ACUTE TOXICITY SUMMARY

HYDROGEN CYANIDE

(formonitrile; hydrogen cyanide; prussic acid)

CAS Registry Number: 74-90-8

I. Acute Toxicity Exposure Levels (for a 1-hour exposure)

Inhalation reference exposure level	**340 µg/m³**
Critical effect(s)	loss of coordination and loss of consciousness, due to cellular hypoxia of the central nervous system
Hazard Index target(s)	Nervous System

II. Physical and Chemical Properties (HSDB, 1994 except as noted)

Description	colorless gas
Molecular formula	HCN
Molecular weight	27.03
Density	1.1 g/L @ 25°C
Boiling point	25.6°C
Melting point	-13.4°C
Vapor pressure	630 mm Hg @ 20°C
Flashpoint	-17.8°C (closed cup)
Explosive limits	upper = 40% by volume in air lower = 5.6% by volume in air
Solubility	miscible in water, alcohol, slightly soluble in ether
Odor threshold	0.58 ppm (w/w) (Amoore and Hautala, 1983)
Odor description	faint, bitter almond odor
Metabolites	thiocyanate, 2-aminothiazo-line-4-carboxylic acid, cyanocobalamin (Vitamin B12) (Ansell and Lewis, 1970)
Conversion factor	1 ppm = 1.13 mg/m³

III. Major Uses or Sources

Hydrogen cyanide (HCN) is used in a variety of syntheses, including the production of adiponitrile (for nylon), methyl methacrylate, sodium cyanide, cyanuric chloride, chelating agents, pharmaceuticals, and other specialty chemicals. Manufacturing activities producing HCN include electroplating, metal mining, metallurgy, and metal cleaning processes. Additionally, HCN has some insecticide and fungicide applications (ATSDR, 1993). Fires involving some nitrogen-containing polymers, often found in fibers used in fabrics, upholstery covers, and padding, also produce HCN (Tsuchiya and Sumi, 1977).

Another common source of HCN is cigarette smoke. Levels in inhaled mainstream cigarette smoke range from 10 to 400 µg per cigarette and decrease to levels ranging from 0.06 to 108 µg in secondary or sidestream smoke (Fiksel *et al*., 1981).

IV. Acute Toxicity to Humans

Cyanide toxicity results from cytochrome oxidase inhibition which prevents cellular utilization of oxygen. The respiratory, cardiovascular, and central nervous systems are the primary target organs of acute cyanide toxicity. Acute effects from inhalation of HCN are characterized by altered sense of smell, headache, tachypnea, nausea, loss of coordination, loss of consciousness, palpitations, convulsions, respiratory distress, and asphyxiation (Chandra *et al*., 1980; Blanc *et al*., 1985; Peden *et al*., 1986; ATSDR, 1993). Eye or dermal contact with liquid HCN, a weak acid, may cause some mild local irritation (Anon., 1970). However, dermal and ocular absorption leading to systemic effects is clearly more cause for concern than possible local irritation. Even though the signs and symptoms of HCN poisoning are recognized, the acute dose-response relationship has not been well defined.

Lethality data from case report studies exist, but specific exposure concentrations are often lacking. As reported by McNamara (1976), several commonly reported inhalation values given as human toxicity data (Kobert, 1912; Henderson and Haggard, 1927; Flury and Zernick, 1931; Dudley *et al*., 1942; Moore and Gates, 1946; Fassett, 1963) may actually be based on pre-1920 animal data. One estimate of the average fatal inhaled dose for humans, 546 ppm (617 mg/m^3), is based on minimal human data and relies on multiple unsubstantiated assumptions including: (1) human susceptibility to HCN is similar to the relatively resistant monkey and goat, and (2) animal data, such as breathing rates, can be substituted for human parameters (McNamara, 1976).

In an accidental human poisoning, a workman collapsed 3 minutes after entering a tank for inspection and cleaning (Bonsall, 1984). The workman was exposed for an additional 3 minutes before being fitted with a breathing apparatus and taken to a hospital, where he later recovered. Later analysis of the tank revealed an HCN concentration of 500 mg/m^3 (442 ppm). In a fatal human poisoning, a workman cleaning the bottom of a silver plating tank was found unconscious by workmates (Singh *et al*., 1989). The duration of exposure was unknown but subsequent analysis of the air in the tank revealed a concentration of 200 ppm HCN.

