SCIENTIFIC PROCEEDINGS.

Vol. XXVI. October, 1928. No. 1.

4106

Relation Between Colloid Osmotic Pressure and Concentration of Serum Proteins.

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Since the initial communication of Starling,[1,2] it has been established that the serum proteins exert an osmotic pressure. The same investigator showed later that the colloid osmotic pressure is approximately proportional to the concentration of protein in the serum. It has been found that as serum is diluted the colloid osmotic pressure falls more sharply than does the concentration of the serum proteins. Verney[3] believes that the explanation of this phenomenon is to be found in the comparatively large molecular volume occupied by the colloidal particles, the line of reasoning being analagous to that employed in deriving the pressure-volume relationship of highly compressed gases. He finds that, where p is the colloid osmotic pressure of the proteins, v the reciprocal of the protein concentration, b is a constant depending on the particular conditions, the formula $p(v—b) = k$ holds for dilutions up to 50% of that of normal serum. Thus he finds that the colloid osmotic pressure of the serum proteins varies with their dilution, within definite limits, in the manner that would be expected of an unionized colloidal solution in which the colloidal particles occupy an effective volume as large as 50% of the original.

It is thus known that the colloid osmotic pressure of the serum per gm. of protein becomes lower, the less the actual concentration of the protein in the serum. If we assume that the rate of change of the colloid osmotic pressure with respect to the concen-

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[1] Starling, *J. Physiol.*, 1896, xix, 312.

[2] Starling, *J. Physiol.*, 1899, xxiv, 317.

[3] Verney, *J. Physiol.*, 1926, lvi, 319.

tration of the protein is proportional to the actual colloid osmotic pressure, we have the differential equation

$$\frac{dp}{dv} = ap$$

where p is the reciprocal of the colloid osmotic pressure and v is the reciprocal of the protein concentration. Separating the variables and integrating

$$\pm a.dv = \int \frac{dp}{p}$$

$$\log p = av$$

$$p = e^{av}$$

where a is a constant, dependent on the initial concentration of protein in the normal serum. We have found this constant in human serum to have a value of 0.75. Applying this constant to the data obtained in our experiments (Table I), as well as that contained in the publications of Mayrs,[4] Krogh,[5] and Verney,[3] the agreement between the calculated values and those ascertained experimentally is striking.

TABLE I.
Relation of protein concentration to osmotic pressure.

Gm. protein in 10 cc. serum	Osmotic pressure Cm/100	v	p	$p = e^{av}$ av. calculated	$p = e^{av}$ av. measured
.721	.353	1.39	2.83	1.04	1.05
.639	.301	1.58	3.35	1.19	1.21
.577	.283	1.72	3.53	1.29	1.26
.505	.219	1.98	4.57	1.49	1.52
.432	.169	2.31	5.93	1.73	1.78
.361	.106	2.78	8.42	2.09	2.13
.289	.075	3.27	13.46	2.60	2.60
.216	.029	4.64	35.1	3.48	3.57

It is to be emphasized that the formula derived above can be utilized only for the calculation of the colloid osmotic pressure of successive dilutions of one and the same serum. It would seem that it cannot be used for the estimation of the colloid osmotic pressure of pathologic sera, in which, in addition to diminution of total protein concentration there is an abnormal relationship between the individual protein fractions.

Summary: The relationship between the concentration of protein in the serum and the osmotic pressure may be expressed by $p = e^{av}$

[4] Mayrs, *Quar. Med. J.*, 1925, xix, 285.

[5] Krogh, *Biochem. Z.*, 1927, clxxxviii, 255.

where p is the reciprocal of the osmotic pressure and v the reciprocal of the concentration of the proteins, that is, when the proteins decrease in arithmetical progression, the osmotic pressure decreases in geometric progression.

4107

Pupillary Reactions During Ether and Chloroform Anesthesia After Morphine.

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In the course of anesthesia by ether and chloroform in the dog, the pupil dilates at 2 stages, in the period of excitement and in the period of deep narcosis. If there is violent excitement the intermediary constriction is not observed. It is commonly held that the primary dilatation is a reflex phenomenon (inhibition of the oculomotor or stimulation of the sympathetic or both). There is no clear statement, however, whether the dilatation of the pupil in the stage of deep narcosis is the result of asphyxia or the direct effect of the anesthetic. While studying the response of the vagus nerve to morphine during ether and chloroform anesthesia, it was observed that in deep ether narcosis, the pupils of the dog under the influence of morphine were widely dilated, while in deep chloroform narcosis under the same conditions, the pupils were constricted. These observations seemed of interest in their bearing upon the mechanism of the pupillary changes produced by ether and chloroform. Twelve experiments were then performed to check and extend these observations and the results are the subject of the present report.

Ether and chloroform were administered by inhalation with the open cone method. The pupils were measured under constant conditions of light for any given experiment. Both eyes were examined; the pupils were found equal in all except one instance. Electrocardiographic records of the heart rate were taken at frequent intervals, making it possible in this way to correlate simultaneous effects upon the vagus and oculomotor nerves. The condensed protocols of the experiments with 2 dogs serve to illustrate the general results. The size of the pupils is expressed in percentage of the diameter of the iris. The stage of anesthesia is designated as "light" when voluntary movements as well as corneal conjunctival reflexes are present; as "deep" when these have disappeared; as "partial re-