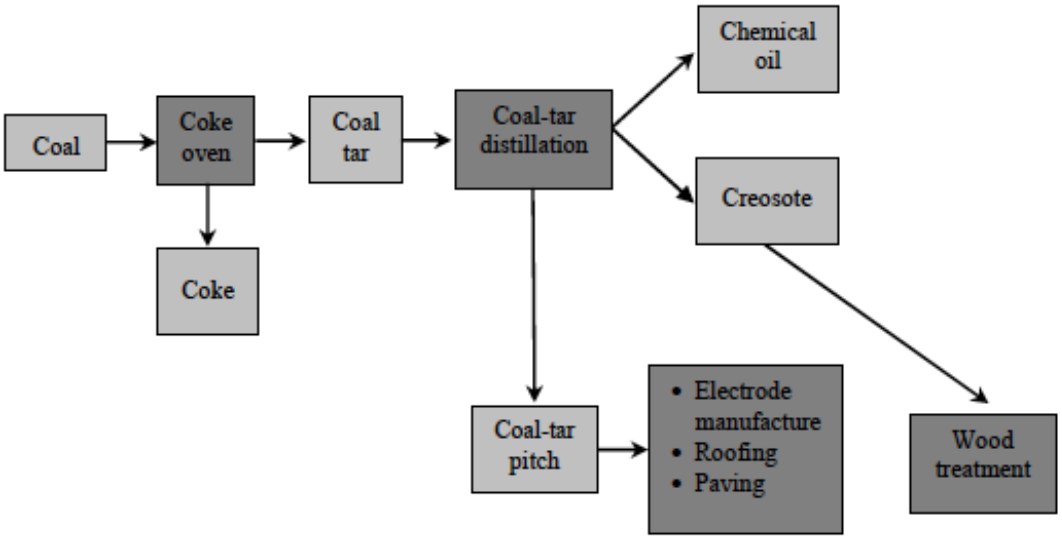
煉焦爐作業引起之肺癌認定參考指引

一、導論

十八世紀以降，自英國開展的工業革命促成人類歷史的進步；十八世紀中葉，英國人瓦特改良蒸汽機，技術革命引起了從手工勞動向動力機器生產的重大飛躍，蒸汽機、煤、鐵和鋼是促成工業革命技術加速發展的四項主要因素。

煤焦（coke）為工業革命後鋼鐵工業裡高爐的主要燃料；煙煤(bituminous coals/soots)在煉焦爐內的無氧環境中加熱乾餾至攝氏1000-1400度，生成以碳元素為主和極少量氫、氧、氮、硫的固態產物煤焦（coke），此過程會精煉出焦油(tar)及輕油(light oils)並產生「煉焦爐蒸氣」(Coke-oven emissions)。經化學分析，煉焦爐蒸氣內含許多已知人類致癌物和潛在致癌物，包括40種以上的多環芳香烴(PAHs)、甲醛(formaldehyde)、丙烯醛(acrolein)、脂肪醛(aliphatic aldehydes)、氨(ammonia)、一氧化碳(carbon monoxide)、氮氧化物(nitrogen oxides)、苯(benzene)、酚(phenol)、鎘、砷和汞的氣體混合物、亞硝胺(nitrosamines)、煤焦油(coal tar)；此外，亦含有數種加強呼吸道效應的致癌物質。[1,2]國際癌症研究中心(IARC)將煤焦油、瀝青及相關製程揮發物所產生的多環芳香烴類物（Non-heterocyclic Polycyclic Aromatic Hydrocarbons）列為第一類人類致癌物。[2]

Figure 1.2. Simple schema for generation of coal tar and coal-tar products



具潛在性暴露之職業：

煉焦爐及煤焦油相關產業及工作場所包括：

1.煤焦油汽化（coal gasification、coal-tar preparation、distillation）製備工業。

2.煤焦、瀝青、焦碳（coke production）製備工業。

3.煙囪清掃工人。

4.煤精煉工人。

5.柏油、瀝青道路鋪設工人。

6.鋁精煉工廠。

7.電極製造工廠。

8.碳煙製造工廠

9.鑄造物混砂工廠

二、醫學評估與鑑別診斷

(一)臨床症狀

肺癌病人的臨床表現可能與局部腫瘤生長，侵犯鄰近的結構，腫瘤轉移有關，也有可能發生腫瘤附屬症候群(paraneoplastic

syndrome)，因腫瘤分泌激素不當而導致鈣離子、鈉離子和鉀離子等電解質失常。原發腫瘤通常造成咳嗽、痰中帶血、哮鳴、呼吸困難、胸痛、或因阻塞引起的肺炎。晚期可能因腫瘤轉移或因對血管、神經、心臟、食道、骨骼等器官直接侵犯或壓迫而造成各種症狀；腫瘤的擴散可造成氣管的阻塞或食道的壓迫，以及血管結構之壓迫所引起的上腔靜脈症候群(superior vena cava syndrome)。周邊神經系統可能受影響，喉返神經(recurrent laryngeal nerve)麻痺造成聲音嘶啞，交感神經侵犯引起Horner's 症候群(患側上眼瞼下垂，縮瞳，患側皮膚乾燥)，或膈神經麻痺。非特異性的症狀，如體重減輕、食慾變差，疲倦等，可以很明顯。

