It is widely believed that women have almost gained equality, that role-sharing is common at a domestic level, and that a difference in sex roles is now in emphasis only. But though it is true that men help around the house and in child care, and that women who work successfully almost always have helpful husbands, domestic life is still considered to be ultimately the woman's responsibility.[20] What we should aim for is a system that neither excludes men from domestic roles nor women from responsible positions in medicine. This year 40% of the entrants to medical school will be women.[4] Who will their models be and where will they find themselves 15 years hence?

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Public Health

CYANIDE EXPOSURE IN FIRES

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Summary The toxic hazard from cyanide produced in fires was assessed in casualties and in firemen exposed to the fire atmosphere. The levels of cyanide and its principal metabolite, thiocyanate, were measured in blood samples from firemen, non-fatal and fatal casualties, and from controls. Although firemen did not differ significantly from controls, casualties showed significant elevation of blood-cyanide, and in a small proportion of fatalities blood-cyanide reached toxic levels.

INTRODUCTION

THE number of fatalities caused by inhalation of gas or smoke from fires has risen fourfold in the U.K. in the past 20 years,[1] and the possibility that this may arise from increased toxicity of fire atmospheres due to the use of plastics in modern construction and furnishing is causing concern. Carbon monoxide is the most important toxic substance produced in fires, but Woolley has shown[2] that substantial quantities of free hydrogen cyanide and other organic cyanides, recognised as potent metabolic poisons,[3] are released during the thermal decomposition of polyurethane foams. This study was undertaken to assess the potential hazard from cyanide to persons accidentally exposed to smoke and to firemen exposed in the course of their occupation.

METHODS

Cyanide and thiocyanate levels were measured in blood-samples taken from four subject groups: 94 firemen on active service whose last severe exposure to smoke occurred between 3 hours and 1 year before sampling; 21 non-fatal fire casualties overcome by smoke; 52 subjects who died in dwelling-house fires (49 cases) or industrial fires (3 cases); 56 controls attending a hospital outpatient clinic. Samples were taken from non-fatal casualties within 24 hours of admission to hospital and from fatalities at necropsy, 24–72 hours after death. The mean tobacco intakes of control and firemen smokers were 18 and 24 cigarettes/day respectively.

Samples were stored at 4°C until analysed, normally within

TABLE I—CYANIDE AND THIOCYANATE LEVELS IN CONTROLS, FIREMEN, AND CASUALTIES

Subject group	Cyanide (μmol/l)				Thiocyanate (μmol/l)			
	No. in group	Range	Mean	S.D.	No. in group	Range	Mean	S.D.
Control non-smokers	29	0–11·7	2·9	2·4	30	10·2–166	30·7	28·8
Control smokers	27	1·3–19·4	6·8	4·2	24	18–110	59·8	26·1
Firemen non-smokers	30	0·1–14·9	3·6	3·5	30	3·9–103	25·8	19·3
Firemen smokers	64	0·5–22·9	8·5	5·2	63	0·7–138	65·5	123
Non-fatal-casualty non-smokers	11	0–29·0	10·4	8·0	11	2–144	66·7	42·4
Non-fatal-casualty smokers	10	3·8–22·6	13·2	6·3	10	49·6–183	96·1	40·5
Fatalities	52	0–130	25·3	27·9	50	1–58·5	19·2	16·6

TABLE II—COMPARISON OF MEAN CYANIDE AND THIOCYANATE LEVELS IN CONTROLS, FIREMEN, AND CASUALTIES BY STUDENT'S T-TEST

Group 1	Group 2	Cyanide		Thiocyanate	
		t-value	P	*t*-value	P
Control smokers	Control non-smokers	4·2	< 0·001	3·9	<0·001
Firemen smokers	Firemen non-smokers	5·3	<0·001	2·5	0·015
Firemen non-smokers	Control non-smokers	0·9	0·358 (N.S.)	0·8	0·445 (N.S.)
Firemen smokers	Control smokers	1·6	0·114 (N.S.)	0·4	0·728 (N.S.)
Non-fatal-casualty non-smokers+smokers	Control non-smokers + smokers	5·7	<0·001	4·8	<0·001
Non-fatal-casualty non-smokers+smokers	Firemen non-smokers + smokers	3·9	<0·001	2·3	0·024
Fatalities	Non-fatal-casualty non-smokers+smokers	3·3	0·001	−8·7	<0·001
Fatalities	Control non-smokers + smokers	5·3	<0·001	−5·1	<0·001

N.S. = Not significant

3 days. Cyanide was measured by colorimetry[4] and gas-liquid chromatography.[5] Thiocyanate was measured by colorimetry.[6] Levels were expressed as micromoles of cyanide and thiocyanate per litre of blood (1 μmol/l = 27 μg HCN/l or 58 μg $^-$SCN/l respectively).

RESULTS AND DISCUSSION

The mean values of blood cyanide and thiocyanate for the different groups are summarised in table I. Within the control, firemen, and non-fatal-casualty groups, smokers show significantly higher cyanide and thiocyanate levels than non-smokers. Statistical analysis (Student's *t*-test) of the differences between the mean concentrations in each group (table II) indicated that there was no significant difference between firemen and controls but that both non-fatal and fatal casualties showed significantly elevated cyanide levels. The differences between the fatal and non-fatal categories may reflect less severe exposure in the non-fatal group.

In our series, the majority of casualties were involved in domestic fires, and exposure to cyanide was likely to have been related to the thermal decomposition of nitrogen-containing polymers, both natural (wool and silk) and synthetic (polyurethane and polyacrylonitrile), which are used extensively in domestic furnishings.[2,7] Our results for casualties are supported by previous observations on fire fatalities.[8,9] The fatal threshold for cyanide exposure is difficult to assess, and a wide range of levels has been quoted.[10–12] Graham et al. suggest that fatal poisoning can occur at levels as low as 112 μmol/l.[12] 4% of the fatalities in our series had levels in the range 100–130 μmol/l and may have been exposed to potentially lethal concentrations of cyanide. The mean level of cyanide recorded in our fatal cases would not be sufficient alone to cause death, and it is likely that, in a fire, the main role of cyanide is its additive contribution to the effects of carbon monoxide in producing asphyxia at the cellular level.[13] The extent to which these elevated levels contribute to death requires further study.

In both smoking and non-smoking firemen mean cyanide levels were higher than in controls, but these differences did not reach significant levels. The firemen taking part in this study were trained in the use of self-contained breathing apparatus which they use routinely in domestic fires. The elevated levels of cyanide found in non-fatal casualties certainly suggest a potential occupational hazard for firemen who do not use such protective equipment. The scope of the present study did not permit the assessment of the firemen during acute fire-fighting, and this aspect is now under investigation.

Cyanide is a normal metabolite present in the body at low concentrations and is principally metabolised to thiocyanate.[10] In the groups studied (with the exception of fatal casualties) thiocyanate levels showed a linear correlation with cyanide; but in fatal cases thiocyanate levels were of little value as an index of metabolised cyanide.

The smoke-inhalation victim who survives the initial exposure is a candidate for close observation and intensive care. In 3 of our non-fatal casualties, evidence of persistent myocardial ischæmia, related to prolonged cyanide elevation, was observed in the absence of elevated HbCO. In other series cardiac and neurological complications have also been described after smoke inhalation.[14,15] Recognition of the role of cyanide may alert the clinician to consider more specific forms of therapy designed to combat the toxic effects.

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TOXICOLOGY/ORIGINAL CONTRIBUTION
carbon monoxide, poisoning
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Cyanide and Methemoglobin Kinetics in Smoke Inhalation Victims Treated With the Cyanide Antidote Kit

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Study objective: To evaluate serial cyanide, methemoglobin, and carbon monoxide levels in smoke inhalation patients.

Setting: Regional poison center and regional toxicology treatment center.

Participants: Seven critically ill smoke inhalation patients referred to the regional poison center.

Interventions: Peak level and half-life were determined by obtaining serial carboxyhemoglobin, cyanide, and methemoglobin levels.

Results: The mean observed half-life of cyanide was 3.0 ±0.6 hours. Methemoglobinemia was evaluated in four patients after sodium nitrite administration. The peak measured methemoglobin levels (mean, 10.5% ± 2%; range, 7.9% to 13.4%) did not occur until a mean of 50 minutes (range, 35 to 70 minutes) following administration of sodium nitrite. The total oxygen-carrying capacity reduced by the combination of carboxyhemoglobin and methemoglobin was never more than 21% (range, 10% to 21%) in this series.

Conclusion: The administration of sodium nitrite to smoke inhalation patients in the presence of concomitant carbon monoxide poisoning may be relatively safe. DANGEROUS

[Kirk MA, Gerace R, Kulig KW: Cyanide and methemoglobin kinetics in smoke inhalation victims treated with the cyanide antidote kit. *Ann Emerg Med* September 1993;22:1413-1418.]

INTRODUCTION

In 1991, the National Fire Protection Association reported 4,605 deaths and 29,375 injuries from fires.[1] A 1985 review of death certificates showed that 67% of fire deaths in 1985 were due to smoke inhalation as opposed to burns or trauma.[2] Cyanide is a product of combustion in many fires, and cyanide toxicity should be suspected in all victims of smoke inhalation.

Concerns that methemoglobin induction is dangerous in the setting of carboxyhemoglobinemia have led authors to suggest withholding the nitrite portion of the cyanide antidote kit.[3-5] Observations on a series of critically ill smoke inhalation victims given the cyanide antidote kit afforded an opportunity to measure serial levels of carboxyhemoglobin (COHb), cyanide, and methemoglobin (MetHb). These data provided peak measured levels and estimations of half-lives. The observations reported here may assist in treatment recommendations for severely ill smoke inhalation victims.

MATERIALS AND METHODS

During the period January 1989 through July 1989, our toxicology consultation service was involved in the care of seven critically ill smoke inhalation patients. Cases were identified prospectively through the poison center, and treating physicians were asked to obtain serial laboratory data and render treatment as clinically appropriate. Supportive care was emphasized with specific attention to airway management and adequate oxygenation.

If the clinical course was consistent with cyanide poisoning, the Lilly® Cyanide Antidote Kit was recommended. The antidote kit was administered if a patient required intubation, exhibited continued altered mental status or cardiovascular instability, or had persistent metabolic acidosis. Administration of the antidote kit was an empiric decision because confirmation of the diagnosis with blood cyanide levels took several hours. An ampule of sodium nitrite (300 mg) was added to 100 mL IV fluid and infused slowly over 15 to 20 minutes. Blood pressure was monitored frequently during the infusion. One ampule (12.5 g) of N sodium thiosulfate was administered simultaneously. The amyl nitrite pearls were not used, as venous access was established rapidly. Serial COHb and cyanide levels were obtained from each patient, and when the antidote kit was administered, serial MetHb levels also were obtained.

Hyperbaric oxygen was recommended if available at the treating facility. Recommendations made to facilities without hyperbaric oxygen were based on the projected risk-benefit of transferring a critically ill patient for that therapy alone. The protocol used for carbon monoxide poisoning at the treating institution was 2.7 atmospheres (ATA) for 30 minutes followed by 2.2 ATA for 60 minutes. At least two additional treatments were given every eight hours at 2.2 ATA for 90 minutes.

Blood cyanide levels were analyzed by the Conway microdiffusion technique at Analytitox, Inc, Denver, Colorado.[6] Both COHb and MetHb levels were analyzed from arterial blood samples by an IL 282 co-oximeter (Instrumentation Laboratories, Inc, Lexington, Massachussetts) at one of the three treating facilities.

