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Emission Control Technology Division
2565 Plymouth Road
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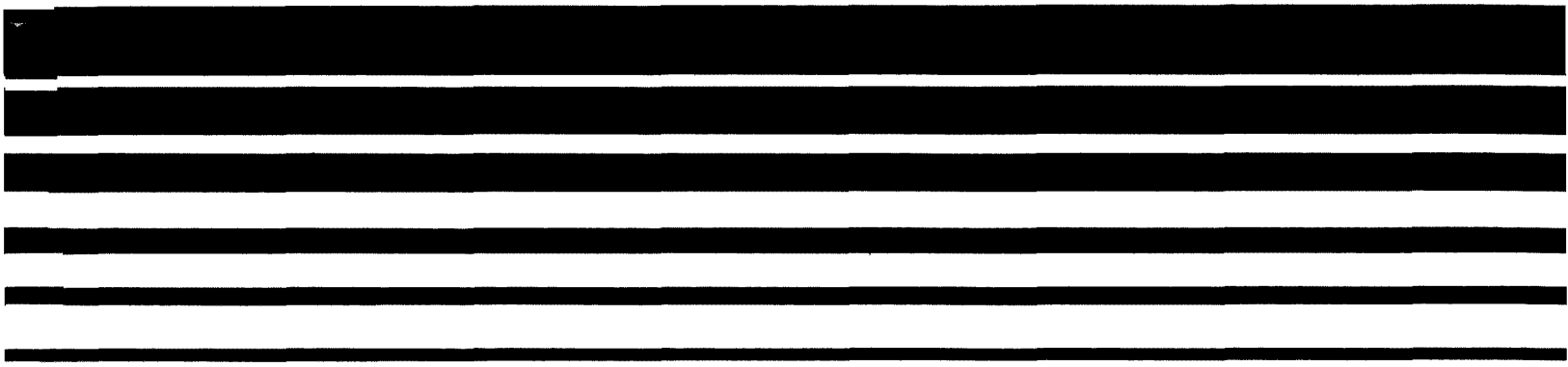
Hydrogen Cyanide Health Effects



HYDROGEN CYANIDE HEALTH EFFECTS

with Contributions by

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FINAL TASK 2 REPORT
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For

Emission Control Technology Division
Office of Mobile Source Air Pollution Control
U.S. Environmental Protection Agency
2565 Plymouth Road
Ann Arbor, Michigan 48105

Attn: Robert J. Garbe

PREFACE

This report on health effects of hydrogen cyanide, was prepared by Midwest Research Institute (MRI) as Task No. 2 under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division" for the U.S. Environmental Protection Agency.

The health effects literature primarily related to inhalation exposures to hydrogen cyanide has been collected, evaluated, tabulated, and summarized so that these results can be used to establish the ranges of human exposure conditions that are of concern for vehicular atmospheric emissions of hydrogen cyanide.

Task activities were coordinated by the project leader, Mrs. Bonnie L. Carson, Senior Chemist. Documents were rated and summarized by senior pharmacologists Drs. Betty L. Herndon and Harry V. Ellis III, of MRI, and epidemiologist Larry H. Baker, M.D., MRI consultant, who is Associate Professor of Community Health at the University of Kansas Medical Center. Data were tabulated by Ms. Eileen Horn, Junior Chemist, and Mrs. Carson. Ms. Carol Hopkin, and Ms. Carol Foret served as literature aides. The annotations were prepared by Mrs. Carson, largely based on notes by the raters of the documents. This study was performed under the general supervision of Dr. Edward W. Lawless, Head, Chemical Impact Assessment Section.

Mr. Robert J. Garbe was the project officer for the Emission Control Technology Division, U.S. Environmental Protection Agency, and Ms. Colleen DeMeyer served as Branch Technical Representative.

Approved for:

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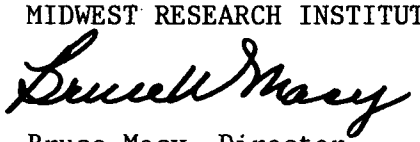

Bruce Macy, Director
Center for Technoeconomic
Analysis

September 11, 1981

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SUMMARY

GOALS AND METHODS

The purpose of this compilation of data on hydrogen cyanide (HCN) inhalation exposures is to assist the Emission Control Technology Division (ECTD) of the U.S. Environmental Protection Agency (EPA) to establish the ranges of exposure conditions that are of concern for HCN in exhausts from vehicles equipped with catalytic converters and to be able to advise automobile manufacturers thereof. The situations of most concern are during vehicle malfunctions and involving exposures in traffic jams, parking and home garages, and other situations where little dilution of the exhaust is expected before inhalation. Most of the report is, as directed by ECTD, in the form of tables. Since the focus is on levels where minimal effects occur, this summary concentrates on exposures that were cited as "tolerated" (in at least some published studies) rather than higher, possibly lethal exposures.

Documents on inhalation effects of HCN identified from manual and computerized literature searches were rated in a two-step process by the project pharmacologists and epidemiologist. First, the document received an A, B, C, or D rating according to its applicability for deriving a range of concern for HCN in automobile emissions. Second, if the paper was not a low-rated, foreign language document,* a theoretical paper, a review, or a nontoxicology experimental paper, it received a numerical score based on itemized features that should be present in an ideal report. For the most part, only A- and B-rated documents were tabulated; but when any C-rated studies involved low-level HCN exposures, these were also tabulated. Blanks in the tables should be construed as denoting missing information in the documents.

BACKGROUND INFORMATION ON HCN TOXICITY AND METABOLISM

High levels of HCN and the cyanide salts are recognized as highly toxic and are controlled in the workplace and in the environment. They act on an organism to stop aerobic metabolism after absorption of the cyanide ion through the respiratory tract or through the skin. The major interest for establishing a level of concern for HCN in automotive emissions lies in the possible long-term effects of repeated exposures to very low-level HCN exposure. Many studies have been made with experimental animals, but a difficulty

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* Most foreign language articles rated C and D were usually not translated. Each foreign language document tentatively rated A or B from an English language abstract or brief examination of the paper was translated in sufficient degree to judge the experimental design and details. These papers were numerically scored from the translation.

exists in extrapolating the exposure data to man. Species differences in susceptibility to the effects of HCN are substantial, and humans and other primates are among the least sensitive (Barcroft, 1931).

Acute poisoning at high levels of HCN produces almost immediate collapse and cessation of respiration. Symptoms comprise giddiness, hypernea, headache, palpitation, cyanosis, and unconsciousness. Convulsions from asphyxia may precede death. At lower doses, early symptoms may include weakness, headache, confusion, nausea, vomiting, and initially increased respiratory rate and depth; breathing becomes slow and gasping in later stages (Fassett, 1963; Swinyard, 1975).

The mechanism of toxicity at the higher levels appears to be the release of the cyanide ion, which forms a stable coordination complex with ferric iron, keeping the iron in a higher oxidation state and thus reducing its efficacy as an electron carrier in ferric-to-ferrous iron transitions. The most important result is that the almost ubiquitous cellular enzyme cytochrome oxidase-Fe(III) is trapped with cyanide. It thus cannot catalyze the reaction of reduced cytochrome + oxygen, and the oxygen cannot be transported. (Cyanide also forms complexes with Fe(III) of methemoglobin, but does not combine appreciably with the oxidized or reduced forms of hemoglobin.) This blockage reduces or stops aerobic metabolism with a shift to the anaerobic biochemical state. The cells become hypoxic, particularly the brain cells, as the products of anaerobic metabolism accumulate.

If death does not ensue, the cyanide is gradually released from the combination with cytochrome oxidase and is converted to thiocyanate (SCN^-). The conversion may involve thiosulfate ($S_2O_3^{2-}$) (which is produced from the metabolism of l-cysteine) according to the following reaction:

$$S_2O_3^{2-} + CN^- \xrightleftharpoons{\text{rhodanase}} SO_3^{2-} + SCN^-$$

Thiosulfate is used in the therapy of severe cyanide poisoning. In less serious poisonings, conversion of hemoglobin to a large fraction of methemoglobin (by nitrite injection or inhalation) promotes trapping of CN^- (Fassett, 1963).

β-Mercaptopyruvate transsulfurase catalyzes the reaction

$$CN^- + HSCH_2COCO_2^- \rightleftharpoons SCN^- + CH_3COCO_2^-$$

Thiocyanate oxidase catalyzes conversion of thiocyanate to cyanide (Maehly and Swensson, 1970).

Thiocyanate conversion reduces the acute hazard of cyanide, and SCN^- is excreted readily in the urine (Fassett, 1963). Hardy et al. (1950) pointed out that because SCN^- excretion is irregular, one cannot correlate the urinary SCN^- concentration with the degree of exposure to CN^-. This was confirmed by Maehly and Swensson (1970).

Hardy et al. (1950) suggested that if thiocyanate excretion is inadequate during chronic exposure, symptoms of thiocyanate toxicity (known from the use of SCN^- to treat hypertension) and goiter may occur. (Excess SCN^- is known to compete with iodide ion for uptake by the thyroid gland.) Fassett (1963) discounted one of the two cases of goiter described by Hardy et al. in persons occupationally exposed to HCN plus dusts of cyanide salts because the patient was from an endemic goiter region. The occupational study by El Ghawabi et al. (1975) does seem to confirm this effect of thiocyanate--56% of the electroplating workers exposed to cyanide salts and HCN vapors showed a mild thyroid enlargement. On the other hand, survivors of rats fed a diet containing ~ 100 or 300 ppm HCN for 2 y showed no histologic abnormality of the thyroids. All pathology was related to old age (Hanzel and Howard, 1955).

Workers constantly exposed to cyanide (as HCN) consistently excrete low levels of thiocyanate. Averages range from 6 to 13 mg SCN^-/L urine (Hardy et al., 1950). By comparison, concentrations of thiocyanate to be expected in the urine of nonsmoking, nonoccupationally exposed persons might be ~ 0.3 to 4 mg/L (Maehly and Swensson, 1970). Smokers also are exposed to HCN; e.g., Gori and Lynch (1978) found 9 to 141 μg HCN/cigarette in modern American brands. In the Levine and Radford study, nonoccupationally exposed young men who were heavy smokers had 0.653 mg SCN^-/L urine. Values reported in the literature for nonexposed smokers are generally < 14 mg SCN^-/L urine (Maehly and Swensson, 1970).

Another confounding cause of thiocyanate in the urine besides occupational or smoking-tobacco exposure to cyanide is a diet rich in high sulfur-containing vegetables, notably Brassica spp.: broccoli, brussel sprouts, cabbage, cauliflower, kale, kohlrabi, mustard, and turnips (Hardy et al., 1950).

BIOASSAYS

The three in vitro studies using hamster lung and hen and rabbit trachea cultures described in Chapter II are aimed at correlating the respiratory effects due to smoking with the various smoke components such as NO, HCN, and acrolein, which are among the most harmful. The levels of HCN studied are not especially relevant to expected levels of HCN in automobile exhaust. For example, eight puffs of 250 mg HCN/m^3 air inhibited ciliary activity of hen trachea in vitro to 50% that of the controls (Battista and Kensler, 1970).

ANIMAL EXPOSURES

The guinea pig is used as a standard model of bronchiolar sensitivity, having one of the most sensitive upper respiratory tract responses to toxicants. It is therefore striking that Barcroft (1931) found that the guinea pig was considerably more resistant to lethal HCN levels than several other laboratory mammals. Dudley et al. (1942) indicated that most mammals showed about the same toxicity to acrylonitrile as they do to a stoichiometrically equivalent level of HCN. Although guinea pigs and rabbits were tolerant of ~ 100 to 200 ppm of either, kidney lesions were more evident in these species

exposed to acrylonitrile. (Experimental details were not given for HCN tests and it is likely that the authors were summarizing earlier literature.) The authors speculated that this might be due to differences in species metabolism or more active excretion of CN^-.

The tabulated data from animal exposures (several acute, a few repeated-dose for rabbits, and no chronic studies) are very sparse in Chapter III. Table S-1 summarizes the data from the lower level tests or from the lowest level studies in Tables III-3 to III-12. Aside from showing large species differences in resistance to HCN, the tests described at $\geq$ 35 mg HCN/m^3 are not especially useful for the goals of this task. Noxious effects were seen in mice at levels as low as 3 ppm for 6 h (with HCN alone).

HUMAN EXPOSURES

Diet and cigarettes

Humans are exposed to cyanide in their diets via residue from HCN fumigation and in foods such as cherries, almonds, sorghum, cassava, and lima beans, which release HCN after hydrolysis of their cyanogenic glycosides (Towill et al., 1978). As mentioned above, the common measure of cyanide exposure is the concentration of the cyanide metabolite thiocyanate in urine or blood. But this measure can be misleading if the diet contains these foods or foods (commonly Brassica spp.) containing glucosinolates (thioglucosides) that release thiocyanate or isocyanate in the body (Towill et al., 1978).

Thus, occupational exposure studies, which frequently recognize the contribution of HCN in cigarette tobacco smoke and stratify the population according to smokers and nonsmokers, seldom mention the possibility of dietary contributions to cyanide or thiocyanate in the urine. Another problem with occupational cyanide exposure studies of workers who are heavy smokers is that their increased exposure to cyanide may be due not only to inhaling HCN in cigarette smoke but also to hand-to-mouth transfer while smoking at work.

Some estimates of cyanide exposure from the diet and cigarettes are derived in parts 1a and 1b, respectively, to place the occupational studies described in part 2 in better perspective.

Dietary Contribution--

Cabbage, kale, and kohlrabi contain the equivalent of 1 to 7 ppm thiocyanate or isocyanate (Towill et al., 1978). An improbable diet consisting solely of such vegetables (based on ~ 2 kg food intake per day) would contribute 2 to 14 mg/d to the thiocyanate content of the body and excreta.

Actual data on cyanide residues on food after fumigation have not been sought, but the Food and Agriculture Association/World Health Organization has set an acceptable daily intake (ADI) of cyanide from food at 0.05 mg/kg body weight (Vettorazzi, 1977), which would be about 3.5 mg/d for a 70-kg adult male (commonly called Reference Man).

