1. Will creatine appear in the urine, even in the presence of an abundant carbohydrate supply, if acidosis is induced?

2. Will the elimination of creatine disappear if the acidosis is abolished, quite independently of the factor of carbohydrate supply?

Upon a diet of oats and corn, containing an adequate supply of carbohydrate, creatine promptly appears in the urine of the rabbit. A marked condition of acidosis, as measured by the hydrogen ion concentration of the urine, is always associated with this phenomenon. Oats and corn are pronounced acid-producing foods. On the other hand, if a base-producing food, such as carrots, is fed to rabbits with creatinuria this symptom rapidly disappears as the urine becomes strongly alkaline.

The protein *per se* is without special significance in the phenomenon under discussion; for upon a diet consisting of oats, corn and carrots creatine fails to appear in the urine, and the reaction of the latter remains alkaline. Equally significant is the further fact that the ingestion of HCl in addition to the mixed diet causes the appearance in the urine of significant quantities of creatine. Simultaneously the hydrogen ion concentration of the urine is markedly increased.

The conclusion seems inevitable that there is an inter-relationship between acidosis and creatine elimination. Creatine excretion may prove to be an index of a condition of acidosis in the organism.

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On the production of soap jellies, and the physical conditions under which jelly formation takes place. (Preliminary communication.)

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In the course of experiments regarding the influence exerted by various electrolytes on the equilibrium of emulsions, published in the year 1913, the writer noted that NaCl, when used at a concentration in excess of .4M, caused a precipitation of some constituent

of the aqueous phase of an emulsion of oil dispersed in water, and that the emulsion subsequently broke down, the oil and water layers separating. This effect was believed to be attributable to the precipitation of the surface film of soap on which the stability of the emulsion depended. To test this question Na oleate was treated with salt at different concentrations, and it was found that at .4 to .45M NaCl complete precipitation of the soap took place. It was noted, however, that prior to precipitation a tendency to jelly formation was exhibited in the zone from .2M NaCl to .4 or .45M NaCl.

An attempt to repeat this experiment with a soap, which had been slightly acidified either by the addition of a minute quantity of oleic acid or of mineral acid, gave an entirely different result, an opalescence with increasing cloudiness and tendency to precipitation was noted between .2M and .4M NaCl, followed by complete precipitation at .45M NaCl. Further tests using varying proportions of soap, varying proportions of NaOH, and of NaCl and other salts of Na, brought out the remarkable fact that, as long as the soap employed was not too greatly diluted and was slightly alkaline, a jelly would be formed at all points between .2M Na and .45M Na regardless of whether the Na was derived from NaOH, from NaCl or other salts of Na.

In very concentrated soap solutions or in very strong alkali the jelly formation commences at a somewhat higher concentration and continues also somewhat above .45M. But it may be stated as a general principle that a zone of jelly formation obtains within these ranges, provided the original concentration of OH ions is in excess of the amount required to produce a strong pink coloration of the soap solution with phenolphthalein. If insufficient alkali is present as a result of the addition of small amounts of organic or mineral acids to the system, precipitation instead of jelly formation is observed. Since jelly formation commences and ends at a given strength of the Na salt almost regardless of the nature of the anions present provided there is a sufficient initial concentration of OH ions, it seems probable that the explanation is as follows:

A dispersion of Na oleate in water represents a dispersion of particles of oleic acid by means of NaOH. Further additions of NaOH lead to a more perfect dispersion of the soap particles,

owing to the fact that the OH ion is more readily adsorbed than the Na ion. NaCl exerts a similar effect to NaOH, the Cl ions exerting a dispersing effect analogous to that of the OH ions, but since they are far less readily adsorbed than the OH ions their effect is considerably smaller. This point may be demonstrated by adding NaCl in increasing amounts to a soap solution containing enough alkali to give a strong pink color with phenolphthalein. A discharge of the color takes place, and the amount of alkali required to compensate for the effect of the NaCl introduced follows a logarithmic curve indicating clearly that the added NaCl either promotes the adsorption of OH ions already present, or that the Cl ions are more readily adsorbed than the Na ions, thus leading to a reduction in the OH ion concentration in the water phase.

The soap particles possess a negative charge attributable presumably to adsorbed anions. This charge prevents their coalescence until the concentration of the Na ions reaches such a point that they also come into play and by adsorption on the particles tend to counteract or diminish the negative charge conveyed by the previously adsorbed OH or Cl ions.

