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CYANIDE POISONING AND ITS TREATMENT.*[,1,2]

BY K. K. CHEN, CHARLES L. ROSE AND G. H. A. CLOWES.

MORTALITY STATISTICS.

Cyanide poisoning is less frequent than mercury or strychnine poisoning, although during recent years the death rate from cyanide poisoning has been increasing. In Table I it will be seen that in the United States Registration Area there were 134 deaths from cyanide poisoning in 1930, and 243, 408 and 416 in 1931,

TABLE I.—MORTALITY STATISTICS FROM CYANIDE POISONING.**

Locality.	Population (1930 Census).	Total Number of Deaths. 1922.	1923.	1926.	1927.	1928.	1929.	1930.	1931.	1932.	1933.	1934.
U. S. Registration Area	122,775,046	102	113	79	84	108	141	134	243	408	416	..*
New York City	6,930,446	...*	...*	14	11	23	21	34	16	42	35	27
Chicago	3,376,438	...*	...*	3	8	14	4	12	16	25	17	6
Philadelphia	1,950,961	...*	...*	2	2	1	3	0	3	4	3	..*
Detroit	1,568,662	...*	...*	2	0	6	2	7	5	15	11	5
Los Angeles	1,238,048	...*	...*	12	14	19	14	18	23	34	33	25
Cleveland	900,429	...*	...*	1	0	3	2	0	1	4	6	1
Saint Louis	821,960	...*	...*	6	2	6	2	7	9	8	6	2
Baltimore	804,874	...*	...*	1	2	1	5	3	2	5	1	1
Boston	781,188	...*	...*	0	6	2	0	3	8	7	3	8
Pittsburgh	669,817	...*	...*	1	1	2	1	2	5	3	1	1
San Francisco	634,394	...*	...*	9	9	8	10	11	12	21	22	23

* Data not available.

** In the compilation of this Table, we were greatly assisted by Dr. T. F. Murphy, Chief Statistician for Vital Statistics, Bureau of Census, Department of Commerce, Washington, who generously turned over to us all the data which he has collected with meticulous care. Our indebtedness must also be acknowledged to Doctors J. C. Geiger, Director of the Department of Public Health, City and County of San Francisco; Herman N. Bundesen, President of the Board

* This article is based on a scientific exhibit held at the joint meeting of the American Medical Association and the Canadian Medical Association, Atlantic City, June 10–14, 1935.

[1] From the Lilly Research Laboratories, Indianapolis.

[2] Scientific Section, A. PH. A., Portland meeting, 1935.

of Health, City of Chicago; W. Thurber Fales, Director of the Bureau of Vital Statistics, Health Department, City of Baltimore; Thomas J. Duffield, Registrar of Records, Department of Health, City of New York; G. Arthur Blakeslee, Director of the Bureau of Vital Statistics, Department of Health, City of Detroit; Joseph W. Monahan, Deputy Commissioner, Health Department, City of Boston, and to health officers of other cities, for their assistance in giving us the figures for 1934. The figures for New York City as given by Dr. Murphy are uniformly lower than those recorded in the office of the Chief Medical Examiner of the City of New York as reported by Gettler and St. George (14).

1932 and 1933, respectively. There was a similar increase in most large cities during the same period. Whether or not it was due to the economic depression is a matter for speculation. The mortality rate from cyanide poisoning in urban areas does not appear always to depend upon the size of the population. For example, San Francisco with a population of 634,394 (1930 census) has a total number of deaths comparable to that of Chicago, the population of which is 3,376,438. Similarly, Los Angeles has a relatively high death rate from the same cause.

SOURCES OF CYANIDE POISONING.

1. Suicidal	
2. Occupational	Fumigation of ships and houses to kill vermin Photography Electroplating Gilding Metallurgy
3. Accidental	Cyanide compounds Bitter almonds (*Amygdalus communis*) Arrow grass (*Triglochin maritima*) Chokecherry (*Prunus virginiana*) Certain mushrooms (*Marasmus*, *Clitocybe*).
4. Homicidal	

In general, over 90 per cent of the cases of cyanide poisoning are suicidal in nature. Owing to the rigid precautionary measures, death seldom occurs in those places where large quantities of cyanides are handled daily, such as the gold or iron mines, cyanide factories, etc.

