

men have attained with them. It seems to Dr. Cook that there are only two questions for consideration: First, is it right that diseases which are causing more suffering and more deaths than any other diseases shall be allowed free course, with no efforts made to control them? Second, whether we are in the wilds of Africa, under the shadows of Harvard, on Commonwealth Avenue, on Fifth Avenue or anywhere else, there are certain subjects concerning which there is a common knowledge. Those subjects are matter of food for the preservation of the body, of clothing suitable for climate and temperature and of the propagation of the species. Every rational human being, sooner or later, is going to know about the relation of the sexes. He asked if the majority of boys and girls in the future, as they have in the past, shall come to this knowledge in a filthy, mysterious way, or if it shall be lifted to a clean, high, self-respected standard. He quoted Garrison to the effect that: "Talking creates zeal; zeal creates inquiry; inquiry creates opposition; opposition creates action; action creates union and union creates victory."

DR. A. D. LAKE, Gowanda, N. Y., said that the only question before us is how to improve the situation. He said that we should invite the clergy, the press, and the teachers to co-operate in the consideration and discussion of this important subject. If much good is to be accomplished in this direction, we must go outside of our profession and endeavor to create a public sentiment in favor of the restriction of this evil by law. When the people generally more thoroughly understand and appreciate the importance of this reformation, some means will be found to bring it about. Legislation is needed. The power which reaches the law-making source is an emphatic public demand, which will come only as the public are educated and understand its necessity. If the papers on this subject, which have been read here, could be published in the newspapers, or if they could become a part of the system of hygiene taught in our public schools, then we would have begun a crusade from which good results might be expected to follow.

DR. H. S. POMEROY, Boston, declared that in the last thousand years civilized society has been cursed by four great physical evils: Smallpox, the so-called Great White Plague, alcoholism, and the social evil. The discovery of that grand master, Dr. Jenner, has put smallpox back into the dark ages. Within the last ten years the light has been let into the public mind in regard to the Great White Plague. When our forefathers were living, it was considered a special dispensation of Divine Providence. Now, after years of fear, tuberculosis has been attacked in its stronghold; and, to-day, we are practically masters of it. In regard to alcoholism, also, the public is being slowly aroused; much is being done; a great deal more is going to be done in the next few years; and in regard to that, he said, we may report progress, thank God, and take courage. In regard to the fourth of these four evils we want more light. Legislation is all very well and it does help; but there is no legislation in a country like this which is of the slightest use beyond the extent to which that legislation is incited in the first instance, and carried out and backed up afterward, by public opinion. There is a little, he declared, which we, as physicians, can do toward prophylaxis directly, and toward curing these diseases; but what we can do individually in that way is a mere bagatelle compared with what can be done by the sentiment of the great American public. He believes that, as physicians, we might better discard for the next five years all our direct efforts toward prophylaxis and toward curing the disease and spend our time, our enthusiasm, our money, our efforts toward arousing a public opinion. He said that he has been criticized and condemned by one of the best men who ever occupied a chair in the Harvard Medical School, because he has committed himself in one of his books to the theory that children should be taught about these things. It is not a question of whether the child shall be taught or shall not be taught; it is not a question of teaching or no teaching; it is not a question of safety through innocence or through ignorance. It is a difficult thing to get safety through ignorance; The ignorance does not exist. There will be knowledge; and if that knowledge is not scientific and pure and sensible and reverent so that the child grows up with a reverential respect for the most important organs that the Master has given him,

after the central nervous system, then the child will grow up with prurient ideas, with false ideas, with ideas which will incite to physical, mental and moral decay. The child has got to know. He is instructed every day. He is instructed by the dogs, by the cats, by the birds, in all sorts of ways; he is instructed by his comrades of the gutter. He will get information. He is curious; he has a right to be curious. There is an insatiable demand in his mind to know about these organs, their origin, uses and destiny. Something about them he will learn. It will be right and it will be safe; or it will be prurient, it will be wrong. It devolves largely on physicians to say what this shall be. Let us lift up our voices, he said, let us use our pens, let us use our influence when we are together, when we are apart, in medical circles and in the public, in our churches, on our school committees, among our friends, in society, everywhere that we can, for a scientific, safe knowledge of these matters, to be put into the child, at least, as early as the dawn of puberty; and then, even, some of us will live to see the time when the diseases of the social evil, instead of being perhaps from 60 to 75 per cent. of those wherein woman needs care, will be a very small percentage. Dr. Pomeroy believes that this time will come.

