

macist to prepare sterile solutions in ampoules with the use of simple apparatus only. He suggests that suitable solutions in non-soluble glass ampoules, may be sterilized after the ampoules are sealed, by placing them in oil or saturated salt solution, and heating for fifteen minutes at a temperature of 115° C. This operation requires only the use of a covered vessel and a thermometer, while the results obtained would approximate those secured through the use of an expensive autoclave; that is, the temperature would be the same as that of the autoclave and the pressure, consequently, inside of each ampoule would be equivalent to the pressure in the autoclave under those conditions.

Such a process is not applicable to all substances, since the temperature required is prohibitive at times, and yet this plan is so simple and where it can be applied so easily and promises such satisfactory results, that it should not be passed over without the emphasis here given.

F. W. Nitardy, of Denver, said his practice was to use steam at 30 pounds pressure in the process of sterilization, keeping it at that point for fifteen minutes. He considered this sufficient sterilization.

Doctor Hitchens, responding to the last speaker, said he thought there was no doubt about the efficiency of this method, provided precautions were taken to have the steam completely replace the air in the chamber. And yet, without control, it would fail. In the ten years he had been doing this work, he had failed many times; but the failure was because somebody had not taken the precaution to remove the air, with the result that the sterilization would not be complete, unless the temperature was raised very high. As he had tried to bring out, and as Mr. Wilbert had kindly emphasized, sterilization must always be controlled by proper cultures. Such cultures are usually made in fermentation-tubes, containing freshly sterilized 2 percent dextrose *bouillon*. With all the precautions ordinarily taken, failure sometimes occurred.

Otto Raubenheimer, of Brooklyn, said he desired to emphasize one point—a thing that should be well known to pharmacists at this time; that distilled water was not necessarily sterile water. Some gentlemen seemed to be of the opinion that sterilization can be attained very easily. But Dr. Hitchens and Mr. Wilbert had properly emphasized the necessity of bacteriological control. He related his observance of a city milk-inspector taking samples of milk for analysis from several milk-wagons, and of the indifference to the exposure of these samples to contamination by bacteria. By the methods pursued by this inspector it must follow that the milk would show excess of bacteria, and he presumed that the milkmen from whom the samples were taken would be disciplined. This incident, he said, would show how carelessly such work is done,—work that should be done with great care and precaution; and all work of sterilization should be guarded with the utmost precaution.

METAL COLLOIDS—THEIR INCREASING IMPORTANCE AS REMEDIAL AGENTS.

CHAS. E. VANDERKLEED AND FRITZ HEIDELBERG.

Perhaps no field of chemical and physical research so well shows how rapidly progress is being made, as a glance at some recent developments in the study of colloids, and particularly at the changes that are being made in our conception of colloids. Just as we no longer believe that atoms are actually indivisible—though for all or nearly all of the purposes of the art of chemistry we may still so consider them; just as we no longer are convinced of the absolute indestructibility of matter—though for all practical purposes in chemistry and mechanics we may so calculate; so do we no longer adhere to Graham's original classification of matter into crystalloids and colloids. We may no longer look upon colloids as a distinct class of substances, separate and apart from other classes

of substances, any more than we can consider gases or liquids or solids as distinct subdivisions of matter. Just as many substances may appear in solid, liquid or gaseous form, so may almost, if not indeed all substances, whether or not they possess the power to crystallize, appear under certain conditions as colloids. In the words of Wolfgang Ostwald in his "Grundriss der Kolloidchemie,"—"Unter geeigneten Bedingungen grundsätzlich alle Stoffe in kolloiden Zustand erscheinen können." (Under certain conditions, fundamentally all substances may appear in colloidal form.) Colloidal chemistry may not therefore be defined as the study of colloidal substances, but rather as the study of the colloidal condition of matter.