TABLE S-1. SUMMARY OF LOW-LEVEL OR NO OBSERVED EFFECT HCN EXPOSURE OF ANIMALS

Level of HCN, mg/m^3 (ppm)	Exposure	Species	Details and References in Table ...	Effects
275 in each 70-ml puff delivered at the rate of 6 puffs/min	~ 0.5 h	Donkeys	III-12	Immediate arrest of bronchial clearance. Recovered within 20 min after the start of exposure.
240	Indefinite	Goats	III-11	Tolerable, yet 360 mg/m^3 for 24 min was 100% lethal for four goats.
125	? 12 min	Rabbit Monkeys	III-6 III-9	No marked toxic effect. Toxic symptoms.
33-44	4-5 h	Cats	III-8	No effect. But 55 mg/m^3 caused severe effects after 1.5 h.
35	Acute	Dogs	III-10	Tolerable, but 125 mg/m^3 was lethal.
11 (10)	2 h	Mice	III-3	Mobility hindrance, labored respiration, reduced food intake.
(3-10)	6 h	Mice	III-3	Wt. loss of 3.4-4.0 g 2 wk after exposure. Controls had gained 1.0 g.
5.5 plus CO, CO_2, 100°F	4 h	Mice	III-3	Lethal to 2 of 10.
1.1 plus CO, CO_2, 100°F	4 h	Mice	III-3	All 10 survived.
0.55 alone or plus NO and/or CO	1-4 wk	Rabbit	III-7	No lung morphology changes. Changes found in the intimal layer of certain blood vessels were not significantly different from those seen in the controls.

Contribution from Cigarettes--

A two-pack-per-day smoking habit might contribute as much as 22 mg HCN to the daily intake (calculated from the data of Brunnemann et al., 1977). This is not a trivial amount compared to occupational exposure. For example, a worker constantly exposed to the TLV (11 mg HCN/m^3) for 8 h could inhale as much as 110 mg HCN per work day. Thus, a worker who is a heavy smoker might derive 17% of his daily cyanide intake from cigarettes and even more if his occupational exposure is regularly less than the TLV. The actual lung contents while smoking may also contain HCN at levels higher than the TLV. For example, we have estimated from the data of Mattina (1972) that after each puff containing 35 μg HCN from a nonfilter cigarette, the lung will momentarily hold air containing HCN at a concentration of ~ 50 mg/m^3 (35 μg/0.7 L tidal lung volume).

Rickert et al. (1980) reported the level of HCN in 102 brands of Canadian cigarettes varied from 4 to 269 μg/cigarette, and that the average Canadian smoker is exposed to 400 ppm (440 mg/m^3) HCN during puffing. Rickert and Robinson (1981) continued the study and calculated that a person smoking < 10 cigarettes/d is exposed to ~ 1.4 mg HCN/d; 17.5-22.5 cigarettes, 3.2 mg/ HCN/d; and > 37.5 cigarettes resulted in exposure to ~ 8.4 mg HCN/d.

Occupational exposures

Human complaints following long-term HCN exposure involve evanescent, general, and nonspecific symptoms, many of which involve parasympathetic nervous system-related symptoms. Since some of the effects occur in some experimental animal species as well as in man, the symptoms involved have been studied in some depth. Colle (1972) and several more recent workers have suggested that low-level exposure appears to cause no symptoms; but when repeated regularly over a long period, HCN exposure leads to the parasympathetic symptoms often described by workers.

It is of interest to the current task whether the halt of aerobic metabolism which occurs with HCN at acute high-level exposures also acts after long-term, low-level exposure of a frequent or infrequent nature. It is also of interest to determine if any short-term, low-level HCN exposure may produce an effect that occurs after cessation of the acute exposure.

The studies of Levine and Radford (1978) may be relevant in this regard. Levine and Radford's population consisted of firefighters who had acute, high-level exposure to HCN in a fire. Over a fourth of them had thiocyanate in their urine, and the cigarette smokers among them had more thiocyanate than the nonsmokers; e.g., the clearance of thiocyanate was not inducible, in that smokers did not clear the additional thiocyanates resulting from the fire exposure any faster than nonsmokers. An increase in urinary excretion of thiocyanate upon exposure to cyanide has been reported in man by several investigators (see the recent review by Chandra et al., 1980), and sensitivity to the thiocyanates and an inability to excrete them rapidly has been suggested to be a mechanism of chronic toxicity to CN-exposed humans (Hardy et al., 1950).

The finding by Levine and Radford (1978) of 6.53 μg SCN^-/mL urine* of heavy smokers otherwise unexposed to HCN versus 3.75 μg SCN^-/mL urine of nonsmokers who were exposed to HCN in a major fire shows that heavy smoking can be as important as occupational exposure to the urinary excretion of thiocyanate.

Radojicic (1973), reporting on a group of 43 Yugoslav workers who had been chronically exposed to cyanides at 7 to 14 mg/m^3 in the annealing and electroplating departments of the electronics industry, were not able to classify the symptoms by a disease syndrome or any specific complaint. A central nervous system component is apparent in some of the complaints. Workers who smoked cigarettes had higher urinary thiocyanate levels than did nonsmokers. Radojicic appears to have overlooked the possibility that the smokers' work-related complaints may have been due to their hand-to-mouth transfer of additional cyanide while smoking. Chandra et al. (1980) found similar results, complaints ascribed to cyanide inhalation exposure and increased thiocyanate, especially in smokers, in a group of 23 Indian electroplaters and casehardeners. This study was careful to request that workers abstain from eating foods that would add to their CN^-/SCN^- exposure for a few days before the concentrations of these anions were measured in their blood and urine.

Other occupational studies have not considered the contributions of diet or smoking to cyanide exposure. Ju'zwiak et al. (1979) found no significant HCN-related disease in a recent industrial study. In 74 employees in 12 galvanizing shops, HCN-exposed females had cardiovascular symptoms less frequently than controls, and exposed males differed from control males in having greatly decreased central nervous system symptoms ("neurosis").

Kiryakov et al. (1978) reported more upper respiratory infections and 15% more time missed from work due to illness in farm workers exposed to HCN, H_2S, and phenol compared to a control population of farm workers exposed to lower concentrations of these air contaminants.

The study of Dinca et al. (1972) found subtle depression of the oxygen-carrying abilities of the blood in HCN-exposed workers. This report is one of the few that describe very long-term, low-level exposure (2.4 mg/m^3 calculated) for an average length of occupation of 5.4 y.

El Ghawabi et al. (1975) reported thyroid changes and effects on sense receptors (taste and odor perception) in workers exposed to mean HCN concentrations in the breathing zones of ∿ 7 to 11 mg/m^3. Other symptoms of a general nature occurred more often in the control population than in the exposed.

CONCLUSIONS

The bioassay, animal, and occupational studies tabulated are not especially helpful in identifying the entire range of concern for HCN in automobile exhaust (especially for long-term, low-level exposure) except that

* This would represent an output of ~ 13 mg SCN^-/d if ~ 2 L urine were voided per day.

one may conclude that the upper boundary of the long-term exposure range should be no higher than the TLV, since workers do register complaints at these levels.

A range of human acute dose-response data, as usually generalized in the literature without original source attribution, has been gathered in Table IV-1. A condensed version is given here in Table S-2. From these generalizations, it appears that the range of concern upon acute inhalation exposure to HCN should be from some value below 0.2 to 5.5 mg/m^3 (the odor threshold) to 11 mg/m^3 (the threshold limit value), or to 5 to < 20 mg/m^3 (levels where headache and vertigo may be the only symptoms). In view of the very steep dose-response curve seen in many animal experiments (wherein twice the no-observed-effect level can be lethal) the upper boundary value should perhaps be decreased by a reasonable safety factor. In this regard, it is interesting to note that the average MAC for HCN is ambient air of populated places is 0.01 mg HCN/m^3 (the workplace MAC of 0.3 mg/m^3 is much lower than the U.S. limit) (USSR, 1972).

When assessing the range of concern for HCN in auto exhaust, the additional contribution of HCN from tobacco should be considered. However, smokers as a class, do not include those individuals who are more susceptible to the noxious effects of the smokestream constituents and are, in fact, relatively inured to these effects. Human experiments are required with subjects who do not smoke and are not occupationally exposed to cyanide to determine a lower limit of the range of concern for HCN in auto exhaust.

TABLE S-2. GENERALIZED DATA ON HUMAN DOSE-RESPONSE TO HCN INHALATION

Dose of HCN		Response
mg/m^3	ppm	
110	100	Fatal in 1 h.
50-60	45-54	Tolerated for 0.5 to 1 h without immediate or late effects.
20-50	18-45	Headache, nausea, vomiting, and tachycardia after several hours.
20-40	18-36	Slight symptoms (headache) after several hours.
5-20	4.5-18	Headache and vertigo.
11	10	Threshold limit value.
0.2-5.5	0.2-5.0	Odor threshold.
0.11-0.99	0.1-0.9	No effect.

SECTION I

INTRODUCTION

This report was compiled as the second of several tasks under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division (U.S. Environmental Protection Agency, Ann Arbor, Michigan)." The goal of the project is to evaluate health effects literature on specific compounds emitted from automobiles equipped with emission-control devices (specifically catalytic converters), not for the purpose of creating a criteria document but to identify a level of concern or a no-observable-effect level for each compound to serve as guidance to automobile manufacturers in their development of future emission-control devices.

Literature related to health effects of inhaled HCN was collected mainly by computer search of TOXLINE and TOXBACK and manual search through the NIOSH criteria document on HCN and cyanides. Approximately 170 papers and other documents were obtained, but few contained original data suitable for tabulation.

Experimental animal exposure studies were evaluated and summarized by senior Ph.D. pharmacologists. There were no studies related to HCN exposures by the general public. Occupational exposure studies were rated by an epidemiologist with an M.D. degree and a senior pharmacologist. Figure I-1 is the form used for rating documents by the project pharmacologists and epidemiologist. Each document was rated in a two-step procedure according to the applicability of its subject matter and to the quality of the experimental methodology. The letter assigned in rating the document A, B, C, or D was derived from the corresponding lower case letters under item 7 in Figure I-1. Thus, a study was rated A if it directly applies to or assists in establishing a level of concern for exposure to HCN. The second part of the rating is the methodology score. The document reviewer checked off which score should be given for each of the first six items in Figure I-1, and the total was written at the top of the page along with the letter that rated the paper's applicability. In some cases, such as reviews, theoretical papers, and low-rated foreign-language documents, a paper may have received an applicability rating but none on methodology.

Data, including the MRI-assigned rating, from the A-, B-, and only if near the range of concern, C-rated papers were tabulated by mid-level and junior-level scientists. Information for each topic heading was carefully sought; so if blanks appear in the summary, the reader can generally assume the data were not given.

CHECK WHERE APPROPRIATE:	PAPER DEFECTIVE 0	PAPER IS SUB-STANDARD 1	STANDARD QUALITY 2	SUPERIOR PAPER 3
1. Do they state/limit the problem?				
2. Adequacy of sample				
3. Replicability				
4. Controls/control procedures				
5. Completeness and comprehensibility of results				
6. Validity of conclusions, interpretation of data				

7. Applicability to health effects of HCN as guidance for establishing a range of concern in automobile emissions.
(circle one)

a. Clearly, directly applies/assists in establishing a range of concern (Chronic human studies; acute exposure of humans if minimal effects.)

b. Research requires major inferences; potentially applicable. (Chronic animal studies; acute human, maximal effect; acute animal, minimal effects.)

c. Useful hints or suggestions; tentatively applicable. (Acute animal, lethal effects; studies in above categories but effects reported not appropriate.)

d. Not directly applicable (peripheral useful information).

Figure I-1 - Form for Report Rating

The final summary of the tabulated data was also performed by the senior pharmacologists. This summary attempts to reflect objectively the important findings related to HCN effects in the literature reviewed.

The references are cited in an annotated bibliography that includes not only each document's rating but also a brief comment on its pertinence (or lack of same) to the study.

The report is organized into the following chapters: II Bioassay Tests, III Experimental Animal Inhalation Exposures, and IV Human Exposures. The Summary precedes the entire report.

SECTION II

BIOASSAYS

The in vitro studies described in Table II-1 are aimed at correlating the respiratory effects due to smoking cigarette tobacco with smoke components such as HCN and acrolein. The levels studied are not particularly relevant to expected HCN levels in automobile exhaust.

TABLE II-1. BIOASSAYS--*IN VITRO* EXPOSURES TO HCN

HCN Concentration	Temperature	Mode of Exposure	Preparation Exposed	Description of Tests and Duration	Results	Reference and Rating
HCN in cigarette smoke 35-77 µg (per 4 puffs) 153 µg/4 puffs extreme value		CSM_{12} Smoking Machine	Hamster lung cultures	12 different experiments with > 7,000 lung cultures including nonexposed control cultures exposed to 4 puffs daily (25 ml at intervals of 58 s). Fresh smoke from 8 different types of cigarettes on 3 consecutive days/wk for a period of 1 wk-6 mo. GC or chemically analyzed and SH reactivity determined.	Malignant transformations were seen in cultures exposed to cigarette puffs containing 40-153 µg HCN and not seen in cultures exposed to puffs containing 35-77 µg HCN. Of the vapor-phase constituents studied, the NO content, however, was best correlated with the frequency of malignant transformations. High SH reactivity was also positively correlated with malignant transformation.	Leuchtenberger et al. (1976) C-14
HCN 200 mg/m^3 (180 ppm)	38°C	9-10° inclined mounting of trachea in chamber pH	Rabbit trachea	*In vivo* assay of ciliary activity quantitated by particulate movement. Exposed for 18 s.	50% inhibitory concentration of ciliary activity. Similar results were described for *in vitro* experiments with hen trachea by Battista and Kensler (1970) (rating C-9). Eight puffs of 250 mg HCN/m^3 inhibited ciliary activity to 50% that of the controls.	Kensler and Battista (1966) B-9

SECTION III

ANIMAL EXPOSURES

Most studies looking only at the lethality of HCN in various animal species have not been considered for tabulation. However, it is interesting to note the variability in resistance of species to lethal and "tolerable" levels of HCN. Table III-1 shows that, at the same HCN level (1,000 mg/m^3), the monkey(s) lived four times longer than the dog(s). Table III-2 shows some reordering of the species; but the dog is still the most sensitive, tolerating 100 mg HCN/m^3 air; the monkey, 180 mg/m^3; and the guinea pig, 400 mg/m^3. Barcroft (1931), however, did not use many animals and without much effort we have found other studies disagreeing with his results (see footnotes of Table III-2). Other discrepancies can also be seen in the following tables when Barcroft's tests are included.

