord conduits to protect cables from sources of heat. At that time vehicles had mechanical parts (brakes, clutch) and coachwork (engine insulation, exhaust and turbine casing, pipe protection, etc.) in asbestos. For maintenance operations the engine insulating barrier would often be pierced by drills or hollow mills to pass electric cables through. This produced asbestos dust which was easily inhaled, as described in the 1985 technical report by the Modena Health Service Preventive Medicine & Workplace Hygiene Department: this found that asbestos was present not just where work was performed but in the remotest places. Contamination of the Officine Padane SpA depended chiefly on the habit of cleaning engines by blasts of compressed air which circulated fibres that had already settled.

Clinical anamnesis
A left-kidney neoplasia was discovered in 2007. Histological examination of the portion excised under eradication surgery revealed the presence of: clear-cell renal carcinoma.

Years of exposure: 28; latency: 44 years; age at diagnosis: 66.

Case 15

IB, born in the province of Reggio Emilia in 21/8/1930; died at Reggio Emilia on 9/9/2008, aged 78. Non-smoker (3-4 cigarettes/day until age 50).

Work anamnesis
– Until 1974 self-employed carpenter.
– 1974-1975: worked as a carpenter for Officine Meccaniche at Leoni di Bogolese, Sorbolo (near Parma) (this period not considered in the overall exposure calculation).
– 1975-1987: worked as a carpenter insulating railway carriages for the bus-train company "*Gallinari SpA*" (railway section) at Reggio Emilia.

Exposure scenario
Fitting and maintaining railway carriages insulated with asbestos. Consequently exposed to environmental contamination. Scenario like case 3. The exposure was recognised by INAIL as a factor causing carcinoma of the larynx which he developed in 2003.

Clinical anamnesis
A left-kidney neoplasia was discovered in 2006. Histological examination of the portion excised under eradication surgery revealed the presence of: malignant renal neoplasia.

Years of exposure:12; latency: 31 years; age at diagnosis: 76.

Case 16

FM, born at Rimini on 16/6/1934 and resident there. Non-smoker.

Work anamnesis

– 1954-1992: worked for the Rimini State Railways as a hand in the locomotive depot (until 1962), steam-engine assistant and stoker (until 1968), steam-engine driver (until 1973), diesel engine driver (until 1980) and later driver of electric engines.

Exposure scenario

FM was an assistant/stoker involved in keeping up pressure in locomotive boilers waiting in the depot, stoking the fire, cleaning out clinker, topping up boiler water and lubricant oil levels. His work brought him in contact with a number of substances including asbestos. Most of an engine-driver's work was inside cabs forming part of carriages, so the exposure was similar to case 3.

Clinical anamnesis

A vesical neoplasia was discovered in 2009. Histological examination of the portion excised under eradication surgery revealed the presence of: highly malignant carcinoma of the bladder, infiltrating the perivisceral muscle and adipose tissue.

Years of exposure: 38; latency: 55 years; age at diagnosis: 75.

Case 17

LC, born in the province of Bologna on 28/5/1937. Non-smoker.

Work anamnesis

– 1974-1990: worked for the firm of Edoardo Weber – Fabbrica Italiana Carburatori, which became Magneti Marelli of Crevalcore (near Bologna); his job was a smelter and forklift operator in the die-casting section.

Exposure scenario

Magneti Marelli Powertrain S.p.A. produces engine control systems for motor vehicles, including injectors, engine control panels, baffle devices, hydraulic pumps and transmissions.

It has three main departments: 1) die-casting of aluminium components; 2) plastic component moulding; 3) manifold assembly. Workers are exposed to various toxic and carcinogenic substances including aluminium, polycyclic aromatic hydrocarbons (PAH) and asbestos. At least until the Nineties those working in the die-casting department were heavily exposed to asbestos since the kilns were lined with asbestos panels and cord. These needed periodic on-site maintenance, involving cutting panels and cords and consequently releasing dust into the environment. When work had to be done inside a kiln, for example electric repairs, they used asbestos sheeting and mattresses which were friable and would be cut to fit on the spot, releasing large quantities of fibre into the workplace. Again, to protect their bodies during very high temperature operations, workers would use asbestos protection, such as gloves, aprons and sheets. These would release asbestos fibres into the environment as they got damaged by thermal and mechanical stress.

Clinical anamnesis

A left-kidney neoplasia was discovered in 1990. Histological examination of the portion excised under eradication surgery revealed the presence of: nephrocarcinoma of clear-cell (70%) and granulous eosinophilic (30%) type.

Years of exposure: 16; latency: 16 years; age at diagnosis: 53.

Case 18

BG, born in the province of Bologna on 5/3/1927. Non-smoker.

Work anamnesis

– 1976-1983: worked for the firm of Edoardo Weber – Fabbrica Italiana Carburatori, later becoming Magneti Marelli of Crevalcore (near Bologna); his job was a smelter and forklift operator in the die-casting section. NFDA.

Exposure scenario

Similar to case 17.

Clinical anamnesis

A left-kidney neoplasia was discovered in 2004. Histological examination of the portion excised under eradication surgery revealed the presence of: multifocal transitional cell carcinoma.

