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ON THE

PHYSIOLOGICAL RELATIONS

OF

COLLOID SUBSTANCES.

BY

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[*Read before the Lancashire and Cheshire Branch of the British Medical Association, June 22nd*, 1865; *and reprinted from the* British Medical Journal, *February 3rd*, 1866.]

LONDON:
PRINTED BY
T. RICHARDS, 37, GREAT QUEEN STREET.

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ON THE PHYSIOLOGICAL RELATIONS OF COLLOID SUBSTANCES.

The recent discoveries by Dr. Graham respecting the class of Colloid Substances, and their remarkable physical and chemical properties, cannot fail to have an important influence upon physiology, and may help to solve many vital problems. By them, not only has an entirely new field for investigation been opened up, but in the method of Dialysis we are supplied with a novel and most powerful instrument of research.

These discoveries are still too recent to permit any report of their effect upon vital science; but even now it may be useful to enumerate the characters of these bodies as described by Dr. Graham, and to endeavour to form some idea of their special action in the animal body.

It is not necessary to name the various colloids which are concerned in vital processes. They exist universally in organised beings; they form the chief part of the blastema, which is the basis of all growth; they appear largely in the blood, and in all the secretions of the body; and take an important part in the various processes of digestion.

An accurate knowledge of the general properties of these substances, therefore, must be essential to the physiologist.

Dr. Graham treats at length of these bodies in his papers on "Liquid Diffusion applied to Analysis" (*Philosophical Transactions*, 1862), and on "The Properties of Silicic Acid" (*Philosophical Magazine*, Oct. 1864, No. 189). From these sources I have extracted the following account, given nearly in his own words; the arrangement only being altered.

He observes that colloids differ radically from all crystalloid substances in their intimate molecular constitution. Every physical and chemical property is characteristically modified in each class. They appear like different worlds of matter, and give occasion to corresponding divisions of chemical science. The distinction between these kinds of matter is analogous to that subsisting between the matter of a mineral and the matter of an organised mass.

The first peculiar property of the colloid bodies, is that by which they were first discovered—their low diffusibility as compared with crystalloid substances. They are slow in the extreme to diffuse themselves either through fluids or through porous membranes, when submitted to osmose.

They are also distinguished by the gelatinous character of their hydrates; and, though often largely soluble in water, they are held in solution by a most feeble force.

Another and eminently characteristic quality of colloids is their mutability. Their condition is a continued metastasis. A colloid may be compared in this respect to water while existing fluid at a temperature

under its usual freezing point, or to a supersaturated saline solution.

Fluid colloids appear to have always a pectous modification (*i.e.*, curdled, from πηκτος); and they often pass under the slightest influences from the first into the second condition. Thus, any solid matter in the form of powder will, simply by its contact, bring about the pectous change in the fluid hydrate of silicic acid. The solution of hydrated silicic acid cannot be preserved. It may remain fluid for days and weeks in a sealed tube; but is sure to gelatinise and become insoluble at last. Nor does the change of this colloid appear to stop at that point; for the mineral forms of silicic acid deposited from water, such as flint, are often found to have passed, during the geological ages of their existence, from the vitreous or colloidal into the crystalline condition. The colloidal is, in fact, a dynamical state of matter, the crystalloidal being the statical condition.

Colloids have little power of chemical combination, and appear singularly inert in the capacity of acids and bases, and in all ordinary chemical relations. The molecular weight of a colloid appears to be always high, although the ratio between the elements of the substance may be simple. Gummic acid, for instance, may be represented by $C^{12}H^{11}O^{11}$; but, judging from the small proportions of lime and potash which suffice to neutralise this acid, the true numbers of its formula must be several times greater. Dr. Graham says:

"It is difficult to avoid associating the inertness of colloids with their high equivalents, particularly

where the high number appears to be attained by the repetition of a smaller number. The inquiry suggests itself whether the colloid molecules may not be constituted by the grouping together of a number of smaller crystalloid molecules, and whether the basis of colloidality may not be this composite character of the molecule."

