fusion. Considering, however, all the evidence up to the present time, it seems probable that even in man the placenta does furnish some regulatory activity, while in some of the more complex types this control is much more elaborate.

These results with sodium ferrocyanide and iron ammonium citrate considered in connection with those of Römer and Wislocki indicate the advisability of extending, as far as possible, the investigation of each type of substance to as wide a group of different placental barriers as possible. This seems especially important in regard to those investigations involving the careful chemical estimation of the normal constituents of maternal and foetal bloods which so far have been studied chiefly in the human.

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Carbon dioxide and the HCO_3 ion as specific respiratory stimulants.

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It has been noted by Howell, Collip, Dale and Evans, the author and others that the intravenous injection of sodium bicarbonate may act as either a respiratory or circulatory stimulant, eliciting hypernea or a marked rise in the blood pressure. Such injection obviously increases the hydrogen ion concentration of the blood and inasmuch as it produces a slight dilution, it decreases the amount of carbon dioxide in the blood eliciting the stimulation. The increased respiration is, therefore contrary to the usually accepted laws of respiration. The only apparent change in the blood which might elicit stimulation is the greatly increased number of HCO_3 ions. Collip, therefore, suggests that the HCO_3 ion exerts a specific stimulating action on the respiratory center.

We believe, however, that this anomalous result may be otherwise explained. When the carbon dioxide is dissolved in water it exists primarily in three forms—dissolved CO_2 molecules, dissolved undissociated H_2CO_3 molecules and dissociated H_2CO_3—thus $CO_2 \rightleftarrows H_2CO_3 \rightleftarrows$ H HCO_3. Addition of sodium bicarbonate to the solution pushes the reaction to the left increasing both the dissolved CO_2 and the undissociated H_2CO_3. If we accept the view that the dissolved CO_2 and the undissociated H_2CO_3 diffuse freely into cells while the ions as such do not penetrate to any appreciable extent it is apparent that the injection of sodium bicarbonate increases the freely diffusable forms of carbon dioxide at the expense of the poorly diffusible ions and in that way increases the acid effects of the blood, at least on the interior of the cells (and possibly in the lymph bathing the cells as will be discussed in a later paper) even though the actual sum total of the original dissolved carbon dioxide in its various forms is not increased and the hydrogen ion concentrate of the blood is actually decreased. This alone should result in the diffusion of carbon dioxide against a positive gradient. That is, the injection of sodium bicarbonate should theoretically tend to produce acidosis along with alkalemia by the accumulation of carbon dioxide in the tissues. The hyperpnea, the rise in blood pressure and the shortening of apnea artificially produced by forced ventilation suggests that a slight degree of acidosis is actually produced.

But this view neglects entirely the effects of the H and HCO_3 ions. The justification of this perhaps might be questioned. In so far as lactic acid appears to diffuse in the dissociated condition from the tissues to the blood there appears to be no reason why the dissociated carbonic acid should not also diffuse.

Arrhenius showed that the addition of a salt to a solution of its acid increased the diffusion of the acid into water solution, for example the addition of sodium chloride to a solution of hydrochloric acid increases the rate of diffusion of hydrochloric acid. The phenomenon depends on the increase of the common anion, Cl and the relative mobility of the cation H and Na.

By means of a simple diffusion experiment without the aid of a membrane and with the use of indicators the diffusion of acid from a point of lower concentration to a point of higher concentration can be demonstrated to occur within a few seconds. This prenomenon would appear to be of considerable significance.

It is obvious that the conditions are somewhat different in the case of a weak acid such as carbonic acid and its salt, sodium bicarbonate. Carbon dioxide occurs in solution in three forms and the relative amounts are varied by the addition of sodium bicarbonate. Though the acid effects of the solution on the interiors of cells placed in such solution are theoretically increased by the increase in the freely diffusible CO_2 and H_2CO_3 molecules, the number of free hydrogen ions is diminished. Yet the effectiveness of these ions is greatly increased by the increase in the common anion HCO_3. If a differential barrier, impeding the migration of the sodium ion, exists between the blood and site of action of the hydrogen ion in the respiratory center a double mechanism exists for the passage of carbon dioxide from the point of low to a point of high concentration accompanied by increased acidity. Michaelis calls attention to the fact that H and OH ions are adsorbed at phase boundaries more than other ions and also that the addition of salts to solution of acids or bases increases this adsorption. This phenomenon should also be carefully considered in relation to the hydrogen ion concentration at the site of stimulation. We hope to show in a later paper the relative importance of the various salt effects of sodium bicarbonate.

In connection with the specificity of carbon dioxide, we have by means of simple diffusion experiments without the aid of a membrane demonstrated striking effects on the hydrogen ion concentration of carbonate buffer solutions on each other, dependent solely on the differences in concentration of carbon dioxide and sodium bicarbonate and their relative rates of diffusion. A relatively alkaline solution of high carbon dioxide tension exerts an acid effect even on a relatively acid solution of lower carbon dioxide tension. The results are comparable to those obtained by Jacobs in the living cell and in the model cell with a lipoid solvent membrane. Our results, however, since they are obtained without a membrane are independent of any peculiar property of the cell membrane. They suggest the possible significance of the relative rates of diffusion, of the numerator and the denominator of the buffer mixture not only in buffer solutions outside the cell, but possibly inside as well.

As Fletcher and Hopkins have shown that the rate of escape of carbon dioxide from saturated living muscle, dead muscle, egg albumin and water follows a similar curve, our experiments further suggest that the acid effects of alkaline buffer solutions with high carbon dioxide tension on living cells depend rather on the relative impermeability of the membrane to the metallic cations preventing free entrance of the sodium bicarbonate than on a specific solubility of carbon dioxide in the cell membrane.

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The mechanism of serum fastness.

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Soon after the discovery of the agglutinins it was observed that some strains of a given microorganism were not agglutinated by a specific immune serum. Such non-agglutinable strains are said to be serum fast. The mechanism of serum fastness is not well understood. Ehrlich's explanation of this phenomenon on the basis of suppressed receptors does enable us to visualize the condition, but a suppression of receptors is probably far from what actually takes place.

In our studies[1] on pellicle formation it has been shown that pellicle forming bacteria are rich in acetone-ether soluble substances. Bacteria which ordinarily do not grow in pellicle were caused to do so by growing them in broth to which had been added glycerine or carbohydrates which they did not ferment. By growing the staphylococcus on glycerine broth for a few generations it began to grow in a pellicle, and finally formed as

[1] *Jour. Inf. Dis.*, 1922, xxxi, 407-415.