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### PHYSICO-CHEMICAL ADJUSTMENTS IN THE BLOOD.

We may regard the material structure of the body as made up of elements of gradually increasing complexity, having as their basal structures the atoms with the positively charged protons and the electrons with an equally great electro-negative charge. All active forces of the body may be finally resolved into those which belong to the electro-magnetic fields surrounding these elementary units, so that all physical and chemical processes may finally be regarded as obeying the laws of electro-magnetism. The old distinctions between matter and energy are no longer valid. The cells of the body have their potentials established as the mean values of the finest ultramicroscopic units. Between the various ultramicroscopic units in the cell there are potential differences; in other words, electric fields are established. The separation of the minute structures of the body, their form, etc., are dependent upon the charge which they carry. In the case of the red blood cells the neutralisation of the charge which they carry results in the loss of their individual character, and they run together or become agglutinated.

The body is essentially made up of disperse systems, consisting of the dispersion medium and the solid elements dispersed in this medium – “the disperse phase.” The material structure of the disperse system is accompanied by its characteristic electric structure. At each interface between the solid and the liquid phase, in the condition of equilibrium, there exist potential differences. Whenever a disperse phase is created, these potential differences are at once established, which can only be destroyed by the complete mixing of the two phases, with loss of characteristic structure. When positively charged, the particles are moved in the direction of the lines of force of the field, from positive to negative, and the reverse when the sign of the charge is negative. Frictional forces oppose the movement. The direction of these movements in the case of very small particles is disturbed by the kinetic energy of heat motion in

the medium, so that it is only in the case of larger particles that the electric forces are dominant in establishing direction in the electric field. It is thus the larger colloidal particles which move according to their charge in one or other directions in the electric field. In the body these movements are continually being checked by contact with porous membranes. If the potential difference between particle and membrane be maintained, a new equilibrium is established and the particle is held in position – so-called polar adsorption. If the potential difference is not maintained and the particle loses its charge, it is then free to be moved in any direction by forces acting upon it. When particles with a particular charge are concentrated on an interface with the opposite charge, there arises an electric double layer, and adsorption ceases when the electric field is fully occupied.

*The electric charge on the red blood corpuscles.* – As is well known, particles suspended in a fluid move along a potential gradient. They therefore possess a surface charge, the so-called electro-kinetic potential, between the suspended matter and the fluid. This potential is readily affected by adsorption of different ions. If the particles be negatively charged, the addition of negatively charged anions will increase the negativity, while positive cations will decrease it. The discharging or neutralising effect of the cations is increased with increase of valency, but valency is not the only determining factor, because certain organic cations of great absorbability may be still more effective. When red cells are suspended in such an electrolyte free solution as isotonic cane sugar; they move towards the positive pole and therefore carry a negative charge. When cations, especially of high valency, are added to the solution, the charge on the cells may be neutralised and finally the cells may acquire a positive charge, the direction of movement then being reversed. The red cells run together or are agglutinated when their charge is neutralised. The agglutination may not take place exactly at the neutral point, but at a so-called “critical point,” when they still possess a slight charge. The closely related phenomenon of rate of sedimentation follows that of agglutination. From the interesting studies of Fahraeus we learn that the rate of sedimentation is increased in the blood during pregnancy. Thus in one case, under similar conditions, the rate of sedimentation in a man’s blood

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was 2 mm. per hour, and in that of two pregnant women 26 and 45 mm. respectively. If the differences are at least in part due to differences in the degree of the negative charge, then this ought to be capable of demonstration by determining the amount of cations which requires to be added to neutralise the charge and cause rapid agglutination and sedimentation. It was found that a concentration of m/500 of a salt of lanthanum was required to neutralise the charge in the man's blood cells, while m/750 was sufficient in the case of the first pregnant woman and m/1250 in the second case.

*The permeability of the red cells and the exchange between them and the plasma.* – Under normal conditions the cells are permeable for anions, not for cations, but by the careful addition of the electro-negative ion OH, the negative charge on the surface of the cells may be increased so that now cations with their positive charge begin to pass through.

