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Mercuric Cyanide Poisoning and Its Treatment in Dogs. (29250)

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Two common cyanides of mercury, mercuric cyanide and mercuric oxycyanide, have some commercial application. The former has been employed in electroplating, and the latter in leather industry. In medicine both have been used in treatment of syphilis and as surgical instrument disinfectants. Bolgert and Levy(1) advocated the combination of penicillin and mercuric cyanide as an ideal antisyphilitic therapy. Although Gettler and Baker(2) emphasized the dominant toxic action of mercury, it is conceivable that cyanides of mercury can cause cyanide and mercury poisoning simultaneously. Indeed Bonciu and Petrovici(3) showed the dual toxicity of mercuric oxycyanide in guinea pigs. The purpose of our investigation was to assess the toxicology of mercuric cyanide in dogs, and to test the efficacy of nitrite-thiosulfate therapy against the CN ions, and that of BAL (British Anti-Lewisite, or 2,3-dimercaptopropanol) against Hg ions. The success of using sodium nitrite and sodium thiosulfate for acute cyanide poisoning has long been known(4,5). The effectiveness of BAL for mercury poisoning was proven by Gilman *et al*(6) and clinically confirmed by Longcope and Luetscher(7). BAL apparently brought about the recovery of a woman who ingested 10 g of mercuric oxycyanide(8).

Methods. Fifty-two dogs were injected subcutaneously with various doses of mercuric cyanide in a 5% aqueous solution. The first group of 32 animals were observed for the appearance of acute toxic signs and their ultimate survival time in days. Sufficient data were obtained to permit calculation of the LD_{50} of the poison. A second group of 15 dogs were subcutaneously injected with larger doses of mercuric cyanide, immediately followed by intravenous injection of sodium nitrite and sodium thiosulfate to detoxify the cyanide portion of the molecule. The smallest dose of the group, 7.5 mg per kg, caused no acute toxic signs, and therefore no cyanide antidote was injected. All the dogs in the second group were treated with BAL, 10% in oil, to detoxify the mercury part of the molecule. In these experiments the first dose of BAL, 7 mg/kg, was injected intravenously at a very slow rate, 30 minutes after mercuric cyanide. Subsequent doses were given by intramuscular injection at 2, 4, 6 and 10 hours after the first dose. All surviving dogs were sacrificed on the 18th day, and their viscera and those of the dead animals were studied grossly and microscopically.

Results and discussion. Thirty-five dogs receiving mercuric cyanide alone ranging from 2 to 5 mg per kg did not develop toxic signs of cyanide poisoning—vomiting, restlessness, rapid respiration, ataxia, convulsions, urination and defecation. However a certain number of them died in an average of 4.1 to 15.6 days (Table I). Two dogs which were injected with a dose of 15 mg/kg had typical signs of cyanide poisoning within 20 minutes. One died of respiratory failure in 2½ hours, the other on the second day, making an average of 1.3 days. By the usual computation(9), the $LD_{50} \pm$ S.E. of mercuric cyanide is 2.71 ± 0.17 mg/kg. The LD_{50} of sodium cyanide was previously

TABLE I. Detoxification of Mercuric Cyanide in Dogs.

Mercuric cyanide, mg/kg	No. dogs died /No. used	CN-antidote: Sodium nitrite, mg/kg	CN-antidote: Sodium thiosulfate, mg/kg	Hg-antidote: BAL, mg/kg	Avg survival time, days
2.0	1/10	none	none	none	15.6
2.4	2/5				11.3
2.9	2/5				10.3
3.5	9/10				7.1
5.0	5/5				4.1
15.0	2/2				1.3
7.5	1/5	none	none	7 (4 doses)	14.9
10.0	4/5	22.5	500	7 (5 doses)	10.5
15.0	5/5	22.5	500	7 (5 doses)	3.7

found to be 5.36 ± 0.28 mg/kg(5). Mole for mole, mercuric cyanide is more toxic than sodium cyanide, the CN content of NaCN being 53.08%, and that of $Hg(CN)_2$, 20.60%.

At necropsy none of the animals that died of mercuric cyanide showed evidence of mucous membrane damage of the gastrointestinal tract. Apparently in these animals the amount of mercury excreted into the colon was not sufficient to cause injury. Microscopically, necrosis and regeneration of renal tubules, typical of mercury effects were extensive. All the dogs that survived 18 days were free from pathological lesions.