Gelatine appears to hold an important place as a colloidal base. This base unites with colloidal acids, giving a class of stable compounds, of which tannogelatine only appears to be known. Gelatine is precipitated entirely by a solution of metaphosphoric acid added drop by drop; 100 parts of gelatine uniting with 3.6 parts of the acid. The compound formed is a semitransparent soft elastic stringy solid mass, presenting a startling resemblance to animal fibrine.

Many other substances, such as alumina, peroxide of iron, certain compounds of copper, of chromium and uranium, and tin, form peculiar colloidal compounds. Thus, soluble silicic acid combines with ordinary alkaline bases, such as potassa, soda, and ammonia; and also with gelatine, forming what Dr. Graham calls colli- or co-silicates, and the compounds are colloidal and differ entirely from ordinary silicates. The new compounds are interesting from their analogy to organic substances, and from appearing to contain an acid of greatly higher atomic weight than ordinary silicic acid.

One most remarkable property of many colloid substances is their power of combining with large quantities of water and other fluids. The water of gelatination thus taken up corresponds to the water of crystallisation of crystalloids. This water has

been described as being retained by "capillary affinity"; *i. e.*, by an attraction partaking of physical and chemical characters. It is, nevertheless, believed that the character of gelatinous hydration is as truly chemical as that of crystalline hydration.

It is further interesting to notice that this water of hydration, whether of a fluid or of a gelatinous colloid, may be replaced by other fluids, such as hydrochloric, nitric, acetic, or tartaric acids; by glycerine, alcohol, and the syrup of sugar; giving rise to new substitution-products, such as the alcogel and glycogel or alcosol and glycosol of silicic acid.

But colloids have no power to crystallise. The hardness of the crystalloid, with its crystalline planes and angles, is replaced in the colloid by a degree of softness, with more or less rounded outline.

Though chemically inert in the ordinary sense, colloids possess a compensating activity of their own arising out of their physical properties. Thus, notwithstanding their apparently feeble affinity for water, anhydrous colloids can decompose certain crystalloid hydratics. The water in alcohol, of greater strength than corresponds with the density 0.926, which represents the definite $C^4H^6O^2 + 6\ HO$, is certainly in a state of chemical union. But alcohol so high as 0.906, contained in a close vessel, is concentrated in a notable degree by contact with dry mucus, gelatine, and gum, and sensibly even by parchment paper. Dilute alcohol, divided from the air of the atmosphere by a dry septum of mucus, gelatine, or gum, is also concentrated by evaporation, as it is in the well known bladder of Sömmering. The selective power is here apparent of the colloid for water; that

fluid being separated from the alcohol and travelling through the colloidal septum by combination with successive molecules of the latter, till the outer surface is reached and evaporation takes place.

A further instance of this physical power of colloid is seen in their adhesiveness, and in the phenomenon of cementation; and the adhesion of colloid to colloid appears to be more powerful than that of colloid to crystalloid. Thus, two pieces of plate-glass left in contact will, after a time, adhere so closely that no division can be detected between them, and they may be cut and ground without separating; and, again, the intense syncœresis of isinglass dried in a glass vessel over sulphuric acid *in vacuo*, enables the contracting gelatine to tear up the surface of the glass.

While the rigidity of the crystalline structure shuts out external impressions, the softness of the gelatinous colloid partakes of fluidity, and enables the colloid to become the medium for liquid diffusion like water itself. Certain colloid substances, accordingly, greatly assist diffusive separations. The jelly of starch, that of animal mucus, of pectin, of the vegetable gelose of Payen, and other solid colloidal hydrates, all of which are, strictly speaking, insoluble in cold water, are themselves permeable when in mass, as water is by the more highly diffusive class of substances.

The diffusion of a crystalloid appears to proceed through a firm jelly with little or no abatement of velocity. But such jellies greatly resist the passage of less diffusive substances, and cut off entirely other colloid substances like themselves that may be in solution. They resemble animal mucus in this respect;

and a mere film of the jelly has this separating effect. The phenomena of Dialysis arise from this property.