In the western states, there are several cyanogenetic plants, chiefly the arrow grass and the chokecherry, which have caused annually heavy losses of live stock. The following interesting account given by Professor B. T. Simms, Oregon State Agricultural College, Corvallis, in a private communication to the authors may be cited:

"You might be interested to know that this type of poisoning (cyanide) has caused rather serious losses in live stock here in Oregon. The common chokecherry has perhaps been the offending plant in the majority of cases. One rancher lost 171 sheep during one night last summer from this plant. Records show that more than 1500 sheep have died in that one area from chokecherry poisoning during the past four years."

DIAGNOSIS.

The diagnosis of cyanide poisoning in men can be easily made if the physician keeps in mind the following points:

1. Personal history.
2. Occupational history.
3. Sudden illness.

4. Early unconsciousness.
5. Characteristic odor of breath (smell of "oil of bitter almonds").
6. Rapid and deep respiration in early stages of intoxication.
7. Convulsions, frequently with involuntary passage of urine and feces. These are followed by depression and paralysis.
8. Cyanosis.
9. Presence of a cyanide container.
10. Positive tests for cyanide in the stomach contents or blood.

CRUCIAL TESTS IMPORTANT FOR EXPERT TESTIMONY.

If a person is poisoned during fumigation, a sample of his blood, 10 to 20 cc., should be drawn. If a person is suspected to have taken poison by mouth, his stomach contents should be evacuated by a stomach tube. If the victim is already dead, the gastric contents should be saved and the liver and kidneys should be removed and analyzed as quickly as possible. It is imperative that the specimens be taken before the body is embalmed. The formaldehyde of embalming fluid reacts quickly with cyanides to form glycollic acid which does not give the chemical reactions characteristic of hydrocyanic acid or its salts. To isolate hydrocyanic acid, the blood, stomach contents or the minced organ, such as the liver or kidney, is definitely acidified with tartaric acid, and subjected to distillation, the poisonous gas being collected in a narrow-mouthed flask. The distillate may be used for various tests.

1. Schönbein's test as modified by Sundberg (1).

Reagents needed: Gum guaiac, 0.2 per cent in alcohol; copper sulphate, 0.1 per cent; and tartaric acid.

Procedure: Place the suspected fluid in a flask, and acidify with tartaric acid. Wet a strip of filter paper with a mixture of guaiac and copper sulphate in the proportion of 10:3, and suspend it in the flask with a cork. Heat the contents on a water-bath.

Interpretation of results: A blue color indicates a positive test. The reaction is not specific but very sensitive.

2. Sulphocyanate test.

Reagents needed: Yellow ammonium sulphide solution; hydrochloric acid, 1 per cent; and ferric chloride, 1 per cent.

Procedure: Add to the distillate yellow ammonium sulphide, evaporate the mixture to dryness, and dissolve the residue in hydrochloric acid. Warm, filter and add ferric chloride.

Interpretation of results: A red color soluble in ether constitutes a positive test. The sensitivity of this reaction is 1:4,000,000.

3. Prussian blue test.

Reagents needed: Ferrous sulphate, 1.5 per cent; ferric chloride, 10 per cent; hydrochloric acid, 10 per cent; and sodium hydroxide, 10 per cent.

Procedure: Alkalinize the suspected fluid with 2 drops of sodium hydroxide, and add to it 2 cc. of ferrous sulphate solution and 1 cc. of ferric chloride. Warm the mixture and cautiously acidify with hydrochloric acid but avoid a great excess.

Interpretation of results: A blue precipitate indicates the presence of hydrocyanic acid. The sensitivity of this test is 1:50,000.

4. U. S. P. method (quantitative).

Reagents needed: Ammonia water, 10 per cent; potassium iodide, $N/1$; and silver nitrate, $N/20$.

Procedure: Treat an aliquot portion of 25 cc. of the suspected fluid with 4 cc. of ammonia water and 3 drops of potassium iodide solution, and titrate with $N/20$ silver nitrate until a permanent turbidity of silver iodide appears.

Calculations: Each cc. of $N/20$ $AgNO_3$ represents 6.5 mg. of KCN, or 7.7 mg. of HCN.