(二)實驗室檢查

痰液細胞學檢查大約可診斷出60%的肺癌案例，使用軟式光纖支氣管鏡檢查在肺癌病人可看見65%的病灶，支氣管粘膜切片(Biopsy)和刷檢(brushing)大致可診斷出90%的病灶。透過X光透視指引(fluoroscopic guidance)進行經胸壁細針抽取術(transthoracic fine-needle aspiration)可運用在支氣管鏡檢查不到的周圍型腫瘤。如果上述較不具侵襲性的診斷工具無法確診時，可能需做探查式胸廓切開術(exploratory thoracotomy)。

(三)影像學檢查

胸部X光是診斷肺癌最重要的工具之一。胸部X光的發現與腫瘤細胞型態，腫瘤位置，及是否有局部侵犯有關。鱗狀細胞癌(squamous cell carcinoma)較常位於中央，合併肺門淋巴結腫大(hilar adenopathy)；肺腺癌(adenocarcinoma)較常表現為周圍型腫瘤結節，並侵犯胸膜及胸壁；大細胞肺癌(large cell carcinoma)則為一個周圍型大腫塊，合併肺炎；中央型腫瘤，合併肺塌陷(atelectasis)及肺門與縱隔腔淋巴結腫大，是小細胞肺癌(small cell carcinoma)常見的特徵。以胸部電腦斷層可較準確地決定肺癌的程度；電腦斷層及高解析度電腦斷層(high resolution computed tomography, HRCT)也能助於診斷肺癌。

（四）鑑別診斷

肺結核(pulmonary tuberculosis)

其他肺炎(pneumonia, bacterial or fungal infection)

類肉瘤症（sarcoidosis）

良性肺部腫瘤（benign lung tumor）

三、流行病學證據

（一）人類研究

在1950之前有許多關於焦煤製造工人發生皮膚癌、膀胱癌和呼吸道癌症的案例。自此開始，美國、英國、日本和瑞士的許多世代研究也都有發現當人類暴露到煉焦爐排放的廢氣時會增加人類肺癌的危險性，而有一些研究也有把抽菸考因素考量進去，但不會干擾所發現的結果。在1969年一個有59000位員工的大型鋼鐵世代研究發現，暴露到煉焦爐排放的廢氣的時間越長、強度越強的話肺癌風險也會越高。許多煉焦爐工廠員工的研究也顯示會增加腎臟癌的風險。此外，關於其他部位的癌症(攝護腺、大腸和胰臟)並沒有超過一個研究有發現。(IARC monograph p122-123, 1984, 1987)

Table 2.1. Cohort and linkage studies of coal gasification workers

Reference, location	Cohort description	Exposure assessment	Organ site	Exposure categories	No. of cases/ deaths	SMR (95% CI)	Adjustment for potential confounders/Comments
Kennaway & Kennaway (1947), United Kingdom	Register-based national mortality analysis of all deaths in England and Wales, 1921–38	Occupational titles	Lung	Gas works labourers	96	1.29 [1.04–1.57]	No data available on tobacco smoking
				Gas producers (male)	12	2.03 [1.05–3.55]	
			Larynx	Gas works labourers	43	0.90 [0.65–1.22]	
				Gas producers (male)	2	0.59 [0.07–2.12]	
Kawai *et al.* (1967), Japan	503 workers at a generator gas plant in a steel industry followed from 1953 to 1965; the plant was closed down in 1953.	Occupational titles	Lung	Gas generator plant	6	33.3 [12.2–72.6]	Precision in the estimation of expected numbers was low.
Doll *et al.* (1972), United Kingdom	3023 gas manufacturing workers aged 40–65 years employed at, or in recpt of pension from, four gas boards ('original gas boards') followed for mortality from 1953 to 1965; minimum duration of employment, 5 years	Occupational titles at start of study	Lung	Heavy exp. to coal gas (A)	99	1.79 [1.46–2.18]	Tobacco smoking habits studied in a 10% sample of the cohort indicated no excess. No excess of atheros-clerotic heart disease supports that smoking habits were not excessive among the gas workers.
				Low or no exp. (C1)	11	0.75 [0.37–1.34]	
			Bladder	Heavy exp. to coal gas (A)	10	2.35 [1.13–4.33]	
				Low or no exp. (C1)	1	[0.77 (0.02–4.29)]	
			Skin	Heavy exp. to coal gas (A)	3	6.0 [1.24-17.5]	
				Low or no exp. (C1)	0 (not possible to calculate expected number)	–	
	4687 men from four additional gas boards followed for mortality from 1957 (one gas board from 1959) to 1965		Lung	Heavy exp. to coal gas (A)	23	1.34 [0.85–2.01]	
				Intermittent exp. (B)	40	1.72 [1.23–2.35]	
				Low or no exp. (C2)	16	0.53 [0.30–0.86]	
			Bladder	Heavy exp. to coal gas (A)	2	1.53 [0.19–5.54]	
				Intermittent exp. (B)	2	1.07 [0.13–3.85]	
				Low or no exp. (C2)	1	[0.40 (0.01–2.23)]	

Table 2.1 (Contd)

