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Process-Dependent Risk of Delayed Health Effects for Welders

by Richard M. Stern*

In most industrialized countries large numbers of workers are exposed to welding fumes. Although the general pattern of welders' health may not significantly differ from that of workers in other dusty industrial occupations which demonstrate elevated incidence of respiratory tract diseases with long latency periods, the extremely wide range of substances at potentially high concentrations produced by various welding technologies may give rise to undetected process-specific high-risk working conditions: ("hot spots"). The origin, prevalence and range of magnitude of such hot spots, especially for cancer of the respiratory tract, is discussed, with emphasis placed on the assessment of risk resulting from exposure to Cr(VI) and Ni accompanying the use of various technologies for the welding of stainless and high alloy steels. The wide variation of health effects found within the industry, however, indicates the need for a standard protocol for future epidemiological studies, as well as for the development of suitable methodologies for experimental risk assessment.

Introduction

The use of welding as a technology for the joining of materials occurs worldwide, engaging of the order of 0.2-2% of the working population in typical industrialized countries. The major processes have been in universal use for of the order of 50 years, and materials and hence exposures have been shown to be, under similar circumstances, comparable throughout the world. The technology is extremely labor-intensive, labor accounting for 80-90% of production costs for all but the most modern automatic processes. However, new processes with higher productivity having an increased range of applicability are continuously being introduced. Since these demonstrate typical doubling times (in terms of their absolute use) of 7-10 years, depending on the details of the economic growth in the individual country, some processes which currently account for significant worker exposure were relatively rare 20 years ago.

The nature of the technology is such that, whenever an arc is struck, the resulting high temperature which melts both work piece and consumable wire or rod produces significant amounts of vaporized metal and (where present) slag formers and flux, which condense in the rising plume of heated air to form a high local concentration (upwards of 100 mg/m^3) of a complex mixture of gases, oxides and other compounds, whose chemistry is determined by the technology, materials and welding parameters used in each case.

The possibility of high, localized concentrations of a wide variety of biologically active substances which in turn have a wide range of toxicity [e.g., O_3, NO_2, Cr(VI), V, As, Mn, Ni, Be, Cu, Na, K, Si, F, Pb] represents a potential source of health risk to significant numbers of workers throughout the world. The magnitude of actual risks which occupational exposures represent are however largely unknown and uninvestigated. Since the fume concentrations of various substances vary a millionfold from process to process, and since individual exposure can depend to a large extent on job situation, one can anticipate that the average risk arising from welding, for a given welder, or any given welding population, and therefore for the welding industry as a whole, is not homogeneous but is made up of a range of process and job-specific risks whose order of magnitude could be estimated by a proper risk assessment (*1*, *2*), based on knowledge

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of the range of process and job specific exposures involved.

The observation of a wide range in the nature and degree of health effects among welders using similar technologies in different localities, and between local users of different technologies indicates that a number of variables determine exposure and hence actual risk, even within a given welding process. Any attempt to reduce occupational health risk must therefore be based on an understanding of these parameters, and the way in which they might affect the nature of the material produced (e.g., the chemistry of the consumables), the rate at which fume is generated (e.g., the values of the welding variables; voltage, polarity, current, arcing time), the local fume concentration (e.g., type of ventilation) or the background exposure (e.g., workshop mix of technologies and applications).

Welders could be used as suitable model populations for studies of process or occupation dependent risk provided one has a knowledge of: (a) the magnitude of available populations and their distribution among various technologies, (b) the types of exposures appropriate to these subcohorts and (c) the techniques necessary to estimate the origin and magnitude of risk accompanying each class of exposure. One useful approach to establishing the necessary methodology is to attempt to identify specific job situations which might be associated with high degrees of excess risk, i.e., process-dependent "hot spots."

Distribution of Welding Populations

Types of Processes

There exist approximately 20 major technologies within the welding industry which are used on ten major classes of materials providing the possibility for of the order of 5000-10,000 different working environments due to the possible variations in composition of workpiece, consumables and welding variables.

Manual metal arc welding (MMA) uses short lengths of electrode coated with a complex material which provides for flux, slag and protection from oxidation through its melting and decomposition. Ten major electrode producers, each offering 100 different electrodes, which can be welded with three types of polarity (AC, ±DC), on several types of joints, account for 3000-5000 separate exposures which differ from each other by a factor of two or more in the absolute concentration of at least one of the 14 major chemical constituants of welding fume.

Metal inert gas welding (MIG) uses a continuous wire electrode and an inert gas (e.g., argon) which provides a shield against oxidation. For some classes of materials, an active gas (e.g., CO_2, O_2) is mixed with the inert gas to provide better surface properties (MAG process).

Tungsten inert gas welding (TIG) uses a nonmelting electrode and occasionally extra filler material.

Gas welding uses an oxy-acetylene or similar flame to melt the work piece.

Submerged arc welding (SA) uses a fully automated process where the arc is maintained under a covering of powdered flux.

In spot welding, material is joined by local resistive heating (provided by a transformed current pulse) under electrode pressure.

Cutting, burning and air (arc) gouging are processes involving the preparation of work pieces and are frequently performed by welders, their assistants, or special workers within the same trade.

The major classes of materials are: mild steel (MS), an alloy of iron, carbon, silicon, and occasionally molybdenum or manganese; stainless and high alloy steel (SS), containing iron, nickel, and chromium, and occasionally cobalt, vanadium, manganese, and molybdenum; aluminum (AL), either pure, or as an alloy with magnesium, silicon and/or occasionally chromium.

Distribution of Welders

Worldwide distribution of welders among the different technologies and their applications is difficult to determine directly because the average number of welders per firm is small (of the order of ten), and a large fraction (30-50%) of individuals exposed to welding fumes are not full-time welders but are also employed in allied trades. The best indirect method of estimating national welding populations is to determine the local use of welding consumables and assume 500 kg of electrodes and 2500 kg of wire per man-year for MMA and MIG welding, respectively. Unfortunately the competitiveness of the market for electrodes tends to make such information a trade secret, but from unpublished trade figures it is possible to estimate the distribution in more common categories, as is shown in Table 1.

Two countries, Sweden and Germany, have recently conducted detailed surveys of their welding industries. The results presented in Table 2 show that there exist wide international variations in the relative distribution of weld ing activity by technology and material. In general, however, the five combinations, MIG/MS, MIG/SS, MIG/Al, MMA/MS, and MMA/SS account for between 60-70% of all welders.

Table 1. Distribution of welders by country for various processes

Country	Process	No. of welders		
		Stainless steel	Other	Total
Sweden, 1974[a]	MMA	5,400	18,600	24,000
Holland, 1978[b]		3,500	31,300	34,800
Japan, 1978[c]		80,000	350,000	430,000
U.S.A., 1976[d]				500,000
Germany, 1970[e]		13,000		97,000
Norway, 1978[b]		1,200 (?)		21,000
Great Britain, 1978[b]		10,000 (?)		87,000
Spain, 1978[b]		1,600		57,000
France, 1978		9,000		81,000
U.S.S.R., 1980[f]				1,500,000
Sweden	MIG + MAG + TIG	3,100	10,000	13,200
Holland				1,460
Japan				30,000
U.S.A.		1,900	57,000	58,900
Germany				66,000
U.S.S.R.				200,000
Sweden	Sub.			780
Holland	Arc			
Japan				15,000
U.S.A.				10,000
Germany				
Sweden	Other			
Holland	(incl. gas)			
Japan				1,000
U.S.A.				
Germany				106,000

[a]Data of Ulfvarson (3).
[b]Data of van der Sluis (4).
[c]Data of Masumoto et al. (5).
[d]Data of Jefferson (6).
[e]Data of Flemming and Sossenheimer (7).
[f]Estimated.

Process-Specific Welders' Exposure

Each technology produces a unique type of aerosol, of which 80-90% of the chemistry is determined by the composition of the consumable material, which is chosen to be metallurgically compatible with that of the work piece. To a first approximation, five combinations of the processes described above with various materials provide upwards of 70% of the total exposure, listed in order of complexicity of fume composition as follows: (a) MIG/AL: aluminum oxide, ozone; (b) MIG/MS (MAG/MS): ferric oxide, manganese, silicon, copper, nitrogen dioxide; (c) MIG/SS: same as MIG/MS plus nickel, chromium, ozone; (d) MMA/MS: same as MIG/MS plus sodium, potassium, molybdenum, fluorine, titanium, calcium, aluminum; (e) MMA/SS: same as MMA/MS plus chromium, nickel, vanadium. (Approximately 40% of MMA/MS welding is performed on plates coated with shop primer, producing in such cases an additional 1-5% organic gas due to the pyrolytic decomposition of the epoxy or other polymer binder: welding fumes are otherwise usually free of organic material. Cutting and gouging provide high exposures to the oxides of iron, carbon and nitrogen and occasionally to zinc, tin, lead, and/or barium).

The amount of fume produced per unit time depends on the choice of welding parameters (current, voltage, wire dimensions, etc.) and the welders' exposure is additionally influenced by the actual job situation and degree of ventilation and/or fume exhaust provided. The approximate cumulative distribution of workplace exposures to total fume for the major technologies is shown in Figure 1. Shop background levels (BG) are also given.

The curves shown are only valid between 15 and 85% and appear to be representative for the trades indicated, data from Sweden, Denmark and the U.K. agreeing to within about a factor of 2. The use

Table 2. Distributions of Swedish welders by process and material.[a]

Process	No. of welders				
	Total	Mild steel	Stainless steel	Al	Other
MMA	25,585	16,854	5,896	1,496	1,339
MIG + MAG	9,143	6,232	1,594	1,141	176
TIG	4,216	1,541	1,529	913	233
Gas	3,823	2,762	479	325	257
Sub. Arc	783	540	210	32	1
Total	43,550	27,929	9,708	3,907	2,006

[a]Adapted from Ulfvarson (*3*). The German data, although unavailable for publication in detail (*8*), indicate that, while in 1980 the total number of welders has remained essentially unchanged from 1970 (see Table 1), there has been a reduction of about 25% in the number of MMA/MS welders and a corresponding increase in the number of welders using semiautomatic metal-gas techniques in this decade. Note that in Sweden the ratio of MMA to MIG/MAG/TIG welders is aproximately 2:1, while in Germany it is currently 1:1. Similarly 9% of the Swedish welding population works on aluminum alloys while only 3–4% of German welders are engaged in these processes. The data generally agree with estimates made based on consumable sales in the individual countries, assuming approximately 500 kg electrodes and 2500 kg wire per man year of MMA and MIG/MAG welding, respectively.