Years of exposure: 7; latency: 28 years; age at diagnosis: 77.

Case 19

MM, born in the province of Bologna on 2/2/1949. Non-smoker.

Work anamnesis

– 1970-2002: worked for the firm of Edoardo Weber – Fabbrica Italiana Carburatori, later becoming Magneti Marelli of Crevalcore (near Bologna); his job was test-inspector working in all departments, including die-casting.

Exposure scenario

Similar to case 17.

Clinical anamnesis

Neoplasia of the right ureter was discovered in 2001. Histological examination of the portion excised under eradication surgery revealed the presence of: papilliferous ureteral carcinoma.

Years of exposure: 32; latency: 31 years; age at diagnosis: 52.

Case 20

EB, born in the province of Modena on 12/4/1952. Non-smoker.

Work anamnesis

– 1974-2012: worked for the firm of Edoardo Weber – Fabbrica Italiana Carburatori, later becoming Magneti Marelli of Crevalcore (near Bologna); his job was electric/electronic maintenance operator working throughout the company, including the die-casting department.

Exposure scenario

Similar to case 17.

Clinical anamnesis
A left-kidney neoplasia was discovered in 2001. Histological examination of the portion excised under eradication surgery revealed the presence of: clear-cell renal carcinoma.

Years of exposure: 38; latency: 27 years; age at diagnosis: 49.

Case 21
EM, born in the province of Bologna on 24/12/1936. Non-smoker.

Work anamnesis
- 1962-1970: worked about 10 months per year at Arra-Artigianato Ravarinese as a basket-maker.
- 1962-1970: seasonal work (~ 2 months/yr) at the Crevalcore Sugar refinery (near Bologna) as a factory hand.
- 1971-1986: more or less continuously employed by the Crevalcore Sugar refinery as a factory hand.
- 1986-1991: worked for the firm of Edoardo Weber – Fabbrica Italiana Carburatori, later becoming Magneti Marelli of Crevalcore (near Bologna); his job was loader/unloader of kilns in the die-casting department.

Work scenario
When working as a basket-maker, EM was certainly exposed occupationally to aromatic amines which have long been known to cause bladder cancer. However, the exposure was relatively short (~ 6 years) and intermittent. One thus also notes the con-causal role of asbestos which he was heavily exposed to right from his sugar-refinery seasonal days and through to continuous employment at Magneti Marelli. As mentioned in case 8, asbestos was greatly used at sugar refineries both in building (gaskets, linings, joints, cables, roofing) and in insulating boilers, pipes and equipment in asbestos-cement, tapes, sheeting and asbestos board – nearly all without any intact outer protective covering. Maintenance operations involved, for example, replacing and cutting out sections of piping, changing and shaping (by hand) gaskets on boilers and heating plants. Fibres released on such occasions dispersed throughout the workplace and cold be inhaled by anyone, whatever their duties. Cleaning was done by broom and hand, leaving dust and asbestos on the floor for days, so that it could easily become airborne again. EM's exposure scenario at Magneti Marelli is similar to case 17.

Clinical anamnesis
A vesical neoplasia was discovered in 1993. Histological examination of the portion excised under eradication surgery revealed the presence of: transitional papillary carcinoma.

Years of exposure: 29; latency: 31 years; age at diagnosis: 57.

Case 22
OS, born in the province of Modena on 20/4/1947. Non-smoker.

Work anamnesis
- 1974-1985: worked for the firm of Claudio Barani at Nonantola (near Modena) as a welder.
- 1985-1987: worked for the firm of Officine Padane SpA as a welder. The same industrial unit housed operations of maintenance and spraying of buses and other vehicles without use of aspirators.
- 1987-1989: worked for the firm of Schiavi Padane SpA as a welder. The same industrial unit housed operations of maintenance and spraying of buses and other vehicles without use of aspirators.
- 1989-1998: worked for the firm of Bobst Group Italia SpA as a welder. The same industrial unit housed operations of maintenance and spraying of buses and other vehicles without use of aspirators at least until 1995 when they moved to a new building.

Exposure scenario
Similar to case 14.

Clinical anamnesis
A right-kidney neoplasia was discovered in 2009. Histological examination of the portion excised under eradication surgery revealed the presence of: clear-cell carcinoma infiltrating the cava inferior and pancreas.

Years of exposure: 24; latency: 35 years; age at diagnosis: 62.

Case 23
DG, born in the province of Ferrara on 14/6/1956. Ex-smoker (had stopped for 15 years).

Work anamnesis
- 1973-1980: worked for the firm of Sasib SpA at Castel Maggiore (near Bologna) which produces machinery and systems for the tobacco industry; his job was that of looking after milling tools (this period not calculated in the overall exposure).
- 1980 till now: DG still works for the firm of Edoardo Weber – Fabbrica Italiana Carburatori, later becoming Magneti Marelli of Crevalcore (near Bologna); his job is to maintain moulds in the die-casting department.

Exposure scenario
Similar to case 17.

Clinical anamnesis
A vesical neoplasia was discovered in 2008. Histological examination of the portion excised under eradication surgery revealed the presence of: transitional carcinoma.

Years of exposure: 32; latency: 28 years; age at diagnosis: 52.