The onset and progression of severe health effects are similar among humans and experimental animals (ATSDR, 1993, Ballantyne, 1987; Wexler *et al*., 1947, Purser *et al*., 1984). These effects are hyperventilation, followed by loss of consciousness, depressed respiration, and bradycardia.

Blanc *et al*. (1985) studied 36 former workers who had been exposed to HCN in a silver-reclaiming facility. A significant dose-response trend was observed between proximity of work to the CN^- source and prevalence of symptoms consistent with CN^- toxicity including headache, dizziness, nausea or vomiting, dyspnea, and syncope (unconsciousness). A 24-hour time-weighted average air concentration of 15 ppm was recorded 1 day after the plant had been closed because of a death from cyanide exposure. Due to poor hygienic conditions at the plant, dermal and oral exposure also occurred. The researchers considered the time-weighted average of 15

ppm to be a low estimate of the occupational exposure due to multiple potential routes of exposure and the retrospective analysis of the air concentration.

Predisposing Conditions for HCN Toxicity

Medical: Individuals with some motor neuron diseases, such as amyotrophic lateral sclerosis, have a decreased ability to convert cyanide to thiocyanate and may be predisposed to HCN toxicity (Kato *et al*., 1985). Individuals with Leber's hereditary optic atrophy, a rare neuroopthalmologic condition, may have low activity of the enzyme rhodanese, an enzyme responsible for converting cyanide to thiocyanate (Wilson, 1983).

Up to 20% to 40% of the population cannot detect the bitter almond odor of cyanide and may therefore be at greater risk for toxicity following exposure (Brown and Robinette, 1967).

Chemical: Individuals taking megadoses of ascorbic acid may diminish the availability of cysteine, an amino acid important in the detoxification of cyanide, thus increasing susceptibility to HCN poisoning (Basu, 1983).

V. Acute Toxicity to Laboratory Animals

The progression of severe health effects is similar among humans and experimental animals (ATSDR, 1993, Kulig and Ballantyne, 1993; Curry, 1992; Ballantyne, 1987; Wexler *et al*., 1947, Purser *et al*., 1984). These effects are characterized by hyperventilation, followed by loss of coordination and consciousness, depressed respiration, bradycardia, convulsions, asphyxiation, and respiratory failure.

In work by Purser (1984), 4 monkeys exposed to 60 ppm HCN developed electroencephalogram (EEG) patterns characteristic of early onset of CNS depression (increased slow wave [delta] activity and decreased fast wave [beta] activity) and increased respiratory rate near the end of the 30 minute exposure period. While both results are indicative of early onset of cellular hypoxia, none of the monkeys lost consciousness. However, with exposures to 80 ppm and above, incapacitation (semi-conscious state with loss of muscle tone) did result within 30 minutes (Purser *et al*., 1984).

Time-to-incapacitation, as a function of HCN concentration, has been measured in mice (Sakurai, 1989), rats (Hartzell *et al*., 1985), monkeys (Purser *et al*., 1984; Purser, 1984), and goats (Barcroft, 1931). The tests used by Barcroft (1931) and Purser *et al*. (1984) essentially defined incapacitation as a semi-conscious state with loss of muscle tone, whereas Sakurai (1989) and Hartzell *et al*. (1985) defined incapacitation as complete loss of consciousness. A linear relationship between gas concentration and mean incapacitation time can be shown as:

$$C = (a/t) + b$$

where C = gas concentration (ppm), t = incapacitation time (min), and a, b = coefficients for HCN gas.

The HCN concentration producing a mean incapacitation time of 30 minutes, using the equation $C = (a/t) + b$, is shown in Table 1.

Table 1. Tabulation of modeling constants for use in the equation $C = (a/t) + b$ for various experimental animal species and determination of HCN concentration resulting in incapacitation following 30 minute exposure to HCN.

Reference	Species	a (slope)	b (y-intercept)	Concentration (ppm)[1]
Sakurai (1989)	mouse	491	25	42
Hartzell *et al*. (1985)	rat	698	92	115
Purser *et al*. (1984)	monkey	685	66	89
Barcroft (1931)	goat	885	152	182

[1] Concentration of HCN producing a mean incapacitation time of 30 minutes.