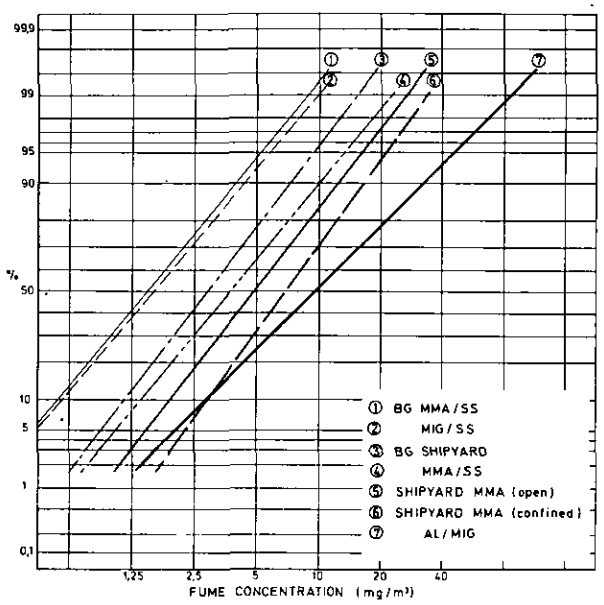

FIGURE 1. Cumulative distribution of working place exposures (%) vs. fume concentration (8 hr average) (mg/m^3) for stainless steel and aluminium welding (in Sweden) and shipyard welding (in Denmark), including background levels (BG), liberally interpreted from Ulfvarson (*3*) and Beck Hansen (*9*).

of point extraction will reduce the average levels by approximately a factor of two to three (*3*). Note that for some applications a significant fraction of welders is exposed above 5-10 mg/m^3: levels above 100 mg/m^3 have been occasionally reported.

Because of local variations in consumable composition and distillation effects in the arc which can cause enrichment of the fume by as much as a factor of 100 for volatile components, it would be extremely difficult to make an a priori prediction of exposure to the individual elemental components of the fume based only on a knowledge of the process technology and work piece composition. Fortunately, however, a great deal is known about the amount and chemistry of welding fumes produced from individual electrodes and processes, and the variations thereof. A comparative study of MMA/MS fumes produced under standardized conditions by Danish, Dutch, British and Swedish welders (*10*) shows that locally, a welder or group of welders produce an amount of fume per unit time for a given electrode which varies by less than 3% within 95% confidence limits, when well supervised, and which varies by less than 18% (95% limits) when unsupervised. National average fume production rates vary by 3% from each other, when corrected for differences in the welding parameters actually used. Variations arise because a given electrode can be welded over a range of currents and voltages. Useful welds can be produced over a range of current of a factor of two, resulting in factor of two variation in burning rate and hence in specific fume production rate. Similarly, fume production per unit electrode length is proportional to arc length (and therefore voltage) which also can vary by a factor of two. Hence absolute fume production rates (and therefore concentrations and exposures) at maximum currents and voltages are approximately four times those at minimum values of the welding parameters. In addition, extreme variations in welding parameters can result in a variation of about ±40% in the relative concentration of the major fume components: Trace elements (< 1% concentration) can show much larger variations.

The results of laboratory measurement (*10*) of total fume and elemental concentrations resulting from the welding of a series of representative tech-

Table 3. Average concentrations of important toxic substances for a representative selection of welding processes.

	Steady-state concn in 10 m^3, 3–5 kW, 25 sec per air exchange, t = 1 sec									
	Ozone concn (20 cm from arc, t = 1 sec), ppm[a]	Ozone, ppm[b]	Fume, $\mu g/m^3$	NO_2, ppm	Cr(VI), $\mu g/m^3$	Ni, $\mu g/m^3$	As. $\mu g/m^3$	Cu. $\mu g/m^3$	Pb, $\mu g/m^3$	Mn, $\mu g/m^3$
TLV	0.1	0.1	5000	0.3 [c]	1.0[d]	15[d]	2	200	150	800[e]
Ceiling limit	0.3	0.3		1.0						
Process										
12.51, A, MIG/MS	0.22	0.8×10^{-5}	15000	0.12	1.5	15	1.5	30	1.5	470
12.51, A + CO_2, MAG/MS	0.15	0.8×10^{-4}	17000	0.015	0.5	1.5	0.5	50	3.0	1700
12.51, CO_2, MAG/MS	0.55	2.8×10^{-3}	12000	0.048	0.5	1.5	1.2	48	4.0	840
FF11, CO_2, MAG/MS[f]	0.88	4.2×10^{-3}	25000	0.23	1.0	5.0	2.0	75	8.0	4000
3RS17, MIG/SS	0.31	5.6×10^{-3}	5000	0.23	35	250	0.5	30	5	350
18.15, A, Al/MIG	0.39	7.1×10^{-3}	22000	0.14	20	0.5	—	1	4	—
18.04, A, Al/MIG	0.72	3.3×10^{-2}	22000	0.11	0	0	—	—	—	—
18.01, A, Al/MIG	0.88	—	23000	0.06	4	1	—	—	—	—
OK 48.15, MMA/MS[g]	—	—	10000	0.02	2	—	5	10	3	350
P 316, MMA/SS[h]	—	—	10000	0.02	300	50	—	30	8	270
PK 46.16, MMA/MS[h]	—	—	10000	0.02	3	1	3	30	3	500

[a]Removal of fume will result in a longer time constant t and an increase in these values by a factor of 2–10; t = halflife in standard welding fume.
[b]Calculated from near zone ($r < 20$ cm) only; practical levels will be higher by a factor of 2–5.
[c]Proposed, NIOSH.
[d]Proposed NIOSH limits for carcinogens.
[e]Change in 1980 from 5000.
[g]Low hydrogen.
[h]Rutile-basic.

nologies produced under comparable, standard conditions (3-5 kW) are presented in Table 3. The values are the estimated steady-state concentrations to be found in a 10 m^3 volume with an air exchange every 25 sec. Ozone concentrations depend on the half-life for this reactive substance, which is in turn determined by the amount and nature of the fume present. For the sake of simplicity, it will be assumed that these few processes are representative for the industry, and these fumes can be considered as surrogates for those comprising the major exposures of welders.

By combining the data of Figure 1 with those of Table 3, it is possible to estimate the relative fraction of welders engaged in a particular trade whose exposure will exceed a given Threshold Limiting Value (TLV), and who by definition can be considered to be at "administrative risk." The fraction of populations at administrative risk for different substances, as a function of technology and material are shown in Table 4. In general, the majority of exposures to other elements do not exceed the respective TLV values provided the TLV for total fume is not exceeded.

The estimates of Table 4 are based on the average elemental concentrations of the surrogate welding fumes listed in Table 3. If one considers all the common consumable types within each major category, which are available industry wide, then a given elemental concentration for a class of fume can vary by a factor of three from these "average" values. In spite of such variations, examination of available data (*1-3, 11*) such as presented in Table 3 permits separation of welders into cohorts having average exposures which can be expected to be distinct with respect to the presence or absence of certain characteristic substances, and hence which might result in unique health risks.

The Health of Welders

Pneumoconiosis and Siderosis

The extremely rich literature of case histories, health surveys, and hygienic measurements in the welding industry has recently been catalogued (*2*). The generalized risks of welding are indicated by reports of cases of accidental death due to electric shock, and occasional acute and sometimes fatal intoxification due to inhalation of high concentrations of Cd, ozone and oxides of nitrogen, and manganese; metal fume fever due to exposure to

Table 4. Estimated fraction of welders at administrative risk, defined as those exceeding the TLV for various substances as a function of the process.[a]

Substance	TLV	Source	Process	Welders at risk, % Mild steel	Stainless steel	Aluminum
Total fume, $\mu g/m^3$	5000	NIOSH accepted	MMA[b]	75	45	
Ni, $\mu g/m^3$	15	NIOSH proposed, 1980 (carcinogenic)			75	
Cr (VI), $\mu g/m^3$	10	NIOSH, probable, 1980 (carcinogenic)			98	
Mn, $\mu g/m^3$	800	NIOSH, in effect, 1980		10	5	
NO_2, ppm	0.6	NIOSH proposed, 1981		10 (?)	20	
Total fume, $\mu g/m^3$	5000	NIOSH accepted	MIG		8	90
Ni, $\mu g/m^3$	15	NIOSH proposed, 1980 (carcinogenic)			30	
Cr (VI), $\mu g/m^3$	10	NIOSH, probable, 1980 (carcinogenic)			75	
Mn, $\mu g/m^3$	800	NIOSH, in effect, 1980		60	5	
NO_2, ppm	0.6	NIOSH proposed, 1981			20	40
O_3, ppm	0.1	Accepted		2	20	40
Total fume, $\mu g/m^3$	5000	NIOSH accepted	TIG		8	1
Cr (VI), $\mu g/m^3$	10	NIOSH, probable, 1980 (carcinogenic)				8
Mn, $\mu g/m^3$	800	NIOSH, in effect, 1980			5	
NO_2, ppm	0.6	NIOSH proposed, 1981				5
O_3, ppm	0.1	Accepted		2	20	1

[a]Derived from Table 3 and Figure 1. The fractional populations shown to exceed TLVs can only be estimated; the relative fractions given are therefore uncertain to about 20% (with an absolute uncertainty of no less than 5% for the small values).

[b]Approximately 40% of all MMA/MS welders work on primed plates and are therby exposed to organic gases of unknown TLV having concentrations ranging from 1 to 5% of those found for inorganic solids.

Zn, Cd, Pb, Sn, and/or Cu appears to be common. Some risks are, however, obviously process-dependent: e.g., exposure during the welding of stainless steel in confined spaces to high concentrations of fume containing water soluble Cr(VI) has been reported to lead to acute and chronic chrome intoxification, dermatitis and asthma (*12-18*).

It is difficult at present to estimate the absolute incidence rates of these acute effects, since case reports are isolated and must be interpreted in terms of the 3-4 million man-years of welders' exposure accumulated annually in the countries whose literature is commonly cited. One might therefore examine epidemiological studies of welders in the hope of determining the absolute level of health effects. Several recent cross-sectional studies would appear to be based on sufficiently large local populations of welders to permit some quantitative determination of the effects of chronic exposure to welding fumes in several different localities and job situations.