The authors of this paper will not presume to enter into a discussion or even a review of the recent theoretical developments of colloidal chemistry and physics. Suffice it to say that to the physicist and student of theoretical chemistry, the subject is of utmost importance and interest. Like radio-activity, the study of the colloidal form of matter may prove to be one of the means of bridging over the gap between matter and energy, while biologic and physiologic chemists may ultimately find in the study of colloids the chemical and physical solution of life itself. Many volumes of researches, discourses, and text-books on the subject have appeared, notable among which may be mentioned, Ostwald's "Grundriss der Kolloidchemie"; "Die Kolloide in Biologie und Medizin," by Bechhold; "Kolloidchemie des Lebens," by Liesegang; and a very interesting little book in English entitled, "An Introduction to the Physics and Chemistry of Colloids," by Hatschek. A monthly journal, the "Zeitschrift für Chemie und Industrie der Kolloide," now in its twelfth volume, has recently been supplemented by an "Ergänzung" called "Kolloidchemische Beihefte,"—all devoted to the development of the theory and practical application of colloids. Ostwald expresses the opinion that such problems as the relationship between color, constitution, molecular form, solvents, etc., may ultimately be solved by the study of colloidal forms of matter.

Neither shall we re-state the well-known, and for practical purposes valuable, classifications of colloids by Graham (1861-1864) into "sols" and "gels"—hydro-sols, organosols, and hydrogels,—reversible and irreversible, etc. For the purpose of this paper it is sufficient that we picture the colloidal form merely as a state of exceedingly fine subdivision,—so fine indeed that the individual particles closely approach in size, the minuteness of molecules themselves. Colloidal solutions become then merely a fine suspension of one material in another,—and theoretically we should be able to produce any known substance in the form of a colloidal solution. Such so-called solutions differ, however, from true solutions in that the latter are, so far as physical means permit us to determine, absolutely homogeneous, whereas colloidal solutions are, ultimately, only suspensions, even though the highest power of the microscope may not enable us to see the individual particles. In other words, in the case of a true solution we are dealing with a single phase system as we say in physical chemistry, whereas in the case of a colloidal solution, we are dealing with a two-phase system. If the colloidal particles are solids, they are called "suspensoids"; if liquids, they are termed "emulsoids," owing to their occupying intermediate places, respectively between suspensions of solids and emulsions of liquids,—and true solutions.

Permit us to emphasize the fact, however, that there is no chemical difference between matter in or out of the colloidal form. There is no chemical difference between ordinary mercury and colloidal mercury, any more than there is any chemical difference between ice, water, and steam. Each is in a physically different form, yet all three are water from a chemical point of view. Even the distinction that may be drawn between colloidal and non-colloidal forms of matter by the process of dialysis, does not betoken any chemical difference. Sodium chloride in solution dialyzes because there are no particles present larger than the pores of the parchment, but a solution of glue will not dialyze because the particles of glue in pseudo-solution are too large to pass through. If, however, a dialyzer with larger pores be used,—such for example as a thin collodion bag,—or if a colloid with more finely divided particles than those in the glue be used, this colloid will pass through the dialyzer, though not so rapidly as the crystalloid.

We will understand clearly the nature of a colloidal solution if we consider the changes which occur in an ordinary suspension. If we put sand in water, the sand will settle very quickly to the bottom of the container; if we grind the particles of sand finer, they will still settle completely after being suspended for some time in the water; the finer we grind the sand, the longer it will take for the particles to settle. This is due to the fact that the force of gravity which acts on the particles of sand is counteracted in part by several factors like friction in the liquid, molecular attraction, etc.

Let us imagine now that we are able to grind the particles so fine that this counteraction,—viscosity of the water, molecular attraction, the motion akin to the Brownian movement of very small suspended particles, and the electrical charges with which small particles become endowed,—is equal to the force of gravity tending to bring each particle of sand to the bottom of the container. What is the result? The particles no longer, or at least no longer quickly, fall to the bottom, but remain in suspension in the liquid,—and we thus obtain a colloidal solution,—colloidal sand dissolved in water. In the same way, we can imagine the production of a suspension of sand in oil, where by grinding the sand particles finer and finer, we could finally obtain a colloidal solution of sand in oil. A colloid therefore may be not only water-soluble; it may be oil-soluble, or soluble in any other solvent; and it will depend only on how we choose the medium in which we produce the fine particles, whether the finished product will be water-, alcohol-, or oil-soluble, etc.