Nothing is more striking than the constancy of the composition of the normal blood. Neither by increased water intake or output can the specific gravity be altered, and the reaction remains so steady that on passing from arterial to venous blood, although carbonic acid enters, it is, almost impossible to detect a change in the alkalinity. This difficulty is not due to lack of refinement in experimental procedure. The reaction is kept steady by a mechanism which prevents it going to the acid side.

When carbonic acid enters the blood, it reacts with the sodium chloride to form traces of HCl and NaHCO<sub>3</sub>. The red cells allow the H + and the Cl – to pass through their capsules while the NaHCO<sub>3</sub> remains in the plasma and the alkalinity of the plasma is thus maintained. The carbonic acid (H<sub>2</sub>CO<sub>3</sub>) also reacts in part with the alkaline salts of the proteins and forms bicarbonate, and the excess H<sub>2</sub>CO<sub>3</sub> passes into the red cells. The effects of a rise in the carbonic acid content of the blood is shown in the following tables more fully.

Plasma		Red Cell Wall
(1) H <sub>2</sub> CO <sub>3</sub> + NaCl = NaHCO <sub>3</sub> + HCl →		HCl
(2) H <sub>2</sub> CO <sub>3</sub> + Na Proteinate = NaHCO <sub>3</sub> + H. Proteinate →		H <sub>2</sub> CO <sub>3</sub>
Red Cell Wall	Red Cell Contents	
HCl	→ { HCl + K <sub>2</sub> HPO <sub>4</sub> = KH <sub>2</sub> PO <sub>4</sub> + KCl HCl + KHbO = HHbO + KCl HCl + KHb = HHb + KCl	
H <sub>2</sub> CO <sub>3</sub>	→ H <sub>2</sub> CO <sub>3</sub> + K <sub>2</sub> HPO <sub>4</sub> = KH <sub>2</sub> PO <sub>4</sub> + KHCO <sub>2</sub> etc.	

The actual differences in the Cl and HCO<sub>3</sub> content of arterial and venous blood are shown in the following table, numbers referring to millimolar concentrations.

	ARTERIAL		VENOUS	
	Serum	Cells	Serum	Cells
Cl	59.59	20.41	58.45	21.55
HCO <sub>3</sub>	15.23	5.21	16.46	6.06

It is evident that the bicarbonate (HCO<sub>3</sub>) concentration is higher in venous than in arterial blood, while the chloride concentration is lower in the serum of venous blood than in that of arterial. The relative amounts of oxyhaemoglobin and haemoglobin in the blood also play a part in the adjustment of the reaction of the blood. Oxyhaemoglobin, being a stronger acid than haemoglobin, parts with the base, which it holds in salt form, less readily to a weak acid like carbonic acid than the haemoglobin does. Therefore in the tissues, when oxygen leaves the capillary blood and oxyhaemoglobin is changed in part into haemoglobin, carbonic acid, on entering the blood from the tissues, more readily secures base from the latter than the former. The alkali reserve of the blood in the form of bicarbonate is therefore kept up. The body possesses many other mechanisms which are concerned in keeping blood reaction steady. To take one example, a rise in carbonic acid stimulates the respiratory centre to act more strongly, breathing rate and amplitude are increased, and excess carbonic acid is thus removed from the blood in the pulmonary capillaries. The steadiness of the blood reaction is dependent upon the constancy of the ratio

$$\frac{\text{CO}_2}{\text{HCO}_3}$$

Both values may be below the normal, but so long as the normal ratio is maintained the reaction is unaltered – a compensated acidosis. There may, however, be an uncompensated fall in the bicarbonate or rise in the carbonic acid, and the condition becomes an uncompensated acidosis. For example, in diabetes the bicarbonate concentration (alkali reserve) may be much below normal and yet the reaction remain unaltered because the carbonic acid is proportionately lowered. This compensation fails in

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diabetic coma, when the reaction of the blood becomes less alkaline than normal from the bicarbonate concentration falling more than the carbonic acid. In tetany there is an uncompensated excess in alkali.

Our present-day knowledge of the physico-chemical adjustments of the body, meagre though it may be, is based upon numerous important investigations carried out within a comparatively short period. We may hope that with the rapid advance in our knowledge of the non-living material world, there may also be an advance, doubtless a much slower one, in the domain of the living one.