While the above equation can estimate the mean time-to-incapacitation for a given concentration of HCN, it cannot provide a NOAEL for incapacitation. However, the coefficient b (y-intercept) could be viewed as the concentration of HCN below which incapacitation will not occur in normal experimental animals.

In mice, Sakurai (1989) has shown that exposure to HCN concentrations of approximately 150 ppm and above results in incapacitation and apnea at about the same time, within 5 minutes. However, exposures to lower HCN concentrations (approximately 150 ppm or less) result in incapacitation in about one-third the time required to cause apnea. This latter situation is observed when incapacitation occurs at 10 minutes or later into exposure to HCN.

Rats inhaling 64 ppm HCN were incapacitated after a mean duration of 35 minutes, while those inhaling 184 ppm HCN were incapacitated after a mean of 5 minutes (Chaturvedi *et al*., 1995). Blood cyanate levels did not predict incapacitation onset, since the blood cyanate at incapacitation following 184 ppm HCN inhalation was half that seen upon incapacitation following 64 ppm HCN inhalation.

In rats, Levin *et al*. (1987) observed that incapacitating levels were approximately 65% of lethal levels for exposure durations ranging from 1 to 10 minutes. Also in rats, Hartzell *et al*. (1985) observed that time-to-lethality was about 2 to 6-fold greater for a given concentration of HCN that produces incapacitation within 1 to 21 minutes. For exposures that produced mean incapacitation times of 10.9 and 21.0 minutes (165 and 127 ppm, respectively), the mean time-to-lethality was 3- to 4-fold greater. Purser *et al*. (1984) noted that a monkey exposed to 147 ppm HCN was incapacitated at 8 minutes and developed apnea at 27 minutes, a 3.4 fold difference. Other monkeys exposed to similar or lower levels of HCN did not develop apnea. Therefore,

there is a clear (though steep) dose-response effect for HCN exposure resulting in incapacitation (a severe adverse effect) followed by apnea (a life-threatening effect) and death.

Numerous citations were located in the literature that contained LC_{50} determinations for HCN at various exposure durations in experimental animals, but many of the studies did not include the raw mortality data from which to estimate an MLE_{05} (maximum likelihood estimate corresponding to 5% lethality) and BC_{05} (benchmark dose at the 95% lower confidence interval of the MLE_{05}) These citations and their respective LC_{50}s are shown in Table 2.

Table 2. Experimental Animal LC_{50}s for Hydrogen Cyanide

Reference	Species	Exposure Time (min)[1]	LC_{50} ppm (95% Confidence Interval)	Post-exposure Time
Ballantyne (1983)	rat	5	436 (329-585)	NR[2]
		30	153 (141-171)	NR
		60	140 (127-154)	NR
	rabbit	5	362 (284-405)	NR
		35	184 (136-244)	NR
Ballantyne (1984)	rat	30	133	NR
Levin *et al.* (1987)	rat	5	570 (460-710)	24 hr
		10	290 (250-340)	24 hr
		20	170 (160-180)	24 hr
		30	110 (95-130)	24 hr
		30	160 (140-180)	none
		60	90	24 hr
Moore & Gates (1946)	mouse	10	204	NR
		30	165	NR
	rabbit	10	283	NR
Esposito & Alarie (1988)	mouse	30	177 (157 -199)	10 min
Hartzell *et al.* (1985)	rat	30	170	NA[4]
Smith *et al.* (1976)	rat	7.9 ± 2.0[3]	450	NA[4]

[1] LC_{50} determinations for exposure durations of less than 5 minutes were not included in the table.
[2] Not reported
[3] Mean time to death (± SD) at 450 ppm HCN
[4] Not applicable, time to death experiment

Table 3 contains the studies which provided adequate data from which an MLE_{05} and BC_{05} could be determined. The MLE_{05} and BC_{05} in Table 3 were extrapolated to 60- minute exposure using a modification of Haber's equation, $C^n * T = K$, where n = 1. The value of n = 1 was based on the lethality studies of Levin *et al*. (1995) and Sato *et al*. (1955) for extrapolation from exposure durations of less than 1 hour to 1-hour exposure. An exponent n = 2.7 was determined by ten Berge *et al*. (1986) based on lethality data from Barcroft (1931). However, the Barcroft study used static HCN exposure conditions based mainly on nominal concentration estimates; the HCN concentration decreased during exposure and sampling of the HCN concentration was apparently not done on a consistent basis.