The time of exposure termination (T_0) was assigned to be the time of the initial 911 call as documented on ambulance records. The apparent half-lives of COHb, cyanide, and MetHb were analyzed if two or more levels were available.

Apparent half-lives were calculated by using the equation: $t_{1/2} = 0.693/K_{el}$ where K_{el} is the elimination rate constant; K_{el}, $[\text{Ln}\ (Cp_1/Cp_2)]/\Delta$ T; Ln, natural log; Cp_1, first blood level; Cp_2, second blood level; and Δ T, time between levels.

RESULTS

Case Presentations Patient 1 (Figure 1A): A 20-year-old man was found unconscious in a motel room fire. En route to the hospital he had a generalized seizure and required intubation. He had burns over 15% of the total body surface area. Admission vital signs were blood pressure of 120/80 mm Hg; pulse, 110; and temperature, 37 C. Admission laboratory results included an arterial blood gas with pH 6.69; P_{CO_2}, 37 torr; P_{O_2}, 187 torr; COHb, 4.9%; sodium, 146 mmol/L; potassium, 4.1 mmol/L; chloride, 107 mmol/L; CO_2 content, 5 mmol/L; blood ethanol, 8 mmol/L; and whole-blood cyanide, 3.38 µg/mL (130 µmol/L). Results were available four hours after admission. The patient was treated with the antidote kit at four and ten hours, the latter for persistent metabolic acidosis. He had full neurologic recovery.

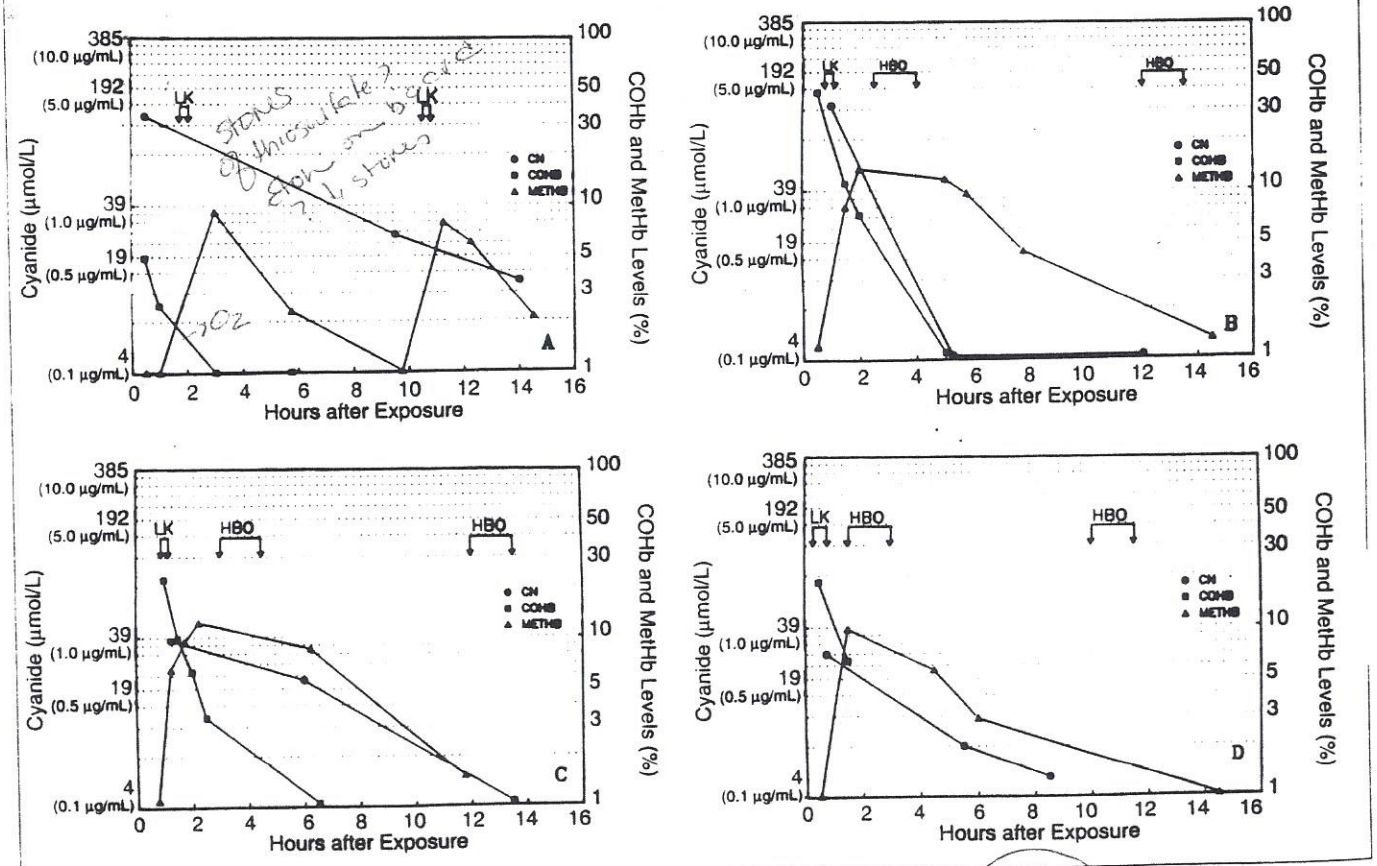
Patient 2 (Figure 1B): A 39-year-old man was found in cardiac arrest in a dwelling fire. At the scene he was intubated, and after advanced cardiac life support drugs, cardiac rhythm resumed. Admission vital signs were blood pressure of 108/40 mm Hg; pulse, 140; no spontaneous respirations; and temperature, 37.7 C. Admission laboratory results included an arterial blood gas with pH 7.17; P_{CO_2}, 30 torr; P_{O_2}, 526 torr; COHb, 38%; CO_2 content, 11 mmol/L; and whole-blood cyanide, 3.16 µg/mL (121.5 µmol/L). ECG showed ischemic changes. The

antidote kit was administered as part of the initial treatment. During the resuscitation, he became hypertensive and no longer required vasopressors. He was treated with hyperbaric oxygen. There was no further cardiovascular instability; however, he died of severe anoxic encephalopathy six days after admission.

Patient 3 (Figure 1C): A 64-year-old man was found unconscious in a dwelling fire with soot in his upper airway. Admission vital signs were blood pressure of 122/60 mm Hg; pulse, 154; respirations, 30; and temperature, 37.5 C. Admission laboratory results included an arterial blood gas with pH 7.37; P_{CO_2}, 30 torr; P_{O_2}, 483 torr; COHb, 22%; sodium, 141 mmol/L; potassium, 3.2 mmol/L; chloride, 114 mmol/L; CO_2 content, 11 mmol/L; and whole-blood cyanide, 0.96 µg/mL (39.9 µmol/L). ECG showed nonspecific intraventricular conduction delay. He was intubated and received the cyanide antidote kit. He was treated with hyperbaric oxygen and returned to his baseline mental status. He was discharged from the hospital after five days.

Patient 4 (Figure 1D): A 26-year-old woman was found unresponsive in a dwelling fire. She was intubated and noted to have soot in the upper airway. Admission vital signs were blood pressure of 100/72 mm Hg; pulse, 106; assisted ventilation; and temperature, 37.6 C. Admission laboratory results included arterial blood gas with pH 7.45; P_{CO_2}, 16 torr; P_{O_2}, 464 torr; COHb, 18.3%; sodium, 138 mmol/L; potassium, 3.5 mmol/L; chloride, 111 mmol/L; CO_2 content, 18 mmol/L; blood ethanol, 79 mmol/L; and whole-blood cyanide, 0.7 µg/mL (26.9 µmol/L). Initial emergency department management included administration of the antidote kit. She received three hyperbaric oxygen treatments and survived without neurologic sequelae.

Figure.
Serial levels of cyanide, COHb, and MetHb for patients 1 (A), 2 (B), 3 (C), and 4 (D). See text for clinical scenerios. Interventions are shown. LK, Lilly Cyanide Antidote Kit; HBO, hyperbaric oxygen.



Patient 5: A 29-year-old man was found at the scene of an apartment fire with altered mental status, 25% body surface area partial thickness burns, and soot in his upper airway. Admission vital signs were blood pressure of 140/82 mm Hg; pulse, 108; respirations, 24; and temperature, 35.7 C. Admission laboratory results included an arterial blood gas (on high-flow oxygen by mask) with pH 7.30; P_{CO_2}, 27 torr; P_{O_2}, 72 torr; COHb, 28.7%; sodium, 144 mmol/L; potassium, 3.3 mmol/L; chloride, 111 mmol/L; CO_2 content, 10 mmol/L; blood ethanol, 60 mmol/L; and whole-blood cyanide, 1.5 µg/mL (57.9 µmol/L). In the ED, he was confused and required intubation for increasing respiratory distress. The cyanide antidote kit was administered because of a persistent metabolic acidosis. Hyperbaric oxygen therapy was not available at that institution. He survived without neurologic sequelae.

Patient 6: A 33-year-old man was found unconscious in an apartment fire. He had respiratory distress with diffuse wheezes and soot in his oropharynx. Admission vital signs were blood pressure of 114/72 mm Hg; pulse, 112; respirations, 28; and temperature, 37.2 C. Admission laboratory results included an arterial blood gas with pH 7.30; P_{CO_2}, 29 torr; P_{O_2}, 237 torr; COHb, 32%; sodium, 142 mmol/L; potassium, 3.8 mmol/L; chloride, 115 mmol/L; CO_2 content, 12 mmol/L; whole-blood cyanide, 2.0 µg/mL (76.9 µmol/L); and blood ethanol, 37 mmol/L. ECG showed atrial fibrillation. He was treated with bronchodilators, steroids, and hyperbaric oxygen. He survived without neurologic sequelae.

Patient 7: A 55-year-old man was found unconscious in a dwelling fire. He was intubated at the scene. He had 5% body surface area burns. Admission vital signs were blood pressure of 166/88 mm Hg; pulse, 92; respirations, 24; and temperature, 35.5 C. Admission laboratory results included an arterial blood gas with pH 7.35; P_{CO_2}, 35 torr; P_{O_2}, 402 torr; COHb, 35%; sodium, 143 mmol/L; potassium, 3.5 mmol/L; chloride, 114 mmol/L; CO_2 content, 19 mmol/L; blood ethanol, 51 mmol/L; and whole-blood cyanide, 2.0 µg/mL (76.9 µmol/L). He was treated with hyperbaric oxygen and survived with neurologic sequelae

Admission COHb and whole-blood cyanide levels were obtained on all seven patients (Table 1). Admission COHb and whole-blood cyanide levels were obtained 25 to

Table 1.
Admission COHb and cyanide levels in seven smoke inhalation victims

Patient	Time of Levels After Exposure (min)	Admission COHb (%)	Apparent COHb $t_{1/2}$ (min)	Admit Cyanide (µmol/L)	Admit Cyanide (µg/mL)	Apparent Cyanide $t_{1/2}$ (hr)
1	25	5	—	130.0	(3.38)	3.67
2	60	38	37	121.5	(3.16)	2.14
3	85	22	33	36.9	(0.96)	3.86
4	45	18	40	26.9	(0.70)	3.19
	120	29	72	57.7	(1.5)	2.69*
	72	32	—	76.9	(2.0)	2.66*
7	43	35	74	76.9	(2.0)	2.94*
Mean	64	26	51	75.3	(1.95)	3.02
(SD)	(29)	(11)	(20)	(36.5)	(0.95)	(0.55)

*Calculations based on only two levels.