Actually, we are not able, by mechanical means, to grind the particles of a substance to such a degree of fineness that we can obtain a colloidal solution, and we therefore have to make use of chemical or of physical (as distinguished from merely mechanical) reactions to get these particles fine enough, although should we have a grinder at our disposal to enable us to grind them sufficiently fine, the resulting colloid would probably be just as good as one obtained by chemical means.¹ Thus, while we are not able to grind sand to a state of colloidal fineness by mechanical means, we can readily prepare a colloidal solution of silicic acid

¹ Colloidal filaments of tantalum, tungsten, etc., are made by grinding the metals to an impalpable powder, mechanically, and then treating them alternately with acid and alkali, when they finally assume colloidal form. But the mechanical grinding alone just falls short of producing the desired result.

by chemical and physical means. It is only necessary to decompose a water-solution of sodium silicate with a slight excess of hydrochloric acid and dialyze the mixture until free from excess of acid and sodium chloride, when there will remain in the dialyzer a perfectly clear, colorless solution of silicic acid.

Such a colloidal solution, in common with other inorganic colloids, is very readily thrown out of the solution or "sol" form, however, on addition of electrolytes, the theory being that these serve to disperse the electric charge with which the colloidal particles are endowed, and which, by its power to enable them to repel each other, helps to maintain the "sol" form. When this charge is dispersed, the particles, no longer antagonistic to each other, aggregate, and soon the whole mass of colloid particles either settles out, or as in case of silicic acid, solidifies to a "gel," enclosing by adsorption the water in which it was suspended.

Colloidal solution of ferric hydroxide, or dialyzed iron, is made by a process analogous to that described for silicic acid,—while colloidal solutions of the metals, such as gold, silver, platinum, copper, and lead, are usually prepared by an electrolytic disintegration method first described by Bredig in 1898. This method consists in passing an electric current, in the form of an arc, between poles of the metal which is desired in colloidal solution, the poles being suspended in the desired liquid, usually water. Under this treatment, particles of the electrodes are broken off in such a fine state of subdivision that they remain suspended in the liquid in colloidal form. Here too, however, the addition of electrolytes soon causes the colloidal metal solutions to precipitate as "gels" which cannot be reconverted into solution-form.

A third method of obtaining inorganic colloids is by reduction. If, for example, we take a solution of a metallic salt like gold chloride, and add a diluted solution of formaldehyde, or any other suitable reducing agent, the gold will be reduced and suspended in colloidal solution if the solution be sufficiently diluted. Again, certain colloids may be prepared by oxidation. If we oxidize hydrogen sulphide gas to sulphur by means of sulphurous acid, the sulphur will assume the colloidal form and remain suspended in colloidal solution.

Just a word as to the probable size of these colloidal particles. First of all, they are so small that they cannot be seen in the ordinary microscope, and as Abbe has shown that the lower limit of visibility is from 800 to 400 millionths of a millimeter, while the wave lengths of light lie between 450 and 760 millionths of a millimeter, it follows that these colloidal particles must be much smaller than these wave lengths themselves. Hence they would forever have remained invisible to the naked eye, had not Zsigmondy and Siedentopf invented the ultra-microscope, which by means of the so-called dark-field illumination, only light reflected or dispersed by the particles, and no direct rays from the source of illumination, enter the microscope. In this way particles calculated to be as small as five millionths of a millimeter can be seen. By a study of so-called "ultra-filtration" methods, Bechhold has passed colloidal particles in solution through filters calculated to have pores not greater than 21 millionths of a millimeter in diameter, whence it follows that the particles must have been smaller than these pores and hence have at least approached in smallness the limits which have been assigned from other investigations for the diameter of molecules.

According to Dr. Conrad Amberger,¹ the effect of gravity on colloidal particles in suspension is neutralized by the action of the electrical charges when the particles are not greater than 60 millionths of a millimeter in diameter. Since, however, the addition of an electrolyte serves to disperse this electric charge, no inorganic colloid solution would appear to be sufficiently stable for use, for example, in medicine. Fortunately, however, it was long since discovered that by adding a portion of an organic colloid to an inorganic colloidal solution, preferably prior to the formation of the latter, the inorganic colloid is rendered quite immune to the precipitating action of electrolytes. This is probably best explained by Bechhold's theory that the organic colloid, such as glue, gelatin, casein, albumin, etc., forms a layer around the inorganic colloid particle, and as the organic colloids are but little affected by the addition of electrolytes, precipitation is thus prevented. For this reason organic colloids used in connection with inorganic colloidal solutions to prevent precipitation have received the name "protective colloids."