The animal tests were grouped into tables by species and by length of exposure. The tables are arranged in this chapter by increasing approximate weight of the test animals. Thus, Table III-3 includes data from acutely exposed mice. Mice exposed to the threshold limit value set by the American Conference of Governmental Industrial Hygienists (ACGIH, 1981) of 10 mg HCN/m^3 air (10 ppm) for 2 h showed mobility hindrance and generally labored respiration and after 6 h, greatly reduced food intake. Five mice exposed to 3 to 10 ppm for 6 h showed a body weight loss of 3.4 to 4.0 g over the next 2 wk compared to a 1.0 g weight gain by the controls (Sato et al., 1955). When combined with combustion products (CO_2 and CO) at 100°F, even 11 mg HCN/m^3 (10 ppm) was lethal to 2 of 10 mice after 4 h (Pryor et al., 1975).

Very little experimental detail was found for the acute rat exposures mentioned in Table III-4. Several more lethality studies were identified, but no studies were found for low-level acute exposures. The situation was similar for acute exposures of guinea pigs (230 to 1,000 mg HCN/m^3) (Table III-5).

Dudley et al. (1942) stated that rabbits showed no marked toxic symptoms when exposed for 125 mg HCN/m^3 (see Table III-6). [Dudley et al. (1942) apparently did not perform the HCN tests they cited to compare with their exposures of various animals to acrylonitrile. Not having identified the original source, we include these values with little experimental detail.] In repeated dose studies (Table III-7), Hugod (1979) found no significant difference in lung morphology or in the vascular intima (aortic arch, thoracic artery, pulmonary artery) from the controls when rabbits were exposed for 1 to 4 wk to 0.55 mg HCN/m^3 alone or plus CO or plus CO and NO.

The lowest dose acutely tested with cats was 33 to 44 mg/m^3, where no effect was seen after 4 to 5 h. However, at 55 mg/m^3 severe pathological symptoms were seen after 1.5 h (Lehmann, 1903). The latter results are very different from those of Barcroft (1931), who reported that the cat could tolerate 180 mg HCN/m^3 "indefinitely." These results are in Table III-8.

Monkeys acutely exposed to 125 mg HCN/m^3 for 12 min showed toxic symptoms (Dudley et al., 1942). The other two tests in Table III-9 are at higher concentrations.

The lowest level used in acute experiments with dogs (Table III-10) was 35 mg HCN/m^3, which is described as a tolerable level by the same authors (Dudley et al., 1942) who reported 125 mg/m^3 to be lethal.

The lowest HCN concentration to which Barcroft (1931), the only author represented in Table III-11, acutely exposed goats was 240 mg/m^3. This level could be breathed indefinitely, yet 360 mg/m^3 killed all four goats exposed within 24 min.

Table III-12 is also very limited. Two donkeys showed bronchial clearance arrest at the onset of ~ 0.5-h exposure to 200 70-ml puffs of smoke at 275 or 1,350 mg HCN/m^3 per puff. Clearance recovered within 20 min of the exposure for the lower level but required 25 min post exposure at the higher level. No effects were seen if clearance studies were performed by initiating exposure to radioactive particles <u>after</u> exposure rather than before as in the tests just described (Albert et al., 1974).

Chronic inhalation studies were not found for any species.

Table S-1 in the summary is a composite of the more interesting tests from Tables III-3 to III-12.

TABLE III-1. SPECIES DIFFERENCES IN LETHAL TIME OF EXPOSURE TO 1,000 mg HCN/LITER
BARCROFT (1931) (B-11)

Animal	Time (min)
Dog	0.8
Mouse	1.0
Cat	1.0
Rabbit	1.0
Rat	2.0
Guinea Pig	2.0
Goat	3.0
Monkey	3.5

TABLE III-2. HIGHEST TOLERABLE CONCENTRATION
BARCROFT (1931) (B-11)

HCN Concentration, mg/m^3	Animal	Effect
100	Dog	Highest approximate concentration which can be breathed "indefinitely." Last experimental values recorded are at 60 min.
100*	Rat	
140	Mouse	
180**	Rabbit	
180	Monkey	
180	Cat	
240	Goat	
400	Guinea Pig	

* The 1-h LC_{50} for male rats was reported to be 484 ppm HCN by Vernot et al. (1977). A review of four other lethal rat studies by Hilado and Cumming (1978) shows a dose-response curve for 250-g rats wherein the LC_{50} falls from ~ 500 ppm at ~ 5 min exposure to ~ 140 ppm at 1 h.

** Nishimaru et al. (1973) reported that ~ 150 ppm HCN killed all the exposed rabbits within 3-5 min.

TABLE III-3. MICE--ACUTE EXPERIMENTAL EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000			Mouse			1 min, once		Lethal	Barcroft (1931) B-11
HCN 165 (150)	85°F	Exposure Chamber	Swiss albino, Webster strain random-bred mice young male and female	10	0	4 h, once		No survivors	Pryor et al. (1975) B-13
HCN 140			Mouse			Indefinite		Highest "tolerable concentration." Last experimental values recorded by Barcroft (1931) are at 60 min.	Barcroft (1931) B-11
HCN 110 (100)	85°F	Exposure Chamber	Swiss albino, Webster strain random-bred mice young male and female	10	0	12 h, once		No survivors	Pryor et al. (1975) B-13
HCN 110 (100)	85°F	Exposure Chamber	Swiss albino, Webster strain random-bred mice young male and female	10	0	4 h, once	10 d	9 survivors (10% mortality)	Pryor et al. (1975) B-13

(continued)

TABLE III-3. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 83 (75) CO_2 30 vol. % CO 0.075 vol. % O_2 16 vol. %	100°F	Exposure Chamber	Swiss albino, Webster strain random-bred mice young male and female	10	10	4 h, once		No survivors. All controls survived the same conditions except HCN (and another 10 survived for 24 h). In all tests where SO_2 or NO_2 was used instead of HCN, the microscopic lung and trachea damage was about the same, i.e., congestion. Signs of excitation and irritability were about the same, too.	Pryor et al. (1975) B-13
HCN ~ 66 (60)		Exposure Chamber	Mice	10	Not given	1 h, once		LD_{50}. The relationship of ppm X time shows only a small variation in the early stages. Also, it appears that the product of concentration X time for 10% deaths is half that for the case of 50% deaths and that the effect of the HCN itself is greater.*	Sato et al. (1955) B-10
HCN ~ 46 (~ 42)		Exposure Chamber	Mice	10	Not given	2 h, once		LD_{50}. The relationship of ppm X time shows an increase of 15 between 1.0-1.5 h.*	Sato et al. (1955) B-10
HCN ~ 42 (38)		Exposure Chamber	Mice	10	Not given	3 h, once		LD_{50}. The relationship of ppm X time shows an increase of 10 between 2.5 and 3.0 h.*	Sato et al. (1955) B-10
HCN ~ 39 (35)		Exposure Chamber	Mice	10	Not given	4 h, once		LD_{50}. The relationship of ppm X time shows an increase of 8 between 3.5-4.0 h and then decreases again.*	Sato et al. (1955) B-10
HCN 33 (30)	85°F	Exposure Chamber	Swiss albino	10	0	24 h, once	10 d	All survived.	Pryor et al. (1975) B-13

(continued)

TABLE III-3. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 33 (30) CO_2 30 vol. % CO 0.075 vol. % O_2 16 vol. %	100°F	Exposure Chamber	Swiss albino, Webster strain random-bred mice young male and female	10	10	4 h, once	10 d	No survivors	Pryor et al. (1975) B-13
HCN 22 (20)		Exposure Chamber 100-L capacity	Mice	10	Not given	4.5 h		20% died.	Sato et al. (1955) B-10
HCN 17 (15)		Exposure Chamber	Mice	10	Not given	4 h		< 10% deaths. The appearance of mobility hindrance occurred at 1 h.	Sato et al. (1955) B-10
HCN 11 (10)		Exposure Chamber	Mice	10	Not given	2 h		Mobility hindrance in 2 h. Generally labored respiration.	Sato et al. (1955) B-10
				3 groups of 10	10	6 h		Food intake by the exposed mice was 20 to 65% that of the control mice. Five mice exposed to 3-10 ppm HCN for 6 h showed a weight loss of 3.4-4.0 g over the next 2 wk compared to a weight gain (1.0 g) by the control group.	
HCN 11 (10) CO_2 30 vol. % CO 0.075 vol. % O_2 16 vol. %	100°F	Exposure Chamber	Swiss albino, Webster strain random-bred mice young male and female.	10	10	4 h, once	10 d	2 mice died. Also, estimated equivalent lethal levels for humans at 17% O_2, 0.01% CO, 10% CO_2, 110°F, and 10 ppm HCN.	Pryor et al. (1975) B-13

(continued)

TABLE III-3. (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 5.5 (5)		Exposure Chamber	Mice	10	10		4 h	The amount of food taken was very much reduced (66-87%) in comparison to that taken by a control group; but on returning to normal air, the amount of food taken returned to normal.	Sato et al. (1955) B-10
HCN 5.5 (5) CO_2 30 vol. % CO 0.075 vol. % O_2 16 vol. %	100°F	Exposure Chamber	Swiss albino, Webster strain random-bred mice young male and female	10	10	4 h, once	10 d	All survived.	Pryor et al. (1975) B-13
HCN $\leq$ 4.4			Albino mice			$\leq$ 7 h		Survival without any symptoms.	Lazarev (1971) C--

* The products of ppm X h for the LD_{50}'s at 0.5-h intervals from 0.5 h up to 4 h were 50, 52, 67, 82, 95, 105, 112, 120. The corresponding values for the LD_{10}'s were 25, 40, 45, 50, 55, 60, 60, 60.

TABLE III-4. RATS--ACUTE EXPERIMENTAL EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/ Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000						2.0 min		Lethal.	Barcroft (1931) B-11
HCN 120 (110)						1.5 h		Lethal.	Dudley et. al. (1942) C-9
HCN 100						Indefinite		Highest "tolerable concentration."	Barcroft (1931) B-11

TABLE III-5. GUINEA PIGS--ACUTE EXPERIMENTAL EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/ Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000						0.8 min		Lethal.	Barcroft (1931) B-11
HCN 400						Indefinite		Highest "tolerable concentration."	Barcroft (1931) B-11
HCN 350 (315)								Lethal.	Dudley et. al. (1942) A-9
HCN 230 (200)						1.5 h		Tolerated without symptoms.	Dudley et. al. (1942) A-9

TABLE III-6. RABBITS--ACUTE EXPERIMENTAL EXPOSURE TO CN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/ Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000			Rabbit			2 min		Lethal.	Barcroft (1931) B-11
HCN 500			Rabbit	1		15 min		Lethal. Total volume of air inhaled in that period - 1,902 cm^3. Total quantity of HCN inhaled - 0.95 mg.	Barcroft (1931) B-11
HCN 350 (315)			Rabbits					Lethal.	Dudley et al. (1942) C-9
HCN 130 (125)			Rabbits					No marked toxic symptoms.	Dudley et al. (1942) C-9

TABLE III-7. RABBITS--REPEATED DOSE EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/ Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 0.55 (0.5)		Exposure Chamber (Animals housed in separate cages within it.)	Rabbits Danish country breed albinos 2.0-2.5 kg	24 M	24 M	4 wk		Lung morphology unaffected in all cases. No significant differences between exposed and control animals could be established for vascular sections.	Hugod (1979) C-11
HCN 0.55 (0.5) CO (200)		Exposure Chamber	Rabbits Danish country breed albinos 2.0-2.5 kg	12 M	12 M	4 wk		Lung morphology unaffected in all cases. No significant differences between exposed and control animals could be established for vascular sections.	Hugod (1979) C-11
HCN 0.55 (0.5) NO (5) CO (200)		Exposure Chamber	Rabbits Danish country breed albinos 2.0-2.5 kg	12 M	12 M	2 wk		Lung morphology unaffected in all cases. No significant differences between exposed and control animals could be established for vascular sections.	Hugod (1979) C-11
HCN 0.55 (0.5)		Exposure Chamber	Rabbits Danish country breed albinos 2.0-2.5 kg	24 M	18 M	1 wk		Lung morphology unaffected in all cases. No significant differences between exposed and control animals could be established for vascular sections.	Hugod (1979) C-11
HCN 0.55 (0.5) CO (200)		Exposure Chamber	Rabbits Danish country breed albinos 2.0-2.5 kg	12 M	12 M	1 wk		Lung morphology unaffected in all cases. No significant differences between exposed and control animals could be established for vascular sections.	Hugod (1979) C-11

TABLE VII-8. CATS--ACUTE EXPERIMENTAL EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000			Cat			1 min		Lethal.	Barcroft (1931) B-11
HCN 350 (315)			Cats			2 min 5-10 min		Respiratory paralysis Death.	Dudley et. al. (1942) C-9
HCN 290			Cat	1		11 min		Death occurred. Total volume of air inhaled in that period - 2,547 cm^3. Total quantity of HCN inhaled - 0.92 mg.	Barcroft (1931) B-11
HCN 180			Cat			Indefinite		Highest "tolerable concentration."	Barcroft (1931) B-11
HCN 140 (125)			Cats			6-7 min		Markedly toxic.	Dudley et. al. (1942) C-9
HCN 130-165 (120-150)			Cats			0.5 h		Severe symptoms described at 55 mg/m^3, but recovered after 0.5 h.	Lehmann (1903) B-3
HCN 55-66 (50-60)			Cats			2.5-5 h		Most died.	Lehmann (1903) B-3
HCN 55 (50)			Cats			1.5 h		Severe pathological symptoms: deep and slow breathing, salivation, vomiting, widening of the pupils, spasms.	Lehmann (1903) B-3
HCN 33-44 (30-40)			Cats			4-5 h		No effect.	Lehmann (1903) B-3

TABLE III-9. MONKEYS--ACUTE EXPERIMENTAL EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000						3.5 min		Lethal.	Barcroft (1931) B-11
HCN 180						Indefinite		Highest "tolerable concentration."	Barcroft (1931) B-11
HCN 140 (125)						12 min		Distinctly toxic.	Dudley et al. (1942) C-9

TABLE III-10. DOGS--ACUTE EXPERIMENTAL EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000						0.8 min		Lethal.	Barcroft (1931) B-11
HCN 550-690						0.5 min		Dog unsteady.	Barcroft (1931) B-11
						1.25 min		Unconscious.	
						1.5 min		Tetanic convulsions (believed dead and removed from chamber; however, the dog was found alive the following day).	
HCN 125 (115)								Lethal.	Dudley et al. (1942) C-9
HCN 100						Indefinite		Highest "tolerable concentration."	Barcroft (1931) B-11
HCN 100 (90)						Indefinite		May be tolerated for hours; death after exposure.	Dudley et al. (1942) C-9
HCN 40-70 (35-65)								Vomiting, convulsions, recovery; may be fatal.	Dudley et al. (1942) C-9
HCN 35 (30)								May be tolerated.	Dudley et al. (1942) C-9