A survey of the occurrence of (legally defined) pneumoconiosis (silicosis, asbestosis and silico-asbestosis) during the decade 1966-1975 has been conducted for the maritime-construction complex La Spezia which has a total work force of approximately 12,000 individuals, among whom are an undetermined number of welders (*19*). The relative cumulative incidence (in percent of all 951 cases) vs. exposure (in years) for the entire work force is shown in Figure 2. Approximately 50% of the total cases occur within 26 years exposure. The relative cumulative incidence for those 143 individuals identified as electric and gas welders is shown for comparison. The median response for this subcohort was at 23 years exposure. Since welders perform their activities throughout the maritime complex, they are exposed (as bystanders) to the same general atmosphere as the average work force, and therefore should have the same general pattern of disease, superimposed upon which is the effect, if any, of their specific welding activity. Since however neither asbestos nor crystalline silica appear in welding fumes, this incidence of asbestosis and silicosis among welders can only be due to bystander exposure. From Figure 2 it can be seen that the effect of welding would appear to be to accelerate by approximately 10% (i.e., 2-3 years) the onset of the pneumoconiosis characteristic for La Spezia, as detected among the welding population. Since the

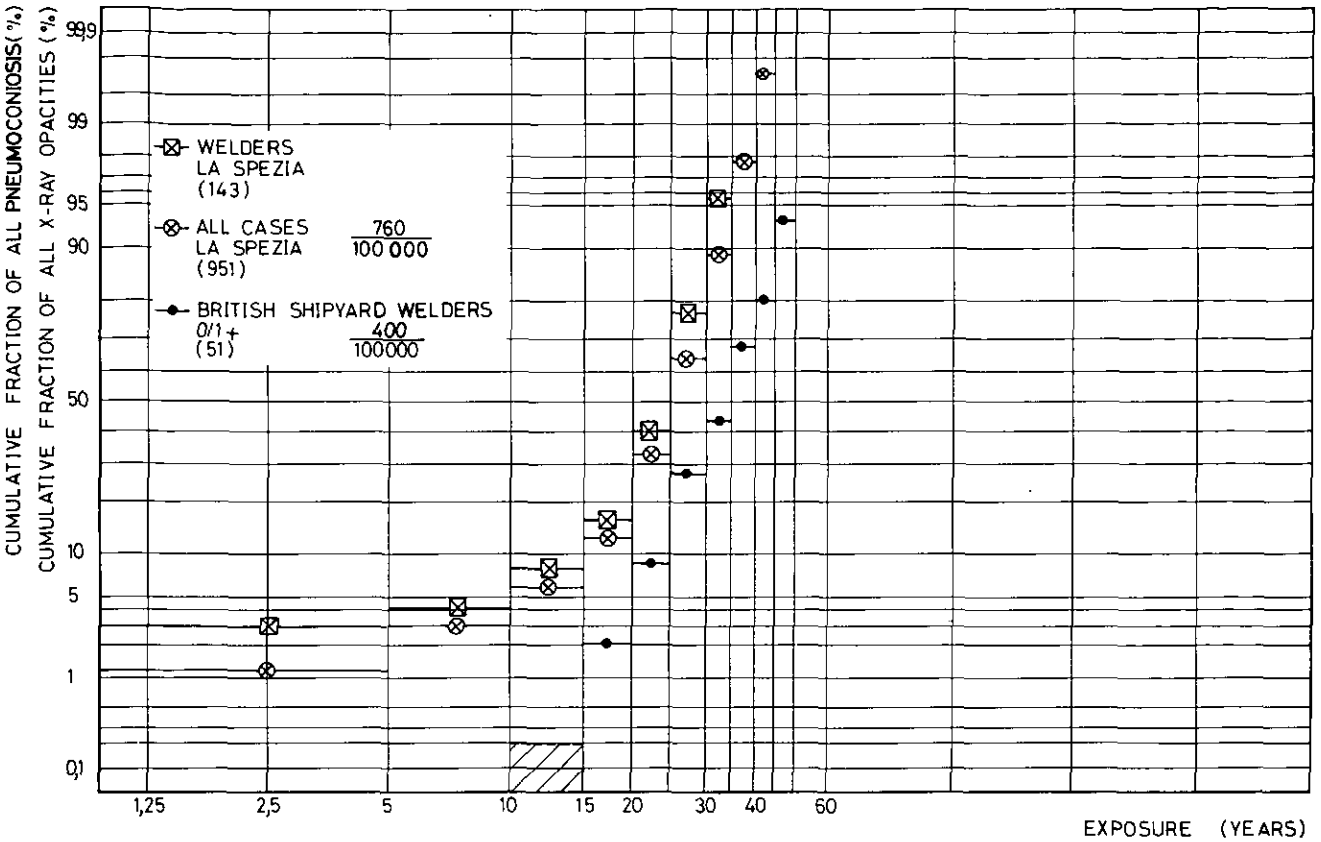

FIGURE 2. Fraction of total incidence of pneumoconiosis (%) vs. length of exposure (years) for the total workforce in La Spezia as well as for the welding subpopulation. Also shown is the fraction of total incidence of small round opacities (1 mm or greater) vs. length of exposure (years) for British shipyard welders.

relative size of the welding population appears to be unknown, the absolute incidence rate for their pneumoconiosis cannot be compared with that of the general shipyard population. It is however difficult to imagine that the numbers of welders with silicosis/asbestosis compared to the entire group (143/951 = 15%) could be different from the ratio of welders to total exposed employees, without there being a significant variation in the respective incidence patterns. This conclusion is justified by the observations of a contemporaneous clinical study of randomly selected shipyard workers in Trieste which shows that welders exhibit a lower incidence of pleural changes (lesions and calcification: 10/37 = 7.3%, 2/137 = 1.5%) than the average of all shipyard employees (63/556 = 11%, 26/556 = 4.4%) who in general exhibit a 10-20 fold excess incidence of bronchopneumopathies compared to the general population (*20*).

In a second article (*21*), diagnostic chest x-rays from 661 British shipyard welders were examined by a panel of three readers to determine the absolute incidence of small round opacities of class 0/1 or higher (i.e., larger than 1 mm: "siderosis") as a function of welding exposure. The relative cumulative incidence for the 51 positive cases is plotted on Figure 2 as well. It can be seen the data follows a lognormal distribution, with approximately a 10 year median delay in detection of siderosis for British welders compared to the detection of pneumoconiosis in Italian welders, and that the low exposure tail appears to be missing. The British welders also worked in all sections of the shipyard, using a wide variety of processes, mostly MMA, but including MIG and TIG techniques (apparently absent in the La Spezia work experience).

The absolute cumulative incidence for siderosis vs. length of exposure among the British welders is shown in Figure 3: Data for a cohort of 220 (East) German welders (*22*) is shown for comparison. After the average length of employment of 17 years, approximately 1.6% of the British welders exhibit detectable x-ray mottling (caused by the local accumulation of welding fumes (mostly Fe_3O_4) having a high x-ray opacity). Doubling the exposure time results in a tenfold increase in incidence. The inci-

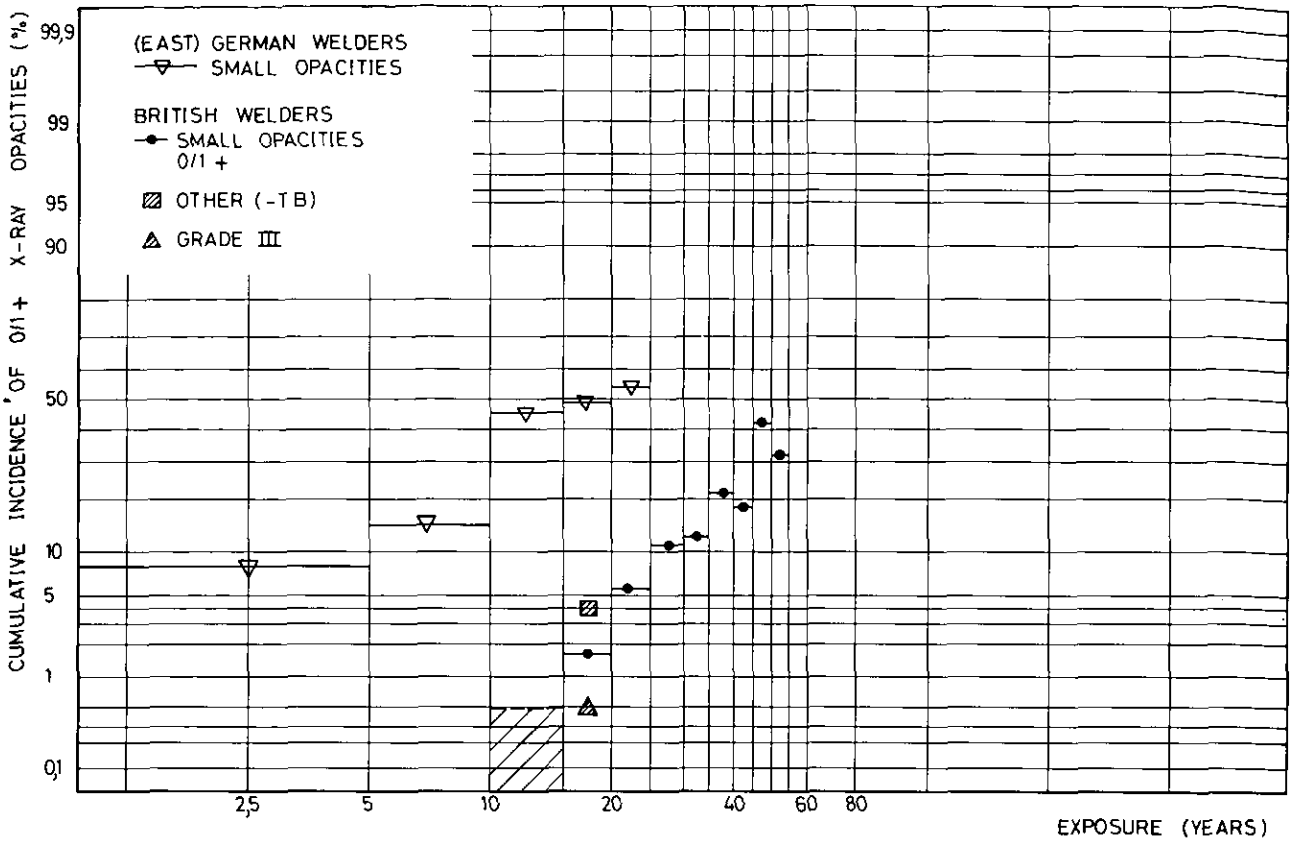

FIGURE 3. Fractional incidence of small round opacities (% of total cohort) vs. length of exposure (years) for British shipyard welders, and for siderosis for (East) German shipyard welders.

dence of other anomalies, and of grade III siderosis (opacities of 3 mm or greater) is also shown for the total population. The (East) German welders show a considerably different pattern of incidence of siderosis, with approximately 45% demonstrating detectable x-ray mottling after an average exposition of approximately 14 years: the incidence of grade III siderosis after this exposure is 1%.