Table 2.
Kinetic parameters of MetHb in patients treated with cyanide antidote kit

Patient	Admission MetHb (%)	Sodium Nitrate Administered (mg)	Peak Measured MetHb (%)	Time After Nitrate Infusion to Peak Level (min)	Apparent MetHb $t_{1/2}$ (hr)
1	0.3	300	9.2	50	2.1
*		300	7.9	35	1.6
2	1.2	600	13.4	54	3.7
3	1.1	300	12.4	70	3.5
4	0.7	300	9.8	40	3.1
Mean			10.5	49.8	2.8
(SD)	(0.7)		(2.0)	(12)	(0.8)

*Dose repeated for persistent symptoms

120 minutes following the fire exposure. The mean admission COHb level was 25.5% (range, 4.9% to 38%). The mean admission cyanide level was 1.95 µg/mL (range, 0.7 to 3.38 µg/mL); 75 µmol/L (range, 26.9 to 130 µmol/L). Patients 2, 3, 4, 5, 6, and 7 were from dwelling fires, whereas patient 1 was exposed to a burning synthetic jacket. A positive correlation ($r = .94$; $P = .004$) was found between admission COHb with cyanide in all patients, excluding patient 1. There was no correlation ($r = -.03$; $P = .95$) when patient 1 was included in the analysis.

Whenever possible, serial COHb and whole-blood cyanide levels were obtained. Apparent half-life calculations were made when two or more levels were available. The mean apparent half-life of COHb was determined to be 46.8 minutes (range, 22 to 89 minutes). The mean COHb was determined from four patients, all on high-flow oxygen, and two were based on only two COHb levels that were obtained prior to hyperbaric oxygen therapy. Five of the seven patients received hyperbaric oxygen. The mean apparent half-life for cyanide was calculated to be 3.0 hours, although in three of the seven patients, only two levels were done. Analysis of data from the four patients with three or more levels showed a comparable half-life of 3.2 hours.

In five of the seven cases, the clinical course was consistent with cyanide poisoning; therefore, the antidote kit was recommended. The peak measured MetHb level generated by sodium nitrite infusion ranged from 7.9% to 13.4% (mean, 10.5% ± 2%) (Table 2). This peak measured level occurred 35 to 70 minutes following the end of the sodium nitrite infusion. Admission hemoglobin levels were 14.1 to 17.0 g/dL (mean, 15.2 ± 0.9 g/dL). The highest total measured nonoxygen-carrying hemoglobin (COHb ± MetHb) was 7.9% to 21% in the patients treated with sodium nitrite. Cyanomethemoglobin measurements were unavailable from the clinical laboratories involved. The mean apparent half-life of the measured MetHb was 2.8 hours (range, 1.6 to 3.7 hours). Admission MetHb levels (secondary to smoke inhalation) were all below 1.2%. The estimated MetHb half-life did not appear to be diminished in the patients treated with hyperbaric oxygen (patients 2, 3, and 4) when compared with the single patient receiving two doses of sodium nitrite and no hyperbaric oxygen (patient 1).

Patient 3 had a blood pressure change from 122/60 mm Hg to 92/50 mm Hg during the sodium nitrite infusion. His blood pressure returned to baseline after the infusion was slowed, and he received the full dose without further hemodynamic changes. No other blood pressure alterations were observed during sodium nitrite infusion in this series.

DISCUSSION

Cyanide has been identified as a product of combustion of polyurethane, wool, silk, polyacrylonitriles, synthetic rubber, nylon, paper, asphalt, nitrocellulose, nitrogen-containing polymers, and fire retardants.[3,7] Clinical evidence of cyanide toxicity is often nonspecific, especially in the smoke inhalation victim, where toxic gases or hypoxia may contribute to the clinical picture. Cyanide production from fires is unpredictable; therefore, any seriously ill smoke inhalation patient should be suspected to be cyanide poisoned.[7-9] Several studies have reported the presence of elevated cyanide levels in both fire survivors and fatalities.[7,10,11] All seven patients in this series had potentially toxic cyanide levels on admission.

Many previous studies of smoke inhalation victims also report elevated cyanide and COHb levels.[7-11] Clark et al reported on 53 fire survivors and found that all but three with elevated (more than 10%) COHb levels had elevated (more than 0.5 µg/mL) cyanide levels.[10] It was also reported that no patient with a COHb of less than 10% had an elevated cyanide level. We also found a high correlation ($r = .94$) between admission cyanide and COHb. The contribution of cyanide toxicity to morbidity and mortality in smoke inhalation victims remains unclear, although evidence from animal studies demonstrates an additive and possibly synergistic effect when carbon monoxide and cyanide are both present.[12-14]

In a study of six smoke inhalation patients, the mean half-life of cyanide was 1.2 ± 0.5 hours.[11] Clark et al estimated a half-life of one hour, although no data were presented.[10] One other report evaluated cyanide kinetics after ingestion of potassium cyanide. The early elimination phase was estimated to be 50 minutes, with a terminal half-life of 19 hours.[15]

The theory of sodium nitrite's efficacy is its ability to induce MetHb, although other mechanisms may be involved.[16] Cyanide is detoxified by binding to MetHb and forming cyanomethemoglobin, which is not measured as cyanide.[16] "Therapeutic" MetHb levels for cyanide toxicity have been suggested in the range of 25% to 40%.[8,17] These recommended levels seem to be based on the highest levels of MetHb that do not seriously compromise oxygen-carrying capacity. Johnson et al reported a case in which a clinical response was obtained with MetHb levels peaking at 9.2%.[18] In view of possible adverse effects of methemoglobinemia, clinical response and not MetHb levels should be the guide to sodium nitrite administration.[18] The formation of cyanomethemoglobin adds additional uncertainty to MetHb measurements. Most clinical laboratories do not have a readily available assay to measure cyanomethemoglobin.

Concerns regarding further impairment of an already compromised oxygen-carrying capacity (from carbon monoxide) in smoke inhalation victims has cautioned the empiric use of the sodium nitrite component of the cyanide antidote kit.[3,5,19] Indeed, a case of hypotension and prolonged impairment of oxygen-carrying capacity of more than 30% has been reported following rapid IV infusion and a full repeated dose of sodium nitrite to a smoke inhalation victim.[19] A study of MetHb induction in human volunteers demonstrated that a 4 mg/kg dose of sodium nitrite (equivalent to one ampule of 300 mg sodium nitrite from the antidote kit) produced maximal MetHb levels averaging only 7%.[17] In our series, the mean of the peak measured MetHb levels was 10.5% ± 2% (range, 7.9% to 15.4%). Serial levels were drawn at varying times, and the true peak may not have been measured. The peak measured MetHb levels occurred at a mean time of 50 minutes after nitrite administration. The method we used of slowly infusing sodium nitrite may have altered the kinetics of MetHb induction.

IV sodium nitrite has been observed to induce significant hypotension.[17,19] If the nitrite component of the kit is used, we would recommend it be administered slowly, as an infusion, with frequent evaluations of the blood pressure during the infusion.

Recognition of methemoglobinemia as a complication of smoke inhalation has introduced yet another variable in considering the use of nitrites on an empiric basis.[20] Therefore, the use of nitrites in victims of smoke inhalation should only be done with the knowledge of both COHb and MetHb levels. Co-oximeters are available in most clinical laboratories and can rapidly provide this information in association with blood gas analysis.

There were several limitations of our pharmacokinetic data. Calculations were derived from a small number of patients and samples. Therapies varied, and the effects of these therapies on elimination were not known. Kinetic calculations for cyanide were based on only two points in three of seven cases. Ideally, valid half-life calculations require at least three levels; however, kinetic calculations for cyanide were based on only two points in three of seven patients. In addition, declining cyanide levels may have reflected not only elimination but also redistribution to other tissues. Finally, because of intermittent sampling, peak measured levels of MetHb may not have detected the highest level actually achieved.

CONCLUSION

Cyanide is a common measurable poison in smoke inhalation victims. In this series, a positive correlation between elevated COHb levels and whole-blood cyanide levels existed in patients with smoke inhalation from dwelling fires. Rapid decline in COHb levels and a delay in peak MetHb formation resulted in a maximum measurable impairment of oxygen-carrying capacity of 21%. These data suggest that administration of the cyanide antidote kit in the presence of concomitant carbon monoxide poisoning in smoke inhalation victims may be relatively safe. Before the routine use of sodium nitrite for smoke inhalation victims can be recommended, we need to know the effects of MetHb formation on onygen delivery, the extent of cyanomethemoglobin formation, and the benefits of this drug in a controlled clinical trial.

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ELEVATED BLOOD CYANIDE CONCENTRATIONS IN VICTIMS OF SMOKE INHALATION

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Abstract *Background.* The nature of the toxic gases that cause death from smoke inhalation is not known. In addition to carbon monoxide, hydrogen cyanide may be responsible, but its role is uncertain, because blood cyanide concentrations are often measured only long after exposure.

Methods. We measured cyanide concentrations in blood samples obtained at the scene of residential fires from 109 fire victims before they received any treatment. We compared the results with those in 114 persons with drug intoxication (40 subjects), carbon monoxide intoxication (29 subjects), or trauma (45 subjects). The metabolic effect of smoke inhalation was assessed by measuring plasma lactate at the time of admission to the hospital in 39 patients who did not have severe burns.

Results. The mean (±SD) blood cyanide concentrations in the 66 surviving fire victims (21.6±36.4 μmol per liter, P<0.001) and the 43 victims who died (116.4±89.6 μmol per liter, P<0.001) were significantly higher than those in the 114 control subjects (5.0±5.5 μmol per liter). Among the 43 victims who died, the blood cyanide concentrations were above 40 μmol per liter in 32 (74 percent), and above 100 μmol per liter in 20 of these (46 percent). There was a significant correlation between blood cyanide and carbon monoxide concentrations in the fire victims (P<0.001). Plasma lactate concentrations at the time of hospital admission correlated more closely with blood cyanide concentrations than with blood carbon monoxide concentrations. Plasma lactate concentrations above 10 mmol per liter were a sensitive indicator of cyanide intoxication, as defined by the presence of a blood cyanide concentration above 40 μmol per liter.

Conclusions. Residential fires may cause cyanide poisoning. At the time of a patient's hospital admission, an elevated plasma lactate concentration is a useful indicator of cyanide toxicity in fire victims who do not have severe burns. (N Engl J Med 1991;325:1761-6.)

SMOKE inhalation has been well established as a cause of death in fire victims.[1-3] The identity of the toxic gases leading to death is uncertain, however. In addition to carbon monoxide, hydrogen cyanide is a major source of concern. The thermal decomposition of various nitrogen-containing materials, either natural (such as wool and silk) or synthetic (such as polyurethane and polyacrylonitrile), can produce toxic levels of hydrogen cyanide.[3-8] For example, the thermal degradation of 1 g of polyacrylonitrile in a 15.6-liter combustion chamber produces a hydrogen cyanide concentration of 1500 ppm.[6] Bertol et al. estimated that a lethal concentration of hydrogen cyanide could be achieved by burning 2 kg of polyacrylonitrile in an average-sized living room.[6] The effect of the hydrogen cyanide content of smoke has been well studied experimentally.[3,4] The exposure of animals to combustion products containing hydrogen cyanide rapidly produced severe incapacitation, and the animals who died had toxic cyanide concentrations in the blood.[4,6,8,9]

Many injuries caused by fire result from an inability to escape from the fire.[5] Obscuration of vision and toxic effects produced by smoke, such as irritation and asphyxia, may impede the victims' escape.[7] So may incapacitation due to cyanide exposure. Delay in escape prolongs the exposure to toxic gases and to flames and increases the probability of death or injury.[4] Forensic and clinical reports on the clinical and biologic importance of blood cyanide concentrations in fire victims are conflicting, because cyanide disappears rapidly from blood and blood specimens have often been obtained from fire victims only several hours after exposure.[4,10-15]

Accordingly, we sought to determine the clinical and biologic importance of blood cyanide concentrations in fire victims who died and those who survived by measuring blood samples obtained at the scene of the fire.