When a certain concentration of the cation is reached, a critical zone commences, in which jelly formation or precipitation appears to depend entirely upon the relative proportions of adsorbed cations and anions. If at the commencement of this critical zone the residual negative charge carried by the particles resulting from an adsorption of anions in excess of cations is sufficient to maintain a perfect dispersion of the particles throughout the system, as indicated by an examination of the suspensions for Brownian movement by means of the ultramicroscope, jelly formation will ensue at higher concentrations. If this residual negative charge on the particles is insufficient, if they no longer exhibit perfect dispersion when examined by means of the ultramicroscope, if agglutination, aggregation and sedimentation under the influence of gravity has already commenced, precipitation necessarily ensues at higher concentrations. It is obvious, therefore, that the formation or non-formation of the jelly in this critical zone is dependent simply upon the relative concentration in the system at the lower critical point of anions like OH, which are more readily adsorbed and anions like Cl which are less readily

adsorbed, and more or less readily adsorbed cations. If at this critical point, the sum total of adsorbed anions is not sufficiently in excess of that of adsorbed cations to insure perfect dispersion, precipitation instead of jelly formation ensues. This explains the necessity for a certain minimum concentration of NaOH, with its readily adsorbed OH ions, to insure jelly formation in the case cited above.

It must be presumed that at the moment at which the particles suffer a sufficient loss of charge no longer to repell one another, they tend to coalesce with one another, and also become distorted and elongated into films and rods under the influence of changing surface tension conditions. It is obvious if they are sufficiently finely dispersed at this point that each particle will coalesce with its neighbor to form a jelly-like structure (analogous in a sense to a honey-comb) enclosing globules of water between the coalescing particles of the original dispersed phase, the structure retaining the form of the original containing vessel. If on the other hand the particles were not sufficiently dispersed at the time at which coalescences commenced, if they were already partly aggregated and no longer exhibiting perfect Brownian movement, they would no longer be perfectly distributed throughout the entire mixture, they would be further apart and, as a result of the diminution of their charge, would tend to aggregate and precipitate to the bottom of the vessel.

There are obviously a large variety of possible intermediary structures between the most perfect jelly formation, resembling a honeycomb, which would be impermeable to water, and the precipitated structure which would be absolutely permeable. Various degrees of permeability would result from the production of systems analogous to a sponge in which two continuous phases exist side by side, and the permeability of such systems would depend upon the extent to which intercommunication between adjacent partially enclosed aqueous phases has been maintained.

Further experiments with $CaCl_2$ and soap suspensions confirmed this theory and afford a satisfactory explanation for the phenomena of blood coagulation, the production of the casein clot, and other cases of jelly formation actuated by salts of Ca. The conversion of a system consisting of particles of fibrinogen dis-

persed in water, into a system consisting of a more or less perfect dispersion of water in an external or continuous fibrin phase may be further explained in a manner analogous to the explanation offered for the transformation of emulsions of oil in water into emulsions of water in oil, by considering the surface tension relations on both sides of a concentration film formed at the interface between the dispersed fibrinogen particles and the surrounding water. This phase of the question will be discussed in a subsequent paper on the process of blood coagulation.

This theory, that jelly formation depends on the extent of dispersion of colloidal aggregates when exposed to the effect of a precipitating agent, offers an explanation for the variations in permeability of a hypothetical protoplasmic membrane, or for that matter of tissues as a whole, under the influence of suboxidation products. A reduction in the concentration of OH ions available for adsorption resulting from the presence of acids would render the dispersion of certain colloidal aggregates less perfect than is normally the case. These aggregates would then tend to precipitate rather than to undergo jelly formation when subjected to the influence of coagulating agents. The structure formed would necessarily be more permeable and would possess less strength and elasticity than that formed under normal conditions of jelly formation. The destruction of emulsions and jellies, with resulting precipitation of the soap present when the concentration of NaCl exceeds .4M, probably bears some relation to the observation of Jacques Loeb that marine organisms are rapidly destroyed when exposed to that strength of NaCl, unless $CaCl_2$ or some other antagonistic salt is added.

The principle involved in the case of soap jellies considered above applies equally well to the reverse type of jelly formation where cations promote dispersion and anions exert an aggregating or precipitating effect.

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