Equally simple and accurate is the gravimetric method for the determination of hydrocyanic acid. This involves the steam distillation of the material acidified with tartaric acid. The distillate is received in a beaker containing an excess of $AgNO_3$. The precipitated AgCN is filtered on a tared Gooch crucible and weighed. From the weight of AgCN, the amount of HCN or cyanide salt may be calculated.

5. Smith's isopurpurate method (quantitative for small amounts) (2).

Reagents needed: Picric acid, saturated solution; sodium carbonate, 5 per cent; hydrochloric acid, 10 per cent; and potassium cyanide, *N*/500.

Procedure: Into a test-tube graduated to 25 cc. are pipetted 3 cc. of picric acid solution, 1 cc. of sodium carbonate solution and 1 cc. of the solution to be tested. Warm the mixture on a water-bath. Upon cooling, dilute with water to the mark. Compare the reddish brown color in a colorimeter with that of the standard, prepared in an identical manner, using 1 cc. of *N*/500 KCN.

Calculation: The total amount in the specimen as KCN in mg. =

$$\frac{0.13 \times \text{Reading of Standard} \times \text{Volume in cc.}}{\text{Reading of Unknown}}$$

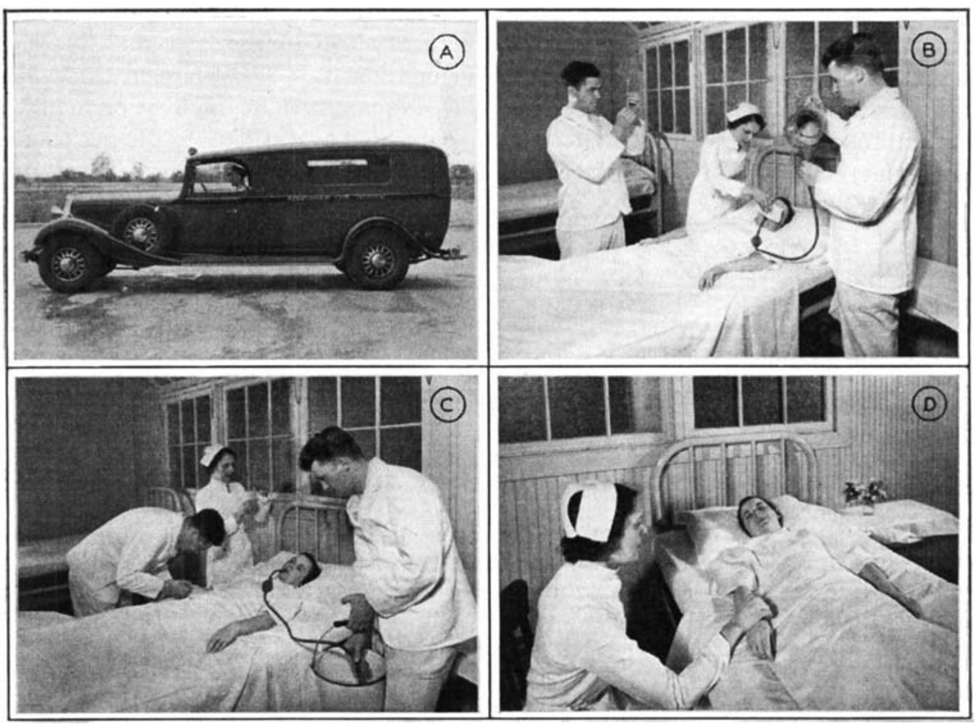

Fig. 1.—Suggestion for managing a case of Cyanide Poisoning. A. The antidote kit should be installed in the ambulance or any place that is most convenient. B, C and D. Showing steps of administering the treatment.

NEW METHOD OF TREATMENT.

The method to be advocated depends upon Hug's and the authors' laboratory work previously published (3), (4). The antidote chiefly consists of a combination of sodium nitrite and sodium thiosulphate, injected intravenously one after the other. Such a combination can detoxify 20 minimal lethal doses of sodium cyanide in dogs, and is ten times as effective as methylene blue. To expedite the treatment, amyl nitrite is also used by inhalation. The recommended dose for sodium nitrite is 0.3 Gm. in 10 cc. of water (3 per cent), and that for sodium thiosulphate 25 Gm. in 50 cc. of water (50 per cent), although an amount of 12.5 Gm. in the same volume of water (25 per cent) is frequently enough. In cases of relapses, one-half of the quantity of each should be repeated. So far, three cases of severe cyanide poisoning have been successfully treated with this procedure: two by Viana, Cagnoli and Cendan (5) and the third by Kempf and Richey (6). All three patients recovered, although they had swallowed large amounts of potassium cyanide. The validity of the laboratory results has therefore been clinically confirmed.

