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TOXICOLOGY
OR
THE EFFECTS OF POISONS

UNDERHILL

TOXICOLOGY

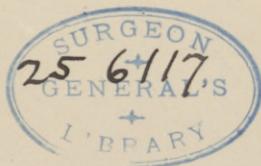
OR

THE EFFECTS OF POISONS

BY

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TO
L. R. U.

PREFACE

This volume has been compiled with the object of presenting a short, concise description of the effects of poisons upon the organism. No attempt has been made to enter into the details of the chemical reactions involved in the isolation and identification of poisons. Such matters have been adequately treated in several well known books. On the other hand, a comparable treatise giving the essentials of the effects of poisons has not been published within recent years. It is hoped that this volume will fill this need and will be of service to medical students and physicians who wish to gain a clear concept of the essentials of the science of poisons.

The subject matter has formed the basis of a course of lectures given to students in the Yale School of Medicine, and has been gathered from the standard text books, reference books and original literature upon the subject. In general, references have been given only to the later articles upon a given topic and then usually to those articles containing the earlier literature.

Acknowledgement is made of the aid of Miss Mary Eloise Montague in preparation of the manuscript and in proof reading.

FRANK P. UNDERHILL.

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TOXICOLOGY

CHAPTER I

THE PRINCIPLES OF TOXICOLOGY

Toxicology is the science of poisons. In its broadest use it is the science that treats of the origin, nature, properties, effects and detection of poisons, and it includes treatment of poisoning. The science falls naturally into two divisions (*a*) that dealing with the effects of poisons and (*b*) that relating to their chemical identification and isolation. From this division it is readily seen that the first relates more especially to *physiological* action, whereas the latter is primarily concerned with *chemical* reactions.

To give a general satisfactory definition of a poison is a somewhat difficult feat. Nevertheless various attempts have been made examples of which follow—"We define poisons as such inorganic or organic substances as are in part capable of artificial preparations, in part existing, ready formed, in the animal or vegetable kingdom, which without being able to reproduce themselves, through the chemical nature of their molecules under certain conditions, change in the healthy organism the form and general relationship of the organic parts, and through annihilation of organs, or destruction of their functions, injure health, or, under certain conditions, destroy life" (Husemann). According to Kobert—"Poisons are organic or inorganic unorganized substances originating in the organism itself, or introduced into the organism, either artificially pre-

pared, or ready formed in nature, which through their chemical properties, under certain conditions, so influence the organs of living beings, that the health of these beings is seriously influenced temporarily or permanently." Blyth prefers the following—"A substance may be called a poison if it is capable of being taken into any living organism, and causes, by its own inherent chemical nature, impairment or destruction of function." Sollmann states that—"A poison is any substance which, acting directly through its inherent chemic properties, and by its ordinary action, is capable of destroying life, or of seriously endangering health, when it is applied to the body, externally, or in moderate doses (to 50 gms.) internally.

CLASSIFICATION OF POISONS

There are at least two ways in which poisons may be classified (*a*) according to chemical properties (*b*) according to physiological effects. From a scientific viewpoint neither system nor a combination is entirely adequate and one must either omit all attempts at classification or else be content to classify poisons from the standpoint of practical utility only. A chemical classification follows:

1. Acids and Alkalies
2. Metallic Poisons
3. Gaseous Poisons
4. Alkaloids
5. Volatile Organic Poisons
6. Miscellaneous Poisons

The physiological classification recognizes the most prominent symptoms as the basis for division of poisons. According to this classification poisons may be divided into three great groups which is that adopted and defined by Sollmann.

1. **Irritants.**—These produce inflammation; if they are taken by the mouth, there is pain throughout the alimentary canal, vomiting, purging, delirium, coma. So many poisons are to some extent irritant, that these symptoms are very commonly present. The irritants can be divided into *corrosives*, which produce destruction of tissue: and simple irritants which do not. If corrosives are taken by the stomach, the vomit is often bloody.

2. **Nerve Poisons.**—These act on the neuromuscular apparatus, and include most of the poisons which are fatal in minute doses. They are subdivided into: *Convulsants*, which cause spasms; *Somnifacients*, causing sleep and coma; and *Cardiac poisons*, which stop the heart.

3. **Blood Poisons.**—Those which alter the hemoglobin or blood corpuscles. These include the toxic gases, nitrites, etc. Their action is generally characterized by cyanosis.

CONDITIONS MODIFYING THE EFFECTS OF POISONS

The influence of a poison upon the organism is very materially modified by a variety of conditions. In general these may be divided into two great classes:—(A) Those relating to the poison itself and the manner of its administration, (B) Those relating to the organism itself.

(A) 1. **The Physical State or Form of a Poison.**—The physical state of a poison has a marked influence in modifying the action of a poison. Thus a poison is more rapidly absorbed in a gaseous form than in a solid or even a liquid state. In order that a substance may act as a poison it must be capable of solution, and absorption by the blood. No substance completely insoluble can be regarded as a true poison. Barium chloride which is readily soluble must be regarded as extremely toxic whereas the insoluble barium sulphate is devoid of toxic properties. In fact

advantage is taken of this in the employment of barium sulphate in X-ray photography in diagnosis of gastrointestinal disorders. The principle of the form of poison modifying its action is made use of in the treatment of various types of intoxication by means of antidotes, the object aimed at being to change the soluble substance to one insoluble and hence incapable of absorption.

In general, dilution of a poison tends to favor rapid absorption and this in turn hastens and intensifies the toxic effect. An exception to this rule is seen in the case of those poisons with a corrosive action. These have their detrimental influence greatly decreased by dilution. Poisons taken into the stomach in the form of a dry powder may not manifest toxic symptoms for hours after administration. Usually the larger the dose the more rapid and severe are the effects. This, however, is not always true. Thus arsenic in large doses may act as an irritant to the stomach, causing vomiting, with prompt ejection of the poison so that few or no toxic symptoms result. On the other hand a very much smaller dose being devoid of irritant action on the stomach allows absorption of the poison with subsequent symptoms which may terminate fatally. Again the solvent containing the poison exerts a marked effect upon its action. Thus of alcoholic, aqueous or oily solutions the first is most rapidly absorbed, the last least so and in consequence more prompt and emphatic effects are to be expected the more rapid the absorption. Hot solutions are usually absorbed more rapidly than cold.

2. The Path of Absorption.—In general a poison exerts its specific action irrespective of the mode of administration. In other words it makes little difference through which path the poison reaches the circulation. The only modifying influence exerted by changing the path of absorption is the time of appearance of symptoms which

varies directly with the rate of absorption. Thus symptoms appear most rapidly when poisons are injected directly into the blood stream. Intraperitoneal injection and intramuscular stand next in order followed by subcutaneous and intra-dermal injection.

Poisons are less rapidly absorbed when taken by mouth. The condition of the stomach greatly modifies the rate of absorption. A diseased stomach may markedly delay the absorption of a poison or on the other hand prove highly susceptible to an irritant poison. Food in the stomach may delay absorption either by retarding the emptying of this organ or by changing temporarily the physical state of the poison. Many apparent anomalies of the effects of poisons may be explained in this manner. Although it may be generally accepted that the path of absorption modifies the action of a poison only in its time relations and does not alter its specific effect, yet there are notable exceptions for in certain instances the mode of administration materially alters the action of the poison. This is particularly true of substances resembling proteins, hence capable of alteration by the digestive enzymes. Snake venom by mouth is entirely harmless even though highly poisonous when it gains direct entrance to the blood. The same is true of the toxic proteins, ricin and abrin, and various bacterial toxins fall into the same class.

(B) The most important conditions residing in the organism that modify the action of poisons are (1) Age, (2), Idiosyncrasy, (3) Habit, (4) Tolerance, (5) Physical state of the individual.

1. Age.—As might be assumed, the age of an individual distinctly modifies susceptibility to poison. Although as a rule the younger the individual the greater is the susceptibility, there are many notable exceptions. Thus for example, children are relatively less susceptible to the

action of strychnine, belladonna, and calomel. Conversely, young children are particularly susceptible to the action of opium and its constituents and the same may be said of the other narcotic drugs. In old age, poisons may react with unusual severity, indicating a reduced resistance.

2. Idiosyncrasy.—The term idiosyncrasy is applied when an individual exhibits peculiar, unusual reactions to certain poisons. Lack of knowledge of this peculiar personal susceptibility or tolerance may result in serious disturbances in bodily function or even terminate in death. In a given case of poisoning the possibility of this distinctive characteristic should always be taken into consideration. Idiosyncrasy may be manifested toward a large number of substances some of which are ordinarily non-toxic, so that this unusual sensitiveness may be both qualitative and quantitative. This feature is brought into prominence in different individuals especially by morphine, calomel, arsenic, mercury, antipyrine, cocaine, etc.

On the other hand, in some individuals a drug will induce an effect exactly opposite that usually produced. Thus morphine will cause wakefulness instead of sleep, or in larger doses convulsions simulating those of strychnine. Many individuals react with severe symptoms after eating or smelling of a large variety of substances, lobsters and other shellfish, honey, various fish, eggs, mutton, strawberries, sewer gas, musk, smell of animals, and odor of flowers.

3. Habit.—Repeated small doses of a poison generally lessen the effect. By gradually increasing the initial small dose of a poison relatively large doses may be taken without evidence of toxic symptoms. Habitual morphine users are pertinent examples, very large doses being necessary finally to produce the desired effect. Again in certain

parts of Europe arsenic eating is notorious, huge quantities being taken daily. Whether in the case of morphine the organism develops an ability to oxidize the drug to an unusual degree or whether the intestine acquires a resistance to absorption remains indiseisive at present. So far as arsenic is concerned the assumption has been made for many years that there was a gradually increasing resistance to its effects. Very recently, however, it has been shown that the apparent habituation to arsenic may perhaps, in part at least, be ascribed to the quality of the arsenic consumed. Thus when arsenic made up of small crystals, or powdered, was ingested, much smaller doses were needed to produce toxic effects than when larger particles were introduced. From this it would appear that the whole matter may be explained on the basis of solubility of the arsenic, the powder or small crystals being much more readily soluble, hence more rapidly absorbed, than the larger, coarser crystals.

This tolerance to poisons, acquired through habit, is not absolute since generally toxic effects and even death may be induced by slightly exceeding the limit of habituation. It is this fact that largely explains the death of the habitué of morphine and of other similar poisons. Habit, however, cannot be acquired with all drugs, for antimony or mercury, for example, cannot be taken long with impunity even in relatively small doses.

4. Tolerance.—Certain individuals exhibit a very noteworthy resistance to the action of certain poisons. This resistance or tolerance is natural, not having been acquired by habituation but it is rarely absolute so that it can hardly be regarded as a natural immunity. Thus some persons are capable of taking large doses of morphine without any apparent effect. The explanation of this peculiarity is not clear. In some instances it may be

due either to non-absorption, rapid elimination, unusual ability to neutralize or destroy the poison or to anatomic peculiarities. In some instances none of these hypotheses seems to hold.

5. Disease.—Pathological conditions in the body may very naturally influence the action and effects of poisons. This modified action may be manifested as an increased susceptibility or the effect may be greatly diminished. These conditions that influence absorption and excretion play a particular role in this respect. Renal disease for example increases the susceptibility to arsenic and other drugs. In paralysis strychnine acts less readily. In peritonitis, delirium tremens, and in those states where intense pain exists the power of morphine is diminished whereas in conditions primarily associated with the nervous system as in inflammatory conditions of the brain an increased susceptibility may be noted. In insanity with maniacal characteristics and in convulsions narcotics may be almost without influence. Exhaustion tends to increase susceptibility. General reduction of vitality from whatever cause usually means a lowered resistance to poisons. } On the other hand sleep, perhaps owing to lessened functional activity has a tendency to diminish or at least to retard the action of poisons.

THE FATE OF POISONS

After absorption, poisons rapidly leave the blood unless indeed they combine with the constituents of the blood and change its characteristics either temporarily or permanently. In general, however, poisons remain in the blood for a comparatively short time, being excreted through the urine, saliva, bile, sweat and feces. In certain instances more of the poison is eliminated by the

feces than by the urine, lead for example. Usually however, most of the poison passes by way of the renal path. Poisons are promptly eliminated from the body but are deposited in all the principal organs and tissues. In general the liver contains the greater amount of stored poison, the amount deposited in the other organs varying with the type of poison. Gaseous poisons are not deposited but are promptly excreted by the lungs.

So far as one may judge a poison deposited in an organ enters into some chemical combination with the cellular constituents and while thus deposited may be regarded as without special detrimental effect. Gradually this combination disrupts and the poison is thrown into the general circulation, injuring sensitive tissues in its passage to the excretory organs which indeed may suffer injury sufficient to cause death. Usually inorganic poisons are eliminated from the body unchanged, the organism being unable to alter them. On the other hand the natural response of the body is to change or modify the poison prior to elimination. Most of the organic poisons are altered in passage through the body by combination with constituents of the body or by undergoing oxidation, hydrolysis or other similar transformation.

SYMPTOMATOLOGY OF POISONS

There are certain outstanding features in poisoning that may be of value to the physician in diagnosis. These symptoms are general and although they do not indicate specific poisons their presence or absence exclude certain possibilities. Special symptoms relating to specific poisons will be considered under individual poisons.

1. Nausea, Vomiting and Purging.—When these suddenly appear in a normal individual it is indicative of

the presence of a gastro-intestinal irritant or of the onset of some acute disease. Many poisons, especially metals and food poisons, are characterized by initial symptoms of nausea, vomiting and purging. If the history of the case agrees with the possibility of poisoning, measures should be taken at once to assist the body in its efforts to rid itself of the noxious substances.

2. Vasomotor Disturbances.—The effects of poisons upon the vasomotor centres is indicated by the fact that many poisons lead to marked changes in the skin. The color may be pale or the natural color much intensified and urticarial rashes are common. Heart action and respiration may be markedly modified in either direction.

3. Cerebral Symptoms.—The influence of poisons upon the cerebrum lead to stupor or coma, or may partake of the nature of convulsions, illusions or hallucinations. Thus, hallucinations and temporary delusions may follow the use of salicylic acid and strychnine may cause convulsions. Stupor and coma may be induced by narcotics or may be due to alcoholism or cerebral hemorrhage.

4. Temperature.—The temperature changes in poisoning have not been sufficiently studied to make definite statements concerning them. Certain it is that usually changes in temperature must be regarded as secondary effects rather than of specific effects of poison. Some poisons, like cocaine, in large doses may elevate temperature but usually in poisoning the temperature is either normal or is low in some instances being as low as 95°F.

5. Pulse.—Generally in acute poisoning the pulse is quick and feeble, the extent to which this is true being determined by the degree of shock that may be present. Poisons that have a specific action upon the respiratory centre may influence the pulse only slightly if at all and the

pulse may continue with a good tone for some time after respiration has ceased.

6. Respiration.—The most common effect of poisons on the respiration manifests itself in dyspnea, which may be due to mechanical obstruction, as in edema of the glottis from local action of a corrosive poison, or to paralysis, as in chronic lead poisoning, or to muscular spasm, as in poisoning with strychnine, or to direct action on the respiratory centre, as may be observed with some poisons of bacterial origin. Cheyne-Stokes respiration marks the approaching termination of many cases of fatal poisoning.

7. Motor Disturbances.—Motor disturbances are so characteristic in certain instances that they lead at once to a correct diagnosis. In lead poisoning the wrist drop is sufficient to arouse suspicion; tetanus due to strychnine poisoning is quite peculiar and the mydriasis of atropine poisoning is characteristic. Retention of urine occurs with narcotic poisons although a general reaction of fatal poisoning is paralysis of sphincters.

8. The Eye.—Only a few reactions upon the eye are of particular value. Thus contraction of the pupil by morphine and dilatation by atropine are quite characteristic. Yellow vision with santonin and blindness from wood alcohol poisoning are quite specific.

9. The Ear.—Quinine causes a ringing sensation in the ear, the hearing is more acute under the influence of strychnine, and salicylic acid causes a buzzing sensation.

10. Modified Sensations.—Various changes of sensation in the skin, such as anesthesia, hyperesthesia, pins and needles sensation, etc., probably have their origin in some form of poisoning. Neuritis from lead, arsenic and alcohol are examples of abnormalities of sensation induced by intoxication.

11. Skin Lesions.—The long continued use of bromides or iodides may result in acnes or fungoid sores. Chronic arsenic poisoning gives rise to the peculiar coloring of the skin called arsenic melanosis, and silver causes the coloration known as argyria. Gangrene may be induced by ergot and members of the arsphenamine group may be responsible for varied skin eruptions partaking of the nature of urticarial, scarlatinoid and morbilliform erythemas together with itching or pruritus of the skin.

THE DIAGNOSIS OF POISONING

At times the diagnosis of poisoning is exceedingly difficult since with a few notable exceptions the effects of poisons are not characteristic. It is, of course, of the utmost importance to be able to make a diagnosis of poisoning so that proper treatment may be instituted.

1. Suspicion of poisoning arises if any individual who has previously been in apparent good health suddenly manifests notable pathological symptoms which rapidly become intensified. This suspicion is strengthened if the symptoms appear a short time subsequent to the ingestion of some food or drink which may have had a peculiar odor or taste. Suspicion is further firmly established if the symptoms agree closely with those characteristic of a certain group of poisons and if they can be differentiated from disease.

In general the physician is guided only by symptomatic evidence. This may entirely mislead him since a variety of diseases may cause symptoms simulating those induced by poisons. Thus, irritant poisoning may be simulated by gastro-enteritis, gastric and intestinal ulcers, acute indigestion, appendicitis, intestinal obstruction, peritonitis, etc. On the other hand, narcotic poisoning may be

simulated by epilepsy, apoplexy, cerebral hemorrhage, certain heart diseases, inflammation of the cerebro-spinal system, uremia, etc. The symptoms of arsenic poisoning and those of cholera morbis are very similar. One may readily mistake apoplexy or uremia for opium poisoning. The resemblance between the symptoms of strychnine poisoning and tetanus is very close.

In acute poisoning a careful examination will many times enable the physician to make an immediate accurate diagnosis. Evidences of corrosion on the lips, tongue, mouth and throat lead one to suspect that a corrosive poison has been taken. Chloroform, carbolic acid, potassium cyanide and other odoriferous substances may be detected on the breath, and examination of the vomitus and even of the feces may reveal important evidence. The urine is of considerable importance in examinations of this kind.

2. The long continued use of sulphonal or trional gives the urine a red color from the presence of hematoporphyrin which may be identified by the spectroscope. Methylene blue imparts a green color to the urine and antipyrin and fuchsin cause it to assume a red hue. In santonin poisoning the fresh urine is normal in color but upon being made alkaline turns bright red. The urine turns dark green with phenol and cresol, the color deepening on standing. Quinine may cause hemoglobinuria which also results from the inhalation of arseniuretted hydrogen. Potassium chlorate induces methemoglobin and blood in the urine may follow the administration of any genito-urinary irritant such as cantharides or turpentine. Phosphorus, mercury or lead may give the urine a brown or greenish brown color.

Chronic poisoning is even more difficult of diagnosis than acute poisoning because the symptoms are usually

not sufficiently definite to arouse the suspicions of the physician.

There are no definite rules to establish a diagnosis of poisoning during life except by chemical analysis of some of the excretions of the body such as urine, feces or vomitus. Any drink, food or medicine suspected should be subjected to analysis also. In no other way is it possible to differentiate absolutely between the symptoms caused by disease and those induced by poisons.

TREATMENT OF POISONING

Each type of poisoning requires specific treatment. In many instances, however, the poison taken is unknown and it is therefore essential that general rules of treatment be established. These are (1) removal of the poison, (2) administration of antidotes, (3) symptomatic treatment.

Removal of the Poison.—The measures taken will depend upon the site to which the poison was applied. If the skin or mucous membranes are concerned the best agent for removal of the poison is water copiously applied. This application not only dilutes the irritant agent but washes the site free from it. If the poison is not freely soluble in water (for instance, carbolic acid) alcohol may be employed. Chemical antidotes may be added to wash-water—thus for acids, soaps or *Linimentum calcis*; for alkalies, lemon juice or vinegar. It should be pointed out that strong acids or alkalies should never be used in the treatment of irritant poisons. After the site has been thoroughly freed from the toxic agent it should be covered with a bland oil or salve.

Most poisons are taken by mouth, hence, in treatment the stomach should be emptied as soon as possible unless indeed sufficient time has elapsed to make this procedure

useless. On the other hand it is always a good plan to follow since the cleansing of the stomach aids greatly in most cases of poisoning. There are only a few instances of poisoning where emptying the alimentary tract is contraindicated. The most notable of these is in strychnine poisoning and in extensive corrosion of the alimentary canal. In emptying the stomach two types of procedure may be followed—the administration of emetics and lavage. Emetics are most easily given and have the advantage of not causing struggling on the part of the patient. If possible, however, lavage, employing the stomach tube, either through the mouth or nose, is to be preferred since it cleanses the stomach more thoroughly and also permits the introduction of chemical antidotes. Moreover, it is less depressing to the patient and must be employed when poisons have been taken that inhibit the vomiting centre—for example, chloral or morphine.

If emetics are administered repetition should be practised at intervals of 15 to 30 minutes if necessary. Apomorphine (5 mgm. (grain $\frac{1}{10}$) in 1 per cent solution = 5 cc.,) subcutaneously is very rapid and effective in its action but has a distinctly depressing influence. Its great advantage lies in the fact that it is the only emetic that can be given hypodermically and is particularly useful when resistance to treatment is offered. Copper sulphate or zinc sulphate are safe and efficient emetics. Copper sulphate is perhaps more effective than zinc sulphate but it is also more irritant. Both produce a minimum of depression. They should not be employed when irritant poisoning is under treatment. The dose of zinc sulphate is 2 gm. in a glass of water; for copper $\frac{1}{2}$ gm. at once or three doses of 0.3 gm. fifteen minutes apart. If vomiting does not occur the copper salt should be removed by lavage. In emergencies a dessert spoonful of ground

mustard stirred into a cup of tepid water may serve as an efficient emetic. At times it is desirable that the entire alimentary tract be cleansed and for this purpose cathartics should be employed. They need not be given, however, until the most acute symptoms have subsided. The saline cathartics are to be recommended for this purpose; oily cathartics in general should be avoided. Enemas are of little value.

Administration of Antidotes.—An antidote neutralizes the action of a poison either by changing its physical state or its chemical composition, thereby preventing its action or retarding its absorption. Since the compounds formed by administration of antidotes may be only slightly less toxic than the original poison or may become poisonous by remaining in the stomach the giving of antidotes should be combined with lavage or the administration of emetics. If lavage is practiced the antidotes may be added to the wash-water; if emetics are used antidotes may be administered between the intervals of vomiting. In general antidotes should be given repeatedly at short intervals. In the selection of an antidote care should be exercised that it be as harmless as possible and that the substance resulting from its action is practically inert, at least, temporarily.

Some antidotes, like raw eggs, acacia, milk, boiled starch or flour, which may be given in quantities as desired, act either by combining with the poison to form an insoluble compound—for example, eggs in the case of metals, especially mercury, or by enveloping the poison temporarily in an impenetrable membrane, hence lessening absorption, accomplished in part by delaying the exit from the stomach. In the case of irritant poisons these antidotes also tend to allay inflammation.

One of the most valuable antidotes is tannin which acts as a precipitating agent. This may be employed in

the form of very strong hot tea which may be given ad libitum. Alcohol diminishes its efficiency since the precipitates formed are, for the most part, soluble in alcohol. The following antidotes will be found useful against specific poisons—*Alkaloidal poisons*—15 drops of tincture of iodine in half a glass of water. *Barium*—either sodium sulphate (Glauber's salt) or magnesium sulphate (Epsom salt). *Oxalates*—calcium either in the form of chalk, lime water, or whiting. *Phosphorus*—copper sulphate or old turpentine. *Acids*—weak alkalies such as chalk, baking soda, soap, burnt magnesia. *Alkalies*—weak acids, as vinegar or lemon juice. *Alkaloids, glucosides and phosphorus*—antidotes for these poisons are oxidizing agents which tend to oxidize and hence to nullify the action of the poison. Potassium permanganate, about 2 grains of the crystals in a glass of water, repeatedly given if vomiting occurs or at least a liter of a 0.05 per cent solution. In no case should any undissolved crystals be administered. For *hydrocyanic acid* poisoning potassium permanganate, hydrogen peroxide or sodium thiosulphate may be employed.

In treatment of poisoning the hypodermic administration of antidotes is sometimes useful, thus for hydrocyanic poisoning sodium thiosulphate may be employed and sodium carbonate may be injected to counteract the action of acids. After poisons have had opportunity for absorption attempts to hasten elimination are sometimes made. The results have not been highly successful. At times, however, some of the measures to be employed are of value. It is, of course, evident that stimulation of the renal function will undoubtedly aid in ridding the body of poison. In choosing a diuretic it should be remembered that water is the best diuretic known. It should be given in large volumes, 4 to 8 liters in 24 hours, if maximum beneficial

results are to be realized. Hypodermic injection of 0.9 per cent solution of sodium chloride repeatedly given in liter quantities will also increase urinary excretion. Intravenous infusion of the same solution may at times be employed. Venesection may be of value in some types of poisoning but the blood drawn (up to a liter) should be replaced immediately by an equal or double volume of isotonic salt solution.

Another class of antidotes is the so-called group termed "physiological antidotes" or "physiological antagonists." These antidotes do not really nullify the effects of poisons; they merely mask the symptoms produced. They are employed only against absorbed poisons and tend to combat the symptoms produced by arousing the opposite action. In this way they sometimes are of value in carrying the patient over a critical period and aid in conserving life. Some of the physiological antagonisms are atropine to pilocarpine, caffeine to morphine, strychnine to nicotine, chloral to strychnine, atropine to morphine, chloroform to strychnine, etc.

Symptomatic Treatment.—In most cases of poisoning symptoms produced by the absorbed poison are the most dangerous and these should receive attention from the beginning of the treatment. One of the first functions to fail is the respiration. Treatment to sustain respiration should not be delayed until respiration has actually ceased but reflex stimulation of the respiratory centre should be begun as soon as any evidence is given of the weakening of respiration. For this purpose use may be made of inhalation of ammonia water, or smelling salts, or by administration of aromatic spirits of ammonia (half a teaspoonful in a glass of water), whipping with wet towels, mustard plasters, etc. Or if desired, agents to act directly upon the respiration may be employed, as hot coffee, atropine (0.001 gram)

or strychnine (0.002 gram). If none of these measures is effectual artificial respiration should be practiced.

In certain types of asphyxiating gas as CO oxygen inhalation alone or inhalation of oxygen with small percentages of CO₂ may be of benefit.

In attempting to stimulate the poisoned heart intravenous infusion of isotonic salt solution alone or with the addition of epinephrin (1:100,000) may be of value. Dilatation of the heart may be relieved by venesection. The patient should be kept quietly in bed, cooling prevented by application of heat; pain controlled by anodynes; convulsions counteracted by chloroform; and coma combatted by stimulants such as coffee or atropine.

For poisoning cases the following suggestion by Sollmann is highly recommended:

“Antidotes for First Aid.—Every physician should keep the following antidotes together, in a special satchel (“Antidote Bag”) so that they can be readily transported. The dose should be written on each container. Amyl nitrite pearls; Apomorphine tablets, 2 mg.; Atropine tablets, 1 mg.; Caffeine-Sodium Benzoate; Chloroform; Cocaine Hydrochloride tablets, 0.03 gm.; Tincture Iodine; Copper Sulphate, powdered; Lime water; Magnesia, calcined; Potassium Permanganate, 1 per cent solution (to be diluted twenty times); Sodium Sulphate; Spiritus Ammoniaë Aromaticus; Strychnine Sulphate tablets, 2 mg.; Whiskey; also a hypodermic syringe in good order, and a stomach tube with funnel. The following should be demanded at the house of the patient: Boiled water; Coffee (strong, hot, and black); Eggs; Hot-water bags; Milk; Mustard; Salad oil; Salt; Soap; Starch, boiled; Tea; Vinegar.”

In criminal cases of poisoning the physician should carefully note and record the symptoms observed and take

possession of any suspected substances such as medicine, food, drink, and he should also preserve vomitus, urine and feces. In the event of an autopsy where a chemical analysis is anticipated it is desirable that the chemist be present. In this way much more satisfactory correlation may be obtained in tracing the origin of the organs than if they are delivered to the chemist by the physician. Moreover, the chemist will also be able to testify that the vessels containing the organs and tissues are chemically clean.

In many instances it is deemed sufficient to examine the stomach and intestines for the presence of poisons. This, however, is not good practice. In addition to the tissues mentioned portions of all the principal organs including the brain, cord and urine of bladder should be secured, especially if the nature of the poison is unknown. In the event that a quantitative estimation of the poison will be called for the total weights of the organs selected should be determined. The various organs and tissues should be preserved in separate vessels without addition of antiseptics and the chemical examination should be begun as soon as possible after the autopsy although in most instances poisons do not rapidly disappear from the body after death. On the other hand poisons that are gaseous or readily volatilized may disappear very rapidly after death.

The autopsy itself may not reveal the cause of death. Indeed in most cases of death by poisoning the autopsy fails to show the cause of death. In this event chemical examination is relied upon to furnish the proof. At times even this fails for the poison may have been largely eliminated and exist in any particular organ in quantities too small to be detected by present day methods or it may be a poison for which there is no specific chemical test. In most instances, however, the chemical examination may be relied upon to give the desired information.

The autopsy is of great value in suspected poison cases though no evidences of poisonous action on the organs and tissues can be demonstrated even on microscopic examination, for it affords an opportunity to determine whether death could be ascribed to natural causes. In the event that the organs and tissues reveal no pathological aspects suspicion of poisoning is even more firmly established.

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CHAPTER II

INORGANIC POISONS

CORROSIVE ACIDS

The action of mineral acids is entirely local and the effects produced depend upon the concentration of the acid. When brought into contact with the skin or mucous membrane these agents cause death of the tissues. Applied to the skin the concentrated mineral acids cause an intense inflammation which may be regarded as a characteristic reaction. When strong mineral acids are swallowed there is an immediate sensation of burning in the mouth and gullet. Intense pain is felt in the stomach, and vomiting of brown or black matter mixed with blood may occur. Portions of the mucous membrane of the stomach may be present in the vomited material; swallowing may be either very difficult or altogether impossible because of the swollen condition or stricture of the œsophagus. There is great thirst, scanty urine and constipation. When the corrosive action has involved the larynx and trachea, there may be difficulty in speech and some cough. Respiration is difficult. The pulse is small and weak, the skin is usually clammy and cold. The face is intensely anxious. The mouth and lips are generally blistered although sometimes such signs are absent. Death occurs suddenly either from suffocation or from shock. Perforation of the stomach or intestines may take place. In those cases where recovery ensues the general health may be impaired, the coats of the stomach specifically suffering more or less permanent injury. When

only a small quantity of acid has been swallowed after effects of the poison are pyloric ulcerations and stenosis.

The mineral acids are rarely employed for the purpose of homicide and in the few cases on record the victims have been either children or insane persons. The concentrated acids, especially sulphuric, have been used more frequently for disfiguring the face. Suicidal deaths by concentrated mineral acids are not uncommon.

SULPHURIC ACID (OIL OF VITRIOL)
(H_2SO_4)

Pure concentrated sulphuric acid is a heavy, oily, colorless liquid (specific gravity 1.800 to 1.845) which when added to water causes a sharp rise of temperature. It has the property of blackening or charring organic substances.

Local Action.—The contact of sulphuric acid with the skin causes great pain and the area of contact becomes first white, then brown. Shortly thereafter the surrounding skin becomes red and swollen. A lasting scar occurs owing to the destruction of the epidermis. Sometimes the destructive action involves also the underlying deeper tissues. Thrown into the eyes an intense conjunctivitis follows or blindness may result.

Treatment of sulphuric acid burns on the skin must be prompt. This consists of dilution of the acid with large volumes of water. If the face is involved it should be immersed in successive basins or pails of water or held under a tap of running water, and the eyes opened under water. Later treatment includes application of a paste of sodium bicarbonate, subsequent washing and bandaging the burned area with a bland oil, or coating with a low melting paraffin. Infection of the wounds should be guarded against by proper dressing.

Symptoms.—When sulphuric acid is taken by mouth there is instant pain which extends along the track of the acid from the mouth to the stomach, especially along the smaller curvature. The tongue may become so swollen that it fills the mouth. It has a white coating and may become a disorganized and shapeless mass of burned flesh. In certain instances swallowing is inhibited and the acid instead of passing down the esophagus runs out of the mouth on to the chin and neck characteristically corroding these areas.

Salivation is profuse and may persist especially because of an inability to swallow owing to the inflamed condition of the pharynx. Sometimes the acid reaches the larynx with resulting spasmodic closure of the glottis causing a gasping respiration and a hoarse voice.

Retching, vomiting and extreme thirst are quite characteristic. The vomitus is very acid, filled with mucus, sometimes blood stained and contains pieces of the mucous membranes of the œsophagus and stomach. The face shows extreme anxiety, the pulse is feeble, the respiration difficult, the skin clammy, the eyes sunken and the extremities convulsed. Death in asphyxia, coma or convulsion may occur in a few hours or be delayed for several days. If death does not occur there is usually a stricture of the œsophagus or pylorus.

Post Mortem Appearances.—Post mortem appearances differ according to the period of life after swallowing the poison. In an early death the characteristic features are those of acute corrosion of the structures of the mouth, œsophagus and stomach. With the exception of the stomach the tissues are white or gray in color and give evidence of distinct erosion. The stomach may be red or brown from the formation of hematin from the hemoglobin of the blood, or black from the charring of the mucous

membrane. The membrane is swollen, and may be so softened that it peels readily. When death occurs only after several weeks characteristic appearances include ulceration and contraction of the œsophagus, absence of mucous membrane of the stomach with its walls thickened and red, and the presence of adhesions, the total capacity being greatly reduced by contraction of the scar tissue.

Fatal Dose.—The fatal dose is quite variable, the outcome depending upon the portion of the alimentary canal most seriously injured. The smallest fatal dose on record for an adult is 3.8 grams. On the other hand, 20 drops may prove fatal to a young child.

Treatment.—Treatment consists in neutralization and dilution of the acid and the relief of other symptoms that may appear, such as asphyxia induced by swelling of the larynx. Neutralization is best effected by the administration of weak alkalis, as the carbonates, or calcined magnesia. In an emergency, soap suds or whiting may be employed. It must be emphasized that all antidotes should be given suspended or dissolved in large volumes of fluid, water or milk. In the event that neutralizing agents are not available large volumes of water may be given with raw eggs. It may be necessary to perform tracheotomy or intubation, and morphine may be essential to allay the pain. Neutralization of the acid will, of course, only prevent further destruction of tissue; it will have no influence upon the tissue already destroyed. Whatever remedial measures are to be taken must be resorted to with great promptness.

NITRIC ACID (HNO_3)

Pure nitric acid is a colorless liquid with a boiling point of 86°C . It is a strong oxidizing agent and in the presence of sunlight decomposes into water, oxygen and lower

nitrogen oxides. In medicine it finds a use as a caustic, corroding organic substances by oxidation. Protein substances are turned a deep yellow and are dissolved by it.

In general poisoning by nitric acid is less frequent than with sulphuric acid. When ingested in solutions of less than 20 per cent, local effects are not prominent. When, however, concentrations of 35 per cent or more are taken a very rapid destruction of tissue occurs. The action is very similar to that of sulphuric acid and the symptoms are quite alike except that the parts in contact with the acid are at first white and later become stained deep yellow. There is intense pain, vomiting and great thirst.

Fatal Dose.—The fatal dose varies greatly in accord with the area with which the acid comes into contact. If it enters the larynx very small quantities are sufficient to produce death from asphyxia. In general, however, it may be stated that three fluid drams constitutes a fatal dose in adults. Death may occur within an hour or less or may be delayed for days or weeks.

Post Mortem Appearances.—The post mortem appearances are those of erosion. The mucous membrane of the mouth and pharynx may be yellow, or greenish in color, much swollen and peels easily. The gullet, stomach or intestines may be perforated, or much contracted and very brittle. Portions or the entire mucous membrane of the stomach may be absent, or ulceration may be prominent.

Treatment.—The general treatment for nitric acid poisoning is similar to that outlined for sulphuric acid. Promptness is of great importance for strong nitric acid acts with such rapidity that aid must be given immediately to be of any value.

HYDROCHLORIC ACID (HCl)

Pure hydrochloric acid is recognized as "a liquid composed of 31.9 per cent by weight of absolute hydrochloric acid, and 68.1 per cent of water. It is a colorless, fuming liquid, of a pungent odor, and intensely acid taste." Its specific gravity is about 1.158 at 25°C.; it is miscible with water in all proportions and also with alcohol. Formerly called Muriatic Acid it finds a useful place in the United States Pharmacopœia where the official preparation is described.

Symptoms.—Although hydrochloric acid is distinctly corrosive to mucous membranes it is not nearly so active in this respect as either sulphuric or nitric acid. For this reason when swallowed stricture of the esophagus is much more common as a sequel than perforation of the stomach. Inasmuch as hydrochloric acid is quite volatile its fumes may cause inflammation of the larynx and air passages. When taken by mouth there is instant pain which later extends to the esophagus, stomach and abdomen. At first the lips, tongue and the buccal cavity in general are white in color but later turn brown. Other symptoms are difficulty in swallowing, husky voice, irregular respiration, feeble pulse, general weakness, retching and vomiting. If recovery follows there is frequently stricture of the esophagus or pylorus.

Fatal Dose.—The fatal dose varies with the manner in which the acid is ingested. A few drops entering the trachea may cause death while a fatal outcome is to be expected from a fluid dram taken directly into the stomach.

Fatal Period.—The period of life may range from 2 hours or less to 24 hours.

Post Mortem Appearances.—Post mortem examination reveals no feature which would differentiate hydrochloric

acid effects from those induced by sulphuric or nitric acids except that with sulphuric acid the destruction of tissues is greater and with nitric acid the appearance of the tissues is quite peculiar.

Treatment.—The treatment for hydrochloric acid poisoning is the same as outlined for sulphuric and nitric acids—namely, neutralization and dilution of the acid by a weak alkali in large volumes of fluid, either water or milk.

POTASSIUM CHLORATE

Commonly employed in saturated solution as a mouth wash in cases of sore throat and stomatitis, especially in mercury poisoning, potassium chlorate frequently gives evidences of toxicity if swallowed. It should not be taken internally since as far back as 1879 Jacobi pointed out the serious effects produced when the drug is absorbed. Upon absorption methemoglobin is formed, an indefinite amount of hemoglobin being used up in this way since the chlorate apparently does not enter into the reaction. As a result of this fact the action of chlorate may be very severe leading to a real asphyxia. Moreover the blood cells disintegrate resulting in embolism. Other secondary symptoms which may appear are jaundice, hemoglobinuria, anuria or suppression of urine, bloody-tube casts, delirium, coma and death from nephritis. The chlorate passes through the body unchanged.

Symptoms.—The symptoms of poisoning indicate gastric irritation, nausea and vomiting, diarrhoea with pain in the abdomen, cyanosis, collapse and perhaps terminal convulsions may appear. The nephritic condition has already been mentioned.

Fatal Dose.—There is great variation in susceptibility to the drug and herein lies one of the great dangers atten-

dant upon its use. If given in divided doses the toxic effect is greater than if administered in a single dose. The fatal dose varies from 15 to 30 grams, 10 grams producing toxic symptoms. In one instance death occurred with 11.65 grams.

Fatal Period.—Symptoms begin quickly and death may result in 5 or 6 hours but usually the fatal termination occurs in 6 or 7 days as a result of the nephritis produced.

Post Mortem Appearances.—On autopsy the findings correspond with what might be expected from the symptoms—gastro-enteritis, and inflammatory changes in the spleen, liver and kidneys. These organs are enlarged and dark brown in color from the contained methemoglobin.

Treatment.—Treatment of poisoning with potassium chlorate consists of thorough lavage of the stomach, and treatment of the secondary symptoms as they arise.

CORROSIVE ALKALIES

SODA, POTASH, AMMONIA

In general, poisoning by the caustic alkalies is accidental rather than intentional. Inasmuch as soda and potash are so similar chemically as well as in the effects they produce a single description will suffice for both.

The forms of potash most commonly encountered are caustic potash or potassium hydroxide (KOH), either as a solid or in solution; potassium carbonate (K_2CO_3) or bicarbonate ($KHCO_3$); pearl-ash an impure commercial product. Soda is found in commerce as sodium hydroxide (NaOH), carbonate (Na_2CO_3) washing soda, or bicarbonate ($NaHCO_3$). In concentrated form all these substances produce similar toxicological effects differing only in degree.

Symptoms.—Applied locally the caustic alkalies destroy tissue in a manner similar to the concentrated mineral acids. As a rule the tissues affected are white and softened, in fact, somewhat gelatinous. The injury usually penetrates deeply and scar formation and contraction of tissue are very much alike with acids and alkalies.

Taken by mouth the caustic alkalies produce a strong soapy taste, which is nauseating. Pain is experienced in the mouth, throat, and stomach which later turns into pain of a colicky nature with great abdominal tenderness. Violent vomiting may take place at once, the vomitus containing mucous shreds and blood. The mucous membranes of the mouth and adjacent tissues become white and swollen, portions being destroyed and the lips and tongue may turn brown. There is difficult respiration due to constriction of the pharynx; the face is extremely anxious, the pulse rapid and feeble, and the entire body is bathed in perspiration, the skin being cold. If death does not occur immediately it may result within a few days from obstruction of the air passages, or unless surgical interference enters death from starvation may occur owing to constriction of the œsophagus.

Fatal Dose.—Ordinarily the fatal dose is about $\frac{1}{2}$ ounce (15.5 grams) of the caustic hydroxide although as little as 30 grains (2 grams) have caused death.

Fatal Period.—Death may ensue within 3 hours although usually not so rapidly. Generally death occurs within 24 hours.

Post Mortem Appearances.—The post mortem picture reveals the mouth and esophagus much softened, swollen and white. The mucous membranes of the stomach and intestines are bright red or black, partially destroyed and disorganized in areas of patches. Ulcerations and strictures of the esophagus or pylorus are quite characteristic.

Treatment.—The treatment consists in neutralization of the alkali by large volumes of weak acid, such as lemon juice or vinegar. The stomach tube should not be passed owing to possible rupture of the injured walls of the stomach and esophagus. Pain may be allayed with morphine, collapse by suitable stimulants.

AMMONIA (NH_3)

Ammonia is a colorless gas, with a characteristic odor, irritating to the eyes and mucous membranes of the air passages. A strong solution in water forms ammonium hydroxide which has all the chemical properties of the gas.

Symptoms.—The character of the pathological effects produced by ammonia depend upon the concentration and the manner of administration. If the vapor penetrates the respiratory passages there is a feeling of suffocation followed by pain and the sense of weight in the chest. Death may occur in a very few minutes from asphyxiation. The gas is a strong irritant to the respiratory tract and even in low concentration is regarded as an irrespirable gas. The influence of ammonia upon the tissues in general is similar to that of sodium or potassium hydroxide, that is, the proteins are dissolved and water is withdrawn.

Take by mouth in solution ammonia causes by its corrosive action burning pain in the mouth, esophagus and stomach, salivation, vomiting, and difficulty in swallowing, or even complete inability to accomplish this reflex. Rapid absorption occurs and the absorbed poison may stop the action of the heart very quickly, or unconsciousness may ensue. There may be delirium and as a sequel, if death does not occur soon, partial or complete stricture of the esophagus.

Fatal Dose.—The fatal dose is quite variable since death has been caused by doses as small as a teaspoonful of con-

centrated ammonia, whereas recovery has followed the ingestion of a fluid ounce.

Post Mortem Appearances.—The post mortem appearances are those characteristic for the other corrosive alkalies—the primary feature being an inflammatory condition of the alimentary canal brought into contact with the poison. The gas produces corresponding inflammatory reactions in the respiratory tract.

Treatment.—Treatment is identical with that outlined for the other corrosive alkalies—namely, neutralization and dilution of the poison. The best antidotes are weak vinegar, lemon juice, oil, butter or milk. Large volumes of fluid should be administered. Other symptoms should be treated as they arise.

IRRITANT POISONS

PHOSPHORUS (P)

Phosphorus ordinarily occurs in two forms—the crystalline, waxy phosphorus, and an amorphous form which is made from the first by high heat in an absence of oxygen. The waxy phosphorus is usually kept under water and turns yellow. This yellow phosphorus is extremely poisonous. Red phosphorus or the amorphous form is non-toxic. It spontaneously takes fire at 50°C. a temperature which may be attained by friction of the hands. To avoid danger of burns phosphorus should always be handled with forceps, never with the fingers. Yellow phosphorus smells and tastes somewhat like garlic. It is only slightly soluble in water, alcohol and glycerol. It is readily soluble in carbon bisulphide, ether and almond oil. White fumes of P_2O_3 are given off when it is exposed to the air, and in the dark a faint phosphorescence may be observed.

Phosphorus poisoning is not so common as in the past since in this country at least its use as the basis of matches has been forbidden. Previously when matches made with phosphorus were common, poisoning by phosphorus accidentally, or with suicidal intent was quite frequent. Even more serious perhaps was phosphorus poisoning from an industrial standpoint since many chronic cases were caused in match factories. In this form of poisoning by phosphorus particularly characteristic were the necrosis of the jaw, especially the lower, and caries of the teeth. Various commercial preparations for the extermination of rats contain phosphorus as a basic principle. According to the researches of Tardieu there exist three acute forms of phosphorus poisoning—(1) the ordinary form, characterized by local irritation and jaundice, (2) hemorrhagic form in which both jaundice and blood effusions occur, and (3) a nervous form, in which jaundice is accompanied by outstanding symptoms indicating nervous action. Nearly all the cases show jaundice and changes in the blood.