METHODS

This study was approved by the Ethics Committee of the Assistance Publique–Hôpitaux de Paris. Because the patients required immediate emergency care, informed consent was not obtained.

Study Subjects

We studied 109 victims of residential fires in the Paris area who were examined by ambulance physicians at the scene of the fire from April 1988 through April 1989. There were 50 women and 59 men, ranging in age from 2 to 87 years (mean, 33). Blood specimens were collected in dry heparin by the first medical squad to reach the scene after the start of isobaric oxygen therapy in all patients who were still alive and the start of mechanical ventilation in some, but before the administration of hydroxocobalamin (an antidote to cyanide) and any hyperbaric oxygen therapy. Thirty-six of these patients had already died at the scene of the fire when the blood sample was collected. Two or three blood samples were collected from six patients to estimate the half-life of cyanide in blood before any antidote to cyanide or any hyperbaric oxygen therapy was administered. These six patients were among those in whom measurements were made early in the course of the study, before we recognized that fire victims had elevated blood cyanide concentrations and before we began to use hydroxocobalamin as an antidote to

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cyanide poisoning. Even so, it was not used routinely, but only when serious cardiovascular compromise was evident.

Control Groups

We also measured blood cyanide concentrations in three groups of control subjects. Since we did not know whether the fire victims who died and those who lived were smokers or nonsmokers, blood samples were obtained from both smokers and nonsmokers among the control subjects.

The first group of controls included hospital inpatients with drug intoxication. For each fire involving one or more victims, a corresponding blood sample was obtained from each of one or more randomly chosen patients who were admitted to the intensive care unit on the same day for treatment of acute drug intoxication. Twenty-one of the patients were women and 19 were men, ranging in age from 15 to 93 years (mean, 35).

The second group of controls included patients with carbon monoxide poisoning caused by the malfunction of a heating appliance. Blood specimens were collected in the homes of patients with carbon monoxide poisoning resulting from the malfunction of a gas water heater or a coal stove. Fifteen of these patients were women and 14 were men, ranging in age from 7 to 80 years (mean, 45). Three were dead at the time the blood sample was collected.

The third group of controls included patients with major trauma from whom blood specimens were collected at the scene of the accident. Five were women and 40 were men, ranging in age from 10 to 91 years (mean, 37).

After collection and during transport, the blood specimens were stored for up to 90 minutes at ambient temperature, then stored at 4°C until the measurements were made[16] — normally on the day after the blood collection, and always within three days. The laboratory personnel who performed the analyses did not know the source of the samples.

Metabolic Study

Plasma lactate concentrations were measured as described elsewhere[17] (normal range, 1 to 2 mmol per liter) on arrival at the hospital in 39 of the fire victims thought to suffer from smoke inhalation. These patients were examined by a physician at the scene of the fire, where blood samples were obtained for the determination of the cyanide and carbon monoxide concentrations. The blood samples used for the plasma lactate measurements were obtained from 32 to 152 minutes (mean [±SD], 80±28) after the samples used for the blood cyanide measurements. Patients with burns over more than 15 percent of their body surface were excluded from this part of the study. The plasma lactate concentrations were correlated with the concentrations of cyanide and carbon monoxide in the blood samples obtained at the scene of the fire. The addition of a high concentration of hydroxocobalamin (300 μmol per liter) in vitro raised the measured plasma lactate concentration by 7 percent.

Analysis of Cyanide and Carbon Monoxide

Blood cyanide concentrations were measured with a colorimetric assay using microdiffusion.[18] The detection threshold was 2.2 μmol per liter, and the interassay coefficient of variation was 8 percent. We assigned a value of zero to blood samples that had cyanide concentrations below the threshold of detection. To determine the extent of artifactual loss of cyanide from blood specimens between collection and analysis, an in vitro study was performed. The blood samples from normal subjects were supplemented with 40 μmol of cyanide per liter, placed in rubber-sealed glass tubes containing lithium heparinate, and stored for three days at 4°C or at room temperature (22±2°C) (one tube per day at each storage temperature, in triplicate). Each day, the tubes designated for that day were opened and their cyanide concentrations immediately measured. The mean (±SD) decrease in the cyanide concentration after storage at 4°C was 10.3±2.2 percent after one day, and the decrease remained constant after three days (11.2±2.1 percent). After storage at room temperature, the mean decrease in the cyanide concentration was 15.3±2.3 percent; after three days the decrease remained constant (16.2±2.7 percent).

Blood carbon monoxide concentrations were measured by infrared analysis[19] in the 109 fire victims and the 29 patients with carbon monoxide poisoning due to the malfunction of a heating appliance.

On the basis of previous reports,[11-13,20,21] nontoxic blood concentrations of cyanide and carbon monoxide were defined as those less than 40 μmol per liter and 1.0 mmol per liter, respectively. Potentially toxic concentrations were defined as those ranging from ≥40 to <100 μmol per liter for cyanide and from 1.0 to 5.8 mmol per liter for carbon monoxide. Potentially lethal concentrations were defined as those ≥100 μmol per liter for cyanide and ≥5.8 mmol per liter for carbon monoxide.

Statistical Analysis

Nonparametric tests were used because of the nongaussian distribution of the variables studied.[22] The results in the three control groups were analyzed with Kruskal–Wallis nonparametric analysis of variance. Since no differences were found between the control groups, the results in the three groups were combined to form a single control group. An overall comparison between the combined control group and the fire victims was made by Kruskal–Wallis analysis of variance. Multiple comparisons were made with Dunn's nonparametric method.[22] Correlations between the carbon monoxide and the cyanide concentrations in blood were assessed with Kendall's rank-correlation coefficients. Correlations between plasma lactate levels and the blood concentrations of carbon monoxide and cyanide were assessed with Kendall's rank-correlation and partial-rank-correlation coefficients. Kendall's rank-correlation coefficients were calculated to determine the correlations between the extent of burns and the blood concentrations of carbon monoxide and cyanide.[22] All the tests were two-tailed, and P values of 0.05 or less were considered significant. The results are expressed as means ±SD.

Results

Blood Cyanide Concentrations in the Control Group

The mean blood cyanide concentration in the 40 inpatients with drug intoxication was 6.0±6.3 μmol per liter. In the 29 patients with carbon monoxide poisoning due to the malfunction of a heating appliance, the mean blood cyanide concentration was 4.3±5.7 μmol per liter, and the mean carbon monoxide concentration 2.9±1.5 mmol per liter. The carbon monoxide poisoning in 23 patients resulted from the malfunction of a gas water heater and in 6 patients from the malfunction of a defective coal stove. Twenty-eight patients had at least temporary loss of consciousness. Three patients were found dead at the scene, two died in the hospital, and another was discharged with severe neurologic impairment.

In the 45 patients with trauma, the mean blood cyanide concentration was 4.6±4.5 μmol per liter. The trauma resulted from a fall in 7 patients, motor vehicle accidents in 30, and penetrating wounds in 8. Eight patients in this group died at the accident scene despite intensive supportive treatment.

Since there were no significant differences in blood cyanide concentrations among these three groups, they were considered as a combined group of 114 patients in the following analysis.

Blood Cyanide Concentrations in the Fire Victims

Of the 109 fire victims from whom we obtained blood specimens, 43 died (39 percent). The mean blood cyanide concentration in these 109 patients was

59.0±77.9 μmol per liter. In those who died, it was 116.4±89.6 μmol per liter, and in those who survived it was 21.6±36.4 μmol per liter. All these values were significantly higher than those for the control group (Fig. 1). The corresponding mean blood carbon monoxide concentration in the 109 fire victims was 1.5±1.7 mmol per liter. In those who died it was 2.8±2.0 mmol per liter, and in those who survived it was 0.7±0.7 mmol per liter.

Of the 43 victims who died, 36 were found dead at the scene of the fire, and 7 died after admission to the hospital. The blood cyanide concentrations were above 40 μmol per liter in 32 of these 43 persons (74 percent), and above 100 μmol per liter in 20 (46 percent).

Thirty patients were less than 14 years old, and 13 of them died. In these 30 patients, the mean blood cyanide concentrations were 27.4±53.0 μmol per liter in those who survived and 87.0±76.1 μmol per liter in those who died (P<0.01). The corresponding mean blood carbon monoxide concentrations were 0.6±0.8 mmol per liter and 1.9±2.0 mmol per liter.

Seventy-nine patients were 14 years old or older, and 30 of them died. In these 79 patients, the mean blood cyanide concentrations were 19.6±28.9 μmol per liter in those who survived and 129.0±93.1 μmol per liter in those who died (P<0.001). The corresponding mean blood carbon monoxide concentrations were 0.8±0.7 and 3.1±2.0 mmol per liter.

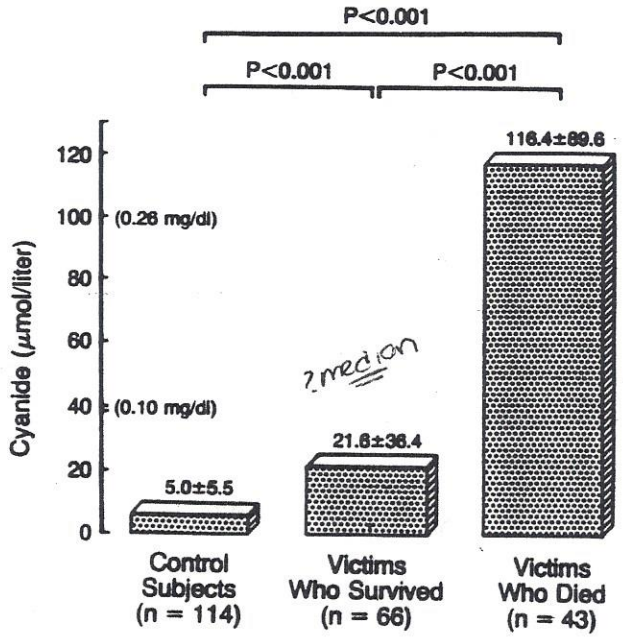

Figure 1. Mean (±SD) Blood Cyanide Concentrations in the Control Subjects, the Fire Victims Who Died, and the Victims Who Survived.

Blood cyanide concentrations below 40 μmol per liter were defined as nontoxic, those from ≥40 to <100 μmol per liter as potentially toxic, and those ≥100 μmol per liter as potentially lethal. Conventional units for cyanide measurements are shown in parentheses.

Twenty-seven of the 109 fire victims had burns. Thirteen of them had burns over more than 80 percent of their body surface that were considered to be life-threatening. There were no significant correlations between the extent of burns and the blood concentrations of either cyanide or carbon monoxide.

There was a significant correlation between the blood concentrations of cyanide and those of carbon monoxide in the 109 patients ($r = 0.50$, $P<0.001$), the 66 survivors of fire ($r = 0.26$, $P<0.001$), and the 43 fire victims who died ($r = 0.26$, $P<0.05$). Fifty-five patients had nontoxic blood concentrations of cyanide and carbon monoxide (Fig. 2); five of them died (9 percent), including four with life-threatening burns. Potentially toxic blood concentrations of cyanide, carbon monoxide, or both were found in 29 patients (Fig. 2), of whom 16 died (55 percent), including 8 with life-threatening burns. Potentially lethal blood concentrations of cyanide, carbon monoxide, or both were found in 25 patients (Fig. 2), of whom 22 died (88 percent), including 1 with life-threatening burns.