TABLE III-11. GOATS--ACUTE EXPERIMENTAL EXPOSURE TO HCN

Compound(s) and Concentration(s), mg/m^3	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN 1,000		Exposure Chamber	Goat			3 min, once		Lethal.	Barcroft (1931) B-11
HCN 360		Exposure Chamber	Goats	4		15 min, once		1 died, 3 recovered.	Barcroft (1931) B-11
				4		20 min, once		3 died, 1 lived.	
				4		24 min, once		All died.	
HCN 240		Exposure Chamber	Goat			Indefinite		Highest approximate concentration that could be breathed indefinitely.	Barcroft (1931) B-11

TABLE III-12. DONKEYS--ACUTE EXPERIMENTAL EXPOSURE TO CN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCN in each puff: (250 or 1,230) corresponding to 10 and 50 cigarette equivalents. Prior exposure to radioactive test aerosol* to measure clearance.		Nasal catheters at the rate of six 70-ml puffs/min for 200 puffs from a smoking apparatus.	Sicilian donkeys F 8-y 169 kg M 5-y 149.1 kg	1 M gelding 1 F	Each served as its own control	~ 0.5 h, once	(Same animals were used in other HCN and cigarette smoke exposures.)	With the 10-cigarette equivalent, there was arrest of bronchial clearance promptly after the onset of exposure. Clearance recovered after 20 of the 30 min of the exposure period, with the second tracheal wave peaking about 50 min later. With the 50-cigarette equivalent exposure, arrest of bronchial clearance persisted for 25 min past exposure period. Recovered clearance was rapid and produced a second tracheal wave that peaked about 50 min later.	Albert et al. (1974) C-11
HCN in each puff: 21 cigarette equivalent: (441) 30 cigarette equivalent: (455) 52 cigarette equivalent: (1,000) 74 cigarette equivalent: (1,080) Exposure to radioactive aerosol* after HCN exposure to measure clearance.		Nasal catheters No. of 70-ml puffs: 285 385 300 400		1 M gelding 1 M gelding 1 M gelding 1 F		~ 0.8 h ~ 1 h ~ 0.8 h ~ 1.1 h		Neither donkey showed any abnormalities in bronchial or tracheal clearance.	Albert et al. (1974) C-11

* Spherical monodisperse ferric oxide particles tagged with ^{99m}Tc sulfide (3.0-3.4 μm MMD).

SECTION IV

HUMAN EXPOSURES

This chapter reviews the literature on occupational studies in detail, while selectively reviewing case histories and related reports. There were no epidemiology studies of HCN exposure of the general public. None of the accidental-exposure papers correlated HCN levels with effects. Except for two occupational studies, accidental overexposures are not included.

Many reviews (see references in Table IV-1) have cited data from original documents when compiling human dose response tables, but it is usually not clear who performed the original observation. In a few instances, compiled values varied as if the author(s) had performed a unit conversion incorrectly. Table IV-1 uses the values most often cited. Note that headache and vertigo (dizziness) have been observed at values below the 1981 ACGIH threshold limit value (ACGIH, 1981). The occupational studies are charted in Table IV-2 and most are discussed in the Summary.

TABLE IV-1. HUMAN DOSE-RESPONSE DATA AS GENERALIZED IN THE LITERATURE[a]

Dose of HCN		Response
mg/m^3	ppm	
22,000	20,000	Even though breathing is through a gas mask, vertigo, weakness, and tachycardia occur after 8-10 min. Loss of work capacity for 2-3 d.
7,000-12,000	6,360-10,900	Level dangerous after 5 min even though a gas mask is used because of skin penetration.
5,000	4,550	Safe for 1 min.
3,750	3,410	Safe for 1.5 min.
3,600	3,270	Safe for 30 min with a gas mask.
2,500	2,270	Safe for 2 min.
$\leq$ 1,000	$\leq$ 909	Safe for an experienced fumigator indefinitely.
550	500	No serious consequences after 1 min exposure.
400	364	Tolerable for 1.5 min without vertigo.
300	270	Immediately fatal. Lazarev (1971) [2-0144] stated that this concentration is tolerable for 2 min without headache. Lazarev (1956) [2-0145] stated a person at rest would withstand this concentration for 2 min without dizziness.
200	180	Fatal after 10 min.
150	140	Fatal after 0.5 h.
120-150	110-135	Fatal after 0.5-1 h.
110	100	Fatal in 1 h.
50-60	45-54	Tolerated for 0.5-1 h without immediate or late effects.

(continued)

TABLE IV-1. (concluded)

Dose of HCN		Response
mg/m^3	ppm	
0.4-50	0.4-45	Headache, vertigo, nausea, regurgitation, heartburn, general weakness, sensation of pressure in the epigastric region, sweating of the hands, instability of the autonomic nervous system, decrease in vascular tone, slowing of blood circulation.
20-50	18-45	Headache, nausea, vomiting, and tachycardia after several hours.
20-40	18-36	Slight symptoms (headache) after several hours.
5-20	4.5-18	Headache and vertigo.
10	10	Threshold limit value (ACGIH, 1981).
0.2-5.5	0.2-5.0	Odor threshold.
0.11-0.99	0.1-0.9	No effect.[b]

[a] Aghoramurthy and Mehta (1977), Dudley et al. (1942), Einhorn (1975), Flury and Zernik (1931), Henderson and Haggard (1943), Hamilton and Hardy (1949), Lazarev (1971) [most levels $\geq$ 300 mg/m^3], McNamara (1976).

[b] Attributed to Lazarev by Czechoslovak Committee of MAC (Wills et al., 1976).

TABLE IV-2. OCCUPATIONAL EXPOSURE TO HYDROGEN CYANIDE

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
Cyanide gas 28-83 (25-75) This was likely higher due to added ventilation before testing.	Worker in photographic darkroom; wet plate process	1 M		Symptoms/complaints of numbness, weakness, vertigo, nausea, rapid pulse, and flushing of the face occurred on three different occasions at the end of the work week followed by headache and vague gastric distress.	Case report showed individual hypersensitivity. Indicating an industrial standard applicable to the general case may not always apply in individual situations.	Parmenter (1926) B--
Cyanides: 7-14 [Yugoslav MPC 5]	Workers in the electroplating department in the electronics industry of Nis, Yugoslavia	28 (18 smokers; 10 nonsmokers)	20	Complaints of exposed workers included fatigue, headache, body weakness, tremor of the hands and feet, pain, and nausea. More pronounced complaints came from workers who had worked for a long time with cyanides. More thiocyanate was eliminated by those who were exposed to CN^- over the controls. The annealing shop was found to be less of a risk than the electroplating shop. The avg. thiocyanate values in the urine for nonsmoking exposed electroplaters and annealing shop workers were 3.10 and 1.90 mg/L; the smokers in these job categories had avg. thiocyanate values 10.00 and 8.00 mg/L, respectively. The values for the controls were 0.17 mg/L for nonsmokers and 4.40 mg/L for smokers. The differences between the exposed and control concentrations were all statistically significant ($P < 0.01$). Workers who had been exposed to cyanides for a longer time generally excreted more thiocyanate in their urine.	Symptoms sound like long-term stress exposure. Interesting that cigarette smoking produced urinary thiocyanate levels higher than work exposure, yet the complaints were working-related not smoking related. Smoking hand-to-mouth may be portal of entry and account for higher levels. Workers constantly exposed to cyanide as HCN consistently excrete low levels of thiocyanate in the urine. Average range from 6 to 13 mg/L (Hardy et al., 1950 [B-7]. Maehly and Swenson (1970) [C-12], who did not report on exposure symptoms, found an average total 20.0 or 23.0 mg SCN^-/L urine when HCN levels were 3.8 or 5.1 ppm, respectively.	Radojicic (1973) B-9
6-9	Workers in the annealing shop of the same plant.	15 (5 nonsmokers; 10 smokers)	same 20 as above			

(continued)

TABLE IV-2. (continued)

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
Combined copper cyanide and NaCN. Mean CN^- concentration in breathing zones: 11.4 (10.375)[a] 7.1 (6.416) 8.9 (8.083)	Electroplating sections of three factories	36 M	20 M	Incidence of symptoms in workers significantly greater than in controls: headache, weakness, changes in taste and smell (especially abhorrence of cigarettes), giddiness, irritation of throat, vomiting, effort dyspnea. Lacrimation, abdominal colic, and precordial pain were less frequent. And only 8.33% of those exposed experienced excessive salivation, disturbances of accommodation, and psychosis. No clinical signs of hypo- or hyperthyroidism, but 56% of the workers had thyroid enlargement to a mild degree. Iodine uptake by the thyroid was increased but the 72-h protein-bound iodine uptake was not affected. Concentration of thiocyanate in urine increased to middle of work week and was almost stationary during its last 3 days. The mean values (M) of SCN^- in urine in the second half of the work week were plotted against the mean values (C) of cyanides in the air during the same period. The regression line is represented by the equation M = 0.65C.	Prevalence data were used to assess exposure. It would have been helpful to use thiocyanate levels to correlate with symptoms.	El Ghawabi et al. (1975) B-9

(continued)

TABLE IV-2. (continued)

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
HCN Average daily concentrations for the 12 shops ranged from 0.05-0.09 to 0.36-2.7.	Workers in 12 galvanizing shops in metallurgic industry, electric, and radiotechnical apparatus plants.	63 M 11 F	11 M 45 F	223 determinations on 73 working posts revealed 46 had ratio of actual concentration to maximum allowable (0.3 mg/m^3) from 1.1 to 9.0. Rhodanase determinations showed only two case values above normal range. Clinical and laboratory investigations showed no characteristics of acute or chronic occupational HCN poisoning. HCN-exposed women had no circulatory system pathologies reported, but had neurosis (CNS symptoms) as frequently as controls. HCN-exposed males had circulatory system problems as frequently as controls but no neurotic symptoms which were seen in control males.	Neurosis may be related to multiple job-related stresses having little association with HCN. Job comparability of workers and controls exposed should have been evaluated.	Ju'zwiak et al. (1979) B-8
Work area: Cyanide (HCN and particulates), 0.2-0.8; mean 0.45 General workroom: 0.1-0.2; mean 0.15 Relative humidity 29.0 - 61.0%; mean 45.0%	Workers engaged in Electroplating and casehardening, ages 23-40 y. Control workers from same factory had never been exposed to chemical hazards and belonged to the same age group, sex, and socioeconomic status. Both groups avoided cyanogenic foods such as cabbage, mustard, and almond for ≥ 48 h before collection of blood and urine samples.	23 M 8 Smokers 15 Nonsmokers	20 M 10 Smokers 10 Nonsmokers	Mean blood thiocyanate level in smokers of exposed and control groups were 0.48 and 0.10 mg/100 ml, respectively, in nonsmokers, 0.42 and 0.04 mg/100 ml, respectively. Corresponding cyanide levels were 56.0, 4.8, 18.3, and 3.2 µg/100 ml, respectively. The mean 24-h thiocyanate in urine of smokers of the exposed and control groups were 0.62 and 0.41 mg/100 ml, respectively; in nonsmokers, 0.57 and 0.08 mg/100 ml, respectively. Corresponding cyanide levels in urine were 6.23, 3.2, 5.4, and 2.15 µg/100 ml, respectively.	Although the author abstract states that the "workers complained of typical HCN poisoning" and there is a similar statement in the conclusions, no health effects are reported. Since detaled clinical examinations and pulmonary function tests are stated to have been performed, perhaps the results will be reported in a future paper.	Chandra et al. (1980) B-11

(continued)

TABLE IV-2. (continued)

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
3.1-37.0°C; mean 45.0°C [sic], presumably 35°C. Duration: 2 mo, June and July	Venous blood was collected at the end of the work shift and urine samples were collected throughout the workday and at home.			Blood values in exposed workers ($P < 0.001$) whether smokers or nonsmokers were significantly higher than among the control group workers. The differences in urine cyanide values were statistically not significant, but the thiocyanate level differences were significant ($P < 0.001$). There was no consistent pattern in thiocyanate levels found in samples collected at 2-h intervals, so a 24-h urine sample should be used.		
1966: avg. acrylonitrile exceeded the MPC (0.5) by an avg. 5-10X. Majority of HCN concentrations < MPC of 0.3, but the MPC was exceeded in one-third of the samples.						
1971: avg. acrylonitrile concentration 0.75. HCN concentrations all at or below the MPC.	Workers employed 4-6 y in an acrylonitrile plant.	75 M&F	25 M&F	Complaints included indisposition, headache, reduced work capacity, poor sleep, irritability, compressive pains in the region of the heart, poor appetite, skin pallor. Some irritation of the skin had occurred but subsequently disappeared. Reduced nos. of erythrocytes, leukocytes, and hemoglobin values were observed. Also noted were changes in the oxidation processes in the tissues.	It would be difficult to attribute effects solely to inhalation since liquid acrylonitrile may be absorbed through the skin.	Zotova (1975) C-8

(continued)

TABLE IV-2. (continued)

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
Over a 5-y period, the avg. concentration was 0.26 (MPC = 0.3)	Avg. length of occupation 5.4 y at an electroplating plant.	12 M 31 F	Not given	Results of tests demonstrate noticeable decline of leukocytochrome oxidase, reduction to peroxidase and succinic dehydrogenase activity, and a reduction of blood catalase levels. These findings demonstrate that HCN inhibits the activity of certain redox enzymes in somatic cells.	Good study. The degree of enzyme depression, however, was not related to age categories.	Dinca et al. (1972) A-12
Acrylonitrile 0.55 ± 0.03 (23.5)[b] HCN 0.08 ± 0.006 (3.7)[b] NH_3 7.9 ± 0.7 (3.0)[b] Total hydrocarbons 41.0 ± 3.8 (0)[b] Unsaturated hydrocarbons 20.2 ± 1.2 (0)[b] 1972-1974 numerous measurements	Workers in acrylonitrile production.	No figures given.		Increased frequency of disorders of the nervous system. Neurasthenic and asthenic syndrome with vegetative-vascular disturbances. Increase in sympathetic nerve system reflexes. Increase in flabby heart and cardiac weakness (both significant at 0.05 level). Changes in the functional condition of the liver. Methemoglobinemia was increased. Tendency to lowering of total work capacity supported by dynamometric data.	Symptom list includes evanescent signs of nervous system change. The progressive symptoms and changes reported, without any good epidemiologic data collection, hint at a toxic effect on long-term human exposure to the levels of the mixture described. Relevance of the signs to HCN toxicity cannot be assessed from data.	Boklag (1975) C-6
HCN 0.01 (0.091) NH_3 2.9 Acid mist	Workers in Massachusetts jewelry plating operations, February 1974.	3-4	-	No hazard exists to employees working in the plating area exposed to HCN, NH_3, and acid mists. "No adverse health effects were evident." Employees interviewed experience "occasional irritation from ammonia."	A NIOSH Health Hazard Evaluation. Paper did not describe the health effects they evaluated or the method of evaluation.	Burton (1974) B-3