Symptoms.—The first symptoms are the garlic-like taste in the mouth, burning sensation in the throat, severe pains in the stomach, and generally intense thirst. Vomiting and purging occur and the breath may be phosphorescent. The vomitus may contain blood, have a garlic-like odor and emit light. Sometimes the symptoms are delayed for many hours. The surface of the body is bathed in sweat, nervous and muscular debility is very great and even in the early stage of poisoning death may result from collapse.

Usually, however, there is a distinct lessening of the symptoms of irritation and the patient may appear on the road to recovery. Jaundice soon appears, however. The liver increases in size, later, however, it may atrophy.

Abdominal pain is severe, vomiting and diarrhœa set in, the ejected matters containing blood. Hemorrhages are common from mucous surfaces and under the skin. Headache, insomnia and itching eruptions of the skin usually occur. The temperature may be subnormal. The urine contains bile pigments, albumin, blood, casts and at times leucine and tyrosine. Additional symptoms are great prostration, rapid, feeble pulse, delirium, convulsions, and coma which gradually ends in death. Death may be caused primarily by the weakness of the heart muscle due to degeneration. At times it is hard to differentiate between the effects of phosphorus poisoning and acute yellow atrophy of the liver.

Fatal Dose.—As small a quantity as $\frac{1}{8}$ grain has proved fatal but ordinarily $1\frac{1}{2}$ grains may be regarded as the fatal dose.

Fatal Period.—The fatal period varies from less than 1 hour to many weeks.

Post Mortem Appearances.—Post mortem examination reveals one characteristic feature, namely, a widespread degeneration of both muscle and glandular tissues—the so-called fatty degeneration, the cellular contents being replaced in large measure by infiltration of fat. The liver, kidneys and muscles, particularly of the heart, are chiefly affected.

When death occurs quickly there may be extensive destruction of the stomach coats, ulceration, perforation or even gangrene. The stomach contents may give evidence of the presence of phosphorus, that is, garlicky odor and phosphorescence. Blood changes are profound, the red cells appearing almost colorless and transparent, the hemoglobin being dissolved in the plasma and the blood clotting only with difficulty. Hemorrhages may be

found in serous membranes, in the pleural and pericardial cavities, and on the surface of the brain and cord.

Treatment.—Treatment of phosphorus poisoning consists in the use of the stomach tube at the first possible moment, the stomach being washed with 1 per cent potassium permanganate solution. Potassium permanganate oxidizes phosphorus to phosphoric acid which is harmless. The lavage with permanganate should be repeated frequently since any food in the stomach will unite with it also and thus leave little or none to act as an antidote. Dilute (1-3 per cent) hydrogen peroxide is perhaps even more effective. Old or oxidized turpentine forms with phosphorus an insoluble compound, hence, turpentine if old may be employed in this connection, one dram to a pint of water, frequently repeated.

Copper sulphate has been recommended as an antidote and is of distinct value although its use in the doses necessary may aggravate the gastro-enteritis already present or may initiate this condition itself. Copper is said to form a coating on the phosphorus preventing its absorption.

Further treatment consists in the administration of mucilaginous drinks containing magnesia in order to have free movements of the bowels. If the bowels do not move freely magnesium sulphate may be given. Oils and fats should be avoided, as they increase solution and absorption of phosphorus. From experiments on animals it is suggested that in acute phosphorus poisoning liquid petrolatum may be of benefit in treatment.

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CHAPTER III

POISONOUS GASES

The group of poisonous gases is readily divisible into two subdivisions—(1) those producing toxic effects by combinations with the hemoglobin of the blood, and (2) those causing poisoning because of their specifically irritant properties upon the mucous membrane of the respiratory tract.

The first group comprises such substances as Carbon Monoxide, Hydrogen Sulphide, and Hydrocyanic Acid. The second group contains the war gases—Chlorine, Phosgene, Chlorpicrin and Mustard Gas, together with Bromine, Iodine and Fluorine. Other gases producing less specific effects are also included in this group.

CARBON MONOXIDE (CO)

Carbon monoxide is a colorless, odorless gas which is practically insoluble in water. As ordinarily encountered it arises from incomplete combustion of coal in stoves, for example, and is one of the chief ingredients of burning charcoal. It is also a constituent of illuminating gas. Owing to the fact that it is inodorous it may be insidious in its action, in many instances accidentally causing death, and it is a favorite method of suicide. It is probable that an atmosphere containing 0.5 per cent will cause death.

Symptoms.—Although the sequence of symptoms which may be induced vary in individual cases the initial stage may be that of excitation. This is followed by intense headache, giddiness, throbbing of the temples, together

with nausea and vomiting. At first there is a rise in blood pressure accompanied by a violent beating of the heart, later the pulse is very rapid but small. Breathing is deep and difficult and as a result of deficient oxygenation there is diminished production of carbon dioxide. When the respiratory center is paralyzed respiration ceases. At times during the period of vomiting inspiration will draw the vomitus into the trachea producing death by suffocation. After a short time the individual loses consciousness and the period of unconsciousness may last for several days. Usually the muscular system is affected, a paralysis being observed which may be either general or may affect certain special groups of muscles. Sensation to pain may be absent for a long period. There is redness of the face and loss of memory, vertigo, fainting, and the heart action, which is at first violent, may become weak and slow and stop. The body temperature is subnormal and there may be an involuntary passage of excreta. A characteristic feature of carbon monoxide poisoning is the distribution of more or less extended patches of a bluish-red color on various parts of the skin. The inhalation of large amounts of carbon monoxide causes a very rapid onset of unconsciousness so that ordinarily the faces of those who have died are placid. The suddenness of loss of consciousness together with some of the other symptoms makes difficult the differentiation of this intoxication from that of the symptoms of drunkenness. Occasionally there are distinct deviations from this picture; for example, there may be tetanic strychnine-like convulsions and a continued condition of excitement in non-fatal cases which simulates alcohol poisoning. In still other cases temporary mania may be seen.

When the poisoning has been severe, but non-fatal, the symptoms are quite similar to those characteristic of

infectious fevers. There may be weakness of the intellect, thought may be irrational and disconnected, and insanity has been observed. There may be even softening of the brain and pneumonia frequently is a sequel. Other results of the intoxication are local inflammations, which may pass into gangrene, and hemorrhages, for example, in the lungs or in the brain. An apparent paralysis of the vasomotor mechanism, resulting in a distention of the capillaries, is evidenced by the red spots shown on the skin. Again there may be eruptions of the skin such as herpes or pemphigus. Generally there is glycosuria. Recovery in some cases is almost instantaneous with no memory on the part of the individual of his condition, whereas in other cases the recovery is very protracted.

With chronic poisoning by carbon monoxide the symptoms are mainly those of anemia. There is impaired digestion, the skin has a gray color, the tongue is coated, there is diminution of the intellectual powers, and sometimes convulsions may occur. There may be muscular weakness which is barely perceptible except by comparative tests.

In certain cases the acute symptoms entirely subside to be followed after some weeks by serious paralyses which often prove fatal.

Poisonous Action.—The poisonous action of carbon monoxide is due to the fact that this gas is easily absorbed by the blood and enters into a definite chemical compound with the hemoglobin forming CO-hemoglobin, which is more stable than oxy-hemoglobin and hence prevents the hemoglobin from carrying oxygen to the tissues. The tissues, therefore, suffer, and particularly is this true of the nervous system. Lack of oxygen in the nerve structures for even a comparatively short period, less than five minutes, is capable of causing permanent damage to these structures.

Fatal Dose.—The fatal dose of this gas is apparently quite variable. It has been shown that when the time of exposure in hours multiplied by the concentration of carbon monoxide in parts per ten thousand of air equals three there is no perceptible physiological effect; when it equals six there is a just perceptible effect; when it equals nine headache and nausea are induced; when it equals fifteen or more conditions are dangerous to life. From certain observations it would appear that about 0.8 of a gram of carbon monoxide is fatal to a man of seventy kilos. The rapidity of death depends more or less directly upon the quantity of gas which has been inhaled so that death has occurred in periods of a few hours to periods of several weeks.

Post Mortem Appearances.—The characteristic features seen at autopsy are the clear rose-red or bluish-red colored patches usually of irregular form scattered over the anterior portions of the body and particularly the neck, face, chest, and abdomen. Since hydrocyanic acid also produces similar patches, in diagnosing, this fact must be kept in mind. As stated previously the cause of this phenomenon is due to the paralysis of the small arteries of the skin which, therefore, become injected with the carbon monoxide hemoglobin. The blood also has a characteristic reddish-blue color which is of diagnostic importance. Congestion of some of the internal organs is quite common and the membranes of the brain are strongly injected. Again the congestion may be localized in the lungs which may be more or less edematous. There is usually a right sided dilatation of the heart, and at times there may be areas of softening in the brain.

Treatment of Carbon Monoxide Poisoning.—To be effective treatment of carbon monoxide poisoning should be carried out as soon as possible. The patient should be

taken at once into the fresh air. Although the combination between carbon monoxide and hemoglobin is much more stable than that between oxygen and hemoglobin nevertheless the carbon monoxide hemoglobin is gradually broken up and the carbon monoxide is breathed out. Moreover in carbon monoxide poisoning it has recently been shown that the blood alkali is greatly decreased. Oxygen deficiency induces excessive over-breathing, thus blowing off an abnormal amount of carbon dioxide from the blood. The result of this acapnial process is that the blood is left abnormally alkaline, and this alkalosis is gradually overcome by the passage of alkali out of the blood. Thus when a man is slowly asphyxiated by illuminating gas the oxygen deficiency, as the blood gradually takes up more and more carbon monoxide, induces such over-breathing that not only is the absorption of the gas increased but an excessive amount of carbon dioxide is washed out of the tissues. As the normal stimulus of breathing is carbon dioxide a point is reached at which the lack of carbon dioxide results in failure of respiration. It is this condition that is chiefly responsible for the failure of breathing frequently observed after the victim of the gassing accident is removed to fresh air. It is only as carbon dioxide reaccumulates in the blood that respiration gradually returns. It may then, for a time, be excessive because of the low alkali in the blood. In order to have correct respiration the alkali must be restored to the blood by the body itself. For this purpose and for the stimulation of respiration the subject is made to inhale oxygen containing ten per cent of carbon dioxide. If it is impossible to subject the patient to this treatment artificial respiration should be resorted to if necessary, or still better, the forced inhalation of oxygen. Transfusion of healthy blood has

been strongly recommended and at times has proved very effective. The patient should be kept as warm as possible. Inasmuch as the carbon monoxide hemoglobin is decomposed below the danger limit within an hour the carbon monoxide being practically eliminated in two to three hours, it is superfluous to use oxygen or transfusion after an hour has elapsed. If the coma continues longer this is due to the earlier injury of the nerve centers by the previous asphyxia. Once this injury has occurred it will not be helped by oxygen. Prognosis is bad if the coma has persisted for more than two days or if edema or cutaneous blebs have appeared. While recovery is usually slow the acute effects generally disappear within three hours.

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HYDROGEN SULPHIDE (H₂S)

Hydrogen sulphide is a colorless, transparent gas which burns with a blue flame and possesses the odor of rotten eggs. It is soluble in water and is a common constituent of the atmosphere of sewers, cesspools, and of the products of putrefaction. In general, hydrogen sulphide is never met with outside of the chemists laboratory so that the few cases of poisoning by the use of the pure gas have been confined to laboratories. On the other hand many cases of intoxication have occurred to men working in sewers or cleaning out cesspools.

Symptoms.—In its pure form in sufficient concentration this gas is very rapidly fatal. In less concentrated form the symptoms produced are nausea, giddiness, cold skin,

labored breathing, irregular action of the heart, great muscular weakness and headache. Death may be ushered in by coma or by convulsions. Even in very great dilutions symptoms may be experienced which are dizziness, headache and febrile symptoms which somewhat resemble those of typhoid fever. Continuous breathing of air contaminated with hydrogen sulphide induces chronic poisoning, the symptoms of which are conjunctivitis, headache, dyspepsia and anemia. Predisposition to boils has also been noticed.

Poisonous Action.—It has been asserted that the toxic action of hydrogen sulphide is due to the formation of a relatively stable compound with hemoglobin, hydrogen sulphide hemoglobin which is not easily decomposed. According to this viewpoint the organs suffer from lack of oxygen and the symptoms induced result from tissue asphyxiation. Recently, however, it has been asserted that when the atmosphere containing hydrogen sulphide is inhaled no combination of the gas is formed with the hemoglobin of the blood nor is any appreciable amount of sodium sulphide formed in the plasma. In the absence of oxygen, blood plasma possesses the property of rapidly oxidizing hydrogen sulphide. These products of oxidation combine in part with the sodium of the plasma. Sodium sulphide is rapidly and completely hydrolyzed by blood or plasma. The absence of oxygen has no effect upon this process. If oxygen is present, however, a large part of the liberated hydrogen sulphide is oxidized. The reduction of blood by hydrogen sulphide or sodium sulphide is the result of withdrawal of oxygen from the corpuscles for the oxidation of the hydrogen sulphide. After inhalation of hydrogen sulphide, or the intravenous administration of sodium sulphide, the sulphide in the blood exists only as dissolved and as yet unoxidized hydrogen sulphide.

The active physiological effects of sulphides are exerted by the hydrogen sulphide in the blood. During the administration of sulphide in any manner the hydrogen sulphide in solution in the blood is a factor in the reaction of oxidation. The rate of oxidation of hydrogen sulphide in the blood is such that in a comparatively short period many times the lethal amount of sodium sulphide may be administered intravenously to animals without any apparent effect. It is quite probable that hydrogen sulphide is not a cumulative poison.

Fatal Dose.—Exact figures on the lethal dose of hydrogen sulphide are lacking but one per cent in air is undoubtedly destructive to life, and 0.02 per cent invariably produces toxic effects. The fatal period depends entirely upon the concentration of the gas. If the gas is in a sufficient concentration death is almost instantaneous. In more dilute concentration death may be delayed for variable periods.

Post Mortem Appearances.—When death has been almost instantaneous the body shows little or no significant change. With slower poisoning the most frequent appearances are edema of the lungs, skin discoloration of the abdomen or of the skin of the whole body, and the offensive and characteristic odor from cavities and soft parts of the body.

Treatment.—Treatment for intoxication of hydrogen sulphide consists in removing the patient to fresh air and if necessary the continuous employment of artificial respiration. The administration of stimulants is helpful.

References

HAGGARD: J. Biol. Chem., 1921, 49, p. 519.

HAGGARD and HENDERSON: Am. J. Physiol., 1922, 61, p. 289.

HYDROCYANIC ACID (HCN)

Hydrocyanic acid or Prussic acid is a colorless, transparent liquid, extremely volatile, intensely poisonous and possesses a peculiar peach blossom odor. This acid is known only in the laboratory except for a 0.2 per cent solution which is used at times medicinally. There are a number of salts of this acid, the cyanides particularly, potassium, sodium, mercury, silver, and gold being the best known. These are employed in commerce, some as constituents of insecticides, others in the process of electroplating. All the cyanides possess very toxic properties and generally the poisoning results from the use of the salts rather than of the free acid. Usually either the acid or the salts are taken by mouth, but cases have been known where intoxication has resulted from inhalation of the gas itself. Hydrocyanic acid is also the product of numerous glucosides, the best known of which is amygdalin of the bitter almond. This glucoside when acted upon by an enzyme known as emulsin hydrolyzes amygdalin into glucose, hydrocyanic acid and oil of bitter almonds. This oil, benzaldehyde, is used as a perfume. Although instances of poisoning with benzaldehyde have been reported it is probable that these have been due to traces of the hydrocyanic acid contained in the oil.

Hydrocyanic acid is rarely employed in criminal poisoning because of its rapid action. Many instances of death by suicide, however, have been reported and such a death is made easy by the fact that the cyanides may be readily obtained. Whether taken by inhalation or by mouth intoxication may take two forms, namely, acute poisoning or chronic poisoning.

Acute Poisoning. *Symptoms.*—The symptoms which come on very rapidly are chiefly dizziness, vertigo, palpitation, intense dyspnea, and unconsciousness. The salts,

especially potassium and sodium, in a concentrated form produce corrosion of the mucous membranes with which they may come into contact producing vomiting. Respiration ceases previous to the heart. Heart action is very feeble and irregular, and the individual may go into violent convulsions which simulate those of epilepsy. Opisthotonos may be observed. The hands are usually clenched. The mortality is very high, being 95 per cent. If the patient survives for an hour recovery generally follows.

Chronic Poisoning.—Repeated administration of small doses of cyanides or inhalation of small quantities of hydrocyanic acid lead to a chronic condition in which the symptoms are chiefly those of cachexia. There may be headache, dizziness, pallor, loss of appetite, and difficult respiration. Peripheral neuritis may also occur.

Fatal Dose.—The smallest fatal dose of hydrocyanic acid is about $\frac{1}{2}$ dram (1.87 c.c. of a 2 per cent solution). In other words about 1 grain of hydrocyanic acid has caused death. In general the minimal fatal dose of hydrocyanic acid is about 2.4 grains. On the other hand recovery has followed much larger doses.

Fatal Period.—Hydrocyanic acid enjoys the reputation of being one of the more powerful poisons, and this reputation is justified more by its extremely rapid action than by its toxic dose. In general, if fatal doses are taken death occurs within $\frac{1}{2}$ hour. On the other hand there have been cases reported in which the individuals did not die for a period of more than 3 hours. With the cyanides there are a few cases in which at least 24 hours have elapsed before death occurred.

Poisonous Action.—Hydrocyanic acid must be regarded as a protoplasmic poison. It forms with hemoglobin a stable compound, cyanhemoglobin, thus depriving the

tissues of oxygen and eventually leading to asphyxiation. The hydrocyanic acid in the body is changed to the sulpho-cyanides which are non-toxic and which are eliminated through the urine and saliva.

Post Mortem Appearances.—The most characteristic feature is that various parts of the body, especially the dependent parts, and the finger nails, show bright red or purple patches. The blood usually is coagulated and dark in color, and hemorrhages are found in various portions of the body such as the pleura and pericardium. If poisoning has been induced by sodium or potassium cyanide characteristic lesions are found in the stomach which resemble those produced by the corrosive action of the strong alkalis. The odor of hydrocyanic acid persists in the body especially in the cavities for a considerable period. On the other hand if the body has undergone a considerable degree of putrefaction this odor may not be present. It is stated that the odor persists in the cavity of the skull for the longest period. In the post mortem examination of a suspected cyanide case, therefore, it would be desirable to open the skull cavity first.

Treatment.—The treatment of hydrocyanic acid poisoning must be prompt. In general the physician should wash out the stomach until the wash water no longer contains the odor of hydrocyanic acid. To this wash water may be added chemical antidotes such as the oxidizing agents, namely, hydrogen peroxide or potassium permanganate. Should a stomach tube not be available vomiting should be induced. Ordinarily, however, the absorption of the poison is so rapid and the effects so prompt that antidotes are usually ineffective. It has been suggested that the patient should be bled profusely, the blood being replaced by double the volume of salt solution. Inasmuch as the primary trouble is in the blood

the last type of treatment deserves serious consideration. Attempts have also been made to transform the cyanide into the sulphocyanide by either hypodermic or intravenous injections of sodium thiosulphate. The symptomatic treatment consists essentially in supporting the respiration. Artificial respiration should be begun at once and maintained so long as the heart beats. Counter-irritation and general stimulants may also be used.

References

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HUNT: Arch. int. Pharmacodyn, et de Ther., 1904, 12, p. 447.
FLURY and HEUBAER: Biochem. Z., 1919, 95, p. 249.

CARBON DIOXIDE (CO₂)

Carbon dioxide is a colorless gas with a slightly acid taste and smell, which does not burn and will not support combustion. It produces suffocation and under the names of "black damp" and "choke damp" it is dreaded in mines because of the possibility of its producing suffocation. Although carbon dioxide is constantly in the atmosphere, even country air containing about 4 parts in 10,000, it is only when it is in the air in excess as in caves, wells, mines, vats, and badly ventilated rooms to the proportion of approximately 7 per cent that it can be said to have detrimental effects. In the atmosphere of rooms poorly ventilated discomfort is produced when about 0.1 per cent of carbon dioxide is present in the air. If 1 per cent is present there is much greater discomfort and headache, dizziness and nausea may be caused by 3 per cent. The exact toxic concentration of carbon dioxide is not definite but it may be stated that an 8½ per cent by volume of carbon dioxide causes distinct dyspnea and rise of blood pressure. The untoward symptoms increase up to 15 per cent but are apparently not dangerous to men.

When 25 and 30 per cent is reached the symptoms are those of depression accompanied by diminished respiration, fall of blood pressure and coma. Much of the discomfort which is experienced in poorly ventilated rooms cannot be laid to the content of carbon dioxide in the atmosphere but to other factors such as increased temperatures, odors, etc., which produce psychic effects.

Symptoms.—According to the degree of concentration of the gas inspired the symptoms may be either sudden or almost imperceptible. If the pure gas is breathed suffocation may be caused by a spasm of the glottis, insensibility results and death follows from apnea unless the patient is taken out of the atmosphere of the carbon dioxide. When the amount is smaller there may be cyanosis and dyspnea on exertion. Profuse perspiration and nausea are common. When a fatal concentration of gas has been breathed the symptoms are those of giddiness, loss of muscular power, sleepiness, pressure in the temples and ringing in the ears. The body collapses, respiration stops, convulsions may ensue, the action of the heart ceases, sensibility is lost, and the limbs become flaccid, the countenance is livid, and death usually occurs without a struggle.

Poisonous Action.—In carbon dioxide poisoning death is ascribed to excessive stimulation of the cerebral spinal system, producing asphyxia.

Fatal Period.—The fatal period is indefinite.

Post Mortem Appearances.—The post mortem appearances are those of typical asphyxia. There is nothing characteristic in the general appearance. Usually there is right-sided dilatation with the vessels of the lungs and brain congested.

Treatment.—Treatment consists in inducing breathing, artificial respiration and administration of oxygen with

stimulation such as application of cold and heat, friction, etc. The body temperature should be maintained.

References

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WINSLOW: Am J. Public Health, 1917, 7, p. 827.

NITRIC OXIDE (NO)

Nitric oxide is a colorless gas which is feebly soluble and neither burns nor supports combustion. If brought into contact with oxygen of the air, brown-red fumes are formed which condense to a yellow liquid. In the manufacture of various products such as gun cotton, oil of vitriol, oxalic acid, and in metal working of various sorts, workmen are exposed to the fumes of this gas, which may produce effects of physiological importance.

Symptoms.—In acute poisoning there is immediate dyspnea, coughing and cyanosis, fainting and diarrhœa and collapse may occur with death within 40 hours. If the poisoning is slight the symptoms may be delayed and are of a slightly different character. Headache, air hunger, thirst, and difficult breathing are quite characteristic. The body may be in a cold perspiration, the face anxious, the eye balls protruded, and there may be intervals of spasmodic coughing followed by vomiting.

Poisonous Action.—The blood is thick and viscid probably owing to a change in its concentration. Inasmuch as this is an irritating gas similar in its effects to those induced by the war gases, it is quite probable that death is provoked by the same type of mechanism (see page 60).

Post Mortem Appearances.—The post mortem appearances are confined to the respiratory tract, inflamma-

tion being very prominent, together with edema of the lungs.

Treatment.—Treatment is that followed in war gas poisoning (see page 63).

NITROUS OXIDE (N_2O)

Nitrous oxide or laughing gas is colorless, possessing a sweet taste and smell, and supporting combustion.

Symptoms.—Nitrous oxide is employed chiefly for its anesthetic effect but at times it assumes physiological importance. In the absence of oxygen asphyxia results.

Post Mortem Appearances.—There are no characteristic changes to be observed.

Treatment.—Treatment consists in the administration of fresh air or oxygen or artificial respiration if necessary, and stimulants.

SULPHUR DIOXIDE (SO_2)

Sulphur dioxide is a colorless gas with a characteristic odor and taste reminding one of the odor of sulphur matches. It does not burn and is formed when sulphur burns. Sulphur dioxide is toxic to both plant and animal life and is a favorite method for fumigation in order to rid rooms of bugs, and fleas, or mosquitos, and bacteria. It is also used as a preservative of foods either as the gas or in the form of its salts, the sulphites and bisulphites (see page 255).

Symptoms.—The first symptoms are those of suffocation with spasms of the glottis, and irritation of the nose, trachea and bronchi, resulting in sneezing and coughing. A certain degree of habituation may be induced in both man and animals. Other effects produced are opacity of the cornea, dyspnea, cyanosis, and sometimes convulsions.

If the poison is taken internally catarrh of the stomach and chronic sulphuric acid poisoning may result.

Poisonous Action.—The primary actions are upon the respiratory tract producing either a catarrhal or an edematous condition.

Post Mortem Appearances.—The post mortem appearances are those characteristic of asphyxia. The respiratory tract presents evidence of an existing inflammatory reaction and the lungs at times may be either slightly or markedly edematous.

Treatment.—For the effects upon the gastro-intestinal tract mild alkalies may be administered and lavage of the stomach should be carried out. For the systemic effects rest in bed and warmth are essential. If evidence of edema arises the treatment should follow that of the war gases (see page 63).

ACETYLENE (C_2H_2)

Acetylene has an odor of geranium and burns with a white flame. When mixed with air it is explosive. It is a product of incomplete combustion and is formed whenever lamps or gas-jets burn without a sufficient air supply.

Symptoms.—In cases of poisoning there is restlessness, hallucinations, laughter. This period of excitement leads finally into deep sleep. These symptoms are associated with vomiting, cyanosis, small irregular pulse and dilated pupils. On coming out of the comatose condition there is dizziness, headache, restlessness and depression for a period of several hours. Acetylene is not a strong poison. Upon continuous exposure it produces edema, malnutrition, and nervous symptoms. So far as the blood is concerned it acts as an indifferent gas.

Treatment.—Treatments consists in the administration of oxygen.

GASOLINE FUMES

With the increase in the use of automobiles a relatively new hazard for life has been introduced. The exhaust gas of automobiles is extremely poisonous. Even when entirely odorless, colorless, and free from soot it is much more poisonous than any other ordinary form of smoke. Therefore neither smoke nor smell is a reliable index of the toxicity of exhaust gas. This gas owes its toxicity for the most part to its content in carbon monoxide, and the intoxication by the fumes from incomplete combustion of gas is due to the content of carbon monoxide. It has been demonstrated recently that the quantity of carbon monoxide in ordinary city streets is considerable and offers a menace to general health. Moreover it has been shown that this low concentration causes and intensifies the development of fatigue.

Every winter there occur throughout the country many deaths in private garages from the exhaust gas of automobiles. Henderson has shown that even a small car produces 1 and a large car or truck 2 or 3 cubic feet of carbon monoxide per minute. When the engine is run idle on a cold day with the garage doors closed the atmosphere of a space large enough to hold a car is contaminated to a very dangerous extent, that is, 25 parts of carbon monoxide in 10,000 of air, within 5 minutes, and to a rapidly fatal extent in 10 minutes. The danger is insidious. The first indication that the victim receives is that his legs give way under him, he lies helpless until consciousness ceases a few minutes later, and in the accumulating gas death by asphyxia follows unless chance brings help within a short period thereafter. There is sufficient oxygen in the air for an engine to continue to run long after it has produced a fatal concentration of carbon monoxide. Although conditions are less threatening to life in public garages

they are nevertheless more continuously dangerous to health. Inasmuch as very few garages have any system of ventilation other than that of simple diffusion of the gas outward and of air inward carbon monoxide headache is an almost daily occurrence with many of the employees in the larger garages. In repair shops the conditions are much worse inasmuch as the employees suffer from headache and nausea. These subacute effects are detrimental to general health and should be recognized.

For the general symptoms and treatment relative to carbon monoxide poisoning see Carbon Monoxide Poisoning, page 36.

Reference

HENDERSON and HAGGARD: J.A.M.A., 1923, 81, p. 385.

ETHYLENE (C_2H_4)

Quite recently this gas has come into use as an anesthetic. It is a colorless, odorless gas constituting one of the components of ordinary illuminating gas to the extent of 4 per cent. Ethylene burns and also supports combustion. It is extremely toxic to flowering plants but to animals and man its chief effect is that of general anesthesia. It produces its anesthetic effects by existing in the blood in a state of physical solution rather than by combination with any of the constituents of the blood. The pure gas itself not only produces anesthesia but may give evidence of asphyxial symptoms. These, however, can be removed by the addition of oxygen without losing the narcotic effect from the ethylene itself.

Ethylene apparently has a direct action on the nervous system, a concentration of 90 per cent maintaining the higher centers in a state of insensibility. The motor reflexes are also abolished at this concentration.

Reference

LUCKHARDT and CARTER: J.A.M.A., 1923, 80, pp. 765 and 1440.

ARSENIURETED HYDROGEN (ARSIN) (AsH_3)

Arseniureted hydrogen is a colorless gas possessing the odor of garlic. It burns with a bluish white flame, and condenses upon a cold body such as a porcelain plate.

Symptoms.—The gas is extremely toxic, being one of the most deadly of the compounds of arsenic. When small quantities are breathed the respiration is slightly quickened with dryness and burning in the throat, temperature is normal, and the pulse rate is increased. If the arsenical atmosphere continues, nausea, shivering, dizziness, and prostration occur, together with chills of more or less severity, and pain in the kidneys. There may be jaundice, the blood becoming dark colored, and the urine may possess a brown or reddish color and perhaps be entirely suppressed. The conjunctiva and skin become yellow and later deepen to a bronze or copper color. The characteristic features by poisoning by arseniureted hydrogen are lumbar pain, icterus and hemoglobinuria. Arseniureted hydrogen besides producing hemolysis causes narcosis and paralysis. Possible contact with arseniureted hydrogen is in chemical laboratories and on board boats. In the latter instance deaths have occurred from ships carrying cargoes of electrolytic ferro silicon containing calcium phosphide, and also batteries of submarines, the arseniureted hydrogen being generated from the lead plates which may contain as much as 0.2 per cent arsenic.

Fatal Dose.—Little or nothing is known relative to the fatal dose for man of arseniureted hydrogen. On the other hand it has been shown that $3\frac{1}{2}$ c.c. per liter of air is rapidly fatal to mammals.

Fatal Period.—Death occurs in a relatively short time, usually within 24 hours, although instances of death at a later period up to 5 or 6 days have been reported.

Post Mortem Appearances.—The characteristic post mortem appearances are those due to the condition of icterus, the skin assuming a dirty yellow or bronzed discoloration, the kidneys are brown, enlarged, and slightly congested, the mucous membrane of the stomach is slate colored or yellow.

Treatment.—Inhalation of oxygen. It has also been suggested that bleeding followed by transfusion of blood is of great value. Other symptoms should be treated as they arise. The channels of excretion should be stimulated if possible.

PHOSPHORETTED HYDROGEN (PHOSPHINE) (PH_3)

Phosphoretted hydrogen is a colorless gas which is sparingly soluble and burns with a greenish flame, or if dry and insufficiently supplied with air the flame is white. This is an extremely toxic gas, although rarely do fatal accidents occur from it.

Symptoms.—The symptoms are irritation of the skin, changed respiration and convulsions.

Post Mortem Appearances.—The most typical of post mortem appearances are anemia of the brain, engorgement of the lungs, liver, and heart, with venous blood.

WAR GASES

CHLORINE, PHOSGENE, CHLORPICRIN, MUSTARD GAS,
PALITE, SUPERPALITE

Chlorine is a greenish, yellow gas, somewhat soluble in water, two and one-half times as heavy as air, and condenses to a yellow liquid, which if perfectly dry, can be stored in steel cylinders.

Phosgene or carbonyl chloride (COCl_2) is a colorless gas with a peculiar odor described as that of "musty hay" by which it may be recognized. Phosgene was first prepared by exposing a mixture of equal parts of carbon monoxide and chlorine to sunlight. The name phosgene was given to the gas to suggest the part played by light in its formation. Phosgene is a liquid at a temperature of 8°C . The toxic action of phosgene is slower than that of chlorine probably because to produce its effects it must undergo hydrolysis.

Chlorpicrin or nitrochloroform (CCl_3NO_2) is a colorless liquid almost soluble in water, but soluble in alcohol. The vapor of chlorpicrin is almost six times as heavy as air. It is not as poisonous as some of the other gases but it was used chiefly because it has a specific action upon the vomiting center. It was used with other gases because it produced nausea and vomiting. This forced the removal of the masks from the soldiers at which time the enemy was overcome by the more poisonous gases which had been fired. In its action it stands mid-way between chlorine and phosgene, being slower in its effects than chlorine, but more rapid than phosgene.

Mustard gas or dichlorethylsulphide ($\text{C}_2\text{H}_4\text{Cl}$)₂S, or yperite is a heavy oily fluid, sinking below water and not mixing with it, of a neutral reaction, having a sweet, ethereal odor and producing extensive burns in relatively small concentrations.

PALITE ($\text{ClCOOCH}_2\text{Cl}$) AND SUPERPALITE (ClCOOCl)
OR DIPHOSGENE

These two gases belong to the same group as phosgene and were extensively used in shells. They are both liquids and inasmuch as their physiological action is similar to phosgene will not be considered separately.

Post Mortem Appearances. Chlorine.—From the pathological aspect chlorine produces injury to the organism by causing immediate death of the epithelium lining the upper respiratory tract. Areas of focal necrosis in the lung itself are attributed to the direct action of chlorine on parts of the lung not protected by bronchiolar spasm. The destruction of the epithelium of the respiratory tract removes the normal protective mechanism and allows pathogenic bacteria from the mouth to find their way into the injured bronchioles within a very short period, resulting in a pneumonia, lobar, lobular or necrotizing—the type depending on the organism concerned. The irritant action of chlorine results in a bronchiolar spasm which eventually causes an acute emphysema or atelectasis. Edema of the lungs, trachea, and bronchi is the most striking feature of acute death from chlorine gassing. It is probably brought about by the direct action of the gas which so damages the bronchi and alveoli as to render the adjacent capillary wall permeable. The coagulation of the plasma as it passes out through the alveolar wall leads to the deposition of fibrin in this situation which must thus seriously interfere with the inflow of blood through the lung, thus putting a strain on the right side of the heart.

Phosgene.—With phosgene gassing the lesions seen at necropsy vary according to the length of time of survival after exposure to the gas. At first, a severe pulmonary edema is associated with extreme congestion and with an inflammatory exudation of fibrin and leucocytes which is most marked in and around the finer bronchioles and which spreads through the lung tissue to a variable extent. A typical lobular or pseudolobar pneumonia is the result. The pneumonia is frequently complicated by a necrotization of the wall of the bronchus, which may involve the adjacent alveoli to form abscesses.

The character of the phosgene lesion is explained by the localization of the action of the gas on the air tubes. The epithelium of the trachea and larger bronchi is not damaged, while that of the smaller bronchi and bronchioles is seriously injured, the more distal portions suffering most. In addition to the changes in the mucosa, the bronchi also show pathological contractions and distortions which result in the more or less complete obliteration of the lumen. These, in turn, lead to mechanical disturbances in the air sacs resulting in a chronic condition of atelectasis or emphysema.

Chlorpicrin.—Chlorpicrin injures the epithelium of the entire respiratory tract, but all portions of the tract are not equally affected. The trachea and largest bronchi, though irritated, suffer only transient injury. The medium size and small bronchi are the most affected. There is a uniform and widespread damage of the alveolar walls which, however, is not severe enough to lead to necrosis.

The overwhelming edema of the lungs rapidly follows exposure to the lethal concentration of the gas. In extreme cases practically every alveolus is filled with fluid. In addition to the fluid in the lung itself there is also marked edema of the mediastinal tissues and pleura which is even more striking than in phosgene or chlorine gassing. Abscess formation, pleurisy, fibrinous or purulent, and organizing pneumonia are common complications. Focal atelectatic emphysematous patches remain as prominent gross evidence of the gas injury.

Mustard Gas.—Mustard gas differs from the other war gases thus far considered in that its effects are not confined to the respiratory tract. Very important actions on other parts of the body especially the skin are of great significance. At first the exposed skin reddens, becomes swollen

and itches, later this skin erythema develops into blisters, sometimes of large size. The mustard burns resemble X-ray and drug dermatitis rather than simple heat burns. In general mustard burns are imperceptible when first received and they remain so until the blisters break. The lesions heal very slowly, due, perhaps, to injury of the blood vessels. They generally become more or less infected although only superficially. After three days exposure the blisters begin to become painful especially on contact with air or mechanical contact of any sort. The wound may remain painful for 3 or 4 weeks or it may take on a gangrenous form. Healing occurs after 5 to 7 weeks by cauterization. Different individuals have a varying susceptibility to mustard gas. Negroes are notably tolerant, and moisture of the skin and perspiration increase the susceptibility.

Symptoms.—Exposure to the gases elicits reactions which are slightly different with the different gases. With chlorine there is at first general excitement as indicated by restlessness, urination, irritation of the eyes, sneezing, copious salivation, retching and vomiting. This is followed by labored respiration with a distinct dyspnoea. The respiratory distress increases until eventually death may occur from apparent asphyxia.

Very small doses of phosgene cause coughing, watering of the eyes and intense dyspnoea. The first symptoms are dizziness and cyanosis on exertion. It usually takes several hours for the symptoms to develop and in the interval there may be no sign of danger. Death is by failure of the respiration.

Chlorpicrin produces coughing, nausea, vomiting, and in large quantity unconsciousness. Secondary effects are bronchitis, shortness of breath, a weak irregular heart and gastritis. A comparison of the three gases shows that

chlorine has a very strong irritating action, the individual becoming excited and in evident distress. With chlorpicrin the character of the reactions produced are very similar to those of chlorine except that they are less pronounced. Phosgene on the other hand appears to cause little or no immediate distress. All these gases have as their most prominent feature the development of an acute intensive pulmonary edema.

With mustard gas an interval of 4 to 16 hours of freedom from distress exists between the actual gassing and the onset of symptoms. There may be a conjunctivitis, leucocytosis, bronchitis, and skin burns. The principal complications are early pulmonary edema and relatively late bronchopneumonia.

Poisonous Action.—With the exception of mustard gas the action of these poisons is confined entirely to the mucous membrane of the respiratory tract. An intense inflammatory reaction is induced which is responsible for the early intensive pulmonary edema. Edema of the lungs causes a very marked concentration of the blood which in turn results in a failing circulation resulting in an inability to proper oxygenation of the tissues, causing death. Body temperature falls very distinctly and there is usually a right sided dilatation of the heart. Mustard gas acts in a similar manner but there is evidence that in addition some of the gas is absorbed and produces additional effects.

On the basis of alterations in blood concentration quite definite stages in gas poisoning may be outlined. These stages stand out most clearly with phosgene, and therefore the picture presented by this gas will be considered first.

First Stage.—In the first few hours (5 to 8) after phosgene poisoning there is a notable decrease in the con-

centration of the blood. The decrease occurs rapidly and then the blood gradually tends to assume the normal concentration. Accompanying the decreased concentration of the blood there is a sharp drop in the chlorides of the blood and a marked increase in the chloride and water content of the lungs. The chlorides of the urine increase immediately after gassing, reaching a maximum between the third and seventh hours, then decreasing. The heart beat is distinctly slowed at first with a tendency to regain the normal or be somewhat above the normal before this period is over. The immediate effect on the respiration is a distinct increase in the rate. Oxygen capacity of the blood, the number of erythrocytes and hemoglobin follow a curve parallel with that of the changes in the blood throughout all stages of phosgene poisoning. The oxygen content of both arterial and venous blood decreases significantly. The saturation of hemoglobin with oxygen decreases somewhat. In general the decrease is more marked in the venous than in the arterial blood.

Second Stage.—The period of blood dilution is followed by an interval during which the blood rapidly becomes concentrated to a point far above the normal value and remains near this level for several hours. In this stage the heart may be markedly decreased in size. During the period of increased blood concentration the chlorides of the blood show a tendency to regain the normal. The water and chloride content of the lungs reach a maximum and then gradually fall. The heart beat and respiration are both accelerated. The temperature drops to a degree or more below normal. Most of the fatalities occur in this stage. The oxygen content of arterial blood remains fairly stationary at a nearly normal value, whereas that of venous blood falls rapidly to a very low level. The saturation of hemoglobin with oxygen decreases rapidly in both

arterial and venous blood, but the fall is greater in venous blood.

Third Stage.—After the period of increased concentration the blood gradually becomes more dilute until it is slightly under the normal value which is eventually gained, and recovery follows. The chlorides of the blood gradually tend to regain the normal level. The chloride and water content of the lungs follows a similar course. The temperature rises to normal or above if recovery is to occur, whereas if death takes place during this period the heart beat and respiration rise but the temperature steadily falls. The oxygen content of arterial and venous blood tends to regain the normal. Chloride excretion by the kidney is markedly decreased but later is much augmented.

It is generally assumed that the cause of death in gas poisoning is due directly to edema of the lungs aided, of course, by the accompanying congestion. It has been stated that death is caused by an individual literally drowning in the water of his lungs. The quantity of water may reach as high as a liter or more and such a conception as the cause of death is quite obvious. The most obvious condition, other than edema, which could lead to death is the concentration of the blood. It is evident that edema and blood concentration are closely associated. Edema is assuredly the cause for blood concentration and thus indirectly, at least, brings about death, but it would appear that blood concentration is much more likely to produce death than is the presence of fluid in the lungs. It has been conceded, however, that blood concentration is immediately responsible for death in these cases. Blood concentration means a failing circulation, an inefficient oxygen carrier, oxygen starvation of the tissues, fall of temperature, and finally suspension of vital activities. The whole aim of treatment in gas poisoning has been to prevent blood

concentration or else restore it to a level more nearly normal. Restoration of blood to a normal concentration permits survival even though an extensive edema exists.

Treatment.—The principles of treatment of gases thus far considered having an effect upon the respiratory tract are very simple, venesection when the blood is diluted and infusion of salt solution during the initial period of blood concentration. Venesection tends to diminish the degree and extent of dilution. Infusion of salt solution tends to keep the blood concentration at a level where it is possible to maintain an approximately efficient circulation. Attempts to change the blood concentration are of little permanent value unless measures are taken in the early period after gassing. Once a highly concentrated blood has been assumed treatment is of little avail. The time and type of treatment is determined by following changes in the concentration of the blood by hemoglobin estimations. Oxygen alone is of little value in gas poisoning since theoretically, at least, there is not a deficiency of oxygen in the arterial blood, and the deficiency in the venous blood is due to the inability of the circulatory organs to push the concentrated fluid rapidly through the capillaries. If, however, the circulation is improved by venesection and salt infusion the addition of oxygen is of distinct value.

The treatment of skin burns from mustard gas poisoning is most successful when the irritation is treated immediately. The successful treatment of the rashes tends to abort the more severe burns. The skin should be scrubbed with kerosene, soap and hot water. The exposed part should be immersed for 1 or 2 hours in Dakin's solution of chlorinated soda or compresses may be applied to the affected part. A 1 per cent solution of alum or aluminum acetate may be substituted for Dakin's solution

which may be too painful. Petrolatum dressings may be alternated with the baths.

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IODINE (I)

It is very unusual for iodine to be employed as a poison with criminal intent owing to the difficulty of disguising its color. It has, however, been used by suicides much more commonly and accidental poisoning is not rare.

Iodine crystallizes in dark gray scales possessing an unpleasant taste and a characteristic odor. Even at ordinary temperature it gives off an invisible vapor which is very irritating to the nose and eyes. It becomes a liquid if heated to 220°F. and then evaporates in violet colored fumes. It is soluble in water with great difficulty, but dissolves readily in alcohol, ether, carbon bisulphide and in water containing potassium iodide. Iodine itself is almost exclusively used externally as the tincture and the liniment. In strong solution iodine may act as a corrosive even when applied to the skin, producing typical blisters and burns.

Symptoms.—The symptoms produced by iodine are those characteristic of irritants in general. Taken by mouth pain results there and follows its passage down the alimentary canal. Subsequently there is vomiting, purg-

ing, extreme thirst, fainting attacks, and collapse. It may also be absorbed from raw surfaces and cause milder symptoms, such as headache, dizziness and gastric irritability. It is excreted by way of the kidneys and may so involve these organs as to cause suppression of urine. As with chlorine and other pulmonary irritants its inhalation leads to inflammation of the lungs and pulmonary edema.

Fatal Dose.—The fatal dose is about one fluid dram of the tincture. On the other hand, recovery has followed after taking one fluid ounce.

Fatal Period.—The fatal period varies from 1 to 6 days.

Post Mortem Appearances.—The post mortem appearances are those common to irritant poisons, namely, inflammation and disorganization of mucous surfaces.

Treatment.—Treatment should be aimed to dilute the stomach contents by large volumes of water, emptying this viscus either by inducing vomiting or by use of the stomach pump. Starch is the specific antidote and it should be given in the form of a decoction of ordinary laundry starch, boiled rice, barley water, etc., so long as it is colored blue by the stomach contents.

For treatment of poisoning by fumes see that given for war gases under "Gaseous Poisons," page 63.

Reference

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IODIDES

The employment of iodides, usually in the form of sodium or potassium iodide, may produce local irritation in the stomach and evidences of irritative reactions on the skin and mucous membranes.

Symptoms.—These reactions partake of the nature of rashes, or of coryza, headache, bronchitis, laryngitis, and conjunctivitis. Stomatitis, parotitis and anorexia may occur but much less commonly. In addition to the general irritation of the mucous membranes of the mouth, throat and trachea there may be salivation with general malaise. The symptoms referred to above lead the patient to believe he has influenza. At times the laryngitis may be so severe that edema of the glottis occurs. The skin lesions consist of irregularly scattered pimples, the chief sites being the face, shoulders, neck and back. In addition to this acne-like appearance "iodism" may manifest itself in the form of furuncles, erythema, purpura, urticaria and vesication, all of which may be accompanied by fever. The more serious eruptions usually occur in patients with a lowered vitality and are especially prominent in chronic nephritis, perhaps owing to inability to excrete iodides which in the normal individual are promptly eliminated.