Thus, there is rendered available for use as therapeutic agents, in relatively stable colloidal solution form, many substances otherwise insoluble. If, however, the colloidal state does not necessarily imply a change in chemical composition, of what possible interest can colloids be in medicine? A consideration of this question brings to light first of all the fact that oftentimes very slight changes in a substance may be the means of materially changing its physiologic effect. Substances of like chemical composition, but differing slightly in the atomic arrangement of their molecules, may differ materially in toxicity and in the effects which they produce. Who shall say therefore that a metal for example, or a metallic oxide or hydroxide or salt in colloidal form, may not differ materially in its potency or in its effect from that of its ordinary form? The question of absorbability, the rapidity with which it may be assimilated, plays an enormous part in treatment with medicinal substances. It is not only conceivable, but highly probable, that this rate of assimilation will be entirely different for mercury, for example, in ordinary globular form, though very finely subdivided mechanically, and mercury many thousands of times more finely subdivided in colloidal form. Hatschek in the closing chapter of his little book says, "The study of colloids shows us that the mere subdivision of matter, or, in other words, *the production of large surfaces*, brings into play energies, the effects of which may be of the most varied character, and of the most profound importance."

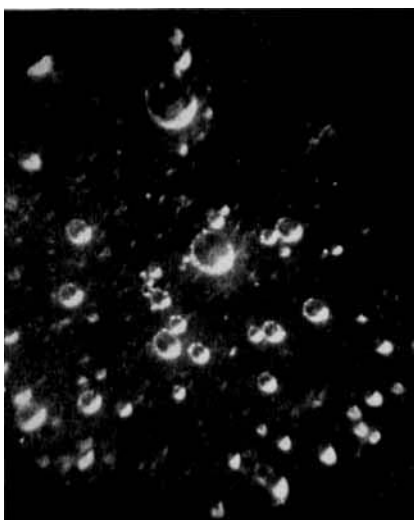
Moreover, the growth of the art of putting into colloidal form and hence making possible the administration of certain substances in solution or liquid form which otherwise could only be administered if at all in solid form,—and then not hypodermically or intravenously but only by mouth or by external application,—shows at once that there is really a promising field for investigation by the therapist of a new line of materia medica products made possible by new discoveries in the production of colloidal solutions.

Another evidence of the possible therapeutic activity of colloid metals, is their possession of the power of catalytic action so resembling in many ways the action of enzymes that Bredig has called them "inorganic ferments." Exceedingly

¹ Pharmazeutische Zeitung, 58, 1913, p. 188.

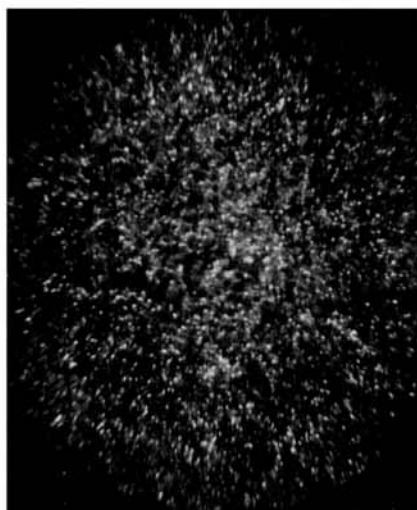
dilute solutions of colloidal platinum and osmium will instantaneously decompose very large quantities of hydrogen peroxide into oxygen and water,—while other colloid metals have been used to polymerize fatty oils into hard masses,—powers not possessed by these metals even when subdivided to the highest possible degree by mechanical means.