Since the British welders are estimated to have exposure of approximately 5 mg/m^3, one can convert the length-of-exposure data to cumulative exposure (mg/m^3 years), as is shown in Figure 4. For comparison are shown the cumulative incidence data for silicosis for gold and for coal miners (*23*), since they represent the classic case of a lognormal dependence of cumulative incidence on total exposure. Average exposure levels in the East German shipyard would have to be 25-35 mg/m^3 for the incidence vs. cumulative exposure data to be comparable in the two cases.

The absolute incidence rates for siderosis for the British and (East) German shipyard populations were 400/100,000 and 1500/100,000 cases/man-year, respectively. The two studies are comparable however only if similar age distributions exist in both shipyards. British welders form a homogeneous group, having started work at age 17 with a universal apprenticeship, while the (East) German welders, who have an average age of 36 (compared to 34 for their British colleagues) commenced their working exposure at the average age of 23, some 6 years later, and presumably have some other type of early working experience. (The Italian working experience is very similar to that of the East German group.) The striking variation in siderosis incidence between the groups may have a number of origins: there is most likely a significant difference in exposure in the shipyards studied, but there might be significant differences in lung retention in the two cohorts due to age or genetic factors. It is also possible that criteria for reading thoracic x-rays may vary from country to country.

The siderosis discussed above, as found in shipyard and other welders is usually described as "benign", the x-ray mottling regressing after cessation of exposure in most cases (*24*). Some smaller

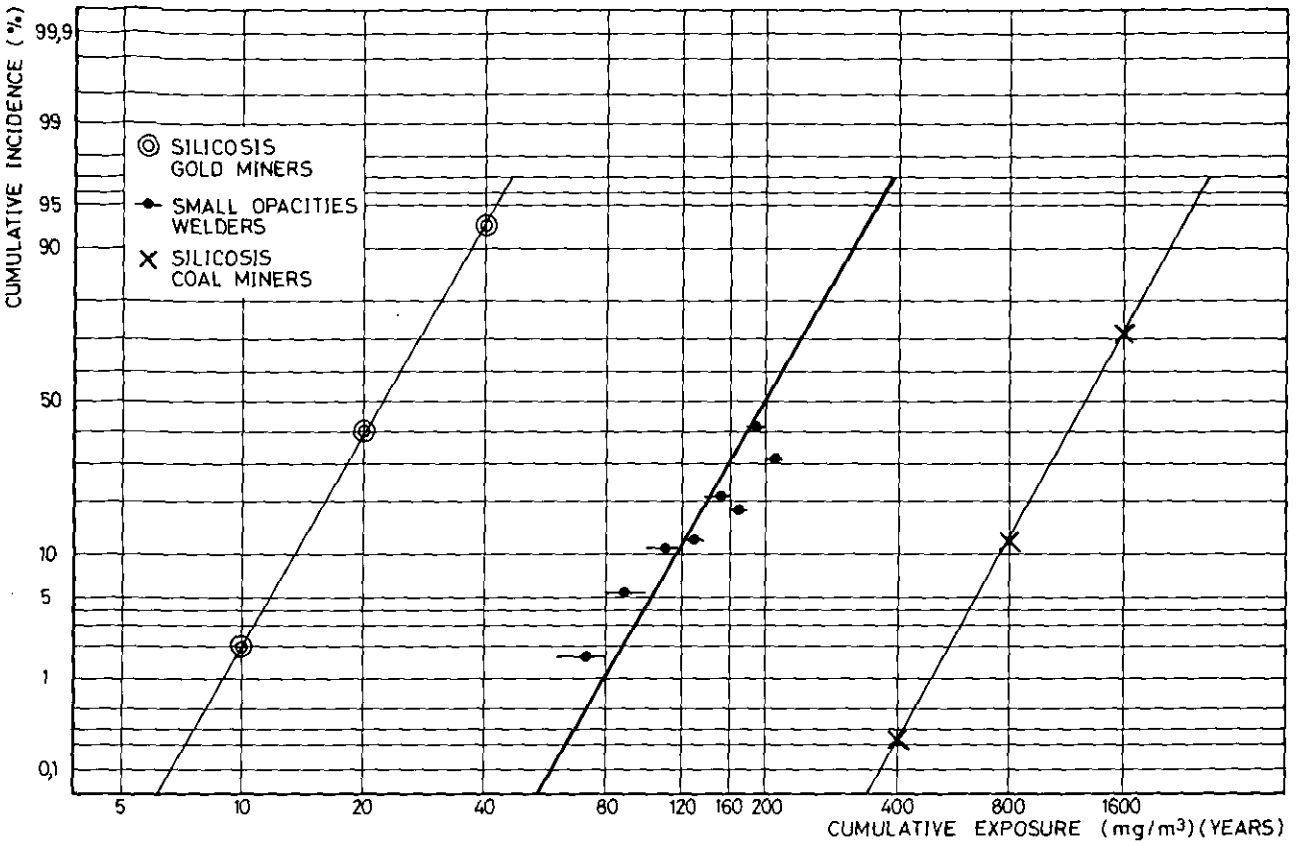

FIGURE 4. Fractional incidence of small round opacities (% of total cohort) vs. cumulative exposure to welding fume (mg/m^3) (years) for British shipyard welders (assuming 5 mg/m^3 average fume concentration). Similar lognormal behavior is found for coal miners and gold miners, each with a characteristic median exposure.

fraction of welders exhibits complex welder's pneumoconiosis characterized by irreversible changes including fibrosis (*17*, *25*) which may be due to specific welding exposure, particular individual sensitivity, or may be an expression of a bystander effect similar to that seen for the La Spezia welding population.

Most shipyard welding is done on primed plates of mild steel. Stainless steel welding is usually performed in shops dedicated to such activity. In one clinical study of 95 welders employed in an Italian metalworking shop using a wide range of technologies on both mild and Ni- and Cr-rich alloy steels, for those welders with more than 10 years experience only 8% show normal thoracic x-rays, 25% have normal respiratory function, and only 8% do not exhibit chronic bronchitis: all demonstrate squamous metaplasia of varying degrees (*26*).

Examination of the cross-sectional studies described above and others published in the literature of the past decade indicates that each subcohort apparently exhibits a health pattern characteristic for its own local working environment, to which a number of factors contribute. The fact that the welding cohort in one English shipyard exhibits approximately 8% abnormal thoracic x-rays (2% siderosis, 0.5% cancer, 3% tuberculosis, 4% other) while the cohort of a German shipyard exhibits 50% siderosis after the same length of employment is most probably an expression of different degrees of exposure to similar materials: productivity, arcing time, and electrode dimensions are probably higher, and ventilation poorer, in the East German yard, although this supposition can only be verified by direct measurement. On the other hand, the fact that 92% of welders in a workshop with mixed exposures to mild and stainless steels have abnormal thoracic x-rays, together with a high incidence of squamous metaplasia is more likely a reflection of the presence of metals such as Cr and Ni in the fumes from alloy steels, usually absent from the mild steels used in shipyard construction.

Pulmonary Function

Cross-sectional studies of pulmonary function, which should be more sensitive than clinical x-ray surveys for the detection of the effects of exposure

to welding fumes, are also difficult to interpret because of two major confounding effects: smoking and population dynamics (e.g., worker self selection). The effects of smoking and age on ventilatory function of the general population have been studied in detail (*27*). In studies on welders (*28*), no statistically significant differences between welders who smoked and controls who smoked could be detected: for nonsmoking welders and controls, only closing volume, closing capacity, total lung capacity and N_2-cardiogenic oscillations were significantly different, presumably due to the deposition of welding fume particles in peripheral small airways. Studies of respiratory effects in other populations in the metal industry can show more pronounced effects (*29*), although they may not become apparent until after 30 years exposure or longer (*30*) for some occupations.

The role of population dynamics through worker self selection among the welding population has been demonstrated (*31*). Of 100 welders first examined in 1963, only 19 could be identified and reexamined in 1978 in an effort to determine the effects of 15 years of exposure to welding fumes. For the two cohorts the average values of forced vital capacity (FVC), maximum expiratory flow volume at 50% vital capacity ($MEFV_{50}$) and forced expiratory volume over the first second (FEV_1) were found to be higher in 1978 by approximately 4%, 0.6% and 4%, respectively. This apparent slight increase in the respiratory function of these welders is however due to the fact that while the initial cohort had values of FVC, $MEFV_{50}$ and FEV_1 of approximately 108, 107 and 105% of normal, respectively, those welders with more nearly average respiratory characteristics left the occupation and could not be reexamined. Those welders who remained, however, were the individuals whose respiratory characteristics were the highest, having in 1963 values of FVC, $MEFV_{50}$ and FEV_1 of 115, 119 and 113% of normal, which in fact had been reduced on the average by 4, 13 and 6% after further 15 years exposure, with various differences in degree and statistical significance due to smoking habits. The opportunity to change jobs is a function of the regional economic situation which has strong variations with time and locality. Thus cross-sectional studies which only examine the age distribution e.g. (*28*) may underestimate the real effects of exposure on a constant population, and variations in population dynamics (i.e., job mobility) may be strongly reflected in differences in cross-sectional studies from widely disparate societies.

The literature discussed above demonstrates the existence of statistically significant exposure related incidence of chronic respiratory tract disease in welders also documented elsewhere (*32*, *33*), and hence there appears to be convincing evidence for a finite risk of delayed health effects for the welding occupation in general. On the other hand, a significant fraction of welders is employed in shipyards, and shipyard workers in general exhibit a statistical overincidence of chronic respiratory tract disease (*34*, *35*), including cancer (*35*, *36*). Thus there is a strong possibility that shipyard welders are partially at risk because of bystander effects related to their place of employment but unrelated to welding.

Possible Cancer Risk for Welders

A number of epidemiological surveys of general welding populations have shown statistically significant overincidence of lung or respiratory tract cancer for this occupation (*32*, *33*, *36-39*) the data of five of these studies (*32*, *33*, *37-39*) is reviewed in Table 5. The five studies encompass some 150,000 welders, represent approximately 420,000 man years at risk, and show an accumulated observed incidence of 415 cases with 308 cases expected, assuming an observed/expected (O/E) ratio of unity for unexposed populations. Although there are slightly different approaches taken in each of the studies, the range of O/E incidence ratios lies between 1.0-2.8 (95% confidence limits) (0.85-3.2 within 99% confidence limits), to be compared with an O/E ratio for unexposed but equivalent populations of the order of 0.6-1.0 (95% confidence limits) (uncorrected for smoking) (*40*). Thus there is sufficient evidence to reject the null hypothesis that welding or being a welder does not contribute to occupationally related cancer incidence.