Usually the less severe skin eruptions are produced by smaller doses and they sometimes disappear when larger doses are given.

Chronic iodism is characterized by anuria, emaciation, nervous irritability, tachycardia, and loss of sexual power. In general, even though definite symptoms are not in evidence large quantities, or long continued use of iodides, tend to lessen body tone and to depress the spirits.

Susceptibility to iodide action varies greatly. In some patients the symptoms appear in a few hours even after a small dose; in others they are manifest only after long continued use. The reactions characteristically induced are not confined to iodides but may be caused by any iodine compound. Thus iodoform may produce the symptoms of iodism. It is probable, however, that these

reactions occur only after dissociation of the compound with liberation of the iodide ion. Formerly the skin symptoms were referred to excretion of the drug by the sebaceous gland, the view being that free iodine was liberated by the fatty acids of the sebaceous secretions. This idea, however, is erroneous and similar symptoms may be induced by the sulphocyanides which in dissociation fail to liberate an irritative ion.

Treatment of Iodism.—The drug should be discontinued. Great cleanliness, particularly of the mouth, the administration of alkalies and arsenic, are indicated. The catarrhal symptoms may be cleared up in one or two days by the use of calcium lactate in doses of 4 grams per day but the calcium treatment should not be prolonged.

IODOFORM (CHI_3)

Iodoform may produce general intoxication when applied as a surgical dressing over a large area. Less frequently it has caused poisoning by internal administration. Iodoform is a local irritant and may cause a dermatitis or a pustular rash. Iodoform is not excreted as such from the body. Instead it reappears in the urine as the iodide or the iodate and as other unknown compounds.

Iodoform occurs in light yellow crystals possessing a penetrating and unpleasant odor and taste. It is insoluble in water, but is soluble in alcohol, ether, glycerol and oils. It melts at 119°C . and volatilizes with steam.

Symptoms.—The symptoms of iodoform poisoning may be of three types (a) gastro-intestinal disturbances as nausea and vomiting, (b) cerebral excitement or delirium, or (c) cerebral depression with melancholia. Death is caused by paralysis of the central nervous system. There may be great lassitude and weakness, hallucinations,

diminished reflexes, mental confusion, light convulsions and coma. The pulse is usually very rapid and there may be a high temperature. In some cases cerebral excitement may be entirely lacking, the only symptoms being those of cerebral depression—stupor and collapse.

Fatal Dose.—Death has been caused by doses of 1.25 grams to 2.0 grams of iodoform and recovery has followed the taking of more than 7 grams.

Fatal Period.—Death may be a matter of less than 24 hours or be delayed for several weeks. This variability depends upon the size of the dose and upon the manner of application.

Post Mortem Appearances.—The characteristic pathological picture presented by iodoform poisoning is fatty degeneration of the liver, heart and kidneys. Edema of the lungs, acute nephritis and congestion of the meninges have also been observed.

Treatment.—If poisoning has occurred from external application the treatment should be stopped. The strength of the patient should be sustained and according to whether there is cerebral stimulation or depression stimulants or sedatives should be administered. For specific treatment potassium iodide has been recommended. Subcutaneous or intravenous injection of large volumes of physiological salt solution are said to be of particular value. Sodium bicarbonate is an antidote.

If taken by mouth, emesis and lavage of the stomach should be practised in addition to the measures indicated above for systemic effects.

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BROMINE (Br)

At ordinary temperatures bromine is a heavy, dark red liquid which if exposed to air is converted into a brownish-red vapor. It boils at 58°C . and at -7.3°C . it is solid. It has an extremely disagreeable odor to which fact it owes its name which signifies a stench. It is soluble in water to a limited extent, and is soluble in alcohol and ether. It acts violently upon organic substances. It attacks the skin causing serious wounds and its effect upon the mucous membranes is very similar to that of chlorine. During the World War bromine was used in hand grenades.

Symptoms.—When inhaled bromine acts as a respiratory irritant. Taken by mouth it exerts a caustic action causing pain from the mouth throughout the alimentary canal producing such profound local effects that death from collapse may ensue in a few hours. The points of local action are characterized by a dark brown stain. The mucous membrane may be softened, inflamed or corroded.

Fatal Dose.—The fatal dose is probably about one ounce of bromine. Generally the quantity taken is too small to cause death.

Treatment.—Treatment of bromine poisoning is identical with that for iodine.

BROMIDES

The more commonly employed bromides are those of potassium, sodium and ammonium and to a less degree those of lithium, strontium and calcium. So far as one may judge sodium bromide is quite capable of fulfilling all the functions and advantages ascribed to the others since it is to the Br ion that the remedial effect is due. The bromides are employed chiefly as sedatives to induce

sleep or to quiet conditions of hyperexcitability as in hysterical states, Basedow's disease, acute cerebral excitement and meningitis, delirium tremens, and convulsions as in epilepsy.

Like the chlorides the bromides are rapidly eliminated through the urine although there is a tendency for the bromides to accumulate in the tissues. The administration of chlorides tends to hasten the excretion of the bromides.

Bromide rashes frequently occur, especially on the face when bromide administration has been continued for a considerable period. These rashes closely resemble those induced by iodides. The reason for the occurrence of these rashes is not clear, a variety of opinions being held but none being above criticism. It is quite probable that the nervous system is involved in some way since vasomotor disturbances accompany the skin rashes.

Symptoms.—Acute poisoning may occur from a single large dose. The symptoms observed are profound depression or apathy, or even a stupor which may last for several days. The respiration is slow and low blood pressure is in evidence. Bromides alone rarely, if ever, cause death.

Bromism or chronic bromide poisoning results from repeated large doses. There is psychic deterioration, the patient being dull, stupid and apathetic; the face is without expression, pale and usually bears diffuse pimples; the memory is weak, speech is disturbed, voluntary movements are sluggish; there may be sexual impotence; somnolence; ataxia, tremors; malnutrition as shown by nausea, gastric irritation, diarrhoea or constipation leading to a general cachexia and a lowered resistance.

Treatment.—Treatment of bromism consists in stopping the administration of the drug and hastening its elimina-

tion as much as possible. Pushing the intake of sodium chloride will aid in this process which should be further assisted by the ingestion of large volumes of water. The nutrition should be improved by careful diet and the depression counteracted by caffeine or strychnine.

CHAPTER IV

METALLIC POISONS

TELLURIUM (Te)

Tellurium occurs free in nature or in combination as a telluride. With other metals it forms grayish white crystals possessing a metallic luster. Chemically it is closely related to sulphur and forms anhydrides which with water produce tellurous (H_2TeO_3) and telluric (H_2TeO_4) acids which are analogous to sulphurous and sulphuric acid. With hydrogen it forms a gas, H_2Te , which resembles hydrogen sulphide in its mode of formation, odor, and reaction with metallic solutions. These solutions, however, are stable and possess odors even more disagreeable than hydrogen sulphide. On combustion dioxide is formed. The compounds which are most often met with are the oxides and the methyl compounds. In general the sodium salts are soluble in water. In medicine sodium tellurate has been employed to suppress sweating in tuberculosis.

Although tellurium is, chemically, closely related to sulphur its pharmacological action resembles very closely that of arsenic. Fatalities from intoxication with tellurium are unknown and its interest from the viewpoint of toxicology is mainly from its employment in industry. In the separation of lead and copper it is met with in the form of fumes as hydrogen telluride, and in dust as tellurous oxide and tellurate.

Symptoms.—The most pronounced symptoms are those of languor, sleepiness, loss of appetite, nausea, pronounced

salivation, depression, garlic odor of the breath, and constipation. The garlic odor of the breath persists for a long time. The toxicity of tellurium is not very great, the oral toxic dose being much less than when the poison is given subcutaneously. The tellurite is much more toxic than the tellurate. Compared to hydrogen sulphide hydrogen tellurite is more irritant and toxic than hydrogen sulphide.

Poisonous Action.—Tellurium compounds produce an action upon the blood which is very similar to that of arsenic, producing leucopenia, a decrease in red count, and hemolysis. With large doses the bone marrow appears red with hyperplasia of the white and red cells. The tellurium compounds are apparently methylated at least in part, and excreted as methyl telluride by the breath, urine and feces. Tellurium appears to diminish and suppress perspiration, and changes the tone of blood capillaries.

Fatal dose and fatal period are unknown.

Post Mortem Appearances.—In animals the post mortem appearances show that the mucosa of the duodenum and jejunum is congested and swollen, contains small hemorrhages, and is covered with a pseudo-membrane. The kidney shows some irritation and the urine has casts, leucocytes and albumin.

Treatment.—The treatment is purely symptomatic.

Reference

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SELENIUM (Se)

Selenium, like tellurium, is chemically closely related to sulphur. It occurs in two forms, either as an amorphous variety which is a black or dark red solid which, on

heating, is transformed to a crystalline fluid possessing a gray color and a metallic luster. Pharmacologically it possesses properties similar to tellurium and arsenic, but is more toxic than tellurium. It has been employed in medicine as a specific treatment for tumors but its use has been discontinued. Selenium is sometimes encountered in industrial plants as selenic acid and sulphates. It has an action in whitening ordinary glass.

Symptoms.—One symptom of selenium poisoning is the typical odor of the breath which is very similar to that of tellurium, that is, a garlic odor, and is due to the production in the organism of the methyl compound. Selenium has a peculiar effect on the mucous membrane of the nose and throat, a catarrh which simulates that of a rose cold. Other symptoms are vomiting and pain in the abdomen and in the lumbar region. Introduction to dogs whether given by mouth or by peritoneal injection speedily causes death.

LEAD—PLUMBUM (Pb)

Lead is a soft, bluish white metal which is very heavy and has a low melting point. If freshly cut the surface presents a brilliant luster which soon disappears owing to the formation of oxide on the surface by its contact with the air. Owing to its characteristic softness, pliability and low melting point it has many industrial uses, such as for solder, type metal, pewter, etc. Although there are a large number of lead salts, all of which possess toxic properties, those which are ordinarily concerned in lead poisoning are the lead acetate, lead carbonate, and lead sulphate. Lead acetate or sugar of lead is soluble in water and has a sweetish taste which later becomes metallic. It forms the basis of various pharmaceutical preparations. Lead carbonate, which is known as white

lead or flake white, or "mineral white," is a mixture of lead hydroxide and neutral lead carbonate. It is employed chiefly as a constituent of paint, and as such is the cause of the so-called painter's colic. Lead sulphate is used to give weight to white silk and is also employed in the painters trade. At times, however, salts, particularly the oxides, cause poisoning owing to the lead dust which is formed in various trades such as lead smelters, zinc smelters, brass molders, workers in type metal, lead type, and shot.

There are various ways in which lead poisoning may occur. In the first place there may be constant contact with lead and its salts in manufactories. It may be caused also by its use in the arts and as a pigment. This is especially noticeable among painters, in the glazing of cards or cardboard, and in makers of Brussels lace. Poisoning may occur by the application of various types of lead-containing ointments, plasters, cosmetics, and hair dyes. A fruitful source of chronic intoxication is from water which has either been stored or conveyed in leaden pipes. Many kinds of foods may contain lead owing to the fact that the containers or wrappers are made of materials of which lead is a constituent. Thus various farinaceous foods, chocolate and tea, may become contaminated and confectionary may contain lead from the use of lead chromate as a coloring agent. Lead poisoning may also occur from the use of tobacco, snuff, since these substances are contained in lead foil wrappers.

Acute Lead Poisoning. *Symptoms.*—Lead is rarely, if ever, used for criminal poisoning. When poisoning does occur it is usually due to an accident. Lead salts in general act as astringents and are also irritant. They are absorbed slowly, chiefly from the alimentary canal, but may be absorbed from the lungs and other tissues or

even in the form of ointments through the skin. The first symptoms of poisoning are a metallic taste in the mouth with dryness of the throat, and intense thirst soon after the poison is swallowed. Within a relatively short period thereafter there is nausea and vomiting which may be persistent. The vomitus may be milky owing to the formation of lead chloride. There is paralysis in the esophagus and stomach with abdominal pain. Either obstinate diarrhoea or constipation may occur, the stools being black from the formation of lead sulphide. The urine may be diminished in volume, the face is anxious, there is a dry skin, the breath is foul, and the tongue is coated. There is more or less specific action upon the nervous system, and although the brain is clear there is pain and cramps in the legs, numbness and local palsies, and paralysis which appears somewhat later. The muscles undergo a form of fatty degeneration. The absorption of lead causes marked anemia with degeneration of the red corpuscles. The symptom which is quite characteristic of lead poisoning is the so-called "blue line" on the gums. This is not present invariably but should always be looked for. Fatal cases eventually pass into coma either with or without convulsions. If the case does not prove fatal apparent recovery takes place within a few days, only later to give rise to the phenomena of chronic poisoning. Perhaps the most characteristic features of lead poisoning are unmistakable colic and wrist-drop.

Inasmuch as lead is a cumulative poison relatively large quantities may be found in the liver, kidneys, brain, muscles, and even in the blood. The excretion of lead is very slow and occurs over a long period of time even when the source of lead absorption has been stopped. The excretion takes place mainly by way of the feces, although

it may be found to a smaller degree in the urine. Saliva and sweat also serve as channels of excretion.

Poisonous Action.—Certain salts of lead possess an astringent property owing to the ease with which they combine with proteins, but this cannot be the entire cause for the toxicity of lead inasmuch as all of the lead salts are more or less corrosive compounds and possess properties as poisonous as the others. Lead appears to produce pathological changes in the kidneys leading to granular degeneration and the kidneys are hard and contracted. There are characteristic local paralyses with atrophy. The muscles involved are wasted and fatty, and there are changes in the large cells in the anterior cornua of the cord and in the peripheral nerve fibers.

Fatal Dose.—According to Kobert the minimal fatal dose of lead acetate is 20 gms., that of white lead 25 gms.

Fatal Period.—The fatal period is quite variable although death usually occurs within a day or two.

Post Mortem Appearances.—The post mortem appearances are not characteristic, the most prominent features being gastro-intestinal inflammation and evidences of inflammation in the liver and kidney.

Treatment.—In acute poisoning it is desirable to rid the stomach as soon as possible of the toxic substances, and this may be accomplished by lavage followed by administration of soluble sulphates such as sodium and magnesium sulphate. If a stomach tube is not available emetics should be employed. For control of the colic and vomiting morphine and atropine are indicated.

Chronic Poisoning. *Symptoms.*—Chronic poisoning is very much more common than the acute manifestations and usually occurs from contact of the metal in industry. Lead possesses a cumulative action and has independent influence upon the blood, upon nutrition, and upon muscu-

lar and nervous structures. The symptoms of chronic lead poisoning are very subtle. Generally the first symptoms are those of ordinary colic and of a general feeling of debility. The appetite is uncertain or may be lost. The mouth is parched, the breath is foul, the skin is sallow and dry, and more or less general emaciation occurs. Anemia, blue line on the gums, local paralysis, especially of the right forearm, presence of blood in the urine, disorders of the central nervous system, the presence of basophilic granules in the red blood cells are all symptoms of chronic lead poisoning, none of which are absolutely peculiar to lead. The basophilic granules and the wrist-drop, lead in urine and feces are usually sufficient to lead to suspicion of chronic lead poisoning. If taken in time the prognosis of chronic poisoning is not unfavorable, if there are no complications such as alcoholism or degeneration of the liver, kidney, heart and blood vessels. If cerebral symptoms occur the prognosis is grave. These cerebral symptoms consist in hallucinations, illusions, delirium, melancholia, pseudoparalysis, coma and epileptiform convulsions.

Chronic lead poisoning may produce changes in the heart and blood vessels leading to arteriosclerosis, valvular degeneration, cardiac hypertrophy, and renal changes with albuminuria. These conditions may be associated with arthritis and gout. The alterations in the vessels may lead to cerebral hemorrhages.

Post Mortem Appearances.—The post mortem appearances in lead poisoning are not characteristic, although the intestines may be constricted with a gray-black discoloration of the mucous lining. The blue line around the gums is highly significant and changes in the cornua of the cord and in the peripheral nerve fibers together with those in the kidney may be prominent.

Treatment.—Treatment in chronic lead poisoning is largely a matter of prophylaxis. The source of lead should be discovered and the patient should be guarded against further exposure to it. The special treatment consists in free bowel movement, best induced by doses of magnesium sulphate, or constipation may be treated with olive oil enemas. The symptomatic treatment is morphine against the pain of colic, hot applications or baths. The palsies may be treated with strychnine, massage and electricity. Although many efforts have been made to hasten the elimination of lead by means of potassium iodide, sweats and sulphur, doubt is expressed as to their efficiency. Perhaps the most promising is the iodide which may at first hasten the elimination but apparently soon loses its effect. Tonics are of considerable importance. Open air exercise and wholesome diet are, however, the best known means of combatting the detrimental effects of chronic lead poisoning.

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SILVER—ARGENTUM (Ag)

Metallic silver is pure white in color with a high luster resisting the action of oxygen. It forms a large number of salts but in toxicology those of importance are the nitrate or protein compounds which are used because of the antiseptic properties of silver. Caustic silver nitrate is extensively employed locally in various affections for purposes of cauterization. In present day therapy argyrisms, or a bluish-black discoloration of the skin, rarely occurs. In true argyrisms the coloring is permanent but no symptoms arise. The application of silver salts to the

skin or mucous membranes causes stains which are quite distinct from argyrisms. These stains may be removed by 10 per cent potassium iodide or cyanide.

Symptoms.—Poisoning from silver usually occurs by the accidental swallowing of pieces of the caustic (Lunar Caustic) silver nitrate especially in infants during the treatment of various conditions of the mouth and lips. Swallowing the caustic causes pain in the throat and stomach, vomiting, gastritis, and later, diarrhœal stools which may show blood. If absorption of the silver occurs dizziness, convulsions, and coma may supervene.

Fatal Dose.—The fatal dose for an adult is approximately 30 grains.

Fatal Period.—Death may occur in a period of 6 hours or more.

Post Mortem Appearances.—The post mortem appearances show the local action of the caustic. Stains on the mucous membranes of the esophagus and gastrointestinal tract will be white at first but will turn black on exposure to light. Inflammation in the stomach and intestines is present.

Treatment of Silver Nitrate Poisoning.—Large volumes of common salt and water (dilute solutions) should be given either as lavage or in combination with an emetic. Usually the salt water itself will act as an emetic. The salt forms the insoluble silver chloride which is not as irritating as the caustic silver nitrate. Lavage should be continued until the wash water no longer gives a test for silver. When this point is reached eggs and milk may be prescribed for their demulcent effect.

MERCURY—HYDRARGYRUM (Hg)

At ordinary temperatures mercury is in a liquid state. It vaporizes at room temperature and has a silver-white

metallic luster. It forms two series of salts—the mercurous and mercuric compounds. Salts of mercury may be regarded as protoplasmic poisons. In virtue of this property mercury salts are active germicidal agents. Their relative insolubility, ease of precipitation, distinctly irritative and toxic properties necessarily limit their wide application. In general, as with arsenic, poisoning occurs only when the salts are dissociated. In this instance, however, the poisonous action is associated with the mercury ion which is very reactive, chemically combining with protein and usually forming an insoluble compound. The mercurous salts in general are less irritative and less toxic than the mercuric salts because of greater insolubility. Certain of the organic mercury compounds, as “*Mercurochrome 220*,” of Young, and *mercuropen* are not irritant although retaining antiseptic properties. The relatively low toxicity and non-precipitation of protein by these compounds are consequences of the non-ionized condition of the substances. Whatever type of mercury compound is employed it may, under favorable conditions, give rise to typical mercury intoxication.

Some of the more common mercury compounds that may cause poisoning when employed medicinally are the various preparations containing metallic mercury, as *Blue Mass* or *Blue Pill* containing 33 per cent of mercury, and used similarly to *calomel*; *Unguentum Hydrargyri* for inunction—50 per cent mercury in suet or lard; or the more dilute *Blue Ointment* (30 per cent mercury) for cutaneous parasites; *Calomel*; *Calomel ointment*; *Yellow Mercurous Iodide*; *Black Mercurial Lotion* (*Black Wash*); *Ammoniated Mercury* in various compound ointment bases; *Yellow Mercuric Oxide* and *Red Mercuric Oxide* in various ointments; *Corrosive Sublimate*, *Potassium Mercuric Iodide*; *Mercury Salicylate*; *Citrin Ointment*;

organic mercury compounds as Mercuraphen, Mercurochrome 220, and Chloromercurphlorescin.

Mercury compounds are readily absorbed from mucous membranes and even from the skin. Mercury disappears rapidly from the blood and is deposited in the various organs probably as compounds of proteins of the cells. Excretion occurs both through the feces and urine and even after a single dose may continue for several days. When mercury has been given continuously for a considerable period its excretion may be a matter of months. Mercury poisoning may be classed into three types—acute, subacute and chronic. Usually the acute effects of mercury poisoning are those induced by corrosive sublimate taken with suicidal or criminal intent. Chronic poisoning or mercurialism is the result of occupation, such as among workers in quick silver mines, in mirror makers, makers of thermometers, barometers, vacuum pumps, furriers and hatters, and munition workers.

Acute Poisoning. *Symptoms.*—The earliest symptom of excessive therapeutic use of mercury is stomatitis. First the breath has a fetid odor, there is a metallic taste, the gums are sore (gingivitis) and salivation (ptyalism) occurs. This stomatitis occurs about as readily when mercury is given otherwise than per os. If the therapeutic administration is continued the edges of the gums become black and the teeth loosen. Later the gums and tongue are swollen and ulceration may occur. Infection sets in and, combined with the accompanying irritation, very severe salivation and progressive exhaustion develop. In the advanced stages the teeth may be lost and necrosis of the jaw may occur. Some grade of stomatitis may follow even the single administration of calomel in certain individuals.

In the more acute types of poisoning the immediate effects are corrosion and irritation. There is a metallic

taste, salivation is pronounced, the mouth and pharynx are ashy in appearance with a burning sensation, swelling of the mucous membrane may occur, and sometimes edema of the glottis is present. There is thirst with abdominal pain, colic, and vomiting with white or bloody mucous shreds. These symptoms usually yield to local treatment including fasting for 1 or 2 days and the patient seems quite well. Symptoms of stomatitis may appear during the first 24 hours.

After absorption the poison appears to act chiefly upon the large intestine and upon the kidney. Generally within 2 or 3 days the urine contains albumin and is greatly diminished in volume, indeed, anuria may develop, followed by death without convulsions in about one week. If the kidneys have not been too severely injured a membranous colitis sets in accompanied by dysentery, tenesmus, ulcerations, hemorrhages and degeneration of the liver. Death may not occur for weeks. In the most severe cases blood pressure may fall, due to cardiac involvement, and there may be vasomotor disturbances, feeble pulse, insensibility of the skin, coma and collapse. Consciousness is usually maintained unimpaired. Sometimes giddiness is experienced or the patient is sleepy and again anxiety and restlessness may be observed.

Should recovery from the acute stage occur subacute poisoning may set in which is characterized by nephritis, stomatitis, and colitis. Sometimes skin eruptions are present. This syndrome is frequently seen in poisoning from the medicinal use of mercury. Usually the stomach and small intestines are not involved.

When mercury poisoning occurs from use other than by mouth the local symptoms are absent.

The kidney appears to be affected even after the ordinary medicinal use of mercury for some albuminuria

is frequently present owing, perhaps, to damage to the renal tissue in its effort to eliminate the poison. When the injury is slight the nephritis partakes of the nature of the interstitial form although the glomeruli and also the epithelium may be affected. Later cirrhosis may develop. If the nephritis is acute it involves the tubules primarily although with severe injury hemorrhagic glomerular nephritis may be induced. Sometimes various portions of the kidney may contain crystals of calcium carbonate. The formation of these crystals is not understood.

The cause for stomatitis, colitis and nephritis is usually attributed to injury of membranes involved during the process of elimination.

Fatal Dose.—The fatal dose varies probably from 3 to 5 gms. of mercuric chloride.

Fatal Period.—The fatal period varies from $\frac{1}{2}$ hour to 2 weeks.

Post Mortem Appearances.—If the poison has been taken by mouth the mucous membranes of the alimentary canal may be ashy colored, congested or corroded. The colon especially may be the seat of inflammation. The kidneys show acute inflammation with calcification. When mercury has been parenterally administered the colon and kidneys show the most change.

Treatment of Stomatitis.—During the administration of mercury the mouth and teeth should be in the best condition possible. Both from the viewpoint of prophylaxis and of treatment a mouth wash, hydrogen peroxide or potassium chlorate (a tablespoonful of the saturated solution to a glass of water) should be used several times daily. The addition of a little tincture of Myrrh will improve the taste of the mouth wash.

Treatment of Acute Mercury Poisoning.—If the poison has been taken by mouth promptness in treatment is of

prime significance and consists in precipitation in the stomach of the mercury as a non-corrosive albuminate. For this purpose white of egg or milk may be given. The mercury-protein compound thus formed should be promptly removed from the stomach by lavage preferably or by use of an emetic. If the poison has had time for absorption this treatment will be less effective. On the other hand frequent lavage of the stomach is of distinct value. Equally efficient but less convenient as an antidote is a hypophosphite-peroxide mixture (sodium hypophosphite 1 gm., water 10 c.c., and hydrogen peroxide 5 c.c., estimated for each 0.1 gm. of mercuric chloride). Lavage with the diluted solution should follow this treatment. In order to protect the kidneys as much as possible a light diet should be given with a plentiful supply of fluid so long as the kidney remains sufficiently active. The administration of sodium bicarbonate may also aid in protecting the kidney from damage.

A detailed outline of treatment which embraces the above principles is that of Lambert and Patterson as follows:

"The first indication is to give the patient the whites of several eggs and then to wash out the stomach thoroughly. This has usually been done before the patients are admitted to the hospital. On admission, the stomach contents are expressed and examined for mercury, the stomach is thoroughly washed, and a pint of milk introduced. If no stomach contents are obtained before lavage, then the lavage water is examined for mercury. The metal appears in the urine in from 3 to 24 hours after it has been swallowed. If more than a day has elapsed since the poisoning occurred, a stool should also be examined for the poison. If the first lavage does not allay the nausea and vomiting, it is repeated after an hour, and the following routine is begun as soon as the stomach will permit:

1. The patient is given every other hour 8 ounces of the following mixture: potassium bitartrate, 1 dram; sugar, 1 dram; lactose, $\frac{1}{2}$ ounce; lemon juice, 1 ounce; boiled water, 16 ounces. Eight ounces of milk are administered every alternate hour.

2. The drop method of rectal irrigation with a solution of potassium acetate, a dram to the pint, is given continuously. The amounts of urine secreted under the treatment are very large.

3. The stomach is washed out twice daily.

4. The colon is irrigated twice daily, in order to wash out whatever poison has been eliminated in that way.

5. The patient is given a daily sweat in a hot pack.

It is imperative to emphasize the necessity of keeping up the treatment with the colonic drip enteroclysis day and night without interruption." When poisoning is not severe a week may be sufficient time for treatment. When large or successive doses have been taken, or when there is a pre-existing kidney lesion, or when treatment begins several days after the poison has been taken, longer periods, even up to three weeks, are necessary. When cases have reached the stage of anuria favorable results cannot always be expected.

A variety of treatments have been proposed aimed to render less active mercury that has been absorbed. None of these has proved of distinct advantage.

Chronic Mercury Poisoning.—In chronic mercury poisoning there is at first loss of appetite, nausea and gastro-intestinal symptoms with constipation or diarrhoea followed by loss of weight, anemia, and pains in the bones and joints. A general cachexia may result. Unlike lead poisoning there is no line on the gums but there may be a gingivitis. Nervous symptoms may be pronounced. The most prominent are tremors, usually of the hands and

lips although the whole body may be affected. Psychic irritability, restlessness, mental weakness, loss of will power, various psychoses, and rarely a peripheral neuritis, muscular atrophy, decalcification of the bone, are all symptoms that may be encountered.

Treatment of Chronic Mercury Poisoning.—There is considerable doubt whether treatment materially modifies the patient's condition. Everything possible should be done to promote elimination of the poison, such as administration of water and perhaps alkali. Potassium iodide is generally recommended but the efficacy of the treatment is very doubtful. For the rest treatment is purely symptomatic, attention being given to the malnutrition, the anemia, and to the nervous manifestations.

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COPPER (Cu)

Copper is a heavy, bright red solid which on contact with air assumes a brown coating of the oxide. The salts which

are of interest toxicologically are those possessing irritant properties, namely, Copper Sulphate (Blue Vitriol), Copper Subacetate (Verdigris), and Copper Acetoarsenite (Paris Green). The salts of copper are extensively employed in industry and occasionally there are cases of poisoning among workers in such industries. It possesses toxic properties when given in large doses, and has been employed for purposes of suicide or criminal poisoning. In the latter instance it is not a favorite inasmuch as its taste militates against such use. Poisoning by copper may take the form of either acute or chronic poisoning. Usually the former is induced by ingestion of the copper salts, whereas the chronic poisoning arises from industrial employment or from the use of copper salts in foods.

Acute Poisoning. *Symptoms.*—Immediately after taking the copper salt there is a coppery, astringent taste and a feeling of dryness in the throat. Inasmuch as copper sulphate, for example, is an emetic, nausea and violent vomiting set in. The vomitus has a green color. The irritant action is continued by gripping pain of a colicky nature, the abdomen being distended, and accompanied by thirst with violent purging. The stools possess a green coloration. Later the absorbed copper causes headache, giddiness, labored breathing with irregular pulse, muscular spasms which may be tetanic in character, paralysis, delirium and death. Inasmuch as the liver may be involved jaundice usually results. Copper is eliminated both through the urine and feces.

Symptoms.—Copper causes the excretion of a urine containing albumin and casts, and it may also contain hemoglobin.

Poisonous Action.—The action of copper may be twofold. In the first place it may lead to death from its simple irritant properties or secondly from the influence

upon the nervous tissues and upon the kidneys and liver.

Fatal Dose.—The fatal dose is uncertain inasmuch as usually a portion of the ingested material is vomited.

Fatal Period.—Usually life persists for several days even in fatal cases, though instances of death within 4 hours are on record.

Post Mortem Appearances.—The post mortem appearances are those of an irritant poison, the gastro-intestinal tract showing congestion, swelling, softening, with perhaps ulcerations, and the mucous membrane may have a bluish color owing to the presence in it of copper. Fatty changes may be present in the liver, and the kidneys are swollen with the tubules clogged with bloody casts.

Treatment.—Treatment consists in emptying the stomach either by means of the stomach tube or by vomiting, and the administration of white of egg or milk. Lavage of the stomach should be practised until it is certain practically all of the copper has been removed. The remaining measures to be taken are purely symptomatic.

Chronic Poisoning. *Symptoms.*—Chronic poisoning is usually not fatal, the toxic phenomena extending over a long course, the symptoms indicating functional disturbances of the muscular nervous systems, anemia and cachexia. The so-called copper colic which simulates lead colic is less severe than the latter and is characterized by the fact that diarrhœa occurs instead of constipation. On the other hand there is evidence tending to show that copper does not produce a symptom complex of poisoning even though copper has been ingested to the point of a blue line on the gums and the urine gives a green color.

Reference

HUBER: J. Pharm. and Exp. Therap., 1918, 11, p. 303.

BISMUTH (Bi)

Under ordinary circumstances even very large doses of bismuth given by mouth are harmless. Under special conditions, however, bismuth salts may become poisonous. The insoluble bismuth salts are employed in X-ray diagnosis, and as adhesive powders forming a protective membrane on inflamed mucous surfaces and on wounds. The subnitrate and subcarbonate are useful against diarrhœa, gastritis and gastric ulcers. Bismuth paste applied to chronic suppurative abscesses and sinus may give rise to toxic symptoms. A certain amount of the basic bismuth salts may be dissolved by the gastric juice, be absorbed into the circulation and find elimination through the intestine, kidney and mouth. Usually the amount thus absorbed is too small to produce symptoms. Quite recently a further possibility of poisoning by bismuth salts has arisen since certain of these salts have been more or less extensively employed in medicine in the treatment of syphilis, especially in the form of an organic acid bismuth compound such as the tartrato-bismuthate. In cases of poisoning bismuth may be found in the kidney, stomach, and liver. Formerly some samples of bismuth subnitrate contained traces of arsenic, antimony, lead and tellurium, and cases of poisoning from these impurities have been reported, arsenic being the chief offender. With more perfect methods of preparation contamination with these substances is no longer probable.

Symptoms.—Poisoning from bismuth may manifest itself in several ways, (a) *nitrite effects* from reduction in the large intestine by bacteria of nitrate to nitrite, the toxic effects therefore being due to nitrite and not to bismuth itself. The symptoms are methemoglobin in the blood, cyanosis, diarrhœa, dyspnea and death from respiratory failure. (b) *Capillary thrombosis*—this is formed from

the precipitation of hydrogen sulphide in the intestinal vessels. Bismuth sulphide is black and very insoluble. When bismuth is absorbed into the blood precipitation of bismuth sulphide may take place in the capillaries of the large intestine causing capillary embolism. Later ulceration occurs and vomiting, cramps, diarrhoea, colic and colitis may follow. The colitis produced is usually much less severe than that observed with mercury poisoning. A "lead line" may appear upon the gums due to the deposition of bismuth sulphide. At times this spreads in patches on the mucous membrane of the mouth and indeed the entire mouth and tongue may become discolored; stomatitis and loosened teeth may also be in evidence. (c) *Chronic Bismuth poisoning.* The symptoms observed in chronic bismuth poisoning are headache, fever, stomatitis, "lead line," and discoloration of mouth and tongue, gastro-intestinal disturbances, diarrhoea with black stools, colic, and albuminuria. Unlike lead, bismuth poisoning usually fails to show specific effects upon the nervous system and upon the blood. In some fatal cases convulsions and tetanus may occur.

Bismuth is excreted both by the feces and the kidneys, and has been detected in the bile, milk and saliva.

Post Mortem Appearances.—The most characteristic appearances of bismuth poisoning are evidences of liver and kidney lesions together with congestion of renal capillaries. The liver cells show cloudy swelling and necrosis. The convoluted tubules of the kidney are necrotic, and the lumen of the tubules is choked with cellular debris.

Treatment.—For the nitrite effects emetics, or lavage of the stomach may be employed. To counteract the systemic influence epinephrine or strophanthin may be used. In treatment of specific bismuth poisoning the

administration or application of the drug should be stopped and everything possible done to favor elimination of the poison, for example, lavage of stomach, catharsis and administration of large volumes of water. For treatment of the stomatitis see under *Mercury*.

Reference

LUCKE and KLAUDER: J. Pharm. and Exp. Therap., 1923, 21, p. 313.

ARSENIC (As)

Arsenic is a steel black mineral with a metallic appearance and forms a series of salts all of which are toxic. The most common compounds of arsenic which may cause poisoning are vapors of arsenic, arsenite of copper, or Scheele's green, or the aceto-arsenite of copper (Paris green), or orpiment or yellow arsenic which has been employed in the arts for coloring of paper and coloring of toys, realgar or red arsenic employed for the same purpose, metallic arsenic in the form of fly powder or in the manufacture of various colors such as magenta, aniline red, or fuchsin. For criminal purposes probably arsenic trioxide (which is also known as arsenic, white arsenic, ratsbane, or arsenious oxide) has been used more extensively than any other.

The characteristic features of arsenic poisoning are elicited by arsenious acid ($\text{As}_2\text{O}_3\text{H}_3$) and its salts or by the anhydride (As_2O_3) which is often spoken of as arsenic. The influence of arsenic is due to the ion of arsenious acid and not to the element. This conception readily explains the fact that compounds of arsenic such as arsenic acid (H_3AsO_4) and its salts, and organic compounds of arsenic, both of which dissociate less readily, are much less toxic than arsenious acid. Upon entrance into the body these latter substances only gradually dissociate forming

arsenious acid in the tissues from which typical arsenic poisoning may occur. It is, therefore, quite evident that poisoning by arsenic is characteristic even though the source of arsenical compounds may be quite varied and the number of arsenical preparations may be large.

The forms of arsenic most commonly prescribed follow: Arsenious oxide (As_2O_3): Fowler's solution (contains 1 per cent solution of arsenious anhydride rendered alkaline with potassium bicarbonate, to which compound tincture of lavender is added to give flavor and color): Sodium arsenate ($\text{Na}_2\text{HAsO}_4 + 7\text{H}_2\text{O}$): Anhydrous sodium arsenate (NaHAsO_4): Pearson's solution (1 per cent solution of dried sodium arsenate); Arsenious iodide (AsI_3): Donovan's solution (contains 1 per cent of arsenic iodide and 1 per cent of red mercuric iodide): Cacodylates: Atoxyl or sodium arsenilate ($\text{NH}_2\text{C}_6\text{H}_4\text{OAsOH.ONa}$): Arsacetin (Acetyl atoxyl): Arsphenamine (p. dihydroxy-m-diamino-arsenobenzene) ($\text{NH}_2\text{OH.C}_6\text{H}_3.\text{As}$): Neo-arsphenamine (Sod. diamino-dihydroxy-arseno-benzene-methanal sulphonylate) ($\text{AsC}_6\text{H}_3\text{OH.NH.CH}_2\text{O.SO.Na}$): Silver arsphenamine.

Irrespective of the method of administration arsenic exerts a poisonous action calling forth characteristic symptoms and inducing pathological changes.

Types of Arsenic Poisoning.—There are at least three distinct types of arsenic poisoning—namely, an acute, a nervous and a chronic form.

Acute Form.—The acute form of arsenic poisoning includes all those cases in which the inflammatory symptoms are severe from the beginning and in which the patient dies within 24 hours or may survive for 2 or 3 days. Usually symptoms appear promptly but may be delayed for $\frac{1}{2}$ to 1 hour. This is especially true when large doses have been taken. The first symptoms appear to be dry-

ness and constriction of the throat, with difficulty in swallowing and general discomfort in the stomach. Violent pain with nausea and vomiting follow. The vomited matters at first consist of food substances together with part of the arsenic swallowed. Later the vomitus may contain bile, blood or consist of a clear fluid. Diarrhoea soon sets in with colicky pains. The fecal matter passed at first has the general characteristics of diarrhoeal stools; later, however, they may partake of the nature of the rice-water stools of cholera. As such they consist almost entirely of small particles or shreds of disintegrated mucous membrane suspended in a somewhat serous fluid. At times, however, the stools are clear. From the great extraction of water from the body by way of the gastrointestinal tract there is thirst and the urine may be greatly diminished. Indeed, a condition of anuria may develop in large measure owing to the action of arsenic upon the kidney. If urine is excreted it may be albuminous or even bloody. Accompanying these gastro-intestinal manifestations nervous symptoms may intervene consisting of dizziness, headache and pain or cramps in the muscles, chiefly of the limbs. The skin is cold and damp and the extremities are cold; cyanosis may be present; there is a feeble pulse with weak, sighing respiration. Toward the end there is collapse which may pass into coma or there may be convulsions or general paralysis with death. Death is perhaps due in large part to exhaustion. In some instances death does not follow immediately, the patient recovering from the acute effects only to develop chronic arsenic poisoning. The fatal dose is uncertain, death having occurred from quantities as small as 0.1 gram ($1\frac{1}{2}$ grains).

Nervous Form.—In the nervous type of arsenic poisoning the usual symptoms associated with gastro-intestinal

disturbances may be slight or even entirely absent. This type is characterized by the influence upon the nervous system. The chief symptoms that may be manifested are narcotism, paresis, deepening into paralysis, delirium, and even acute mania and convulsions. These cases are not common but occasionally one occurs and attention is called to the possibility since the symptoms encountered are so unlike those usually seen in arsenic poisoning.

Chronic Form.—Chronic arsenic poisoning may be initiated either by the ingestion of a single large dose or the repeated administration of small doses. The latter is the more common method of its induction. In the therapeutic use of arsenical preparations the earliest form of intoxication is manifested by diarrhœa, colicky pains, conjunctivitis or swelling of the eyelids. There may be sensations of weakness, loss of appetite, nausea, occasionally vomiting, and even constipation may result. Should the arsenic be continued the second phase of chronic arsenic poisoning soon sets in. This is characterized by inflammation of the conjunctiva, coryza, sneezing, hoarseness and cough arising from an inflammatory reaction upon the mucous membranes of the nose and larynx. Jaundice may appear with swelling of the liver. Skin eruptions are usually quite marked, the so-called "eczema arsenicale." These may take the form of exfoliation, the skin falling off in fine brownish flakes, or even in large flakes, especially on the hands and feet. The hair falls out and the finger nails may become loose or detached. Again an acne-like eruption may appear. A form of melanosis is also quite prominent which is probably caused by the formation in the layers of the skin of organic pigment granules. It has been erroneously assumed that the pigmentation is caused by deposition of arsenic in the skin. This symptom is much more prominent in individuals of

dark complexion than in those with a fair skin. In the latter it partakes more of the nature of freckles. Usually this arsenic melanosis, so-called, disappears when the individual becomes arsenic-free but in some instances the pigmentation is permanent. Chronic intestinal catarrh develops which ultimately may lead to ulceration. When the poisoning is very slow there is persistent capillary paralysis leading to widespread fatty and other degeneration. The endothelium of the capillaries is first attacked, subsequently the cells of other organs and tissues, particularly the liver, kidney and heart-muscle. There is also considerable tendency for the development of local effusions.

The symptoms referable to the third phase of chronic arsenic poisoning are indicative of an action upon the peripheral nerves giving rise to polyneuritis, atrophy of the muscles involved, disturbance and paralysis of sensation which may involve the eye producing blindness. This phase of poisoning is initiated usually by intense headache, or acute pain in the knee, ankle or foot. It is less commonly observed in the hand or wrist. The palms of the hands and the soles of the feet become red and swollen and are extremely sensitive to pressure. The sensory paralysis, especially of the extremities, closely resembles that of locomotor ataxia. In the later development of motor paralysis, which is usually confined to the extremities, and generally although not invariably symmetrical, diagnosis of arsenic poisoning is sometimes quite difficult, the disturbances closely resembling those seen in lead poisoning and in alcoholic neuritis. If other differentiation fails the urine and hair should be tested for arsenic. If the period of poisoning is prolonged the individual sinks into an apathetic, semi-idiotic condition, or indeed may become epileptic. If the poison is removed the condition generally improves and the symptoms disappear although

some trace of paralysis may persist for years. If the muscles are markedly degenerated little hope of improvement may be anticipated. Death usually results from malnutrition and exhaustion, emaciation being a striking feature.

Pathology of Arsenic Poisoning.—The most marked changes to be observed are the fatty degeneration and infiltration of the liver and kidney. This change in the liver may proceed to such an extent that the entire organ is distinctly yellow. In acute poisoning there may or may not be evidences of an inflammatory reaction either in the stomach or intestines or in both. The inflammatory changes may be recognized many months after death since the presence of arsenic in tissues tends to prevent or at least to retard putrefactive changes.

Treatment of Arsenic Poisoning.—Acute arsenic poisoning is best treated by lavage with warm water. The lavage should be continued until one may be assured that all the arsenic has been removed from the stomach. If lavage is impossible emetics should be employed. They however, are not so effective as lavage and are detrimental inasmuch as they tend to induce depression. Whichever treatment is carried out should be prompt. Attempts to wash the intestine by high rectal tube are usually of little value. When the stomach has been thoroughly washed the intestine is best emptied by purgatives. For this purpose the saline cathartics are to be preferred since they act promptly. Chemical antidotes, such as the so-called "arsenic antidote," are of doubtful value. It is much better to rely upon repeated and copious lavage with subsequent purgation. The collapse usually observed in acute arsenic poisoning is to be treated by the ordinary measures employed, such as warmth and stimulants for example, caffeine and digitalis. In view of the water

deprivation of the body, incident to the extensive vomiting and diarrhœa, large volumes of fluid should be administered over a period of 3 or 4 days. Such a procedure will also facilitate the excretion of that portion of the arsenic absorbed.

In the treatment of chronic poisoning the cause should be removed and symptomatic measures taken. The paralysis may be combatted by stimulating the muscles with the galvanic current.

Toxicology of the Arsphenamine Group.—In the use of arsphenamine and neo-arsphenamine there are a certain number of cases that exhibit systemic effects which are not completely understood. The percentage of cases in which the reactions occur varies from 1 to 15 per cent. In most instances the symptoms are alarming and distinctly annoying to the patient but only occasionally is there a fatality. There are several types of reaction elicited by these compounds.

Type A. Nitritoid Reactions.—In the first type which is spoken of as the "nitritoid" reactions there may be vasodilatation, as in nitrite action, hence the name, which characterizes this group. If the reaction is very severe the symptoms partake of the nature of anaphylaxis. The symptoms may start during the intravenous injection or immediately after. There is flushing of the face, inflammation of the conjunctiva; an anxious expression, peculiar burning sensation of the tongue, nausea, vomiting and profuse perspiration, edema of the tongue and eyelids. Sometimes there is cough and dyspnea, precordial distress and cyanosis. The pulse is full at first then weak with a pallid skin. Unconsciousness with feeble pulse may intervene in the severe cases. At times during the period of injection there may be severe lumbar pain. The symptoms thus indicated may disappear within

15 to 30 minutes or may grade into the group of symptoms described below as Type B. The symptoms observed immediately usually give place to speedy recovery even though there is a condition of actual collapse. The condition of actual collapse is much more frequent following the second dose.

The cause of the nitritoid reactions has been variously given. It has been ascribed to lack of purity in the preparations employed, the impurity being spoken of as substance "X," to a "colloidal reaction," precipitation or "anaphylaxis;" to the liberation of decomposition products, which, however, are usually less toxic than the original substances; to the formation of an insoluble base, by certain salts of the blood, which forms emboli; to a special supersensitiveness to the drugs themselves. Of the foregoing hypotheses the most likely appear to be associated with the presence of substance X and the susceptibility of the patient.

