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Pathological Changes in the Viscosity of Blood Serum.

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Measurements of the viscosity of blood serum reported by clinical observers have shown results that are seemingly paradoxical. We have attempted to investigate the physical-chemical basis of these empirical relationships.

Blood serum, as seen from the viscosity at different dilutions, shows a remarkable ability to keep its viscosity constant in spite of dilution. If we compare the effects of dilution on the viscosity of such a protein as gelatine, we find that not alone is the absolute viscosity of the same percentage concentration of serum protein very much lower than that of a similar strength of gelatin, but the gelatin manifests a much greater change in viscosity for each increasing unit of dilution. The importance of this point in maintaining the circulation of the blood in such conditions as nephrosis, where the blood proteins are reduced to one half their normal concentration, is obvious.

Loeb has distinguished between two types of protein, one represented by gelatin and the other by egg albumin. In the former there is an enormous tendency toward the formation of submicroscopic particles of solid gelatin which, as a result of the inability of the protein ion to freely diffuse, set up a Donnan equilibrium with the result that water is occluded and these particles increase in size. On the other hand, we have such proteins as albumin, which show no tendency at a pH in the neighborhood of neutrality and at body temperature toward the formation of these submicroscopic particles. These show a low viscosity and no tendency to jell. There are certain exudates, especially pleural exudates, which after standing become jellified. If Loeb's hypothesis were correct, these exudates should show a higher viscosity than other exudates and transudates that do not jell. We have found that abdominal exudates of higher protein concentration that did not jell had a lower viscosity than some other exudates of lower protein concentration that did jell. This would seem to prove Loeb's theory of the presence of submicroscopic particles, in this case probably of fibrin, which cause the solution to manifest higher absolute viscosity and which make it occlude water.

Those proteins which show no tendency to jell also show very

little effect on the viscosity of their solutions through changes in the hydrogen ion concentration. The viscosity of blood proteins is very insensitive to changes in the hydrogen ion concentration, the viscosity remaining almost constant between the ranges of pH 7.8 and 8.1.

In an effort to explain the high viscosity found in the serum of patients suffering from cyanosis, CO₂ was passed through blood serum. After that the cells were put back with the serum and the CO₂ passed through again. After centrifuging, the viscosity of the serum was again measured and was found to have increased. Von Limbeck shows that saturating the blood with CO₂ causes the cells to swell up with water which passes into them from the serum, and it is for this reason we find that the viscosity of serum containing cells through which CO₂ has been passed is increased.

In cases of nephritis we should expect that owing to the increase in total solids such as urea, cholesterol, etc., the viscosity of the blood serum would be much increased. Such, however, is not the case. The figures for the viscosity of blood serum of patients suffering from nephritis have always been found normal. We have found that the saturation of serum with cholesterol reduces its viscosity. This is probably due to the tendency of hydrophobe colloids such as cholesterol to emulsify water in oil in contradistinction to the hydrophile colloids such as albumin, globulin, lecithin, etc., which tend to emulsify oil in water. W/O emulsifiers increase the size of the fat particles and cause a fall in the viscosity.

It has been known for a number of years that the effect of urea has been to decrease the viscosity of water. We have found that the viscosity of blood serum is similarly decreased by the addition of urea. It is of some significance that just those blood constituents, such as cholesterol and urea, which are found higher as a result of kidney lesions, have the power of lowering the serum viscosity. In about 5 cases of uremia, all of which showed abnormally high urea and cholesterol figures, we found, again in agreement with findings of clinical investigators, that the viscosity was fairly normal.

The serum of patients suffering with pernicious anemia and hemolytic jaundice, though showing an increase in the concentration of bilirubin, does not have a higher viscosity. On the other hand, sera of patients suffering with obstructive jaundice show an enormous increase. The presence of bile acid in cases of obstructive jaundice would seem to offer an explanation for the difference in the viscosities of the sera of patients suffering with these diseases. The bile acids are known to greatly decrease the surface tension and increase the viscosity. We should, therefore, expect

that a blood serum showing a positive direct Van den Bergh reaction will have a much higher viscosity than one showing only a positive indirect. Such we found to be the case.

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Relationship Between Vitamin C and Oestrus in the Guinea Pig and the Fertilizing Power of Sperm.*

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Papanicolaou and Stockard¹ have shown that dioestrus is prolonged when guinea pigs are underfed. The effect of vitamin C deprivation was studied by their method in the following way.

After their oestrus rhythm had been observed on a complete natural food diet, 3 guinea pigs were transferred to the Sherman scorbutic diet with a daily protective dose (3 cc.) of orange juice. The regular occurrence of oestrus was soon resumed and maintained for about 150 days, during which the orange juice was fed successively at the levels of 3 cc. $\frac{1}{2}$ cc., and $\frac{1}{4}$ cc. daily for about 50 days on each level. Two of the pigs manifested oestrus after the level of orange juice had been reduced to $\frac{1}{8}$ cc., just before the rapid decline in growth, due to scurvy, set in. Two of the pigs were autopsied within 20 days of the last cycle and showed large follicles as well as the marked symptoms of scurvy. The third pig was cured by the administration of 3 cc. of orange juice daily, and the ovulation rhythm was reestablished within 10 days of the rise in the growth curve.

Daily weighings indicated that during oestrus, the guinea pig lost from 30 to 40 gm. in weight and regained it shortly thereafter. There was no corresponding decrease in food consumption, such as Slonaker² has observed in the rat.

Lindsay and Medes³ found that guinea pigs with mild chronic scurvy did not reproduce, and they described extensive histological

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¹ Papanicolaou, G. N., and Stockard, C. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1919, xvii, 143.

² Slonaker, J. R., *Am. J. Phys.*, 1924-1925, lxxi, 362.

³ Lindsay, B., and Medes, G., *Am. J. Anat.*, 1926, xxxvii, 213.