THE CHEMISTRY OF THE ORGANIC SILVER COMPOUNDS.*

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Believing that a knowledge of the chemistry of medicines will tend to their more intelligent use in the treatment of disease, a brief account of the chemical behavior of some of the organic silver compounds proposed for use in medicine is here presented. While in recent years the country has been deluged with new organic remedies the information offered regarding them has been meager and, being almost exclusively furnished by the promoter of each new article, is not always clear and to the point. More particularly is there a dearth, especially in the English language, of systematic discussion of the many new remedies, the available literature consisting either of the incomplete statements found in books on chemistry or pharmacy, or else the rather more comprehensive treatises hastily compiled from the manufacturers' literature. It is, therefore, hoped that the following, while presenting nothing new, may contribute to some extent to a better interpretation of the therapeutic effect of the many silver compounds placed before the medical profession.

THE CONSTITUTION OF SILVER COMPOUNDS: SIMPLE SILVER COMPOUNDS.

When to a solution of silver nitrate there is added solution of sodium chlorid, or potassium chlorid, or almost any other chlorid, a white, curdy precipitate of silver chlorid is produced; a solution of any soluble iodid produces a precipitate of yellow silver iodid; addition of an albumin solution produces insoluble silver albuminate. Precipitates having the same composition will be obtained if, instead of a solution of silver nitrate, one of silver sulphate or of silver acetate is used. In many other ways silver salts show similar behavior regardless of the acid with which the silver is combined, and they are said to be peculiar to silver and are used to identify silver compounds. This similar behavior of different silver compounds is now generally believed to be due to the

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

separation (ionization) of the silver compounds, when in solution, into their constituent parts (ions) thus:

Silver nitrate into silver ions and nitrate ions, or
 $\text{AgNO}_3 = \text{Ag}^+ + (\text{NO}_3)^-.$

Silver sulphate into silver ions and sulphate ions, or
 $\text{Ag}_2\text{SO}_4 = 2\text{Ag}^+ + (\text{SO}_4)^{--}.$

Silver acetate into silver ions and acetate ions, or
 $\text{AgC}_2\text{H}_3\text{O}_2 = \text{Ag}^+ + (\text{C}_2\text{H}_3\text{O}_2)^-.$

The dots and accents are used to indicate that these parts do not exist as such but are still combined with, or attracted toward, each other.

Since such solutions all contain identical silver particles or ions, it is but natural that they should show similar properties.

COMPLEX SILVER COMPOUNDS.

If, on the other hand, to a solution of silver nitrate considerable potassium cyanid is added, and if now to this solution a chlorid, bromid, iodid or albumin solution is added, no precipitation will occur. In general, such a solution will not show the behavior characteristic of silver solutions. The generally accepted explanation for this behavior is that the addition of the alkali cyanid caused the formation of another silver compound, thus: $\text{AgCN} + \text{KCN} = \text{KAg}(\text{CN})_2$, which, when dissolved in water separates (ionizes) into potassium ions and silver cyanid ions, thus: $\text{KAg}(\text{CN})_2 = \text{K} + (\text{Ag}(\text{CN})_2)^-.$ Since such a solution contains no silver ions it is not surprising that it fails to show the properties of ordinary silver solutions.

But by appropriate tests it can be shown that such a solution containing the complex silver-cyanid ions does contain very small amounts of silver ions: that the complex ion itself undergoes to a slight extent dissociation into Ag^+ and $2(\text{CN})^-$.

Many other silver compounds have been prepared which, when dissolved in water, contain the silver in complex radicles or ions, which themselves, to a slight extent, dissociated to form silver ions. On this behavior of the complex silver compounds just indicated their proposed use in medicine is based. Solutions of simple silver compounds, such as silver nitrate, reacting to form insoluble compounds when mixed with solutions containing chlorids or albumin bodies, both abundantly found in the body fluids, the reaction between silver and chlorid, albumin, etc., occurs at once and hence the effect of silver will only be obtained superficially and there it will act as a cauterant. On the other hand, solution of complex silver compounds containing but few silver ions will be but slowly affected by the body fluids; hence they may penetrate deeper and exerting the specific action of silver compounds very gradually do not act as cauterants. This slow action of such complex silver compounds can, of course, occur only if the compound is undecomposed by the body fluids; in the same way that a chlorid may be added to an ammoniacal solution of silver nitrate without causing precipitation only as long as alkalinity obtains.

COLLOIDAL SILVER.