Treatment of Nitritoid Reactions.—In the treatment of nitritoid reactions epinephrin may be employed prophylactically and after appearance of symptoms. If used as a prophylactic 1 mg. may be administered intramuscularly just before the injection of the arsphenamine compound. If symptoms have arisen $\frac{1}{2}$ to 1 mgm. may be given intravenously. Good results have been reported by this treatment. If the individual is susceptible to arsphenamine it is quite possible that he will also exhibit sensitiveness to epinephrine resulting in symptoms quite as alarming as those induced by the arsphenamine compounds.

Type B. Early Symptoms.—These symptoms consist of chilliness or a distinct rigor, headache, vertigo, nausea, vomiting, diarrhoea, and rise of temperature, usually 100° to 102° F. All of these symptoms may not be present and the patient may merely feel "queer" or there may be

chills, attacks of emesis and profuse and protracted diarrhœa. Sometimes complaints are made of severe pains in the legs and back. This group of symptoms usually passes off in 12 to 14 hours and is followed by a feeling of lassitude and weakness. More rarely vomiting and diarrhœa with slight rise of temperature may continue for a number of days, nourishment not being retained during this period. Sometimes the urine is small in volume and may contain albumin and casts. Various types of eruptions may appear within a few hours or not for several days. The most common are urticarial, scarlatinoid, morbilliform erythemas, rarely purpura. Sometimes an itching of the skin or pruritus without accompanying eruption may be observed. Generally these eruptions disappear within a day or two. Late eruptions occurring from 6 to 10 days after the administration of the drug are much more persistent, universal exfoliating dermatitis occurring which may last for weeks with fever and debility and at times ends in death.

Type C. The Late Symptoms.—The reactions may be delayed for more than 24 hours, in which event they usually consist of vomiting, fever and diarrhœa, similar to the immediate reactions. More rarely serious and even fatal reactions may develop about 3 days after the administration of the drug. In these instances the symptoms are referable either to the brain or to the liver. In the severe cases there may be headache, vomiting, muscular twitchings, epileptiform convulsions, dilatation of the pupils, absent reflexes, coma and death. These symptoms are usually the expression of edema of the brain or of encephalitis hemorrhagica. A rare syndrome subsequent to arsphenamine administration is characterized by severe jaundice accompanied by rise of temperature. This may appear in from 3 days to several weeks after treatment.

Most cases pursue a favorable course but sometimes a fatality occurs with the symptoms and autopsy findings of acute yellow atrophy of the liver.

The treatment of the later manifestations of poisoning by the arsphenamine group is purely symptomatic.

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ANTIMONY (Sb)

Antimony is a solid with grayish white appearance. It is tasteless and odorless. Chemically it is closely related to arsenic and forms the same types of compounds. In general only two compounds of antimony are of toxicological importance. These are tartrated antimony and antimony chloride which is also known as butter of antimony. These substances have been employed in the past in medicine, the tartar emetic, as its name implies, being used as an emetic; the antimony chloride in the form of an external application. Antimony chloride is at the present time used in industry especially in certain forms of bronzing.

There are two types of poisoning, the acute and the chronic. Previous to 1850 poisoning by antimony was rather common. To-day, however, antimony poisoning is very rare.

Acute Poisoning. *Symptoms.*—Salts of antimony must be regarded as irritant poisons and the clinical picture of arsenic poisoning might be substituted for that of antimony. Soon after taking the poison violent, frequent

vomiting occurs, the vomitus sometimes being mixed with bloody matter. There is a sense of constriction in the throat and pain in the stomach. Vomiting may continue even though the stomach is completely empty. Colicky pains attended by diarrhœa with watery stools occur, and there may be fainting attacks with profuse sweating. Nervous symptoms may supervene as indicated by spasmodic contraction of the limbs, with delirium, convulsions or coma. The urine may be suppressed and the skin may be covered with an eruption. In general antimony poisoning has a more hopeful prognosis than arsenic poisoning even though the case seems desperate.

Poisonous Action.—The poisonous action consists in the local effects upon the gastro-intestinal tract with a remote influence upon the liver, kidneys, and the central nervous system. Elimination occurs both through the urine and feces.

Fatal Dose—The exact fatal dose is uncertain owing to the fact that the antimony compounds produce vomiting. The smallest dose that has proved fatal to a child is $\frac{3}{4}$ grain, and a healthy woman died from the effects of $1\frac{1}{2}$ grains. On the other hand recovery has followed a dose of 170 grains.

Fatal Period.—The fatal period varies from a few hours even to several months.

Post Mortem Appearances.—The mucous membrane of the gastro-intestinal tract is softened and corroded. There may be fatty degeneration of the internal organs such as the liver and kidneys. This latter condition, however, is much more likely to occur after chronic poisoning rather than from the acute intoxication. The mucous membranes of the stomach and intestine may show a varied coloration from yellowish to reddish color due to the presence of antimony salts.

Treatment.—Usually vomiting is induced by the ingestion of antimony salts. If vomiting does not occur spontaneously it should be induced and the stomach emptied so far as possible from all the antimony. The stomach should be washed thoroughly with warm water containing tannic acid or tea, these tending to form the insoluble tannate of antimony. For the relief of pain morphine may be given and the depression treated by the administration of stimulants. The stomach and bowels may be soothed by demulcent drinks and the patient should be kept warm.

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TIN—STANNUM (Sn)

Tin is a silver white metal which resists the action of air and water. It is also present in many forms of alloy such as that of bronze or Britannia metal, and in soft solder. Tin forms two types of salts, the stannus and the stannic compounds. Intoxication from tin is rather uncommon but occasionally it does occur. A considerable controversy has arisen as to the possibility of poisoning from tin containers for fruits and other foodstuffs. It has been demonstrated that if the contents of these cans possess an acid reaction a considerable portion of tin may be contained in the food products. The consensus of opinion appears to be that in this instance poisoning by the soluble tin is doubtful or if it does occur the effects are so subtle and vague as to escape detection. Inasmuch as very few cases of poisoning have been reported from this source some doubt has been expressed as to the absorbability of tin compounds. This matter, however, has

been settled in the affirmative, the tin finding its way into the urine within a relatively short time. The major portion of tin, however, is eliminated by way of the gastro-intestinal tract and may be distributed in the liver, skin, brain and spinal cord.

Symptoms.—The salts of tin must be regarded as gastro-intestinal irritants, the symptoms produced being a metallic taste, nausea, vomiting, abdominal pain, diarrhœa, cyanosis, and collapse. Tin poisoning may also give indications of an influence upon the nervous system, the effects being similar to those of ataxia. Again there may be sore throat, a feeling of coldness and a condition of marked anemia.

Poisonous Action.—The poisonous action is probably caused by the local action of the tin as an irritant. In the more chronic types of cases the influence upon the nervous system and the blood are the characteristic features.

Fatal Dose.—The quantity of tin salts necessary to produce death is unknown.

Fatal Period.—The fatal period is unknown.

Post Mortem Appearances.—The post mortem appearances are confined almost entirely to the gastro-intestinal tract which presents the picture of irritation.

Treatment.—The stomach should be emptied and lavage employed. To sooth the irritated gastro-intestinal tract demulcent drinks should be given together with stimulants and agents to allay the pain.

Reference

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CHROMIUM (Cr)

Chromium is a white, hard crystalline metal which is insoluble in alkalies and in all acids except hydrochloric.

The chromium compounds which are of interest from the toxicological standpoint are potassium chromate, chromic acid, and lead chromate. Lead chromate, known otherwise as chrome yellow, possesses quite toxic properties but the characteristic effects are undoubtedly elicited by the lead rather than by the chromium. The salts of chromium cause poisoning mainly from the industrial use since the salts of chromium are employed in various types of trade such as dyers, furriers, stainers, battery fluids, etc. In medicine, chromic acid has been employed externally as a caustic and even here its employment is attended with considerable danger. In dye works the employees occasionally suffer from irritation on the arms. Chromate dust produces ulcers which develop slowly but penetrate very deeply and heal with difficulty. It also causes ulceration of the mucous membrane of the septum of the nose.

Symptoms.—Chromium compounds must be regarded as gastrointestinal irritants. After absorption they also have an effect upon the central nervous system. The acute symptoms are those characteristic of gastrointestinal irritants. There is at first a disagreeable taste, with vomiting, diarrhœa, and pain. The pupils are dilated and respiration is greatly slowed. Muscular cramps ensue followed by collapse and unconsciousness.

Chronic poisoning produces severe dermatitis and ulcers. After absorption a characteristic feature of chromate poisoning is the induction of a severe nephritis accompanied by a glycosuria. In these respects chromium resembles uranium.

Poisonous Action.—The poisonous action of chromium salts is three-fold. First, that of a gastro-intestinal irritant; secondly, the influence upon the nervous system; and thirdly, the action upon the kidneys.

Fatal Dose.—The fatal dose of potassium dichromate is less than 8 gms. and for chromic acid about 6 gms.

Fatal Period.—The fatal period is variable, death having occurred in 40 minutes after the taking of 1 ounce.

Post Mortem Appearances.—Upon necropsy there may be gastrointestinal inflammation and ecchymoses. The kidneys exhibit a parenchymatous nephritis.

The chromium is found in the blood, urine, feces and gastric contents. The main avenue of excretion is by way of the kidney which causes a detrimental influence upon this organ, but it is also eliminated by way of the bowel and the bile.

Treatment.—Treatment consists in evacuation and lavage of the stomach followed by demulcent drinks. For the pain the ordinary sedatives should be given, and cerebral and respiratory stimulants as indicated.

References

MACNIVEN: *Lancet*, 1883, 2, p. 496.

BRIEGER: *Zeit. exp. Path. u. Therap.*, 1920, 21, p. 393.

THALLIUM (TI.)

Thallium is a heavy metal resembling in its toxic properties lead. All thallium compounds are toxic. They possess a toxicity almost equal to that of arsenic. Thallium acetate has been employed therapeutically, externally as a depilatory, and against the night sweats of tuberculosis. The medicinal use has caused poisoning, the chief symptoms being stomatitis, diarrhoea and dyspnea. There is salivation, trembling and pain in the limbs followed by paralysis. The hair falls out and hemorrhages may occur in the stomach and from the lungs. The effects are cumulative, somewhat like those of mercury and inasmuch as it is eliminated through the kidney in

part it produces a persistent nephritis which is characterized by albuminuria. Thallium is also found in the feces, the elimination being very slow. It is also excreted into the milk. It causes death from asphyxia.

Reference

SWAIN and BATEMAN: *J. Biol. Chem.*, 1910, 7, p. 137.

IRON—FERRUM (Fe)

Iron generally occurs as oxides, carbonate, or the sulphides. Pure iron is of a silver white color and capable of being highly polished. It is plastic like wax and can be pressed or forged into all sorts of forms. It readily forms oxides and possesses two types of salts, the ferrous and the ferric. Iron occurs throughout the body particularly in the hemoglobin of the blood, and is a frequent constituent of food. Inasmuch as the organism has a need for iron, various salts have been extensively employed in medicine as tonics. Iron itself has no specific toxic action on protoplasm but the salts in sufficient quantities produce gastro-intestinal irritation. Iron salts are eliminated for the most part by the gastro-intestinal tract. The salts most commonly met with from a toxicological viewpoint are ferrous sulphate and ferric chloride. The ferrous sulphate or copperas or green vitriol, as it is sometimes called, has been administered as a poison but has been employed more frequently to produce abortion.

Symptoms.—When these salts have been taken there is a metallic taste which resembles that of ink, accompanied by vomiting, abdominal pain and diarrhoea. Later there may be pain in the extremities together with paralysis, suppression of urine, convulsions and death. The feces are black from the formation of iron sulphide.

Poisonous Action.—The poisonous action must be regarded as that of a gastro-intestinal irritant, and after absorption has, however, an influence upon the central nervous system and upon the kidneys, leading to the suppression of urine.

Fatal Dose.—The fatal dose is quite variable, recovery having followed after taking 3 ounces of the tincture of iron, and on the other hand death having followed from $1\frac{1}{2}$ ounces. Bile and vomiting and urinary symptoms have resulted from the taking of 1 ounce.

Fatal Period.—Acute death is uncommon, the fatal result usually occurring after several weeks although in one instance it followed after 4 hours.

Post Mortem Appearances.—In acute cases the gastro-intestinal tract is covered with a greenish black substance. The kidneys and liver show congestion and swelling with ecchymoses. The brain and its membranes may give evidence of hyperemia.

Treatment.—Treatment consists in the administration of emetics and lavage of the stomach with large volumes of water containing alkaline bicarbonates or carbonates. Further treatment is purely symptomatic.

Reference

BERENGER-FERAND and PORTE: *Annales d'Hyg. Pub.*, 1879, 3 S., i, pp. 312 and 508.

ZINC (Zn)

Zinc is a white, soft metal which at a high temperature volatilizes and burns. If the temperature is above 100°C . it becomes soft and may be rolled into sheets. Zinc is a common constituent of many foods and probably is constant in the animal body. Chemically zinc resembles manganese and chromium, and forms a series of salts,

especially the oxide, which is used in the preparation of paint. In general intoxication from zinc occurs with those salts which are soluble, either the sulphate or the chloride, which may be mistaken for other substances. In medicine zinc sulphate is employed as an emetic and locally as an astringent and antiseptic. It is less irritant to the gastro-intestinal tract than copper. Zinc chloride finds medicinal use in external application for purposes of its escharotic action. Spelter chills or brass founders' ague are conditions which result from the industrial use of zinc. The spelter chills are characterized by chilliness, sneezing, pains in the limbs and abdomen, and a heightened temperature. Irritated mouth, nausea, diarrhœa, rapid pulse and prostration are sequels. Exhaustion, sweating, and a deep sleep follow the chills. The brass founders' ague is induced from inhalation of finely divided zinc oxide which gives rise to irritation of the throat, malarial chill, with temperature, and the other general symptoms already indicated.

Zinc fumes may cause chronic lesions of the respiratory, digestive, excretory and nervous systems.

Symptoms.—Poisoning from sulphate of zinc occurs only after large doses when it produces gastro-intestinal disturbances such as vomiting and purging resulting in a serious prostration. These symptoms may be entirely absent and death result from the depressant action on the nervous system. The symptoms from zinc chloride are immediate pain in the throat, mouth and stomach, swallowing is difficult and painful, and there is excessive salivation. There is vomiting, diarrhœa and collapse which may end in coma and death within a few hours. Should death be delayed nervous symptoms make their appearance which are particularly noticeable in the special senses, especially taste and smell. Again aphonia, muscu-

lar and localized tetanic affections may be observed. The caustic action may result in stricture of the esophagus or pylorus and cause destruction of the mucous membrane of the stomach so that death from inanition may result. Handling zinc chloride which may be used in the preservation of wood causes dermatoses and burns which are ascribed to the influence of the zinc chloride.

Poisonous Action.—The poisonous action of the zinc salts is similar to that of the other metals, that is, the influence which it exerts as a gastro-intestinal irritant and the action which it induces upon the nervous tissues after absorption. Like the other heavy metals it is present in the liver and muscles and is eliminated both by the gastro-intestinal tract and also in the urine.

Fatal Dose.—The fatal dose of zinc sulphate may be taken as about $1\frac{1}{2}$ ounces. So far as zinc chloride is concerned 6 gms. have caused death although recovery has followed after a dose of 200 grains.

Fatal Period.—The fatal period varies greatly inasmuch as death has occurred in 4 hours from both zinc sulphate and zinc chloride, yet other cases are on record in which death followed more than 100 days because of the secondary constriction of the esophagus.

Post Mortem Appearances.—The autopsy findings are those characteristic of irritant poisoning, and mainly more or less intense inflammation of the mucous membrane and intestine. With zinc chloride there may be in addition ulceration or even perforation.

Treatment.—The stomach should be emptied as rapidly as possible, the stomach tube being employed carefully when vomiting is not readily induced. Large volumes of water or milk should be given. White of eggs and tannin, best in the form of tea, may be regarded as antidotes for zinc chloride.

Reference

MCCORD and KILKER: *J.A.M.A.*, 1921, 16, p. 442.

CADMIUM (Cd)

Cadmium is chemically very similar to zinc and although it has similar toxicological properties is much more poisonous. Kobert claims that cadmium sulphate is twice as toxic as zinc sulphate. The toxicological interest of cadmium compounds is the intoxication which results from its industrial use. Workers in zinc are exposed to cadmium fumes and present symptoms which are typical for lead poisoning. Absorbed the cadmium is eliminated by the gastro-intestinal tract and the urine, inducing gastro-enteritis and nephritis together with degeneration of the liver and heart. Cadmium chloride is a powerful emetic and experimentally it produces nephritis. Its hypodermic injection induces local necrosis and when administered intravenously death is caused by failure of respiration. So far as one may find, no deaths have been reported from employment of cadmium salts and in man the acute effects are those of a gastro-intestinal irritant.

Reference

STEPHENS: *J. Industrial Hygiene*, 1920, 2, p. 129.

MAGNESIUM (Mg)

Magnesium is a white tough metal forming salts which are relatively little absorbed by the alimentary canal. Magnesium sulphate probably possesses the greatest importance toxicologically because of its frequent therapeutic use as a purgative. Owing to obstruction or sluggishness of the intestine the onward passage of the magnesium may be so delayed that a considerable degree of absorption occurs especially if the salt is given in high

concentration. In conditions of marked dehydration, in animals at least, the same action occurs. Under these circumstances typical magnesium effects are induced—namely a condition of general anæsthesia, scanty or suppressed urine with abolition of reflexes, and respiratory paralysis which may cause death.

In treatment of tetanus magnesium sulphate has been employed to control the convulsions. Attempts to use the salt as a local and general anesthetic have caused magnesium poisoning. In fatal cases there are fatty changes in the liver with small hemorrhages of the pleura, and peri- and endocardium.

Elimination occurs by way of the urine which in consequence may have a very high specific gravity a fact in itself pointing to magnesium sulphate poisoning.

Treatment of poisoning aims to increase elimination and to counteract the respiratory depression. For the purpose of hastening excretion large volumes of saline may be given intravenously and the bowel may be emptied by calomel. Calcium is antagonistic in action to magnesium and the respiratory depression may be alleviated by calcium chloride solution (0.02 per cent in physiological saline) up to 600 c.c. or more. Physostigmine $\frac{1}{2}$ to 1 mgm. subcutaneously will act in the same manner. In the absence of either remedy or as an adjuvant artificial respiration should be instituted.

References

- MELTZER and AUER: *Am. J. Physiol.*, 1905, 14, p. 366.
MELTZER: *J.A.M.A.*, 1916, 66, p. 931.

CALCIUM (Ca)

Calcium is a grayish white metal whose salts are widely distributed in nature. It is of minor significance

from a toxicological viewpoint since its salts are relatively non-poisonous. Occasionally, however, cases of poisoning occur from the ingestion of some form of lime. The symptoms indicated are burning abdominal pain, intense thirst and obstinate constipation. Treatment of the condition is neutralization of the lime by large volumes of weak acid as lemon juice or vinegar and evacuation of the stomach. Demulcents, as white of egg, milk, barley or oatmeal gruel, control of pain, and saline purgatives as magnesium or sodium sulphate are indicated.

BARIUM (Ba)

Barium is a white metal belonging to the group of alkaline earths together with calcium and strontium. Its ion is toxic and the common salts—chloride, nitrate and carbonate, all irritant compounds, may give rise to poisoning. Barium salts are employed in wood staining and glass-making. The carbonate mixed with arsenic constitutes "Rough on Rats" and common salt, sodium chloride, may contain significant quantities. Barium sulphate is employed in X-ray work and poisoning has occurred because of errors in using a barium salt other than the sulphate. The excretion of barium is largely by way of the feces.

Symptoms.—Barium closely resembles digitalis in its physiological action but because of its toxicity is not employed therapeutically. Its principal effects are increased excitability of heart muscle, contraction of arterial muscle, causing rise of blood pressure, strong peristaltic action of the intestines, initial stimulation and final paralysis of the central nervous system.

The first symptoms are those of gastro-intestinal irritation—vomiting, abdominal pain (colic) and diarrhoea. When absorption occurs the pulse is slow and hard, and

the blood pressure is high. Later convulsions and paralysis may occur. Death results from arrest of the heart.

Fatal Dose.—The fatal dose approximates 1 gram although much larger quantities have been taken with recovery.

Fatal Period.—Death results after an hour or less, or may be delayed for several days.

Post Mortem Appearances.—Autopsy reveals gastrointestinal irritation and some degree of corrosion. The stomach, intestines and kidneys may show hemorrhages.

Treatment.—Treatment consists in the first place of attempting to change any unabsorbed soluble barium salt into an insoluble form as the sulphate. For this purpose the best chemical antidote is magnesium sulphate or sodium sulphate. Gastric lavage with milk and water should be thoroughly carried out. Pain and cardiac depression should be treated by the usual appropriate measures.

Reference

SALANT and KLEITMAN: *J. Pharm. and Exp. Therap.*, 1922, 20, p. 247.

LITHIUM (Li)

Lithium is a silver-white metal closely resembling sodium in many of its properties. Lithium salts are present in many natural mineral waters and is a constituent of many foodstuffs. The chief interest in lithium salts from a medical standpoint lies in the fact that they were formerly employed quite extensively in therapeutics as uric acid solvents in rheumatic and gouty conditions.

Toxicologically in animals lithium resembles potassium except that when taken into the body, irrespective of the avenue of introduction, gastro-enteritis is in evidence. Lithium is excreted by the urine, saliva and feces, the

gastro-enteritis probably being caused by the gastro-intestinal excretion. In man large doses of lithium salts produce general muscular weakness, tremors, vertigo, impaired vision and ringing in the ears, but gastro-intestinal disturbances, may at times be absent.

References

- GOOD: *Am. J. Med. Sci.*, 1903, 125, p. 273.
CLEVELAND: *J.A.M.A.*, 1913, 60, p. 722.

ALUMINUM (Al)

Aluminum is a bluish, silvery metal which has extensive use in industry. In the form of its salts it is widely distributed in nature, especially in soils. It forms a series of salts, the most important of which, from a medical viewpoint, are the double sulphates of aluminum and the alkalies, sodium, potassium, and ammonium, to which the name alum has been given. In medicine these salts have been employed as local caustics and as astringents against diarrhœa. In properties these salts are so similar that they may be interchanged without perceptible alteration of physiological effects. When alum is heated it loses its water of crystallization and is transformed from a crystalline form to a spongy white mass. This is called "burnt alum." Both types of alum possess marked caustic and astringent properties, the burnt alum to the greater degree.

Aluminum salts are toxic to plants, animals and man exerting an irritant influence upon protoplasm. Aluminum in the form of alum has caused violent irritant symptoms sometimes ending in death. The symptoms produced are gastro-intestinal disturbances as vomiting and pain, the vomitus containing blood stained mucus. The urine shows albumin and blood.

The chief interest in aluminum compounds centres around the employment of the alums, especially sodium alum, in baking powders, as an acid agent to liberate CO_2 from the sodium bicarbonate. There is left a residue of aluminum hydroxide, sodium sulphate and perhaps some unchanged alum. It has been held by some that the aluminum hydroxide is not absorbed, hence cannot exert a detrimental influence. Notwithstanding the report of the Referee Board to the contrary there is evidence that the aluminum contained in baked bread or biscuits is absorbed and is thus free to act upon any cells with which it may come into contact (Steel). Aluminum finding its way into the blood stream causes paralysis of sensation and motion, with fatty degeneration of the liver and kidneys (Siem).

According to Mallet the aluminum of bread dissolves in the human gastric juice. "It is likely that the action of this soluble chemical would be deleterious to the gastric processes. Persons with temporary illness or those with permanently feeble digestion would suffer greater detriment than the many in health or of average peptic strength, whose power of resistance would enable them to withstand the tax without obvious harm. It is probable that the insidious strain repeated daily would in time be hurtful, and yet the cause of this effect go unrecognized" (Holland).

"For these reasons it is just to demand that positive proof be furnished that these chemicals foreign to the normal body are harmless. This proof beyond a reasonable doubt is still lacking" (Holland).

References

- HOUSE and GIES: *Am. J. Physiol.*, 1906, 15, p. XIX.
STEEL: *Am. J. Physiol.*, 1911, 28, p. 94.

SIEM: Schmidt's Jahrbuch., 1886, 211, p. 128.

HOLLAND: In Peterson, Haines and Webster's Legal Medicine and Toxicology, 2nd Edition, 1923, p. 165.

Report of Referee Board, U. S. Dept. Agri. Bull. 103.

URANIUM (U)

Uranium, like radium, is a source of radiant energy and its salts have been employed in medicine for the treatment of diabetes. The soluble salts, the acetate and nitrate are the most common uranium preparations. Ingestion or injection of uranium salts leads to respiratory paralysis which is the cause of death. In sublethal doses uranium causes nephritis and glycosuria, the tubules and glomeruli both being affected. Other mechanisms that may be acted upon are the gastro-intestinal tract, blood vessels and the nervous system. At times the liver undergoes a degeneration, which is similar to that seen in mercury poisoning, and which is accompanied by acidosis.

References

MACNIDER: J. Exp. Med., 1916, 23, p. 171.

KARSNER, REIMANN and BROOKS: J. Med. Res., 1918, 39, pp. 163, 169, 177.

VANADIUM (V)

Vanadium is a rare metal belonging to the nitrogen and phosphorus group. It is grayish-white with feebly basic and strong acid properties and has valences of 1, 2, 3, 4, and 5, the last being the most stable. Vanadium salts, especially the chloride and trioxide, are employed in industry chiefly in dyeing and in the manufacture of steel. Vanadium pentoxide has been used therapeutically in diseases of metabolism without sufficient justification. Vanadium poisoning, vanadiumism, is experienced by persons employed in manufactories where vanadium is produced, dust and fumes being responsible. Poisoning

may also result from using or wearing clothing dyed by vanadium chloride, trioxide or pentoxide.

Symptoms.—Anemia is an early symptom (a peculiar cachexia) somewhat resembling chlorosis. At first there is an increase in hemoglobin content and red cell count followed shortly by a reduction of the cells and hemoglobin. Cough is a prominent and characteristic symptom. It is dry, irritating and paroxysmal, becoming so intense that hemorrhages are frequent and severe, even causing death. The victims of the poisoning are especially susceptible to tuberculosis. Emaciation, irritation of the nose, throat and eyes are always present. Gastro-intestinal disturbances are indicated by anorexia, nausea, diarrhoea, alternating with constipation. The urine may contain albumin, casts and blood.

Later sequels of exposure to the poison are nervous disturbances, as headache, fine tremors of the extremities, neurorretinitis, amaurosis, vertigo, hysteria and melancholia.

Post Mortem Appearances.—The action of the poison seems directed on the gastro-intestinal tract, the lungs and the kidneys. The lungs show marked congestion and destruction of alveolar epithelium. The kidneys are highly congested and sometimes there is an acute hemorrhagic nephritis. The gastro-intestinal tract is irritated and inflamed. The drug is excreted by the urine, feces, and saliva.

Treatment.—The prognosis is good in the absence of serious renal, blood, nervous and lung involvement. The patient should be kept out of the poisonous environment, given open air exercise, tonics, and symptomatic treatment when needed, as for example, for cough.

Reference

DUTTON: J.A.M.A., 1911, 56, p. 1648.

MANGANESE (Mn)

Manganese closely resembles iron in its physical and chemical properties. It has a reddish-gray lustrous color. Like iron it forms two series of salts, theous and ous compounds. Manganese occurs in traces in the organs of man and animals due to the presence of manganese in the food. Salts of manganese in general produce no noticeable effects when taken by mouth. Absorption occurs to a certain extent and excretion takes place mainly by the intestines although some manganese is eliminated in the urine. Injected intravenously manganese salts produce fatty degeneration of the liver. Potassium permanganate which must be regarded as a strong oxidizing agent is a gastro-intestinal irritant, large doses causing death. Treatment of potassium permanganate poisoning consists in administration of white of egg and gastric lavage, the general symptoms being combatted as they arise.

The main toxicological interest in manganese arises from its use in industry when workers are brought into contact with manganese dust.

Symptoms.—According to Edsall, Wilbur and Drinker the symptoms which are clear cut and lend themselves readily to diagnosis are produced by contact with manganese dust for a period of three months. The characteristic signs are langour and sleepiness, stolid, mask-like facies, a low monotonous voice, muscular twitchings which may be generalized, cramps in the calves and stiffness of the leg muscles, cramps usually coming on at night and being worse after a day of exertion. There is a peculiar slapping gait, the patient maintaining a broad base. Occasionally there is uncontrollable laughter and sometimes crying. There are no disturbances of deep or superficial sensation, eye changes, genito-urinary or gastro-intestinal disturbances, reactions of degeneration, blood, urine or spinal

fluid alterations. It is significant that, unlike lead, manganese does not shorten life by the production of degenerations. If severely poisoned the victims are life-long cripples. The metal apparently makes a very definite attack upon some non-vital portion of the neuro-muscular system, destroys it thoroughly, if time for action is permitted, and leaves the patient quite well in every other respect. There seems to be a certain degree of idiosyncrasy to the action of manganese only a small proportion of workers being attacked.

The disease is never fatal although autopsy has been performed by Casamajor upon a single case of advanced manganese poisoning, death being caused by pneumonia. No gross changes were present in the brain, kidneys, liver or spleen. Histologically examined there was a moderate chronic interstitial nephritis and in the liver there was considerable biliary cirrhosis. The brain showed evidences of digeneration in certain areas.

When poisoning has actually occurred no form of treatment has any value. Prevention is the only known means of combatting the conditions. In incipient cases spontaneous recovery follows when the patient is removed from the contaminating atmosphere.

References

- CASAMAJOR: J.A.M.A., 1913, 60, p. 646.
EDSALL, WILBER and DRINKER: J. Ind. Hyg., 1919, 1, p. 183.
DAVIS and HUEY: J. Ind. Hyg., 1921, 3, p. 231.

CHAPTER V

ALKALOIDAL POISONS

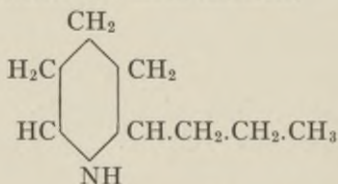
The alkaloids are organic nitrogenous bases occurring naturally, for the most part, in plants and they may be regarded as substituted ammonium compounds or amines, generally tertiary amines. Some contain oxygen whereas in others oxygen is absent. Certain of the alkaloids are liquid and volatile, others are solid and non-volatile. The oxygen-containing alkaloids belong to the latter group, the non-oxygen-containing alkaloids, like nicotine, and coniine are liquid and volatile. They are further divided into three great groups according to their chemical structure, thus derivatives of (a) pyridine, as atropine and nicotine, (b) quinoline, as quinine and strychnine, and (c) phenanthrene, as morphine and codeine.

Several alkaloids may occur in the same plant and these may possess physiological actions similar or completely antagonistic to each other. On the other hand they all possess certain characteristic properties as a group. They are bitter, and give an alkaline reaction to litmus. As the free base they are generally insoluble in water, but form soluble crystalline salts with the common inorganic acids. The free bases are readily soluble in oils, ether, chloroform and alcohol, whereas the salts are relatively insoluble. They are precipitated from solution by forming compounds with a variety of reagents both organic and inorganic in nature and from this fact these substances are spoken of as "alkaloidal reagents." The list of alkaloidal reagents includes, mercuric chloride,

potassium mercuric iodide (Mayer's Reagent), potassium bismuth iodide (Dragendorff's Reagent), phosphomolybdic acid and phosphotungstic acid, tannic acid, picric acid, platinic chloride, gold chloride, potassium dichromate, and picrolonic acid. Again many of the alkaloids give color changes with concentrated acids either with or without addition of oxidizing agents, the reaction aiding in the identification of a particular alkaloid.

In general the alkaloids act upon the nervous system producing varied effects.

CONIINE (HEMLOCK ALKALOID)



Conium maculatum or "poison hemlock," is a plant growing wild in various parts of the United States. It closely resembles parsley and from this fact cases of poisoning have occurred. Coniine, a volatile alkaloid, is the principal active constituent of this plant and is a derivative of pyridine. The poison of hemlock has been well known since Socrates killed himself by drinking it. There are at least five other alkaloids in hemlock and they are closely related to coniine chemically. Formerly, the fluid extract of conium was employed as a sedative and antispasmodic but to-day it is not used to any extent. The concentrated free alkaloid is a local caustic.

Pure coniine has been prepared synthetically but is of the racemic form whereas that occurring naturally is dextro-rotatory. Coniine is a colorless, oily liquid with a peculiar odor resembling that characteristic of mice. Its boiling point is 166°C . and has a specific rotation $[\alpha]_D = 15.7^\circ$ at

19°C. When the solid is sufficiently chilled coniine becomes a solid crystalline mass. It is relatively insoluble in water but easily soluble in alcohol, ether, chloroform, benzol and acetone.

Symptoms.—The poisonous action develops very rapidly, the symptoms consisting of a burning, smarting sensation in the mouth and throat, pain in the head, drowsiness, faintness, lassitude, muscular weakness, muscular twitchings, stiffness and rigidity, and pupil dilation. Nausea is usually present and at times vomiting may occur, speech and deglutition being difficult. The intellect generally remains clear although the special senses may be dulled. Paralysis of the extremities may set in. The respiration is chiefly affected, at first being rapid, later slow and labored, eventually becoming weak and irregular, death resulting from respiratory failure.

Poisonous Action.—Coniine causes paralysis of the ends of the motor nerves eventually extending to the trunks and the motor centre itself. The sensory nerves are less affected but may share in the paralysis. The final action is paralysis of the respiratory centre. Coniine is eliminated from the body by the lungs and by the kidneys. Probably a portion is burned or otherwise destroyed by the organism.

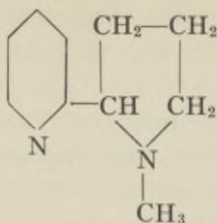
Fatal Dose.—The fatal dose is between 2 and 3 grains.

Fatal Period.—Death may occur within a few minutes and the longest case on record is fifty-two hours.

Post Mortem Appearances.—There is nothing characteristic, the appearances being for the most part those peculiar to death by asphyxia. The gastro-intestinal membrane may be inflamed and congested.

Treatment.—Treatment of coniine poisoning consists in lavage of the stomach, employing tannin as an antidote, stimulation and maintenance of the respiration.

NICOTINE GROUP



American, Havana, French and Dutch tobaccos are in general obtained from the tobacco plant, *Nicotina tobacum*. Turkish, Syrian and Latakia tobaccos are derived mainly from *Nicotina rustica*. In either event there are at least four alkaloids present in the plant, chief of which is nicotine. It exists in all parts of the plant but occurs in largest quantity in the leaves, from which tobacco of commerce is prepared.

Nicotine is a colorless, oily fluid with little odor but when allowed to stand or diluted with water the characteristic odor of tobacco develops. Its taste is sharp and irritating. In contact with air nicotine assumes a dark brown color and gradually becomes a resin. The free base is levorotatory $[\alpha]_D = -166.4$ at 20°C . whereas its salts turn the plane of polarized light to the right. Nicotine is soluble in alcohol, ether and water.

Symptoms.—Intoxication with nicotine, other than through the use of tobacco is rare although there are several cases on record. Irrespective of whether nicotine is taken in the form of the alkaloid or in the use of tobacco the symptoms produced are quite characteristic, the only significant difference being in the time of onset and development of symptoms. The pure nicotine acts with a rapidity equal to that of hydrocyanic acid, and if in

concentrated form, leaves behind evidences of irritation since nicotine has some caustic action.

If nicotine is taken by mouth there is a hot, burning sensation from the mouth to the stomach. Absorption occurs rapidly. The first symptoms are nausea, salivation, vomiting, and purging with abdominal cramps. A considerable degree of dizziness, mental confusion and muscular weakness follow. The pulse is weak, slow and sometimes intermittent. There may be clonic convulsions and tetanic spasms. Respiration is rapid and labored and the eyes protrude, the pupils at first being contracted, later dilated. Later a condition of unconsciousness may set in, with symptoms of shock, or delirium, death resulting from respiratory failure.

Poisonous Action.—Nicotine is readily absorbed as such and is then free to act upon the nerve centers. The first action is one of stimulation of the brain followed by depression. The convulsions are probably of cerebral origin, although nicotine acts powerfully upon the heart causing it to beat slowly and irregularly through vagus inhibition. Death does not occur from paralysis of the heart but from arrest of the respiration. Nicotine appears to possess a strong, almost specific effect upon the small intestines and uterus causing them to contract vigorously. Bile and saliva secretions are increased. It is probable that a portion of nicotine is oxidized or otherwise changed in the body, the major portion, however, being eliminated by the urine and saliva.

Fatal Dose.—One to four drops of pure nicotine will probably kill an adult in a few minutes. Perhaps the smallest fatal dose is about one grain. The fatal dose varies somewhat according to whether the individual has an established tolerance for nicotine through the use of tobacco.

Fatal Period.—Death may occur within a few seconds depending upon the rate of absorption of the nicotine, which in turn would be influenced by the state of the alimentary canal, food content, etc. A fatal outcome has been recorded as long as two days after ingestion of the poison.

Post Mortem Appearances.—Post mortem appearances are not especially characteristic. The odor of nicotine may be present in the gastro-intestinal contents and the mucous membranes of the stomach and intestines may show signs of irritation.

Treatment.—Evacuation of the stomach and thorough gastric lavage are indicated. To the wash-water may be added tannic acid or oxidizing agents as hydrogen peroxide. The symptoms are to be combatted by stimulation, maintenance of the respiration, and body temperature. Oxygen inhalation may be of value.

THE USE OF TOBACCO

Under ordinary circumstances the moderate use of tobacco in the form of smoking or chewing tobacco is not attended by any perceptible untoward effects except the establishment of a habit which in some instances is very difficult to break. Symptoms of poisoning which resemble mild nicotine intoxication, are, however, usually experienced in the first use of tobacco in any form, and even in the experienced user of tobacco when an excess is consumed. In spite of statements to the contrary, it is quite generally accepted that the symptoms which may be called forth by the excessive use of tobacco are due to the nicotine content of the smoke or juice. Inhalation of the smoke produces more marked symptoms than are experienced when the smoke is not inhaled. This un-

doubtedly is due to the greater absorption of nicotine by the blood vessels of the lungs.

As stated previously the acute toxic symptoms which may be produced by the use of tobacco resemble those of acute nicotine poisoning. The long continued excessive use of tobacco may also give rise to chronic poisoning which is manifested especially upon the gastro-intestinal tract, the central nervous system and the heart. The symptoms indicative of chronic poisoning are loss of appetite, with various types of gastric inability to handle foods and chronic intestinal catarrh, which may lead to anemia and emaciation; nervous disturbances take the form of heightened reflexes, insomnia, tremors and lack of control of voluntary movements, and rarely nicotine blindness which may be completely cured by stopping the use of tobacco unless degeneration of the optic nerve has set in. The heart symptoms are so characteristic as to lead to the designation of the trouble as "tobacco heart." There is palpitation, increased rate, arrhythmia which is due to extra systoles of the auricles, and heart block. All these symptoms disappear on stopping the use of tobacco. The heart irregularity may become sufficiently grave to cause fainting. Angina pectoris is rare in these cases but arteriosclerosis is said to be favored by the use of tobacco.

The therapeutic use of tobacco or nicotine at the present time is very limited. Numerous cases of poisoning have been recorded attendant upon the employment of tobacco therapeutically, as in the form of a poultice applied to local swellings or to stop bleeding, or as an enema.

Analyses of tobacco of diverse origin have shown a wide variation in nicotine, the range being from 0.6 to 8.9 per cent. It is often stated that different brands of cigarettes contain added opium derivatives. This is incorrect since

several investigations have failed to show the presence of any foreign narcotic drug.

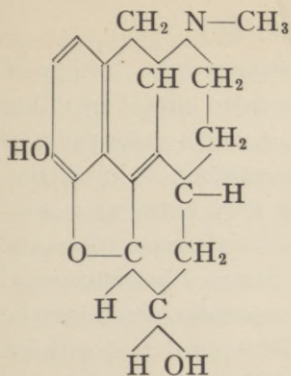
References

- VAN LEEUWEN: Arch. Neerl. Physiol., 1918, 2, p. 650; Arch. f. exp. Path. u. Pharm., 1918, 84, p. 282.
BAUMBERGER: J. Pharm. & Exp. Therap., 1923, 21, pp. 23, 35, 47.

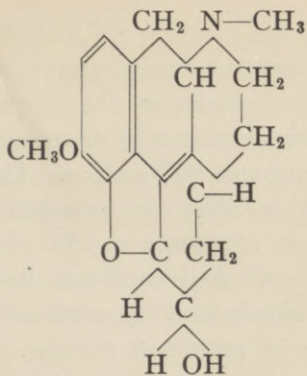
THE OPIUM GROUP

When the unripe capsules of the garden or opium poppy, *Papaver somniferum*, are cut the juice flows out and this when air-dried is called opium. This brownish material contains twenty or more alkaloids which are divisible into two groups, namely, the morphine group and the papaverine group. The morphine group is the most important, and the members may be regarded as phenanthrene derivatives. In addition to morphine this group contains esters formed by replacing the hydrogen of one or both hydroxyl groups in morphine. Codeine, or methylmorphine; thebaine, or dimethylmorphine are natural constituents of opium. Others, as dionine, or ethylmorphine, and heroine or diacetylmorphine are synthetic products. The second group of alkaloids in opium are iso-quinoline derivatives, the most important being papaverine and narcotine. The characteristic effects of this group is associated with the benzyl radicle. From a toxicological viewpoint the important constituents of opium are morphine, codeine, and heroine. The alkaloids of opium occur in combination with acids usually sulphuric and meconic acids although sometimes the combination is with acetic and lactic acids. In the dried form opium contains about 10 per cent of morphine.

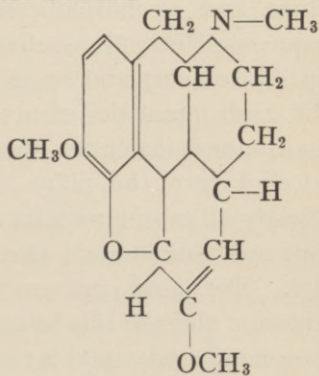
The structural relationships of the different opium derivatives may be represented by the following formulæ:



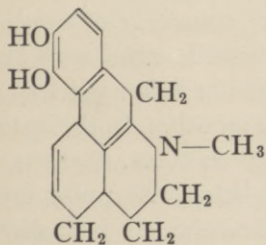
Pschorr's Formula
for Morphine



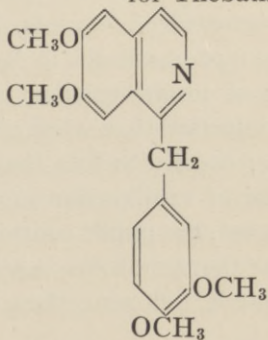
Pschorr's Formula
for Codeine



Pschorr's Formula
for Thebaine



Pschorr's Formula
for Apomorphine



Papaverine

OPIUM AND MORPHINE

Inasmuch as opium and morphine are so similar in action toxicologically, the characteristic effects in either case being produced by morphine, a single description of the symptoms will suffice. The number of medicinal preparations into which morphine may enter as a constituent is very large and for the official preparations the reader is referred to the United States Pharmacopœia.

Morphine is found as a crystalline powder which may be made up of prisms or needles. This powder is without odor and is bitter to the taste. Relatively insoluble in water, ether and benzene it readily dissolves in chloroform and alcohol especially if the latter is hot. Its aqueous solution is alkaline to litmus and dissolves readily in dilute acids and in an excess of the caustic alkalis. In small quantities of potassium and sodium hydroxides morphine is insoluble. Solutions of morphine in acid and alcohol turn the plane of polarized light to the left. Nearly all morphine salts are crystalline, soluble in water but insoluble in amyl alcohol, ether, chloroform and benzol. The most common morphine salts are the hydrochloride and the sulphate which exist as white crystalline powders readily soluble in water.

Symptoms.—The symptoms of poisoning in man may be divided into three stages (*a*) a period of excitement, (*b*) an interval of narcosis, and (*c*) coma. The rate at which symptoms begin to be manifested varies with the manner of administration, being earlier following hypodermic injection than when given by mouth. In the latter instance, usually in less than thirty minutes, there is a sensation of exhilaration and well being, the pulse rate is increased, the pupils contracted, and the face is flushed. Thus far the symptoms closely resemble those of alcohol. Immediately following these sensations there is a feeling

of giddiness, and mental heaviness which gradually is succeeded by drowsiness, sometimes nausea and vomiting, the pulse being slow and reduced in volume. In certain cases skin eruptions may appear. An irresistible desire for sleep follows accompanied by feelings of great muscular relaxation and loss of sensation. The pupils become contracted, the bowels are generally constipated and voluntary control of the bladder is lost. Unconsciousness ensues which is succeeded by coma from which the patient cannot be aroused. The respiration is stertorous and slow and gradually becomes shallower. Cyanosis is present, the skin is covered with a cold sweat and near to death the pupils may dilate. Dilated pupils in a dead body, therefore, do not contraindicate morphine or opium poisoning. Death occurs from failure of respiration. As in other types of faulty respiration the blood shows typical features, accumulation of CO_2 , insufficient oxygen, etc.

All cases of opium or morphine poisoning do not necessarily present the same train of symptoms. At times death is sudden without preliminary symptoms other than sleep, and death occurs quickly. Again in individuals more or less accustomed to the drugs convulsions may be the characteristic feature. A relapsing form is also sometimes to be observed, the patient apparently being on the road to recovery, consciousness being restored, only to sink back into a fatal narcosis. Vomiting may or may not be present and the same is true with respect to diarrhoea.