(continued)

TABLE V-2. (continued)

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
Exposed:						
HCN 0.00035-0.00087 (0.00032-0.00079) Phenol 0.00875-0.9154 H_2S 0.0075-0.0093 (0.0050-0.0062)	Bulgarian farm workers - 1973-1975	No numbers given.		Suffered more acute infections of the upper respiratory pathways and neurosis than workers exposed to the less contaminated air. In this period, 65.7% of the workers exposed to the more contaminated air experienced morbidity of average duration 14.3 d compared to 50.5% of the workers exposed to the lesser contamination experiencing sickness of average duration 9.3 d.	Multiple factors besides air quality could have contributed to the observed variation of "sickness duration." Job comparability between the groups is not given.	Kiryakov et al. (1978) C-5
Controls: HCN 0.00012-0.00083 (0.00011-0.00075) Phenol 0.00504-0.01701 H_2S 0.0032-0.0063 (0.0021-0.0038)	Bulgarian farm workers - 1973-1975					
HCN concentration not given; infrequent intoxication incidents in 1953.	17 workers in fumigation employment of miscellaneous job classifications. Ages - 24-59 y Periods of service - < 2-27 y.	13 M		4 workers employed 7-8 y and 24-27 y had not inhaled HCN gas on any occasion, and showed no symptoms or physical changes resulting from employment. Of the 13 exposed workers, 12 showed some signs of gastritis. Objective signs of disturbance included dizziness, headache, tremors, pain around the heart, Romberg's sign, nystagmus, heartburn, dyspnea, cough, tachycardia, and diarrhea. 3 or more of those exposed had odd atrioventricular lead patterns (as shown by EKG). Other parameters were tested and results given. Loss of consciousness was reported in one subject for a period of ≤ 10 min.		Carmelo (1955) C-6

(continued)

TABLE IV-2. (continued)

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
HCN concentration not given. Serum thiocyanate (SCN^-) levels measured after CN^- exposure in fumes while fighting major fires: Oct. 1, 1973 - Mar. 31, 1974	Baltimore, Maryland firefighters population (not stratified by cigarette use)	479 Presumably all male.	46	28% showed minor symptoms after a fire: 7%, cough and increased sputum; 2%, nausea and vomiting; 8%, headache; and 10%, other symptoms. Significantly higher mean serum SCN^- levels (5.6 vs. 4.36 µg/ml). Occupational exposure also related to shift in range of serum SCN^- evidenced by 12% of the exposed having levels above the highest values for controls (9.9 µg/ml).	No attempt was made to correlate minor symptoms with serum SCN^- levels due to concomitant CO exposure. The population studied was quite small after stratification for smoking. There was a lack of age correspondence with the controls, who were fire academy students and administrative personnel.	Levine and Radford (1978) A-10
HCN concentration not given. Serum thiocyanate (SCN^-) levels measured after CN^- exposure in fumes while fighting major fires.	Baltimore, Maryland, firefighters (heavy smokers category)	114	11	Increase in serum SCN^- levels for heavy smoking exposed firefighters (7.8 µg/ml) over heavy smoking unexposed controls (6.53 µg/ml).	~ 10-15% of the exposed men had values above the highest control values in each smoking group.	Levine and Radford (1978) A-10
HCN concentration not given. Serum thiocyanate (SCN^-) levels measured after CN^- exposure in fumes while fighting major fires.	Baltimore, Maryland, firefighters (light-to-moderate smokers category)	132	13	Increase in serum SCN^- levels for light-to-moderate smoking exposed firefighters (6.74 µg/ml) over smoking unexposed controls (4.61 µg/ml).		Levine and Radford (1978) A-10
HCN concentration not given. Serum thiocyanate (SCN^-) levels measured after CN^- exposure in fumes while fighting major fires.	Baltimore, Maryland, firefighters (nonsmoking category)	193	20	Increase in serum SCN^- levels for nonsmoking exposed firefighters (3.75 µg/ml) over unexposed nonsmoking controls (3.21 µg/ml).		Levine and Radford (1978) A-10

(continued)

TABLE V-2. (concluded)

Compound(s) Concentration(s), mg/m^3 (ppm) Duration	Description of Workers	Exposed	Controls	Effects	Remarks	Reference and Rating
HCN vapors from hot liquid bath of cyanide salts. Dusts of the latter. No concentrations given. Subject 1: 1910-1920 1941-1943 Subject 2: 1940-1948 (less frequent exposure 1942-1948)	Subject 1: Case hardener exposed continuously, at work. Heavy cabbage eater. From known area of endemic goiter. Age 62 in 1946, the year his goiter was removed. Subject 2: Worked in machine shop where case hardening was performed. Began iodine treatment for neck swelling 5 mo after beginning of exposure. Age 36 in 1948, when admitted to hospital with goiter. Heavy pipe smoker until 1945. Sister had a simple colloid goiter.	2 M	None	Case 1: Persistent headache, sweating, chest pains, dizziness, fatigue, weakness, mental confusion, disturbed motor function (e.g., tremor), nervousness, coughing, sneezing, cramping in lower abdomen, paralysis, auricular fibrillation, thyroid enlargement 2-3 X normal, high blood pressure. After a thyroidectomy, the patient did not resume contact with cyanides. Case 2: Thyroid enlargement.	Case reports of goiter in two men occupationally exposed to unquantitated HCN vapors. Family history, endemic goiter region, and dietary history combined make these reports of doubtful value in establishing thyroid toxicity of HCN vapors.	Hardy et al. (1950) B-7

[a] No local exhaust system.

[b] Percent of measurements that exceeded the USSR maximum allowable concentration.

BIBLIOGRAPHY*

- ACGIH, American Conference of Governmental Industrial Hygienists. 1979. TLVs.® Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1979. Publications Office, ACGIH, Cincinnati, Ohio. p. 37.

  A--. Recommended time-weighted TLV of 10 mg/m^3.

2-0035 Aghoramurthy, K., and S. K. Mehta. 1977. Toxicological Involvement in Acrylonitrile Plant. Environ. Pollut. Hum. Health, Proc. Int. Symp., 1st. pp. 519-539.

  C--. Review of toxicity of HCN and other materials that would be used at a planned acrylonitrile plant.

2-0001 Aguado Matorras, A., S. Carrasco Novella, and A. Perez Carvajal. 1972. Intoxicacion por el Acido Cianhidrico y sus Derivados [Poisoning by Hydrocyanic Acid and Its Derivatives]. Rev. Esp. Anestesiol. Reanim. 19:215-223.

  C-2. Mostly a toxicology review. Hyperbaric oxygen was used to treat a worker overcome by cyanide fumes in a metal plating factory.

2-179 AIHA, American Industrial Hygiene Association. 1969. Hygienic Guide Series; Hydrogen Cyanide. American Industrial Hygiene Association, Akron, Ohio.

  D--. Summary of various exposure standards such as TLV's toxicity data, recommended industrial practices and medical treatment.

2-0034 Albert, R. E., J. Berger, K. Sanborn, and M. Lippmann. 1974. Effects of Cigarette Smoke Components on Bronchial Clearance in the Donkey. Arch. Environ. Health. 29:96-101.

  C-11. Two donkeys were exposed for ~ 30 min to puffs of cigarette smoke containing avg. concentrations of 250 or 1,230 ppm HCN. They showed a transient impairment of tracheobronchial clearance.

2-0066 Anonymous. 1966. FAO/WHO Monographs on Fumigants. Food Cosmet. Toxicol. 4:433-436.

* Numbers in the left margin are MRI acquisition numbers.

D--. Acceptable daily intake of 0.05 mg CN^-/kg body weight in food for man given; no data for the choice or reason behind it.

2-0071 Aoyama, M. 1975. Effect of Anti-Flame Treated Cloths at Combustion on the Living Body. Nagoya Med. J. 20:1-10.

D-11. Time of death was recorded for mice exposed to mixed products of antiflame-treated cloth combustion. No HCN concentrations were given.

2-0120 Barcroft, J. 1931. The Toxicity of Atmospheres Containing Hydrocyanic Acid Gas. J. Hyg. 31:1-34.

B-11. Classic LD_{50} - concentration - time studies. Multispecies comparison very good.

5-191 Battista, S. P., and C. J. Kensler. 1970. Mucus Production and Ciliary Transport Activity. In Vivo Studies Using the Chicken. Arch. Environ. Health 20:326-338.

C-9. In vitro, a dose of 10 μg HCN/40 ml puff [250 mg/m^3] for 8 puffs inhibited ciliary activity to 50% that of the trachea of control hens. The corresponding ED_{50} in vivo was 38 μg/40 ml puff for 8 puffs. A log concentration - percent inhibition curve for HCN is given.

2-0036 Baxter, R. 1977. Cyanide Can Be Handled Safely. Ind. Finish. 53(12):38-41.

C--. Review. The odor threshold for HCN is 2 ppm.

2-0020 Boklag, E. P. 1975. Hygienic Characteristics of Working Conditions in the Production of Acrylonitrile. Zdravookhr. Beloruss. No. 8: 41-44.

C-6. Group changes upon exposure to acrylonitrile, HCN, NH_3, and hydrocarbons included evanescent signs of increased immunity, premature aging, and borderline central nervous system change. One assumes the mixture to which this population was exposed was slightly toxic.

2-0037 Brunnemann, K. D., L. Yu, and D. Hoffmann. 1977. Chemical Studies on Tobacco Smoke. XLIX. Gas Chromatographic Determination of Hydrogen Cyanide and Cyanogen in Tobacco Smoke. J. Anal. Toxicol. 1:38-42.

C--. A "standard" cigarette contained 479 μg HCN in mainstream smoke. A profile of brands contained 279-551 μg in smoke.

2-0032 Burton, D. J. 1974. Health Hazard Evaluation/Toxicity Determination Report 73-147-134, H. F. Barrows Company, North Attleboro, Massachusetts. PB-246 459, U.S. Nat. Tech. Inform. Serv. U.S. Dept. of Commerce, Springfield, Virginia. 6 pp.

B-3. Three or four electroplaters were exposed to acids, 0.01 mg HCN/m^3, and 2.9 mg NH_3/m^3. No ill effects were noted. Paper did not describe the health effects evaluated or any method of evaluation, which is a shortcoming.

2-0121 Carmelo, S. 1955. Nuovi Contributi allo Studio della Intossicazione Subacuta-Cronica da Acido Ciandrico nell'Uomo [New Contributions to the Study of Subacute-Chronic Hydrocyanic Acid Intoxication in Man]. Rass. Med. Ind. 24:254-271.

C-6. Most fumigators who had inhaled sufficient HCN to experience symptoms of poisoning within the past 2 y suffered from gastritis. Those who had never inhaled HCN showed none of the CNS and cardiopulmonary symptoms observed in the exposed fumigators.

2-0003 Castello, C., A. Giussani, and A. Berti. 1969. Avvelenamento da Acid Cianidrico. Considerazioni Clinico-Terapeutiche e Presentazione di un Caso. [Poisoning by Hydrocyanic Acid; Clinical and Therapeutic Considerations and Presentation of a Case]. Minerva Anestesiol. 35:437-447.

D-2. Paper describes the medical treatment of a sailor found unconscious in his berth onboard ship after disinfection of the ship with HCN.

2-0178 Chandra, H., B. N. Gupta, S. K. Bhargava, S. H. Clerk, and P. N. Mahendra. 1980. Chronic Cyanide Exposure--A Biochemical and Industrial Hygiene Study. J. Anal. Toxicol. 4(4):161-165.

B-11. Case hardeners and electroplaters were exposed to cyanide at concentrations up to 0.8 mg/m^3. They showed significantly elevated thiocyanate in blood and urine and significantly elevated cyanide in blood. There were only small differences between values for exposed smokers and nonsmokers. Although this article mentioned that HCN toxicity symptoms occurred, the full report was cited as having been communicated (by these authors with Gupta first) in 1979 to an obscure journal that we tried but failed to locate: Indian J. Occup. Health.

2-0122 Chaumont, A. J. 1960. L'intoxication chronique par les cyanures et l'acid cyanhydrique [Chronic Intoxication Caused by Cyanides and by Hydrocyanic Acid]. Soc. Med. D'Hyg. Trav. 660-662; copyrighted English translation provided by the National Institute for Occupational Safety and Health, Rockville, Maryland.

C-4. Review of work by Koopman (1936) [2-0173] and Teleki. Additional case histories given, but no HCN concentrations given. Paper demonstrates definite low level symptoms that are secondary to low oxygen-carrying power of red blood cells: increased heart size, increased red blood cell count, enzyme change. Poor, scientifically. Not strong numbers.

2-0123 Colle, R. 1972. L'intoxication cyanhydrique chronique [Chronic Hydrogen Cyanide Poisoning]. Maroc. Med. 50:750-757; copyrighted English translation provided by the National Institute for Occupational Health Science, Rockville, Maryland.

C--. Good review of symptoms of occupational chronic exposure to HCN, but research and control level are deficient.

2-0172 Columba, D. 1940. Die ersten klinischen Beobachtungen über die Blausäure bein Menschen verursachten chronischen Veränderungen durch. [First clinical observations on the chronic changes in man due to hydrocyanic acid]. Ber. Gesamte Physiol. Exp. Pharmakol. 120:176.

C-3. Pneumo-cardio-diaphragmatic changes, hematologic changes, and changes occurring in carbohydrate metabolism were observed in 15 workers who had been exterminating with HCN for 2 to 7 y. Changes included widening of the lungs and bronchi, a change in the position of the diaphragm, hypotension, hyperhemolysis followed by hyperchromy, a diminution of the neutrophil polynuclei, a reduction in peroxidase levels, lymphocytosis accompanied by monocytosis, and hyperglycemia.

2-0124 Creel, R. H., F. M. Faget, and W. D. Wrightson. 1915. Hydrocyanic Acid Gas--Its Practical Use as a Routine Fumigant. Public Health Rep. 30:3537-3550.

D-9. Lethality experiments with rats were performed.

2-0068 Dalhamn, T. 1972. Factors Influencing the Respiratory Toxicity of Cigarette Smoke. J. Nat. Cancer Inst. 48:1821-1824.