When an aqueous solution of silver nitrate or other silver salts is treated with a reducing agent, metallic silver is formed and being insoluble in water it separates out of the solution. But, under certain conditions, silver solutions may be treated with reducing agents, when no precipitate of metallic silver is formed, although the reduction plainly occurs. This reduction product when collected and purified is almost pure silver. It differs on the one hand from metallic silver, especially in being soluble in water; on the other hand, its

solutions fail to show many characteristics of silver solutions. While a solution of this substance is readily changed so as to show the behavior of solutions of ordinary silver salts, it differs in that no precipitate is produced by albumin solutions and that in the presence of such albuminous bodies no precipitation is produced on the addition of chlorids.

It is on this property that its use in medicine has been based. This form of silver is commonly known as colloidal silver because it is held back by certain membranes non-permeable to non-crystalline substances, such as proteins, gums, mucilages, and generally known as colloids.

As regards the chemical nature of this "colloidal silver" there is still much doubt. It was pointed out that analysis shows it to be nearly pure silver, yet all attempts to obtain a preparation containing 100 per cent. of silver have been unsuccessful. And some investigators believe that the so-called colloidal metallic silver really is a compound containing the silver in a complex molecule and that on this account the properties of silver compounds are not shown. This is especially true of a preparation known as collargolum; thus Hanriot¹ found it to contain only 87.3 per cent. metallic silver and concludes that its properties were due to the presence of an organic acid (see silver lysalbinat below) which he calls collargolic acid. More generally, it is accepted that in the process of manufacture the silver has been reduced to the metallic state, but that its separation as solid, insoluble silver has been prevented (postponed?) in some way. The silver being in the metallic state and not in the ionic condition is, of course, not affected by chlorids, albumin, etc., just as little as a silver coin would be.

Besides the colloidal metallic silver, a number of compounds of silver, such as the oxid, chlorid, carbonate, have been proposed for use in medicine in colloidal water soluble form. Here, too, the true chemical condition is still in doubt. It is generally held that in such substances the insoluble silver compound has been produced, but that its separation has been prevented or retarded by such bodies as albumin, gelatin, gums, etc. Other investigators hold to the belief that the silver is a part of a complex molecule and hence masked. Still others believe that the silver compound exists in an insoluble form, but that its precipitation is postponed indefinitely because of its fine state of subdivision and also because of the presence of the colloidal gelatin, etc.

CLASSIFICATION OF ORGANIC SILVER SALTS.

In the following a brief account of the many organic silver salts proposed for use in medicine is offered. The discussion of each article is usually confined to two particulars, namely, the chemical composition and the chemical properties, i. e., the behavior in the test tube. Often the method of manufacture and the patents governing the same must be taken up in order to make clear the probable composition of the article. To facilitate reference, an alphabetic classification has been adopted; and although these substances are almost exclusively known by coined names, yet it has seemed more rational to discuss them under their chemical titles, references to these being made whenever possible.

Actol: A trade name for silver lactate, which see.

Aktol: A trade name for silver lactate, which see.

Albargin: See silver gelatose.

Albargol: See silver gelatose.

1. *Cr. d. l'Acad. des Sciences*, vol. cxxxvi, pp. 680, 1448, and vol. cxxxvii, p. 122; also, *Chem. Centbl.*, 1903, vol. 1, pp. 1916 and 1903, vol. ii, p. 280 and 543.

Argentamine: A trade name for a solution of silver nitrate in diaminoethane (ethyldiamine); see diaminoethane silver nitrate.

Argentol: A trade name for silver oxyquinoline-sulphonate, which see.

Argonin: See silver caseinate.

Argonin L.: See silver caseinate.

Argyrol: See silver vitellin.

Diaminoethane Silver Nitrate: Diaminoethane or ethyldiamine may be considered as an ammonia derivative of ethane in

which two hydrogen atoms of ethane $\begin{array}{c} \text{H} & \text{H} \\ | & | \\ \text{H}-\text{C}- & -\text{C}-\text{H} \\ | & | \\ \text{H} & \text{H} \end{array}$, CH_3CH_3

or C_2H_6 have been replaced by two ammonia residues, NH_2

thus: $\begin{array}{c} \text{H} & \text{H} \\ | & | \\ \text{H}_2\text{N}-\text{C}- & -\text{C}-\text{NH}_2 \\ | & | \\ \text{H} & \text{H} \end{array}$, $\text{CH}_2(\text{NH}_2)\cdot\text{CH}_2(\text{NH}_2)$ or $\text{C}_2\text{H}_4(\text{NH}_2)_2$.