At times the diagnosis of opium or morphine poisoning is difficult since the symptoms so closely simulate those of disease and other types of intoxication. "Insensibility from chloral, from alcohol, from belladonna or atropine, and from carbon monoxide gas are all more or less like opium poisoning. With regard to chloral, it may be that

only chemical analysis and surrounding circumstances can clear up the matter. In alcohol poisoning the breath commonly smells very strongly of alcohol, and there is no difficulty in separating it from the contents of the stomach, etc., besides which the stomach is red and inflamed. Atropine and belladonna invariably dilate the pupil, and although just before death opium has the same effect, yet we must hold that mostly opium contracts, and that a widely dilated pupil during life would, *per se*, lead us to suspect that opium had not been used, although, as before mentioned, too much stress must not be laid upon the state of the pupils. In carbon monoxide, the peculiar rose-red condition of the body affords a striking contrast to the pallor which, for the most part, accompanies opium poisoning. In the rare cases in which convulsions are a prominent symptom, it may be doubtful whether opium or strychnine has been taken; but the convulsions hitherto noticed in opium poisoning seem to have been rather of an epileptiform character, and very different from the effects of strychnine. No rules can be laid down for cases which do not run a normal course; in medicine such are being constantly met with, and require all the care and acumen of the trained observer. Cases of disease render a diagnosis often extremely difficult, and the more so in those instances in which a dose of laudanum or other opiate has been administered.

Apoplexy will only simulate opium poisoning during life; a post mortem examination will at once reveal the true nature of the malady. In epilepsy, however, it is different, and more than once an epileptic fit has occurred and been followed by coma—a coma which certainly cannot be distinguished from that produced by a narcotic poison. Death in this stage may follow, and on examining the body no lesion may be found" (Blyth).

“In differential diagnosis of morphine poisoning it is observed that, as a rule, it differs from alcohol narcosis in the contraction of the pupil; from cerebral hemorrhage, in the two pupils being alike in contraction; from carbolic poisoning in showing no white stain in the mouth; and from the narcosis of chloroform or ether, in absence of the odor of these agents on the breath. In whatever diseases and from whatever poisons there are failure of respiration and excessive venosity of the blood, there are certain grave symptoms which are likewise found in morphine poisoning. Then the history of the case must be relied upon for a differential diagnosis, and, if possible, the question must be settled by a chemical analysis of the liquid vomited or drawn from the stomach” (Peterson, Haines and Webster).

Morphine varies in its action on different animals. Thus in frogs, strychnine-like convulsions are caused; in the herbivora, as in the rabbit and goat, the narcotic influence is lacking but death follows from respiratory failure; in the cat and related species the feature is great excitement, culminating in convulsions and death; the dog behaves in a manner very similar to man.

Morphine is rapidly absorbed from all mucous surfaces. It is combined in the organs in part and in part is oxidized. As it is excreted into the stomach it may be reabsorbed. More is eliminated from the body by way of the feces than by the urine.

Fatal Dose.—Doses of morphine above one grain are undoubtedly dangerous and death will generally occur after 2 grains. Doses of three to four grains of opium will probably cause death. Children are much more susceptible to morphine than are adults.

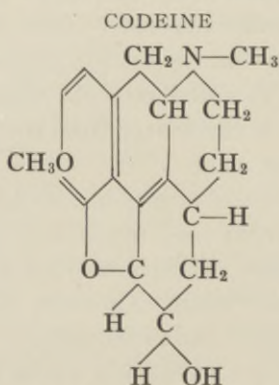
Fatal Period.—The fatal period varies from about one to twelve hours. If respiration can be maintained for a period of 24 hours or more recovery is possible.

Post Mortem Appearances.—The only characteristic appearances after death are those common to other respiratory deaths, hyperemia of the brain and pulmonary congestion.

Treatment.—The stomach should be evacuated as soon as possible even though the drug has been administered subcutaneously. Potassium permanganate ($\frac{1}{2}$ gram per liter of water) is the best chemical antidote. Tannic acid is not very satisfactory. Every means should be taken to keep the patient awake and in motion if possible. Stimulation should be pushed, strong black hot coffee or strychnine. Atropine may aid if not more than $\frac{1}{40}$ grain is given. The patient should be kept warm and if the respiration shows signs of weakening artificial respiration should be instituted. When recovery is certain the bowels should be emptied by cathartics. The intestines should be emptied soon since a relapse may occur from reabsorbed morphine in the intestines.

Reference

MACHT: J. Pharm. and Exp. Therap., 1915, 7, p. 339.



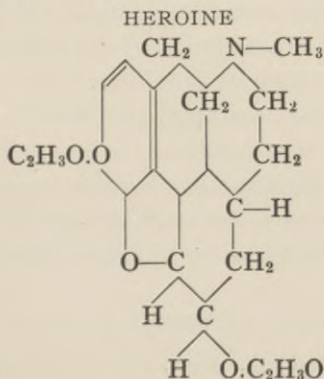
The quantity of codeine present in opium is less than one-twentieth that of morphine. Codeine is very similar

to morphine in its pharmacological and toxicological effects but very much weaker. Codeine occurs in crystalline prisms which possess the same solubilities as morphine, being relatively insoluble in water, petroleum ether, and the hydroxides of sodium and potassium. It is soluble in ether, chloroform, benzol, amyl alcohol, acids and ammonium hydroxide. It is levorotatory in watery solutions. By treatment with strong acids it yields apomorphine under the same conditions as does morphine. The common salts of codeine are the phosphate and the sulphate which are readily soluble in water but insoluble in chloroform and ether. Unlike morphine codeine apparently does not readily form a habit.

Symptoms.—Codeine produces less profound sleep than morphine and in large doses tends to increase excitability. The symptoms of poisoning are disturbances of vision, muscular weakness, slight delirium, increased heart rate, dyspnoea and collapse. Codeine does not appear to cause constipation.

Fatal Dose.—Doses of more than 4.5 grains (0.3 grams) are dangerous.

Treatment.—Treatment for codeine poisoning would be similar to that for morphine.



Heroin is a synthetic derivative of morphine, diacetylmorphine. It forms a white powder of crystalline prisms which are difficultly soluble in water and ether but readily soluble in hot alcohol and chloroform. Treated with potassium hydroxide it yields morphine and acetic acid. With hydrochloric acid it forms heroine hydrochloride, a white crystalline powder, soluble in water and alcohol and insoluble in ether and chloroform. In the body morphine is formed from heroine.

Symptoms.—Poisoning from heroine resembles closely morphine intoxication. In general there is a greater action on the respiratory mechanism, the cerebral symptoms being less pronounced. The symptoms most characteristic are disturbed vision, headache, restlessness, slow pulse, slow, deep respiration, some cyanosis, pains in the extremities. Death is due to failure of respiration.

In many instances death from heroine intoxication results from over-dosage by individuals with the heroine habit, acquired in many cases by the taking of the drug in the form of snuff.

Fatal Dose.—The fatal dose is approximately 0.5 gram.

Fatal Period.—This varies from a few hours to 2 or 3 days.

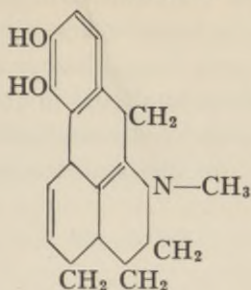
Post Mortem Appearances.—Autopsy of heroine victims reveals nothing characteristic beyond those features usual with deaths from respiratory failure.

Treatment.—The treatment indicated for heroine poisoning is exactly that outlined for morphine intoxication (see page 134). Inasmuch as heroine possesses an action upon the respiration more marked than morphine special attention should be given to its maintenance.

Reference

McNALLY: J. Lab. and Clin. Med., 1917, 2, p. 570.

APOMORPHINE



Apomorphine is a synthetic derivative of morphine made by the action of concentrated acids upon the alkaloid. It possesses little or no narcotic action but instead exercises an excitant action upon the nerve centres, particularly the vomiting centre. This is stimulated to a marked degree whether the drug is administered by mouth, vein or subcutaneously. Therapeutically and toxicologically its chief significance lies in its property of causing vigorous vomiting and advantage may be taken of its use in cases of other types of poisoning especially when resistance is offered to treatment or cooperation on the part of the patient is lacking. In general, however, in poisoning with narcotics apomorphine fails to work. This statement is particularly true with respect to chloroform, chloral, morphine and its derivatives.

Poisoning by apomorphine rarely occurs, its appearance for the most part resulting from accidents in therapeutic employment.

Symptoms.—The chief symptoms of poisoning are marked excitement, anxiety, dizziness, fainting, irregular respiration, violent convulsions, and death from respiratory failure.

It is generally conceded that these untoward effects are produced by impurities, such as decomposition products,

in the apomorphine preparations employed. Accidents are particularly likely to occur if vomiting is not elicited, especially in lung and heart diseases, in patients with lowered resistance in general, and in children.

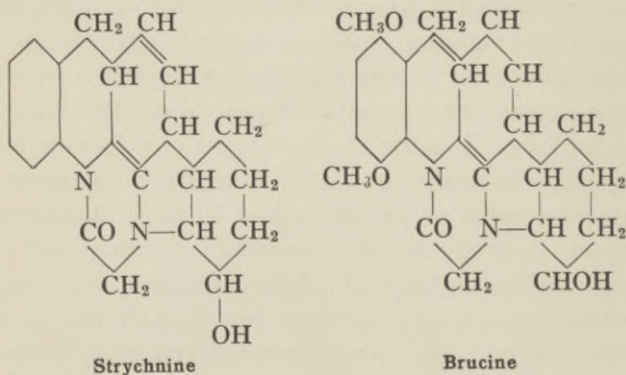
The fatal dose is indefinite and treatment should be directed especially to the maintenance of respiration.

References

- HARNACK: Münch. med. Wochenschr., 1910, 57, p. 1745.
 MACHT: J.A.M.A., 1917, 68, p. 1230; Proc. Soc. Exp. Biol. and Med., 1917, 15, p. 26.

STRYCHNINE GROUP (Nux Vomica)

STRYCHNINE AND BRUCINE



The seeds of *Strychnos nux vomica*, or Koochla tree, contain approximately three to four per cent of the alkaloids, strychnine and brucine, which occur in about equal quantities. The mixture obtained from dried ripe seeds constitutes the therapeutic preparation known as *nux vomica*. Both alkaloids have the same type of action in man, although the brucine effect is only about $\frac{1}{30}$ to $\frac{1}{8}$

as strong as the strychnine action. Practically, therefore, the action of nux vomica is represented by the strychnine present.

The preparations of nux vomica commonly employed are nux vomica which officially must contain 2.5 per cent of alkaloids (1 grain = 0.06 gm.); the extract, 16 per cent of alkaloids ($\frac{1}{6}$ grain = 0.01 gm.); the fluid extract, 2.5 per cent (1 minim = 0.06 c.c.); the tincture, 0.25 per cent (10 minims = 0.6 c.c.). The official salts of strychnine are the nitrate and the sulphate.

Strychnine is insoluble in water but soluble in acids and chloroform. It has an intensely bitter taste and forms salts with acids which are soluble in water.

Brucine is somewhat more soluble in water than strychnine and is readily soluble in chloroform and amyl alcohol. Its salts possess physical properties similar to those of strychnine.

Symptoms.—The first signs of strychnine poisoning consist of restlessness, nervousness, abrupt movements, and stiffness of the face muscles. These symptoms are soon succeeded by more pronounced twitchings of the muscles which may partake of the nature of muscle spasm and lead to general convulsions of the spinal type. In these convulsions all the voluntary muscles are involved, so that of two opposing sets of muscles the stronger predominates. The extensor muscles usually being the stronger, the legs, arms and back are extended and the head is thrown back, the whole action at times being sufficiently aggravated so that the back is arched, the weight resting upon the heels and back of head (opisthotonus). The hands are clenched, eyes open and the lips may part in a characteristic grin, the *risus sardonius*, from the fact that the corners of the mouth are spasmodically drawn out. The patient's mind is clear which

leads to great anxiety and during the convulsions there is great pain from the muscle cramps.

The convulsions at first are rapidly intermittent (clonic) but soon become tonic resulting in a typical tetanus. The muscles of the diaphragm are also involved so that ultimately it becomes rigid, and this together with the tense muscles of the thorax and abdomen stops respiration. Cyanosis is therefore present, the eyes protrude with dilated pupils and the pulse is small and tense and often cannot be detected.

The convulsion usually lasts about a minute, the muscles relax, and a condition of depression almost amounting to paralysis sets in. An interval of 10 to 15 minutes may elapse before the next attack which usually follows some kind of stimulation. If death does not occur during a convulsion the remissions become progressively shorter, the convulsions become weaker and paralysis more prominent.

Convulsions in the higher degrees of poisoning are induced usually by reflex stimulation such as the slamming of a door, a touch, a light, a puff of air, any voluntary movement, etc. In more serious cases the spasms are undoubtedly spontaneous but even in this instance just as few reflex stimuli as possible should be allowed to play upon the patient. Death follows usually from failure of respiration, the heart continuing to beat for some time after cessation of breathing. On the other hand, in long continued cases of strychnine poisoning the patient may die from the exhaustion induced by the tetanus. Strychnine is excreted unchanged in the urine. Little is eliminated by the feces.

Repetition of administration leads to increased susceptibility rather than to tolerance, hence the possible danger of too large doses continuously administered.

At times it is difficult to differentiate strychnine tetanus from other types of tetanus, as traumatic tetanus, spinal meningitis, epilepsy or hysteria. In traumatic tetanus there has been previous malaise and slow development and the course of the condition will establish the diagnosis. If any doubt is present treatment for strychnine poisoning should be instituted. Fever and history will differentiate in spinal meningitis and in epilepsy consciousness is lost and the reflexes are normal. In certain cases of hysteria the diagnosis is impossible hence such cases should also be treated as for strychnine poisoning.

Fatal Dose.—The smallest fatal dose on record is $\frac{1}{4}$ grain of strychnine sulphate. On the other hand a dose of 20 grains has been taken with recovery.

Fatal Period.—The symptoms generally appear in about 20 minutes after administration of the drug although they may be delayed for a much longer period, an hour or more. If the dose is very large death generally occurs within two hours although it may be delayed for many hours. Even when the patient has apparently recovered a sudden, severe spasm may occur terminating in death.

Post Mortem Appearances.—The appearances after death are not characteristic beyond an early and maintained rigor.

Treatment of Nux Vomica Poisoning.—If the drug has been taken by mouth and prominent symptoms have not appeared thorough lavage of the stomach should be practiced, employing a chemical antidote in the washwater or administered at short intervals—potassium permanganate is probably the most effective ($\frac{1}{4}$ teaspoonful of the crystals should be dissolved in one pint of warm water, carefully decanted so as not to include any crystals). Iodine (15 drops of the tincture in $\frac{1}{2}$ glass of water) or tannin (teaspoonful in $\frac{1}{2}$ glass of hot water) are also useful

since they render the alkaloids insoluble. They should, however, be immediately removed. Tea and coffee are less desirable since their content of caffeine, if allowed time for absorption, acts synergistically to nux vomica or strychnine.

When convulsions have already set in quick action is demanded and the patient should be anesthetized with ether or chloroform. Anesthesia with ether and chloroform should not be continued longer than possible since both these anesthetics tend to depress the respiration. Ether is to be preferred since chloroform may give rise to delayed poisoning. For prolonged effect bromides in massive doses, 15 grams by mouth or rectum act in a manner antagonistic to nux vomica. Paraldehyde may also be useful since it does not depress the respiratory centre. Morphine should be employed with extreme caution owing to its marked depressant action upon the respiratory centre. If necessary artificial respiration must be given. A patient should be kept as quiet as possible.

References

- HATCHER and EGGLESTON: *J. Pharm. and Exp. Therap.*, 1917, 9, p. 359; 10, p. 281.
GITHENS and MELTZER: *J. Pharm. and Exp. Therap.*, 1911, 2, p. 357.

ACONITINE

Aconitum or monkshood contains several alkaloids of which aconitine is chief. The structure of aconitine has not yet been established. The principal therapeutic effects of aconitine are upon the circulation producing slowing of the pulse and fall of pressure. Employed locally as the tincture it has value for the relief of pain, in toothache, neuralgia and rheumatic conditions. The

principal preparations are aconitum U.S.P. containing not less than 0.5 per cent of alkaloids; the extract representing 2 per cent of alkaloids, the fluid extract containing 0.5 per cent of alkaloids, and the tincture 10 per cent of drug or 0.05 per cent of alkaloids. A characteristic action of aconitine is the tingling sensation in the mouth which is followed by numbness and loss of sensation. This action is produced locally wherever the drug may be applied.

Aconitine is unstable, decomposing readily and on hydrolysis yields benzoic and acetic acids and an inert base aconine. Aconitine is alkaline to litmus, soluble in chloroform, ether and benzene, and insoluble in water. It turns the plane of polarized light to the right; its salts to the left.

Symptoms.—Symptoms of poisoning consist in tingling in the mouth, stomach and skin, and may be most pronounced in the finger tips. This characteristic feature is of considerable importance in the diagnosis of aconitine poisoning. There may be nausea, diarrhœa, vomiting and pain in the stomach. The burning and tingling sensations pass into anesthesia. There are peculiar chilly sensations, the pupils are dilated and vision is misty, the skin is cold and pallid, respiration is dyspnoëic, the pulse is weak and feeble and arrhythmic. Speech may be impaired and convulsions are not infrequently encountered. Death occurs from respiratory failure or from heart block, or ventricular fibrillation.

When large doses are taken death may result very rapidly from heart paralysis.

Fatal Dose.—Aconitine is one of the most powerful poisons known and has caused death in amounts of $\frac{1}{10}$ grain or less.

Fatal Period.—Death usually occurs within 4 or 5 hours, but in certain cases has been delayed for 3 or 4 days.

Atropine occurs in the racemic form and may be obtained as crystalline plates. Difficultly soluble in water it readily dissolves in alcohol and chloroform. Atropine sulphate, a white crystalline powder, is the official preparation which is soluble in water but relatively insoluble in chloroform and ether.

Atropine actions fall into two groups (*a*) stimulation of nerve centres, principally cerebral and medullary, (*b*) depression of nerve endings as sensory nerve endings, motor nerve endings in the smooth muscle of the viscera, secretory nerve endings, the ends of the third nerve in the eye and vagus nerve endings. Poisoning may occur from administration of the isolated drug or from absorption through the skin by the use of plasters, oily or alcoholic preparations as ointments or liniments. Toxic symptoms in ophthalmic practise are fairly common.

Symptoms.—The first warnings of toxic action are the dilated pupil, dry throat and mild cerebral symptoms. The symptoms occur promptly but may last several hours or days. In fatal cases the course of intoxication may run for two weeks or more. With severe poisoning there may be cerebral stimulation as evinced by delirium. Later this is followed by collapse, and coma. Death usually occurs in coma. Convulsions at the terminal stage are rare.

During the stage of stimulation there is great thirst, burning and constriction of the throat, difficult swallowing, flushed skin, especially, of face and neck which resembles a scarlatinal rash. Accomodation of the eye is paralyzed so that vision is disordered. The pulse is rapid, respiration deep and rapid, arterial pressure is high, the temperature may rise several degrees, there is vertigo, muscular incoördination, often nausea and vomiting, and retention of urine. During the stage of delirium patients with atropine poisoning strongly resemble maniacs, and in the earlier

period of the poisoning the condition has been mistaken for scarlet fever.

After the period of stimulation collapse follows which is characterized by feeble heart action, low blood pressure, a slow and shallow respiration, and coldness of the extremities, death resulting usually from respiratory failure.

Fatal Dose.—The fatal dose of atropine may be taken as 0.1 gram for adults and 0.01 gram for children. The other members of the atropine group are less toxic.

Fatal Period.—Death usually occurs within 24 hours, although it may be delayed for several days.

Post Mortem Appearances.—The autopsy reveals findings typical of asphyxia.

Treatment.—Treatment of atropine poisoning is quite effective since death does not usually occur rapidly, and it consists of lavage of the stomach, tannic acid or tea being added to the wash water. The general symptoms should be combatted by pilocarpine (10 mg. ($\frac{1}{8}$ gr.) subcutaneously repeated until mouth is moist). For the delirium, bromides and the ice cap. Because of their depressant effect upon the respiratory centre, morphine, chloral and chloroform should not be used, although the cautious use of morphine in the early excitement may be beneficial, or ether may be inhaled to lessen excitement. In the stage of collapse depression should be antagonized by strong coffee and artificial respiration persistently resorted to if necessary.

Reference

CUSHNY: *J. Pharm. and Exp. Therap.*, 1921, 17, p. 41.

VERATRINE GROUP

There are three types of plants in which veratrine-like alkaloids may occur. Each type consists of a mixture of alkaloids, the classification differing widely and the whole subject being in more or less confusion. However,

two substances stand out clearly, veratrine or cevadine, and protoveratrine. Cevadine (veratrine) is present in the seeds of *Veratrum Sobadilla* or *Cevadilla*. The active poisonous principle of both *veratrum alba*, or white hellebore, and *veratrum viride*, or green hellebore is protoveratrine. The official veratrine has as its principal constituent cevadine. The official *veratrum viride* contains protoveratrine as its chief constituent.

Therapeutically cevadine has been employed in the form of an ointment as a counterirritant in neuralgic conditions, especially of the face. As it is highly toxic its internal administration is not advised and poisoning has occurred from absorption through the skin.

Protoveratrine (*Veratrum viride*) has been used to slow and soften the pulse and to lower blood pressure. Its chief action is that of a cardiac depressant from vagus stimulation, resulting in slowed pulse, fall of systemic blood pressure and reduction of temperature, the latter probably from the profuse sweating induced. It has enjoyed a wide use in conditions of high blood pressure particularly that associated with eclampsia. The preparations most employed are *veratrum viride*, the fluid extract and the tincture.

Symptoms.—Death from overdoses of *veratrum viride* is rare owing to the fact that it is a strong gastric irritant and promptly causes vomiting. Typical symptoms of veratrine poisoning consist of burning in the stomach, vomiting, diarrhoea, abdominal pain, increased salivation, giddiness, headache, dilated pupils, irregular heart action, collapse, paralysis or convulsions, death from respiratory failure and accompanying cardiac collapse.

Fatal Dose.—Little is known concerning the exact fatal dose although death may occur after taking 4 or 5 c.c. of the fluid extract of *veratrum viride*.

Fatal Period.—Although death may occur rapidly it is usually delayed for more than 24 hours.

Post Mortem Appearances.—These are not characteristic. There may be irritation of the gastro-intestinal tract and hyperemia of the brain and its linings, but these features are not constant.

Treatment.—Alkaloidal antidotes and lavage of the stomach should be employed. For the collapse stimulants, as ammonia, brandy, atropine, strychnine and warmth, may be administered. Artificial respiration is of great value when indicated and the heart may be helped by intravenous injection of epinephrine or strophanthine should the need arise.

References

- PILCHER and SOLLMANN: *J. Pharm. and Exp. Therap.*, 1915, 7, p. 295.
PILCHER: *Ibid.*, 1917, 9, p. 350; *Am. J. Physiol.*, 1917, 44, p. 1.

PHYSOSTIGMINE

Physostigmine (also called Eserine) is the principal alkaloid of Calabar bean, or the ordeal bean. It is a basic substance, containing nitrogen, and on treatment with potassium hydroxide yields carbon dioxide and methylamine. It occurs in crystalline form, is tasteless, difficultly soluble in water, readily soluble in alcohol, ether, chloroform and benzene, and turns the plane of polarized light to the left. Official preparations are the salicylate, the alkaloid itself, the extract and the tincture. The chief action of physostigmine is that of stimulating secretory nerve endings of glands and the nerve endings of striated and smooth muscle. It causes a powerful contraction of the smooth muscle of the eye and of the intestine. It is employed in diseases of the eye and in intestinal paresis. Paralytic effects may be observed as the action on the

nervous system. It is antagonistic in its action to atropine. In many respects it resembles nicotine in its physiological effects.

Symptoms.—The symptoms of poisoning by physostigmine are marked muscular weakness without loss of consciousness, nausea, vomiting and sometimes purging. The pupils are noticeably contracted, the skin is covered with sweat, there is epigastric pain, salivation, lachrymation, palpitation with slow pulse, low blood pressure, dyspnoea, muscular twitchings, and convulsions. The loss of muscular power starts in the legs and travels upwards. Respiration is depressed and the breathing may be asthmatic in character from contraction of the bronchial muscles. Death is caused by failure of respiration.

Fatal Dose.—The fatal dose is unknown. However, 3 grains would be much beyond the minimum lethal dose.

Fatal Period.—In the very few cases reported in the literature death has been a matter of a few hours.

Post Mortem Appearances.—Autopsy reveals nothing characteristic, changes from the normal being those common to an asphyxial death.

Treatment.—Treatment consists of lavage of the stomach, stimulants, and atropine ($\frac{1}{2}$ to 1 mg.). Magnesium sulphate is also antagonistic to the action of physostigmine and its subcutaneous use in physostigmine poisoning has been recommended.

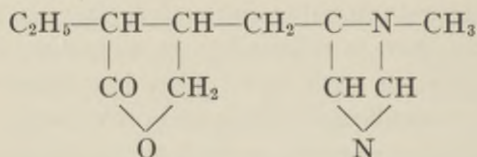
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PILOCARPINE

Pilocarpine is the principal alkaloid of jaborandi leaves and it is distinctly antagonistic to the action of atropine,

peripherally stimulating the secretory nerves, the nerves governing smooth muscle, etc. The principal secretion affected is the sweat, pilocarpine being a powerful diaphoretic. The preparations commonly employed are pilocarpine the alkaloid, the fluid extract, the hydrochloride and the nitrate.



Pilocarpine

Pilocarpine the alkaloid is a soft gelatinous mass which, however, forms with mineral acids crystalline salts possessing the power of dextrorotation.

Although the toxicology of pilocarpine is not very important cases of poisoning from overdoses occasionally occur. After toxic doses pilocarpine is an arterial dilator; it acts as a cardiac depressant, both from the action on the vagus and from its direct influence on the heart; in conditions of cardiac weakness collapse and death may follow even from relatively small doses; respiration is also depressed leading to pulmonary edema and asphyxia.

Symptoms.—The symptoms of poisoning resemble those of muscarine and start with greatly increased secretion of saliva, sweat and tears. This may be followed by nausea, vomiting and diarrhoea with severe abdominal cramps. Changes in the eye are quite noteworthy, there being contraction of the pupil and spasm of accommodation. There is at first slowed heart beat, low blood pressure, and later collapse. These symptoms are due to the action of pilocarpine upon the vagus and upon the vasomotor centre, resulting respectively in vagus heart block and

low pressure. Respiration is usually labored and of the asthmatic type and the lungs may give evidence of edema. Muscular relaxation which ascends from the lower limbs sometimes occurs. Generally consciousness is present although there may be confusion of ideas, vertigo, tremors, and feeble convulsions. Death results from paralysis of the heart or from pulmonary edema.

Less dangerous symptoms of overdoses of pilocarpine manifest themselves by gastro-intestinal disturbances, nausea, and vomiting which may be long continued and very depressing. These symptoms may occur even though the drug is not introduced by mouth. Another characteristic symptom is a burning sensation in the urethra accompanied by an irresistible desire to urinate. A large portion is eliminated in the urine unchanged.

Fatal Dose.—Two grains subcutaneously administered may be considered as a dangerous dose.

Fatal Period.—Death ordinarily occurs quickly.

Post Mortem Appearances.—There is nothing characteristic.

Treatment.—Treatment for pilocarpine poisoning consists in the use of atropine to combat the pilocarpine effects and symptomatic treatment, especially artificial respiration for the collapsed state. The atropine tends to lessen bronchial secretion, hence prevent edema, modifies the asthmatic respiration and abdominal cramps and counteracts the pilocarpine action upon the vagus, thus releasing the heart from its block.

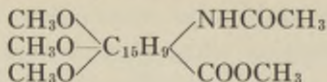
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McNALLY: J.A.M.A., 1915, 65, p. 1640.

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EGGLESTON: Ibid., 1916, 9, p. 11.

COLCHICINE



All portions of the common meadow-saffron, *Colchicum autumnale*, possess toxic properties because of the presence of the alkaloid colchicine. This alkaloid has been employed extensively for gouty conditions without definite indications for its use. Intoxication with colchicine is usually due to accident, mistaking the preparation for something else, or else from an overdose. At times, however, it has been administered with criminal intent. It is stated that the alkaloid itself is not toxic but upon oxidation in the body yields oxydicolchicine which induces the toxic symptoms. The excretion of the poison is slow.

Symptoms.—The initial symptoms are burning in the throat and stomach, nausea, vomiting and purging, intense thirst, abdominal colic. Hematuria or anuria may follow. There is great depression and weakness. The pulse is irregular and weak, the respiration shallow, the pupils dilated, the mind may or may not be affected. At times there may be delirium or convulsions. Eventually collapse results and death occurs from respiratory failure.

Fatal Dose.—About $\frac{1}{3}$ grain (0.02 gram) of the pure alkaloid may cause death.

Fatal Period.—Death usually occurs within 24 hours from a single dose although it may be delayed for several days.

Post Mortem Appearances.—Autopsy reveals nothing characteristic.

Treatment.—The stomach should be evacuated as soon as possible and to the wash-water add tannic acid or strong tea. For the irritated stomach demulcents (egg-white,

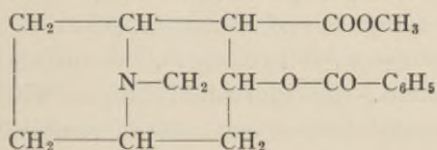
milk, oatmeal group) may be given. Pain may be combatted by morphine and the collapse treated with strychnine and atropine. If necessary institute artificial respiration.

References

DIXON and MALDEN: *J. Physiol.*, 1908, 37, p. 50.

DENIS: *J. Pharm. and Exp. Therap.*, 1915, 7, p. 601.

COCAINE



Cocaine is the principal alkaloid obtained from the leaves of *Erythroxylon coca*, a plant indigenous in South America. The natives of Peru, Chili and Bolivia have chewed these leaves from ancient time for the psychic stimulation produced. Cocaine exists in the dried leaves, to the extent of approximately 0.75 per cent. Other alkaloids are found with cocaine but they possess less significance.

From a chemical viewpoint cocaine is closely related to atropine and occurs in three stereoisomeric forms, l-cocaine, d-cocaine, and r-cocaine. It is the l-cocaine that is of value from a medicinal standpoint.

Cocaine occurs as a white crystalline powder which is almost insoluble in water and cold alcohol, but soluble in warm alcohol, ether, chloroform and olive oil. It forms cocaine hydrochloride which is the official preparation and constitutes a white crystalline powder, soluble in water and alcohol but insoluble in ether and olive oil. The solution in water is neutral to litmus and turns the plane of polarized light to the left.

Cocaine is rapidly absorbed, being partly destroyed in the organism, but is eliminated in large measure unchanged in the urine. Poisoning with cocaine resembles in some respects intoxication with epinephrine, namely, stimulation of the sympathetic nervous system.

Symptoms.—Cocaine poisoning is not infrequent and fatal results may follow. In many instances intoxication results from carelessness in administration, mistakes in dosage or because of the idiosyncrasy of the individual.

The first symptoms of cocaine intoxication are restlessness or excitement, talkativeness, the speech is confused and incoherent, the individual laughs without cause, and there may be other evidences of mental disturbance, as delirium with hallucinations which may assume a maniacal condition. The mouth and throat are dry, swallowing is difficult, there may be dizziness, a rapid pulse, quickened respiration, the pupils are dilated and exophthalmic, nausea, vomiting, abdominal pain and numbness and tingling of the hands and feet may be experienced. The heart is at first rapid and strong, later becoming weak and irregular. The skin is pale and covered with sweat and there may be creeping sensations. Dyspnea, Cheyne-Stokes respiration, unconsciousness, convulsions, cyanosis, and respiratory failure close the scene.

In other instances fatal results are induced in a very few minutes, the severe symptoms appearing without warning. The patient may collapse, go into convulsions or unconsciousness and die.

Chronic poisoning, induced through habit, is like other drug habits, characterized by peculiar features which, however, have no direct interest for the toxicologist. A discussion of the cocaine habit and its peculiarities is therefore not included here.

Fatal Dose.—The fatal dose of cocaine depends upon the manner of the introduction. When taken by mouth probably 1 gram may be considered as capable of producing death. Such a dose has caused death and in others large quantities have been taken with recovery. A dose of 0.03 gram per urethra, 0.04 gram under the conjunctiva, have caused death.

Fatal Period.—This depends upon the dosage and the rapidity of absorption. If the patient survives for $\frac{1}{2}$ an hour the chances of recovery are good. Death, however, may be delayed for several hours.

Post Mortem Appearances.—With rapid death there is hyperemia of the brain, spinal cord, liver, spleen and kidneys.

Treatment.—If cocaine has been taken by mouth the stomach should be emptied and well washed out. Chemical antidotes, such as potassium permanganate, may be added to the wash-water. When the poison has been introduced parenterally every means should be employed to delay absorption, such as ligation, etc. If symptoms of poisoning have manifested themselves every means employed to delay death gives an opportunity for recovery since in the body cocaine is rapidly oxidized and thus rendered inert. For the depression or collapse, stimulants such as caffeine, aromatic spirits of ammonia, hot alcoholic drinks are indicated. The convulsion may be controlled by ether or chloral. Artificial respiration may be necessary.

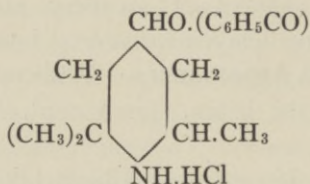
COCAINE SUBSTITUTES

There are a large number of substitutes which are employed in medicine in place of cocaine. The purpose of their preparation was the endeavor to form a compound which would possess the anesthetic properties of cocaine

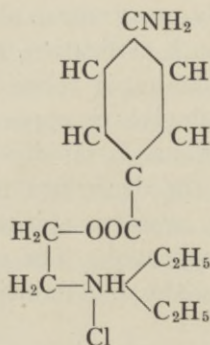
without its toxicity. In general these substitutes are less poisonous than cocaine but they still have a certain degree of toxicity. Even with these less toxic compounds cases of poisoning occasionally occur, the symptoms manifested resembling those induced by cocaine. Treatment indicated is symptomatic.

The most important of the cocaine substitutes are—

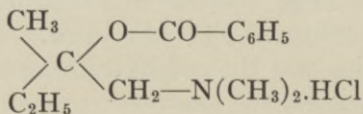
Eucaine—beta eucaine chloride or lactate (trimethyl-benzoyl oxypiperidine).



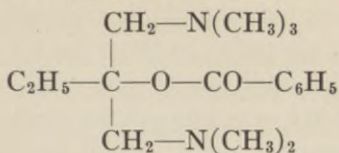
Novocaine or Procaine.—(para-amino-benzoyl-diethyl amino ethanol) generally employed as the hydrochloride—



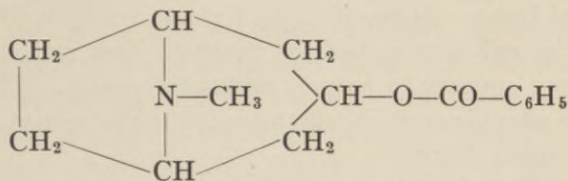
Stovaine—(dimethyl-amino-benzoyl-pentanol chloride).



Alypine—(the hydrochloride of tetra-methyl-diamino-dimethyl-ethyl-carbinyl-benzoate).



Tropacocaine—(the benzoyl ester of pseudo-tropine chloride).



References

- EGGLESTON and HATCHER: *J. Pharm. and Exp. Therap.*, 1919, 13, p. 433; *Proc. Soc. Exp. Biol. and Med.*, 1918, 16, p. 16.
 ROTH: *Hygienic Lab. Bull.*, 109, 1917.
 HOFVENDAHL: *Biochem. Z.*, 1921, 117, p. 55.

IPECAC

Ipecac is obtained from the root of a Brazilian plant, which contains two potent alkaloids, emetine and cephæline. Therapeutically they are employed for the production of nausea and emesis, as a sedative expectorant and as specifics in amebic dysentery. The emetic effects are not so prompt as with apomorphine.

Chemically they are isoquinoline derivatives, emetine ($\text{C}_{25}\text{H}_{28}\text{N}_2(\text{OCH}_3)_4$) being the mono-methyl ether of cephæline ($\text{C}_{25}\text{H}_{28}\text{N}_2(\text{OH})(\text{OCH}_3)_3$).

The therapeutic use of the various ipecac preparations has given rise to many cases of poisoning in some instances with fatal results. The toxic effects are particularly

prominent if the drug is given intravenously. Special care should, therefore, be exercised when it is so administered. Emetine, for example, is excreted by the kidney but very slowly, appearing in the urine for several weeks.

Symptoms.—In addition to the well marked gastro-intestinal irritation ipecac preparations may induce general edema consequent to renal insufficiency, hemoptysis, flaccid paralysis, peripheral neuritis, delirium, coma and failure of the heart.

Fatal Dose.—Approximately 2 grams are fatal whether administered over a short or relatively long period since the drug appears to have a cumulative effect. Thus, 2 grams administered subcutaneously in the course of 20 days caused death.

Fatal Period.—Most of the fatalities have occurred only after continued administration, hence little can be said relative to death after acute poisoning.

Post Mortem Appearances.—Autopsy reveals severe gastro-intestinal irritation together with renal congestion.

Treatment.—Since poisoning occurs generally only after repeated doses stoppage of the drug usually leads to cessation of symptoms and recovery. When acute intoxication occurs the remedial measures are purely symptomatic, heart depression being the most serious symptom and most to be guarded against.

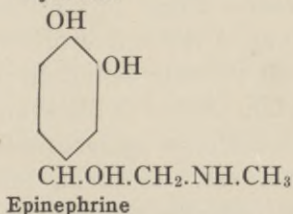
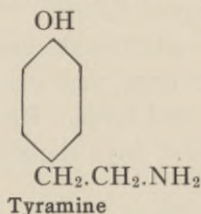
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- LEVY and ROWNTREE: *J. Pharm. and Exp. Therap.*, 1916, 8, p. 120; *Arch. Int. Med.*, 1916, 17, p. 420.
JOHNSON and MURPHY: *Mil. Surg.*, 1917, 40, p. 58.

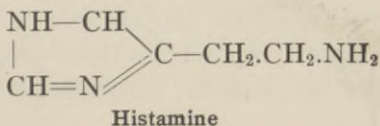
ERGOT

Ergot is a parasitic fungus which grows upon cereals. That which is obtained from rye constitutes the official preparation which may be either the extract or the fluid

extract. There are several stages in the development of the fungus, the drug being obtained from the resting stage. The chemistry of ergot is complex, several basic substances being present which are responsible for the characteristic effects of the drug. The substances which are important in contributing to ergot pharmacological effects are ergotoxine, tyramine and histamine. Ergotine is perhaps responsible for ergot producing gangrene in the cock's comb; the rise of blood pressure is attributed to tyramine and the characteristic effect of ergot in stimulating the uterus to contraction is caused by histamine. The structure of ergotine has not been established. That of tyramine is p.hydro-xyphenylethylamine—which is closely related to tyrosine from which it may be formed by loss of CO_2 , and also to epinephrine—



Histamine, or β -iminazolethylamine, is closely related to the amino acid histidine from which it may be formed by loss of CO_2 .



In previous time ergot poisoning, or ergotism, was quite common. With better methods of handling grain ergotism has become of merely historic interest although it has been said that even to-day ergotism is present in certain portions of Russia. Intoxication from ergot is caused either by overdosage in therapeutic use or its employment by women in attempts at abortion. Generally therefore the symptoms produced are those of acute poisoning.

Symptoms.—The early characteristic symptoms are those of intense gastro-intestinal irritation, vomiting, colic and diarrhoea being prominent. A second type of action is upon the cerebral nervous system as indicated by disturbances of vision, delirium, anesthasias, muscular weakness, convulsions, coma, suppression of urine, and death by respiratory failure.

In pregnancy additional symptoms, abortion followed by severe hemorrhage, may ensue which may prove fatal to both mother and fetus. Recovery from ergot poisoning is slow, several days elapsing before a normal condition is regained.

Fatal Dose.—Ergot preparations may vary widely in their content of the active principles and for this reason it is difficult to state definitely the fatal dose. There is also a certain degree of idiosyncrasy with respect to the drug which militates against positive statements concerning the toxic dose. Death has been produced by 12 grains (0.77 gram) whereas recovery has followed the administration of 150 grains (9.72 grams).

Fatal Period.—Death is usually a matter of 3 or 4 days and is not so frequent after a single large dose as after small repeated doses for considerable periods which may induce the same symptoms as those produced by eating contaminated rye, namely, gangrene of the various por-

tions of the body as fingers, toes, arms, legs, nose, or even the internal organs.

Post Mortem Appearances.—The stomach and intestines show evidence of intense irritation. The lungs, kidney and uterus may be hyperemic. The tissues in general putrefy very quickly.

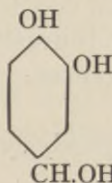
Treatment.—The gastro-intestinal canal should be thoroughly cleaned out—the stomach by stomach tube and repeated lavage—the intestines by purgatives. If indicated, stimulants as tea, coffee or strychnine should be administered.

References

BARGER: The Simpler Natural Bases, 1914.

KOESSLER and HANKE: J. Pharm. and Exp. Therap., 1917, 9, p. 360.

EPINEPHRINE



Epinephrine is the active principle of the medulla of the adrenal gland. It can be prepared synthetically and as its formula indicates is an amine closely related to the amino acid, tyrosine. It forms characteristic crystals which in solution in water readily decompose unless a preservative is present. The naturally occurring base is levo-rotatory, the synthetic is optically inactive.

Therapeutically epinephrine is employed locally to stop hemorrhage by constriction of the arterioles; in bronchial asthma; and to stimulate circulatory failure. Its chief actions are as follows: in the intestines and bronchioles it produces relaxation; in the heart and blood vessels it

causes constriction and raises blood pressure. In the body epinephrine is very quickly oxidized.

Toxicologically epinephrine is of interest only because of over-dosage or hypersusceptibility of the individual.

Symptoms.—The first indications of a toxic effect are excitement, anxiety, tremors, palpitation, precordial distress, rise in pulse and respiration, high blood pressure and increased temperature. If too great quantities are given intravenously, death may result from acute cardiac dilatation. Generally death results from failure of the respiration. There is also danger of intravenous administration in cerebral arteriosclerosis from rupture of a cerebral artery owing to the sudden increase in blood pressure. At times the condition of pulmonary edema may be aggravated when epinephrine is given intravenously in this condition.

Fatal Dose.—The fatal dose is unknown.

Fatal Period.—Death is usually sudden.

Post Mortem Appearances.—Autopsy reveals nothing characteristic.

Treatment.—This is purely symptomatic.

References

CUSHNY: *J. Physiol.*, 1909, 38, p. 259.

HEWLETT: *Arch. Int. Med.*, 1918, 21, p. 421.

GELSEMIUM

Obtained from the rhizome and roots of *Gelsemium sempervirens*, the yellow jasmine, the alkaloid gelseminine acts in a manner similar to nicotine and coniine, although its influence upon the central nervous system is more depressing. Another alkaloid found in company with gelseminine is gelsemine which has a weak strychnine action. Official preparations are the fluid extract, dose

1 minim (0.06 c.c.), and the ten per cent tincture, dose 10 minims (0.6 c.c.). Although it has been employed therapeutically in neuralgias the mechanism of its action is not understood.

Symptoms.—The symptoms consist of double vision, relaxation of the muscles of the eye and jaw, general muscular weakness and prostration. The pulse is slow and temperature falls. The respiration is slow and shallow. The mind remains clear up to the time of death which results from respiratory failure.

Fatal Dose.—Relatively small doses may cause toxic symptoms and even death. A dram of the fluid extract has caused death and 15 minims have provoked evidences of poisoning.

Fatal Period.—Death usually occurs in from 1 to 8 hours.

Post Mortem Appearances.—There is nothing especially noticeable beyond the appearances characteristic of a respiratory death.

Treatment.—The stomach should be emptied and thoroughly washed. Atropine and stimulants are indicated.

Reference

CUSHNY: Arch. f. exp. Path. u. Pharm., 1892, 31, p. 49.

CHAPTER VI

MISCELLANEOUS ORGANIC POISONS

BENZOL (C_6H_6)

The term benzol is used in two senses, first as a synonym for benzene and second to designate a variable mixture derived from the distillation of coal tar. When coal tar is subjected to fractional distillation there are four products that result: (1) crude naphtha, (2) dead oils or creosote oils, (3) green or anthracene oil, and (4) a pitch, the residue. Commercial benzol is obtained from the first fraction. Benzols of commerce vary widely in composition and in general they consist chiefly of benzene and its homologues, toluene ($C_6H_5CH_3$), and xylene ($C_6H_4(CH_3)_2$), and small percentages of other substances. Benzine with which these two substances has been confused is a derivative not of coal tar but of petroleum, consisting chiefly of hexane (C_6H_{14}) and heptane (C_7H_{16}). Usually it contains no benzene (C_6H_6). The fate of benzol in the body, so far as it has been determined, is that from 15 to 30 per cent is oxidized to phenol, catechol, and quinol, and excreted as phenol sulphates. A part is changed to muconic acid and a considerable portion is excreted unchanged by the lungs. Two types of poisoning occur, acute poisoning and chronic poisoning. These intoxications are encountered either from the industrial use of benzol or from its employment as a symptomatic remedy in the treatment of leucemia.