The half-life of cyanide in blood was approximately one hour in the six patients in whom it was serially measured (Table 1). One patient had no neurologic symptoms, two were agitated and confused, and three were comatose. All these patients had increased plasma lactate concentrations (range, 3.0 to 20.6 mmol per liter). None of them received hyperbaric oxygen therapy or any antidote to cyanide before the blood samples were collected.

Metabolic Consequences

Blood specimens were obtained from 39 fire victims thought to have had smoke inhalation on arrival at the hospital. The mean interval from the blood collection for the measurement of cyanide to the blood collection for the measurement of plasma lactate was 80±28 minutes.

Of these 39 patients, 10 had minor burns, 25 had transient or prolonged impairment of consciousness, 8 were agitated, confused, or both, and 29 had rhonchi or wheezing. Only three patients had no neurologic or respiratory symptoms. Nine of the 39 patients eventually died. At the time of admission to the hospital, however, only one fire victim, a two-year-old baby, was in refractory cardiac arrest, and the arterial origin of the blood sample could not be ascertained. The mean systolic arterial blood pressure recorded when the 38 remaining fire victims were admitted to the hospital was 129±25 mm Hg. The mean pH was 7.31±0.10, the mean partial pressure of oxygen in arterial blood was 33.0±23.3 kPa, and the mean plasma bicarbonate concentration was 19.1±4.5 mmol per liter.

Six fire victims had plasma lactate concentrations ≥29 mmol per liter. These six were discovered in cardiac arrest and required mechanical ventilation and infusions of epinephrine and sodium bicarbonate; five had already received hydroxocobalamin. One of these fire victims was the two-year-old child. In the five

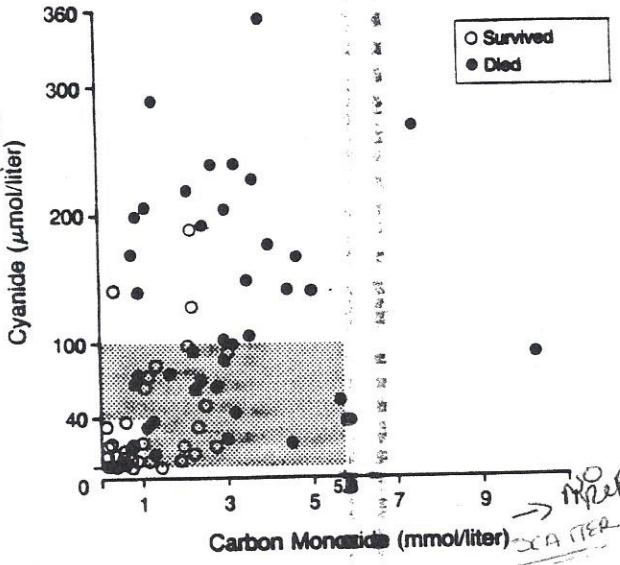

Figure 2. Correlation between Blood Concentrations of Carbon Monoxide and Those of Cyanide in Fire Victims Who Died and Victims Who Survived.

Blood concentrations of cyanide and carbon monoxide below 40 μmol per liter and 1 mmol per liter, respectively, were considered to be nontoxic (open square at lower left); those ranging from ≥40 to <100 μmol per liter for cyanide and from 1 to 5.8 mmol per liter for carbon monoxide were considered to be potentially toxic (stippled area); and those ≥100 μmol per liter for cyanide and ≥5.8 mmol per liter for carbon monoxide were considered to be potentially lethal.

others, the mean systolic arterial blood pressure at the time of admission to the hospital was 130±27 mm Hg, the mean pH 7.22±0.14, the mean partial pressure of oxygen in arterial blood 57.5±19.2 kPa, and the mean plasma bicarbonate concentration 13.1±2.5 mmol per liter. Despite the use of hyperbaric oxygen therapy and the administration of high doses of hydroxocobalamin, these five fire victims died. The deaths occurred two to seven days after admission to the hospital, and all were related to brain death.

The mean plasma lactate concentration in the 39 patients thought to have had smoke inhalation (11 of whom had received hydroxocobalamin) was 14.0± 12.3 mmol per liter. The mean blood carbon monoxide and cyanide concentrations measured at the scene of the fire were 2.1±1.5 mmol per liter and 76.2±75.1 μmol per liter, respectively. There was a significant correlation between the plasma lactate concentration and both the blood cyanide ($r = 0.55$, $P<0.001$) and the blood carbon monoxide ($r = 0.38$, $P<0.001$) concentrations. There was also a significant correlation between the blood concentration of carbon monoxide and that of cyanide ($r = 0.43$, $P<0.001$). The correlation between the blood carbon monoxide concentration and the plasma lactate concentration, with the effect of blood cyanide held constant, was 0.18, as expressed by the partial correlation coefficient. The partial correlation coefficient between the blood cyanide concentration and the plasma lactate concentration, with the effect of carbon monoxide held constant, was 0.47. We concluded that the plasma lactate concentrations measured at the time of admission in patients suffering from smoke inhalation who did not have severe burns correlated more closely with the blood concentrations of cyanide than with those of carbon monoxide.

Among these 39 patients, 23 had blood cyanide concentrations at the scene of the fire that were higher than 40 μmol per liter. Only 3 of these 23 patients had plasma lactate concentrations below 10 mmol per liter (Fig. 3). Sixteen patients had blood cyanide concentrations below 40 μmol per liter, and only 1 of the 16 had a plasma lactate concentration above 10 mmol per liter. Hence, in the context of smoke inhalation without severe burns, the sensitivity of a plasma lactate concentration above 10 mmol per liter for cyanide poisoning, defined by a blood cyanide concentration above 40 μmol per liter, was 87 percent; the specificity was 94 percent, and the positive predictive value 95 percent.

Table 1. Estimated Half-Life of Blood Cyanide Concentrations in Six Fire Victims before the Administration of Any Hydroxocobalamin or the Initiation of Hyperbaric Oxygen Therapy.

Patient No.	Blood Cyanide Concentration		Estimated Half-Life*
	Initial Sample	Follow-up Samples	
	μmol/liter	μmol/liter (hr elapsed†)	hr
1	128.6	36.6 (2)	1.1
2	11.5	4.2 (1)	0.7
3	98.9	52.3 (1)	1.1
4	80.9	11.6 (2.5), 6.9 (3.5)	0.9
5	50.0	21.2 (2), 7.7 (4)	1.5
6	73.1	33.5 (5), 4.6 (7.5)	2.1
Mean ±SD			1.2±0.5

*Calculated for each patient by linear regression analysis.
†Since the time the initial sample was taken.

Discussion

Several potential pitfalls have been noted in the measurement of blood cyanide concentrations in patients with either fatal or nonfatal poisoning. Cyanide may disappear rapidly from body tissue after death from acute cyanide poisoning,[21] and its half-life in blood is short in cases of nonfatal cyanide poisoning in dogs and humans.[15,23,24] Our finding that the half-life of cyanide is approximately one hour agrees with the results of previous studies. Such rapid disappearance precludes accurate evaluation of cyanide poisoning by delayed blood sampling in surviving fire victims. Furthermore, the production of cyanide has been described in various tissues, including blood. The potential for postmortem cyanogenesis is uncertain, however, since some have failed to demonstrate it.[16,21]

The conditions of blood sampling, storage, and analysis in our study were those known to influence blood cyanide concentrations the least.[21] The blood samples were collected by the first medical team to

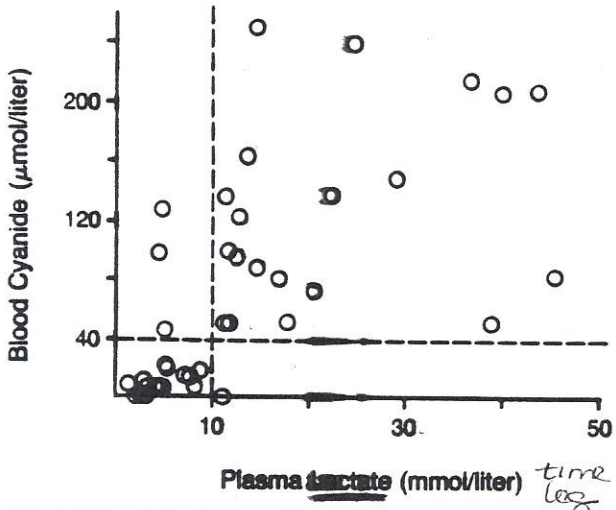

Figure 3. Correlation between Plasma Lactate and Blood Cyanide Concentrations in 39 Fire Victims with No Severe Burns.

arrive at the scene of the fire, even when there were fatalities. Furthermore, the samples were collected from the victims of carbon monoxide poisoning or major trauma under the same conditions as those used for the collection of blood from fire victims.

In the fire victims who survived, the mean blood cyanide concentration was significantly higher than that in the control subjects. Nine patients had blood cyanide concentrations above 40 μmol per liter, and three had values above 100 μmol per liter. Survival despite a blood cyanide concentration in the potentially lethal range has been reported previously.[12,14] These results indicate that there is no blood cyanide concentration above which the outcome is invariably fatal.[16,21] Among the 43 fire victims who died, the blood cyanide concentrations were above 40 μmol per liter in 74 percent and above 100 μmol per liter in 46 percent. These results suggest that it is reasonable to suspect cyanide poisoning whenever fire victims have smoke inhalation.

As reported elsewhere,[11-14] the blood carbon monoxide and cyanide concentrations were significantly correlated. Blood carbon monoxide concentrations may be considered an index of cyanide poisoning in fire victims. However, the low value of the Kendall's rank-correlation coefficient indicated a wide spread in blood cyanide concentrations for a given blood concentration of carbon monoxide. This finding precludes the possibility of predicting the blood cyanide concentration accurately on the basis of the blood carbon monoxide concentration. Furthermore, a few of the fire victims who died in our study had potentially lethal blood cyanide concentrations despite having blood carbon monoxide concentrations in the range generally considered nontoxic. Thus, in contrast to those of previous studies,[11,12] our results suggest that cyanide poisoning may prevail over carbon monoxide poisoning as the cause of death in some fire victims.

In accordance with the results of an earlier study,[25] 36 of the 43 victims we studied who died (84 percent) were found dead at the scene of the fire. The major lethal factors in fires are toxic gases, heat, and oxygen deprivation.[5] By far the most commonly reported cause of smoke inhalation–related death is carbon monoxide, which is a systemic toxin with no irritant properties. However, respiratory irritants alone produce a chemical tracheobronchitis that contributes to thermal injury of the upper respiratory tract and to chemically mediated alveolar injury in the lower respiratory tract. The exact contribution of each toxic gas to the rapid deaths of fire victims is difficult to quantitate in the setting of a fire.[26] One of the most striking results was the fact that 55 percent of the 29 patients who died had blood concentrations of either carbon monoxide or cyanide that were within the potentially toxic but not the potentially lethal range. In addition to severe burns that might have occurred after death,[27] these patients may also have suffered from low inspired-oxygen content and smoke-induced damage to the respiratory tract. However, studies in animals have shown that there may be physiologic potentiation of toxicity from carbon monoxide and cyanide combined.[4,28] Our data suggest that both gases may have an additive toxic effect in humans.