Just as ammonia reacts with water to form ammonium hydroxid, $\text{NH}_3 + \text{H}_2\text{O} = \text{NH}_4\text{OH}$, so diaminoethane reacts to form a hydroxid, $\text{C}_2\text{H}_4(\text{NH}_2)_2 + 2\text{H}_2\text{O} = \text{C}_2\text{H}_4(\text{NH}_3\text{OH})_2$, and, as might be expected, aqueous solutions of the two products, namely, ammonium hydroxid and diaminoethane hydroxid have very similar properties; thus, with silver salt both form solutions (compounds) which are not precipitated with chlorids. Based on this latter property of diaminoethane, and on the property that it does not precipitate, but rather dissolves, albumin, attempts have been made to use compounds of silver and diaminoethane in medicine. Argentamine (German patent No. 74,634) formerly was stated to be made by dissolving silver phosphate and diaminoethane in water. The silver phosphate solution having been found to be unstable the same name is now applied to a solution obtained by dissolving 10 parts silver nitrate and 10 parts diaminoethane in 100 parts of water. Chemically this may be considered as a complex silver compound, permanent only in alkaline solutions and then showing the characteristic properties of silver salts to a very limited extent and at the same time the alkaline properties of the solvent.

Credé's Antiseptic: See silver citrate.

Ethyldiamine Silver Nitrate: See diaminoethane silver nitrate.

Ichthargan: See silver ichthyolate.

Ichthargol: See silver ichthyolate.

Itrol: A trade name for silver citrate, which see.

Largin: See silver protalbinat.

Novargan: See silver proteid.

Picratol: See silver picrate.

Protargol: See silver proteid.

Silberol: See silver phenolsulphonate.

Silver Acetate: This is the silver salt of acetic acid, $\text{HC}_2\text{H}_3\text{O}_2$ or CH_3COOH , and its composition is $\text{AgC}_2\text{H}_3\text{O}_2$ or $(\text{CH}_3\text{COO})\text{Ag}$. Its solubility in water is much less than that of silver nitrate; in all other ways it shows the properties of simple silver salts.

Silver Albuminate: See silver protein.

Silver Caseinate: Sodium caseinate, the sodium salt of casein, is obtained by reacting on casein with sodium hydroxid solution. If to such a solution silver nitrate is added and then alcohol, precipitates are obtained which have been taken to be sodium silver-casein, that is, a salt in which sodium is the basic ion, while the silver is a part of the acid radicle. A solution of such a compound will, of course, fail to show the reactions of silver compounds, and hence will not react with chlorids, albumins, etc., whence its use in medicine. Argonin (U. S. patent 575,277) is a trade name applied to such a sodium silver caseinate. It is claimed to contain about 4.3 per cent. of silver, to be slowly soluble in cold water, quickly in hot water, so that a 10 per cent. solution may readily be prepared which is neutral to litmus and not affected by chlorids, albumin, hydrogen sulphid or alkaline sulphids. Argonin L. or argonin, soluble, said to be a compound of similar composition, but containing 10 per cent. of silver, and to be readily soluble in cold water, has recently been offered for sale as an improvement on argonin. Recent investigations

(see silver lysingenate) seem to indicate that this and other similar compounds, which form solutions that are neutral or alkaline, contain silver compounds in colloidal condition.

Silver Citrate: This is known also by the coined names *Itrol* and *Credé's Antiseptic*, is the normal silver salt of citric acid, $\text{H}_3\text{C}_6\text{H}_5\text{O}_7$, and has the composition $\text{Ag}_3(\text{C}_6\text{H}_5\text{O}_7)$. It occurs as a heavy white powder, contains about 63 per cent. of silver, and is almost insoluble in water, one part requiring about 3,800 parts for solution. While all silver salts are rather easily reduced, usually liberating silver in the metallic state, this tendency is somewhat more pronounced because citric acid itself tends towards oxidation, and hence acts as a reducing agent, thus the salt is decomposed with separation of metallic silver when boiled with water.

This ease of decomposition is also illustrated by the manner of marketing *Itrol Credé prooculis*, a very finely powdered silver citrate. It is put up in opaque vials, sealed and containing only 0.5 or 1 gm. of substance, and it is recommended that if the vials are opened frequently the contents remaining after two weeks should be rejected. On the readiness with which silver citrate decomposes, its introduction in medicine was based. It was one of the precursors of colloidal metallic silver and has largely been abandoned in favor of the latter because of its insolubility.