Acute Poisoning.—The acute poisoning gives rise to the following symptoms—dizziness and confusion followed by

excitation, unconsciousness, and death from respiratory paralysis. The symptoms arising from its medicinal use are heart-burn, flatulence, nausea, vomiting, diarrhœa, bronchial irritation, minute hemorrhages of skin and mucous membranes (purpura hemorrhagica) albuminuria, ringing in the ears, and vertigo.

Fatal Dose.—The fatal dose is undetermined but it is quite apparent that 15 mg. per liter of air produce listlessness and confusion after $\frac{1}{2}$ hour, and exposure to 20 to 30 mg. or from 2 to 3 parts per 100,000 parts of air for a few hours may cause loss of consciousness.

Post Mortem Appearances.—The blood in the heart and vessels is fluid, and the veins of the abdomen are engorged. There are hemorrhages into the gastric mucosa and bloody foam in the air passages. Liver, kidney, and intestinal disturbances contraindicate benzol.

Chronic Poisoning. *Symptoms.*—Chronic benzol poisoning takes the form of an aplastic anemia with subcutaneous hemorrhages and bleeding from the mucous membranes as terminal changes. There is a direct destruction of leucocytes with reduced formation of the elements. A destructive action on blood platelets and the megakaryocytes of the marrow from which the platelets are formed is also in evidence. There is a destruction of the adult red corpuscles and the prevention of the formation of new ones. These changes occur in the order given, the effect on the red corpuscles being especially characteristic of very slow poisoning, the last to appear and the last to disappear with recovery. It may cause headache, vertigo, narcosis, and inability to walk, with vomiting. Bleeding from various mucous membranes together with bruise-like blotches on the body are quite characteristic. Some individuals are very much more sensitive than others, instances being cited of individuals dying from typical

benzene poisoning in air containing only 1 part of benzene to 10,000 of air. Benzol also exerts a catabolic influence upon the body tissues as a whole inasmuch as nitrogenous metabolism is stimulated by it.

If after medicinal administration of benzol the leucocytes show a rapid fall in number the benzol should be stopped at once no matter how high the count, for this is an indication of severe aplasia, otherwise the leucocytes will continue to fall with fatal results. Under the circumstances the bone marrow is very red with myelocytes, with much new connective tissue and new vessels and hemorrhages.

Treatment.—Treatment is purely symptomatic. If swallowed the stomach tube should be used and ether and strychnine given hypodermatically. When overcome by the vapor removal to the open air, artificial respiration, oxygen inhalation, and stimulants are necessary. Poisoning from a medicinal use may result in anemia which can be combatted successfully only by repeated transfusions of blood.

References

HAMILTON: J.A.M.A., 1922, 78, p. 627.

UNDERHILL and HARRIS: J. Ind. Hyg., 1923, 4, p. 491.

NITROBENZOL-NITROBENZENE ($C_6H_5.NO_2$)

By the action of nitric acid on benzene, nitrobenzene, which is also sometimes called "essence of mirbane," is formed. It is extensively employed in the preparation of aniline and various explosives, and because its odor resembles benzaldehyde, or oil of bitter almonds, finds considerable use as a substitute. Various flavoring extracts, perfumes, floor polishes, inks, shoe dyes, soaps,

alcoholic liquors, confectionery and pastry may contain nitrobenzene. It has also been used to induce abortion and with suicidal intent. Nitrobenzene must be regarded as a powerful narcotic poison. Poisoning has resulted from the external application, as by spilling upon the clothing, wearing dyed shoes, from employment as a delousing agent, from the use of soap containing it, etc. Needless to point out it should never be a constituent of any substance intended for internal administration. Industrially poisoning occurs chiefly in aniline plants. The vapor is even more toxic than the liquid.

Nitrobenzene is an oily yellow liquid which may be obtained in crystalline form at low temperatures. It boils at 205°C . and has a specific gravity of 1.186. It is combustible, burning with a yellow flame.

Symptoms.—Taken by mouth nitrobenzene may cause no symptoms for a period of three hours or more beyond a burning sensation in the throat and stomach which may be followed by numbness and tingling sensations. The vapor is more powerful than the liquid. In either case definite symptoms appear suddenly. In certain instances the victim has complained of feeling drunk. There is headache, giddiness, faintness, nausea and vomiting, the vomitus having the characteristic odor of nitrobenzene. The vision is disturbed, the face is steel gray in color, coma supervenes, sometimes ending in death. The general symptoms closely resemble prussic acid poisoning except that with nitrobenzene the coma is delayed for a considerable period and does not come on at once as with prussic acid poisoning. The temperature is lowered, respiration takes on the Cheyne-Stokes type and the pupils are not sensitive to light. The urine is dark in color, with an odor of nitrobenzene, and contains reducing substances. The phenolsulphonephthalein excretion may be consider-

ably decreased. The blood is chocolate colored. Death occurs from respiratory failure. After the acute symptoms have subsided jaundice may persist for several days.

Inhalation of relatively large quantities of the vapor may produce very sudden symptoms, chief of which are nausea, vomiting, unsteady gait and actions similar to those of alcoholic intoxication, stupor and coma finally appearing with intense cyanosis and respiratory failure. The habitual contact in industry produces a chronic condition having as outstanding features languor, breathlessness, cyanosis and failing eye-sight. The urine is dark red in color, and there may be multiple neuritis, fatigue, indigestion, emaciation and anemia.

Physiological Action.—Nitrobenzene has at least a two-fold action. In the first place it first stimulates, then paralyzes the central nervous system. Secondly it may be regarded as a blood poison since nitrobenzene so changes the blood that it is no longer capable of transporting oxygen. This is accomplished by nitrobenzene combining with hemoglobin to form nitrobenzene hemoglobin or acting upon hemoglobin in such a manner as to form methemoglobin. It is possible that both compounds may be formed. At any rate the action is temporary and in acute cases at least there is no destruction of red cells or diminution of hemoglobin. The oxygen capacity of the blood is markedly decreased. Some of the nitrobenzene appears in the urine as p.amino-phenol.

Fatal Dose.—One gram will undoubtedly cause death in an adult, although recovery has followed from the ingestion of more than three ounces. Taken in an alcoholic mixture nitrobenzene appears to be more toxic than when taken alone.

Fatal Period.—Death may occur in less than an hour although usually it is delayed for several hours and even

for several days. Generally, however, death takes place within 24 hours.

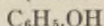
Post Mortem Appearances.—The most characteristic features are the dark-brown or black color of the blood, which usually remains liquid, the appearance of ecchymoses in the gastro-intestinal tract, hyperemia of the brain, venous engorgement, and the characteristic odor of nitrobenzene which may persist for several days.

Treatment.—This consists in prompt evacuation of the stomach and thorough lavage. There are no special antidotes. When indicated general stimulation should be carried out. Since the most serious feature is due to the changed conditions in the blood this should be remedied as soon as possible. Experience has demonstrated that this can be best accomplished by venesection and subsequent saline infusion or blood transfusion. Fatty or alcoholic substances are contraindicated. If the intoxication has been caused by spilling nitrobenzene on the body a bath should be given immediately so as to prevent absorption.

References

- SCOTT and HANZLIK: J.A.M.A., 1920, 74, p. 1000.
HAMILTON: J. Ind. Hyg., 1919, 1, p. 200.
SANDERS: J.A.M.A., 1920, 74, p. 1518.
LOEB, BOCK and FITZ: Am. J. Med. Sci., 1921, 161, p. 539.

PHENOL (CARBOLIC ACID)



Perhaps phenol poisoning is more frequent than any other type, since phenol is readily available and its use is a favorite method of suicide. It rarely occurs from a criminal motive. Many cases of accidental poisoning occur annually through the ingestion by mistake of phenol for other drugs or alcoholic fluids. Owing to its

valuable antiseptic properties it has been employed extensively as an antiseptic or disinfectant and such use has caused many cases of poisoning from absorption through the skin or wounds produced surgically.

Pure phenol or carbolic acid obtained from coal tar synthetically is a white crystalline substance having a peculiar aromatic odor. The crystals melt at 40°C . "It is soluble in about 15 parts of water, but becomes liquid when 10 parts of water are added to 90 parts of the crystals; the liquified phenol of the U.S.P. contains not less than 87 per cent of pure phenol. Phenol is readily soluble in alcohol, ether, chloroform, and glycerine. The aqueous solution is neutral, or at most only faintly acid to litmus."

Phenol must be regarded as a general protoplasmic poison. It precipitates proteins forming with them a relatively loose chemical combination which is insufficient to prevent the diffusion of phenol into the deeper tissues of the body, where it causes necrosis. Upon its reaction with protein depends its antiseptic properties. As an antiseptic it is, however, not so powerful as corrosive sublimate or the cresols. Phenol exerts an anesthetic action upon sensory nerves and is employed as an analgesic against itching. In addition to the local action phenol in minute doses produces central effects which are at first in the nature of stimulation, later of depression.

Phenol is readily absorbed from any mucous membrane, abraded skin, wound or even from the intact skin. A small portion of the phenol is burned in the body, the remainder being eliminated by the kidneys as the ethereal sulphates, and glycuronates of phenol, and as hydroquinone and pyrochatechin. The latter substances are oxidation products of phenol. The urine generally assumes a smoky appearance.

Symptoms. *Local Action.*—Applied to the skin phenol causes local tingling and numbness or even complete anesthesia. The skin becomes wrinkled and soft, the color changing from a white stain to brown. The effect is not that of a direct corrosive action but rather a local necrosis. An eschar forms which eventually falls off without pus. The continued application may give rise to gangrene. Another distinct feature of the local application even in dilute solution is the production of a severe eczema. The absorption of phenol from local application may give rise to systemic effects.

Systemic Effects.—Taken by mouth in more or less concentrated form phenol induces a burning pain in the mouth, pharynx and stomach. Vomiting may or may not occur. The contact of the poison produces local burns which generally heal promptly but which temporarily leave brownish stains. The most characteristic symptom of phenol poisoning is the rapid collapse which may occur in a few minutes. The face is pale, and covered with a cold sweat. Unconsciousness ensues, the heart action is weak and rapid and the respiration is irregular. Cyanosis is intense. At times convulsions occur or there may be convulsive twitchings of the face or limbs. The pupils contract and the temperature is subnormal although this low temperature may be preceded by a rise above normal. The urine, which is diminished in volume, has a smoky appearance and may contain albumin, casts, blood or bile pigments. Little or no preformed sulphates are present, having been used up to form ethereal sulphates. Death occurs from respiratory failure. Generally phenol may be detected on the breath.

In less intense poisoning there may be headache, vertigo, excitement and mild delirium. The face is pale, the pulse

is feeble and respiration is irregular. Vomiting usually occurs and there may be evidences of renal irritation.

From injudicious use of phenol dressings a form of chronic poisoning may occur which is characterized by disturbances of digestion, skin eruptions and renal irritation ultimately causing death.

Fatal Dose.—The fatal dose may be taken as 8 to 15 grams, although recovery has followed the ingestion of three times the quantity and death has resulted from $\frac{1}{10}$ the fatal dose as given above. Introduced by routes other than the alimentary canal death is induced by much smaller quantities. Thus, a uterine douche containing a dram of phenol in one quart of water caused death in less than two hours.

Fatal Period.—Death may occur in a few minutes; nearly always in less than 24 hours.

Post Mortem Appearances.—Autopsy reveals brown patches on the site of local application or about the mouth if ingested. In the latter instance the mouth, pharynx, esophagus and stomach membranes are white and when the acid has been taken in a concentrated form these mucous membranes are eroded. Sometimes the gastrointestinal tract gives evidences of an intense inflammatory reaction. The odor of phenol may be present. The respiratory tract and the lungs may be congested. The blood vessels of the brain may be gorged with blood and there may be right sided dilatation of the heart since death usually occurs from asphyxia. When death is sudden, however, these appearances may be lacking.

Treatment. (a) *Local Effects.*—The affected parts should be washed thoroughly with alcohol in which phenol is soluble, and oil dressings should be applied. Oils and fat solvents prevent the penetration of phenol into the tissues and indeed may absorb phenol from the tissues.

(b) **Systemic Effects.**—Since phenol stays in the stomach for a considerable period the stomach should be thoroughly washed out even though the poison has been ingested for a considerable period. The lavage fluid should be at first 10 per cent alcohol, later warm water. Potassium permanganate is perhaps the most valuable chemical antidote. Sulphates have been used but their employment seems without special benefit. White of egg by forming a compound with phenol may help to retard absorption but the compound thus formed should be promptly removed. In the period of circulatory depression saline infusions may be of value. When collapse occurs the application of heat is indicated.

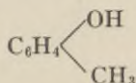
References

CLARKE and BROWN: J.A.M.A., 1906, 46, p. 782.

SOLLMANN, HANZLIK and PILCHER: J. Pharm. and Exp. Therap., 1910, 1, p. 409.

WILBERT: Public Health Reports, 1916, 31, p. 1046.

CRESOL



Cresol occurs in three forms, the ortho, meta and para, so designated from the position of the alkyl radical in the phenol ring. Under ordinary conditions, however, the term cresol relates to the commercial preparation which is a mixture of the three cresols and is obtained from the distillation of coal tar. This cresol is a liquid with a boiling point between 198° and 203°C. If sufficient ammonia is added it separates in crystalline scales. The same action is induced by 6 per cent soda solution. It is soluble in water and mixes in all proportions with alcohol, ether and glycerol.

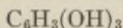
Cresol enters into the composition of many of the commercial disinfectants of which perhaps lysol is the preparation most often causing intoxication.

The symptoms of poisoning with cresol and its derivatives are so similar to phenol intoxication that a separate discussion is unnecessary. Treatment of poisoning would likewise be that for phenol.

Reference

HALE: U. S. Hygienic Lab. Bull., 1913, No. 88.

PYROGALLOL



Pyrogallol (pyrogallic acid) or trihydroxybenzene is a strong reducing agent which is closely related to phenol. The typical phenol effects, however, are lost in the overwhelming reducing action of the compound. Commercially pyrogallol is employed in photography, in hair dyes, and inks. In medicine it finds use externally in skin diseases, such as psoriasis, lupus and ring worm, as an ointment. Such use, however, is always dangerous as it is absorbed by the skin. It acts as a mild caustic to membranes and wounds.

Pyrogallol occurs as colorless crystals possessing a bitter taste. It is soluble in water, less soluble in alcohol and ether and quite insoluble in chloroform and benzol. In alkaline solution it rapidly oxidizes changing to a brown or black color and staining skin or hair with which it may come into contact.

Symptoms.—When absorbed pyrogallol acts chiefly upon the blood producing hemolytic effects and the outstanding symptoms are those induced by rapid destruction of the red corpuscles. The hemoglobin is thrown into the plasma and is transformed into methemoglobin. If this

change occurs to a sufficient degree asphyxial symptoms eventually appear and death occurs from respiratory failure. The most prominent symptoms are at first headache, chills, vomiting, diarrhœa, cyanosis, and sometimes icterus. The urine is dark colored, contains hemoglobin and is diminished in volume. Intense nephritis with casts and protein may be observed. Coma and collapse usher in death.

Fatal Dose.—The fatal dose has not been accurately determined but death has been caused by one-half ounce or less taken internally and from the use of the 10 per cent ointment applied to one-half the body in the treatment of psoriasis.

Fatal Period.—Death usually occurs within 3 or 4 days.

Post Mortem Appearances.—The internal organs are generally intensely congested, and the kidneys assume a purple or black color.

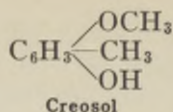
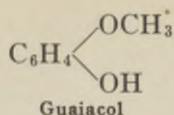
Treatment.—The poison should be removed from the stomach if taken internally and this organ thoroughly washed with warm water. Inhalations of oxygen may help. Stimulation should be pushed and the body temperature should be maintained. Bleeding followed by saline infusions are recommended. If these measures fail blood transfusion should be carried out.

References

- NEISSER: *Annal. d'Hyg. Pub.*, May, 1881.
REILLY: *Brit. Med. J.*, 1897, ii, p. 81.

CREOSOTE

Creosote is a mixture of crude phenols obtained in the distillation of wood. The principal substances present are guaiacol and creosol.

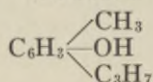


These substances partake of the nature of phenol but the toxic effects are less convulsive. Medicinally they have been employed in tuberculosis, as intestinal antiseptics, and as local anesthetics in dentistry.

Creosote is a yellow liquid with a characteristic smoky odor.

The symptoms produced are those of phenol poisoning, the lethal dose approximating 7 grams and death occurring usually within 24 hours. Treatment would be similar to that of phenol.

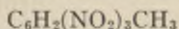
THYMOL



Thymol is allied to the creosote constituents and in its action resembles phenol. Contained in a number of aromatic oils, for example, thyme, it has high antiseptic value, low germicidal properties and relatively low toxicity. It is employed chiefly as an anthelmintic in the treatment of hookworm disease. In about one-half the cases treated unfavorable symptoms are observable and in rare instances severe poisoning occurs and even death. The symptoms resemble those of phenol except that convulsions do not occur, the chief action being depression of the central nervous system. In therapeutic use alcohol or oily solutions or mixtures should be avoided since toxicity is greatly favored owing to the more rapid absorption of the dissolved thymol.

Treatment consists of emptying the stomach, lavage, saline cathartics (not castor oil) and stimulants for the central nervous system.

TRINITROTOLUENE (T.N.T.)



Trinitrotoluene poisoning came into prominence during the World War. It was used chiefly as an explosive, and in its manufacture and especially in the process of loading it into shells and grenades, many cases of intoxication resulted, of which a relatively large number were fatal.

Trinitrotoluene may be absorbed from the skin, through the lungs or be introduced by way of the alimentary canal. While all three methods of introduction probably contribute to the poisoning in its industrial aspect the absorption through the skin is undoubtedly of prime importance. It must be classed with the irritant poisons and produces local irritation, the symptoms varying, of course, with the site of application. Contact with the skin induces dermatitis, with the alimentary canal gastric pain, etc., with the respiratory tract bronchitis, congestion and edema. Absorbed it exerts a specific influence upon the red cells of the blood transforming hemoglobin into methemoglobin, hematin and nitric-acid-hemoglobin. Ultimately there is red cell destruction resulting in an aplastic anemia. The poison also exerts a marked influence upon the liver, jaundice being a prominent feature. In addition the kidneys may show irritation. It is excreted by the urine for the most part and in smaller measure by the bile and feces. Trinitrotoluene is a hard, pinkish yellow crystalline powder which melts and sublimates at 82°C .

Symptoms.—The symptoms of intoxication vary with the manner of application of the poison. Thus, in the so-called acute gassing which occurs in the nitrating room it is probable that other substances than trinitrotoluene play a part. In this room there may be present large quantities of nitric acid, nitrous oxide, methane, hydrogen and

chlorine gases. The first symptoms are those of choking, cyanosis, and at times loss of consciousness. Upon removal from the room the sputum contains blood, and exposure to the gases results within a day of the onset in a chill, in bronchitis and moderate pulmonary edema, sometimes pneumonia.

From swallowing the poison gastric intestinal disturbances come to the front as evidenced by nausea, eructations, vomiting, bitter taste in the mouth, diarrhoea, or constipation, abdominal pain and colic.

When in contact with the skin an intense itching dermatitis results partaking of the nature of an eczema usually most severe where sweating is greatest. The skin assumes an orange color.

After absorption the systemic effects are associated with the action upon the blood cells, liver and kidneys. The symptoms include "pallor or cyanosis, dyspnea on exertion, dizziness, headache, fatigue, pains in the legs, drowsiness, blurring of vision; those due to renal irritation, urgency and frequency of micturition and lumbar pain; those due to degeneration of the liver; pain and tenderness in the right epigastrium." In many instances death is preceded by delirium, anuria and coma. In the stage of liver degeneration a toxic jaundice is prominent. When death results primarily from the aplastic anemia there may be bleeding from the gums and nose, and death occurs in delirium and coma. In all severe poisonings the red cells and hemoglobin content of the blood are very markedly reduced. In some instances the hemoglobin may be 30 per cent with a red cell count under one million.

Fatal Dose.—The fatal dose of trinitrotoluene is unknown.

Fatal Period.—Death may occur within 24 hours but is usually delayed for days or even weeks.

Post Mortem Appearances.—The most striking post mortem appearances are those of an extensive hepatic necrosis and atrophy closely resembling the liver of acute yellow atrophy. In the kidney the glomeruli are congested and the tubules contain casts, cellular debris and in some instances the lumen is closed by the swollen cells. Fatty degeneration may also be present.

Treatment.—Treatment is largely preventative. All possible care should be taken to prevent contact of the patient with the dust. Especially should the skin be protected. Thorough cleansing of the skin is particularly recommended. Rest is essential for patients suffering from the effects of contact. The channels of elimination should be stimulated by the use of purgatives and the ingestion of large volumes of fluid. A well balanced diet containing a sufficiency of meat is recommended in attempts to combat the anemia. In the incipient form this treatment will undoubtedly prove successful but in the stage of aplastic anemia the prognosis is unfavorable.

References

- MARTLAND: J.A.M.A., 1917, 68, p. 835.
VOEGLIN, HOOPER and JOHNSON: U. S. Pub. Health Report, 1919, 34, p. 1307.
HAYTHORN: J. Ind. Hyg., 1920, 2, p. 298 (literature).
HAMILTON: Ibid., 1921, 3, p. 102.

ANILINE ($C_6H_5.NH_2$)

Aniline is a colorless, oily liquid, with a characteristic odor and a burning taste. It is inflammable, and on exposure to air gradually turns brown. Its boiling point is $184^{\circ}C$. It is slightly soluble in water but dissolves readily in alcohol, ether and chloroform. Formed by the reduction of nitrobenzol it possesses basic properties and forms

typical salts. It is readily absorbed by the unbroken skin as well as by mucous membranes.

In general poisoning by aniline occurs from its industrial use. Under these circumstances pure aniline intoxication is not to be considered but rather the effects of aniline oil which contains several impurities, such as the toluidines, and xylydine. Poisoning may occur in the manufacture of aniline dyes, various pharmaceutical preparations, photographic materials, and in dyeing establishments and in rubber industries. Absorption may occur through the skin, which is the ordinary method of poisoning, by spilling upon clothing, etc., by inhalation of vapors and dust, and by swallowing of the dust with saliva or food. There are on record a few cases of suicide by the use of aniline.

Aniline must be regarded as a blood poison causing methemoglobin and disintegration of the red cells, and in addition an influence upon the nervous system. It has been stated that in the blood aniline black is formed. Aniline is excreted in the urine, in part, unchanged, in part as an ethereal sulphate.

Symptoms.—Pallor is the first symptom of aniline poisoning. A blue color, especially on the lips and finger nails succeeds this pallor. There is weariness, sleepiness, flushed face, fulness in the head, mental confusion. There is dryness of the throat, difficulty in swallowing, weak pulse, low temperature, severe headache, dizziness, a staggering gait, nausea, loss of consciousness, convulsions, coma and death. In mild poisoning there may be pallor with cyanosis, weakness, unsteady gait, labored speech, irritability, and defective orientation with other symptoms resembling alcoholic intoxication. At a later period there may be loss of appetite, constipation, marked air hunger, and cyanosis, loss of reflexes, jaundice, vomiting, painful micturition and bloody urine.

In chronic poisoning the chief characteristic is anemia, with slow pulse, disturbances of digestion, headache, dizziness, head noises, and muscular pains. Skin eruptions of an eczematous and pustular character on various parts of the body especially on the scrotum are common.

Perhaps the most reliable means of diagnosing aniline poisoning, particularly of the chronic type, is by estimation of hemoglobin content. A reduction of 15 to 20 per cent accompanied by stippling of the cells is indicative of aniline poisoning. A dark colored urine, due to the presence of hemoglobin and aniline decomposition products is quite characteristic.

Fatal Dose.—The fatal dose is unknown. Death has been caused by quantities varying from 25 c.c. to 100 c.c. although recovery has followed the ingestion of 75 c.c. On the other hand, 0.1 to 0.25 gram aniline will produce serious symptoms.

Fatal Period.—In acute cases death has generally followed within 24 hours. In chronic poisoning recovery takes several weeks and in many instances the individual is unable to return to his former work because of increased susceptibility.

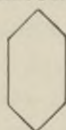
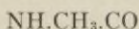
Post Mortem Appearances.—Beyond the finding of methemoglobin autopsy reveals nothing characteristic of aniline poisoning.

Treatment.—For acute symptoms treatment consists in removing the patient to the fresh air. If aniline has been swallowed lavage of the stomach should be instituted. The saline purgatives and stimulants (hot, black coffee) are recommended. If the case is serious and the patient can stand it bleeding with saline infusion may be carried out or bleeding with transfusion of blood. Oxygen inhalations may help and body temperature should be maintained.

References

- HARRINGTON: Boston Med. and Surg. J., 1918, 179, p. 497.
 LUCE and HAMILTON: J.A.M.A., 1916, 66, p. 1441.
 HAMILTON: J. Ind. Hyg., 1919, 1, p. 200.
 BIRGE: J.A.M.A., 1914, 62, p. 314.

ACETANILID



Poisoning from acetanilid usually results from the careless or ignorant use of this antiseptic for its analgesic effect, usually in the form of headache powders. When employed for its action in lowering a febrile temperature care must also be taken for the side action of the drug may result in sudden collapse. Both acute and chronic poisoning may occur, death resulting from either. Previously intoxication resulted from absorption of acetanilid, which has some antiseptic properties, applied to wounds.

Acetanilid crystallizes in lustrous white plates, which possess no odor and only a slight burning taste. It melts at 113°C . and is sparingly soluble in cold water. It dissolves readily in hot water, alcohol and ether, and when heated with acids or alkalis decomposes to aniline and acetic acid. Acetanilid is rapidly absorbed and reappears promptly in the urine transformed into para-aminophenol combined either with sulphuric or glycuronic acids. This derivative of acetanilid gives to the urine the "indophenol reaction."

Acetanilid produces toxic effects chiefly by its action upon the red blood cells forming methemoglobin and causing destruction of the erythrocytes. This blood destruction gives rise to a characteristic cyanosis.

Symptoms.—The outstanding features of acetanilid poisoning are cyanosis, profuse perspiration, muscular weakness, prostration and collapse. The pulse is weak, the extremities are cold, the respiration is shallow and dyspnoëic, the temperature is subnormal, and there may be unconsciousness, convulsions or delirium. Death occurs from circulatory failure. The blood has a lowered oxygen capacity, and contains methemoglobin. Nephritis with anuria and an acute jaundice may be observed.

There have been reported a number of cases of chronic acetanilid poisoning, the characteristic symptoms being weakness, insomnia, increased nervous excitability, digestive disturbances, dyspnoëa, cyanosis and anemia. The heart sounds are indistinct and there may be murmurs. The urine contains methemoglobin and is generally brown in color.

Fatal Dose.—With a weak heart small doses (10 to 20 grains (0.6 to 1.3 grams) may cause alarming symptoms. With individuals with normal hearts death has been caused by doses varying from 8 to 30 grains although recovery has followed the administration of 60 to 120 grains.

Fatal Period.—Death may be sudden or be delayed for a period of several days.

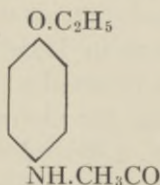
Post Mortem Appearances.—In acetanilid poisoning autopsy reveals nothing characteristic beyond the chocolate colored blood due to the presence of methemoglobin.

Treatment.—The alimentary canal should be thoroughly cleansed by lavage and saline purgatives. Stimulants, such as strychnine, camphor, ammonia, brandy, warmth, are indicated. In desperate cases venesection with subsequent saline infusion is recommended. Epinephrine or strophanthin may be used intravenously to stimulate the heart. Perform artificial respiration if necessary. For chronic poisoning the treatment is symptomatic.

References

- ARCULI: *Lancet*, 1921, 1, p. 965.
 McELLROY: *J.A.M.A.*, 1919, 73, p. 1027.
 NADLER: *Ibid.*, 1920, 74, p. 1717.
 SHUMAN: *Ibid.*, 1921, 77, p. 526.

ACETPHENETIDIN (PHENACETIN)



Acetphenetidin is closely allied to acetanilid both chemically and toxicologically. In general it is less toxic than acetanilid and its effects are produced more slowly. As with acetanilid para-aminophenol is formed which may be the cause of the toxic symptoms.

Acetphenetidin occurs in white glistening crystals or powder. It is odorless, slightly bitter and causes a faint numbness of the tongue. In water solution it is neutral to litmus. It is rather difficultly soluble in cold water but readily soluble in hot water, in alcohol and chloroform. It is less soluble in ether although appreciable quantities are dissolved by this solvent. It melts between 133° and 135°C .

Symptoms.—Symptoms of poisoning are practically identical for those of acetanilid (which see). The skin eruptions, however, appear to occur more frequently than with acetanilid.

Fatal Dose.—This is indefinite since in most of the fatal cases some pathological condition has contributed to the outcome. Doses as small as 10 to 15 grains have caused death under these circumstances.

Fatal Period.—Death may be sudden or be delayed for several days.

Post Mortem Appearances.—Autopsy reveals nothing characteristic beyond the brown color of the blood due to the presence of methemoglobin.

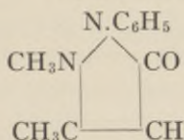
Treatment.—Treatment is identical with that for acetanilid (which see).

References

WEST: *Lancet*, 1895, I, p. 91.

TOBEY: *Mon. Bull. State Board Mass.*, Jan., 1908.

ANTIPYRIN



In general antipyrin (phenyl-dimethyl-pyrazolon) has a toxicological action similar to that of acetanilid. It causes a tumultuous action of the heart and there may be erythematous or herpetic eruptions of the skin. These eruptions may be accompanied by edema and itching. Poisoning generally results from overdoses and a habit may be formed. Unlike acetanilid and acetphenetidin it does not cause the formation of methemoglobin. It is in part eliminated as such in the urine and in part in combination with sulphuric acid.

Antipyrin occurs as a white crystalline powder or as tubular crystals. It is odorless and possesses a slightly bitter taste. It is soluble in water, alcohol and chloroform but relatively insoluble in ether. It melts between 111° and 113°C .

Symptoms.—The symptoms are principally those of depression, rapid, feeble pulse, collapse, cyanosis, cold

perspiration, loss of body temperature, nervous symptoms (restlessness, convulsions, sense disturbances) delirium, coma, sometimes albuminuria. A type of chronic poisoning is characterized by skin eruptions, digestive disturbances and muscular weakness.

Fatal Dose.—Death has followed the administration of doses varying from 15 to 30 grains.

Fatal Period.—Death in acute cases is generally sudden.

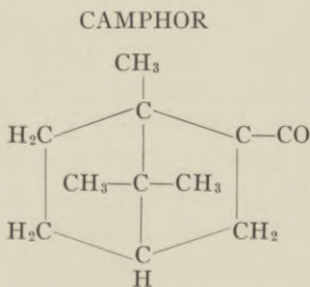
Post Mortem Appearances.—Nothing characteristic is revealed by necropsy.

Treatment.—Follow that outlined for acetanilid.

References

Report of Therapeutic Committee, B.M.A. Brit. Med. J., 1891, 1, p. 85.

BLAKENEY: Ibid., 1899, ii, p. 85.



Camphor, a substance closely related chemically to terpene, is a solid obtained by distillation of the wood of camphor-laurel growing in China, Japan and the East Indies. Recently it has been made from turpentine. Medicinally it is employed as a mild irritant and antiseptic, as a counterirritant, or as a stimulant to the central nervous system. It assumes toxicological importance mainly with children, being given either by mistake for something else or in overdoses. On the other hand it has been

employed as an abortifacient with fatal results and it may cause poisoning through its use as a common cold remedy.

Camphor may be regarded chemically as a solid ketone, insoluble in water but readily soluble in alcohol, ether, benzene, oils and chloroform. In the body it is oxidized to camphorol and eliminated in the urine in combination with glycuronic acid.

Symptoms.—Camphor produces toxic effects mainly through its action upon the central nervous system. At first stimulation is in evidence followed by depression and paralysis of the central nervous system. The symptoms induced are nausea, vomiting, a burning sensation in the mouth, throat and stomach, thirst, disturbed vision, ringing in the ears, excitement, incoördinated movements, dizziness, headache, rapid pulse, hallucinations, delirium, epileptiform convulsions, especially in children, sometimes anuria, unconsciousness. Death is rather rare in adults and results from asphyxia and collapse. The breath smells of camphor.

Fatal Dose.—For an adult the fatal dose is unknown although one gram or less will cause toxic symptoms. This dose, however, is fatal to young children.

Fatal Period.—With fatal doses death usually occurs within 24 hours.

Post Mortem Appearances.—There are no characteristic post mortem appearances. The tissues generally smell of camphor.

Treatment.—In camphor poisoning the stomach should be emptied and thoroughly washed. All use of oils and alcohol is contraindicated since they tend to hasten the absorption of camphor. The bowels should be purged with saline purgatives or calomel. The convulsions may be relieved by morphine or bromides. Stimulation

should be practiced and if necessary artificial respiration should be instituted.

References

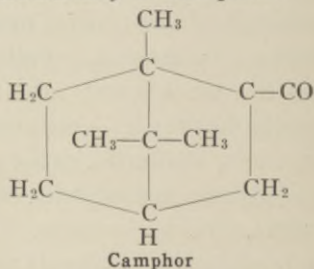
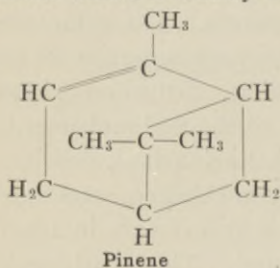
AUSTRAGESILLO: J.A.M.A., 1915, 64, p. 1694.

MACLEOD: Brit. Med. J., 1896, 1, p. 1556.

BENZ: J.A.M.A., 1919, 72, p. 1217.

TURPENTINE

Turpentine is obtained from various species of pine by distillation. When purified turpentine consists chiefly of pinene which is closely related chemically to camphor.



Turpentine is a thin, colorless, or slightly yellowish oil. It is inflammable, somewhat soluble in alcohol, only slightly soluble in water, and possesses a characteristic odor and taste, which increases on exposure and becomes more unpleasant. It is employed in medicine internally to diminish bronchial secretions. Externally it finds use as a counterirritant. It has also been used to induce abortion and as a means of suicide. The vapors are toxic. Whether inhaled or taken by mouth absorption into the blood occurs, excretion taking place mainly through the urine, turpentine leaving the kidney in the form of a glycuronate. The urine has the odor of violets. Poisoning may be either acute or chronic. The latter usually occurs from exposure of workmen to the fumes in varnish factories, etc.

Symptoms.—Taken internally the symptoms induced by turpentine are those of gastro-intestinal irritation. The respiration is slow, the pulse weak, and nervous symptoms are present, resembling in part alcoholic intoxication. There is excitement, muscular incoördination, and sometimes delirium. The urinary tract is greatly irritated as indicated by painful micturition, bloody urine, albuminuria, and at times anuria. In some cases skin eruptions of a scarlatinoid type are in evidence.

In the chronic cases of poisoning the chief symptoms are headache, dizziness, rapid respiration, palpitation, ataxia, pain in chest, bronchitis, nephritis, stupor, unconsciousness and convulsions.

Fatal Dose.—The fatal dose of turpentine is unknown. Death in an adult has occurred from swallowing six ounces and in children from a teaspoonful to one ounce has caused death.

Fatal Period.—Death usually occurs within 24 hours.

Post Mortem Appearances.—There is nothing characteristic except the action upon the gastro-intestinal tract and the kidney.

Treatment.—The stomach should be emptied and thoroughly washed, the lavage being followed by demulcents to allay the gastro-intestinal irritation. Stimulation by hot black coffee is indicated.

References

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ALCOHOLS

ETHYL ALCOHOL— $C_2H_5.OH$

Alcohol poisoning is extremely common, the chronic type, however, being much more usual than the acute. In

the chronic type the toxicologist has only slight interest. Death from acute alcoholism is infrequent but not rare. It has resulted in children from administration of relatively large quantities of alcoholic drinks, and in adults as the result of wagers or sprees.

Alcohol, also called ethyl or grain alcohol and ethanol, "is a transparent, colorless, mobile, and volatile liquid having a characteristic odor, and a burning taste." "It is very hygroscopic, specific gravity not higher than 0.797 at 15°C. (60°F.). It boils at 78.4°C. (173.1°F.), and is congealed at -130.5°C. (-202.9°F.). It burns with a non-luminous flame. It dissolves resins, fats, volatile oils, bromine, iodine, etc., also many salts and gases. On oxidation it is converted into aldehyde and acetic acid. The alcohol of commerce always contains some water (usually about nine parts by weight) and various impurities. The different alcoholic beverages vary widely in the percentage of alcohol they contain: beers have from 2 to 6 per cent; light wines from 7 to 12 per cent; strong wines, such as port and sherry, from 15 to 20 per cent; spirits, such as whiskey, brandy, rum, and gin, have from 45 to 60 per cent of alcohol by weight. It is the latter class of beverages (spirits) that is responsible for most cases of acute poisoning with alcohol. These beverages, which contain in addition to ethyl alcohol higher alcohols of the same series, such as amyl alcohol or "fusel oil," and certain little known bodies called "enanthic ethers," are, as a rule, slightly more poisonous than pure alcohol diluted to the same extent with water; there is no justification, however, for the view, sometimes held, that the toxicity of these spirits is due more to the impurities than to the ethyl alcohol."

Alcohol must be regarded as a local irritant. If applied to the skin or mucous membrane it produces redness and a

burning sensation with some anesthesia. It hardens tissues by withdrawing water, causing precipitates of the proteins. In a concentration of 70 per cent alcohol is an effective germicide. In concentrations above or below this figure it is almost inactive. Taken by mouth in relatively large volumes it causes irritation of the gastric membrane resulting in nausea and vomiting.

Alcohol has long enjoyed a reputation as a general stimulant to the body. At the present time the concensus of pharmacological opinion is to the effect that alcohol is in reality, especially in large doses, a distinct depressant. The apparent stimulating effects, namely, the increase in heart and respiration rate, the rise in blood pressure, the sensations of flushing and warmth, are to be ascribed to the paralysis of inhibitory functions.

Alcohol readily passes into the blood and in alcoholic intoxication the blood may contain 0.13 per cent. In large measure (about 90 per cent) alcohol is oxidized in the tissues to carbon dioxide and water, the remainder being eliminated by the lungs and kidneys. It also passes into the milk and probably permeates every tissue in the body. It appears to have a specific influence upon the germ cells causing degenerative changes which induce abnormalities in the offspring.

Symptoms.—Four stages of intoxication are recognized, namely, the "stimulant" stage, the narcotic stage, the anesthetic stage and the paralytic stage. In the "stimulant" stage a flushing of the skin and a feeling of warmth constitute the first symptoms. Excitement quickly follows and assumes various forms of expression, some individuals becoming foolish in speech and action, others angry or violent.

The narcotic stage quickly follows and is characterized by diminished psychic activity. There is generally

nausea, vomiting, vertigo, loss of coördinated movement and more or less incoherent speech. The individual is drowsy.

In the anesthetic stage there is a gradual loss of consciousness, sensation and muscular tone, and the patient may be partially aroused from the stupor but soon relapses.

The paralytic stage is characterized by medullary paralysis, slow and stertorous respiration, small, slow pulse, cold cyanotic skin, dilated pupils, lost reflexes, low temperature (86°F. or lower). The breath smells of alcohol. Death results from respiratory failure. Death may not be the immediate result of the alcohol poisoning but may result from pneumonia.

During acute alcohol intoxication acute insanity may develop in which the patient may attempt acts of violence, or suicidal melancholia may be present. Various forms of unconsciousness or coma may complicate the diagnosis of alcohol poisoning. The breath, however, is generally diagnostic.

Fatal Dose.—The fatal dose of alcohol is variable, being conditioned by several factors, such as the state of health of the individual, the period of digestion, habituation, the strength of the solution and the manner of administration. One to two pints of whiskey or brandy taken at one time may perhaps be considered a fatal dose, although recovery has followed the ingestion of even larger quantities. In terms of pure alcohol the above figures would correspond to 8 to 16 ounces of pure alcohol. The smallest fatal dose of pure concentrated alcohol varies from 3½ to 7 ounces. Children require much smaller doses, since 2½ ounces have caused death in children from 5 to 7 years of age.

Fatal Period.—Death usually occurs within a few hours (6 to 12), although in some instances it was delayed for 5 or

6 days. The prognosis is unfavorable if the coma persists for more than 12 hours.

Post Mortem Appearances.—The most characteristic autopsy findings are inflammation of the stomach mucous membrane with punctiform ecchymoses. The membranes of the brain are generally hyperemic and there may be well marked edema of the brain or of the lungs. The stomach contents and the brain especially may have a noticeable odor of alcohol which may persist for a considerable period after death.

Treatment of Acute Alcohol Poisoning.—The stomach should be emptied, best by apomorphine since this also serves as a hypnotic, and thorough lavage with warm water is advisable. Stimulation should be instituted by the administration of strong hot coffee, or aromatic spirits of ammonia, or strychnine. The body temperature should be maintained by hot applications and the rubbing of the limbs. Restlessness and headache, may be combatted by caffeine and bromides. Morphine is not recommended except to control mania. With respiratory failure artificial respiration should be instituted.

References

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METHYL ALCOHOL (WOOD ALCOHOL) CH₃.OH

Methyl alcohol is obtained by distillation of wood. It is also known as wood alcohol, methyl hydrate, methanol, wood spirit, wood naphtha, and carbinol. When purified it is commercially known as acetone alcohol, Columbian spirits, Colonial spirits, Eagle spirits, Lion d'Or, etc., and

is employed in the manufacture of paints, shellac, dyes, rubber, essences, bay rum, perfumes, and in the denaturation of grain alcohol. Commercial wood alcohol occurs in varying conditions of purity, some of the impurities being acetone, ethyl-methyl-ketone, methyl and dimethyl acetate, furfural, and allyl alcohol. The admixture of these substances may impart an unpleasant taste and odor to the fluid. On the other hand, it is difficult if not impossible to differentiate between methyl and ethyl alcohol by taste or smell.

Methyl alcohol, when pure, is colorless with a specific gravity of 0.8021 at 15.5°C. It boils at 66°C. It readily yields formaldehyde and formic acid when subjected to oxidation.

Poisoning from wood alcohol has come into prominence since the establishment of prohibition in the United States by passage of the 18th Amendment to the Constitution. In many instances ignorance has led to death by drinking methyl alcohol as a substitute for ethyl alcohol in various preparations sold for beverage purposes. Poisoning has also resulted from inhalation of the fumes in factories, from external application, and from the drinking of denatured alcohol.

Even though death has not always resulted from wood alcohol poisoning, a characteristic result of severe intoxication is impairment of vision which may be temporary or permanent, partial or complete blindness, due to atrophy of the optic nerve. Usually a central scotoma develops. At times the color sense is chiefly affected. In some instances the only untoward symptom of poisoning has been the blindness.

Poisoning in man by wood alcohol differs distinctly from ethyl alcohol intoxication. Although in animal experiments methyl alcohol is less toxic than ethyl alcohol

yet in man the reverse is true. This may perhaps be explained by the fact that methyl alcohol seems to possess a degree of specificity for the nervous structures and man being more highly organized than animals in the development of the nervous system is therefore more susceptible. From animal experimentation it has been shown that the intoxication from wood alcohol does not markedly differ from that of ethyl alcohol except that the onset of symptoms is much slower and the effects are much more prolonged. This influence is explained by the difference in the fate of the two alcohols. Ethyl alcohol is, in large measure, quickly burned in the body to carbon dioxide and water, whereas methyl alcohol is only slowly oxidized, one product of combustion being formic acid which undoubtedly plays a part in the symptoms produced. An acidosis also results but it is questionable how large a share this plays in the serious features of the intoxication. The formic acid formed from the incomplete oxidation of methyl alcohol is only slowly eliminated from the body which accounts in a measure at least for the prolonged period of intoxication. The ingestion of repeated doses of ethyl alcohol establishes a degree of tolerance; with methyl alcohol the same procedure induces a cumulative effect.

Symptoms.—With methyl alcohol poisoning the stage of excitement characteristic of ethyl alcohol intoxication is usually absent. Instead the most outstanding feature is depression and weakness. There is headache, nausea, vomiting, violent abdominal pains, muscular incoördination, weak, rapid pulse, dyspnœa, cyanosis, restlessness, non-sensitive dilated pupils, low temperature, cold, moist skin, sometimes delirium, generally coma, infrequently convulsions, and death from respiratory failure. Total blindness may be sudden. Eye effects are usually

manifested within 48 hours by pain sensations around the eyes, tenderness on pressure of the eye balls, some photophobia, pupil dilatation, blurring of vision, blindness. At times complete or nearly complete vision is regained which may remain but frequently is again permanently lost. It is only when the optic nerve atrophies sufficiently that total blindness occurs.

Fatal Dose.—Individuals show remarkable variations in their susceptibility to wood alcohol. It may be stated, however, that, in general, the fatal dose varies between 1 to 2 ounces. Blindness or disturbances of vision have been reported after taking quantities as small as $\frac{1}{2}$ ounce. It has been stated that if 4 ounces of wood alcohol were drunk by each of 10 persons all would have abdominal pain within 3 hours, 4 would die, 2 of these being blind before death, 6 would ultimately recover, but 2 of these would be blind permanently.

Fatal Period.—Usually death occurs within 36 hours, but may be delayed for 3 or more days. Death has occurred within 1 hour.

Post Mortem Appearances.—The stomach and duodenum are inflamed, the lungs may be edematous and the brain and its membranes may show edema and congestion.

Treatment.—The stomach should be emptied and repeatedly washed with warm water. Methyl alcohol is in part eliminated into the stomach hence the need for lavage at intervals after the evacuation of the organ. Stimulation by caffeine or strychnine should be instituted if deemed necessary. Sodium bicarbonate by mouth or intravenously may be given to overcome the acidosis present. The evidence seems to show, however, too much dependence should not be placed upon this measure since it is quite probable that the acidosis is only an accompanying factor. Acidosis is not responsible for the condition.