D-8. Cats were exposed tracheally to mixed combustion products from nonfilter cigarettes containing 60-480 µg HCN/cigarette. Physiological effects on bronchial clearance were studied. The number of 10-ml puffs to produce ciliostasis ranged from 39 to 154. Acrolein, tar, CO, nicotine, and HCN concentrations were highly correlated with the number of puffs required.

2-0006 Delga, J., J. Motin, P. Bouletreau, and I. M. Rouzioux. 1970. Actual Problems of Hydrocyanic Acid Poisoning. Therapeutique 46:887-892.

D--. Review. Chronic HCN poisoning is similar in its manifestations to carbon monoxide poisoning.

2-0111 Dequidt, J., D. Furon, F. Wattel, J. M. Haguenoer, P. Scherpereel, B. Gosselin, and A. Ginestet. 1974. Intoxication with Acetonitrile with a Report on a Fatal Case. Eur. J. Toxicol. Environ. Hyg. 7:91-97.

D-12. Well-followed fatal case report. Concentrations of free HCN were determined in the victim's tissues. Acetonitrile, CH_3CN, was used by the fatally intoxicated worker and others to clean a floor. Upon pouring boiling water on the floor, hydrolysis caused the release of HCN and HCHO.

2-0126 Dinca, C., L. Pod, and I. Galetariu. 1972. [Considerations on Leukocytic Oxidative Enzyme Changes in Subjects Exposed to the Prolonged Action of Cyanhydric Acid in Industry]. Med. Int. 24:1385-1392; Copyrighted English translation provided by the National Institute for Occupational Safety and Health, Rockville, Maryland.

A-12. The case is convincing--a human population exposed at moderate levels (0.26 mg/m^3) to HCN had significantly depressed enzymes.

2-0029 DiPasquale, L. C., and H. V. Davis. 1971. Acute Toxicity of Brief Exposures to Hydrogen Fluoride, Hydrogen Chloride, Nitrogen Dioxide, and Hydrogen Cyanide Singly and in Combination with Carbon Monoxide. AD-751 442, National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 13 pp.

C-10. Data same as those in MacEwen and Vernot (1971) [2-0027].

2-0127 Drinker, P. 1932. Hydrocyanic Acid Gas Poisoning by Absorption Through the Skin. J. Ind. Hyg. 14:1-2.

D-8. Industrial gas masks give respiratory protection in atmospheres containing 2% HCN, but unprotected skin should not be exposed to such concentrations.

2-0128 Dudley, H. C., T. R. Sweeney, and J. W. Miller. 1942. Toxicology of Acrylonitrile (Vinyl Cyanide). II. Studies of Effects of Daily Inhalation. J. Ind. Hyg. Toxicol. 24:255-258.

C-9. The effects of inhaled acrylonitrile are quite similar at comparable levels to HCN in several animal species. No experimental protocol is given for the HCN tests so that they are probably only a review of the literature.

2-0039 Einhorn, I. N. 1975. Physiological and Toxicological Aspects of Smoke Produced During the Combustion of Polymeric Materials. Environ. Health Perspect. 11:163-189.

C--. The human HCN dose-response data are reviewed again.

2-0021 Eitingon, A. I., L. T. Poddubnaya, L. S. Naumova, and G. P. Gribunova. 1977. Toksichnost i Sostav Produktov Goreniya Nekotorykh Khimicheskikh i Prirodnykh Tkanei i Volokon [Toxicity and Composition of Combustion Products of Some Synthetic and Natural Fabrics and Fibers]. Khim. Volokna No. 4:49-51.

D-6. Lethal doses were determined for mice exposed to mixed combustion products.

2-0129 El Ghawabi, S. H., M. A. Gaafar, A. A. El-Saharti, S. H. Ahmed, K. K. Malash, and R. Fanes. 1975. Chronic Cyanide Exposure: A Clinical, Radioisotope, and Laboratory Study. Br. J. Ind. Med. 32:215-219.

B-9. Controlled study reports multiple symptoms in exposed group. Prevalence data were used to assess exposure. It would have been helpful to use thiocyanate levels to correlate with symptoms. Twenty (56%) of 36 electroplaters had mild to moderate thyroid enlargement after long-term exposure to 4.2-12.4 ppm CN^- in the air.

2-0130 Etteldorf, J. N. 1939. The Treatment of Gaseous Hydrocyanic Acid Poisoning by Sodium Thiosulfate and Sodium Nitrite Combination. J. Pharmacol. Exp. Ther. 66:125-131.

D-9. Exposure of dogs to convulsing concentrations of HCN (~ 500 ppm) for $\geq$ 0.25 h was lethal.

2-0131 Fairley, A., E. C. Linton, and F. E. Wild. 1934. The Absorption of Hydrocyanic Acid Vapour Through the Skin with Notes on Other Matters Relating to Acute Cyanide Poisoning. J. Hyg. 34:283-294.

C-7. The skin of guinea pigs and rabbits was exposed to an atmosphere "saturated with" HCN vapor. This is a lethality study; no other effects were well studied.

2-0132 Fassett, D. W. 1963. Cyanides and Nitriles. In: Industrial Hygiene and Toxicology, Vol. 2, F. A. Patty, ed. Interscience Publishers, New York, New York. pp. 1991-2036.

C--. Review of effects of high HCN concentrations.

2-0133 Flury, F., and F. Zernik. 1931. Cyanwasserstoff (Blausäure, Ameisensäurenitril) [HCN (Hydrocyanic Acid, Prussic Acid)]. In: Noxious Gases--Vapors, Mist, Smoke, and Dust Particles. Verlag von Julius Springer, Berlin, Germany. pp. 400-415.

C--. A good review of early literature on animal and human poisoning by HCN.

2-0134 Gettler, A. O., and J. O. Baine. 1938. The Toxicology of Cyanide. Am. J. Med. Sci. 195:182-198.

C--. The distribution of HCN in a 68.30 kg human female who had died inhaling HCN was (in mg/kg): brain, 0.032; lungs, 0.075; blood, 0.041; liver, 0.021; kidney, 0.033; heart, 0.42; and stomach wall, 0.10. Distribution in dogs poisoned fatally by HCN inhalation was similar.

2-0135 Gordh, T., and B. Norberg. 1947. Studies on Oxygen Treatment in Connection with Experimental Hydrocyanic Poisoning. Acta Physiol. Scand. 13:26-34.

D-10. Rabbits were exposed to lethal HCN concentrations (284-1,290 mg/m^3).

2-0040 Gori, G. B. and C. J. Lynch. 1978. Toward Less Hazardous Cigarettes. J. Am. Med. Assoc. 240:1255-1259.

C--. Compare data with Brunnemann et al. (1977) [2-0037], where smoke was analyzed. In this study, the range of HCN found in 27 modern brands of U.S. cigarettes was 9 to 141 μg/cigarette.

2-0136 Grabois, B. 1954. Exposure to Hydrogen Cyanide in the Processing of Apricot Kernels. NY State Dept. Labor Mon. Rev., Div. Ind. Hyg. 33:33-36, 1954.

D--. No exposure effects are described in the plant personnel exposed to ≦ 17 ppm HCN. Since the paper is mainly an analytical methods development paper, no attempt was made to examine the workers. In fact, we had totally discarded this paper until we found the observed levels described as "No observed effects" in Table XIV-5, p. 178, of Wills et al. (1976) on human responses.

2-0137 Grubbs, S. B. 1917. Detection of Hydrocyanic Acid Gas--Use of Small Animals for This Purpose. Weekly Public Health Rep. 32:565-570.

D-9. Several species, but few doses and single animals. Guinea pigs were resistant to HCN concentrations that may be dangerous to man. Mice and tame rats were almost as susceptible as the "most delicate live indicators"--sparrows or other small birds.

2-0138 Hamilton, A., and H. L. Hardy. 1949. In: Industrial Toxicology, ed. 2. Paul B. Hoeber Inc., New York, New York. pp. 248-262.

C--. Good review. Human symptoms (more applicable than Fassett, 1963 [2-0132]).

2-0061 Hanzal, R. F., and J. W. Howard. 1955. Chronic Toxicity for Rats of Food Treated with Hydrogen Cyanide. J. Agric. Food Chem. 3:325-329.

D--. Survivors of 20 rats (10 of each sex) fed 2 y a diet containing ~ 100 or 300 ppm HCN (HCN vaporized from the fumigated food) showed significant amounts of SCN^- in tissues but no pathology that was not linked to their advanced age. Specifically, the thyroid was one of the organs studied histologically. Hardy et al. (1950) [2-0175] had suggested goiter in chronically CN^- exposed humans was due to SCN^- toxicity.

2-0175 Hardy, H. L., W. M. Jeffries, M. M. Wasserman, and W. R. Wadell, 1950. Thiocyanate Effect Following Industrial Cyanide Exposure. Report of Two Cases. New England J. Med. 242:968-972.

B-7. Two case studies are presented, and other so-called chronic cyanide poisoning studies are reviewed. Many of the symptoms ascribed to chronic cyanide poisoning may be due to the toxicity of its metabolic product thiocyanate. Both of the cases described exhibited goiter, presumably due to the mimicking of iodide by thiocyanate. Heavy smoking and eating of cabbage-related vegetables may exacerbate the symptoms of occupational cyanide exposure due to additional formation of thiocyanate.

2-0072 Haroz, R. K., and L. Mattenberger-Kreber. 1977. Fassett, 1963 [2-0132]. Effect of Cigarette Smoke on Macrophage Phagocytosis. Energy Research and Development Administration Symp. Ser. 43 (Pulmonary Macrophage Epithelial Cells):36-57.

D--. The decrease in immunity was not adequately related to HCN.

2-0139 Haymaker, W., A. M. Ginzler, and R. L. Ferguson. 1952. Residual Neuropathological Effects of Cyanide Poisoning. A Study of the Central Nervous System of 23 Dogs Exposed to Cyanide Compounds. Mil. Surg. 111:231-246.

D-7. Two of five dogs exposed for 1.75-2.0 min to 590 to 700 ppm HCN survived 24 and 28 h (until sacrificed), whereas the other 3 died within 16-20 h. Another dog, exposed to 165 ppm HCN for 10 min survived 26 h until sacrificed. All were rendered comatose and apneic.

2-0140 Henderson, Y., and H. Haggard. 1943. In: Noxious Gases and the Principles of Respiration Influencing Their Action, ed. 2, No. 35, ACS Monograph Series. Reinhold Publishing Corporation, New York, New York. pp. 172-176.

C--. Old review with commonly given human dose-response data. The rapidly fatal dose is in error, being > 10-fold higher than the 270 ppm value or 0.3 mg/L value given by Flury and Zernik (1931) [2-0133].

2-0028 Higgins, E. A., V. Fiorica, A. A. Thomas, and H. V. Davis. 1971. Acute Toxicity of Brief Exposures to Hydrogen Fluoride, Hydrogen Chloride, Nitrogen Dioxide and Hydrogen Cyanide Singly and in Combination with Carbon Monoxide. AD-735 160. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 9 pp.

C-12. LC_{50} for HCN and HCN plus toxic dose of CO. Good data but only 5-min. exposure.

2-0095 Higgins, E. A., V. Fiorica, A. A. Thomas, and H. V. Davis. 1972. Acute Toxicity of Brief Exposures to Hydrogen Fluoride, Hydrogen Chloride, Nitrogen Dioxide, and Hydrogen Cyanide with and without Carbon Monoxide. Fire Technol. 8:120-130.

C-12. Lethality studies of rats and mice exposed to HCN and HCN plus CO. Data duplicated in Higgins et al. (1971) [2-0028].

2-0041 Hilado, G. J., and H. J. Cumming. 1978. Short-term LC_{50} Values: An Update on Available Information. Fire Technol. 14:46-50.

D--. Review of 4 lethality studies in mice and rats. Values taken from a curve representing LC_{50} values for 250-g rats showed that at ~ 5 min the LC_{50} was ~ 500 ppm; at 10 min, ~ 350 ppm; at 20 min, ~ 210 ppm; at 30 min, ~ 180 ppm; and at 60 min, ~ 140 ppm. Note that Barcroft (1931) had reported that 100 ppm was a level that rats could "breathe indefinitely."

2-0096 Hoffmann, L. D., and E. L. Wynder. 1972. Smoke of Cigarettes and Little Cigars: An Analytical Comparison. Science. 178: 1197-1199.

C--. The HCN content of single puffs of cigarettes and little cigars was 36.1 to 88.7 μg.

2-0043 Hoffmann, D., L. D. Sanghvi, and E. L. Wynder. 1974. Comparative Chemical Analysis of Indian Bidi and American Cigarette Smoke. Int. J. Cancer. 14:49-53.

C--. Cigarettes (200) of a U.S. non-filtered brand purchased in 1973 contained 445 and 240 μg HCN when smoked mechanically at the rates of 2 and 1 puff/min, respectively.

2-0031 Hollett, B. A. 1976. Health Hazard Evaluation Determination. Report Number 75-182-334, New England Foundry, Lawrence, Massachusetts. PB-273 778, National Technical Information Service, U.S. Dept. of Commerce, Springfield, Virginia. 25 pp.

C--. Core makers exhibited respiratory problems due more probably to SiO_2 than to HCN, whose concentrations were well within accepted exposure limits.

2-0074 Hugod, C. 1979. 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. 44:13-23.

C-11. Rabbits were exposed for 1-4 wk in an interaction study at low levels; only morphological effects sought; none found, which limits usefulness. Same design with more data, especially physiological, would be very useful.

2-0119 Hugod, C., and P. Astrup. 1980. Exposure of Rabbits to Carbon Monoxide and Other Gas Phase Constituents of Tobacco Smoke. Influence on Coronary - and Aortic Intimal Morphology. MMW, Muench. Med. Wochenschr. 122:18-24.

C-11. Identical experiments for HCN were reported by Hugod (1979).

2-0044 Hugod, C., L. H. Hawkins, and P. Astrup. 1978. Exposure of Passive Smokers to Tobacco Smoke Constituents. Int. Arch. Occup. Environ. Health. 42:21-29.

D--. People were exposed to $\leq$ 0.014 mg HCN/m^3 from sidestream cigarette smoke for up to 2.5 h. Authors have attempted to quantitate "annoyance"; no control on cigarette type. They concluded that a passive smoker would require 50 h to inhale as much HCN as an active smoker would from inhaling the mainstream smoke of one cigarette.

02-0142 Jandorf, B. J., and O. Bodansky. 1946. Therapeutic and Prophylactic Effect of Methemoglobinemia in Inhalation Poisoning by Hydrogen Cyanide and Cyanogen Chloride. J. Ind. Hyg. Toxicol. 28:125-132.