Hansen *et al.* (1986), Esbjerg, Denmark	47 gas production workers employed >1 year any time between 1911 and 1970.; an age-matched reference cohort of 141 persons selected from population registers		Lung		7	**OR** 3.94 (p <0.05)	No data on tobacco smoking habits available; analytical method may not have been appropriate. A shorter time to death from lung cancer was noted among the gas wokers than among the referent cohort (p = 0.01)
Wu (1988), China	3107 workers active in 1971 at any of six coal gas plants followed for mortality until 1982		Lung		[not stated]	SRR (90% CI) 3.66 (2.36–5.43)	The short report does not allow an assessment of the validity of the study.
Gustavsson & Reuterwall (1990), Stockholm, Sweden	295 male blue-collar workers from a gas production plant in Stockholm employed > 1 year between 1965 and 1972; followed for mortality from 1966 to 1986 and for cancer incidence from 1966 to 1983	Department	Lung Nose and sinuses	Entire cohort Coke-oven department Entire cohort	4 0 (0.9 expected) 2	1.35 (0.36–3.46) – 29.57 (3.57–106.89)	
Berger & Manz (1992), Hamburg, Germany	4908 male employees from a gas- producing plant, employed >10 years between 1900 and 1989 were followed for mortality from 1953 to 1989	Department	Lung Stomach Colon and rectum	Gas furnace workers Other labourers White-collar workers Gas furnace workers Other labourers White-collar workers Gas furnace workers Other labourers White-collar workers	78 102 12 31 72 10 13 48 7	2.88 (2.28–3.59) 0.96 (0.78–1.17) 0.45 (0.23–0.79) 1.77 (1.20–2.51) 1.13 (0.88–1.42) 0.57 (0.27–1.05) 1.84 (0.98–3.15) 1.70 (1.25–22.5) 0.92 (0.37–1.90)	Data on tobacco smoking available for about 80% of the cohort; no smoking- adjusted SMR for lung cancer was presented. Causes of death were obtained by different methods for the cohort and the national reference group.

Table 2.1 (Contd)

Martin *et al.* (2000), France	Case–control study nested within a cohort of male workers employed >1 year at a company producing gas and electricity. 310 lung cancer cases occurring between 1978 and 1989 were included, 1225 referents were selected from the cohort.	Industry-specific job–exposure matrix with index of cumulative exposure	Lung	Coal gas production Unexposed Q1 Q2 Q3 Q4	 298 7 7 7 5	 1.0 1.02 (0.21–4.94) 1.59 (0.39–6.49) 0.55 (0.07–4.57) 3.87 (1.15–12.9)	Risks adjusted for exposure to asbestos and socioeconomic status. There may be residual confounding from tobacco smoking.

(二)動物研究

關於煉焦爐排放廢氣的致癌性動物研究證據是足夠的，暴露到煉焦爐排放的廢氣會導致兩種品系老鼠的腫瘤。連續52週，每週將煉焦爐排放物塗到老鼠皮膚上會導致皮膚癌，顯示這些物質也有tumor initiation的角色。在許多的研究發現，吸入煉焦爐排廢氣會導致老鼠肺部發生良性和惡性腫瘤，除此之外也會導致雌性老鼠的皮膚腫瘤。(IARC 1984)

(三)有關致癌機轉的研究

煉焦爐排放物的化學物質分析發現裡面有許多已知致癌物、極可能致癌物，像是多環芳香碳族、硝酸鹽、焦油、砷化合物和苯。除此之外，煉焦爐排放廢氣中也有許多已知會增加化學致癌性的物質，特別是會對呼吸道造成影響。(IARC 1984)

煤焦油、瀝青、油，及焦炭之不完全燃燒所產生的多環芳香烴(PAHs)，長久以來被認定是致癌物。最早提出PAHs致癌是1775年Pott報告清掃煙囪工人因為皮膚暴露於煤灰以致陰囊癌風險增高。PAHs與肺癌相關的流行病學證據是1936年日本一家煤炭焦化工廠的暴露工人肺癌發生率顯著增加[Rugo, 2007]。

暴露於PAHs 與肺癌風險增高的關連性已經在煉焦爐作業（coke oven emissions），屋頂維修工人(roofers)，印刷工人，卡車司機中發現。此外，橡膠廠工人，以及瀝青製造，煤炭氣化(coal gasification)，焦炭生產(coke production)鋁還原電解設備的員工也有暴露的風險。最佳呈現PAHs暴露的職業是煉焦爐工人，直接暴露於煉焦爐會增加肺癌的風險，工人與煉焦爐的距離有明顯的劑量效應關係[Rugo, 2007]。王榮德曾報告台灣煉焦爐工人罹患職業性肺癌的案例[Wang, 1991]。

四、暴露證據收集之方法

(一)個人工作史、工作時間、作業名稱、作業環境控制情形均需詳細紀錄。

(二)環境偵測

煉焦爐排出物及多環芳香烴(PAHs)化合物以採樣管收集後，以苯或環己烷萃取，可以氣相層析儀分析，定量個體之吸入量。

(三)生物偵測

可偵測尿液中1-hydroxy-pyrene(1-OHP)之含量，或測量DNA結合物[3]。

(四)容許濃度標準

1.煤焦油產品(蒸發物)(Coal tar products, volatiles)：

(1)美國工業安全衛生技師協會(ACGIH) TLV：確定人類致癌物

(2)美國職業安全衛生研究所(OSHA) PEL：0.2mg/m3 TWA

(3)美國職業安全研究所(NIOSH) REL：0.1mg/m3

(4)我國容許濃度標準：0.2mg/m3

2.萘(Naphthalene)：

(1)美國工業安全衛生技師協會(ACGIH)TLV：10ppm TWA, 15ppm STEL

(2)美國職業安全衛生研究所(OSHA) PEL：10ppm TWA, 15ppm STEL

(3)美國職業安全研究所(NIOSH) REL：10ppm TWA, 15ppm STEL

(4)我國容許濃度標準：10ppm

3.瀝青精(Bituments)：

美國職業安全研究所(NIOSH) REL：5mg/m3 ceiling (15 minutes)