This process simply consists in the diffusion of crystalloids and the retention of colloids by means of a septum of gelatinous matter. The septum may consist of well sized paper, animal membrane, or mucus; but the most convenient material is the parchment paper manufactured by Messrs. De la Rue. This paper, applied to a hoop of gutta percha, forms a vessel which constitutes the dialyser. The mixed fluid, containing both colloids and crystalloids, is poured into the hoop, upon the surface of the parchment-paper, to the depth of about half an inch. The dialyser is then floated on a basin containing a considerable volume of water; and, in about twenty-four hours' time, the principal portion of the crystalloid ingredients will have passed through the septum into the water, and the colloids will still be found within the dialyser.

Dr. Graham supposes that the crystalloid owes its power of thus diffusing through a colloid septum, to the greater affinity for water possessed by crystalloids over colloids.

It may, perhaps, be of little consequence what explanation of the action is given, so long as the facts relating to it are observed; but I would notice, with great deference to so high an authority, that this theory scarcely accords with what has been said before respecting the attraction of colloids for water. Moreover, the endosmotic power of a fluid does not depend solely upon its affinity for water; but rather upon its molecular affinity for the material of the septum—in other words, upon its power of wetting

the septum—and upon its miscibility with the opposite fluid. Thus, when an animal membrane forms the porous diaphragm, water will pass into alcohol; but when India-rubber or gutta percha is substituted, the alcohol current is the strongest; the molecular affinities of the membrane thus determining the result.

In the case of dialysis, the same influences are at work, but in a much higher degree. The particles of the colloid cling powerfully to the substance of the septum, and thus are unable to pass off into the opposite fluid, even if they had less tenacity of constitution; but, as we have seen, this colloid substance is easily penetrated by crystalloid solutions—as easily as is water itself. The crystalloid, therefore, readily traverses the colloid lining the pores of the membrane, and is taken up by the molecular affinities of the colloid solution on the opposite side.

The physiological bearings of his discovery have been fully recognised by Dr. Graham; and numerous allusions to vital problems occur in the papers in which the properties of these substances are described. There can be no doubt that both their physical and chemical characters render them peculiarly well fitted for the processes of organic life; and on many important points we may need to bring our views of these processes into accordance with a more accurate knowledge of the colloid constitution of many organic substances.

It is probable that we shall have to modify our views as to the relative proportions of colloid and crystalloid materials forming constituents of the different fluids of this body.

We have seen that colloids are capable of uniting with large quantities of water and other fluids; and it would seem that the hydrated form of a colloid is its most powerful dynamical condition. In physiology, we have to do with these substances in their most energetic forms; and it seems desirable, in any analysis of animal fluids, not only that we should have the quantities of their component parts estimated dry, as is usually done, but that the natural degree of hydration of the colloids they contain should be ascertained, and that the quantities of these should also be given to us. Thus, the quantity of ptyaline in the saliva, according to recent analyses, is less than two parts in the 1000; and that of pepsine in the gastric juice is less than one part per 1000. If we knew more correctly the active condition of these substances it is most probable that these proportions would have to be greatly altered.

The whole subject of the physiology of digestion will need to be studied afresh by the light of these researches. Thus, as Dr. Graham observes: "The secretion of free hydrochloric acid during digestion, at times most abundant, appears to depend upon processes of which no distinct conception has been formed. But certain colloidal decompositions are equally inexplicable upon ordinary chemical views. To facilitate the separation of hydrochloric acid from the perchloride of iron, for instance, that salt is first rendered basic by the addition of peroxide of iron. The comparatively stable perchloride of iron is transformed by such treatment into a feebly constituted colloidal hydrochlorate. The latter compound breaks up under the purely physical agency of diffusion, and

divides in the dialyser into colloidal peroxide of iron and free hydrochloric acid. The superinduction of the colloidal condition may possibly form a stage in many analogous organic decompositions."

The theory thus cautiously indicated may or may not prove to be well grounded; but it certainly points out a wide field for fresh physiclogical investigations. There seems reason to hope that a study of the characteristic properties of these bodies may assist in explaining the action of the digestive fluids upon the food—the change of starch into sugar by the saliva, and the liquefaction of fibrine in the stomach.