Nor have physicians been slow to take up this line of investigation. We refer of course to a study of the therapeutic effects of colloidal solutions of metals, oxides, hydroxides, and salts, which in ordinary form are insoluble in water or in other suitable vehicles for their administration. It is hardly to be conceived that any advantage would ensue from the administration in colloidal form of a substance naturally soluble in a suitable solvent. But there remains a large number of substances, of which the metals and some of the non-metallic elements are



A

Ultra-micro-photograph (x1000) of Blue Ointment U. S. P. dil. to 10%.



B

Ultra-micro-photograph (x1000) of Colloidal Mercury Ointment, 10%.

examples, which, unless made “soluble” by rendering them colloidal, must remain unsuitable for use in the *materia medica*.

Perhaps the first of metal colloids to be introduced into medicine, colloidal ferric hydroxide, or dialyzed iron, is now acknowledged to be a therapeutic failure,—or at least to possess no advantages that are not to be gained from the administration of iron in other forms. This, however, need not deter us from investigating other colloids, for it must be remembered that dialyzed iron was only administered by mouth, and it is probable that slighter differences will be noted between colloidal and non-colloidal forms when thus administered, than when used hypodermically, intramuscularly, or intravenously.

Among the earliest of the metallic colloids to be employed in medicine was silver,—in the form of pseudo-salts with protein and other organic acids,—colloidal in nature, though tried out and used before many of the investigations of colloids had disclosed their real nature. Of undoubted value in the treatment

of certain bacterial diseases from the clinicians' point of view, these colloidal silver preparations possessed little or no direct bactericidal power,—particularly in comparison with solutions of crystalline silver salts. True, they possessed the advantage, much appreciated by the patients, of being non-irritating,—but of what use is a negative advantage unless accompanied by decided positive advantages? Satisfactory, or at least helpful results, however, were consistently claimed by, not a few, but by very many able practitioners. Some explanation other than the possession of antiseptic power must therefore be sought.

Recent investigations of certain French authors (Pastia,¹ Bossani and Marcelet²) have shown that colloid metals influence the opsonic strength of a serum against various bacteria. Bossani and Marcelet think that this influence is not due merely to the colloid nature of the substances, in which case one colloidal metal might act as well as another, but varies with the kind of colloid used.

The experiments of these authors along this line were carried on with the purpose of determining how the action of the leucocytes upon streptococci is influenced by colloidal silver. Experiments were made with animals, men and *in vitro*. The serum used in all the experiments was taken directly before the injection of colloidal silver, one hour after the injection, and 24 hours after the injection.

In the work with rabbits, mixtures were made of serum, a 1:3 suspension of a 24-hour *bouillon* culture of streptococcus, washed white corpuscles, and physiological salt solution. These were incubated for 15 minutes at 30°, slides were made, and from the cocci contained in 100 polymorphonuclear leucocytes mixed with serum there was subtracted the number contained in the leucocytes of the control tubes, namely those in salt solution only.

The results showed that in every case the injection of colloidal silver, while causing no increase after one hour, caused a decided increase of phagocytosis after 24 hours.

Experiments upon people were carried out in the same way and showed practically the same results.

To determine whether the colloidal silver influenced the phagocytic power of the leucocytes directly, or increased the opsonic strength of the serum, a number of experiments were made *in vitro*. Increasing dilutions of colloidal silver were mixed with serum in one series, with physiological salt solution in another, and white blood corpuscles were added to both. Slides made from each series were examined.

The results showed that colloidal silver does influence the leucocytes directly, but the colloid can increase the opsonic strength of the leucocytes only in the presence of serum.

Colloidal mercury and colloidal mercurous chloride have also been introduced into medicine, but have not apparently been used very extensively, the former possibly because of the unstable character of the marketed product. Dimond in

¹ Pastia: *La presse medicale* 1910.

² Bossani and Marcelet: *Gazette des Hopitalz* 1908.

a recent article¹ speaks of highly satisfactory results from the injection of colloidal mercury and silver solutions in various infectious diseases, particularly in connection with specific vaccine and serum treatments, and attributes the favorable results to increased phagocytosis. Dimond has used metal colloid solutions both "protected" and "unprotected" by the presence of "Schultz-kolloid," and declares that the use of the latter has not been followed in his experience by any loss of therapeutic activity.