4.碳黑(Carbon black)：

(1)美國工業安全衛生技師協會(ACGIH) TLV：3.5mg/m3 TWA

(2)美國職業安全衛生研究所(OSHA) PEL：3.5mg/m3 TWA

(3)美國職業安全研究所(NIOSH) REL：3.5mg/m3 ; in presence of PAH, 0.1mg/m3 TWA

(4)我國容許濃度標準：3.5mg/m3

5.蒽(Anthracene)：

(1)美國工業安全衛生技師協會(ACGIH) TLV：0.2mg/m3 TWA

(2)美國職業安全衛生研究所(OSHA) PEL：0.2mg/m3 TWA

(3)美國職業安全研究所(NIOSH) REL：0.01mg/m3(環己烷可萃取部份)

6.安息香比林(Benzoapyrene)：

(1)美國工業安全衛生技師協會(ACGIH) TLV：疑似人類致癌物，no TWA

(2)美國職業安全衛生研究所(OSHA) PEL：0.2mg/m3 TWA

(3)美國職業安全研究所(NIOSH) REL：0.01mg/m3

四、總結

(一)主要基準

1.疾病證據：

有明確的疾病證據證實為原發性之肺癌；肺組織切片等病理檢查證實肺癌，或細胞學檢查證實有肺癌細胞並且配合實驗室及影像學檢查之證據。

2.暴露證據：

(1)工作史及作業場所調查：

在煉焦爐頂部工作至少五年。或在非煉焦爐頂工作至少十五年。或同時在煉焦爐頂頂和其他部門工作，爐頂作業一年約相當於其他部門工作三年，再將工作年限換算成其他部門的年資至少十五年。

(2)若可行，測量作業環境中煤焦油產品(蒸發物)、萘、瀝青精、碳黑、蒽、安息香比林等濃度，並與管制標準(permissible exposure limit)比較。

(3)若可行，提出該認定致癌物之已被人體吸收的證據，含生物偵測(biological monitoring)，如尿液中1-hydroxy-pyrene(1-OHP)之含量，或測量DNA結合物[3]

3.時序性：

在煉焦爐頂部工作至少五年；或在非煉焦爐頂工作至少十五年；或同時在煉焦爐頂頂和其他部門工作，爐頂作業一年約相當於其他部門工作三年，再將工作年限換算成其他部門的年資至少十五年。

4.合理排除其他原因：

如吸菸，個案終生累積吸菸暴露量在15 pack-year 以內者以及戒菸超過15年者，則可視其吸菸之致癌性為低度風險，相對於職業暴露的致癌物，未達顯著差異之危險因子。另亦需注意抽菸與該致癌物質為相加或相乘性之關係。

若個案不抽菸則視為無干擾因子, 個案總抽菸量15pack-year 以內者以及戒菸超過15 年者可視其抽菸之致癌性為低度風險,另亦需注意抽菸與該致癌物質為相加或相乘性之關係。

職業性致癌物暴露引起肺癌的相對風險在2倍及以上者(RR≧2)，其致癌強度即足以合理排除其他原因。若無法排除其他原因，可依專家共識決定職業性致癌物暴露為一有意義的共同致病因子。

(二)輔助次要基準

1.癌症個案發生有時空的叢集性（cluster），例如同一工作場所至少

超過一個以上的人發生相同種類癌症，臨床判斷比例明顯偏高，也可作為懷疑是職業性癌症的輔助判斷基準，建議進行流行病學調查。

2.作業環境空氣中致癌物濃度測定記錄資料，可作為職業暴露的證據。

五、參考文獻

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(三)Biomonitoring of polycyclicaromatichydrocarbons in human urine, Journal of Chromatography B, Volume 778, Issues 1–2, 5 October 2002, Pages 31–47

(四)英國「Department for Work and Pensions」2011 年發表有關『煉焦爐勞工之肺癌』認定指引 （請見附件一）

附件一）

以下為英國「Department for Work and Pensions」2011 年發表有關『煉焦爐勞工之肺癌』認定指引之原文摘要：

Introduction

In 1986 the Industrial Injuries Advisory Council (IIAC) published its Command paper 'Occupational Lung Cancer' which included consideration of hematite (iron ore) miners, coke oven/gas retort workers, foundry workers (heat treatment loaders, furnace men, fettlers, foundry laborers, furnace repairers, iron and steel foundry workers), rubber workers, manufacturers of man-made mineral fibers, workers exposed to formaldehyde and fur skin workers. At that time there was insufficient evidence to warrant prescription for any of these occupations, but IIAC agreed to keep the matter under review. In September 2009 the Council revised the evidence relating to these occupational categories and now finds that evidence relating to lung cancer in coke oven workers is sufficiently strong to consider prescription for this exposure. The other occupational categories have been ('Lung cancer in foundry workers', 'Silica and lung cancer in the absence of silicosis'), or will be, considered in separate reports.

Clinical features

For some diseases attribution to occupation may be possible from specific clinical features of the individual case. For example, the proof that an individual's dermatitis is caused by his/her occupation may lie in its improvement when s/he is on holiday, and regression when they return to work, and in the demonstration that they are allergic to a specific substance with which they come into contact only at work. It can be that the disease only occurs as a result of an occupational hazard (e.g. coal workers' pneumoconiosis).