Pain may be controlled by morphine. It has been stated that the eye symptoms are relieved by the use of pilocarpine, potassium iodide, strychnine and purgatives. For mania hyocine may be given. Venesection may be useful in edema of the lungs. If indicated give artificial respiration. Large volumes of fluid are of value in hastening elimination of the products of combustion.

References

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AMYL ALCOHOL (FUSEL OIL)



In general the different alcohols increase in toxicity with increase of the size of the molecule. Amyl alcohol, therefore, possesses a greater degree of toxicity than either methyl or ethyl alcohol. There are eight amyl alcohols possible; seven are known. Only isoamyl alcohol is of significance in toxicology at present. It occurs as the principal constituent of the so-called "fusel oil" formed in fermentation.

Isoamyl alcohol is an oily liquid with a penetrating odor and acrid taste. It is only slightly soluble in water but mixes in all proportions with alcohol, ether and benzene. It boils at 131.6°C . and has a specific gravity of 0.8148.

Fusel oil is employed in industry and several cases of poisoning by it have occurred.

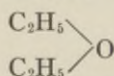
The symptoms of amyl alcohol poisoning are characterized by coma, glycosuria and sometimes methemoglobin. The toxic dose of amyl alcohol for man is unknown but from animal experiments it may be stated that it is about five times as toxic as ethyl alcohol.

References

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ETHER



Ether poisoning is rare although there are records of deaths by suicide and as a result of chronic poisoning induced by its habitual use as an intoxicant. In certain types of industry, such as the manufacture of smokeless powders, acute ether intoxication may occur by inhalation of the vapor. A certain degree of tolerance may be induced by ether as with alcohol. In certain parts of Europe ether drinking has been recognized for a long time. The quantities thus consumed may amount to as much as a pint or more, daily.

Symptoms.—Ether is a colorless, readily volatile liquid, with a characteristic penetrating odor and a sweet, sharp taste. Evaporated on the skin it causes cold sensations. It possesses a specific gravity of 0.713 and boils at 35°C. Ether burns readily and when mixed with air forms an explosive mixture. It is practically insoluble in water but mixes with alcohol and chloroform.

Death from ether during anesthesia is rare. The danger signals of overdosage of ether occur suddenly and consist of pupil dilatation, pallor and a changed facial expression.

Usually death in deep anesthesia is caused by respiratory paralysis with more or less involvement of the circulation. Respiration ceases even while the heart action is good.

Serious but not necessarily fatal sequelæ to ether anesthesia may be exhibited upon the respiratory organs and the kidney. Thus, bronchitis, pulmonary edema, and the flaring up of an old tuberculous lesion of the lung are some of the common after effects of ether induced in part perhaps by the irritative properties of the ether. Albuminuria and nephritis also sometimes occur.

Ether taken by mouth produces a strong burning sensation in the throat and stomach. The intoxication resulting from absorption is in every respect similar to that of alcohol except that the onset is much more rapid and the duration is much shorter. Owing to the volatility of ether the stomach may be greatly dilated soon after the ether is swallowed. This gastric dilatation at times causes serious interference with respiration.

Fatal Dose.—The fatal dose of ether by inhalation is very indefinite. The important factor is one of concentration rather than the total quantity inspired. The maintenance of surgical anesthesia requires a concentration of nearly 7 per cent ether vapor by volume in the air inspired. A marked depressing effect is caused by concentrations of 9 per cent and concentrations of 11 per cent or more cause paralysis of the respiratory centre. Taken by mouth it is stated that one ounce of ether would probably be fatal to most adults.

Fatal Period.—From ether narcosis death may occur suddenly or be delayed for days. In delayed death complications, such as pneumonia and nephritis, usually play a predominating part.

Post Mortem Appearances.—Autopsy fails to reveal characteristic features in death from ether. Usually the

brain and lungs are greatly congested, sometimes also the liver and kidneys. The odor of ether may often be recognized in the different tissues and organs.

Treatment.—In anesthesia if the pulse is weak, rapid or irregular the administration of the ether should be stopped. In case of collapse the head should be lowered giving the patient free access to air. Maintain body temperature. Artificial respiration should be instituted if indicated. Give hot saline by rectum or slow intravenous infusion containing 1 c.c. epinephrine per liter. For collapse strychnine or caffeine may be injected subcutaneously or ammonia by inhalation is often effective. For stoppage of the heart rapid rhythmic pressure over the heart or on the epigastrium should be tried.

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CHLOROFORM (CHCl₃)

Chloroform plays little role in toxicology from the standpoint of administration with criminal intent. At times it figures in suicide from swallowing the liquid and death is sometimes caused by drinking it in mistake for some other fluid. Chloroform, therefore, is of more significance from the accidents that have occurred in its use as an anesthetic.

Chloroform is a heavy, colorless liquid with a characteristic odor and a sweet taste. It is neutral in reaction, difficulty soluble in water but is miscible in all proportions with alcohol and ether. Its specific gravity is 1.491 and it boils at 62°C. Chloroform is not inflammable.

Symptoms.—Chloroform must be regarded as an irritant whether applied to mucous membranes or to the skin.

When taken by mouth chloroform induces pain, vomiting and sometimes diarrhœa.

Chloroform anesthesia is attended by at least three sources of danger (1) early heart failure, (2) depression of the heart with limited margin of safety, (3) delayed chloroform poisoning. In the early stages of chloroform anesthesia the common symptoms are sudden cessation of respiration, asphyxia leading to dilatation of the heart, vagus stimulation, and finally failure of the heart because of the asphyxial condition. In light chloroform narcosis the heart muscle becomes over-stimulated sometimes inducing ventricular fibrillation followed by death. It is probable that this type of action is due to excessive reflex inhibition of the vagus and the direct action of the chloroform upon the heart muscle, chloroform being recognized as a protoplasmic poison. Even after the heart has stopped respiration may be resumed but generally the heart cannot be revived. In most instances therefore the heart ceases before respiration and the former must be regarded as the real cause of death. When death occurs in deep anesthesia with chloroform the blood pressure steadily falls, respiration fails and the heart stops. Generally, however, the pulse cannot be felt before respiration ceases. Usually such accidents occur when the concentration of the chloroform vapor has been too high. Warning signs of this type of chloroform poisoning are shallow or irregular respiration, a pulse that is either very slow or very rapid, dilatation of the pupil and cyanosis.

Delayed Chloroform Poisoning.—By delayed chloroform poisoning is meant the condition which develops in some patients a few hours or days after chloroform administration and which is marked by great prostration, delirium, coma and death. The symptoms may appear suddenly or gradually. When the onset is sudden recovery from

the anesthesia has hardly been attained before the untoward symptoms appear. These consist of shrieking and struggling alternating with intervals of stupor or coma; profuse vomiting which may be blood stained; cyanosis; jaundice, edema, renal hemorrhage, acetone breath. The urine contains albumin and casts and the ammonia coefficient may be high. The urine also usually contains acetone, diacetic and β -oxybutyric acids. The blood shows retention of non-protein nitrogen, urea and amino acids.

Fatal Dose.—By mouth the probable fatal dose of chloroform is $1\frac{1}{2}$ ounces. By inhalation of chloroform death has been caused by 15 drops. Much larger quantities (20 ounces) have not caused fatality. Patients should not receive air containing more than 3.5 per cent of chloroform by volume even for a short period.

Post Mortem Appearances.—Autopsy shows extensive vacuolization and fatty degeneration of the liver, swelling and necrosis of the cells, especially about the central veins. Fatty degeneration also occurs in the kidney and sometimes in the heart and arteries. Children are especially susceptible to this type of chloroform poisoning and patients with diabetes, hepatic diseases, cyclic vomiting, rickets or wasting diseases, renal disease, alcoholism and anemia are particularly likely to succumb to this condition. In general, delayed chloroform poisoning almost certainly causes death, very few cases ever having recovered.

Impurities in the anesthetic are not responsible for the untoward effects, contrary to popular opinion. They may contribute to the local irritative symptoms but are probably not concerned in the dangerous effects. Swallowing of chloroform may cause gastritis and the phenomena characteristic of delayed chloroform poisoning.

Treatment.—Treatment of chloroform poisoning (excluding delayed chloroform poisoning) consists in stopping

the anesthetic, the head lowered, and artificial respiration resorted to immediately. This prevents asphyxia and aids in the elimination of the poison. In order to aid the action of the heart the cardiac region should be strongly compressed at the rate of 40 times per minute. Saline solution containing 1 c.c. of 1:1000 solution of epinephrin per liter should be injected into the cardiac end of an artery. None of these measures are of value unless they can be taken immediately.

References

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CARBON DISULPHIDE (CS₂)

Acute poisoning with carbon disulphide is rare. From the fact that this substance is employed to a considerable extent in industry as a solvent for sulphur, phosphorus, oils, resins, rubber, etc., and as a disinfectant, chronic poisoning is much more common.

Carbon disulphide is a colorless, volatile fluid possessing the property of refracting light. When impure its odor is most offensive and disagreeable. The pure substance lacks this repulsive odor. Its specific gravity is 1.293 at 0°C. and it boils at 47°C. Very inflammable, it burns with a blue flame, forming sulphur dioxide. It is difficulty soluble in water but readily dissolves in alcohol or ether.

Symptoms.—Carbon disulphide* must be regarded as a blood poison forming methemoglobin and destruction of

the red cells. It produces total anesthesia and causes death by respiratory failure.

The symptoms prominent in acute intoxication are pallor, dilated pupils, rapid, weak pulse, lowered temperature, and convulsions. Carbon disulphide is eliminated through the lungs and the kidneys. In chronic poisoning two stages are recognized—a stage of excitement and a stage of depression. In the first stage, there is headache and gastro-intestinal disturbances. There is increased sensitiveness of the skin, head noises, irritable temper, pain in the limbs and spasmodic contractions of various groups of muscles.

Anesthesia of the skin and mucous membranes ushers in the second stage—that of depression. Digestive disturbances, weakness of the muscular system and mental debility may be prominent and paralysis of the limbs may occur. Recovery from the effects of chronic poisoning by carbon disulphide may take a year or more and if paralysis has taken place the injury may be permanent.

Fatal Dose.—The fatal dose of carbon disulphide is unknown. Two ounces or more have failed to produce death when taken with suicidal intent.

Fatal Period.—This is generally prolonged being a matter of days and sometimes of weeks.

Post Mortem Appearances.—Autopsy reveals appearances with acute poisoning quite similar to those of delayed chloroform poisoning.

Treatment.—If taken by mouth, evacuation and lavage of the stomach and general stimulation should be attempted. If indicated, blood transfusion is recommended. Artificial respiration and maintenance of body temperature should be carried through.

Reference

HAMILTON: U. S. Bur. Labor Bull., 1915, p. 179.

CHLORAL—CHLORAL HYDRATE
 $\text{CCl}_3\cdot\text{CHO}\cdot\text{H}_2\text{O}$

Chloral has been extensively employed as a hypnotic. Most cases of poisoning have resulted from overdoses prescribed by physicians, from self-medication by individuals or from the use of proprietary preparations advertised as remedies for insomnia. A few instances are on record where it has been given with criminal intent. Death from chloral by suicides is not uncommon. Chloral constitutes the so-called "knock-out drops" which have been administered for purposes of robbery or rape. Generally poisoning has occurred from chloral taken by mouth although there are records of deaths from its injection into the blood stream and introduction by rectum.

Chloral, which is an oily liquid, is generally used in the form of its hydrate, $\text{CCl}_3\cdot\text{CHO}\cdot\text{H}_2\text{O}$. The latter occurs in the form of white crystals. At ordinary temperature it is somewhat volatile, melts at 58°C . and boils at 97.5°C . Easily soluble in water and alcohol it possesses a melon-like odor and an unpleasant taste which may be completely masked by solution in alcoholic fluids. The addition of alkalis to chloral solutions decomposes it into chloroform, formic acid and water.

The general action of chloral hydrate is depression and paralysis of the central nervous system. In these respects it closely resembles alcohol and chloroform. It has been extensively employed for the purpose of inducing sleep which closely resembles natural sleep. The analgesic effect is not pronounced until large doses have been given. Continued use of chloral may lead to fatty degeneration of different organs. Chloral must be regarded as a local irritant possessing some antiseptic properties, which might be anticipated from its aldehyde nature. It is excreted in the urine as a conjugated glycuronate which

imparts to the urine a reducing action, hence, may simulate the appearance of sugar in the urine.

Symptoms.—Generally with doses up to 2 grams drowsiness and heavy sleep are the only symptoms. With large doses uncontrollable narcosis results. The intoxication may closely resemble that induced by alcohol or chloroform. With weak heart death may occur in a short period from heart failure. Nausea and vomiting may occur induced by the local action of chloral upon the gastric membrane. The temperature declines sharply in from 5 to 20 minutes after taking the drug. Respiration is shallow, the pupils are usually contracted and cyanosis may be prominent. Sleep may pass directly into death without marked change or may be preceded by collapse or delirium and convulsions. Death results from respiratory failure. Pulmonary edema at times contributes to a fatal outcome.

In chronic poisoning by chloral the symptoms may be so varied as to render diagnosis extremely difficult. Types of symptoms are digestive disturbances; skin troubles, as rashes, vesicle formation, ulceration at the nail roots; inflammation of the eyes; nervous symptoms, insomnia, depression, or melancholia; at times a condition resembling delirium tremens, especially on withdrawal of the drug, or a type of dementia. In chloral habitues death from sudden heart failure is frequent.

Fatal Dose.—The fatal dose of chloral is extremely variable death having been caused by 2 grams and recovery following 30 grams. Children are less susceptible than adults but old individuals are particularly susceptible to its effects. It is quite probable that doses of 8 grams or under may not prove fatal, especially if proper treatment is instituted, but with doses of more than 10 grams it is probable that death will surely result.

Fatal Period.—The fatal period is determined in large measure by the size of the dose and the condition of the individual. Sudden death, that is, within 15 minutes, to an hour, is common after large doses or in persons with a weak heart. Most of the deaths appear to occur during a period of 6 to 10 hours.

Post Mortem Appearances.—The post mortem appearances are not characteristic. The esophagus and stomach membranes may show an inflammatory reaction and the odor of chloral may sometimes be detected in the stomach contents. Edema of the lungs may be present in acute intoxication. In chronic poisoning there may be fatty degenerations, especially of the heart and muscles.

Treatment.—Lavage of the stomach should be instituted especially if the drug has not had time for absorption. Owing to the depressant action of chloral on the nervous system emetics may fail to act. Owing to the rapid absorption of chloral other measures are likely to be more successful than gastric lavage. General stimulation is indicated and this is best attained by subcutaneous injections of strychnine and hot coffee by mouth or rectum. Atropine and camphor may also be useful. The body temperature demands maintenance by application of hot water bags, etc. At times artificial respiration is essential.

Chronic chloral poisoning is best treated in the hospitals especially conducted for the cure of drug addicts.

References

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BENNETT: *Ibid.*, 1922, 79, p. 1048.

FORMALDEHYDE (H.CHO)

Formaldehyde is a colorless irritant gas formed by the oxidation of methyl alcohol. The official solution of

formaldehyde contains about 37 per cent by weight of the gas with small amounts of methyl alcohol. Formaldehyde is soluble in water and these solutions tend to decompose, on standing, but particularly on heating, into insoluble decomposition products. By treatment with ammonia formaldehyde is transformed into hexamethylenamine. Because of its antiseptic properties formaldehyde has been extensively employed for disinfectant purposes and to some extent as a food preservative, especially for milk. At present, however, its use as a food preservative is prohibited by law in the United States. It possesses an irritant action for the skin and mucous membranes and according to concentration its solutions by continued application may induce an eczema or ulcerations and gangrene. Its vapor is extremely irritating to mucous membranes and it may produce bronchitis and pneumonia.

Formaldehyde is absorbed by all mucous surfaces and in small quantities is oxidized to formic acid in the tissues. Some of the formaldehyde may be eliminated as such or be transformed into hexamethylenamine.

Symptoms.—Poisoning by formaldehyde is not very common but there are a number of cases on record. "The symptoms consist of immediate and severe abdominal pain; often sudden and prolonged loss of consciousness, and collapse." There is sometimes diarrhœa, sore mouth, irritation of the respiratory tract, and an action upon the central nervous system resembling that of acute alcohol intoxication, such as staggering gait, stupor, coma and sometimes convulsions. The urine may be suppressed for several hours and then it may contain casts and blood. If recovery occurs it is usually rapid and complete.

Fatal Dose.—An ounce of "formalin" (40 per cent commercial solution) has caused death, and the largest quantity from which recovery has occurred is 2 ounces.

Fatal Period.—Death may be sudden, that is, within 2 to 3 hours but generally takes place within 36 hours.

Post Mortem Appearances.—Autopsy reveals gastritis with erosions, and the kidneys may show congestion.

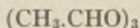
Treatment.—Gastric lavage should be practised promptly and should be followed by administration of dilute ammonia and ammonium acetate with the purpose of transforming the irritating formaldehyde into the non-irritating and non-toxic hexamethylenamine.

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PARALDEHYDE



Poisoning by paraldehyde is rare. A few deaths have resulted from overdoses either given therapeutically or from overdosage as the result of the formation of a habit.

Paraldehyde, a polymer of acetaldehyde, is a volatile, colorless liquid with an ethereal odor which is penetrating and disagreeable. It has a burning taste and resembles ether inasmuch as it irritates the mouth, throat and stomach. It is soluble in water, alcohol, ether and oils and becomes a solid at low temperatures. Its boiling point is 124°C .

Rapidly absorbed it produces sleep, and in its action it resembles chloral but does not cause noteworthy depression of the nervous centers. It is eliminated in part by the lungs and imparts a characteristic odor to the breath. A portion is also excreted by the kidneys.

Symptoms.—Toxic doses of paraldehyde result in stupor, muscle relaxation, depression of medullary centers, collapse and death.

With chronic paraldehyde poisoning the symptoms closely resemble those of chronic alcoholism. These may be followed by delirium tremens, convulsions, high temperature, marked thirst, profuse sweating, weak pulse and polyuria.

Fatal Dose.—The toxicity of paraldehyde is low. As much as 100 grams have been followed by recovery.

Fatal Period.—Little is known concerning this. When death has occurred it has taken place within a few hours.

Post Mortem Appearances.—Autopsy reveals nothing except possibly gastric irritation. The stomach contents, lungs and in fact most of the organs may have the odor of paraldehyde.

Treatment.—Gastric lavage is indicated in acute intoxication. Stimulation by strychnine, hot coffee, atropine and camphor are recommended. The body temperature should be maintained by hot water bags, blankets, etc. Artificial respiration may be necessary. Chronic paraldehyde poisoning should be treated in a manner similar to treatment for chronic alcoholism.

References

KRAEPELIN: *Biochem. Bull.*, 1916, 5, p. 223.

FORNACA and QUARELLI: *Berl. klin. Woch.*, 1912, 49, p. 2451.

CARBON TETRACHLORIDE



Carbon tetrachloride has recently become of toxicological importance chiefly because of its extended employment in various fields. It is used in industry as a rubber solvent, as an ingredient of certain types of paint, as a fire extinguisher, and as a shampooing agent. In medicine it has been quite extensively employed as an anthelmintic, and to a small degree as a delousing agent.

In the presence of heat carbon tetrachloride may form phosgene and hydrochloric acid which may cause serious poisoning. Such possibilities exist under suitable circumstances when carbon tetrachloride is used as a fire extinguisher.

Carbon tetrachloride is a colorless liquid with a pleasant odor. It solidifies to a solid mass at -30°C . and has a boiling point of 76°C . It possesses a narcotic action somewhat similar to that of chloroform. The physiological action at times is obscured by the influence of carbon disulphide which is often present in carbon tetrachloride as an impurity.

Symptoms.—The symptoms of poisoning by carbon tetrachloride are nausea, vomiting, abdominal pain, at first stupor later deepening into coma, absence of reflexes, clonic convulsions, weak pulse, increased temperature and death.

Fatal Dose.—The fatal dose is unknown but is several times the therapeutic dose (3 to 4 c.c.).

Fatal Period.—Death usually occurs within 36 hours.

Post Mortem Appearances.—The most characteristic feature on necropsy is severe necrosis of the liver. The kidneys are not affected.

Treatment.—The treatment is purely symptomatic.

References

- LAMBERT: J.A.M.A., 1923, 80, p. 526.
SMILLIE and PESSOA: Am. J. Hyg., 1923, 3, p. 35.
LAMSON and McLEAN: J. Pharm. and Exp. Therap., 1923, 21, p. 237.

NITRITES

The nitrite group of drugs includes the inorganic nitrites, the nitrous esters, as amyl nitrite, ethyl nitrite or

“Sweet Spirits of Niter,” and those nitrates which are reduced to nitrites in the body.

Amyl Nitrite.—($C_5H_{11}NO_2$) is a clear yellow fluid with a peculiar ethereal fruit odor and aromatic taste. It is practically insoluble in water but mixes with alcohol and ether. It is very volatile, even at low temperatures and is inflammable.

Nitroglycerine.—($C_3H_5(NO_3)_3$) is a clear yellow, oily liquid insoluble in water but soluble in alcohol, ether and chloroform. Upon concussion it will explode.

Symptoms.—Although death rarely, if ever, occurs after the therapeutic use of the nitrites it is quite common for untoward symptoms to appear which, however, usually pass over rapidly. The effects seem to be aggravated if the patient is in an upright position. The symptoms most obvious are a pounding heart, flushing of the face and neck, throbbing and fulness of the head “as if the top of the head were coming off,” and intense headache. There may also be confusion of ideas, visual disturbances, dizziness, a feeling of faintness, or indeed actual fainting may occur. At times there may be localized edema and excessive sweating. The symptoms are probably referable to low cerebral blood-pressure.

There is a wide range of susceptibility to the action of the nitrites, some patients displaying marked toxic symptoms with very small doses, others being unaffected with very great quantities.

In general the nitrites in large doses form methemoglobin which produces cyanosis and asphyxia. Excessive doses of nitroglycerine may produce nausea, vomiting, colic, and at times bloody diarrhoea. There is a flushed and perspiring skin; headache is persistent; vertigo is present; and very rarely blindness and delirium. Respiration is markedly altered, hyperpnea at first obtaining,

being followed by dyspnea. The body surface is cold with cyanosis, the heart is slowed, paralysis occurs, convulsions appear and death results within seven or eight hours from respiratory failure.

Nitrite poisoning may also occur from the administration of bismuth subnitrate (which see).

Fatal Dose.—The fatal dose of amyl nitrite is unknown. With nitroglycerine a few drops may prove fatal.

Fatal Period.—With nitroglycerine death may occur within an hour or two or may be delayed for several hours.

Post Mortem Appearances.—Beyond the reddish-brown color of the blood, due to the presence of methemoglobin, the only noteworthy features of nitrite poisoning revealed on autopsy are hyperemia of various organs and tissues.

Treatment.—Gastric lavage is indicated in the case of nitroglycerine. To hasten further elimination purgation may be induced by saline cathartics. When the case is desperate venesection with subsequent infusion of physiological saline is recommended. For the attendant severe headaches caffeine in the form of large volumes of black coffee is useful.

References

CADWALLADER: Med. Record, 1896, 50, p. 816.

EVANS: J.A.M.A., 1912, 58, p. 550.

DIGITALIS

The active principles of digitalis, or foxglove, are obtained from the leaves of *Digitalis purpurea* an ornamental garden flower which also grows wild both in Europe and America. The active constituents are glucosides and therefore prone to chemical change. The glucosides present in digitalis are divisible into at least four groups (*a*) digitoxin, is a crystalline alcohol soluble compound of the

formula $C_{34}H_{45}O_{11}$ which is probably the most important substance of the leaves. On hydrolysis digitoxin yields a hexose and digitoxigenin. (b) Digitalin, an amorphous alcohol-soluble compound of the formula $C_{35}H_{36}O_{14}$ which on hydrolysis yields dextrose, digitaligenin and digitalose. It is about one-half as active as digitoxin. (c) Digitalein, an amorphous water-soluble substance which is probably a mixture of closely related compounds. They have typical digitalis effects. (d) Digitonin, which is a water-soluble saponin occurring in both a crystalline and an amorphous form. The digitonin has properties similar to saponins, that is, irritant and hemolytic effects and the typical digitalis action is lacking.

Various other glucosides, notably the strophanthins, have digitalis effects, the action differing quantitatively rather than qualitatively. There is considerable confusion relative to the chemistry of the different commercial preparations. The official strophanthin, is strophanthin amorphous, although the same plant, the Kombe, also yields a crystalline strophanthin whose action is very similar. Oubain is a crystallized strophanthin which has about twice the toxicity of strophanthin. It is of particular value for intravenous administration.

Digitalis and strophanthins are of great importance in therapeutics in correcting irregularities of the heart beat as in auricular fibrillation or in chronic dilatation of the heart.

Great care in administration must, however, be exercised since digitalis and its allies are highly toxic. The best preparations of digitalis are undoubtedly the tincture and the infusion.

Poisoning from the clinical use of digitalis is not rare, indeed the border line between the necessary efficient therapeutic dose and the toxic dose is so narrow that toxic

symptoms may appear simultaneously with the desired therapeutic effects. This toxic action is not permanently harmful if care in administration and dosage is properly regulated.

Symptoms.—Early indications of toxicity are nausea, malaise and headache which may be very severe. Diarrhœa sometimes occurs but is more common with strophanthin. The dosage of the drug should either be reduced or stopped altogether when these symptoms make their appearance. In one or two days they usually disappear.

In advanced digitalis poisoning various heart irregularities may be noted. The most common and the earliest to appear being the result of overstimulation of the vagus, the heart beat dropping to 50 or lower. Extra systoles are frequent although the rhythm may be maintained. The next stage of poisoning is partial heart block which may be permanent. Finally there may be muscular irritability of the heart, with extra systoles and high blood pressure.

Acute poisoning from digitalis is characterized by the symptoms appearing late and the course of the intoxication being prolonged, death in many instances not occurring for a week or more. The most notable symptoms are nausea, vomiting, diarrhœa, slow arhythmic pulse, lassitude, sensory and muscular disturbances. Sudden death with asphyxial convulsions is quite characteristic.

Fatal Dose.—The fatal dose of digitalis is quite variable, 2.5 grams having caused death whereas with 4.0 grams recovery has been noted. The difference in results appears to be associated with the different degrees of absorption taking place, and the effect of vomiting, diarrhœa, etc. upon this absorption.

Fatal Period.—Death is usually delayed for a period of several days.

Post Mortem Appearances.—Sometimes there is evidence of gastric irritation.

Treatment.—In the simplest type of poisoning treatment consists in stopping the drug and keeping the patient quiet in bed until the symptoms have disappeared. To counteract over-stimulation of the vagus atropine sulphate in doses of $\frac{1}{65}$ grain (0.001 gram) may be given subcutaneously. Atropine action, however, is short lived, its influence lasting not more than 1 hour. Bromides (1 to 2 drams (4 to 8 grams) of sodium bromide or morphine sulphate, $\frac{1}{4}$ grain (0.015 gram) and a hot water bag, or ice bag over the heart may reduce excessive irritability.

When severe poisoning is present absolute quiet and freedom from exertion must be maintained, since even the slightest effort may cause circulatory failure and sudden death. The other measures to be followed are purely symptomatic, warmth, stimulants, etc.

In acute poisoning, evacuation of the stomach, catharsis, quiet and general symptomatic treatment are advocated.

Reference

HATCHER and EGGLESTON: *J. Pharm. and Exp. Therap.*, 1912, 4, p. 113.

PICROTOXIN ($C_{30}H_{34}O_{13}$)

Picrotoxin may be taken as the pharmacological representative of the active principles of a number of plants. It occurs in the seed, *Cocculus indicus*, of the plant *Anamirta paniculata*. The fruit is also known as fish berries and in powdered form has been employed as fish and bird poison, and as a remedy against parasites and vermin. Poisoning has been induced by eating the berries, or the flesh of fish poisoned with it, by drinking beer to which it has been added as an adulterant and as an ingredient of so-called "knock-out" drops.

Active principles of other plants capable of inducing picrotoxin-like effects upon the organism are Cicutoxin from the root of *Cicuta virosa* or "Water Hemlock" which has been eaten for parsley; Coriamyrtin from *Coriaria myrtifolia* and Tutin from *Coriaria tutu*, both glucosidal in nature.

Pure picrotoxin occurs as colorless crystals with a neutral reaction, slightly soluble in cold water, more readily soluble in warm water and easily soluble in alcohol, ether and chloroform. The solutions are odorless but possess an intensely bitter taste. The crystals melt at 192° – 200° C.

Picrotoxin stimulates the medullary centres and the spinal cord causing typical convulsions. The stimulation is followed by paralysis. Picrotoxin is excreted by the urine in part at least in unchanged form. Picrotoxin is not employed therapeutically.

Symptoms.—The initial symptoms of poisoning are a burning sensation in the mouth, throat, esophagus and stomach with subsequent salivation, nausea, vomiting, abdominal pain, and diarrhœa. Closely following these symptoms are profuse sweating, pallor, weakness, headache, shallow respiration, palpitation. Confusion and stupor soon pass into unconsciousness. Early in the intoxication convulsions, both clonic and tonic, may set in and opisthotonus may be in evidence. Sometimes the jaws are firmly closed, thus resembling strychnine poisoning. The convulsions ultimately cease and paralysis ensues, death resulting from respiratory failure.

Fatal Dose.—No cases of fatal poisoning have occurred in man from the pure picrotoxin, hence, the exact fatal dose is unknown. From animal experimentation it has been inferred that the fatal dose probably varies between 0.13 and 0.20 gram. Death has been caused, however, from

eating 2.4 grams of the powdered berries which contained much less than the toxic dose given above.

Fatal Period.—Death may be very rapid—30 to 60 minutes—or be delayed for several hours. In some recorded cases several days elapsed before death occurred.

Post Mortem Appearances.—The post mortem appearances are those of death by asphyxia.

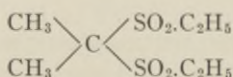
Treatment.—If vomiting has not been free, emetics should be administered. The convulsions may be controlled by ether, chloroform or chloral. Ether presents less danger than the others, chloroform may lead to delayed chloroform poisoning, and chloral possesses a depressant action on respiration. Stimulation by hot mustard baths and minimal doses of atropine may be given in the later stages.

References

BROWN: Brit. Med. J., 1875, i, p. 540.

GRUENWALD: Arch. f. exp. Path. u. Pharm., 1909, 60, p. 249.

SULPHONAL



Sulphonal was introduced into medicine as a hypnotic by Baumann and Kast in 1888. Since then at least 34 fatal cases have been recorded due either to overdosage from a single administration or from long continued use. Its effects are cumulative and it is possible that it may form a habit without the induction of tolerance. Sulphonal is a strong hypnotic but has only slight analgesic properties. It is excreted by the urine in part as ethylsulphonic acid and partly unchanged, but the elimination is very slow.

Sulphonal occurs in the form of crystals which are odorless and almost tasteless. It is almost insoluble in cold water but dissolves readily in hot water, alcohol and ether. The crystals melt at 125°C .

Symptoms. Acute Poisoning.—Large doses of sulphonal are followed by stupor, unconsciousness, and sometimes convulsions. The respiration is profoundly affected, being stertorous and irregular, and cyanosis develops. The pulse is weak, the temperature may be increased and the urine may be partially or entirely suppressed. At times the urine becomes red in color from the presence of hematoporphyrin from disintegration of the red corpuscles. Diagnostically this condition is regarded as an unfavorable symptom.

Chronic Poisoning.—The use of the drug for long intervals leads to a type of poisoning which is characterized by disturbances of digestion, nausea, vomiting, either constipation or diarrhœa, headache, noises in the head, vertigo, mental and physical incapacity, difficulty in speech, more or less paralysis, great emaciation, albuminuria, hematoporphyrin in the urine, and various skin eruptions.

Fatal Dose.—Death has been reported from the use of doses varying from 5 to 30 grams. Much larger doses (100 grams for instance), have been followed by recovery. The use of sulphonal over a period of several months has caused death in daily doses varying from 0.6 to 1.3 grams.

Fatal Period.—Death may be rapid from single doses varying from a few hours or may be delayed for several days. Death from chronic poisoning is usually a matter of months.

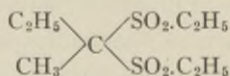
Post Mortem Appearances.—The post mortem appearances are not characteristic.

Treatment.—In acute poisoning the stomach should be emptied and washed out. Excretion should be hastened by the use of purgatives, saline cathartics preferably, the administration of diuretics, best large volumes of water. Stimulation is indicated, strychnine and other stimulants may be given. In chronic poisoning the drug should be discontinued. Rest, regular diet, free movement of the bowels, large volumes of fluid, and tonics are recommended. Recovery is generally slow and prognosis is unfavorable when hematoporphyrin appears in the urine.

References

- TAYLOR and SAILER: Contributions from Pepper Laboratory, 1900, p. 120.
 ROGERS: J.A.M.A., 1912, 58, p. 1510.

TRIONAL



Trional is closely related both chemically and pharmacologically to sulphonal. A few cases of acute poisoning have been described and at least one instance of chronic intoxication is on record. The symptoms are so similar to those induced by sulphonal that a separate description is unnecessary. Treatment would also follow that of sulphonal poisoning. The fatal dose is not definitely known, but it probably smaller than that for sulphonal since trional is more soluble and its effects are therefore correspondingly more rapid and intense.

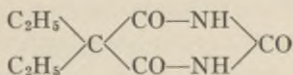
Trional occurs in crystalline scales, which are colorless, odorless, and possess a bitter taste. In aqueous solution it is neutral to litmus and has a melting point between 74° and 76°C. Above this temperature it decomposes yielding sulphur dioxide.

References

COLEMAN: *Med. News*, 1900, 77, p. 129.

v. NOORDEN: *Therap. Mon.*, 1916, 30, p. 426.

BARBITAL (VERONAL)



Barbital, as may be seen from its structure is an urea derivative, which was first introduced into medicine in 1903-05 as an hypnotic. In many ways it possesses distinct advantages over other preparations having similar pharmacological effects. Compared with chloral it is more powerful and agreeable and it is not a local irritant. There is also a greater range between the therapeutic dose (0.5 gram) and the dose likely to produce toxic symptoms (8-10 grams). On the other hand it has certain disadvantages, for example, it acts more slowly than chloral, and after depression effects are more usual than is true for chloral. These depression effects, however, are rather exceptional for in therapeutic doses there is generally little or no influence upon the circulation and respiration. The general action of the therapeutic use of barbital is to produce a deep, dreamless sleep from which the individual awakes without bad after effects. Certain individuals, however, exhibit a variety of symptoms such as lassitude, dizziness, headache, diarrhoea, nausea and skin eruptions.

Barbital is chiefly eliminated through the urine although small quantities may appear in the feces. Usually more than one-half is excreted unchanged. Excretion is very slow, hence cumulative effects appear and constitute a menace if continuous doses are maintained for a considerable period of time. Tolerance is not readily established although the barbital habit may be formed.

It has been stated that the toxic action of barbital is especially directed to the blood vessels. It resembles arsenic in this action. In addition to its employment as a general hypnotic barbital has been used in epilepsy, delirium tremens, prolonged labor, pernicious vomiting of pregnancy and sea sickness.

A large number of deaths have been reported from the use of barbital. Most of these have been caused either by overdosage of the drug taken in single doses or from continued use. A number of deaths by suicide are also on record.

Barbital is a white crystalline powder with a slightly bitter taste. It is soluble in hot water and alcohol and ether. The sodium salt is readily soluble and generally barbital sodium is the form in which barbital is prescribed.

Symptoms.—The acute symptoms of poisoning with barbital consist of coma, low blood pressure, weak heart action, slow and shallow respiration, increased reflexes, temperature either high or subnormal, cyanosis, and asphyxia. There may be renal irritation, the urine secretion may be suppressed either partially or completely, skin eruptions, death from respiratory failure.

Symptoms of chronic poisoning are gastro-intestinal disturbances, nausea, vomiting, diarrhoea, confusion, staggering gait, loss of memory, general debility, delusions, anemia, hematoporphyrinuria and skin rashes somewhat resembling those of measles.

Fatal Dose.—The fatal dose varies enormously probably depending upon the rate of absorption and the factors present which may modify this. Quantities as small as 1 gram have caused death whereas recovery has followed the administration of more than 8 grams. It is probably fair to state that the usual fatal dose lies somewhere between 8 and 10 grams.

Fatal Period.—Death rarely occurs under 24 hours, and may be delayed for 2 or 3 days.

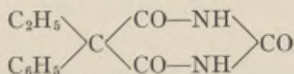
Post Mortem Appearances.—Autopsy reveals no characteristic symptoms although there may be present hyperemia of various organs, notably, the brain and liver and kidneys, and the latter may show tubular degeneration. At times from the nature of the death edema of the lungs may be observed.

Treatment.—Prompt lavage of the stomach is indicated together with measures for stimulating excretion, such as the administration of diuretics (best large volumes of fluid) and saline purgatives. Since a failing circulation is one of the most prominent features of barbital poisoning attempts should be made to increase blood pressure. Hypodermic injections of camphor may help. The extremities should be bandaged and caffein is especially useful. At times saline infusion may tide the patient over the critical period. Artificial respiration may be necessary.

References

- ZÖRNLAIB: Wien. med. Wochen., 1906, 56, p. 2544.
 WILLCOX: Lancet, 1913, ii, pp. 734 and 1178.
 RAEMER: Deut. med. Wochen., 1919, 45, p. 1305.
 HASSIN and WIEN: J.A.M.A., 1920, 75, p. 671.

LUMINAL



Luminal, which is the trade name for phenylbarbital, is closely allied in properties and effects to barbital. It is a more powerful hypnotic than barbital and usually is given as the sodium salt which is freely soluble whereas the free acid is insoluble. There is perhaps more danger

of poisoning with luminal than with barbital since the zone between the therapeutic dose and the toxic dose is very narrow.

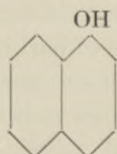
The symptoms of poisoning so closely resemble those of barbital that a separate discussion is unnecessary.

References

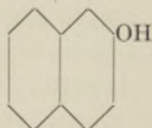
FARNELL: J.A.M.A., 1913, 61, p. 192.

SHONLE and MOMENT: J. Am. Chem. Soc., 1923, 45, p. 243.

NAPHTHOL



α -naphthol



β -naphthol

There are two naphthols, the Alpha and Beta compounds. The first is very toxic and has not been used in medicine. β -naphthol has an action similar to that of phenol and is even more germicidal. It has been used especially in the form of ointment in various skin diseases, such as psoriasis, acne, etc., and internally it is employed as an anthelmintic especially in hookworm disease.

β -naphthol is a white crystalline powder with a burning taste and the odor of phenol. It is difficultly soluble in water but dissolves easily in alcohol, ether, chloroform, glycerol and alkalies.

In the body β -naphthol has an influence similar to that of phenol. It destroys the red cells and is irritant to the kidney. It is absorbed from the skin and its application to the diseased skin has led to several cases of poisoning.

Symptoms.—The symptoms of poisoning apparently vary according to conditions of administration. In some

cases the application to the skin produces a severe nephritis, whereas in others vomiting, stupor, and unconsciousness were most in evidence. Taken by mouth as in the treatment of hookworm disease nausea, vomiting, abdominal pain, destruction of red cells, with resulting anemia, large spleen and liver may be the chief symptoms, or again an acute nephritis may develop. The urine is dark in color from the conjugated glycuronate and sulphate formed.

Fatal Dose.—The precise fatal dose is unknown. Death has been caused by the absorption of the 2 per cent ointment applied to the skin of children or by 3 or 4 grams in adults. By mouth doses of 18 grams cause serious symptoms.

Fatal Period.—The fatal period is usually delayed for many days. Death may occur in from 24 hours to a month.

Post Mortem Appearances.—The most characteristic feature is the presence of an acute nephritis.

Treatment.—Follow the treatment for phenol poisoning—see page 173.

References

- SMILLIE: J.A.M.A., 1920, 74, p. 1503.
BUSQUET: J.A.M.A., 1921, 79, p. 51.

CUBEB AND COPAIBA

The oleoresins of copaiba and cubeb are employed as urinary antiseptics in subacute and chronic urethritis. They are used as aids to local treatment to diminish pain and the discharge and to hasten healing. Cubeb is also sometimes used in bronchitis. The oleoresins are rich in terpenes and resin acids which are mildly irritant. This irritant action is induced along the urinary tract as a

stimulus to repair, the terpenes at the same time acting as antiseptics.

These substances are also irritating to the gastro-intestinal tract causing anorexia, colic, eructations and diarrhœa. Scarlatinal rashes occur in some patients whether from the direct action of the drugs or secondary to the gastro-intestinal disturbance is uncertain. With large doses there is intense irritation of the urinary tract resulting in renal pain and albuminuria.

OIL OF SAVIN

Savin is a volatile oil present in the leaves of the common savin plant (*Juniperus Sabina* or *Sabina Communis*) which is indigenous in Europe and certain parts of the United States. The tops of this evergreen have been employed in the form of a decoction from time immemorial to produce abortion and most of the fatalities have occurred from such use. The intoxication with savin resembles turpentine poisoning except that it is much more serious.

Symptoms.—There is a burning sensation in the throat and stomach followed by nausea, vomiting, violent abdominal colic, and bloody diarrhœa. There is severe congestion in the pelvic organs including the uterus upon which it may exert a specific effect. If the uterus is pregnant the fetus is generally expelled. The menstrual flow is said to be greatly increased. The urinary organs are intensely irritated, blood and protein appearing in the urine, the passing of which is painful and may be entirely suppressed. The respiration is irregular. Later unconsciousness and convulsions may be manifested and death occurs in collapse.

Fatal Dose.—Since death generally occurs from home made decoctions it is impossible to state the exact

fatal dose. According to Lewin 6 drops of the oil may produce toxic effects.

Fatal Period.—Death usually occurs only after several days but may result in a few hours.

Post Mortem Appearances.—In a case described by Blyth the pharynx was much reddened, and the gullet even congested. The stomach was inflamed and contained some greenish matter in which savin tops could be identified. The odor of savin may be detected in the gastro-intestinal contents. The kidneys are irritated.

Treatment.—Treatment of savin poisoning consists in evacuation of the stomach and lavage. The administration of demulcents and stimulants is indicated.

Reference

BLYTH: Poisons, 5th Edition, 1920, p. 485.

OIL OF CEDAR

Oil of cedar is contained in the tops of the red cedar (*Juniperus Virginiana*) indigenous in the United States. This oil resembles closely the oil of savin and like the latter has caused toxic effects and death mainly from its use by the laity as an abortifacient. On the other hand it has been taken by mistake and also with suicidal intent. It rarely produces abortion.

Symptoms.—The symptoms produced are somewhat similar to those evoked by savin—burning in the throat and stomach, nausea, vomiting, the vomitus at times containing blood, convulsions, irregular respiration, slow, intermittent pulse, unconsciousness, coma and death in collapse. The kidneys are irritated and there may be anuria.

Fatal Dose.—The smallest fatal dose on record is one ounce. As small a quantity as 90 minims (5.5 c.c.) have caused serious symptoms.

Fatal Period.—Death may occur within an hour or be delayed for more than a day.

Post Mortem Appearances.—There is gastro-intestinal irritation and congestion of the renal organs. The stomach contents have the odor of oil of cedar.

Treatment.—The treatment should be prompt, evacuation of the stomach with lavage and general stimulation if indicated.

References

McNALLY: *Med. Record*, 1916, 89, p. 330.

DeNEEN: *Am. J. Surg.*, 1919, 33, p. 277.

CROTON OIL

Croton oil is a fixed oil which is obtained by pressure from the seeds of *Croton Tiglium*. It is a pale yellow liquid, with a faint fatty odor, and contains about 10 per cent of the active constituent "croton resin." Poisoning has occurred accidentally from mistaking it for castor oil, from overdoses and from homicidal motives. The ingestion of the seeds of the plant has also caused intoxication. In medicine it has been employed as a purgative in obstinate constipation when other measures have failed.

Symptoms.—The chief symptoms are gastro-intestinal irritation with subsequent collapse. Applied to the surface of the body croton oil is an irritant, producing sensations of burning, redness of the face and formation of vesicles, which may develop pus, and sometimes sloughing of the tissues.

Taken by mouth croton oil produces a burning sensation in the mouth and throat, irritation, salivation and vomiting. Intense abdominal pain occurs accompanied by profuse diarrhoea, the stool often containing blood. The skin

is moist and cold, the face pinched, the respiration is slow and shallow, the pulse small and thready, and the temperature falls. There may be delirium. Collapse sets in, cyanosis develops and death occurs from respiratory failure. It is reported that death may take place without special gastro-intestinal disturbances, as purging.

Fatal Dose.—Death has been caused by the ingestion of 20 drops of the oil whereas recovery has followed the administration of one-half dram. The toxicity of different specimens of the oil varies considerably. In general the freshly prepared samples are less toxic than those which have stood for a considerable period.

Fatal Period.—Death usually occurs in from 4 to 12 hours, although there are cases of poisoning on record where death was delayed for several days.

Post Mortem Appearances.—The characteristic features observable on necropsy are intense inflammation of the gastro-enteric tract, sometimes with erosion.

Treatment.—The stomach should be emptied either by the tube or by an emetic as apomorphine. The stomach should be washed with warm water, and after thorough lavage demulcent drinks are indicated. The circulation and respiration should be stimulated. This may be accomplished by aromatic spirits of ammonia, strychnine and strong coffee.

SANTONIN ($C_{15}H_{15}O_3$)

Santonin is the inner anhydride or lactone of santonic acid obtained from Levant wormseed, *Santonica*. Santonin forms colorless crystals, which become yellow on exposure to light. They are odorless and at first tasteless, leaving an after bitter taste. The crystals are only slightly soluble in water but dissolve readily in alcohol. The crystals melt at 170°C .