Groups of 10 rats inhaled hydrogen cyanide for 30 minutes and were observed over the next 24 hours (Lynch, 1975). Deaths noted occurred within 1 hour of exposure. No deaths were reported following exposure to 60 or 68 mg/m³. Some but not all rats survived exposure to HCN at concentrations between 90 and 166 mg/m³. There were no survivors following exposure to 168 or 192 mg/m³.

Table 3. Animal Lethality Benchmark Dose Determinations for Hydrogen Cyanide

Reference	Species	Exposure Time (min)[1]	MLE_{05} (ppm) 60 min[2]	BC_{05} (ppm) 60 min[2]	Post-exposure Time
Lynch (1975)	rat	30	35	29	24-hr
Bhattacharya *et al*. (1991)	mouse	30	337	169	24 hr
Matijak-Shaper *et al*. (1982)	mouse	30	51	25	10 min
Sato *et al*. (1955)	mouse	varied	35	26	NA[3]
Higgins *et al*. (1972)	mouse	5	19	16	7 days
	rat	5	28	24	7 days
Levin *et al*. (1985)	rat	30	87	73	none

[1] Exposure durations of less than 5 minutes were not included in the table.
[2] Exposure time was extrapolated to 60 minutes using a modification of Haber's equation ($C^n * T = K$), where n = 1.
[3] Not applicable

Experimental animals incapacitated and brought near death during HCN exposure can appear to recover quickly following cessation of exposure (Purser *et al*., 1984). However, while most deaths occur during the exposure period, Levin *et al*. (1987) noted that deaths of additional experimental animals may occur within 24 hours of exposure. Therefore, LC_{50} studies without a post-exposure period may overestimate the exposure necessary to cause death. Similarly, time to death studies (Hartzell *et al*., 1985; Smith *et al*., 1976; Sato *et al*., 1955) may also overestimate the concentration of HCN necessary to produce death.

One mortality study reported an inhalation NOAEL of 16 ppm (18.1 mg/m³) for rats and mice exposed for 16 hours (Weedon *et al*., 1940). Of the four experimental HCN concentrations

(1,000, 250, 63, and 16 ppm, or 1,130, 282, 71, and 18 mg/m³, respectively), only 16 ppm produced no distress (excitement, loss of coordination, or respiratory difficulties) throughout the exposure period. However, no other physiological indicators or measures of toxicity were used. Necropsy revealed lung and coronary artery changes in one of the two rats exposed to 16 ppm HCN.

Continuous exposure of rabbits to 0.5 ppm HCN (0.57 mg/m³), for either 1 or 4 weeks, produced no microscopically detectable morphological changes in the lung parenchyma, pulmonary arteries, coronary arteries, or aorta (Hugod, 1979; 1981).

Due to the lipophilic nature of HCN, dermal absorption during exposure to high atmospheric concentrations of HCN can occur. Moore and Gates (1946) exposed mice, cats, and dogs to body-only exposure to HCN gas, which resulted in 10 minute lethality at concentrations of 20,000 mg/m³ (17,700 ppm), 50,000 mg/m³ (44,250 ppm) and 100,000 mg/m³ (88,500 ppm), respectively. Dermal exposure through whole body or shaved region exposures of guinea pigs, rabbits, and dogs also resulted in systemic signs and symptoms of HCN poisoning (Walton and Witherspoon, 1926; Fairley *et al*., 1934).

VI. Reproductive or Developmental Toxicity

No information is available regarding developmental and reproductive effects in humans for any route of exposure to HCN. Also, no animal studies utilizing inhalation or dermal exposure have been reported for either HCN or cyanide salts.

Certain plants, such as cassava, contain naturally occurring cyanide compounds, cyanogenic glycosides, that produce HCN when hydrolyzed. Hamsters fed a cassava diet exhibited adverse effects, such as stunted growth and decreased ossification (Frakes *et al*., 1986). However, rats fed cassava or cassava supplemented with potassium cyanide failed to display this toxicity (Tewe and Maner, 1981). Furthermore, no reproductive or developmental effects were reported in hamsters fed cassava during gestation (Frakes *et al*., 1986).