If the statistically significant overincidence of respiratory tract cancer among welders is due to their occupation, is not a bystander effect (*36*) and is not due to some systematic confounding effect such as smoking habit (welders exhibit an overprevalence of smoking by 22%) (*32*) or other lifestyle effect, then it may have its origin partially in the general working place exposure of all welders, and partially in specific, high risk exposures. A general occupational risk might arise from the lung burden of dust [approximately 2 g in older welders (*14*)] which, if it resulted in an increase of the order of five years in "lung age" over chronological age, could account for the observed overincidence in age specific cancer rate. Technology or job specific risk would be associated with processes which produce welding fumes possessing high carcinogenic potency (i.e. "hot spots").

Table 5. Summary of epidemiological studies of welders which demonstrate a statistically significant excess incidence of respiratory tract cancer.

Author	Locality	Reference population[a]	O[b]	E[a,c]	O/E	p[d]	O/E 95%[e]	Study design and population
Milham (39)	Wash. state, U.S.	U.S. age-adjusted	67	49	137 (PMR)	0.05	1.2–1.7	White males; deaths from cancer of trachea, bronchus, lung (1951–70); 2000–3000 welders
Menck (*37*)	Los Angeles Co.	LA Co. age-specific	21(d) 27(i)	34	137 (d + i) (SMR)	0.05	1.0–1.8	White males; lung deaths (d) (1968–70) plus 2 yr incidence (i) (1972–73); 15,300 welders
Dec. Suppl. (*32*)	Great Britain	National age-adjusted	246	192	127 (PMR)[f]	0.01	1.3–1.8	All males; lung deaths (1968–69); 128,000 welders
					151 (SMR)	0.01		
					116 (SMR)[g]			
Beaumont and Weiss (*33*)	Seattle, Wash.	U.S. age-adjusted	53	40	1.31 (SMR)	NS	0.98–1.6	White males; respiratory cancer deaths (1950–76); 3200 welders
			40	23.7	1.69 (SMR)	0.01	1.1–2.3	and burners (base rate 38/100,000)
Breslow et al. (*38*)	California	Noncancer patients in same hospitals	14/16[h]	9/16[h]	1.5	0.05	1.1–1.9	Males, lung cancer patients (1949–52); 493 cases; 493 controls matched for smoking habits; 5 yr employment as welders and sheet metal workers doing welding

[a]The number expected for any given cohort is extremely dependent on the reference population chosen and hence the observed/expected ratio will exhibit the same sensitivity.
[b]Observed.
[c]Expected.
[d]Significance.
[e]Limits to O/E within 95% confidence interval.
[f]PMR social class adjusted.
[g]SMR adjusted for smoking [excess incidence = 122% = SMR (expected) 110–160 = 135 smoking adjustment: 151–135 = 116).
[h]Proportion of cases among welders (14 cases, 2 controls).

Individuals who occupationally perform welding fall into several distinct categories. In countries, like Great Britain, with a well defined apprenticeship system, workers enter the welding trade at the age of 17 and remain for the major fraction of their working life (*21*). Approximately one half of this population is itinerant within the trade, being occupied with a wide range of technologies both daily and within a working lifetime. Perhaps an equal number of individuals are engaged in rather well defined and limited range of welding situations, and are exposed over relatively long periods to a narrow range of types of welding fumes (e.g. stainless steel welders). In addition to these fulltime welders there exists a large population of individuals in other jobs who weld occasionally and who contribute of the order of 30% fulltime equivalents to the populations listed in Table 3.

Since the nominal composition of the fumes from most welding processes is known (*1-3*, *10*), it is instructive to examine the technologies most representative for the industry in order to determine if there exist well defined cohorts who might suffer excessive exposure to suspected carcinogens, and conversely, to identify unexposed cohorts who might serve as control groups. If the welding population can be shown to have a sufficiently inhomogeneous exposure to carcinogens, one could then address the problem of identifying, quantifying, and eliminating the "hot spots" thereby defined.

Of the five metals which have been identified or strongly suspected as being human carcinogens (in some frequently unknown form) [As, Be(?), Cd, Ni, Cr] (*41-47*), nickel and chromium appear in significant concentrations only in the fumes from stainless and alloy steels, arsenic is a ubiquitous trace impurity in most welding fluxes, cadmium is absent from welding consumables but occurs in many brazing alloys (an allied but separate trade), and beryllium is most probably present only in certain highly unique situations. Approximately 40% of all MMA welders (on mild steel), mostly those employed in

Table 6. Typical exposures (8 hr).

% of welding population	Process	Exposure, $\mu g/m^3$ Total fume	Fe_3O_4	Benzo (a) pyrene	Total organic (gaseous)	Total Cr	Cr(VI) (water-soluble/ insoluble)	Total Ni	As	Asbestos	Cutting Oil	NO_2	O_3
36 ± 5	MMA/MS unprimed[a]	5000	2000	0.06	15	0.5	0.25/0.25	–	2.5	+[b]	+	+	–
24 ± 5	MMA/MS shop primed surfaces[a]	10000[c]	4000	?	300[c,d]	1.0	0.5/0.5	–	5	+[b]	?	+	
10 ± 5	MMA/MS	5000	500	–	–	200	140/10	50	–	–	+	+	–
2 ± 1	MIG/SS	2500	1250	–	–	250	20/5	125	–	–	+	+	–
3 ± 2	AL/MIG	10000	800	–	–	8	4/4	–	–	–	–	+	+

[a]MIG/MS and MAG/MS values are expected to be similar to corresponding MMA/MS exposure but depend to such a great extent on consumables etc. that MIG/MS and MAG/MS welders cannot be assumed to form a homogeneous exposure group.
[b]Shipbuilding and structural steel trades.
[c]Assuming a zinc-based primer.
[d]Assuming a formation rate of 3 ± 2% of that of total fume.

shipyards, utilize base material coated with shop primer, an antirust compound, usually a polyvinyl butyral or phenolic or epoxy resin, containing iron oxide and/or zinc tetraoxychromate. Welding on this material produces a fume containing 1-3% organic gases from the pyrolytic decomposition of the primer. In addition to aldehydes, alcohols and ketones, this organic "soup" has been shown to contain a vast variety of compounds such as naphthalene, methylbenzofurene, phenol, cresol, dioxane, pyridine, 2,4-dexadienal, 2-hexanone, and benzene and other saturated and unsaturated alphatic and aromatic hydrocarbons (C_6-C_{14}) (*48*, *49*) and therefore must be suspected of possessing some carcinogenic potency of unknown but nonzero magnitude. Most other welding fumes are free of organic material (a notable exception being that from cellulose electrodes used on pipelines).

In addition to welding fumes, bystander exposure to carcinogens might be significant: at least 40% of all welders have some historical contact with asbestos (*21*, *39*), while those working in machine shops have occasional exposure to cutting oil mist, a suspected sinonasal carcinogen (*50*, *51*). Most welders are exposed to iron oxide particulates, which alone are probably inactive, but which appear to be a cocarcinogen for benzo(a)pyrene (*52*) which has been identified in some workshop backgrounds (*3*). The magnitude of possibly carcinogenic exposures which are expected to accompany the use of some representative welding technologies is summarized in Table 6, derived from nominal concentrations and compositions shown in Figure 1 and Table 3, respectively.

Semiquantitative Risk Assessment

The ubiquitous exposure of most welders to possible work place carcinogens as illustrated in Table 6 might well explain the observed excess incidence of respiratory tract cancer summarized in Table 5. The demonstrated 5:1 excess incidence of mesothelioma among dockyard welders in Plymouth, England (*36*), giving an absolute rate of 80/100,000 cases/man year could contribute only of the order of 10% to the average overincidence of welders respiratory tract cancer if this "signal" cancer due to asbestos exposure is included, although no specific mention of this tumor is found in the studies listed in Table 5. Naval dockyards in general, and Plymouth in particular, may represent a mesothelioma "hot spot." On the other hand, it is tempting to try to estimate what fraction of actual risk is represented by the exposure of stainless steel welders to Cr(VI) and Ni since, because of their skills, they represent a coherent cohort with reasonably well defined exposures with a minimum of confounding effects (no asbestos), and the health effects of occupational exposure to Ni and Cr have been studied to a great extent in the respective (nonwelding) Ni and Cr industries (*41-47*).

Although a linear dose-response model is probably inappropriate for human cancer (*53*), and the available and relevant information is fragmentary and frequently inaccurate, one can attempt a survey of exposure-response data found in the literature of epidemiological studies carried out in the chromium and nickel industry. A tentative summary of relevant data is presented in Table 7. Here

Table 7. Approximate carcinogenic dose-response relationship.

	Total metal (cumulative exposure), $mg/m^3 \cdot yr$[a]	Absolute lung cancer incidence rate/100,000	Latency, yr (average)	Age group at risk (average)
Chromium industry	Total Cr(VI)			
Cr plating (*54*)	0.5	< 360[b]	(16)	(58)
Ferrochrome (*55*)	0.44	100	5–42 (21)	54–79
Chromate (*56*)	2–25 (4)	600	8–39 (22–32)	45–64
Chrome pigment (*57*)	2.0	760	5–21	
Chrome pigment (*58*)			(15)	(50)
Average Cr(VI)	3 ± 2	500 ± 250	(21)–(15)	45–79
Nickel refining industry (Clydach) (*59, 60*)	Total Ni 11–110[c]	64 (lung)	15–40	44–79
Average[c]	33	21 (nasal)	20–34	(68)

[a]Estimated geometrical average.
[b]Maximum consistent with observed nonsignificant overincidence.
[c]Exposure is to $Ni(CO)_4$ + Ni + NiO + Ni_3S_2.

estimated geometrical-average cumulative exposures to Cr(VI) and average lung cancer rates are listed together with the relevant age group and range in latency period for the four industries: chromium plating and ferrochrome, chromate and chrome pigment production (*54-60*). Exposure in the case of chromium plating is principally to water-soluble Cr(VI), while in the other three industries it is to a varying mixture of Cr(VI) and Cr(III) of different solubilities. The values shown must be considered highly uncertain and the tentative conclusion that these industrial exposures can be considered to result in an approximately similar risk per dose in the range shown must be considered extremely speculative, since an additive model of carcinogenicity with a single causitive agent is implicitly used. Note that if the distributions of exposure shown in Figure 1 are typical in other industries, there is approximately a range of a factor of 16 for the exposure levels of 90% of the cohorts studied.

Historical exposures are extremely difficult to estimate since even in those cases where reliable concentration measurements have been made, they show such a wide interindividual range that one can question the statistical use of a geometrical (or any other) average: compositions can frequently only be arrived at by an educated guess, leading to an order of magnitude uncertainty in estimates for total exposures. Furthermore, for the case of Ni and Cr, the actual causative agents are unknown and there is emerging evidence that at least for Ni, there is an extremely wide variation of carcinogenic potency for different substances.