Silver Eosolate: This is said to be silver acetguaiacol-trisulphonate. The chemical makeup of such a salt may best be illustrated by its synthesis. From guaiacol, $\text{C}_6\text{H}_4(\text{OH})(\text{OCH}_3)$, the acetguaiacol, $\text{C}_6\text{H}_4(\text{CH}_3\text{COO})(\text{OCH}_3)$, is obtained. This is then converted by treatment with strong sulphuric acid to the acetguaiacol-trisulphonic acid $\text{C}_6\text{H}_3(\text{CH}_3\text{COO})(\text{OCH}_3)(\text{SO}_3\text{OH})_3$, and from this the silver salt, $\text{C}_6\text{H}_3(\text{CH}_3\text{COO})(\text{OCH}_3)(\text{SO}_3\text{OAg})_3$ or $\text{Ag}_3(\text{C}_6\text{H}_3\text{O}_{12}\text{S}_3)$, is prepared. The properties of such a compound are indicated by its composition: it is a simple silver salt and should on the one hand show the characteristic silver properties, modified to a slight degree, if at all, by the acid radicle, while the acid radicle should possess the properties of a phenolsulphonate or sulphocarbolate. It should here be noted that at the same time that objectionable properties, disagreeable taste, insolubility, etc., of guaiacol are removed by sulphonation, that also its medicinal effect is decreased or destroyed.* As with sulphonates generally, we here have a water soluble, permanent salt.

Silver Ethylenediamine Salts: See diaminoethane silver nitrate.

Silver Gelatose: Under the title albargin a silver preparation was placed on the market which was prepared (German patent No. 141,967) by adding to a solution of "gelatose" a solution of silver nitrate, neutralizing and evaporating to dryness. The term gelatose is used to indicate the products produced by the hydrolysis of gelatin, also known as gelatin-peptone or gelatone. While the claims made by the manufacturer or his agents have been vague and confusing, it appears to be a simple mixture of silver nitrate and the decomposition products of gelatin. Its chemical properties are those of silver nitrate modified by the presence of the protein bodies, which, as was noted when discussing the colloidal silver compounds, have a tendency to retard or prevent the typical silver reactions.

Silver Ichthyolate: Compounds of ichthyol and silver have, from time to time, been proposed for use in medicine. Just as ichthyol is a complex mixture, so the composition of the ichthyol-silver compounds is indefinite; also, just as ichthyol largely is the ammonium salt of a mixture of acids, known as ichthyol-sulphonic acid, obtained by treating the crude ichthyol oil with sulphuric acid, so the ichthyol-silver compounds are, at least largely, salts in which silver is the basic or positive part and the ichthyol-sulphonic acid the negative part or acid radicle. Several methods resulting in widely differing preparations have been proposed (German patent Nos. 99,124, 112,630, 114,394). The article now on the market, ichthargan, also known as silver ichthyolate, silver ichthyol-sulphonate, is a brown powder, odorless and claimed to contain 30 per cent. silver and 15 per cent. sulphur in permanent combination. It is readily soluble and possesses on the one hand the properties of

2. Ther. Mon., 1899, p. 96; also Arch. f. Exp. Path. and Pharm., vol. 1, p. 340.

a simple silver salt, on the other hand the properties of the ichthyol derivative. It has been claimed that the process (German patent No. 114,394) which rendered the salt soluble, odorless and permanent also rendered the ichthyol less active or even inert.³ Under the name *Ichthargol* a silver ichthyolate at one time was offered which was insoluble in water and contained 12 per cent. of metallic silver.

Silver Lactate: This is known also by the coined name *Actol*, or *Aktol*. It is the silver salt of lactic acid, $\text{CH}_3\text{CHOH.COOH}$. Its composition is $\text{AgC}_2\text{H}_3\text{O}_3 + \text{H}_2\text{O}$, and therefore it contains about 50 per cent. of silver. It is soluble in 15 parts of water. Lactic acid, or 1,2-hydroxy propanoic acid, in common with other 1, 2-hydroxy acids, being readily oxidized, and the silver in silver compounds being readily reduced to the metallic state, silver lactate is a decidedly unstable salt of silver. The ease with which the salt is reduced is shown by the discoloration which its solutions undergo. Its use in medicine has also been based on the tendency to set free metallic silver, as when gauze, ligatures and drains are impregnated with the solution and then exposed to light, so as to cause the reduction. It is one of the precursors of the colloidal metallic silver.