The high lactate concentrations in the fire victims' plasma were probably related to cyanide poisoning, for several reasons. First, the values for partial pressure of oxygen in arterial blood excluded hypoxia as a cause of lactic acidosis. Second, despite initial cardiac arrest in a few fire victims, the values obtained for systolic arterial blood pressure at the time of admission to the hospital could not easily explain the very high plasma lactate concentrations. Third, in the 39 fire victims thought to have had smoke inhalation, a significant correlation was found between the plasma lactate and the blood cyanide concentrations. Lactic acidosis is known to be an important consequence of cyanide poisoning.[29] Metabolic acidosis occurs frequently in fire victims, and cyanide poisoning may be an unrecognized cause of lactic acidosis.[12,14] Carbon monoxide poisoning is also a cause of lactic acidosis, which depends not only on blood carboxyhemoglobin levels but also on the duration of exposure.[30,31] However, the exposure of fire victims to toxic gases is usually short. Our results indicate that in victims with no burns or only minor ones, high plasma lactate concentrations are strongly suggestive of cyanide poisoning in addition to carbon monoxide poisoning.

The basic treatment for severe cyanide inhalation includes mechanical ventilation with pure oxygen and the administration of an antidote to cyanide. Although a variety of agents have proved effective in experimental studies, the choice of an antidote in the clinical setting remains a matter of debate.[32] Only a kit containing nitrites and thiosulfate is approved for use in the United States. However, the potential hazards of nitrite therapy in cases of combined poisoning with cyanide and carbon monoxide have recently been outlined.[33] Because of the strong affinity of cyanide for

cobalt, cobalt compounds (such as cobalt edetate and hydroxocobalamin) are rapid and powerful cyanide antidotes. However, cobalt edetate induces side effects that may be deleterious in patients with suspected but not confirmed cyanide poisoning.[32] Hydroxocobalamin combines with cyanide to form cyanocobalamin (vitamin B_{12}).[34] We began to use it during this study because of its promise as an antidote whose action appears to be rapid and efficient and because, in comparison with nitrites and cobalt edetate, it appears to have low toxicity.[34-37]

We are indebted to Colonel R. Noto, M.D., and Colonel H. Julien, M.D., who made it possible to conduct these studies; to the Service d'Aide Médicale Urgente de Paris for help in collecting the data; and to A. Hall, M.D., from the Rocky Mountain Poison and Drug Center, University of Colorado Health Sciences, and R. Garnier, M.D., from the Paris Poison Control Center, for helpful criticism in reviewing the manuscript.

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fertility in all IUD users is needed.[29] Meanwhile, the risk is clear: there is a greatly increased association between IUD use and pelvic sepsis,[30,31] and the risk to fertility from pelvic sepsis is established.[32] Tubal damage is the main cause of the infertility and treatment is unlikely to be successful. For women who are particularly concerned about their future fertility, especially the nulliparous, and are choosing between an IUD and oral contraception, we strongly recommend oral contraception (in the absence of any other specific medical contraindication) whatever the previous menstrual history.

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BLOOD CARBOXYHAEMOGLO CYANIDE LEVELS IN FIRE SURVIVORS

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Summary Blood carboxyhaemoglobin and cya concentrations were measured in 53 survivors, 36 of whom had clinical evidence of sm inhalation. Carboxyhaemoglobin and cyanide levels v raised only in patients with smoke inhalation. B carboxyhaemoglobin measurement can be used to con the diagnosis of severe smoke inhalation in cases in whicl clinical data are inconclusive, provided that the tim sampling after exposure is taken into account. A nomog has been constructed for this purpose. There is no q method of measuring blood cyanide levels, but the c relation between cyanide and carboxyhaemoglobin l suggests that carboxyhaemoglobin concentrations, whicl be rapidly and easily measured, could be used to ide those who might benefit from treatment with cya antidotes.

Introduction

THE number of fire casualties, and the proportio victims overcome by smoke or noxious fumes, has rise recent years.[1] Concern that this rise is due to the widesp introduction of highly flammable synthetic polymers household decorations and furnishings has led to legislat requiring special display labels[3] for such furnish Hydrogen cyanide gas is a noxious decomposition pro produced by the thermal degradation of many of t modern plastic furnishings.[4] The possible hazards of metabolic poison in persons exposed to fire are highlighte the finding of raised blood cyanide levels in fire fatalities. have therefore screened the survivors of home fires who have been exposed to smoke and measured their whole-b cyanide concentration to obtain further information potential cyanide toxicity during a fire.

To identify patients with smoke inhalation injury an house-fire survivors attending the casualty departmer Glasgow Royal Infirmary, we ask about the circumstanc the fire and in particular the state in which the patient found. We have also investigated the value of b carboxyhaemoglobin levels as an index of smoke inhal injury since the blood carboxyhaemoglobin concentra has been shown experimentally[6] to correlate directly wit dose of smoke inhaled.

Patients and Methods

53 patients, all survivors of domestic fires, were studied. were suffering from inhalation of smoke alone, from burns a from a combination of inhalation and burns, or from r symptoms such as abrasions or agitation requiring initial evalu at the casualty department before being allowed home. Pa were classified as cases of smoke or no-smoke inhalation acco to clinical data (table I), arterial gas concentrations, and chest findings. When the patient was unable to give a clear history event the relevant information was obtained directly from th officer in charge of operations.

Blood samples were taken in all patients 2–3 h after the fir interval between smoke exposure and sampling being accur recorded in all cases (patients in whom sampling was delaye more than 3 h were excluded from the study). Venous samples stored at 4°C and all were analysed within 48 h of sampling. I

TABLE I—IMPORTANT DATA TO OBTAIN RELATING TO SMOKE EXPOSURE

—	Details to obtain
History of accident	Exposure in a smoke-filled environment and duration of exposure Consciousness level on removal Resuscitation required before hospital admission
Clinical history	Smoking history Dyspnoea, sense of suffocation or choking Irritation of eyes, nose, and throat Cough Expectoration of carbonaceous sputum
Examination	Consciousness level, evidence of cerebral irritation General appearance (cyanosis, cherry-red appearance, soot deposits) Inflammation or soot deposits on oropharyngeal mucosa Respiratory rate and character of respirations Evidence of airways obstruction, e.g., stridor, bronchospasm Other auscultatory abnormalities

cyanide was measured by gas-liquid chromatography.[7] Chloramine-T (sodium *p*-toluene sulfonchloramide) was used to convert cyanide to cyanogen chloride which was then extracted with hexane and subjected to gas chromatography. The blood carboxyhaemoglobin saturation and methaemoglobin concentrations were measured by the use of an Instrumentation Laboratory co-oximeter ('IL 282'). Arterial blood-gas measurements were made at the time of initial admission and at intervals thereafter on an 'ABL2' pH/blood gas analyser (Radiometer, Copenhagen).

Results

17 of the 53 patients seen at the casualty department had no evidence of inhalation of fumes: 6 of these were treated for burns injury alone and 11 were treated for minor symptoms, then discharged. The mean blood cyanide level (table II) for these 17 patients was 5·0 μmol/l (range 0·5–13); within this group smokers (n = 11) had a higher mean blood cyanide level than non-smokers (n = 6), but all had levels within the normal range.[5] The carboxyhaemoglobin levels in these no-smoke-inhalation patients were also within the normal range.[8]

36 patients had evidence of smoke inhalation and 11 of these patients also had burns. 24 of the 36 had only minor effects of smoke inhalation (i.e., one or two transient symptoms, and no abnormality on examination, in arterial gases, or on chest X-ray). The other 12 were considered to be suffering from serious smoke inhalation. The mean blood cyanide level of 36 patients who had inhaled smoke was 25·8 μmol/l (range 2·0–126) which is greater ($p<0·05$) than that in the non-inhalation group (table II). 10 of the 36 patients who had inhaled smoke had raised blood cyanide levels, in some cases to around near lethal levels (fig. 1). All these 10 had been clinically classified as suffering from serious smoke inhalation. No patient with minor inhalation was found to have a raised blood cyanide level.

The mean carboxyhaemoglobin concentration of the 36 patients who had inhaled smoke was 14·5 (range 0·3–45), which was greater ($p<0·005$) than that for the patients with no clinical evidence of smoke inhalation (table II). All the 12 patients with clinical evidence of considerable smoke inhalation had raised carboxyhaemoglobin concentrations, and of the remaining 24 patients with minor smoke inhalation only 2 showed marginal elevation of carboxyhaemoglobin above the upper limit of normal for their respective smoking categories.

Fig. 1 also shows two distinct groups of patients, one having normal levels of both carboxyhaemoglobin and cyanide (sector C), and the other having raised levels of both carboxyhaemoglobin and cyanide (sector B). Only 3 patients with raised carboxyhaemoglobin levels had normal cyanide levels (sector D). No patient with a normal carboxyhaemoglobin concentration had a cyanide level above normal limits (sector A).

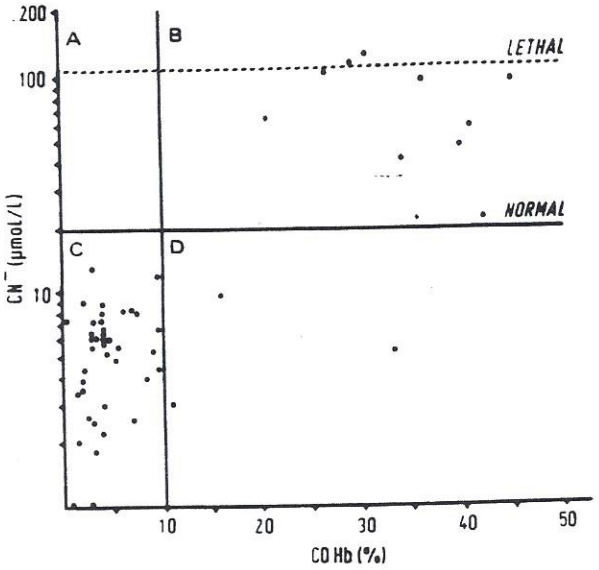

Fig. 1—Blood cyanide and carboxyhaemoglobin concentrations in 53 fire survivors.

The uninterrupted lines indicate the upper limits of normal values for cyanide and carboxyhaemoglobin in smokers. The interrupted line indicates the approximate lethal level in cyanide intoxication. (For clarity of illustration the cyanide concentrations are plotted on the vertical axis on a logarithmic scale.)

CO<10 = CN < 11

From the interval between smoke exposure and time of blood sampling and assuming the half-life of carboxyhaemoglobin to be 4 h when the subject was breathing air,[9] we calculated the approximate carboxyhaemoglobin level at the time of exposure in our patients. No patient with values within the normal range on admission would have had raised carboxyhaemoglobin levels consistent with significant smoke inhalation at the time of exposure. Fig. 2 shows the blood

TABLE II—WHOLE BLOOD CYANIDE AND CARBOXYHAEMOGLOBIN CONCENTRATIONS IN 53 HOUSE-FIRE SURVIVORS

	Cyanide (μmol/l)	Carboxyhaemoglobin (%)
No smoke inhalation (n = 17)	5·0 (0·5–13)	3·8 (0·8–9·6)
Smokers (n = 11)	6·6 (2·2–13)	4·7 (2·9–9·6)
Non-smokers (n = 6)	2·1 (0·5–3·9)	2·1 (0·8–3·2)
Smoke inhalation (n = 36)	25·8 (2·0–126)	14·5 (0·3–45)

Results are given as mean and range.
The upper ranges of normal cyanide in smokers and non-smokers are 20 μmol/l and 10 μmol/l, respectively.[5] Those for carboxyhaemoglobin are 10% and 5%, respectively.[8]

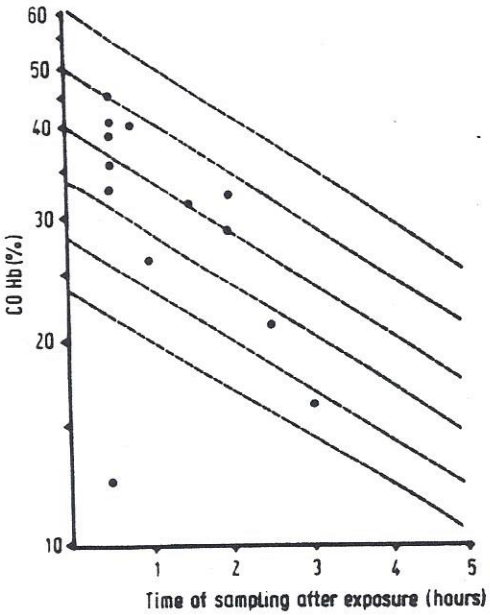

Fig. 2—Blood carboxyhaemoglobin levels and time of sampling after exposure in the 13 patients with raised admission levels.