Santonin is employed medicinally as an anthelmintic and nearly all the cases of intoxication have been due to overdoses generally by the laity in attempts at self-medication. Most deaths have occurred among children although occasionally adults have succumbed. Santonin is changed in the intestine to sodium santoninate and the major portion is passed out as such through the feces. The portion absorbed is changed in the organism, probably by oxidation, and the decomposition products impart a yellow color to the urine. Upon rendering the urine alkaline the yellow color becomes pink.

Symptoms.—The symptoms observed in santonin poisoning are gastro intestinal disturbances and an influence upon the central nervous system. The symptoms of gastro-intestinal trouble are nausea, vomiting, abdominal pain and diarrhœa. The nervous symptoms are headache, vertigo, weakness, sleepiness. Later unconsciousness, clonic convulsions, and fall of temperature may occur. There seems to be a special influence upon the eye since even with large therapeutic doses there may be "yellow vision" which in severe poisoning may result in temporary, partial or complete blindness. The blindness may last for a week or more. At times taste, smell and hearing are also affected. At times also there may be skin eruptions, fever, nephritis, hematuria, and urine suppression. Death is due to respiratory failure.

Fatal Dose.—The fatal dose of santonin for children between the ages of four to seven years lies somewhere between 2 and 3 grains (0.06 to 0.16 gram). With adults as much as 1 gram has been taken without fatal results.

Fatal Period.—The fatal period is variable. Some deaths have occurred in less than 1 hour, others in 15 hours and in other cases death has been delayed for 1 or 2 days.

Post Mortem Appearances.—Beyond the possibility of gastro-intestinal irritation autopsy reveals no characteristic features of santonin poisoning.

Treatment.—The stomach should be emptied and thoroughly washed with warm water. The bowels should be emptied preferably by saline cathartics, as magnesium sulphate. The convulsions may be controlled by ether or chloral hydrate. Chloroform may be used but it is not advisable because of the danger of delayed chloroform poisoning. For the collapse stimulants are indicated.

References

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HARNACK: Ibid., 1901, 45, pp. 272 and 447.

MALE FERN

The employment of male fern, *Aspidium filix-mas*, as an anthelmintic dates from ancient times. The form in which it is generally employed is that of the dried ethereal extract, the constituents of which are a number of closely related substances, filicic acid, aspidium, flavaspidin, etc., of which filicic is probably the active ingredient.

The oleoresin is a green, oily liquid sometimes containing a crystalline deposit which should be discarded. It possesses a disagreeable taste and odor. The active constituent, filicic acid, is a derivative of phloroglucin. It is insoluble in water but soluble in oils.

Nearly all the cases of poisoning by male fern have been due to overdoses or to the administration of castor oil with or subsequent to its administration. Being soluble in castor oil it is thought that the toxic effect is increased owing to the better absorption of the drug. Filicic acid is decomposed in the body yielding trimethylphloroglucin.

Symptoms.—The symptoms of poisoning induced by male fern are indicative of gastro-intestinal disturbance and an action upon the nervous system. The gastro-intestinal disturbance is manifested by nausea, vomiting, abdominal pain, and profuse diarrhœa. The influence upon the nervous system is indicated by headache, muscular twitching, dizziness, confusion, sleepiness, dyspnœa, sometimes convulsions, delirium, muscle cramps, coma, collapse and death by respiratory failure. Glycosuria sometimes occurs and albuminuria with casts may be present. In many instances icterus may be observed.

Male fern also causes serious trouble by an action upon the eye resulting in temporary and sometimes permanent blindness. Out of 78 cases of poisoning 18 became permanently blind in both eyes, and 15 lost the vision of one eye. In others while actual blindness was not permanent the vision was distinctly impaired. The influence upon the eye is caused by spasm of the retinal vessels with subsequent atrophy of the optic nerve.

Fatal Dose.—For adults the fatal dose varies from 5 to 6 drams (18.5 to 22.2 c.c.) although death has resulted from 1 dram. For children the fatal dose is probably from 1 to 2 drams (3.7 to 7.4 c.c.).

Fatal Period.—Death usually occurs within 24 hours.

Post Mortem Appearances.—The gastro-intestinal tract is much congested and the small intestine may contain many hemorrhagic areas. The kidneys may show nephritis.

Treatment.—The stomach should be emptied and saline cathartics should be administered. Fats and oil are contra-indicated. Demulcent drinks are recommended. In the period of convulsions ether may be given and stimulants in the stage of collapse. Artificial respiration may be necessary.

References

STUELP: Zent. f. Biochem. u. Biophys., 1904, 12, p. 470.

SIDLER-HUGUENIN: Correspondenzbl. f. schweiz. Aertze., 1898, 28, p. 512.

OIL OF CHENOPODIUM

Oil of *Chenopodium* has caused fatal poisoning almost entirely from overdosage in its therapeutic use as an anthelmintic. Severe intoxication may result even with ordinary therapeutic doses. During fasting the drug is more toxic than when food is given, especially fatty food and carbohydrates. This fact is recognized by the present manner of therapeutic administration during which period liquid food is given. The probable active principle of the oil is Ascaridole which is more toxic than the oil itself. The oil is distinctly constipating and for this reason its administration is followed by castor oil. The oil is absorbed from the stomach and intestines and is in part eliminated by the lungs.

The oil of *Chenopodium* is obtained by distillation of the American wormseed, *Chenopodium ambrosioides* anthelminticum.

Symptoms.—The symptoms of poisoning are gastrointestinal irritation and depression of the nervous system. The first indications of intoxication are nausea, vomiting, abdominal pain and colic, diarrhœa with bloody or mucous stools, headache, and tingling in the hands and feet. There may be temporary deafness which may last as long as two years but usually clears up in a few days or weeks. The pulse becomes irregular and drowsiness is prominent. Hallucinations, clonic convulsions, paralysis, collapse and coma may intervene and death close the scene by respiratory failure.

Fatal Dose.—The fatal dose is unknown. Four drops of the oil 3 times a day for seven doses caused the death of an infant of one year, and death has occurred in an adult after 2 doses of 3 c.c. each.

Fatal Period.—Death may occur within a few hours and may be delayed for several days.

Post Mortem Appearances.—The only noteworthy autopsy findings are gastro-intestinal irritation.

Treatment.—Treatment of oil of *Chenopodium* intoxication consists in immediate purgation, and central stimulation by strychnine or caffeine, in the form of hot, black coffee.

References

PREUSCHOFF: *Zeit. f. exp. Path. u. Pharm.*, 1920, 2, p. 425.

DARLING, BARBER and HACKER: *J.A.M.A.*, 1918, 70, p. 499.

SALANT and LIVINGSTON: *J. Pharm. and Exp. Therap.*, 1916, 8, p. 119.

CANTHARIDIN

Cantharidin is the active principle of the commercial cantharides which is either dried entire, or the dried and powdered blister beetle, Spanish fly (*Cantharis vesicatoria*). It is highly toxic and many cases of poisoning have resulted from its supposed action of stimulating sexual feeling and from its abortifacient properties. Poisoning has also resulted from its use as a vesicant and as a counterirritant in pleurisy, neuralgia and rheumatic pains. In a few cases it has been used to cause death with criminal intent.

Cantharidin is probably the lactone of a ketonic acid, cantharidic acid. It is insoluble in water and difficulty soluble in alcohol, chloroform and ether, but readily dissolves in alkaline solutions. With bases, cantharidin forms salts. The pharmaceutical preparations are the plaster, tincture and the dried beetle.

Symptoms.—Cantharides is an irritant to the skin and mucous membranes. Consequently irrespective of the manner of administration local irritation will be in evidence. Taken by mouth there is a burning sensation in the mouth and throat succeeded by swelling and blistering, thirst and difficulty in swallowing. Generally there is salivation, nausea, vomiting, the vomitus sometimes bloody, abdominal pain, and bloody diarrhoea. The poison exerts a specific action upon the genito-urinary mechanism resulting in renal pain, pain in the penis with sometimes erection, urethral burning, frequent micturition, scanty urine, albuminuria, hematuria, casts, and in pregnant women abortion. The pulse is weak and slow, chills may occur, delirium and tetanic convulsions have been observed and death is preceded by collapse and coma. If recovery occurs chronic nephritis may result, although this is by no means constant. In many instances the urine regains its normal aspects within a few days.

Fatal Dose.—Death has been caused by doses varying from 1.5 to 3.0 grams although recovery has followed the ingestion of larger amounts. Distinctly toxic symptoms may be produced by 0.5 gram or less.

Fatal Period.—In the acute deaths, which occur from shock, the period varies from a few hours to a day or two. In those instances in which a fatal outcome is due to the induced nephritis death may be delayed for many days.

Post Mortem Appearances.—Autopsy reveals blistering of the mouth and pharynx, and gastro-enteritis, which may be accompanied by intestinal perforation. An acute nephritis is generally present and there may be evidences of an urethritis.

Treatment.—The type of treatment to be carried out depends upon the conditions in the alimentary canal. The first step is to empty the stomach and whether this shall be

done by lavage depends upon the degree of injury to the mucous membrane of the throat, esophagus and stomach. If the inflammatory reaction appears to be sufficiently severe so that the passage of the stomach tube would probably cause further damage to the mucous membrane, the stomach should be emptied by apomorphine. To soothe the pain demulcent drinks and opiates are indicated. Oils and fats are contraindicated. The body temperature should be maintained. Large volumes of water are recommended.

References

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FOLIN, KARSNER and DENIS: *J. Exp. Med.*, 1912, 16, p. 789.
LIPSITZ, FUERTH and CROSS: *Arch. Int. Med.*, 1917, 20, p. 913.
MORGULIS and MUIRHEAD: *Ibid.*, 1919, 23, p. 190.

ACETIC ACID (CH_3COOH)

In concentrated form, that is, as glacial acetic acid, acetic acid is a corrosive. In dilute solution it acts as an irritant. As pure glacial acid it occurs as crystals melting at 17°C . The liquid is colorless and dropped upon the skin or mucous membranes it forms blisters and erodes the tissues beneath.

In some European countries, particularly Russia, poisoning with acetic acid is quite common although quite infrequent in England and the United States.

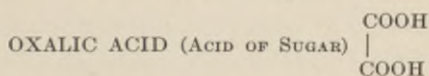
Symptoms.—The symptoms resemble those of the concentrated mineral acids so closely that a detailed description need not be repeated. The parts exposed to the action of the acid become softened and turn yellowish in color. Since the acid is very volatile the larynx may be involved.

Fatal Dose.—The fatal dose has not been accurately estimated although it is said that 2 tablespoonfuls have proved fatal.

Post Mortem Appearances.—Post mortem examination reveals typical evidences of corrosive action throughout the mouth and those portions of the alimentary canal with which the acid came into contact.

Treatment.—Treatment consists in neutralization of the acid by large volumes of weak alkali, as magnesia, emptying the stomach by vomiting and dilution of any remaining acid by more dilute alkali. Other symptoms should be treated as they arise, and may even include tracheotomy because of the swollen condition of the larynx.

OXALIC ACID GROUP



Oxalic acid, or its acid potassium salt (salt of lemons) $\begin{array}{c} \text{COOH} \\ | \\ \text{COOH} \end{array}$ occurs in many types of plants, as rhubarb, sorrel, dock, etc. It possesses marked bleaching properties and is used in commerce to remove rust and ink from linen, to bleach straw for hats, to polish metals, etc. Owing to its close resemblance to Epsom Salts (Magnesium Sulphate) accidental poisoning is not infrequent with oxalic acid. Its acid taste prevents its employment by criminals. On the other hand, owing to the ease with which it may be bought, it is frequently used by suicides. Salt of lemons so closely resembles in appearance cream of tartar that poisoning may easily result if a mistake in identity is made.

In large doses oxalic acid acts as a corrosive. With small doses it is an irritant or may produce serious results

by its remote inhibitory action on the respiratory or cardiac centres. With large doses death sometimes occurs so rapidly that treatment cannot be instituted.

Symptoms.—With large doses there is an acid taste with burning pain in the throat, esophagus and stomach. There is vomiting, the vomitus consisting of mucus, or mucus admixed with blood, presenting a coffee-ground appearance. The pulse may be imperceptible and weakness is pronounced at first, later, leading to complete collapse owing to the action of the poison on the heart. Should a dose of oxalic acid insufficient to produce death, be taken, the absorbed poison produces characteristic effects indicative of an action upon the nervous system. These consist of headache, cramps, tetany, convulsions, delirium and coma. It is probable that these effects are associated with a combination of the acid with calcium which temporarily at least eliminates the normal function of this element. Convalescence is very slow. During this period the patient complains of numbness and tingling, soreness of the mouth and throat, and painful swallowing. The urine may contain significant quantities of protein. Oxalic acid differs from the other corrosive acids in that it is still poisonous even after dilution which has eliminated its corrosive and irritant properties. Sometimes subsequent to the ingestion of a small dose immediate symptoms are lacking, later nervous phenomena being the first indication of poisoning.

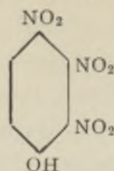
Fatal Dose.—The fatal dose varies between 1 and 3 drams. In general death follows $\frac{1}{2}$ to 1 ounce. With large doses vomiting usually occurs which offers a degree of relief and may lead to recovery. When more than 1 ounce has been retained death usually follows in spite of proper treatment.

Fatal Period.—The shortest fatal period on record is three minutes. There is an individual variation in this respect even when the same dose has been taken. Death generally occurs within 4 or 5 hours although it may not ensue for an equal number of days.

Post Mortem Appearances.—Post mortem appearances are not especially characteristic, the acid leaving no stain upon the lips, face or mouth. On the other hand, the tissues with which it has come into contact are white in color and mucous membranes are loose giving evidence of erosion in spots and there may be areas of contraction. The stomach may contain bloody or coffee ground matter. The walls may be white and smooth or present a highly inflamed appearance. Generally perforation does not take place. The kidneys show marked congestion and contain large amounts of oxalates.

Treatment.—Treatment calls for special attention inasmuch as alkalis and water cannot be employed. Alkalis transform the acid into its salts which are more soluble than the acid and which are about equally toxic and much more readily absorbed. Water increases the solubility and accordingly correspondingly increases the quantity immediately available for absorption. The best antidote is some preparation containing calcium or magnesium which uniting with the acid or its salt forms an insoluble salt. Finely divided chalk, calcined magnesium, or whitening from the wall suspended in large volumes of water may be given. The stomach tube should be used with caution since its contact against the corroded mucous membrane may cause perforation. Emetics, especially apomorphine, are indicated. When an antidote is to be given its administration should be prompt since oxalic acid acts with great rapidity.

PICRIC ACID



At present picric acid is one of the most common therapeutic agents for the local treatment of small superficial burns. It has been advised in a number of affections of the skin—acute eczema, intertrigo, and herpes labialis. For the unbroken skin alcoholic solutions may be used but in superficial burns only the aqueous solution should be employed, otherwise poisonous symptoms may arise.

Picric acid is a yellow, crystalline substance, without odor, and possessing an extremely bitter taste. It is somewhat soluble in water, readily soluble in alcohol, ether and chloroform. It explodes when subjected to percussion or heated rapidly.

Symptoms.—Evidences of the toxic action of picric acid applied locally consist of an acute inflammation of an erythematous nature, the later appearance of vesicles and considerable local edema. The usual constitutional symptoms are headache and an annoying insomnia. Itching of the affected part is almost unendurable. Later the acute lesions involute to an erythemato-aqueous type accompanied by considerable thickening and possibly infiltration of the skin. This stage is not unlike an eczema.

Taken internally picric acid is probably absorbed as the sodium salt. The picric acid is in part reduced to picramic acid by the liver and other tissues of the body as a method of detoxication. Elimination is chiefly through the urine to which an intense yellow color is imparted, or the urine may be colored a peculiar red or reddish-brown. After a

single dose of a gram, the excretion of picric acid may continue for a week.

The symptoms of intoxication are referred to either the gastro-intestinal, nervous, circulatory, or urinary systems or more commonly to several of these locations. Depending on the degree of the intoxication the gastro-intestinal symptoms vary from a mild anorexia, dyspepsia and flatulence to a severe diarrhœa accompanied by gastrodynia, abdominal cramps and emesis, the vomited matter being stained yellow. The irritant action of picric acid on the mucous membranes is responsible for the gastritis found. The nervous manifestations vary from a slight headache and vertigo to stupor with convulsions followed by collapse in the extremely severe cases. Picric acid is a respiratory and cardiac depressant, but symptoms referable to these systems are rare. At times a primary tachycardia with a subsequent slowing of the pulse rate may be noted. Occasional symptoms are strangury and anuria. Asthenia and fever may accompany the above constitutional manifestations of internal picric acid poisoning. Toxic doses may also destroy the red corpuscles, and induce hemorrhagic nephritis and acute hepatitis.

Yellow pigmentation of the mucous membranes is usually observed and superimposed upon this may be an erythema or even a generalized eruption of eczematous character and itching in nature. This dermatitis may partake of the nature of a measles rash.

Fatal Dose.—The fatal dose is unknown. Six grams have failed to cause death.

Fatal Period.—The fatal period is unknown.

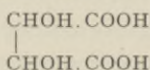
Post Mortem Appearances.—The only characteristic feature revealed by autopsy is the yellow color of the organs and skin.

Treatment.—(a) *Taken internally and with constitutional effects.* Lavage of the stomach with administration of large volumes of water to hasten elimination is indicated. (b) *Local evidences of poisoning.* The treatment to be followed is identical with that for acute eczema.

Reference

PACK: J. Ind. Hygiene, 1923, 4, p. 501.

TARTARIC ACID



Tartaric acid in concentrated solution acts as an irritant producing an intense inflammatory reaction on the stomach. Toxicologically it is of little importance, poisoning rarely occurring and then only when taken in mistake for some other substance. Some cases of poisoning are on record in which tartaric acid was taken in concentrated form as a fruit acidulant. Injected under the skin of animals or given by mouth in large doses tartaric acid and its salts cause acute nephritis leading to death. The quantities necessary to produce this effect are very greatly in excess of those ever employed in therapeutic application of this acid and its salts.

References

UNDERHILL, WELLS and GOLDSCHMIDT: J. Exp. Med., 1913, 18, p. 317.

POST: J.A.M.A., 1914, 62, p. 592.

CITRATES

From the toxicological point of view the citrates are of little importance since given by mouth they are harmless even in large quantities. Since 1915 when Weil suggested

the use of sodium citrate to prevent blood coagulation during transfusion there have been numerous cases showing untoward symptoms which although not dangerous or of much practical significance are nevertheless sufficiently outstanding to be worthy of note. The symptoms consist of fairly severe chill and fever of 2.5° F. in about one-half hour subsequent to transfusion of citrate blood but within 4 to 8 hours normal conditions are restored.

Varied views have been held relative to the cause of such symptoms and perhaps the most likely hypothesis is that the corpuscles and platelets are changed or injured by the citrate withdrawing calcium from the blood elements and combining with it to form a stable compound.

Reference

DRINKER and BRITTINGHAM: *Arch. Int. Med.*, 1918, 23, p. 133.

SALICYLATES

Because of their close relationship to phenol one might suspect that the salicylates would possess toxic properties. In general the early evidences of toxicity are nausea, vomiting and sometimes diarrhœa, or headache, ringing in the ears, and deafness or mental excitement.

Salicylism resembles cinchonism although the ear symptoms are not so common as with quinine. These may be due to either congestion or anemia or to changes in the nervous tissue of the cochlea. Disordered vision may also occur which is associated with degenerative changes in the retina or optic nerve. Other characteristic symptoms are a feeling of fulness of the head, angioneurotic swelling of the face and throat, general urticaria, mental dulness and apathy, muscular weakness, or mental excitement with loquacity, a talkative delirium, the so-called "Salicylic jag" the cerebral symptoms of which resemble those of

atropine. Alcoholics are especially susceptible to this type of reaction.

With very large doses, or because of idiosyncrasy, there may be weakening of the heart and depression of respiratory and vasomotor centres followed by collapse. Hanzlik asserts that even with full therapeutic doses albumin, leucocytes and casts appear in the urine of both normal individuals and rheumatic patients. The administration of bicarbonate with the salicylate has practically no demonstrable influence upon the albuminuria and renal functional changes produced by the salicylate. This evidence of inflammation of the kidney promptly ceases upon stopping administration of the drug. With full therapeutic doses there may be diminution of the urine with corresponding increase of body weight due to fluid retention in the tissues. Although edema is not visible this is probably an edemic condition.

All toxic effects of salicylates are usually without danger disappearing as soon as the drug is stopped. On the other hand, a few deaths have been reported from large doses or because of idiosyncrasy. It is, however, difficult to determine whether death in these cases was induced by the drug or whether the accompanying disease was responsible. Autopsy findings in these instances show hyperemia of the brain and its membranes, of the kidneys and lungs and ecchymoses of the pericardium.

In a clinical statistical study of the toxicity of different salicylates in adult males and females, respectively, Hanzlik found the toxic dose to be as follows: 180 and 140 grains of the synthetic salicylates; 200 and 135 grains of the natural sodium salicylate; 120 minims of the methyl salicylate; 165 and 120 grains of acetyl salicylate; 100 and 83 grains of salicylo-salicylic acid. For females the toxic dose was approximately 80 per cent of that for males.

The toxic dose of the different salicylates was uninfluenced by age between 16 and 75 years; by racial differences; various diseased conditions, and therapeutic response with the synthetic salicylate. Individuals showed idiosyncrasy toward toxic doses of the synthetic salicylate, but no relationship was found to exist between this and such factors as age, race and diseased condition. Idiosyncrasy varies in the same patient, and was not influenced by previous salicylate medication. The toxic dose for children is higher than would be calculated for the age.

Treatment.—The drug should be stopped. Usually the symptoms quickly disappear. Bromides control, in a measure at least, the cerebral excitement. Renal excretion should be stimulated, best by large volumes of water.

References

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HANZLIK, SCOTT and THOBURN: Arch. Int. Med., 1917, 19, p. 1029
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FOOD POISONING

Food poisoning may be due to a variety of causes. The idiosyncrasy of the individual toward some special type of food, as in the case of eggs, milk, oatmeal, strawberries, etc., must be regarded as a condition of food sensitization or alimentary anaphylaxis. The symptoms in such poisonings are usually some form of skin affection (such as urticaria or eczema) sneezing, nausea, vomiting and diarrhoea. Such symptoms usually do not lead to serious consequences, disappearing without sequelæ after a short interval. By food poisoning, however, is generally meant an intoxication due to some peculiarity of the food itself rather than to some idiosyncrasy of the individual.

According to this concept food poisoning may be due to substances inadvertently added to the food in their preparation or preservation as in the case of metals (lead, arsenic, tin, etc.); to the presence of poisons occurring naturally, as in mushrooms, or to toxic substances eaten by animals themselves subsequently eaten and their flesh giving rise to poisonous effects; and finally to products produced by bacterial activity or to infection induced by the ingestion of food contaminated with pathogenic organisms.

For many years the term "ptomaine poisoning" has been applied to that condition induced by the ingestion of spoiled or contaminated foods. By this term was meant originally the presence in the food of certain bases formed by putrefaction which are assumed to be responsible for the effects produced. A few such substances have been isolated from spoiled foods but their effects do not correspond with those originally produced by the foods themselves. The term "ptomaine poisoning," therefore, has come to have an indefinite meaning and is really applied in many instances when no more definite description seems adequate. Nevertheless the significance of its meaning has been lost and the term should be discarded as obsolete. Food decomposed by putrefactive organisms is not so toxic as hitherto has been supposed which explains the apparent paradox of the harmless custom of eating "ripened" cheeses or game well on the road to putrefaction. A misconception of the toxicity of such products has been engendered by the method of testing experimentally the toxicity of products contained in spoiled foods, that is these substances are usually injected either subcutaneously or intravenously into animals rather than given by mouth, the way in which the food would naturally be taken. When spoiled food is given by mouth to animals, even very

young cats, no untoward symptoms result, which leads Savage to state that "a study of the evidence along these accessory lines of inquiry singularly fails to bring forward any evidence associating the consumption of food in a state of incipient putrefaction with illness in those who consume it."

Food poisoning today means contamination with the paratyphoid group or other organisms, or the type of intoxication produced by *B. botulinus*. Two types of food poisoning are therefore recognized. Investigation reveals that food poisoning in the United States is steadily increasing. Generally poisoning occurs from food preserved either commercially or in the home. Of the commercially prepared foods, meat products, as beef, are responsible for most of the cases of poisoning; of fish, salmon is first and sardines second; of the vegetables and fruits the list is as follows, the incrimination of the product being in the order given—tomatoes, corn, beans, string beans, pork and beans, peas, peaches and olives. Of the home prepared products the order is for meat products, beef, sausage and pork; of fish, salmon; of vegetables, string beans, corn, and asparagus; of fruits, apricots and peaches.

The season of the year appears to play little role in the outbreaks of food poisoning and the physical appearance, taste and odor of the food do not necessarily bear any relation to the toxic symptoms produced.

Food Poisoning by the Paratyphoid Group.—"The diagnosis of food infection depends on: the history of exposure to the suspected food; symptoms suggestive of food poisoning, isolation of the infecting organisms from the suspected food and also from the blood, urine, feces or viscera of the patient; specific identification of the causative organism by agglutination tests; demonstration of agglutinins in the blood serum of patients."

All degrees of poisoning are encountered from rapid fulminating cases fatal within 24 hours to those of slight diarrhœa and general malaise insufficient to keep the patient from work. The incubation period varies considerably, in some instances symptoms arising in less than four hours, in others being delayed for two or three days.

Symptoms.—The symptoms are chiefly those of gastro-intestinal disturbances, nausea, vomiting, abdominal pain diarrhœa and fever. The diarrhœa may continue for several days and be associated with tetany or suppression of urine. In other instances there may be a more or less generalized erythema. Great mental depression is marked.

Treatment.—Treatment consists of gastric lavage, purgation and stimulants as indicated.

Food Poisoning from Botulinus.—Botulism has been recognized for a great many years but its significance has only recently received merited attention and study due undoubtedly in large measure to the many recent outbreaks identified as this condition. It differs fundamentally from most types of food poisoning in that acute gastro-intestinal disturbances are lacking. Although some cases exhibit pain in the abdomen, nausea, vomiting, and diarrhœa, these symptoms are not outstanding. On the contrary an obstinate constipation appears to be a prominent symptom.

Symptoms.—Early symptoms of botulism are an indefinite, indisposition associated with fatigue, sometimes headache or giddiness, muscular weakness and constipation. Eye symptoms, dimness of vision, mydriasis, loss of accomodation, etc., due to retrobulbar neuritis, occur early in the intoxication. Shortly after the eye symptoms are noted the patients complain of difficulty

in swallowing and talking and a sense of constriction in the throat. The tongue is generally heavily coated. Inability to speak is caused by paralysis of the laryngeal and pharyngeal muscles. The mouth is very dry which undoubtedly increases the difficulty in swallowing. Extreme muscular weakness is a striking feature of botulism and if it progresses sufficiently simulates paralysis. The patient is usually apathetic, semicomatose, or frequently restless with insomnia. At times there may be loss of memory, loss of sight or hearing, neuralgia in the neck, disturbance or loss of sensation in the arms or fingers. The secretions in general tend to diminish and the skin becomes hard and dry. The pulse is rapid, reaching in some cases to 150 per minute and the heart sounds may be distinct and weak. Usually the temperature is below normal ranging between 96° and 98°F. and unless complications set in the low temperature continues until death. Sometimes fever develops when pneumonia intervenes. Respiration at first normal, later becomes irregular with extreme dyspnoea which may merge into partial or complete asphyxia. Death may occur from cardiac or respiratory failure, usually the latter. The length of the period of illness shows great variation; some patients die within 48 hours but in the majority of cases death occurs in from 4 to 6 days, although it may be delayed for as long as 3 weeks. If recovery occurs convalescence is slow. Difficulty in swallowing disappears first, but the muscular weakness persists for several weeks. Eye disturbances are the last to regain the normal, and the patient may retain a tendency to constipation.

The diagnosis of botulism is sometimes difficult but "when one has decided that he is dealing with cases of food-poisoning the disturbances of vision, the difficulty in swallowing and talking, the absence of sensory dis-

turbances, the marked muscular weakness, and the subnormal temperature at once suggest botulism" (Dickson). Botulism may be confused with acute poliomyelitis, cerebrospinal syphilis, bulbar paralysis, various toxic ophthalmophgias, and poisoning from belladonna, gelesemium, hyocyamus, and methyl alcohol. The average mortality in the United States is 64 per cent.

Post Mortem Appearances.—Beyond congestion and hyperemia of various organs, autopsy reveals nothing characteristic in deaths from botulism.

Treatment.—Treatment has not been especially effective as the high mortality figures testify. That which has been most often employed is the institution of emesis and lavage with active purgation induced by magnesium sulphate or castor oil. The colon should be thoroughly irrigated. The patient should remain in bed and be kept quiet. Simple nourishing food with plenty of water should be given but care should be taken that none gets into the trachea because of the difficulty in swallowing. Water by rectum or salt solution under the skin are recommended. Strychnine is advocated for stimulation of the central nervous system and may be given freely. Pilocarpine is given to increase the secretion and in many cases affords temporary relief. Cardiac stimulants, as digitalis or strophanthin, should be administered as indicated and artificial respiration with oxygen administration should be continued so long as the heart beats.

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POISONING FROM FOOD PRESERVATIVES AND DYES

The preservation of food by addition of chemicals has long been practised and it is probable that upon no other topic has a greater controversy been waged than upon the question of the influence upon health of the addition of these chemicals to food. In spite of the great amount of work that has been done upon the subject an actual demonstration is lacking that the addition of preservatives to food, as practised, is harmful. On the other hand it is granted that in sufficient doses these substances must be regarded as distinct poisons and occasionally, in circumstances other than from their use as preservatives, poisoning occurs.

So far as dyes or coloring matters are concerned some, such as annatto, employed to color butter are believed to be entirely harmless, whereas others, for example the salts of copper and other metals, as well as various aniline derivatives, are either known to yield distinctly toxic effects or else are regarded with definite suspicion. Indeed in many states of this country, and in European countries in general, specific laws are in force against their employment to color foods since these substances are classed as poisons.

Below is given a brief resumé of the toxicology of the most commonly employed food preservatives that are of interest in this connection. Our knowledge concerning the specific toxic action of aniline dyes as employed in foods is not sufficiently definite to allow a detailed account of the toxicology of these substances.

Poisoning from addition of salts of toxic metals is, however, different, a short review of the toxicology of substances usually employed being given below.

BORIC ACID AND BORAX

Both boric acid and borax have been extensively employed as food preservatives. One must assume that they exert an identical influence upon the nutrition of the body and as ordinarily consumed in small quantities occasionally there is little or no evidence that any deleterious influence is exerted. On the other hand there is no question concerning the continued use of even relatively small quantities of the substances for they tend to accumulate in the body, the digestion becomes somewhat deranged, body weight is lost, and the feces become more fluid without actual diarrhoea being present. The effects may be even more detrimental for individuals with digestive or renal disturbances. Indeed it has been shown that if an albuminuria were present it is increased under administration of food containing borax or boric acid. In general borax and boric acid are excreted through the urine, little or none being eliminated by the bowel. When doses of 1 to 3 grams per day are ingested pronounced effects follow so that it may be stated that doses of more than 2 grams per day are distinctly harmful, the effects being seen mainly in gastro-intestinal and renal disturbances.

Symptoms.—With acute poisoning from larger doses the following symptoms are to be observed—gastro-enteritis, skin eruptions resembling those of scarlet fever, disturbances of vision, muscular weakness, lack of co-ordination, fall of temperature and collapse.

Post Mortem Appearances.—On post mortem examination evidences of fatty degeneration are present rather generally.

Treatment.—Treatment of the chronic type of poisoning consists of preventing ingestion of these substances and measures to hasten elimination. For acute poisoning

lavage of the stomach, catharsis, and stimulants are advocated.

References

- TUNNICLIFFE and ROSENHEIM: J. Hygiene, 1901, 1, p. 168.
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SALICYLIC ACID

Salicylic acid exists in combination in the volatile oils of birch and wintergreen and possesses about the same anti-septic powers as benzoic acid and phenol. It is irritant to mucous membranes and in strong solution effects destruction of the skin. It possesses a biting taste and distinctly retards gastric digestion. It is rapidly absorbed from the intestines and has analgesic properties resembling acetanilid in this respect. Rapidly excreted by all the secretions but principally through the urine it leaves the body mainly as the salicyluric acid, a compound of salicylic acid and glycocoll. In large doses the urine may give a green color.

The toxic effects of salicylic acid, aside from the local irritant action are characteristic of *salicylates*, which see.

BENZOIC ACID AND BENZOATES

Benzoic acid occurs in the balsams, in cranberries, and in various vegetables and fruits. The free acid even in concentrations as low as 0.1 is distinctly irritant whereas the salts are not. The toxicity of benzoic acid is low due probably to its being transformed in the organism to hippuric acid by union with glycocoll.

Investigations by various Governmental commissions have led to the conclusion that the presence of small quantities of benzoate in food is without evidence of harmfulness although in larger doses the conclusions do not

appear to be concordant. It is quite apparent that benzoate in food as ordinarily preserved may be taken by normal individuals without serious detriment. With patients with gastro-intestinal or kidney lesions the inherent irritant properties of the acid may prove deleterious.

Symptoms.—In sufficient doses benzoic acid and its salts exhibits symptoms of toxicity strikingly similar to those of phenol poisoning. There is gastric irritation, nausea and vomiting. The respiration is dyspnoëic in character, the reflexes are diminished, and either coma or convulsions may ensue.

Treatment.—Treatment consists of evacuation and lavage of the stomach and stimulants.

References

- CHITTENDEN, LONG and HERTER: Report 88, U. S. Department of Agriculture.
WILEY: Report 84, Ibid.

SACCHARIN

Saccharin, or benzosulphinid, has an intense sweet taste, even in greatly diluted solution. It passes through the body practically unchanged within a period of 24 hours almost all being eliminated by the kidneys. It has a sweetness about 500 times that of sugar and has been extensively employed to give a sweet taste to the food of diabetics and as an adulterant of sweet foods.

Although the older literature reveals reports of various digestive and other disorders following the use of saccharin later work has all tended to demonstrate its low toxicity although even here large doses tend to produce minor derangements. Distinctly poisonous effects in man are unknown.

Reference

- HERTER and FOLIN: Report 94, U. S. Department of Agriculture.

FORMALDEHYDE

Formaldehyde at times has been employed as a food preservative especially of milk, but its characteristic irritant properties renders its employment in this connection extremely dangerous. When large doses have been swallowed there is immediate agonizing abdominal pain, loss of consciousness and general collapse. Death usually occurs within 48 hours. Post mortem examination reveals acute and extensive gastritis. When death does not occur the urine may be suppressed for 24 hours and usually when secretion is resumed the urine contains blood, albumin and casts. Sometimes there is diarrhœa. (See also p. 207.)

Formaldehyde is probably oxidized to formic acid, a part of which may appear in the urine.

References

- MACLACHLAN: Cleveland Med. J., 1909, 8, p. 606.
WILEY: U. S. Bureau of Chemistry Circular, 42, 1908.
TUNNICLIFFE and ROSENHEIM: J. of Hygiene, 1901, 1, p. 321.

SULPHITES

By the term sulphites is meant sulphurous acid, sodium sulphite and sodium thiosulphite. The substances are strongly reactive and readily combine with oxygen to form sulphates which tends to render harmless their native toxicity. Even in large quantities this transformation into sulphates prevents a general systemic intoxication, their employment in food being associated with deleterious action because of local irritant properties through the liberation of sulphuric acid.

Symptoms.—Systemic effects are in evidence only when quantities sufficient to overwhelm the oxidative capacity of the body have been ingested. Under these circumstances

blood pressure is lowered, there is central nervous depression and depression of the musculature of the heart and arteries. At times violent colic and diarrhœa may be observed. Death results from paralysis of the respiratory centre.

Treatment.—Treatment consists in evacuation of the gastro-intestinal tract by lavage and catharsis and general stimulation.

NITRATES

Potassium nitrate, or Saltpeter, has been and still is extensively employed in the preservation of meats. In general it acts like other neutral salts although it probably is distinctly more irritant to the stomach and intestine. Readily absorbed it is chiefly eliminated by the urine and has diuretic properties.

Symptoms.—With large doses the characteristic symptoms include severe abdominal pain, vomiting and at times bloody stools. The pulse becomes irregular, convulsions occur and collapse ensues. The urine may be entirely suppressed or if passed may contain albumin and blood. Death may result from the gastro-intestinal disturbances provoked by the salt action.

Treatment.—Potassium nitrate poisoning should be treated by administration of large volumes of water and by gastric lavage. To allay the irritation of the gastro-intestinal tract milk, eggs, etc., should be given.

COPPER

Copper in food is employed mainly for the purpose of giving a green color to peas and beans. It combines with the chlorophyll of young vegetables to form a stable compound but with older vegetables the combination is not so firm. Consequently in the ingestion of these colored foods more copper gains entrance into the tissues when the older

vegetables are eaten than when the young peas and beans colored with copper are taken. Even though the maximum quantities of the latter are eaten distinct toxic symptoms are not in evidence. With large quantities of old vegetables colored with copper gastro-intestinal disturbances may occur.

Symptoms.—The symptoms of poisoning are associated with the gastro-intestinal tract since copper is irritant and causes vomiting, diarrhoea, and pain. Lesions in the kidney and spleen are characteristic.

Treatment.—Treatment of copper poisoning consists in the prompt administration of precipitants as white of egg, milk or acacia, with thorough lavage of the stomach, and stimulants if indicated.

Reference

LONG: Preservatives, Trans. Internat. Congress of Hygiene, 1912.

MUSHROOM POISONING

Mushroom poisoning has been well recognized from ancient times. Certain varieties of mushrooms are edible, others are toxic at certain seasons of the year and still others always possess poisonous properties. The toxic properties of these fungi may perhaps be modified by climate since reports concerning the toxicity of various species vary in some degree, at least, according to the locality in which they have grown. In Italy and Hungary certain mushrooms are eaten which are regarded as poisonous in England, and the same holds true for others eaten in Russia and France. Some mushrooms are more toxic to certain individuals than to others, so that it is quite likely that idiosyncrasy may play a part in the severity of the effects produced.

Although the number of mushrooms considered capable of causing toxic symptoms is large most attention has

been directed to two species, namely, *Amanita phalloides* and *Amanita muscaria* or "fly mushroom." The fungus most often responsible is *Amanita phalloides* perhaps because of its widespread and abundant distribution and its pleasant taste. Moreover, it is perhaps possessed of greater toxicity than any other mushroom. In the United States it is popularly termed "toadstool." Because of the deadly character of the two species cited above considerable attention has been devoted to their toxicology and the knowledge gained constitutes our definite knowledge of the nature of the toxic substances present in mushrooms. On the other hand, more than 70 species are capable of producing toxic symptoms in man.

Amanita Phalloides. *Symptoms.*—Several hours usually elapse before any symptoms appear. The first effects are great abdominal pain, vomiting, and diarrhœa. The vomitus and stools may contain blood. There may be periods when vomiting and pain may cease. These intervals are usually brief. The suffering is intense and rapidly leads to loss of strength. The period of intoxication may last in adults for six or eight days, in children for a shorter period, and during this time a variety of symptoms may develop. Especially important is the partial or complete suppression of urine due to acute nephritis. There may be jaundice, cyanosis and lowered temperature. Death is usually preceded by deep coma.

An influence upon the nervous system may also be observed as indicated by convulsions and delirium in some cases. In some instances death occurs rapidly—within 24 hours.

If recovery occurs health is regained very slowly. In rare cases a chronic poisoning may result, death being delayed for several weeks.

Post Mortem Appearances.—Autopsy shows that *amanita phalloides* contains a poison which causes an extensive disintegration of cells, especially the endothelial cells of the blood vessels, renal cells, cells of the liver and central nervous system. The liver and kidney show extensive fatty degeneration. In general when large quantities of the poison have been ingested the cellular destruction is so widespread as to render impossible continued functional activity of the organism as a whole and death results. This destruction of cells once established is so great as to render treatment of little use.

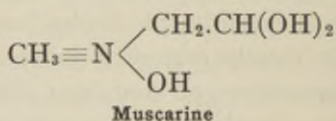
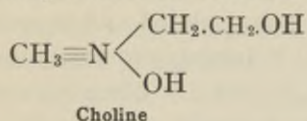
The Poison of Amanita Phalloides.—The active principle of *Amanita phalloides* has been isolated and is probably closely related to indole. It partakes of the nature of an amine and contains C, H, N, and S. When injected into animals the lesions produced closely resemble those induced in man by ingestion of the fungus.

Amanita Muscaria. *Symptoms.*—Poisoning by *amanita muscaria* may be readily diagnosed because of the characteristic symptoms. Soon after eating the mushrooms there is salivation, perspiration and weeping together with violent gastro-intestinal disturbances as indicated by vomiting, watery stools, and great thirst. There is a slow, irregular pulse, rapid respiration with dyspnoea. An influence upon the nervous system becomes apparent. In some cases there are present the symptoms characteristic of alcoholic intoxication, or there may be merely mental confusion and dizziness. In other cases the nervous effects may be so great as to lead to delirium, convulsions, profound coma, and eventually death from respiratory paralysis. In still other cases after the preliminary exhibition of gastro-intestinal upset sleep overtakes the patient from which he awakes after several hours, greatly weakened but out of danger. The pupils of the eye are

usually contracted and do not respond to light. This fact is of importance in diagnosis.

Post Mortem Appearances.—Beyond the fact that the alimentary tract shows great congestion with hemorrhages, little is known concerning changes in man induced by the active principle of *amanita muscaria*. Certain it is that this poison does not lead to widespread degeneration so typical of *Amanita phalloides*.

The Poison of Amanita Muscaria.—It has been assumed for many years that the active principle of *Amanita muscaria* is muscarine, a base stronger than ammonia and closely related to choline.



Its chief action is the production of typical peripheral stimulation of the parasympathetic system. It provokes the characteristic pilocarpine reactions and in addition possesses a nicotine and curare effect. Muscarine and atropine are antagonistic, atropine depressing the nerves stimulated by muscarine, in particular the inhibitory nerve endings of the vagus. Muscarine paralyzes the heart and respiration by stimulating the inhibitory fibres of the vagus—atropine depresses these fibers and is therefore a physiological antidote for muscarine.

Classification of Mushroom Poisoning.—Although the symptoms of poisoning characteristic of *Amanita phalloides* and *Amanita muscaria* have been presented in some detail other symptoms are at times observed by ingestion of different mushrooms which may be quite dissimilar to those described. The classification most widely adopted is that of Huseman who recognized three types. Mushroom poisoning was designated by him by the term myce-

tismus. According to Huseman the three forms were mycetismus intestinalis, mycetismus cholericiformis and mycetismus cerebrialis—the terms being sufficiently descriptive. More recently Ford has modified and extended this classification so that five types are recognized.

FORD'S CLASSIFICATION OF SYMPTOMS

1. **Mycetismus Gastro-intestinalis.**—The symptoms are mainly gastro-intestinal and are short lived. Death is only infrequent. The symptoms are characteristic of the *Boleti*, certain of the *Entolomas*, *Lactarii* and *Lepiotas*.

2. **Mycetismus Cholericiformis.**—Gastro-intestinal disturbances are prominent at first. Later the characteristic features are weakness, pain, nephritis, anuria, delirium and coma. Death occurs in nearly 50 per cent of cases. This type of poisoning is produced by *Amanita phalloides* and closely related species.

3. **Mycetismus Nervosus.**—Initial gastro-intestinal disturbances accompanied by excessive perspiration, salivation and by lachrymation. Later there may be delirium, mental confusion, convulsions and coma. Death is unusual but may occur. The muscarine-containing fungi are responsible for this group of symptoms—especially *Amanita muscaria*, the *Inocybes* and the *Clitocybes*.

4. **Mycetismus Sanguinareus.**—Gastro-intestinal symptoms are prominent at first. Jaundice and anemia develop later. The urine may contain hemoglobin from hemolysis of the red cells. The symptoms are characteristic of the fungus *Helvella esculenta*.

5. **Mycetismus Cerebrialis.**—Only temporary excitement and hallucinations are characteristic. There is

dilatation of the pupils and collapse may result. The patient generally recovers. Only two fungi are known definitely to produce the effects, namely, *Panæolus campanulatus* and *Panæolus papilionaceus*.

Treatment of Mushroom Poisoning.—In order that the best type of treatment be instituted it is very desirable to learn the nature of the mushroom taken. This may, perhaps, be learned from descriptions of the fungus by the patient or better by examination of the vomited material. Such identification, however, may be impossible and no time should be lost in applying treatment irrespective of the type of mushroom eaten. Even though vomiting and diarrhœa may be present the gastro-intestinal canal should be cleaned out by gastric lavage and if possible by saline purgatives. If these are not retained high enemas may be given. The possibility exists that *amanita muscaria* may be the cause of the symptoms and atropine should be administered even though this hypothesis fails to be substantiated. Atropine will do no harm and if *muscaria* has been eaten it will act as a physiological antidote. Other general measures to employ, especially with symptoms of collapse, are stimulants as strychnine, digitalis, application of heat, and large volumes of fluid. If it is known that *Amanita phalloides* is responsible for the symptoms there is nothing specific that can be done. The measures outlined above for general treatment are applicable here and in line with the best type of treatment.

If *amanita muscaria* is the cause of the symptoms atropine is the specific antidote. It should be given repeatedly hypodermically or even intravenously. The collapse should be combatted by strychnine and digitalis. Large volumes of fluid are especially recommended.

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