Recently renewed interest in colloidal medication has been aroused, first in France by the use of a form of colloidal copper for the treatment of cancer and tumors, and later by Dr. Leo Loeb in St. Louis, who has reported² on the experimental use both of colloidal copper solutions prepared electrolytically and used intravenously, and of colloidal copper protected with protein substances. His results have been partially successful, and he closes his article in the May, 1913, number of the *Interstate Medical Journal* with these words, "It seems to us necessary, in the interest of science and of practical medicine, to follow to the utmost these lines of investigation."

Following the preparation some time ago of a colloidal silver oxide, our research laboratory has been engaged in a study of the production of other colloids. Renewed interest in the use of mercury by intramuscular injection, usually in the form of "Grey Oil" of the British Pharmaceutical Codex, a mechanically subdivided suspension of mercury in liquid petrolatum and lanoline, suggested to us the advisability of preparing a colloidal mercury soluble in oil, thereby possessing the advantage of stability, if not indeed possessing greater therapeutic activity because of the many thousands of times more highly subdivided nature of the mercury particles.

Such a colloidal solution, containing five percent of colloidal mercury, is here shown, together with a specimen of the ordinary "Grey Oil" diluted also to a five percent strength for the purpose of comparison.

An interesting fact was brought out in our experimental work in preparing these colloids, namely, that the solubility of the resulting product, if protected by a so-called "Schutz-kolloid," depends upon the nature of the "Schutz-kolloid" or protective colloid employed. If, for example, metal colloid be protected by means of a caseinate which is water-soluble, the product will dissolve to a clear solution in water, which may be shaken with petroleum or with chloroform without the latter taking up anything from the water solution. On the other hand, if an oil or chloroform-soluble protective colloid, such for example as lanoline, has been used, the product will dissolve to a clear solution in chloroform, which in turn may be shaken with water without loss of any material to the water layer.

This is here shown by two samples of colloidal selenium, one protected by a water-soluble colloid,—the other by an oil-soluble colloid. Selenium has been used in the form of a selenium-eosin compound by Wassermann in the experimental treatment of cancer,—and this metal has ardent advocates who claim therapeutic virtues for it in many forms. These colloidal forms are now being

¹ *The Practitioner XCL* July, 1913, p. 132.

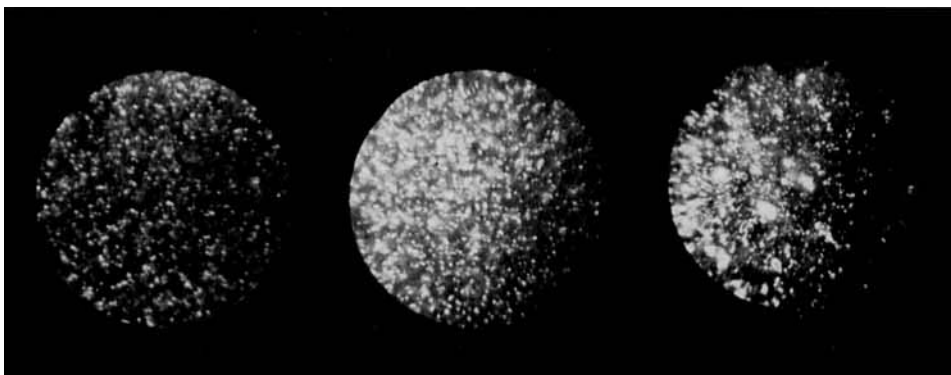
² *Interstate Medical Journal*, 1913.

Journal of the American Medical Association LX, June 14, 1913, p. 1857.

tested experimentally and clinically for their possible value in the treatment of malignant growths.

The production of an oil-soluble colloidal mercury also suggested to us the possible advantage of mercurial ointment in colloidal form. Here is shown such a 10 percent ointment, the vehicle consisting of lanoline and petrolatum, and the whole ointment, mercury and all, being soluble in chloroform, unlike ordinary Blue or Mercurial ointment which, when treated with chloroform, separates into a solution of the vehicle and metallic mercury which settles to the bottom of the tube.