It must be pointed out here that the antidotal action of amyl nitrite against cyanide was first demonstrated by Pedigo (7), that of sodium nitrite by Mladoveanu and Gheorghiu (8), and that of sodium thiosulphate by Lang (9). It is the combination therapy that is of recent development.

In order to make the treatment most effective, it is suggested that a kit containing 12 pearls of amyl nitrite, 2 ampuls of sodium nitrite, 2 ampuls of sodium thiosulphate, 2 sterile syringes, 10- and 50-cc. sizes, respectively, 1 file and 1 stomach tube be installed in the ambulance, as is practiced at the Indianapolis City Hospital (Fig. 1A), or in any place where it is most easily accessible. These ampuls have proved to be stable for more than a year with appropriate preservatives and the usual precaution. A team of three individuals is necessary for the best management of a case of cyanide poisoning. In step 1 (Fig. 1B), the physician in charge loads his 10-cc. syringe with sodium nitrite, assistant No. 1 washes out the patient's stomach, and assistant No. 2 initiates the treatment by giving inhalation of amyl nitrite. In step 2 (Fig. 1C), the physician injects sodium nitrite by vein, assistant No. 1 finishes washing the stomach, and assistant No. 2 withdraws the amyl nitrite and loads the 50-cc. syringe with sodium thiosulphate. In step 3, the patient should be watched for 24 to 48 hours after the completion of the thiosulphate injection by the physician. If poisoning results from fumigation, gastric lavage is of course not necessary.

The rapidity of death from cyanide poisoning has been justly emphasized in teaching and textbooks, for most patients do die within 30 to 60 minutes. On the other hand, one must also remember that many others may linger for several hours. Doctor G. F. Kempf of the Indianapolis City Hospital showed us the record of a man poisoned with hydrocyanic acid gas in fumigation. The victim did not die instantly but lived a little more than three hours. This happened in 1928. Oxygen therapy and stimulants were the only measures employed. Hanzlik and Richardson (10) adequately state "that clinical cyanide poisoning is not always as rapidly fatal as may be imagined from animal experiments or textbook statements. There is generally considerable cyanosis in man, and symptoms or unconsciousness may be present for two or three hours, which ordinarily will be ample time for administering treatments suggested." The combined therapy with sodium nitrite and sodium thiosulphate has saved dogs even after their respiration has ceased. It is reasonable to assume that this also holds true in men. As long as the victim's heart still beats, the clinician should consider the case hopeful and treat it without delay.

Clawson, Bunyea and Cough (11), (12), (13) conducted numerous experiments in sheep and cattle, and clearly demonstrated that the same method of treatment can be applied to live stock poisoned by cyanogenetic plants.

SUMMARY.

This paper is a general but brief résumé of cyanide poisoning. It deals with the mortality statistics, sources of poisoning, the diagnosis, crucial tests for legal pur-

poses, and the treatment. The new antidote advocated chiefly consists of a combination of sodium nitrite and sodium thiosulphate. Precise instructions as to how a case of cyanide poisoning should be managed are given.

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CARBO ACTIVATUS.*,[1]

BY JOSEPH ROSIN,[2] GEO D. BEAL[3] AND CHESTER R. SZALKOWSKI.[4]

The demand on the part of the medical profession for a charcoal superior in adsorptive powers to Carbo Ligni U. S. P. X culminated in instructions from the present Sub-committee on Scope to admit a carbon from any source, standardized for its adsorption potency.

Decolorizing carbons have, during the past twenty years, assumed a prominent position both in industry and in the chemical laboratory. Such carbons have had their decolorizing powers greatly beneficiated by chemical treatment, and it is likely that such beneficiation received its greatest impulse during the late war in the production of adsorbent carbon for gas mask canisters.

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