D-10. Dogs were exposed to lethal concentrations (500 to 2,200 ppm) of HCN without an antidote. The protective action of methemoglobin was not so marked for HCN poisoning as for CNCl inhalation.

2-0165 Jaroschka, R., and R. Kropp. 1966. Chronische Cyanidvergiftung [Chronic Cyanide Poisoning]. Int. Arch. Gewerbepath. u. Gewerbehyg. 22:202-207.

C--. One case history of exposure to KCN, trichloroethylene, H_2SO_4, HCl, HNO_3, bleaching lye, and caustic soda. No concentrations were given. Extensive description of his blood chemistry and EKG. The victim must have had a toxic hepatosis.

2-0099 Jouglard, J., G. Fagot, B. Deguigne, and J. A. Arlaud. 1971. Acute Hydrogen Cyanide Poisoning and Its Emergency Treatment. Mars. Med. pp. 571-575.

C-7. The accidental inhalation exposures of 5 humans to HCN are described, but the symptoms are discussed with those for cyanide salts.

2-0019 Ju'zwiak, I., B. Pollak-Korkus, J. Bugajska, M. Menzel-Lipi'nska, H. Go'zdzik, J. Suchowiak, W. Pelc, Z. Kaplicka, B. Rybacka, Z. Pruszy'nska, and A. Gruszka. 1979. Badania nad Zagrozeniem Zawodowym Cyjanowodorem Pracownikow Galwanizerni Przemyslowych [Occupational Exposure to Hydrogen Cyanide in Workers of Industrial Galvanizing Workshops]. Pol. Tyg. Lek. 34(9):337-340.

B-8. Electroplaters exposed to HCN had a different health profile than the control group: HCN-exposed women had no circulatory system pathologies reported, but had neurosis (CNS symptoms) as frequently as controls. HCN-exposed men, on the other hand, had circulatory problems as frequently as controls but none of the neurotic symptoms that were seen in control males.

2-0100 Kensler, C. J., and S. P. Battista. 1966. Chemical and Physical Factors Affecting Mammalian Ciliary Activity. Am. Rev. Resp. Dis. 93:93-102.

B-9. Ciliary activity in rabbit trachea was inhibited to 50% that of the controls when exposed to 200 mg HCN/m^3 for 18 s.

5-367 Kettner, H. 1978. Indoor Contamination by Chemical Substances of Daily Use and Their Hygienic Significance. In: Org. Verunreig. Umwelt: Erkennen, Bewerten, Vermidern, K. Aurand, V. Hasselbarth, E. Lahmann, G. Muller, and W. Niemitz, eds. Erich Schmidt Verlag, Berlin, Germany. pp. 448-453 (Ger).

C--. Maximum allowable indoor air in the USSR:

Acrolein	0.1 mg/m^3
NH_3	0.2
HCN	0.002
HCHO	0.01
MeOH	0.5

2-0018 Kiryakov, K., T. S. Vodichenska, V. Markovska, and E. Tsutsulova. 1978. Contamination of the Atmospheric Air and Morbidity with Temporary Loss of Working Capacity Among Agrarian Workers. Khig. Zdraveopaz. 21:42-48.

C-5. Bulgarian article. Workers were exposed to H_2S, phenol, and HCN. The details that were understandable to a reader facile in Russian are given in Table IV-2. Multiple factors besides air quality could contribute to the variation in "sickness duration" observed. Job comparability between groups is not given.

2-0047 Kishitani, K., and K. Nakamura. 1974. Toxicities of Combustion Products. J. Fire Flammability/Combust. Toxicol. Suppl. 1:104-123.

D-12. Mice were exposed to lethal concentrations of mixed combustion products in almost all tests. However, the mice survived $\geq$ 1 week in fresh air after the tests when the HCN concentrations were 9 to 60 ppm and the CO concentrations were low. In some tests at > 100 ppm HCN, the mice survived; yet in others, where the combustion constituents were nearly the same, they died.

2-0024 Kondrashov, Y. A. 1978. O Sootnosheniyakh Opasnosti Otravleniya Parami i Gazami Toksicheskikh Veshchestv pri Kozhnom i Ingalyatsionnom Putyakh Vozdeistviya [Relative Hazards of Poisoning with Fumes and Gases of Toxic Substances with Their Dermal and Inhalation Routes of Action]. Gig. Tr. Prof. Zabol. No. 2:34-38.

D-2. The LC_{50} for rats by inhalation of HCN is ~ 200 mg/m^3 compared to ~ 22,000 mg/m^3 by skin absorption.

2-0173 Koopman [no initial]. 1936. Beitrag zur Frage der chronichen Blausävievergiftung [On the Question of Chronic Cyanide Poisoning]. Deut. Z. ges. gerichtl. Med. 36:382-384.

D-6. Complaints of employees that had been in contact for years with the rooms that had been used for disinfection with cyanide are enumerated. They included eye itching and watering, headache, light coughing, and various gastrointestinal symptoms. The conclusions are broad and sweeping without the data base that is expected in current studies. No HCN concentrations are given.

2-0145 Lazarev, N. V. 1956. [Harmful Substances in Industry-Part II - Inorganic and Organometallic Compounds]. State Technical Publishings, Warsaw, 1956, pp. 224-235; copyrighted English translation by the National Institute for Occupational Safety and Health, Rockville, Maryland.

C--. Review duplicated in 1971.

2-0144 Lazarev, N. V. 1971. Toxic Substances in Industry. Inorganic and Elementary Compounds. A Manual for Chemists, Engineers and Physicians. ed. 6. Khimiya, Leningrad, pp. 228-240; copyrighted English translation provided by the National Institute for Occupational Safety and Health, Rockville, Maryland.

C--. Review. Duplicates information in Lazarev (1956).

2-0146 Lehmann, K. B. 1903. Ueber die Giftigkeit der gasförmigen Blausäure und des Phosphorwasserstoffs mit Demonstration [About the Toxicity of Gaseous HCN and Hydrogen Phosphide with a Demonstration]. Klin. Wochensch. 40:918-919; copyrighted English translation provided by the National Institute of Occupational Safety and Health, Rockville, Maryland.

B-3. Cats tolerated 30-40 ppm HCN for 4-5 h, but more severe symptoms appeared at higher concentrations.

2-0080 Leuchtenberger, C., R. Leuchtenberger, I. Zbinden, and E. Schleh. 1976. Significance of Oxides of Nitrogen and Sulfhydryl Reactive Components in Pulmonary Carcinogenesis. An Experimental Study Related to Tobacco Smoke. Colloq. Inst. Natl. Sante Rech. Med. 52(Environ. Pollut. Carcinog. Risks):73-79.

C-14. A good paper; a valuable assay for lab. workers. Not useful for identifying a level of concern for HCN in automobile emissions.

2-0048 Levine, M. S., and E. P. Radford. 1978. Occupational Exposures to Cyanide in Baltimore Fire Fighters. J. Occup. Med. 20:53-56.

A-10. Exposure to a fire atmosphere was correlated with a significant increase in mean serum thiocyanate levels over controls in each smoking category. The population studied was quite small after stratification on smoking. There was a lack of age correspondence with controls. The blood thiocyanate levels could not be correlated with the exposure composition (materials burned in fire), symptoms in firefighters (undescribed), or mask use (safety protection). The authors hypothesized that there are some individual differences in response, which sounded theoretical and unbased but possible.

2-0149 Levine, S., and W. Stypulkowski. 1959. Experimental Cyanide Encephalopathy. Arch. Pathol. 67:306-323.

D-10. Rats were exposed to lethal and near-lethal concentrations and the brain histopathology was described.

2-0148 Levine, S., and B. Weinstein. 1959. Neurotoxicity of Hydrogen Cyanide. J. Am. Pharm. Assoc. 48:224-226.

D-7. Rats were exposed to near-lethal and lethal concentrations of HCN. The concentrations were varied according to the condition of the animal so as to produce a high incidence of brain lesions.

2-0102 Levine, S., A. Hirano, and H. M. Zimmerman. 1967. Experimental Cyanide Encephalopathy: Electron Microscopic Observations of Early Lesions in White Matter. J. Neuropath. Exp. Neurol. 26:172-174.

D-2. Rats were acutely exposed to unknown HCN concentrations.

2-0009 Lutsenko, L. A. 1970. Voprosy Gigieny Truda pri Obagashchenii Sul'fidnykh Mednykh Rud na Fabrikakh Urala [Industrial Hygiene in the Concentration of Sulfide Copper Ores at Mills in the Urals]. Gig. Tr. Prof. Zabol. 14:11-15.

D--. Workers were exposed to numerous agents including HCN, CS_2, H_2S, noise, vibration, and low temperature as well as the ore dusts containing free silica [and probably numerous accessory elements in the ore minerals].

2-0027 MacEwen, J. D., and E. H. Vernot. 1971. Toxic Hazards Research Unit Annual Technical Report. AD 734543. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 102 pp.

C-10. Acute toxicity (mortality) study of rats and mice exposed to high levels of HCN alone and combined with CO.

2-0150 Maehly, A. C., and A. Swensson. 1970. Cyanide and Thiocyanate Levels in Blood and Urine of Workers with Low-Grade Exposure to Cyanide. Int. Arch. Arbeitsmed. 27:195-209.

C-12. "Total" SCN^- in urine of 13 exposed workers (including five nonsmokers) averaged 20.0-23.0 mg/L when the HCN levels were 3.8-5.1 ppm. Concentrations of free CN^- or SCN^- in the urine vary and cannot be used for detecting undue chronic exposure to workplace cyanide. Average urinary thiocyanate values in nonsmokers not exposed in the workplace were 1.1-3.8 mg/L and were 3.1-6.5 mg/L in nonexposed smokers.

2-0167 Mattina, C. F., Jr. 1972. Potentiometric Method for the Determination of Hydrogen Cyanide and Hydrogen Sulfide in Cigarette Smoke. Tob. Sci. 16:113-114.

C--. Nonfilter cigarettes were consumed by a smoking apparatus in 32 puffs. Each puff contained 4.3 µg H_2S and 35 µg HCN. [If this is drawn into the lungs with ~ 0.7 L air/puff, the resultant HCN concentration in the lungs would be ~ 50 mg/m^3 (which exceeds the 1979 TLV for HCN).]

2-0152 McNamara, B. P. 1976. Estimates of the Toxicity of Hydrocyanic Vapors in Man. ADA 028501. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 25 pp.

A--. Good review of old animal and human data as regards human exposure. Estimated 1-min LC_{50} of 3,404 ppm.

2-0151 Merzbach, G. 1899. Ueber einen Fall von gewerblicher chronischer Blausäurevergiftung [On a Case of Chronic Industrial Hydrocyanic Acid Intoxication]. Beil. Hyg. Rundsch. 9:45-56.

D--. The patient, an electroplater, was chronically exposed not only to HCN fumes but also to a AgCN-KCN solution. From the description of his ash-gray colored face with a bronze-colored luster, he might have suffered from argyria.

2-0049 Mohler, S. R. 1975. Air Crash Survival: Injuries and Evacuation Toxic Hazards. Aviat. Space Environ. Med. 46:86-88.

C--. The importance here is the author's conclusions that HCN is dangerous as a combustion product in a large fire - say on an airplane. At ~ 5 μg CN^-/ml blood, death occurs in mammals. Incapacitation occurs at about half that level.

2-0154 Moss, R. H., C. F. Jackson, and J. Seiberlich. 1951. Toxicity of Carbon Monoxide and Hydrogen Cyanide Gas Mixtures--a Preliminary Report. Arch. Ind. Hyg. Occup. Med. 4:53-64.

D-6. Interaction study of combustion products in rats; superceded by later work.

2-0114 Myers, W. G., J. F. Lamb, R. W. James, and H. S. Winchell. 1973. ^{11}C Distribution in Dogs Visualized after Intravenous ^{11}C-Cyanide in High Specific Activity. Nucl. Med. 12(2):154-162.

D--. High ^{11}C uptake by some organs (heart, fundus of stomach, kidneys, and parotid glands) may be due to complex formation between HCN and ferricytochrome oxidase.

6-124 Newsome, J. R., V. Norman, and V. L. Zaratzian. 1965. Vapor Phase Analysis of Cigarette Smoke. Tob. Sci. 9:102-110; or Tobacco 161(4): 24-32.

D--. Levels in tobacco smoke (μg/40 ml puff):

	Unfiltered	Filtered
methanol	13	10
HCHO	4.1	3.6
acrolein	8.2	7.9
HCN	32	29
H_2S	3.4	3.1
NH_3	12	13

2-0026 Nishimaru, Y., M. Shimada, and Y. Tsuda. 1973. Experimental Examination on the Case of Inhaled Hydrogen Cyanide Gas. Yokohama Igaku. 24:1-8.

D-5. Time-lethality study at very high levels. Rats more resistant than rabbits. Not all of the rabbits were killed after 30 min at $\leq$ 80 ppm HCN, but ~ 150 ppm HCN killed all the rabbits within 3-5 min. Rats required 30 to 50 min. to expire from < 500 to 700 ppm HCN. [Comments based only on English summary.]

2-0109 Owsianowski, M. 1975. Cholesterol Metabolism in the Rat Brain During Experimental Cyanide Encephalopathy. Neuropatol. Pol. 13:423-431.

D-10. Rats were dosed to unconsciousness. About 30% died within 24 h of intoxication. No HCN concentration was given.

2-0030 Paabo, M., B. Pitt, M. M. Birky, A. W. Coats, and S. E. Alderson. 1976. Measurements and Observations of the Toxicological Hazard of Fire in a Metrorail Interior Mock-up. PB-250768. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 20 pp.

D--. Acute exposures of rats to combustion products (HCl, CO, CO_2, HCN) from a full-scale mock-up.

2-0155 Parmenter, D.C. 1926. Observations on Mild Cyanide Poisoning: Report of a Case. J. Ind. Hyg. 8:280-282.

B--. A case report showed individual human hypersensitivity. Indicating an industrial standard applicable to the general case may not always apply in individual situations.

2-0050 Pryor, A. J., D. E. Johnson, and N. N. Jackson. 1975. Hazards of Smoke and Toxic Gases Produced in Urban Fires. Combust. Toxicol. 2:64-112.

B-13. Mixed combustion products and HCN alone - good interaction study. Good effort at separation and interaction of variables - see Table 21 and 23.

2-0157 Radojicic, B. 1973. [Determining Thiocyanate in Urine of Workers Exposed to Cyanides.] Arh. Hig. Rada 24:227-232; copyrighted English translation provided by the National Institute for Occupational Health Science, Rockville, Maryland.