Great differences of opinion even now exist respecting the parts taken in digestion by ptyaline and pepsine; some observers attributing all the activity of the digestive fluids to their influence, whilst others assert that any decomposing material would do as well. It seems to be agreed to affix to these substances the title of of *ferments*; but their mode of action remains in doubt. I believe, however, that their influence has never yet been ascribed to the presence of living organisms of low degree of organisation, such as M. Pasteur has discovered to be necessary to alcoholic, lactic, butyric, mucous, and other fermentations. The operation of digestive ferments has rather been compared to the so-called catalytic action of emulsine upon amygdaline in the formation of hydrocyanic acid; to the action of erythrozym upon rubian (described by Dr. Schunck); and to the kindred fermentations by which most of the essential oils are produced.

With reference to these actions, the views of Ber-

zelius and Liebig are very generally accepted; and these may be thus briefly epitomised. "1. Nitrogenous matter, by contact with atmospheric oxygen, undergoes a change of composition by which the equilibrium of the attractive forces which holds its particles together is disturbed and new compounds are formed; and 2. The *motion* thus produced by the altered arrangement of the atoms is propagated through the whole of the nitrogenous body, and affects the atoms of any contiguous matter, producing movements in them which bring about new combinations."

It must be admitted that there are strong objections to this view of the action of this class of ferments, which may be briefly enumerated thus:

1. Contact with atmospheric oxygen is not by any means a necessary condition for the production of fermentation.

2. It has not yet been proved that decomposition of the ferment is essential to the action.

3. On the contrary, the preserving power of the gastric juice, and the fact that many of these fermentations will go on in the presence of the most powerful antiseptics, would lead us to an entirely opposite conclusion.

4. Moreover, in the case of a kindred ferment—erythrozym—Dr. Schunck found that, when it began to change and to putrefy, it lost in great measure its power over rubian.

5. The action of the so-called ferments, also, is a very specific one. Not only is it certain that any decomposing nitrogenous material will not effect the changes described, but each ferment will only act

upon its appropriate material. Ptyaline will not liquefy fibrine; and pepsine will not change starch into sugar.

6. The result of these fermentations, in many instances, is not decomposition, but synthesis. In the case of salivary digestion, the starch is made to unite with at least two, probably four, equivalents of water.

It seems certain that these gastric ferments, however they may act, are of the nature of colloid substances; but, as we are ignorant of the peculiar arrangement of atoms to which colloids owe their properties, we cannot say whether or not these properties are due to the motion or vibration of their particles. We may discern, however, that the colloid constitution is one exceedingly well adapted for giving full play to the molecular attraction of these particles.

It would be sufficient if I were to adduce, in support of this statement, the singular property, common to these substances, of instability of molecular condition. The fluid forms of their hydrates, as we have seen, constantly tend, with time, to change to a semi-solid consistency; and the presence of small quantities of certain substances is sufficient to alter their condition from the fluid to the solid, or from the solid to the fluid form. This property must arm them not only with all the influence due to change of physical condition, but must give full play to any peculiar molecular force which their separate particles may possess.

But this is not all. It is remarkable how closely organic ferments resemble, in many points, the most

powerful inorganic catalytes—such, for instance, as animal charcoal or platinum-black. Thus, like these bodies, colloids generally are singularly inert in all chemical relations; and nitrogen, the most indifferent of all the metalloid elements, seems to be an essential component in all ferments. This character, in fact, is essential to substances acting by contact. Although very little is known of molecular forces, it is certain that they require extreme approximation of the particles influencing each other; and that their power increases inversely as the distance, in some enormous ratio. It may easily be conceived, therefore, that this chemical indifference of catalytes enables the ultimate particles of these bodies to come into close contact with substances which would otherwise unite chemically with them and destroy their molecular power. This chemical inertness will be found, upon examination, to be characteristic of the whole range of substances which are capable of bringing about the so-called actions of catalysis.

Colloids further resemble inorganic catalytes in their penetrability. All these substances are easily permeated by the material upon which they act. Their molecules are loosely aggregated together; thus presenting a large surface and a series of points of force, from each of which any peculiar molecular influence (whatever it may be) can arise and act without perturbation from other surrounding molecules.