The interrupted lines indicate carboxyhaemoglobin decay with time, assuming a half-life of four hours. (The carboxyhaemoglobin concentrations displayed on the vertical axis are on a logarithmic scale.)

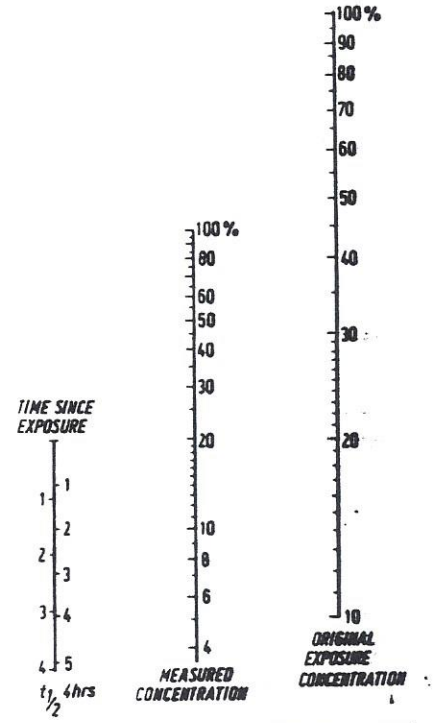

Fig. 3—Nomogram for calculating carboxyhaemoglobin c tration at time of exposure.

The time since exposure is given on two scales in order to allow for th of previous oxygen administration on the half-life of carboxyhaemoglo hand scale assumes a half-life of 3 h).

carboxyhaemoglobin concentration of the 13 patients with raised admission levels plotted against the time after exposure that sampling was done. It shows that there were several patients with severe smoke inhalation in whom a delay in sampling of 2 h or more resulted in lower levels than seen in other patients with similar degrees of exposure.

Arterial blood gas analysis was not routinely done in patients who clearly had no clinical evidence of smoke inhalation. A few of the patients with minor smoke inhalation showed changes consistent with hyperventilation. None of these patients showed arterial oxygen desaturation. In patients with raised blood carboxyhaemoglobin and cyanide concentrations metabolic acidosis of variable severity was very common; so was hypoxaemia and hypocapnia (pH range 7·23–7·35; base excess range −16 to −3). Methaemoglobin concentrations, measured in all patients, were not significantly raised. I wouldn't be

Discussion

Three points emerge from this study. One is the importance of as complete a clinical history as possible (which includes information on the circumstances of the fire). Smoke inhalation is often not diagnosed because of the heterogeneity of the effects of fumes produced by combustion; because the patient may be assessed during a quiescent period after removal from exposure, so the extent of inhalation may be underestimated;[10] and because at the time of clinical assessment in the casualty department accurate details of the extent of exposure and other facts relating to the fire may be unavailable. Our questionnaire case-sheet asked for specific features apart from those usually noted routinely at a clinical assessment, and we had an arrangement with the fire services so that they provided the information when the patient was unable to. We suggest that our practice be adopted in the routine evaluation of patients surviving domestic fires.

The second point relates to carboxyhaemoglobin which should be measured within a few hours of the i since they broadly correlate with the degree of inhalation. They should be measured to substantiate evidence of smoke inhalation, to provide evidence in c which the clinical data may be incomplete, and to rati the use of oxygen therapy in patients in whom raise are found. To ease interpretation of carboxyhaemc levels obtained on admission, we have prepared a nom (fig. 3) from which likely carboxyhaemoglobin le exposure can be calculated from levels on admission interval between exposure and sampling. The nom assumes a half-life of carboxyhaemoglobin of 4 h in a breathing room air. Most patients will not have r supplementary oxygen before admission, and at best t have been administered via a face mask, giving a ina fractional inspired oxygen concentration of 50–60% has little effect on carboxyhaemoglobin eliminatio scale on the left hand side of the time column nomogram makes an allowance for prior oxygen supp by assuming a shorter half-life of 3 h. This nomogram hope, help burns units to decide quickly whether smoke inhalation is likely to have occurred. It has be in the Regional Burns Unit at the Royal Infirmary, G to select patients at high risk of pulmonary complicat early management in the intensive-care unit.

The third point to emerge from our study conce raised blood cyanide levels. Cyanide is a potent m poison that inhibits cellular respiration.[11] Letha

yanide levels[11] have been found in necropsy studies of fire ıtalities.[5] The source of cyanide is the hydrogen cyanide gas roduced by thermal degradation of complex nitrogen olymers found in modern plastic furnishings and in natural ıbrics such as wool and silk. The massive growth of the olymer industry makes it likely that hydrogen cyanide will : encountered with increasing frequency in fires.[12]

We found that fire survivors without clinical evidence of noke exposure did not have raised cyanide levels when the ıbjects' smoking habits were taken into account. However, veral of the survivors who had inhaled a considerable nount of smoke had high blood cyanide concentrations, owing that cyanide inhalation need not necessarily be sociated with fatalities only. The dependence of hydrogen anide production in fires on a variety of factors, such as aterials combusted and temperature of the environment, eans that cyanide inhalation in domestic fires could be a ry variable occurrence.

Several of our patients had near-lethal cyanide levels and ost had levels liable to produce serious toxicity.[13] Since the sults of our work still in progress agree with those of Ansell d Lewis[11] that the half-life for cyanide elimination is very ort (approximately 1 h) the initial exposure levels in our rvivors were probably considerably higher than the levels easured on admission.

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These observations have important therapeutic lications. There is no rapid screening test for cyanide soning since it takes about 2 h to extract cyanide from od for analysis. None of the cyanide antidotes is free from -effects,[18] so they cannot be given empirically to all house- survivors. However, carboxyhaemoglobin can be sured quickly and easily, and patients most likely to have cyanide levels are those with high carboxyhaemoglobin ls. Had cyanide antidotes been used in those of our ents with carboxyhaemoglobin levels above an arbitrary centration of 15%, the measure would have proved arranted in only 1 case (fig. 1), and more importantly no ent with cyanide toxicity would have been missed, even out the use of the nomogram in this particular series. The of carboxyhaemoglobin level as a marker of inhalation of other toxic products of combustion has been suggested in general terms previously,[19] but our findings are the first to show its use in a specific (cyanide) poisoning.

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TRANSMISSION OF IN-VITRO RADIORESISTANCE IN A CANCER-PRONE FAMILY

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Summary Neoplasms of possible radiogenic origin developed in two members of a family prone to a diversity of cancers, including bone and soft-tissue sarcoma, brain and breast cancers, and leukaemia. Gamma-irradiation survival studies in these two patients and three other relatives, but not their spouses, over three generations demonstrated resistance to cell killing. The D_{10} value (radiation dose required to reduce survival to 10%) was significantly higher for the five radioresistant strains (491±30 rad) than for control cultures (405±18 rad). There was a significant correlation between individual D_{10} values and D_0 survival-curve parameters, indicating that changes in the exponential slope of the survival curves accounted for much

fertility in all IUD users is needed.[29] Meanwhile, the risk is clear: there is a greatly increased association between IUD use and pelvic sepsis,[30,31] and the risk to fertility from pelvic sepsis is established.[32] Tubal damage is the main cause of the infertility and treatment is unlikely to be successful. For women who are particularly concerned about their future fertility, especially the nulliparous, and are choosing between an IUD and oral contraception, we strongly recommend oral contraception (in the absence of any other specific medical contraindication) whatever the previous menstrual history.

We thank Prof. M. P. Vessey for supplying detailed data to enable us to construct the graph in fig. 2 and for his helpful advice.

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THE LANC

BLOOD CARBOXYHAEMOGLO CYANIDE LEVELS IN FIRE SURVIVORS

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Summary Blood carboxyhaemoglobin and cya concentrations were measured in 53 survivors, 36 of whom had clinical evidence of s inhalation. Carboxyhaemoglobin and cyanide levels raised only in patients with smoke inhalation. E carboxyhaemoglobin measurement can be used to cor the diagnosis of severe smoke inhalation in cases in whic clinical data are inconclusive, provided that the tim sampling after exposure is taken into account. A nomo has been constructed for this purpose. There is no c method of measuring blood cyanide levels, but the relation between cyanide and carboxyhaemoglobin suggests that carboxyhaemoglobin concentrations, whic be rapidly and easily measured, could be used to ide those who might benefit from treatment with cy antidotes.

Introduction

THE number of fire casualties, and the proporti victims overcome by smoke or noxious fumes, has ris recent years.[1] Concern that this rise is due to the wides introduction of highly flammable synthetic polymers household decorations and furnishings has led to legisla requiring special display labels[3] for such furnis Hydrogen cyanide gas is a noxious decomposition pr produced by the thermal degradation of many of modern plastic furnishings.[4] The possible hazards o metabolic poison in persons exposed to fire are highlight the finding of raised blood cyanide levels in fire fatalities have therefore screened the survivors of home fires wh have been exposed to smoke and measured their whole- cyanide concentration to obtain further informatio potential cyanide toxicity during a fire.

To identify patients with smoke inhalation injury a house-fire survivors attending the casualty departm Glasgow Royal Infirmary, we ask about the circumstan the fire and in particular the state in which the patien found. We have also investigated the value of carboxyhaemoglobin levels as an index of smoke inha injury since the blood carboxyhaemoglobin concentr has been shown experimentally[6] to correlate directly wi dose of smoke inhaled.

Patients and Methods

53 patients, all survivors of domestic fires, were studied were suffering from inhalation of smoke alone, from burns from a combination of inhalation and burns, or from symptoms such as abrasions or agitation requiring initial eval at the casualty department before being allowed home. P were classified as cases of smoke or no-smoke inhalation acc to clinical data (table I), arterial gas concentrations, and chest findings. When the patient was unable to give a clear history event the relevant information was obtained directly from t officer in charge of operations.

Blood samples were taken in all patients 2–3 h after the fi interval between smoke exposure and sampling being acc recorded in all cases (patients in whom sampling was delay more than 3 h were excluded from the study). Venous sample stored at 4°C and all were analysed within 48 h of sampling.

TABLE I—IMPORTANT DATA TO OBTAIN RELATING TO SMOKE EXPOSURE

—	Details to obtain
History of accident	Exposure in a smoke-filled environment and duration of exposure Consciousness level on removal Resuscitation required before hospital admission
Clinical history	Smoking history Dyspnoea, sense of suffocation or choking Irritation of eyes, nose, and throat Cough Expectoration of carbonaceous sputum
Examination	Consciousness level, evidence of cerebral irritation General appearance (cyanosis, cherry-red appearance, soot deposits) Inflammation or soot deposits on oropharyngeal mucosa Respiratory rate and character of respirations Evidence of airways obstruction, e.g., stridor, bronchospasm Other auscultatory abnormalities

cyanide was measured by gas-liquid chromatography.[7] Chloramine-T (sodium *p*-toluene sulfonchloramide) was used to convert cyanide to cyanogen chloride which was then extracted with hexane and subjected to gas chromatography. The blood carboxyhaemoglobin saturation and methaemoglobin concentrations were measured by the use of an Instrumentation Laboratory co-oximeter ('IL 282'). Arterial blood-gas measurements were made at the time of initial admission and at intervals thereafter on an 'ABL2' pH/blood gas analyser (Radiometer, Copenhagen).