Silver Lysalbinat: C. Paal⁴ has prepared two new organic silver salts which promise to throw much light on the chemistry of silver compounds. He has shown the formation of two bodies of weak acid character by treatment of egg albumin with dilute warm sodium hydroxid. These bodies, which he terms protalbinic acid (*Protalbinsäure*) and lysalbinic acid (*Lysalbinsiure*), are weak acids and form definite compounds with silver and other metals. Silver lysalbinat he concludes to be a simple salt of silver, which has the peculiar property that when treated with alkalis, silveroxid or hydroxid is formed, but which, because of the protecting action of the protein body, remains in colloidal solution. These experiments suggest the thought that many silver compounds of protein bodies which are said to contain the silver in a complex or masked combination really contain colloidal water-soluble compounds of silver.

Silver Nucleinate: Nargol is the trade name of a compound of silver and nucleic acid. According to the patent this article is prepared from a purified nucleic acid made from yeast fermentation residues (German patent Nos. 113,164, 118,050). It is claimed to contain 10 per cent. of silver, is readily soluble in water, yielding a faintly alkaline solution, which is not precipitated by chlorids or albumin. What was said regarding the chemical nature of silver caseinate and silver lysalbinat applies to silver nucleinate. While generally considered to be a complex silver compound containing the silver combined with the nucleic acid in such a way as not to show ordinary silver reaction, it is possible that instead it is a colloidal compound of silver.

Silveroxyquinoline Sulphonate: Under the trade name *Argentol*, silver oxyquinoline sulphonate, also called silver hydroxyquinoline sulphonate and silver quinasseptolate, the silver salt of the sulphonic acid derivative of oxyquinoline is sold. Its formula is given as $\text{C}_8\text{H}_7\text{N}(\text{OH})(\text{SO}_3\text{Ag})$, and indicates that it contains about 32 per cent. of silver. It shows the properties of a simple salt of silver, modified by the slight solubility in water and by the character of the acid radicle. This acid radicle, still retaining its phenolic hydroxyl, possesses the properties of acting as a reducing agent when in alkaline solutions; thus when the salt is boiled with water it decomposes, with liberation of silver. On this reduction of the silver to the metallic state in alkaline solution the use of the argentol as a dusting powder for wounds and also as an intestinal antiseptic has been based.

Silver Phenolsulphonate: Under the trade name *Silberol* the silver salt of paraphenolsulphonic acid has been introduced; it is variously called silver phenolsulphonate, silver phenylsulphonate, silver sulphocarbonate. Its composition being $\text{C}_6\text{H}_4(\text{OH})(\text{SO}_3\text{Ag})$ or $\text{C}_6\text{H}_4\text{O}_2\text{SAg}$, it contains nearly 38.5 per cent. silver. It is very soluble in water, and in solution shows the properties of a simple silver salt on the one hand, on the other hand those of a phenolsulphonate or sulphocarbonate.

Silver Picrate: Silver picrate, or silver trinitrophenolate, is marketed under the name *Picratol*. Trinitrophenol or picric acid, $\text{C}_6\text{H}_2(\text{NO}_2)_3\text{OH}$, being a body of very decided acid properties, forms a well-defined silver salt. Its composition is $\text{C}_6\text{H}_2(\text{NO}_2)_3(\text{OAg}) + \text{H}_2\text{O}$, and it therefore contains about 30 per cent. of silver. It is claimed to be soluble in 50 parts of water, and, being a simple salt of silver, the solution shows all the characteristic properties of silver salts and also those of picrates.

Silver Protalbinat: Under the names *Largin* and *Silver Protalbin*, Lilienfeld, a silver compound has been introduced which is of the general nature of silver lysalbinat (see) and silver nucleinic (see). It is said to be obtained⁵ by hydrolysis of nucleoproteids with alkalis, whereby a body soluble in alcohol and free from phosphorus (protalbin or protalbinic acid) is produced. An alcoholic solution of this product on treatment with ammonium-silver nitrate solution yields the silver compound *largin*. It is said to contain 11 per cent. of silver, to be soluble in 10 parts of water, yielding a slightly alkaline solution, which is not affected by chlorids or albumin. The statements regarding the chemical nature of silver caseinate, silver lysingenat and silver protein (see) apply here.