Doubling of risk

Other diseases are not uniquely occupational, and when caused by occupation, are indistinguishable from the same disease occurring in someone who has not been exposed to a hazard at work. In these circumstances, attribution to occupation on the balance of probabilities depends on epidemiological evidence that work in the prescribed job, or with the prescribed occupational exposure, increases the risk of developing the disease by a factor of two or more.

The requirement for, at least, a doubling of risk follows from the fact that if a hazardous exposure doubles risk, for every 50 cases that would normally occur

in an unexposed population, an additional 50 would be expected if the population were exposed to the hazard. Thus, out of every 100 cases that occurred in an exposed population, 50 would do so only as a consequence of their exposure while the other 50 would have been expected to develop the disease, even in the absence of the exposure. Therefore, for any individual case occurring in the exposed population, there would be a 50% chance that the disease resulted from exposure to the hazard, and a 50% chance that it would have occurred even without the exposure. Below the threshold of a doubling of risk only a minority of cases in an exposed population would be caused by the hazard and individual cases therefore could not be attributed to exposure on the balance of probabilities; above it, they may be.

The epidemiological evidence required should ideally be drawn from several independent studies, and be sufficiently robust that further research at a later date would be unlikely to overturn it.

Lung cancer is not exclusively occupational and does not have unique clinical features when it occurs in an occupational context. The case for prescription, therefore, rests on reliable evidence of a doubling or more of risk in coke oven workers after allowance for other non-occupational risk factors.

Lung cancer

Lung cancer is the second most common cancer in the United Kingdom with around 39,000 people diagnosed per year. The predominant risk factor for lung cancer is cigarette smoking (associated with 9 out of 10 cases). Other risk factors include exposure to certain substances, such as asbestos or radon, or familial predisposition. Over two-thirds of people diagnosed with lung cancer are over 65 years old.

Lung cancers can be classified into two types: small cell lung cancers and non-small cell lung cancers based on the appearance of the tumor cells under a microscope. The latter is the most common form, accounting for 80% of all lung cancers.

Symptoms of lung cancer include cough, shortness of breath, coughing up blood stained sputum, chest pain and loss of appetite or weight. Lung cancer can be diagnosed by chest radiograph, computer tomography (CT) or magnetic resonance imaging (MRI) scans, or bronchoscope with lung biopsy. Treatment may include chemotherapy, radiotherapy or surgery. The prognosis for lung cancer is highly dependent on the progression and type of the tumor.

Coke oven work

Coke is produced in coke making plants, by blending and heating coal at high temperatures in the absence of oxygen. These plants transform coal into a dense, crush resistant fuel, known as coke, for use in blast furnaces and other industries and allow the collection of usable chemical and gas by-products, such as ammonia, benzene, toluene, tar, oil and methane. A coke making plant consists of the coal handling area, the coke oven batteries (where coke is produced), the coke handling area and the by-products plant.

Coke batteries are organized into large numbers of ovens, typically 25 to 66 ovens on each battery grouped in one, two (most often) or three operating units, comprising of 42-88 chambers which are made up of heating chambers, coking chambers and regenerative chambers (for storing and re-using heat). The ovens are arranged side-by-side and charged and discharged in a cyclical manner in a continual process. Coal is charged through holes in the top of the oven, and then coke is discharged through doors located at the sides of the oven and sent to the coke handling plant, while by-products are routed through pipes to the by-product plant.

In the UK, coke is used mostly in blast furnaces at integrated iron and steel works. Currently there are 6 coke making plants in the UK, 5 of which are situated at integrated steel works. Coke may also be used in the synthesis of calcium carbide.

Health Risks

Coke oven emissions are complex mixtures of chemicals and gases which may include known or suspected carcinogens and toxins, such as polycyclic aromatic hydrocarbons (PAHs), formaldehyde, phenol, cadmium, arsenic and mercury. Coke oven emissions have been linked to various cancers, including lung cancer, the focus of the present report.

Consideration of the evidence

A number of studies investigating the link between exposure to coke oven emissions and lung cancer have been carried out since the early 1960s. The majority of these have been cohort studies in which the rate of death due to lung cancer in coke plant workers is compared to that either in the general population, or in another worker population. Cohort studies typically overcome the practical problem of long latency (the many years an investigator has to wait between exposure and cancer onset) by studying populations in retrospect using records of employment, linked with databases of cancer registry or more usually death certification. Such studies usually focus on specific workforces and contain information about employment duration, sometimes supplemented by supporting exposure measurements.

However, they rarely contain information on important confounders such as the smoking habits of the workforce, an important factor in studying causes of lung cancer.

Much of the evidence in this field derives from a single long-term mortality study carried out by a research group at Pittsburgh University in the USA and published in a series of papers between 1969 and 1983. The results of this study provide the most compelling evidence for an association between employment as a coke worker and lung cancer.

The original cohort consisted of 58,828 steelworkers employed in 1953 at seven plants in Allegheny County, Pennsylvania. The seven plants included two coke plants employing 2,543 workers (subsequently termed the 'Allegheny cohort'). Steel workers who had never worked in the coke plants were used as a comparison group for calculating expected deaths and mortality ratios. Findings over the first follow-up period, from 1953-1961, indicated an excess risk of lung cancer in coke plant workers overall (Relative Risk (RR) 1.70, $p<0.05$) (Rockette and Redmond, 1985). However, separate analysis for coke oven workers showed that in this group the risk was more than doubled (RR 2.48, $p<0.01$), while that for non-oven workers was 0.47.