In spite of the obvious speculative nature of the data of Table 7 one could attempt to use the dose-incidence data to predict order of magnitude effects for stainless steel welders. A 20-year exposure to the average Cr(VI) concentration of 0.15 mg/m^3 found for MMA/SS welders would give an average total Cr(VI) exposure of 3(mg/m^3) (years), similar to that found in Table 7 in the chromium industry, and hence might be expected to lead to the same magnitude of cancer incidence. Obviously the exposure, and hence on this simple model the expected incidence rates, for MIG/SS welders are of the order of a factor of six lower than for MMA/ SS welders. The risk for Ni for these trades, although non-zero, is negligible compared to that for Cr(VI), with the exception of the relatively few MIG welders using pure Ni filler wire. Such interindustrial comparisons, if appropriate, can also be used as an aid in the proper design of epidemiological studies by indicating those exposure levels, latency periods, and cohort sizes consistent with detection of an effect at an acceptable level of significance. For example, a cohort of some 200 MMA/SS welders exposed at high total fume concentrations (10 mg/m^3) for the period 1950-1955 and followed to 1980 should provide statistical material just sufficient to verify or reject the model presented above.

One unavoidable conclusion to be made based on the preceeding discussion is that unless water soluble Cr(VI) is not a carcinogen of potency comparable to that of other industrial Cr(VI) exposures, the manual metal arc welding of stainless steel with conventional electrodes represents a "hot spot" for risk of occupationally related respiratory tract cancer. Should this exposure represent a potential

overincidence of a factor of three (SMR = 300), then the 10% subcohort of MMA/SS welders could contribute to approximately a 30% overincidence for the entire industry (SMR = 130). It is not clear in which direction systematic errors and bias in the selection of data will effect such a zeroth order risk assessment. Certainly the probable nonlinearity of the dose-incidence relationship will provide for a disproportionately large effect among those individuals with significantly higher than average exposures.

Since there is as yet little epidemiological data (on selected subcohorts of welders with restricted exposures) on which to attempt an evaluation of the type of risk assessment proposed above, justification for the supposition of process-dependent "hot spots" (especially of genetic risk) must be sought on the basis of indirect (i.e., nonhuman) experiments on the (geno)toxic properties of welding fumes.

Screening Tests for Mutagenesis and Carcinogenesis

Utility of Screening Tests

Because of the existence of an extraordinarily wide variety of welding atmospheres, a direct determination of toxic risk for welding fume by traditional *in vivo* methods is impractical: such studies would only provide information concerning a single process or group of processes and only with difficulty could be extrapolated to a larger segment of the industry. Similarly evaluation of most single processes by means of human epidemiology is impractical. On the other hand, short-term screening tests for mutagenesis and carcinogenesis would appear to be ideally suited for use in evaluating the relative genetic risk entailed by exposure to various welding fumes assuming that the obvious problems concerning exposure-related dose for such complex aerosol systems can be resolved. The fumes have an aerodynamic mass median diameter (MMD) of the order of 0.2 μm (*61*) (MMA fumes have an additional component with MMD = 1 μm) and a demonstrated elemental deposition in the human respiratory tract of the order of 30-40% (*62*).

Despite the uncertainty in the relationship between mutagenicity and carcinogenicity of metals (*41, 42, 47, 63-66*), semiquantitative fast *in vitro* screening methods could be used to assess relative risks of welding fumes of similar composition by studying the origin of variations of genotoxicity and hence by implication their possible carcinogenic potency (*67-69*). Such conclusions can be based on the expectation that a number of steps which determine specific (i.e., molar) genotoxicity *in vitro* (solubility, species formation rate and activity of intermediate metalorganic metabolites, membrane diffusion, the nature and efficiency of detoxification pathways and repair mechanisms, and particle cell interactions (such as phagocytosis)) can be expected to exist *in vivo* as well (*70-75*).

Although at present there is not sufficient information to be able to interpret the significance of the general observation of mutagenicity of a large number of the metals many of which can be found to some degree in various welding fumes, there would appear to be strong incentive to examine the possibility for the *in vitro* risk assessment of nickel and chromium, not only because of their importance in welding, but because of the widespread worker exposure in other industries. The development of specific screening techniques for Ni and Cr welding aerosols, and the subsequent demonstration of their general applicability would be a significant step in industrial hygiene.

Mutagenicity of Ni and Cr

The present state of understanding of the mutagenicity of Ni and Cr has recently been reviewed (*42, 47, 66, 76*). Nickel induces base-pairing aberrations of nuclear acids, infidelity of DNA replication, chromosome aberrations in cultured mammalian cells, sister chromatid exchange in cultured human lymphocytes *in vitro* and aberrant DNA synthesis and/or repair and binding to nuclear macromolecules *in vivo*. Neoplastic cell transformation can be induced by particulates of crystalline Ni_3S_2 (a potent experimental animal carcinogen) which excite phagocytosis but not by amorphous NiS (a concarcinogen).

Hexavalent chromium, Cr(VI), induces infidelity of DNA replication, is mutagenic in bacterial test systems (*B. subtillis*, *S. typhimurium*), and induces chromosomal aberrations and aberrant DNA synthesis or repair in tissue culture cells *in vitro*. The cytotoxic activity of Cr(VI) is eliminated by the extracellular reduction to Cr(III), an oxidation state for which there is little membrane permeability. On the other hand Cr(III) is highly effective in inducing infidelity of DNA synthesis, indicating that Cr(III) may be the ultimate carcinogen and that reduction of Cr(VI) at a target molecule may be the critical carcinogenic step (*77*). Only $CaCrO_4$ has been established as an experimental animal carcinogen, and there is considerable uncertainty about the exact role played by solubility of Cr(VI) compounds in the determination of their carcinogenic potency (*42, 43, 47*).

Table 8. Range of distribution in oxidation state and solubility fraction for Cr and Ni in stainless steel welding fumes.

Process and oxidation state	Water-soluble, %	Serum-soluble, %		Insoluble, %	Total, %
		pH = 8.8	pH = 7.0		
MMA/SS					
Cr (III) + Cr	0			0.2–2.1	0.2–2.1
Cr (VI)	2.2–4.3			0.03–0.42	2.2–4.3
Total Cr	2.2–4.3			0.2–2.5	2.4–6.4
Ni	0.01–0.3			0.27–1.6	0.38–1.9
MIG/SS					
Cr (III) + Cr	0			3.56–13.78	3.56–13.78
Cr (VI)	0.005–1.5[a]			0.01–0.42	0.02–2.0
Total Cr	0.005–1.5			3.60–13.8	4.06–15.3
Ni	0.05–0.25			3.5–6.3	3.5–6.5
MIG/Ni[b]					
Ni					
Ni:NiO = 1:1	0.2–0.4	0.5–1.2	13–43		69–72
Ni:NiO = 1:10	0.2–0.35	0.5–0.6	7–9		56.3–68.3

[a]Decays rapidly (is reduced to 0.5% after 24 hr at room temperature) (*78*, *79*).
[b]Data of Nieburh et al. (*80*).

Mutagenicity Studies of Welding Fumes

A number of pilot studies have recently been undertaken to determine the extent and origin of genotoxicity of welding fumes. Such a study is necessary in any attempt to rank fumes from various processes in terms of relative genetic risk. The need for rapid screening methods can be inferred from Table 8, which shows the range of Cr and Ni in various solubilities and oxidation states in some typical MIG/SS and MMA/SS welding fumes. It can be seen that relative concentrations of individual components vary by an order of magnitude even in the limited sample shown here, and presumably some rapid method must be developed to determine the risk associated with each of the various combinations of metals produced.

Stainless steel welding fumes are positive in the Salmonella histidine revertant plate incorporation test (*81*, *82*), where the active mutagen has now been shown to be Cr(VI) (*83*, *84*). Fumes from MIG/SS show a specific (molar) revertant rate equal to that for their water soluble Cr(VI) content while those from MMA/SS show a reduced rate indicative of an antisynergistic effect. The addition of microsomes results in a (occasionally complete) reduction of the effect. The test system is negative for fumes which contain only Ni, and for others in which Cr(VI) is absent (including those from mild steel welding processes).

A slight but statistically significant increase in mutagenicity is observed for stainless steel welding fumes in the *N*-thioguanine resistence of V79 chinese hamster cells which survive exposure to the highly toxic material (*82*).

The recessive lethal test in drosophila is negative for exposure in the larval stage to MIG/Ni fumes (a mixture of Ni:NiO) and to MIG/SS particles, and to fresh MIG/SS fume in the adult stage. No significant enhancement for adult sensitivity to DES was found to result from fresh MIG/SS exposure (*83*).

Aqueous solutions of $NiSO_4$ and aqueous and (fetal calf) serum-soluble fractions prepared from a Ni rich welding fume (MIG/Ni) demonstrate equal specific activity in inducing sister chromatid exchange in human peripheral lymphocytes in culture. The serum solubility of both Ni and NiO is extremely high at physiological pH (7.2), as shown in Table 8 (*80*).

Water-soluble Cr(VI) and fumes from an MMA/SS welding process representing an equivalent Cr(VI) dose show similar transplacental genotoxic potency in interperitoneal administration in the mouse spot test (Fleckentest) (*85*, *86*). Stainless steel fume particles are cytotoxic and genotoxic in cultured mammalian cells (*87*, *88*).

From these pilot studies it can be seen that Cr(VI) and Ni as contained in welding fumes apparently exhibit the same types of genotoxicity as is expected for these metals in general (*60*, *73*, *89*, *90*). Since there is no evidence to the contrary, one should assume that the actual risk for genetic damage and other delayed health effects to welders can be expected to be similar to that found in other industries with exposure to these substances. The presence of some unique combinations, such as ozone-Cr(VI), Ni-Mn, however, might result in local

synergistic or antisynergistic effects, which should be studied in detail.

Summary and Conclusions

Throughout the industrialized world the welding industry is found to provide a relatively large population with a potential exposure to high concentrations of a wide range of toxic and biologically active material, occupational exposure to some of which, albeit in other forms and in other industries, is suspected of inducing human respiratory tract cancer. *In vitro* and *in vivo* studies of some representative welding fumes demonstrate mutagenic, embryotoxic, cytotoxic and genotoxic potential. Epidemiological studies show that welders exhibit a statistically significant excess incidence of respiratory tract disease, including cancer, which appears to depend on cumulative exposure. Further evidence implies that specific occupational risk, especially of delayed health effects, may be extremely process-dependent. There is also strong evidence that the local workshop environment significantly influences the degree of such risk. The factors which can effect the absolute health risks experienced by different welding cohorts should in principle be controllable if they can be identified. A demonstration that inhomogeneous risks are primarily restricted to "hot spots" would have major implications for the assignment of priorities for the use of limited resources for risk reduction within the industry.