We also show herewith ultra-micro-photographs of ordinary mercurial ointment in comparison with 10 percent colloidal mercurial ointment. These photographs, taken with an enlargement of approximately 1000 diameters by means of a dark-field illuminating apparatus, seem to bear out a calculation, based upon a measurement of the particles in the ordinary ointment and the theoretical size of the colloidal particles, that in amounts of the two ointments containing equal weights of mercury, there is approximately 60,000 times as much mercurial sur-



C
Ultra-micro-photograph
(x1000) of Colloidal Mercury
Ointment with lowest possible
illumination.

D
Same as C, but with increased
illumination.

E
Same as C and D, but with
more intense illumination.

face exposed in the colloidal ointment as in the ordinary form. In this connection it is of interest to point out, however, that the individual particles in the colloidal ointment, though theoretically magnified only about 1000 diameters in the photograph, are actually many times smaller than this, due to the fact that to the observer, the particles themselves are luminous and sources of light. Consequently, the brighter the illumination (a high power arc is required), the larger the particles will appear. This is well shown in photographs C, D and E, which represent the same colloidal ointment with gradually increasing intensity of illumination. The particles appear to coalesce into luminous nebulae with increase in luminosity, while if the latter be decreased, the individual character of the particles again becomes discernible. Moreover, no adequate conception of the actual size of the particles can be had, because they are in indescribably rapid motion similar in appearance to the so-called Brownian movement of floating dust particles. Thus each bright spot, as shown particularly well in photograph B, represents not the size of one colloidal particle magnified 1000 times, but rather

the entire circumference of the glow of a particle rapidly vibrating throughout a space very many times its own actual dimensions.

These ointments are also undergoing clinical tests and investigations. It may be of interest, however, to report that the toxicity of colloidal oil-soluble mercury, as determined upon guinea pigs, compared with ordinary metallic mercury appears to be about four times as great. The bactericidal power of water-soluble colloidal mercury has also been determined and appears to be equivalent to a phenol-coefficient of about 27.7.

Here also are samples of water-soluble colloidal copper, protected with casein, and ampoules of the aqueous solution ready for hypodermic or intravenous injection. Each ampoule contains 10 milligrams of substance corresponding to 2 milligrams of metallic copper, this quantity being the minimum lethal dose for 250 gm. guinea pigs. All these metallic colloids have been produced by the reduction method, starting with soluble salts.

Without doubt many things remain to be learned by the employment of these products in medicine, and the earnest co-operation of careful laboratory and clinical investigators along these lines may lead to discoveries of untold importance in the treatment of disease.

RESEARCH LABORATORY OF H. K. MULFORD COMPANY, July 28, 1913.

A PHARMACODYNAMIC STUDY OF THE PITUITARY GLAND WITH TESTS OF A NEW PRODUCT.

FRITZ HEIDELBERG, PAUL S. PITTENGER AND CHARLES E. VANDERKLEED.

The role which the pituitary body or hypophysis plays in life has until recently been a mystery. It was at first thought that its function was to lubricate the nasal cavities. This belief, however, was soon discarded and replaced by the supposition that the gland was, like the appendix, of no use at all. Later, however, it was proven by Vassale and Sacchi,¹ Caselli², and others that the gland plays a very important role and is absolutely necessary to life. It has also been found that acromegaly and other diseases are due to functional disturbances produced by an over or an under secretion of this gland, and that its removal causes death. According to Sajous³ the anterior lobe may prove to be the center of the adrenal system.

The pituitary body varies in size according to the age and species of the animal. The gland most commonly used in therapeutics is that obtained from the ox, and is about $\frac{3}{4}$ inch in diameter.

The gland is composed of two parts or lobes,—the anterior and the posterior or infundibular. The smaller or posterior lobe, which forms only about ten to fifteen percent of the total gland, is the more important therapeutically. This

¹ Vassale and Sacchi: *Rivista Sperimentale de Freniatria* p. 83, 1894.

² Caselli: *Studi anatomici e sperimentali sulla Fisiopatologia della Glandola pituitaria*, 1900.

³ Sajous: *Internal Secretions and the Principles of Medicine*. Vol. 1, p. 216.