Moreover, as platinum-black and its congeners act with the greatest energy when their surfaces have been freed from all taint of vapour other than that

upon which they are about to take effect, so these organic ferments are most active when they are in a nascent condition—their particles freshly formed, or at least freshly arranged, and free to attach themselves to the material which is appropriate to them.

I venture to think that the changes produced during digestion are brought about chiefly by purely molecular influences, analogous to the so-called catalyses wrought by many inorganic substances. On the hypothesis now brought forward, it is not difficult to understand why a very small proportion of a ferment suffices to act upon large masses of suitable material; for the molecular action once completed upon one part of the mass is not necessarily exhausted or neutralised thereby. If the substances formed by contact with the catalyte have less molecular affinity for it than the original material had, they will readily be given up; the original energy of the catalyte will return, it will attract fresh portions of the more appropriate material, and the action may go on almost indefinitely.

It is quite possible that, even in fermentations brought about by living organisms, the eminently catalytic powers of nascent nitrogenous colloids may come into play. In his recent researches upon these fermentations, M. Pasteur concludes that the mycodermic plant which effects the change of alcohol into vinegar, or into carbonic acid and water, "does not act by means of some agent which it secretes", and then leaves to work by itself; but, as he goes on to remark, "the chemical phenomena which accompany the life of the plant depend upon some peculiar physical condition analogous to platinum-black." "It

is, however, essential to remark that this physical condition of the plant is in some way closely bound up with its life." This observation of M. Pasteur need not be confined to fermentative operations; it is capable of much wider application. We cannot but feel sure that, in the vital processes in which colloid bodies are constantly being evolved in a nascent state, their peculiar physical constitution must have had a most important influence.

The changes wrought upon fibrine, albumen, and other protein compounds, by means of the gastric juice, are not without a parallel in the history of other colloid substances. Thus certain gelatinous colloids are liquefied in short spaces of time by very minute quantities of reagents. Gelatinous silicic acid is liquefied by very small portions of caustic potash. One part of this agent, in ten thousand of water, dissolves two hundred parts of silicic acid (estimated as dry) in sixty minutes, at 100° cent. The alkali, too, after liquefying the colloid, may be separated again from it by diffusion into water upon a dialyser. This solution, says Dr. Graham, is analogous to solution of insoluble organic colloids in animal digestion. Liquid silicic acid may be represented as the *peptone* of gelatinous silicic acid. Certain other colloids, such as the pure jellies of alumina, peroxide of iron, and titanic acid, are even more closely assimilated to albumen in this respect, since they are peptised by minute quantities of hydrochloric acid. These facts also recall forcibly the observations of Dr. B. W. Richardson with reference to the power possessed by ammonia and other alkalies in preserving the fluidity of the blood.

The remarkable osmotic characters of colloid substances have a most important bearing upon the subject of animal absorption. It seems very singular that substances like albumen and gluten, which, in their ordinary state, are perfectly "fixed" as to diffusiveness, should yet, after digestion, be capable of rapidly permeating the stomachal and intestinal walls, and become absorbed into the blood or lacteal vessels.

Dr. Graham suggests that the property exhibited by the hydrogels of some colloids of forming substitution-products with other fluids may partly explain this process. Thus, as the hydrogel of silicic acid assumes other fluids, such as alcohol or glycerine, in place of the water of combination, without disintegration or change of form, producing the so-called alcogels and glycogels of silicic acid—so may the albuminous matter of the membranous walls of the intestines take up fatty and other insoluble bodies from among the products of digestion.

So far as the absorption of albuminous matter is concerned, this theory would probably be received with considerable hesitation; but it seems quite possible that the fatty matters of the food may form, with animal colloids, compounds in which the oleine is substituted for the water of gelatinisation; compounds not only soluble in the blood, but capable of traversing animal membranes.

The rapid absorption of *albuminous* fluids after digestion seems rather to point to some change of molecular constitution effected by the catalytic action of the ferments, making the peptones, if not

crystalloid in their character, at any rate diffusive and able to traverse membranous septa.