Silver Proteid: Protargol, or protein-silver salt, also known as silver protein and silver methylenealbumose, is a silver compound, obtained, according to the patents (German patent Nos. 102,455, 105,866, 118,353, 118,496), by treatment of insoluble silver protein compounds with a soluble albumose. The silver protein compound is said to be obtained by treating protein bodies, such as egg albumin, serum albumin, albumoses or peptones, with silver salts. The method of obtaining albumoses given depends on the treatment of egg albumin with formaldehyd, whereby a product is obtained which, dissolved in water, is not coagulated by heat. Protargol is yellow powder, contains about 8.3 per cent. metallic silver and is very soluble in water. No precipitation occurs on addition to the solution of albumin, chlorids or free hydrochloric acid. Addition of alkali sulphids gradually causes darkening and finally formation of a precipitate.

The chemical nature of this article is still in doubt. It is generally stated to be a complex silver compound in which silver forms a part of the protein molecule, forming solutions which contain no silver ions and hence do not show the ordinary silver reactions. On the other hand it is very possible that we are dealing with silver compounds, retained in the colloidal soluble form by the presence of the proteins.

Novargan, described by the manufacturers as a proteinate of silver, appears to resemble protargol closely in composition and properties.

Silver Vitellin: Argyrol and silver vitellin are names applied to a silver compound of a protein resembling vitellin, obtained from serum albumin by hydrolysis. It contains from 20 to 25 per cent. silver and is freely soluble in water. The solution is not sensibly affected by albumin, chlorids or free hydrochloric acid. The statements regarding the composition of compounds containing masked silver (see silver caseinate, silver lysingenat, etc.) are probably equally applicable to this compound.

DISCUSSION.

DR. S. SOLIS-COHEN, Philadelphia, said that he would discuss the therapeutic aspect. Physicians, he said, should consider, in both the external and internal applications of the metals and metallic compounds, the probability of developing the ionic state of the element. An atom set free from combination is by that very action rendered ionic, or is in a nascent state. It is thus prone to enter into a new combination and by reaction with the elements of the tissues produces certain definite chemical results. On the other hand, when preparations are administered in which the ionic state of the metallic atom is prevented or obscured, or is slow of development, certain other effects than those due to combinations of the metal with the tissue may be brought about; and it has seemed to Dr. Solis-Cohen that this is the explanation of the therapeutic action of colloidal silver as distinguished from the salts of silver. In the case of the latter, decomposi-

3. Frankel, S.: *Argneimittelsynthese*, second edit., p. 321.

4. Ber. d. chem. Ges., vol. xxxv. pp. 2195, 2206.

5. Wien. klin. Wochft., vol. xi, p. 260.

tion of the salt and combination of the silver with the proteid molecule or with some atom acting as a negative ion takes place. In consequence, partial destruction of the tissues ensues as when mercury or any other metal combines with the cell. If enough silver enters into combination, the cell is completely destroyed; if but little combines there is a stimulation of the vital chemistry of the cell by which the damaged portion may be thrown off and regeneration occur. This, he said, seems to be the way in which mercury and iodine compounds bring about the substitution of healthy for diseased tissue in syphilitic degenerations of cells and perhaps in some inflammatory sequelæ. The chemistry of the masked silver compounds to which Professor Puckner referred, Dr. Solis-Cohen said, is to him *terra incognita*. He does not know of any literature on the subject which will enlighten anyone except the expert chemist, although he has seen more or less intelligible statements of the empirical composition of most of these compounds. He has seen therapeutic results, however, which show that some of these preparations at least have value altogether apart from what might be attributed to them from our knowledge of the action of the ordinary inorganic salts of silver. Dr. Solis-Cohen said that he could not explain this, and has seen no explanation which satisfies him; for the present he is content to accept and to utilize the fact. Some of these substances have bactericidal power especially as regards the gonococcus, but one of the most useful of them has little, if any, value as a germicide, yet it reduces inflammatory action and promotes absorption of chronic exudates. As to the colloidal salts in general, it is quite probable that in the organism they may play the part of catalytic agents, similar in many respects to the organic enzymes. The therapeutic value of colloidal silver may thus be largely due to catalytic action in taking up and again yielding oxygen, thus destroying toxins, bacteria or diseased cells—a chemical ambceptor action, to take an illustration made familiar by Ehrlich—and through such an action it may prevent or retard sepsis. It certainly, he said, has a definite therapeutic action and should be employed more extensively in larger and more frequent doses than we have been using. In regard to the external application of nitrate of silver Dr. Solis-Cohen agrees with Fraenkel that the cauterizing action is due to free nitric acid and that hence organic compounds which do not possess an acid element give us equal disintegrating, resolvent and absorbent effect, and in some instance antiseptic action also, without cauterization. In many cases this is to be preferred. The rules laid down by Fraenkel for the ideal silver compound are simple. They are four—two positive and two negative. Positively the compound should contain the largest amount of silver possible and should be soluble. Negatively it should be non-irritating and should not be decomposed by the tissues. There are some cases, however, in which we do wish decomposition of the agent in order to utilize the ionic effect of the metallic atom. Hence there are special uses for each type of compounds described, and Puckner's classification ought to aid us in deciding which class, and which agent of the class, to use in any given case.