In the second series of experiments a dose of 7.5 mg/kg of mercuric cyanide caused no acute toxic signs. No cyanide antidote was therefore administered, but BAL was injected 30 minutes after the poison, and repeated. The dogs receiving 10 and 15 mg/kg of mercuric cyanide were treated with both nitrite-thiosulfate combination and BAL. Four out of 5 animals on 7.5 mg/kg and one out of 5 animals on 10 mg/kg, survived 18 days, but none on 15 mg survived in spite of detoxifying medication. The early toxic signs of cyanide (nausea, vomiting, rapid breathing and ataxia), with 10 and 15 mg per kg subsided after intravenous injection of sodium nitrite and sodium thiosulfate. The LD_{50} of the treated group is 8.66 ± 0.66 mg per kg. The difference between the two LD_{50}'s is highly significant, P being <0.001. The beneficial effects are contributed by both the cyanide and mercury antidotes. It is possible that additional doses of BAL might have saved more dogs.

The principle of treating the poisoning by mercuric cyanide can be then expressed by the following equations:

I. $NaNO_2 + \text{Hemoglobin} \longrightarrow \text{Methemoglobin}$

II. $\text{Methemoglobin} + CN^- \longrightarrow \text{Cyanmethemoglobin}$

III. $Na_2S_2O_3 + CN^- + 0 \xrightarrow{\text{Rhodanese}} NaSCN + Na_2SO_4$

IV. $\begin{matrix} CH_2SH \\ | \\ HOCH_2CHSH \end{matrix} + Hg^{++} \longrightarrow \begin{matrix} CH_2—S \\ | \\ HOCH_2CH—S \end{matrix} > Hg$

The detoxification of cyanide with nitrite and thiosulfate has been amply demonstrated (5). For mercury, BAL not only forms the inactive cyclic mercaptide, but also protects enzymes which the metal inhibits.

In clinical medicine the ideal treatment of poisoning by mercuric cyanide requires double antidotes. Both should be available in first aid stations or poison centers. If mercuric cyanide is swallowed, gastric lavage must be immediately applied. As soon as possible sodium nitrite and sodium thiosulfate are injected by vein consecutively, and quickly followed by intramuscular injection of BAL. The latter should be repeated until urinary abnormality disappears. Because of similar symptomatology, the cyanide antidote is better administered than omitted. In case of anuria, hemodialysis with an artificial kidney is a last resort.

Summary. Mercuric cyanide has a dual mechanism of poisoning. In dogs receiving this poison intramuscularly, the cyanide radicle may be detoxified by intravenous injection of sodium nitrite and sodium thiosulfate, one after the other; and the mercury radicle, by prompt injection of BAL. The latter can be given first by intravenous in-

jection, and repeated by intramuscular injection. The LD_{50} of mercuric cyanide in dogs without treatment is 2.71 ± 0.17 mg per kg; and that with nitrite-thiosulfate therapy and BAL injections, 8.66 ± 0.66 mg per kg.

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Trachoma Viruses Isolated in United States.*† VII. Relative Toxicity of Different Strains for White Mice. (29251)

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Since 1959 several strains of virus have been isolated in this laboratory from cases of trachoma and inclusion conjunctivitis(1). These strains were adapted to growth in the yolk sac of embryonated hens' eggs by serial passage. When high, constant egg-lethal titers of between 10^{-6} and 10^{-7} ELD 50/g of yolk sac were reached, usually after 4-5 passages, 50% yolk-sac pools were stored in stoppered glass vials at —50°C in a mechanical freezer. It was of interest to determine if these suspensions were lethal for mice following intravenous inoculation, to compare toxicity with egg lethality and with the total numbers of virus particles present, and to determine if strains with different biological properties differed in relative toxicity(2,3,4). The results of such studies are presented here.

Materials and methods. Viruses.§ Isolates from the United States were employed at the following yolk-sac passage levels: Trachoma isolates BOUR YS 14 and 16, ASGH YS 14, AP 2 YS 10 and inclusion conjunctivitis isolates IC Cal 3 YS 10 and 13, IC Cal 4 YS 11, IC Cal 5 YS 12.

In addition, one of the strains originally isolated in Peking(6), and passed for many years in mouse brain and in eggs, was supplied to us by Dr. J. Snyder. It was TE55 and used as our YS6. Stock virus suspensions were made from pools of infected yolk sacs harvested from live eggs and stored at —50°C for 1-9 months as 50% suspensions in broth-saline. They were titrated for egg lethality (ELD 50/g of yolk sac) as previously described(2). Bacteriologically sterile pools of high egg-lethal titer were rapidly thawed, serial 2-fold dilutions made in chilled broth saline, and 0.5 ml amounts inoculated intravenously into weanling (3 week old, 12-15 g) Swiss white mice obtained from a commercial,

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§ The nomenclature of these isolates by the proposed system(5) is as follows: BOUR = TRIC/ /USA-Cal/Cal-1/OT; ASGH = TRIC/ /USA-Cal/ Cal-2/OT; AP 2 = TRIC/ /USA-Cal/Cal-4/OT; IC Cal 3 = TRIC/ /USA-Cal/Cal-9/ON; IC Cal 4 = TRIC/ /USA-Cal/Cal-10/ON; IC Cal 5 = TRIC/ /USA-Cal/Cal-11/ON.