Subsequent follow-up of this cohort to 1966, and later to 1970 confirmed a significantly increased risk which was confined specifically to coke oven workers (Redmond *et al.*, 1976). In 1966, for cancer of the lungs, bronchus and trachea, the RR for coke oven workers (n=1,316) was 3.31 ($p<0.01$) and for non-oven workers (n=1,227) it was 1.01. The difference in risk associated with the two groups was accentuated when workers only employed for more than five years were considered (oven workers RR 3.67, $p<0.01$, non-oven workers RR 0.51).

In the 1970 report, coke oven workers were further sub-divided into three exposure groups reflecting increasing duration of exposure. The results indicated increasing risk with employment duration (5 or more years, RR 3.02; 10 or more years, RR 3.42; 15 or more years RR 4.14). In all cases $p<0.01$.

In the 1970 follow-up further analysis on the basis of employment type indicated higher risks in topside oven workers than side oven workers. For those employed full-time as topside oven workers RRs for the three employment duration groups were 9.19, 11.79 and 15.72 respectively (in each case $p<0.01$). For those employed part-time as topside oven workers the respective figures were 2.29, 3.07 and 4.72 (in each case $p<0.01$). For side oven workers the figures were 1.79, ($p<0.005$); 1.99, ($p<0.05$) and 2.00, (not statistically significant) (Rockette and Redmond, 1985).

In addition to this analysis of the Allegheny cohort a further follow-up to 1966 was carried out which included the Allegheny cohort plus ten additional plants, (the 'non-Allegheny cohort'), situated in various locations around the US and Canada. This additional cohort included all coke oven workers (n=4,661), who were compared with other workers matched on age, employment date and race. All participants had been originally employed between 1951 and 1955 and follow-up was from 1951. A particular focus of this analysis was the investigation of suggestions of a higher risk among non-white workers. Results indicated similar risks in white and non-white workers when exposure levels were taken into account. Overall the RR for workers employed in all plants was 2.85, ($p<0.01$). Subsequent follow-up of the two cohorts to 1975 indicated RRs of 2.63, $p<0.01$ (Allegheny cohort) and 2.49, $p<0.01$ (non-Allegheny cohort) (Redmond *et al.*, 1983).

A final follow-up was carried out in 1982 (Costantino *et al.*, 1991. This included the non-Allegheny cohort plus a subset of the original Allegheny cohort which included all coke oven workers from the two coke plants in the original cohort (n=2,025), and a matched sample of non coke oven workers (n=4,032). (Minor discrepancies in worker numbers compared with earlier cohorts were due to some reclassification of job titles following more detailed assessment of work histories.) Overall the RR for cancer of the lungs, bronchus and trachea in coke oven workers was 1.95 (95% confidence interval (95% CI) 1.59-2.33).

Further analysis indicated increasing risk by duration of employment (Costantino *et al.*, 1991). After ten years of employment a statistically significant risk was observed (RR 1.82, 95% CI 1.26-2.99), which was more than doubled after 15 years of employment (15-19 years RR 2.91, 95% CI 2.27-4.52; $\geq$20 years, RR 2.71, 95% CI 1.76-2.85). For the subset of topside oven workers risks were higher. A statistically significant risk was observed after 1-5 years of employment (RR 1.67, 95% CI 1.41-2.51) and following five years of employment this risk was more than doubled (5-9 years RR 2.58, 95% CI 1.75-4.23), rising to 4.34 (95% CI 2.89-6.97) after 20 or more years of employment.

Although data on smoking were unavailable in this study, the authors argued that there were no particular reasons to suppose that coke oven workers differed markedly from the non coke oven workers in terms of smoking habits. In addition, the magnitude of some of the increased risks reported in this study would be unlikely to be accounted for by smoking alone.

In addition to the Pittsburgh study, two mortality studies have been carried out in the UK, those of Davies, (1977) and Hurley *et al.* (1983, 1991).

Davies (1977) studied mortality in 610 coke oven workers employed in May 1954 at two steelworks in South Wales. Follow-up was from 1954 to 1965. Using the general population for comparison, no excess of lung cancer was observed in the coke oven workers (8 observed cases, 9.76 expected). However, this was a relatively small study and the follow-up period was short given the long latency (interval to disease onset) associated with lung cancer.

Hurley *et al.* (1983) studied a total of 6,767 coke plant workers employed at the British Steel Corporation (BSC) and National Smokeless Fuels (NSF). Follow-up periods were again relatively short, for 12 years and 13 years respectively. Information on smoking habits obtained from some workers suggested that smoking habits were similar to those in the general population. The combined Standardised Mortality Ratio (SMR) for lung cancer in the 27 plants of the two companies was 1.17[1] when compared to regional rates and 1.05 when compared to rates for semi-skilled men in the general population. There was no convincing evidence in either cohort that risks related to years of employment in oven work.

However, a subsequent follow-up of these workers (Hurley *et al.* 1991), which extended the follow-up period to 20 years and introduced a more detailed occupational classification system, found evidence of a more than doubled risk in certain circumstances. For coke plant workers overall, compared to regional rates, the increased risk was moderate (SMR for NSF workers was 1.25 and for BSC workers 1.27). Similarly, compared to rates for semi-skilled workers, SMRs were unremarkable (1.04 and 1.10 respectively). However, risks were higher among oven workers, with some variation by employer and statistical model of analysis. For NSF workers, RRs tended to increase with duration of work on general oven jobs (which included foremen and general maintenance work, but not the specialized jobs on ovens tops or sides), and in one statistical (Cox) model a more than doubling of risk (RR 2.29, 95% CI 1.21-4.33) was estimated per ten years of work on general ovens jobs. A possible relation between lung cancer mortality and length of employment in top oven work at NSF was also found, although this did not reach statistical significance. However, for BSC workers the relationship was more clear-cut, with risks more than doubled among those in top oven work for more than five years (RR 2.10, 95% CI 1.22-3.61), relative to men with no recorded experience of this type of work[2]. An analysis which allowed for smoking habits estimated a RR of 2.40 (95% CI 0.76-7.55) per 10 years of top oven work. These results show some consistency with those of the Pittsburgh study in identifying an increased risk in oven workers and in top oven workers in particular, although the magnitude of the increased risk was smaller in the British data.