Dr. W. J. ROBINSON, New York City, said that while we call collargol soluble silver, the adjective soluble is hardly correct. It does not make a true solution, only an exceedingly fine suspension. True, it is the finest suspension obtainable, but still it is a suspension and not a solution. That this is not merely theory, but fact, can be positively demonstrated by the aid of the ultra-microscope. A "solution" of colloidal silver in water, examined under the ultra-microscope, shows the beautiful, shining particles of silver, as clear and distinct as grains of sand. These can not be seen under the ordinary microscope. Dr. Robinson's opinion is that in acute gonorrhea the organic silver compounds are much superior to silver nitrate. In fact, in the acute stage of gonorrhea, silver nitrate, he thinks, should never be used. In chronic urethritis, however, silver nitrate seems to act best, and is still the remedy *par excellence* in spite of the multitude of organic compounds. Dr. Robinson believes that the nitric acid radical plays an important and hitherto unrecognized rôle. It can not be the silver alone that acts, for there are many compounds with a large

silver percentage that are much less active than other compounds with a lesser silver content. Dr. Porosz of Budapest had been making experiments in treating gonorrhea with very dilute solutions of nitric acid, and he claims very good results. This goes to show the importance of the NO₃ radical.

Dr. C. S. N. HALLBERG, Chicago, said that the relative percentage—amount of silver—ranges from about 10 to about 25 per cent., and he wished to know whether or not the preparations are correspondingly more potent on account of the silver percentage.

Prof. W. A. PUCKNER, Chicago, said that he did not attempt in any way to take up the therapeutic effect. The paper is intended as a conservative statement of the present state of knowledge for physicians who may wish to consult it. In reply to Professor Hallberg's query he said that the organic silver compounds vary from 5 to possibly 30 per cent. of silver. He has no doubt at all that their action is largely dependent on the amount of silver present. The silver ion is colorless; the ions of the complex silver compounds, so far as established, are colorless. Professor Puckner believes that the color of colloidal silver solutions is due to reduction processes. On close inspection it gradually shows various colors as the particles aggregate, so the color is due to that. In reply to Dr. Robinson's comment, he said that he tried to make a conservative statement of the present theories; it is generally believed that the silver is there in solution, possibly in the metallic form.

THE INFLUENCE OF X-RAYS IN THE TREATMENT OF LEUKEMIA AND HODGKIN'S DISEASE, WITH A REPORT OF TWO CASES.*

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Since the therapeutic value of x-rays in Hodgkin's disease and leukemia is still in the experimental stage, and requires the report of more cases which have been under careful observation and treatment for longer periods of time, in order to arrive at definite conclusions, the two following cases are submitted with their detailed histories, and results of treatment; together with an account of some experimental observations concerning the action of x-rays on the blood and urine in leukemia.

HODGKIN'S DISEASE: REPORT OF A CASE WITH A SYMPTOMATIC CURE.

Patient.—Mrs. R. came to the medical clinic of Dr. Dock, May 13, 1904, because of nodules in the sides of the neck and pain in the neck and thorax.

History.—The patient's family history is negative. She has had measles, scarlet fever and three attacks of "la grippe." Five years ago she noticed a mass on the left side of the neck above the clavicle. The mass was soft and puffy and movable beneath the skin. It became harder in about six weeks. At first there was no pain, but later she had intermittent attacks of pain of a sharp-shooting character. The skin over the mass became sore to the touch. In the winter of 1903 she had noticed a shortness of breath at times and a sort of a catch on inspiration; so that she breathed with considerable discomfort. During the three weeks before coming to the clinic she had been somewhat hoarse, and had increased difficulty in breathing at night. The patient said that other lumps or masses have appeared since the first one described. The order of appearance was as follows: (1) On the neck above the clavicle, (2) under left arm in axilla, (3) behind angle of the left jaw, (4) on the chest, (5) behind angle of right jaw. The last four occurred within four or five weeks. The patient used to weigh 160 pounds, she now weighs 139. She has a poor appetite, is habitually constipated, has no cough.

* From the Medical Clinic of Dr. Dock, University Hospital.