The first indication of a significantly enhanced lung cancer risk (i.e., a "hot spot") for a cohort of stainless steel welders which satisfies the necessary criteria of length and magnitude of exposure, and latency period has recently been published (*91*). For the cohort studied (234), mostly MMA/SS welders with a minimum of 5 years experience: average exposure of 16 years (3735 man-years) to Cr(VI) concentrations of approximately 216 $\mu g/m^3$) three cases of respiratory tract cancer were found vs. 0.68 expected. The average cumulative exposures of 3.4 (mg/m^3 years) result in a risk rate of 82/100,000 cases/man-year with a local background of 18/100,000: a risk ratio of 4.4:1. These observations lie within a factor or two for the risk ratio and within a factor of six for the absolute excess incidence rate predicted for this exposure to Cr(VI) by the crude semiquantitative risk assessment model presented. Although it is obvious that there is not as yet sufficient evidence on which to test any health risk model for welders, it is clear that the combination of risk assessment methodologies and good epidemiological data will be a powerful tool for the future.

The international welding industry would appear capable of providing a large number of model populations on which to base the development of techniques of multifocal epidemiological studies to determine the origin and extent of process-specific risk. Great care must, however, be taken in design of the study protocols to cope with the observed differences between various welding populations. Recent discussions concerning the variation in age adjusted lung cancer incidence with occupation found for local populations (*55*), and the strong urban-rural gradient (*92*) which they exhibit, point to a possible uncertainty in expected incidence rates of a factor of from two to four: the results of multifocal epidemiological studies carried out on essentially similarly exposed populations would be extremely useful in helping to establish guidelines for the choice of appropriate reference populations, without which it may be extremely difficult to prove the existence of occupationally related excess cancer risks. The parallel development of *in vitro* fast screening tests for mutagenesis and/or carcinogenesis appropriate for use with metallic particulate aerosols might provide a unique opportunity for the establishment of practical risk assessment protocols for use in the metal industry in general. The resulting protection against exposure to carcinogens should reduce the risk for genetic effects in general (*93*).

Without the development of risk assessment methodologies, protective legislation (i.e., TLVs) based on the concept of homogeneous risk, if set at the lowest feasible level, will penalize industries with low risk exposures, while elevated compromise levels might permit dangerous exposures to unidentified high risk material. Finally, it should be pointed out that the wealth of technologies available to this important, populous industry ensures that if "hot spots" of risk can be identified, the means of reducing risk at the source are at hand, provided appropriate alternate low risk procedures can be identified.

Added in proof: Analysis of the citations of a recent literature search (*2*) has uncovered over 100 cases of welders who exhibit abnormal epithelial proliferation ("fibrosis"). For the more than 70 cases for which welding history is known and diagnosis is verified by pathology, the observed incidence is uniformly distributed over starting age (13-52 years) and length of exposure (3-40 years), and does not appear to indicate any specific process-dependent risk (e.g., stainless steel welders account for 5-10% of the welding population), although *in vitro* studies show that fumes from stainless steel welding have a high fibrogenic potential compared to those from other processes (*94*).

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REFERENCES

1. Stern, R. M. Identification, evaluation and elimination of risk in the welding industry. In: Proceedings of the Colloquium on Welding and Health, Instituto de Soldadura, International Institute of Welding, Commission VIII, Lisbon 1980. SVC Report 80.26 from The Danish Welding Institute, Park Alle 345, 2600 Glostrup, Denmark.
2. Stern, R. M. A preparatory study of the exposure of welders to toxic substances and the resulting health effects. Report for Commission of the European Communities, Directorate General for Employment and Social Affairs, Health and Safety Directorate, Luxembourg, 1980; Danish Welding Institute Report 80.36.
3. Ulfvarson, U. Arbetsmiljöproblem vid svetsning. Del II: Kartläggning av luftföroreningar vid svetsning. Arbete och Hälsa Vetenskaplig Skriftserie, Vol. 31, Arbetarskydsverket, Stockholm, 1979.
4. Van der Sluis, H., TNO Appeldorn, private communication.
5. Masumoto, I., Godai, T., and Okuda, N. Recent trends in welding consumables in Japan. Kobe Steel Ltd., Japan, 1979.
6. Jefferson, T. B. Welding has a record year. Welding Design Fabrication, July 1977.
7. Flemming, D., and Sossenheimer, H. Schweissen Heute und Morgen. DUS, Düsseldorf, 1972.
8. Dorn, L. (Technische Universität Berlin), personal communication of unpublished data.
9. Beck Hansen, E. Fumes from welding and cutting in Danish shipyards. Report SF77.01, Danish Welding Institute, 1977.
10. Stern, R. M. The classification of welding electrodes using the Swedish fume box technique. SVC Report SF 78.08, The Danish Welding Institute, Park Alle 345, 2600 Glostrup, Denmark, 1978.
11. Stern, R. M. The production and characterization of a reference standard welding fume: Introduction, Parts I, II, III. SVC Reports 76.00, 76.05, SF 78.01, SF 78.09, The Danish Welding Institute, Park Alle 345, 2600 Glostrup, Denmark, 1976, 1978.
12. Franchini, I., Mutti, A., Cavatorta, A., Corradi, A., Cosi, A., Olivetti, G., and Borghetti, A. Nephrotoxicity of chromium. Contr. Nephrol. 10:98-110 (1978).
13. Jindrichova, J. Chromium-induced injuries in electric welders. Z. Gesamte Hyg. 24:86-88 (1978).
14. Kalliomäki, P.-L., Kalliomäki, K., Kelhä, V., Sortti, V., and Korhonen, O. Measurement of lung contamination among mild steel and stainless steel welders. Welding in the World 18:67-72 (1980).
15. Keskinen, H., Kalliomäki, P.-L., and Alanko, K. Occupational asthma due to stainless steel welding fumes. Clin. Allergy 10:151-159 (1980).
16. Mutti, A., Cavatorta, A., Pedroni, C., Borghi, A., Giaroli, C., and Franchini I. The role of chromium accumulation in the relationship between airborne and urinary chromium in welders. Int. Arch. Occup. Environ. Health 43:123-133 (1979).
17. Stettler, L. E., Groth, D. H., and Mackay, G. R. Identification of stainless steel welding fume particulates in human lung and environmental samples using electron probe microanalysis. Am. Ind. Hyg. Assoc. J. 38:76-82 (1977).
18. Tola, S., Kilpiö, J., Virtamo, M., and Haapa, K. Urinary chromium as an indicator of the exposure of welders to chromium. Scand. J. Work Environ. Health 3:192-202 (1977).
19. Coggio, L. P. Statistical survey of pneumoconiosis in the La Spezia shipyard. Riv. Infortuni Malat. Prof. 66:297-353 (1979).
20. Gobbato, F., Cova, F., Munafo, G., and Zanin, T. Frequency and nature of pleural alterations in naval shipyard welders. Riv. Med. Lav. Ihiene Ind. Napoli 3:49-59 (1979).
21. Attfield, M. D., and Ross, D. S. Radiological abnormalities in electric arc welders. Brit. J. Ind. Med. 35:117-122 (1978).
22. Mehl, J. Problems of pulmonary siderosis in electric welders. Szczecin. Tow. Nauk, 19:113-124 (1976).
23. Hatch, T. Permissible dustiness. Am. Ind. Hyg. Assoc. Quart. 16:30-35 (1955).
24. Doig, A. T., and McLaughlin, A. I. G. Clearing of x-ray shadows in welder's siderosis. Lancet i:789-791 (1948).
25. Guidotti, T. L., DeNee, P. B., Abraham, J. L., and Smith, J. R. Arc welders pneumoconiosis: application of advanced scanning electron microscopy. Arch. Environ. Health, 33:117-124 (1978).
26. Caudarella, R., Cascella, D., Tabaroni, G., Corso, T., and Raffi, G. B. Occupational disease of welders—I. Respiratory effects. G. Ital. Med. Lav. 1:31-37 (1979).
27. Bosse, R., Sparrow, D., Costa, P. T., and Weiss, S. T. Cigarette smoking, aging, and decline in pulmonary function: a longitudinal study. Arch. Environ. Health 35:247-252 (1979).
28. Oxhöj, H., Bake, B., Wedel, H., and Wilhelmsen, L. Effects of electric arc welding on ventilatory lung function. Arch. Environ. Health 34:211-217 (1979).
29. Pham, Q. T., Mastrangelo, G., Chau, N., and Haluszka, J. Five year longitudinal comparison of respiratory symptoms and function in steelworkers and unexposed workers. Bull. Eur. Physiopathol. Respir. 15:469-480 (1979).
30. Langaard, S. A survey of respiratory symptoms and lung function in ferrochromium and ferrosilicon workers. Int. Arch. Occup. Environ. Health 46:1-9 (1980).
31. Lob, M. Problèmes medicaux poses par le soudage. J. Soudure 7:178-183 (1979).
32. Office of Population Censuses and Surveys. Occupational Mortality. The Registrar General's Decennial Supplement for England and Wales, 1970-72. HMSO, London, 1978.
33. Beaumont, J. J., and Weiss, N. S. Mortality of welders, shipfitters, and other metal trades workers in boilermakers local No. 104-AFL-CIO. Am. J. Epidem., in press.
34. Puntoni, R., Russo, L. K., Zannini, D., Vercelli, M., Parodi Gambaro, R., Valerio, F., and Santi, L. Mortality among dock-yard workers in Genoa, Italy. Tumori, 63:91-96 (1977).
35. Blot, W. J., Harrington, J. M., Toledo, A., Hoover, R., Heath, C. W., Jr., and Fraumeni, J. F. Lung cancer after employment in shipyards during World War II. New Engl. J. Med. 299:620-623 (1978).
36. Sheers, G., and Coles, R. M. Mesothelioma risks in a naval dockyard. Arch. Environ. Health 35:276-282 (1980).
37. Menck, H. R., and Henderson, B. E. Occupational differences in rates of lung cancer. J. Occup. Med. 18:797-801 (1976).
38. Breslow, L., Hoaglin, L., Rasmussen, G., and Abrahms, H. K. Occupations and cigarette smoking as factors in lung cancer. Am. J. Publ. Health 44:171-181 (1954).
39. Milham, S., Jr. Cancer mortality patterns associated with exposure to metals. Ann. N. Y. Acad. Sci. 271:243-249 (1976).