There would be nothing contrary to experience even in the first supposition. Dr. Graham has shown that colloids are capable of taking on the crystalloid form. Thus, in the so-called "blood-crystals of Funke", a soft and gelatinous albuminoid body is seen to assume a crystalline contour. The solid form of water, as in ice and snow, is either colloid or crystalloid; and quartz declares the same power to be possessed by silica.

But it seems very probable that something short of true crystalline constitution may confer the power of diffusion upon colloids. Mialhe and Pressat have noticed that albuminose—the substance produced by the action of gastric juice upon albumen and its kind—is endosmotic. And this observation is easily confirmed by dialysing some chyme from a calf's stomach, evaporating the diffusate, and precipitating the albuminose, by means of alcohol or tannic acid. It would be sufficient to account for the diffusion of albuminose, if it were to be proved that digested albumen is so far altered as to make it less adhesive to animal membrane, and more easily miscible with the blood than pure unaltered albumen.

Many other interesting applications of Dr. Graham's observations to physiology might be noticed. I will, however, only mention one other, which he has himself brought forward, respecting the physiology of the organs of taste;—"that, while soluble crystalloids are always highly sapid, soluble colloids are singularly insipid. It may be questioned," he says, "whether a colloid, when tasted, ever reaches

the sentient extremities of the nerves of the palate, as the latter are probably protected by a colloid membrane, impermeable to soluble substances of the same physical constitution."

In conclusion, it may be observed that, as a practical instrument for physiological and pathological research, and for the prosecution of toxicological analysis, Dr. Graham's dialyser will be most valuable.

Numerous experiments, illustrating the application of dialysers to medico-legal inquiries, are given in the work on *Liquid Diffusion applied to Analysis.*

The process has the advantage of introducing no metallic substance or chemical reagent of any kind into the organic fluid.

The arrangement for operating is also of the simplest nature. The organic fluid is placed, to the depth of half an inch, on a dialyser formed of a hoop of gutta percha ten or twelve inches in diameter, covered with parchment paper. The dialyser is then floated in a basin containing a volume of water about four times greater than the volume of organic fluid in the dialyser. The water of the basin is generally found to remain colourless after the lapse of twenty-four hours; and, after being concentrated by evaporation, it admits of the application of the proper reagents to precipitate and remove a metal or other poisonous ingredient from the solution. One-half to three-fourths of the crystalloid and diffusible constituents of the organic fluid will generally be found in the water of the basin.

By this means, arsenic was separated from albumen, gum, gelatine, and milk; also from porter,

from blood, and from animal intestines. Tartar emetic was diffused from defibrinated blood, and from milk; and strychnine was obtained from organic fluids impregnated with it. "All soluble poisonous substances, whatever their origin, appear to be crystalloid, and accordingly pass through colloidal septa;" whilst the organic fluids which make their detection difficult are retained by the dialysing instrument.

In the examination of urine, the method will prove of much service. Thus, in one experiment given by Dr. Graham, half a *litre* of urine, dialysed for twenty-four hours, gave its crystalloidal constituents to the external water. The latter, evaporated by a water-bath, yielded a white saline mass. From this mass, urea was extracted by alcohol in so pure a condition as to appear in crystalline tufts upon the evaporation of the alcohol.

Even in bedside examination of albuminous urine, the method may be used. Thus a piece of well-sized letter-paper was folded into the form of a filter, and filled with urine from a patient suffering from Bright's disease of the kidney. This was placed in a tumbler containing a known quantity of pure water. The relative specific gravities of the fluid within the paper, and of the diffusate, after twenty-four hours' dialysis, gave a much closer approximation to the proportion of albumen to urea, than could have been obtained by the use of the urinometer alone.

The importance of the subject must be my excuse for venturing to bring before your notice so much that is yet doubtful or hypothetical. I can only trust that sufficient has been said to induce mem-

bers of our profession to contemplate with interest the physiological bearings of these discoveries, and to turn to practical advantage the instrument placed in their hands by Dr. Graham.

T. RICHARDS, PRINTER, 37, GT. QUEEN STREET.