Three other studies have investigated lung cancer rates in retired workers. Bertrand *et al.,* (1987) studied 534 French workers who had retired from two coke plants after January 1st 1963 and followed them to 1982. Mortality from lung cancer was compared with national rates. Overall the SMR for coke plant workers was 2.51 ($p<0.01$), although it was much higher in plant A (SMR 3.05) than in plant B (SMR 1.75). No increase was observed in those employed in coke oven work compared to non oven work or with duration of coke oven work (<5 years SMR 2.35; ≥5 years SMR 2.78). Although smoking was not taken into account in this study the authors conducted a separate analysis of 77 lung cancer cases whose smoking habits were known and matched to these controls in terms of smoking. They observed that 47% of cases were occupationally exposed to dust, gas and fumes compared to 35% of the controls, suggesting a role for occupational exposure over and above that of smoking, although they noted that the difference was not statistically significant.
43. Bye *et al.* (1998) carried out an incidence and mortality study at a coke plant in Norway involving 888 former workers employed for at least one year. Rates were compared with national population rates. Follow-up was from 1962-1993. The Standardized Incidence Ratio (SIR) for lung cancer was 0.82 (95% CI 0.33-1.70). However, a significant increase in lung cancer incidence was observed for those with the highest cumulative exposure to PAHs (≥150 mg/m^3-years). In this group the SIR was 3.60, although there were no cases in other exposure categories (p value for trend 0.08).

Sakabe *et al.* (1975) studied 2,178 retired coke oven workers from 11 firms, which included iron and steel works and city gas companies. The authors noted a significant excess of lung cancer deaths in workers employed in the iron and steel works (Standardized Mortality Ratio (SMR) 2.37), although not in workers from the gas companies.

Two further studies indicate a moderately increased risk of lung cancer in coke workers. Swaen *et al.* (1991) studied mortality rates in 5,659 workers employed for at least six months at three coke plants in the Netherlands. They were compared with 5,740 nitrogen fixation plant workers and follow-up was from 1945-1969. For all coke oven workers the SMR was 1.29 (95% CI 99.0-165.5). In top oven workers the authors report a significantly increased risk of mortality from respiratory disease, although this was not exclusively lung cancer (SMR 1.75, 95% CI 1.07-2.70). Side oven workers showed a significantly increased risk of lung cancer (SMR 1.41, 95% CI 1.03-1.90).

In Italy, Franco *et al.* (1993) studied 538 workers at a coke production plant

employed between 1st January 1960 and 31st December 1985. Follow-up was from 1960-1990. The SMR for lung cancer was 1.90 (95% CI 1.14-2.96) compared with national rates and 1.70 (95% CI 1.02-2.65) compared with regional rates.

In addition to these mortality and morbidity studies two case-control studies have been carried out in Canada (Finkelstein, 1994) and in China (Xu *et al*. 1996). The occupational history in case-control studies is obtained retrospectively (usually by asking the subject) and may be subject to reporting bias. For example, those suffering from disease may be more likely to recall certain occupations or exposures than those not suffering from disease. However, the opportunity exists to ask about smoking habits and other possible relevant exposures and thus allow for these factors in the analysis.

Finkelstein (1994) carried out a population-based case-control study in two cities in Ontario, Canada where two steel plants were situated. Males who died from lung cancer (n= 967) between 1979 and 1988 were compared to 2,827 age and sex matched subjects who died from other causes. In this case researchers obtained each subject's last occupation from death certificates and, where these were recorded as steelworkers, sought more information on occupational history from previous employers. No increased risk was identified for steelworkers overall when compared either with general population rates or with rates for blue collar workers. The authors note that because of small numbers the statistical power to investigate lung cancer risk by specific work area, such as coke plants, was low. At two plants there was no increased risk among coke workers. However, in one plant, they reported an RR of 1.78 (95% CI 0.3-9.3) for coke oven workers with more than 5 years employment. At this plant five of the seven men who had ever worked at the coke ovens died from lung cancer.

Xu *et al*. (1996) studied 610 cases (552 men, 58 women) and 959 controls in a nested case-control study derived from a proportional mortality study of workers at a large iron and steel complex. Following adjustment for smoking and other pulmonary disease the Odds Ratio (OR) for ever having worked in coke oven work was 3.6 (95% CI 1.7-7.5). There was no increased risk with years of employment, (<15 years employment OR 3.9, 95%CI1.3-12.4; $\geq$15 years employment OR 3.4, 95%CI 1.4-8.5).

Conclusions

The studies considered here are consistent in indicating a statistically significant increased risk of lung cancer associated with work involving coke ovens. The majority found a more than doubling of risk either in certain groups of workers

or in association with certain durations of exposure.