40. Vinni, K., and Hakama, M. Defining expected mortality in occupational studies. Scand. J. Work Environ. Health 5:62-65 (1979).
41. IARC. Evaluation of the Carcinogenic Risk of Chemicals to Man, Vol. II. Cadmium, Nickel, Some Epoxides, Miscellaneous Industrial Chemicals, and General Considerations on Volatile Anasthetics. IARC, Lyon, 1976.
42. IARC. Evaluation of the Carcinogenic Risk of Chemicals to Man, Vol. 23. Some Metals and Metallic Compounds, IARC, Lyon, 1980.
43. NIOSH. Criteria for a Recommended Standard for Occupational Exposure to Chromium VI. USDHEW Publ. 76-129, Washington, D.C., 1975.
44. NAS. Chromium: The Medical and Biological Effects of Environmental Pollutants. NAS, Washington, D.C., 1974.
45. NAS. Nickel: The Medical and Biological Effects of Environmental Pollutants. NAS, Washington, D.C., 1977.
46. NIOSH. Criteria for a Recommended Standard for Occupational Exposure to Inorganic Nickel. USDHEW Publ. 77-164, Washington, D.C., 1977.
47. Nordiska Expertgruppen för Gränsvärdesdokumentation. Krom. Arbete och Hälsa Vetenskaplig Skriftserie, Vol. 33, Arbetarskyddsverket, Stockholm, 1979.
48. Bille, M., Rosendahl, C.-H., Steen, A., Svensson, L., and Wallen, K.-A. Determination of decomposition products formed during welding on painted steel. Svetsaren, 2:6-13 (1976).
49. Linden, G., Lindskog, G., and Neverland, P. Chemical health hazards in welding and thermal cutting of coated materials. Institutet för verkstadsteknisk forskning resultat 78501—Feb. 1978: Sveriges Mekanförbund, Box 5506, 11485, Stockholm.
50. Roush, G. C., Meigs, J. E., Kelly, J. A., Flannery, J. T., and Burdo, H. Sinonasal cancer and occupation: a case-control study. Am. J. Epidemiol. 111:183-193 (1980).
51. Huygen, P. L. M., van den Broek, P., and Fischer, A. J. E. M. Nasopharyngeal cancer and occupation. Tijdschr. Soc. Geneeskunde 57:733-736 (1979).
52. Safiotti, V. R., Montesano, A. R., Sellakumar, A. R., and Kaufman, D. G. Respiratory tract carcinogenesis in hamsters induced by different numbers of administrations of benzo(a)pyrene and ferric oxide. J. Natl. Cancer Inst. 44:1073 (1972).
53. Peto, R. Epidemiology, multistage models and shortterm mutagenicity tests. In: Origins of Human Cancer, Cold Spring Harbor Laboratory, 1977, pp. 1403-1428.
54. Royle, H. Toxicity of chromic acid in the chromium plating industry, I, II. Environ. Res. 10:39-53, 141-163 (1975)
55. Langård, S., Andersen, Å., and Gylseth, B. Cancer incidence among ferrochromium and ferrosilicon workers. Brit. J. Ind. Med. 37:114-120 (1980).
56. Mancuso, T. F. Consideration of chromium as an industrial carcinogen. Paper presented at the International Conference on Heavy Metals in the Environment, Toronto, Ontario, Canada, Oct. 27-31, 1975.
57. Davies, J. M. Lung cancer mortality of workers in chromate pigment manufacture: an epidemiological survey. J. Oil Color Chemists Assoc. 62:157-163 (1979).
58. Langård, S., and Norseth, T. A cohort study of bronchial carcinomas in workers producing chromate pigments. Brit. J. Ind. Med. 32:62-65 (1975).
59. Barton, R. T. Nickel carcinogenesis of the respiratory tract. J. Otolaryng. 6:412-422 (1977).
60. Anon. Nickel and Its Inorganic Compounds. International Nickel Company, unpublished report, 1976; cited by Langaard (*23*).
61. Stern, R. M. Gesundheit in der Industrie-Forschungsarbeiten am Dänischen Schweissinstitut. Zeit. Schweisstech. 6:127-138 (1979).
62. Akselsson, K. R., Desaedeleer, G. G., Johansson, T. B., and Winchester, J. W. Particle size distribution and human respiratory deposition of trace elements in indoor work environments. Am. Occup. Hyg. 19:225-238 (1976).
63. Sunderman, F. W., Jr. Carcinogenic effects of metals. Fed. Proc. 37:40-46 (1978).
64. Sunderman, F. W., Jr. Carcinogenicity and anticarcinogenicity of metal compounds. In: Environmental Carcinogenesis, P. Emmelot and J. Kriek, Eds., Elsevier/North-Holland Press, 1980.
65. Sunderman, F. W., Jr. Mechanisms of metal carcinogenesis. In: Biological Trace Element Research, Vol. 1, Humana Press Inc., 1979.
66. Flessel, C. P. Metals as mutagenic initiators of cancer. In: Trace Metals in Health and Disease, N. Kharasch, Ed., Raven Press, New York, 1979, pp. 109-122.
67. Casto, B. C., Meyers, J., and DePaolo, J. A. Enhancement of viral transformation for evaluation of the carcinogenic or mutagenic potential of inorganic metal salts. Cancer Res. 39:193-198 (1979).
68. DiPaolo, J. A., and Casto, B. C. Quantitative studies of *in vitro* morphological transformation of Syrian hamster cells by inorganic metal salts. Cancer Res. 39:1008-1013 (1979).
69. Sirover, M. A., and Loeb, L. A. Infidelity of DNA synthesis *in vitro*: screening for potential metal mutagens or carcinogens. Science 194:1434-1436 (1976).
70. Weinzierl, S., and Webb, M. Interaction of carcinogenic metals with tissue and body fluids. Brit. J. Cancer 26:279-291 (1972).
71. Hopfer, S. M., Sunderman, F. W., Jr., Fredriksson, T. N., and Morse, E. E. Nickel-induced erythrocytosis: efficacies of nickel compounds and susceptibilities of rat strains. Ann. Clin. Lab. Sci. 8:396-402 (1978).
72. Costa, M., Nye, J., and Sunderman, F. W., Jr. Morphologic transformation of Syrian hamster fetal cells induced by nickel compounds. Fed. Proc. 37:231 (1978).
73. Oskarsson, A., Andersson, Y., and Tjävle, H. Fate of nickel subsulphide during carcinogenesis studied by autoradiography and x-ray powder diffraction. Cancer Res. 39:4175-4185 (1979).
74. Kasprzak, K. S., and Sunderman, F. W., Jr. Mechanisms of dissolution of nickel subsulphide in rat serum. Res. Commun. Chem. Pathol. Pharmacol. 16:95-108 (1977).
75. Costa, M., and Mollenhauer, H. Phagocytosis of nickel subsulfide particles during early stages of neoplastic transformation in tissue culture. Cancer Res. 40:2688-2693 (1980).
76. Sunderman, F. W., Jr. Recent research on nickel carcinogenesis. Environ. Health Perspect. 40: 131 (1981).
77. Gruber, J. E., and Jennette, K. W. Metabolism of the carcinogen chromate by rat liver microsomes. Biochem. Biophys. Res. Comm. 82:700-706 (1978).
78. Thomsen, E., and Stern, R. M. A simple analytical technique for the determination of hexavalent chromium in welding fumes and other complex matrices. Scand. J. Work Environ. Health 5:386 (1979).
79. Thomsen, E., and Stern, R. M. Collection, analysis, and composition of welding fumes. Danish Welding Inst. Rept. 81.09; Scand. J. Work Environ. Health, submitted.
80. Niebuhr, E., Stern, R. M., Thomsen, E., and Wulf, H.-C. Relative solubility of nickel welding fume fractions and their genotoxicity in sister chromatid exchange *in vitro*. In: Nickel Toxicity, S. S. Brown and F. W. Sunderman, Jr., Eds., Academic Press, London, 1980, pp. 129-132.
81. Maxild, J., Andersen, M., Kiel, P., and Stern, R. M. Mutagenicity of fume particles from metal arc welding on stainless steel in the Salmonella microsome test, Mutat. Res. 57:235-243 (1978).

82. Hedenstedt, A., Jensson, D., Lidsten, B.-M., Ramel, C., and Stern, R. M. Mutagenicity of fume particles from stainless steel welding. Scand. J. Work Environ. Health 3:203-211 (1977).
83. Stern, R. M. A chemical, physical and biological assay of welding fume. In: The *In Vitro* Effects Of Mineral Dusts, R. C. Brown, I. P. Gormley, M. Chamberlain, and R. Davies, Eds., Academic Press, London, 1980, pp. 203-209.
84. Stern, R. M., Thomsen, E., and Larsen, H. Origin of welding fume mutagenicity in *S. typhimurium*. In preparation.
85. Knudsen, I. The mammalian spot test and its use for the testing of potential carcinogenicity of welding fume particles and hexavalent chromium. Acta Pharmacol. Toxicol. 47:66-70 (1980).
86. Knudsen, I., and Stern, R. M. Assaying potential carcinogenicity of welding fume and hexavalent chromium with the mammalian spot test. In: Colloquium on Welding and Health, Instituto de Soldadura, International Institute of Welding, Commission VIII, Lisbon, 1980; SUC Report 80.28.
87. Koshi, K. Effects of fume particles from stainless steel welding in sister chromatid exchanges and chromosome aberrations in cultured Chinese hamster cells. Ind. Health, 17:39-49 (1979).
88. White, L. R., Richards, R. J., Jakobsen, K., and Østgaard, K. Biological effects of different types of welding fume particulates. In: The *In Vitro* Effects of Mineral Dusts, R. C. Brown, I. P. Gormley, M. Chamberlain, and R. Davies, Eds., Academic Press, London, 1980, pp. 211-218.
89. Newbold, R. F., Amos, J., and Connell, J. R. The cytotoxic, mutagenic and clastogenic effects of chromium-containing compounds on mammalian cells in culture. Mutat. Res. 67:55-64 (1979).
90. Levis, A. G., and Majone, F. Cytotoxic and clastogenic effects of soluble chromium compounds on mammalian cell cultures. Brit. J. Cancer 40:523-533 (1979).
91. Sjögren, B. A retrospective cohort study of mortality among stainless steel welders. Scand. J. Work Environ. Health 6:197-200 (1980).
92. Doll, R. Atmospheric pollution and lung cancer. Environ. Health Perspect. 22:23-31 (1978).
93. Hemminki, K., Saloniemi, I., Luoma, K., Salonen, T., Partanen, T., Vainio, H., and Hemminki, E. Transplacental carcinogens and mutagens: childhood cancer, malformations and abortions as risk indicators. J. Toxicol. Environ. Health, in press.
94. Stern, R. M., Pigott, G. H., and Abraham, J. L. Fibrogenic potential of welding fume. Report 81.29, Danish Welding Institute, to be published.