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Mild Adverse Effect Level

The most sensitive, measurable endpoints, loss of coordination and consciousness, are potentially disabling (severe adverse effects). Acute symptoms of HCN toxicity which may qualify as mild adverse effects, such as headache, dizziness, and nausea or vomiting, have been described in humans (ATSDR, 1993; Blanc *et al*., 1985). Flury and Zernik (1931) described similar symptoms in humans following exposure to 45 ppm. However, no adequate acute dose-response trends can be determined from these data to develop a mild adverse effect level.

Reference Exposure Level (protective against severe adverse effects): 340 μg/m³

Study	Purser, 1984; Purser *et al*., 1984
Study population	4 cynomolgus monkeys
Exposure method	inhalation
Critical effects	CNS depression/incapacitation
LOAEL	80 ppm
NOAEL	60 ppm (68 mg/m³)
Exposure duration	30 minutes
Extrapolated 1 hour concentration	30 ppm (60^{1}ppm* 0.5 h = C^{1} * 1 h) (see Table 12 for information on "n")
LOAEL uncertainty factor	1
Interspecies uncertainty factor	10
Intraspecies uncertainty factor	10
Cumulative uncertainty factor	100
Reference Exposure Level	0.30 ppm (0.34 mg/m³; 340 µg/m³)

This value of 0.30 ppm protective against severe adverse effects is consistent with the conclusion of a review by Kaplan and Hartzell (1984), which determined that HCN exhibits a steep dose-response effect with incapacitating doses of HCN about one-third to one-half of those required to effect death (see below).

Level Protective Against Life-threatening Effects

From Table 3, the best estimate of the BC_{05} is 66.1 mg/m³ for 30 minute exposures and is derived from the Lynch (1975) data. This study included 9 exposure groups, 10 animals per group, and an adequate post-exposure observation period (24 hours), which made the data superior to that of other data presented in Table 3. Uncertainty factors of 3 to account for interspecies differences and 10 to account for increased susceptibility of sensitive human individuals were applied to the 60 minute BC05 (33 ppm).

level protective against life-threatening effects = BC05 /(UF)

Incorporation of these factors (cumulative uncertainty factors = 30) yielded a level protective against life-threatening effects of 1.1 ppm (1.2 mg/m³) for a 1-hour HCN exposure.

VIII. References

Amoore JE, Hautala E. Odor as an aid to chemical safety: odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air water dilution. J Appl Toxicol 1983;3:272-290.

Anonymous. Hydrogen cyanide. Am Ind Hyg Assoc J 1970;31:116-119.

Ansell M, Lewis FAS. A review of cyanide concentrations found in human organs: A survey of literature concerning cyanide metabolism, 'normal', non-fatal and fatal body cyanide levels. J Forensic Med 1970;17:148-155.

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological profile for cyanide. TP-92/09. Atlanta: U.S. Department of Health and Human Services; 1993.

Ballantyne B. The influence of exposure route and species on the acute lethal toxicity and tissue concentrations of cyanide. In: Hayes AW, Schnell RC, Miya TS, editors. Developments in the science and practice of toxicology. Amsterdam, The Netherlands: Elsevier Science Publishers BV; 1983. p. 583-586.

Ballantyne B. Relative toxicity of carbon monoxide and hydrogen cyanide in combined atmospheres [abstract]. Toxicologist 1984;4:69.

Ballantyne B. Toxicology of cyanides. In: Ballantyne B, Marrs T, editors. Clinical and experimental toxicology of cyanides. Bristol: Wright; 1987. p. 41-126.

Barcroft J. The toxicity of atmospheres containing hydrocyanic acid gas. J Hyg 1931;31(1):1-34.

Basu TK. High-dose ascorbic acid decreases detoxification of cyanide derived from amygdalin (laetrile): studies in guinea pigs. Can J Physiol Pharmacol 1983;61:1426-1430.

Bhattacharya R, Vijayaraghavan R. Cyanide intoxication in mice through different routes and its prophylaxis by α-ketoglutarate. Biomed Environ Sci 1991;4:452-459.

Blanc P, Hogan M, Mallin K, Hryhorczuk D, Hessl S, Bernard B. Cyanide intoxication among silver-reclaiming workers. JAMA 1985;253:367-371.