B-9. Smokers and long-time cyanide workers eliminated more thiocyanates (CNS) in their urine. The test was valuable for quantitating chronic exposure if the smoking history was also known.

2-180 Rickert, W. S., and J. C. Robinson. 1981. Estimating the Hazards of Less Hazardous Cigarettes. II. Study of Cigarette Yields of Nicotine, Carbon Monoxide, and Hydrogen Cyanide in Relation to Levels of Cotinine, Carboxyhemoglobin, and Thiocyanate in Smokers. J. Toxicol. Environ. Health 7(3-4):391-403.

C--. Study calculated that a person smoking < 10 cigarettes/d is exposed to ~ 1.4 mg HCN/d; 17.5-22.5 cigarettes, ~ 3.2 mg HCN/d; and smoking > 37.5 cigarettes resulted in exposure to ~ 8.4 mg HCN/d. In small groups of smokers studied no significant difference was found in blood thiocyanate level of those smoking high HCN cigarettes versus those smoking low HCN cigarettes.

6-036 Rickert, W. S., J. C. Robinson, and J. C. Young. 1980. Estimating the Hazards of "Less Hazardous" Cigarettes. 1. Tar, Nicotine, Carbon Monoxide, Acrolein, Hydrogen Cyanide, and Total Aldehyde Deliveries of Canadian Cigarettes. J. Toxicol. Environ. Health 6(2):351-366.

C--. Canadian cigarettes (102 brands purchased in March and April 1978) smoked usually to a 30-mm butt length contained 4-269 μg HCN/cigarette and 3-85 μg acrolein per cigarette. Average values were 168 and 65 μg, respectively, or 432 and 78 ppm [it is not clear how these latter values were derived; presumably the alveolar concentrations were meant]. Smoking 20 cigarettes per day would give 4 and 68% of the total exposure in the workplace for an 8-h day at the OSHA limits.

2-0051 Rylander, R. 1973. Toxicity of Cigarette Smoke Components: Free Lung Cell Response in Acute Exposures. Am. Rev. Respir. Dis. 108:1279-1282.

D-5. Guinea pigs were acutely exposed to HCN in mixed combustion products from 5 cigarettes containing 60-260 μg HCN/cigarette. The numbers of free macrophages and leukocytes in the lungs after exposure to the smoke from unfiltered cigarettes were inversely correlated to HCN and other smoke components except NO.

2-0081 Sakai, T., and A. Okukubo. 1979. Application of a Test for Estimating the Relative Toxicity of Thermal Decomposition Products. Fire Retardants: Proc. 1st Eur. Conf. Flammability and Fire Retardants, Belgium, 1977. pp. 147-153.

D-6. Lethality study with mice of mixed combustion products.

2-0159 Sato, T., T. Fukyama, and M. Yamada. 1955. The Allowable Concentration of Hydrogen Cyanide in Air. Bull. Inst. Public Health (Tokyo) 4(4):3-5; copyrighted translation provided by the National Institute for Occupational Safety and Health, Rockville, Maryland.

B-10. Very good; the paper would have been excellent had it contained more data on gas concentrations. Sublethal effects were studied in mice exposed to HCN at and near the TLV.

2-0052 Schmeltz, I., D. Hoffmann, and E. L. Wynder. 1974. Toxic and Tumorigenic Agents in Tobacco Smoke: Analytical Methods and Modes of Origin. Proc. Univ. Mo. Annu. Conf. Trace Subst. Environ. Health 8:281-295.

C--. A U.S. nonfilter cigarette contained 240 μg HCN/cigarette in the gas phase of the smoke and 74 μg/cigarette in the particulate phase.

2-0160 Smith, A. R., 1932. Cyanide Poisoning. N.Y. Dept. Labor Ind. Bull. 11:169-170.

D--. Symptoms of poisoning by exposure primarily to cyanide salts are reviewed with a few case histories.

2-0115 Smith, L., H. Kruszyna, and R. P. Smith. 1977. The Effect of Methemoglobin on the Inhibition of Cytochrome Oxidase by Cyanide, Sulfide or Azide. Biochem. Pharmacol. 26:2247-2250.

D-6. Azide and sulfide are more toxic cellularly in vitro than cyanide on cytochrome c oxidase system.

2-0078 Smith, P. W., C. R. Crane, D. C. Sanders, J. K. Abbott, and B. Endecott. 1976. Effects of Exposure to Carbon Monoxide and Hydrogen Cyanide. Nat. Academy Sciences, Nat. Res. Council, Comm. Sociotech., Comm. Fire Res., eds. Physiological and Toxicological Aspects of Combustion Products: Int. Symp., Utah. 1974. pp. 75-88.

D-12. Lethality study of rats exposed to HCN and HCN plus CO. Times to physical incapacitation at lethal concentrations were also recorded.

2-0084 Spurgeon, J. C. 1978. The Correlation of Animal Response Data with the Yields of Selected Thermal Decomposition Products for Typical Aircraft Interior Materials. AD-A062938, Iss. FAA-NA-78-45, FAA-RD-78-131. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 40 pp.

C-12. LD_{50} of mixed combustion products. Sixteen percent of the lethal HCN dose produced incapacitation of a 200 g rat in 5 min. The calculated incapacitating concentration was 193 ppm HCN.

2-0053 Swinyard, E. A. 1975. Noxious Gases and Vapors. Carbon Monoxide, Hydrocyanic Acid, Benzene, Gasoline, Kerosene, Carbon Tetrachloride, and Miscellaneous Organic Solvents. In: The Pharmacological Basis of Therapeutics. L. S. Goodman and A. Gilman, eds. MacMillan Publishing Co., New York, New York. pp. 900-911.

C--. Brief review of HCN metabolism and therapy covers the same material that Fassett (1963) did.

2-0177 Towill, L. E., J. S. Drury, B. L. Whitfield, E. B. Lewis, E. L. Galyan, and A. S. Hammons. 1978. Reviews of the Environmental Effects of Pollutants. PB-289-920. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia.

C--. Review of effects of HCN, metal cyanides, and organic nitriles.

2-0161 Trautman, J. A. 1933. Methylene Blue in the Treatment of HCN Gas Poisoning. Public Health Rep. 48:1443-1447.

D-10. Guinea pigs, rats, and rabbits were exposed to lethal concentrations of HCN. Methylene blue injections were of no value as on antidote.

2-0015 Truhaut, R., C. Boudène, and J. M. Jouany. 1975. Etude de la toxicité aiguë, par voie aérienne, des toxique majeurs pouvant être libérés lors d'incendies [Toxicity of Combustion and Pyrolysis of Materials Used in Construction. I. Acute Toxicity by Pulmonary Route of Major Toxicants Released During Fires]. Arch. Mal. Prof. Med. Trav. Secur. Soc. 36:707-738.

C-6. Elaborate interaction study; mostly dose-lethality studies on rabbits and rats.

2-0169 Ubisch, H. von. 1968. The Assessment of Environmental Hazards from Large-Scale Storage of Hydrogen Cyanide. Nord. Hyg. Tidskr. 49(1):31-35.

Not rated. Experiments showed the rate of evaporation of HCN from simulated spills. Health effects were not considered.

5-425 Urban, C. M., and R. J. Garbe. 1980. Exhaust emissions from malfunctioning three-way catalyst-equipped automobiles. SAE Tech. Pap. Ser. 800511. 11 pp.

C--. Maximum emission rates (mg/m^3) in 4 malfunctioning, 3-way catalyst-equipped automobiles:

NH_3	254
CN^-	67
H_2S	8
HCHO	3

3-094 U.S.S.R. State Committee of the Council of Ministers for Construction. 1972. Sanitary Norms for Industrial Enterprise Design. Izdatel'stvo Literatury po Stroitel'stvu [Publishing House of Literature on Construction]. Moscow. 96 pp.

C--. In the USSR, the MAC for HCN in workplaces was 0.3 mg/m^3, and 0.01 mg/m^3 as the average limit in populated places.

2-0162 Valade, P. 1952. Lésions du système nerveux central dans les intoxications chroniques experimentals par l'acide cyanhydrique gazeux [Injuries to the Central Nervous System in Chronic Experimental Poisoning by Hydrocyanic Acid Gas]. Bull. Acad. Natl. Med. Paris. 136:280-285.

D-8. Five of 17 dogs died after repeated short exposures to 50 ppm HCN. The morphology of the vascular and nervous systems was described. There were no controls.

2-0056 Vernot, E. H., J. D. MacEwen, C. C. Haun, and E. R. Kinkead. 1977. Acute Toxicity and Skin Corrosion Data for Some Organic and Inorganic Compounds and Aqueous Solutions. Toxicol. Appl. Pharmacol. 42:417-423.

D-11. The inhalation 1-h LC_{50} for male rats was 484 ppm HCN. The 5-min LC_{50} for male mice was 323 ppm.

2-0057 Vettorazzi, F. G. 1977. State of the Art of the Toxicological Evaluation Carried Out by the Joint FAO/WHO Expert Committee on Pesticide Residues. III. Miscellaneous Pesticides Used in Agriculture and Public Health. Residue Rev. 66:137-184.

D--. Review. No-effect level for man of oral HCN is 0.05 mg/kg or 3.5 mg/day for 70-kg Reference Man.

2-0170 Vickroy, D. G., and G. L. Gaunt, Jr. 1972. Determination of Cyanide in Cigarette Smoke by a Cyanide Ion-Selective Electrode. Tob. Sci. 16:22-25.

C--. An average 306 μg CN^- was determined in each standard domestic brand cigarette by analyzing the smoke.

2-0059 Wagner, R. P., C. H. Haddox, R. Fuerst, and W. S. Stone. 1950. The Effect of Irradiated Medium, Cyanide, and Peroxide on the Mutation Rate in Neurospora. Genetics. 35:237-248.

D-6. Treating the conidia of Neurospora crassa with a nutrient broth that had been pre-irradiated by ultraviolet light produced biochemical mutations at a rate significantly higher than the control rate. Biochemical mutations were also produced at a higher rate by treating with KCN or H_2O_2. The mutation rates induced by these treatments were not much different from each other but were significantly lower than the rate induced by direct ultraviolet irradiation.

2-0163 Walton, D. C., and M. G. Witherspoon. 1926. Skin Absorption of Certain Gases. J. Pharmacol. Exp. Ther. 26:315-324.

D-8. The skin of individual dogs was exposed to very high concentrations of HCN (5,500-16,900 ppm). Some died; some survived, showing no symptoms or facial twitching during the test.

2-0113 Wender, M., A. Piechowski, and A. Wajgt. 1974. The Activity of Arylsulphatases in Experimental Cyanide Encephalopathy. Exp. Pathol. (Jena). 9:122-124.

D-11. The effect of cyanide on sulfatase activity appears not to be a decisive factor in demyelination resulting from experimental cyanide encephalopathy in rats. The HCN concentrations inhaled were not given.

2-0117 Wender, M., J. Stanislawska, and H. Filipek-Wender. 1978. Cerebral Cholesteryl Esters in Cyanide Encephalopathy. Neuropatol. Pol. 16:163-172.

D-11. Encelphalopathy was induced in rats by unknown HCN concentrations.

2-0060 Wills, J. H., F. L. Mitchell, and B. J. Vos. 1976. Criteria for a Recommended Standard. Occupational Exposure to Hydrogen Cyanide, and Cyanide Salts (NaCN, KCN, and $Ca(CN)_2$). U.S. Dept. of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio. Vol. 77-108. 191 pp.

No rating. Bibliography used for source of documents.

2-0017 Yamamoto, K. 1976a. Acute Combined Effects of HCN and CO, with the Use of the Combustion Products from PAN (Polyacrylonitrile)-Gauze Mixtures. Z. Rechtsmed. 78:303-312.

D-11. Interaction of HCN and CO was studied in rats and mice, mostly at maximum concentrations of HCN > 200 ppm. In one test, all nine mice survived when a maximum concentration of 37 ppm was attained within 18 min.

2-0070 Yamamoto, K. 1976b. Acute Combined Effects of Hydrogen Cyanide and Carbon Monoxide, with Special Reference to a Theoretical Consideration of Acute Combined Effects on the Basis of the Blood Cyanide and Carbon Monoxide-Hb Analyses. Nippon Hoigaku Zasshi. 30:401-406; Chem. Abstr. 1977. 87:79238 m.

D--. This Japanese interaction study was not rated in detail. Rats were acutely exposed to HCN and CO in combustion products. The HCN concentration was not given. Blood cyanide in the rats dying from the exposure was 3.14 to 3.70 μg/ml.

2-0013 Yamamoto, K., and Y. Yamamoto. 1971. Toxicity of Gases Released by Polyurethane Foams Subjected to Sufficiently High Temperature. Nippon Hoigaku Zasshi. 25:303-314.

C-12. Studies of acute inhalation exposures of rats to mixed combustion products and HCN alone. HCN seems to be the most toxic component of the mix because thiosulfate predosing protected. One dose - death curve for HCN.

2-0014 Yamamoto, K., and Y. Yamamoto. 1978. On the Acute Toxicities of the Combustion Products of Various Fibers, with Special Reference to Blood Cyanide and P_{O_2} Values. Z. Rechtsmed. 81:173-179.

C-9. Dose-lethality for rabbits and HCN and mixed combustion products, with some blood CN^- measures.

2-0025 Zotova, L. V. 1975. Working Conditions in the Production of Acrylonitrile and Their Influence on the Workers. Gig. Tr. Prof. Zabol. No. 8:8-11; copyrighted English translation provided by the National Institute for Occupational Safety and Health, Rockville, Maryland.

C-8. Workers were exposed to vapors of acrylonitrile and HCN as well as to acrylonitrile absorbed via the skin.

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(Please read Instructions on the reverse before completing)

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16. ABSTRACT

Health effects literature primarily related to inhalation exposures to hydrogen cyanide was collected, evaluated, tabulated and summarized. Approximately 170 documents were collected from computerized and manual literature searches covering the period 1899-1981. Pharmacologists and an M.D. epidemiologist rated the documents according to their applicability to the study and their methodology. The approximately 20 documents considered useful for deriving a range of concern for human exposure to hydrogen cyanide from automotive emissions were tabulated. The 25 pages of tables detail the results of acute and repeated dose testing of mice, rats, guinea pigs, rabbits, cats, monkeys, dogs, goats, donkeys and humans as well as human occupational studies. Most of the documents evaluated are described in an annotated bibliography.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS		b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
Toxicity	Toxic Tolerances	Inhalation Health Effects	06 T
Hydrogen cyanide	Occupational diseases		
Cyanides			
Mammals	Respiratory system		
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