Results

17 of the 53 patients seen at the casualty department had no evidence of inhalation of fumes: 6 of these were treated for burns injury alone and 11 were treated for minor symptoms, then discharged. The mean blood cyanide level (table II) for these 17 patients was 5·0 μmol/l (range 0·5–13); within this group smokers (n = 11) had a higher mean blood cyanide level than non-smokers (n = 6), but all had levels within the normal range.[5] The carboxyhaemoglobin levels in these no-smoke-inhalation patients were also within the normal range.[8]

36 patients had evidence of smoke inhalation and 11 of these patients also had burns. 24 of the 36 had only minor effects of smoke inhalation (i.e., one or two transient symptoms, and no abnormality on examination, in arterial gases, or on chest X-ray). The other 12 were considered to be suffering from serious smoke inhalation. The mean blood cyanide level of 36 patients who had inhaled smoke was 25·8 μmol/l (range 2·0–126) which is greater ($p<0·05$) than that in the non-inhalation group (table II). 10 of the 36 patients who had inhaled smoke had raised blood cyanide levels, in some cases to around near lethal levels (fig. 1). All these 10 had been clinically classified as suffering from serious smoke inhalation. No patient with minor inhalation was found to have a raised blood cyanide level.

The mean carboxyhaemoglobin concentration of the 36 patients who had inhaled smoke was 14·5 (range 0·3–45), which was greater ($p<0·005$) than that for the patients with no clinical evidence of smoke inhalation (table II). All the 12 patients with clinical evidence of considerable smoke inhalation had raised carboxyhaemoglobin concentrations, and of the remaining 24 patients with minor smoke inhalation only 2 showed marginal elevation of carboxyhaemoglobin above the upper limit of normal for their respective smoking categories.

Fig. 1 also shows two distinct groups of patients, one having normal levels of both carboxyhaemoglobin and cyanide (sector C), and the other having raised levels of both carboxyhaemoglobin and cyanide (sector B). Only 3 patients with raised carboxyhaemoglobin levels had normal cyanide levels (sector D). No patient with a normal carboxy-haemoglobin concentration had a cyanide level above normal limits (sector A).

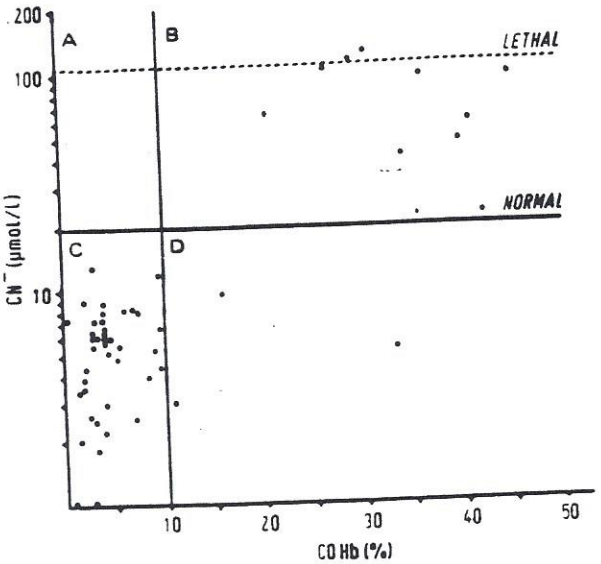

Fig. 1—Blood cyanide and carboxyhaemoglobin concentrations in 53 fire survivors.

The uninterrupted lines indicate the upper limits of normal values for cyanide and carboxyhaemoglobin in smokers. The interrupted line indicates the approximate lethal level in cyanide intoxication. (For clarity of illustration the cyanide concentrations are plotted on the vertical axis on a logarithmic scale.)

From the interval between smoke exposure and time of blood sampling and assuming the half-life of carboxy-haemoglobin to be 4 h when the subject was breathing air,[9] we calculated the approximate carboxyhaemoglobin level at the time of exposure in our patients. No patient with values within the normal range on admission would have had raised carboxyhaemoglobin levels consistent with significant smoke inhalation at the time of exposure. Fig. 2 shows the blood

TABLE II—WHOLE BLOOD CYANIDE AND CARBOXYHAEMOGLOBIN CONCENTRATIONS IN 53 HOUSE-FIRE SURVIVORS

	Cyanide (μmol/l)	Carboxyhaemoglobin (%)
No smoke inhalation (n = 17)	5·0 (0·5–13)	3·8 (0·8–9·6)
Smokers (n = 11)	6·6 (2·2–13)	4·7 (2·9–9·6)
Non-smokers (n = 6)	2·1 (0·5–3·9)	2·1 (0·8–3·2)
Smoke inhalation (n = 36)	25·8 (2·0–126)	14·5 (0·3–45)

Results are given as mean and range.
The upper ranges of normal cyanide in smokers and non-smokers are 20 μmol/l and 10 μmol/l, respectively.[5] Those for carboxyhaemoglobin are 10% and 5%, respectively.[8]

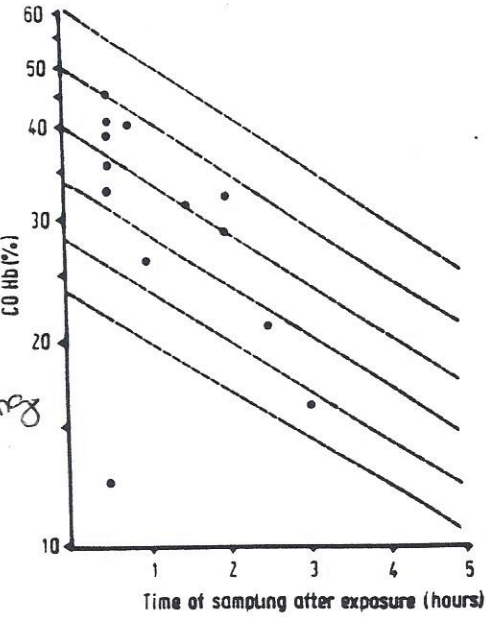

Fig. 2—Blood carboxyhaemoglobin levels and time of sampling after exposure in the 13 patients with raised admission levels.

The interrupted lines indicate carboxyhaemoglobin decay with time, assuming a half-life of four hours. (The carboxyhaemoglobin concentrations displayed on the vertical axis are on a logarithmic scale.)

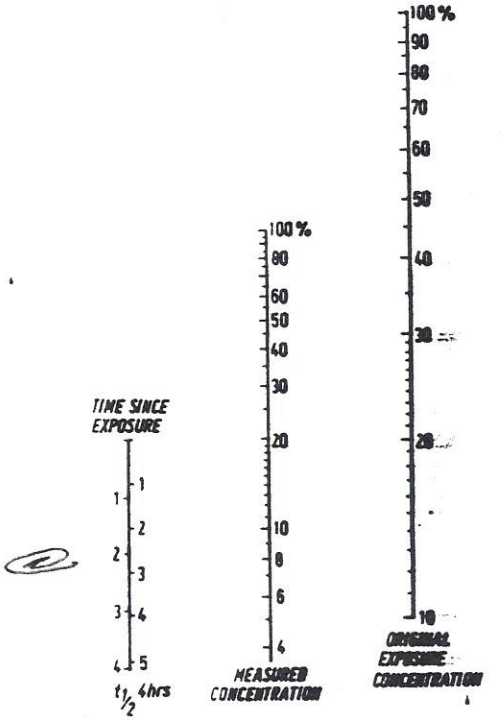

Fig. 3—Nomogram for calculating carboxyhaemoglobin tration at time of exposure.

The time since exposure is given on two scales in order to allow for of previous oxygen administration on the half-life of carboxyhaemo hand scale assumes a half-life of 3 h).

carboxyhaemoglobin concentration of the 13 patients with raised admission levels plotted against the time after exposure that sampling was done. It shows that there were several patients with severe smoke inhalation in whom a delay in sampling of 2 h or more resulted in lower levels than seen in other patients with similar degrees of exposure.

Arterial blood gas analysis was not routinely done in patients who clearly had no clinical evidence of smoke inhalation. A few of the patients with minor smoke inhalation showed changes consistent with hyperventilation. None of these patients showed arterial oxygen desaturation. In patients with raised blood carboxyhaemoglobin and cyanide concentrations metabolic acidosis of variable severity was very common; so was hypoxaemia and hypocapnia (pH range 7·23–7·35; base excess range −16 to −3). Methaemoglobin concentrations, measured in all patients, were not significantly raised.

Discussion

Three points emerge from this study. One is the importance of as complete a clinical history as possible (which includes information on the circumstances of the fire). Smoke inhalation is often not diagnosed because of the heterogeneity of the effects of fumes produced by combustion; because the patient may be assessed during a quiescent period after removal from exposure, so the extent of inhalation may be underestimated;[10] and because at the time of clinical assessment in the casualty department accurate details of the extent of exposure and other facts relating to the fire may be unavailable. Our questionnaire case-sheet asked for specific features apart from those usually noted routinely at a clinical assessment, and we had an arrangement with the fire services so that they provided the information when the patient was unable to. We suggest that our practice be adopted in the routine evaluation of patients surviving domestic fires.

The second point relates to carboxyhaemoglob which should be measured within a few hours of the since they broadly correlate with the degree o inhalation. They should be measured to substantiat evidence of smoke inhalation, to provide evidence i which the clinical data may be incomplete, and to r the use of oxygen therapy in patients in whom rais are found. To ease interpretation of carboxyhae levels obtained on admission, we have prepared a n (fig. 3) from which likely carboxyhaemoglobin exposure can be calculated from levels on admissio interval between exposure and sampling. The n assumes a half-life of carboxyhaemoglobin of 4 h in breathing room air. Most patients will not have supplementary oxygen before admission, and at bes have been administered via a face mask, giving a i fractional inspired oxygen concentration of 50–6(has little effect on carboxyhaemoglobin elimina scale on the left hand side of the time colum nomogram makes an allowance for prior oxygen su by assuming a shorter half-life of 3 h. This nomogra hope, help burns units to decide quickly wheth smoke inhalation is likely to have occurred. It has in the Regional Burns Unit at the Royal Infirmary, to select patients at high risk of pulmonary compli early management in the intensive-care unit.

The third point to emerge from our study co raised blood cyanide levels. Cyanide is a potent poison that inhibits cellular respiration.[11] Let

ide levels[11] have been found in necropsy studies of fire ities.[5] The source of cyanide is the hydrogen cyanide gas luced by thermal degradation of complex nitrogen mers found in modern plastic furnishings and in natural ics such as wool and silk. The massive growth of the mer industry makes it likely that hydrogen cyanide will ncountered with increasing frequency in fires.[12]

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TRANSMISSION OF IN-VITRO RADIORESISTANCE IN A CANCER-PRONE FAMILY

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Summary Neoplasms of possible radiogenic origin developed in two members of a family prone to a diversity of cancers, including bone and soft-tissue sarcoma, brain and breast cancers, and leukaemia. Gamma-irradiation survival studies in these two patients and three other relatives, but not their spouses, over three generations demonstrated resistance to cell killing. The D_{10} value (radiation dose required to reduce survival to 10%) was significantly higher for the five radioresistant strains (491±30 rad) than for control cultures (405±18 rad). There was a significant correlation between individual D_{10} values and D_0 survival-curve parameters, indicating that changes in the exponential slope of the survival curves accounted for much