Bonsall J. Survival without sequelae following exposure to 500 mg/m³ of hydrogen cyanide. Human Toxicol 1984;3:57-60.

Brown KS, Robinette RR. No simple pattern of inheritance in ability to smell solutions of cyanide. Nature (London) 1967;215:406-408.

Chandra H, Gupta BN, Bhargave SH, Clerk SH, Mahendra PN. Chronic cyanide exposure - a biochemical and industrial hygiene study. J Anal Toxicol 1980;4:161-165.

Chaturvedi AK, Sanders DC, Endecott BR, Ritter RM. Exposures to carbon monoxide, hydrogen cyanide and their mixtures: interrelationship between gas exposure concentration, time to incapacitation, carboxyhemoglobin and blood cyanide in rats. J Appl Toxicol 1995;15(5):357-363.

Curry SC. Hydrogen cyanide and inorganic cyanide salts. In: Sullivan J, Krieger G, editors. Hazardous materials toxicology, clinical principles of environmental health. Baltimore (MD): Williams and Wilkins; 1992. p. 698-710.

Dudley HC, Sweeney TR, Miller JW. Toxicology of acrylonitrile (vinyl cyanide). II. Studies of effects of daily inhalation. J Ind Hyg Toxicol 1942;24:255-258.

Esposito FM, Alarie Y. Inhalation toxicity of carbon monoxide and hydrogen cyanide gases released during the thermal decomposition of polymers. J Fire Sci 1988;6(3):195-242.

Fairley A, Linton EC, Wild FE. The absorption of hydrocyanic acid vapour through the skin: with notes on other matters relating to acute cyanide poisoning. J Hyg 1934;34(3):283-294.

Fassett DW. Cyanides and nitriles. In: Patty, FA, editor. Industrial hygiene and toxicology. Chapter XLIV. Vol. II. 2nd ed. New York (NY): Interscience Publishers; 1963.

Fiskel J, Cooper C, Eschenroeder A. Exposure and risk assessment for cyanide. EPA/440/4-85/008. NTIS PB85-220572. Springfield (VA) NTIS; 1981.

Flury F, Zernik F. [Hydrogen cyanide]. In: [Noxious Gases--Vapors, Mist, Smoke- and Dust Particles]. Berlin: Verlag von Julius Springer; 1931. p. 340-493.

Frakes RA, Sharma RP, Willhite CC, Gomez G. Effect of cyanogenic glycosides and protein content in cassava diets on hamster prenatal development. Fundam Appl Toxicol 1986;7:191-198.

Hartzell GE, Priest DN, Switzer WG. Modeling of toxicological effects of fire gases: II. Mathematical modeling of intoxication of rats by carbon monoxide and hydrogen cyanide. J Fire Sci 1985;3:115-128.

Henderson Y, Haggard HW. Noxious gases and the principles of respiration influencing their action. New York: The Chemical Catalog Co., Inc.; 1927. p. 110-112.

Higgins EA, Fiorca V, Thomas AA, Davis HV. Acute toxicity of brief exposures to HF, HCl, NO_2 and HCN with and without CO. Fire Technol 1972;8:120-130.

(HSDB) Hazardous Substances Data Bank. National Library of Medicine, Bethesda (MD) (CD-ROM version). Denver (CO): Micromedex, Inc.; 1994. (Edition expires 4/30/94).

Hugod C. Effect of exposure to 0.5 ppm hydrogen cyanide singly or combined with 200 ppm carbon monoxide and/or 5 ppm nitric oxide on coronary arteries, aorta, pulmonary artery, and lungs in the rabbit. Int Arch Occup Environ Health 1979;44:13-23.

Hugod C. Myocardial morphology in rabbits exposed to various gas-phase constituents of tobacco smoke. Artherosclerosis 1981;40:181-190.

Kaplan HL, Hartzell GE. Modeling of toxicological effects of fire gases: I. Incapacitating effects of narcotic fire gases. J Fire Sci 1984;2:286-305.

Kato T, Kameyama M, Nakamura S, Inada M, Sugiyama H. Cyanide metabolism in motor neuron disease. Acta Neurol Scand 1985;72:151-156.

Kobert R. Kompendium der Praktischen Toxikologie zum Gebrauche für Ärzte, Studierende und Medizinalbeamte. Stuttgart, Germany: Ferdinand Enke (publisher); 1912.