The various results deriving from the Pittsburgh investigation provide the most compelling evidence of an association between coke oven working and lung cancer. In this study, a more than two-fold increase in risk appeared to be confined to those employed in oven working and increased with years of employment. Moreover, particularly high risks were identified in those employed in top oven, as opposed to side oven, work. The more conservative estimates of the Pittsburgh study, reported at final follow-up, continue to point to an increased risk which is more than doubled after five years employment for top oven workers, and fifteen years for other oven workers.

Other studies provide support for the view that increased risks are largely confined to oven workers and that these risks are further increased in those with experience of top oven work. Hurley *et al.* in their later follow-up found that, in one group of workers, more than ten years employment in general oven work and more than five years in top oven work was associated with more than a doubling of risk. Bye *et al.* did not distinguish occupational groups but identified a more than three-fold risk in those with the highest exposure to PAHs (which would include oven workers and particularly top oven workers). In a nested case-control study Xu *et al.* reported an OR of 3.6 for ever having been employed in coke oven work and the population-based case-control study of Finkelstein, although based on small numbers of coke oven workers, provides some supporting evidence for an increased risk. Set against this, Bertrand *et al.* found no difference between oven and non-oven workers, although reporting a more than two-fold risk for coke workers overall. Sakabe *et al.*, who reported a two-fold risk and Franco *et al.*, who reported a risk slightly less than doubled, did not distinguish between oven and non-oven workers.

Smoking is a potent risk factor for lung cancer and an important potential confounder in occupational studies. Few studies had access to data on smoking history and most relied on an assumption that exposed subjects were unlikely to differ markedly from controls in terms of smoking habits. It was noted in a number of studies, however, that increased risks in coke oven workers were much above those which could be attributed to smoking alone. Moreover, in the case-control study described in paragraph 49, which included adjustment for smoking, a more than three-fold risk was identified.

When the Council originally considered this subject the evidence base was limited to the early results of one US based study (the Pittsburgh study) and two UK based studies, which excluded the later follow-up of the Hurley *et al.* study

reported in 1991. Neither of the UK studies suggested that risks were as much as doubled.

The Council considered that in these circumstances prescription could not be justified. However, the availability of a further follow-up of the study by Hurley *et al.* and the publication of several other studies has altered this picture considerably.

Current evidence appears to be consistent in indicating a more than doubling of risk of lung cancer in coke oven workers. Further, the balance of evidence supports the view that for top oven workers, the risk is more than doubled after five years and for other oven workers after 15 years of employment. The Council recommends prescription under each of these circumstances.

The possibility exists that some workers may have moved between top oven and other oven duties over the course of their career. In doing so they may fail to meet the threshold of five years of employment in top oven work. However, by virtue of the more highly exposed portion of their employment, they may nonetheless bear added risk relative to workers who have worked solely in general oven duties. In light of the epidemiological evidence indicating that risks of lung cancer in top oven workers tend to double after an interval of about five rather than 15 years, the Council considers that it would be equitable to count each year of top oven work as contributing three years towards the 15-year target in the assessment of claimants with such combined exposures.

During the course of its enquiries, the Council received evidence from representatives of the industry indicating substantial improvements in working conditions since the early 1970s, and a considerable reduction in workers' exposures to PAHs. Likewise, a research report from Norway has indicated a reduction of some 60% in exposures in 1977 – 1987 as compared with 1976 (Romanstad *et al.*, 1998). Better exposure controls are likely to have lessened risks of lung cancer. Consideration was given, therefore, to whether a cut-off date for employment could be defined after which prescription might no longer apply. However, in the absence of published evidence to confirm that reduced exposures have translated into reduced health risks, or any exact understanding of exposure-response relationships, the Council has decided that there is no certain basis for defining such a cut-off date. Should further evidence on this emerge in future, the Council will revisit the question.

The Council has also received evidence to suggest that exposure levels to potential carcinogens have been higher historically in the US than in British industry. Nevertheless, the Council considers the evidence in British industry

sufficiently compelling to accept the case for prescription.

Recommendations

The Council recommends that lung cancer associated with (i) at least five years of work at the top of coke ovens in aggregate, or (ii) at least 15 years of coke oven work in aggregate should be included in the list of prescribed diseases.

Should the first of these thresholds not be met, then the total duration of employment in top oven work should count towards the second threshold, and be aggregated such that one year of top oven work is regarded as equivalent to three years of general oven work. Thus, for example, a worker employed in top oven work for four years in aggregate, and so failing to meet the first criterion for prescription, could satisfy the second if it were to be established that they had also been employed for at least three years in total in other oven duties.

The Council further recommends that to be reckonable against these qualifying time limits, workers should be wholly or mainly employed in the relevant job category or categories.

The term 'top oven work' includes a number of job titles and evidence has been sought on the extent to which the work activities of top oven and non-top oven workers overlap, and can be distinguished under the practical circumstances of the IIDB scheme. As a result of these enquiries the Council recommends that the following job titles should be included as counting specifically to top oven work: lidsman, car man (chargerman), valveman or tarman, top oven maintenance worker. This is not an exhaustive list but includes job titles which were employed in the British study carried out by Hurley *et al.* and are judged to be readily understood within the current industry.

The recommendations for prescription are described in the table below.

Where these conditions of prescription are satisfied, a claimant's lung cancer should be presumed to arise from their occupation, regardless of their smoking history.

參考文獻：Lung cancer in coke oven workers. Report by the Industrial Injuries Advisory Council in accordance with Section 171 of the Social Security Administration Act 1992 considering prescription for lung cancer in coke oven workers. Department for Work and Pensions, 2011(available for download at www.official-documents.gov.uk)