Kulig KW, Ballantyne B. Cyanide toxicity. Am Family Physician 1993;48(1):107-114.

Levin BC, Gurman JL, Paabo M, Baier L, Holt T. Toxicological effects of different time exposures to the fire gases: carbon monoxide or hydrogen cyanide or to carbon monoxide combined with hydrogen cyanide or carbon dioxide. 9th Joint Panel Meeting of the UJNR Panel on Fire Research and Safety, May, 1987. U.S. Department of Commerce; 1987. p. 368-385.

Levin BC, Braun E, Navarro M, Paabo M. Further development of the N-gas mathematical model: An approach for predicting the toxic potency of complex combustion mixtures. In: Nelson GL, editor. Fire and polymers II: Materials and tests for hazard prevention. ACS Symposium Series No. 599. American Chemical Society; 1985. p. 293-311.

Lynch RD. On the non-existence of synergism between inhaled hydrogen cyanide and carbon monoxide. Fire Research Note No. 1035. Borehamwood, Hertfordshire, WD6 2BL, England: Fire Research Station; 1975.

Matijak-Schaper M, Alarie Y. Toxicity of carbon monoxide, hydrogen cyanide and low oxygen. J Combust Toxicol 1982;9:21-61.

McNamara BP. Estimates of the toxicity of hydrocyanic acid vapors in man. Edgewood Arsenal Technical Report. EB-TR-78023. Edgewood (MD): Dept of the Army; 1976.

Moore S, Gates M. Hydrogen cyanide and cyanogen chloride. In: Summary Technical Report of Division 9, NDRC, Volume 1: Chemical warfare agents and related chemical problems, Parts I-II, PB-158 508; 1946. p.7-16.

Peden NR, Taha A, McSorley PD, Bryden GT, Murdoch IB, Anderson JM. Industrial exposure to hydrogen cyanide: implications for treatment. BMJ 1986;293:538.

Purser DA. A bioassay model for testing the incapacitating effects of exposure to combustion product atmospheres using cynomolgus monkeys. J Fire Sci 1984;2:20-36.

Purser DA, Grimshaw P, Berrill KR. Intoxication by cyanide in fires: a study in monkeys using polyacrylonitrile. Arch Environ Health 1984;39(6):394-400.

Sakurai T. Toxic gas tests with several pure and mixed gases using mice. J Fire Sci 1989;7(1):22-77.

Sato T, Fukuyama T, Yamada M. The study of allowable concentration of hydrogen cyanide in air. Bull Inst Publ Health (Jap) 1955;4(4):3-5.

Singh BM, Coles N, Lewis P, Braithwaite RA, Nattrass M, FitzGerald MG. The metabolic effects of fatal cyanide poisoning. Postgrad Med J 1989;65:923-925.

Smith PW, Crane CR, Sanders DC, Abbott JK, Endecott B. Effects of exposure to carbon monoxide and hydrogen cyanide. In: Physiological and toxicological aspects of combustion products: International Symposium. Washington (DC): National Academy of Sciences; 1976. p. 75-84.

ten Berge WF, Zwart A, Appelman LM. Concentration-time mortality response relationship of irritant and systematically acting vapours and gases. J Hazard Mater 1986;13:301-309.

Tewe OO, Maner JH. Long-term and carry-over effect of dietary inorganic cyanide (KCN) in the life cycle performance and metabolism of rats. Toxicol Appl Pharmacol 1981;58:1-7.

Tsuchiya Y, Sumi K. Thermal decomposition products of polyacrylonitrile. J Appl Polym Sci 1977;21:975-980.

Walton DC, Witherspoon MG. Skin absorption of certain gases. J Pharmacol Exp Ther 1926;26:315-324.

Weedon FR, Hartzell A, Setterstrom C. Toxicity of ammonia, chlorine, hydrogen cyanide, hydrogen sulphide, and sulphur dioxide gases. V. Ann Contri Boyce Thompson Inst 1940;11:365-385.

Wexler J, Whittenberger J, Dumke P. The effect of cyanide on the electrocardiogram of man. Am Heart J 1947;34:163-173.

Wilson J. Cyanide in human disease: a review of clinical and laboratory evidence. Fundam Appl Toxicol 1983;3:397-399.