mation of a bothersome turbidity that developed when benzene was used. Any slight turbidity appearing upon the addition of water to the solution of the residue dissolved in ethyl alcohol either disappeared during the reduction process or was removed by filtration.

Approximately 250 separate analyses were made during the course of the experiment. At no time was any parathion found in the milk from any of the cows fed parathion. Biological assays of the milk from the parathion-fed cows, using adult houseflies (*Musca domestica* L.) were conducted, and the absence of mortality among the flies served to confirm the negative analytical findings. No objectionable flavor was noted in the milk of the cows fed parathion, and no harmful effects to the health of the cows have been observed.

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A Rational Method for Calculating Colloid Osmotic Pressure of Serum

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The usual equation for calculating the osmotic pressure of a solution is:

$$\pi = CRT \qquad (1)$$

in which π is the osmotic pressure, T is the absolute temperature, R is the ideal gas constant, and C is the concentration of the solution in moles of solute per liter.

Capillary endothelium is a dialyzing membrane permeable to ordinary ions but not to a colloid or its ion. Within the capillary is blood serum, and outside of it is interstitial fluid.

The symbols y and $y+z$ are respectively the sum of nonprotein anion and cation normalities in blood serum, and x the same for interstitial fluid. The normality of the serum protein is z, and n its valence. According to the Donnan equilibrium relation (*4*),

$$x^2 = y(y+z). \qquad (2)$$

Because of the complexity added by consideration of bivalent ions (*9*), their low concentration, and consequently, the small scale of their effect, we omit them from this discussion. The observed pressure of equilibrium is the difference between the total osmotic pressures of the two solutions (*10*), or

$$\pi = RT(z + z/n + 2y - 2x). \qquad (3)$$

[1] The suggestion of this problem by Joseph B. Kirsner is gratefully acknowledged. This paper was written while the author was with the Frank Billings Medical Clinic, Department of Medicine, University of Chicago.

The symbol π represents in equation (3) what is generally called the colloid osmotic pressure. Putting the expression for x obtained from equation (2) into (3), we have

$$\pi = RT[z + z/n + 2y - 2\sqrt{y(y+z)}]. \qquad (4)$$

Since albumin and globulin are the components of serum protein, let

$$z = z_A + z_G,$$

where z_A is the molarity of albumin and z_G the same for globulin. If the law of partial pressures applies,

$$\pi = RT[z_A/n + z_G/n + z_A + z_G + 2y - 2\sqrt{y(y + z_A + z_G)}]. \qquad (5)$$

In order to use equation (5), molecular weights for globulin and albumin as determined by ultracentrifugation (*2, 3, 5, 16*) may be utilized, choosing 70,000 for albumin and an average value of 165,000 for globulin. Because protein is a titratable anion, it has been possible to determine the amount of alkali necessary to neutralize a specimen of serum protein when the pH of the medium is known (*14*).

The above information is used to formulate the expression for Z below. Let

A = g of albumin per 100 ml of serum,
G = g of globulin per 100 ml of serum,
pH = serum pH,
$[HCO_3^-]$ = mEq./l of serum bicarbonate,
$[Cl^-]$ = mEq./l of serum chloride,
T = temperature in °C + 273,
R = 0.849 liter-mm H_2O/millimole-(°C + 273), and
organic acid (in serum, assuming its acidity due to univalent carboxyl groups) = 6 mEq./l (*7*).

Define

$$Y = 0.849([HCO_3^-] + [Cl^-] + 6) \qquad (6)$$

and

$$Z = 1.061A(\text{pH} - 5.16) + 0.654G(\text{pH} - 4.89). \qquad (7)$$

Then, if P is the colloid osmotic pressure of the serum, we have

$$P = T[0.1212A + 0.0514G + Z + 2Y - 2\sqrt{Y(Y+Z)}]. \qquad (8)$$

Equations (6), (7), and (8) stand in distinction to previously proposed empirical relations derived from curve fitting of a set of experimental data (*1, 6, 8, 12, 17, 18*). Scatchard (*15*) attempted a theoretical derivation, but made an erroneous substitution invalidating his result.

The impression exists that, in order to make a colloid osmotic pressure determination, a direct measurement with an appropriate osmometer should be carried out. To show that for clinical purposes this is not necessary, colloid osmotic pressures calculated with equations (6), (7), and (8) are compared with measured ones in Fig. 1.

If the effect of $[HCO_3^-]$ and $[Cl^-]$ on serum colloid osmotic pressure is known, the effect of serum sodium may readily be determined from the following equation:

$$1.178Z + [HCO_3^-] + [Cl^-] = [Na^+] + 4, \qquad (9)$$

remembering the normal concentrations of the more dilute ions, as well as the original omission of consideration of

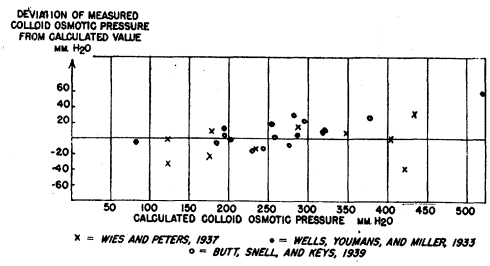

FIG. 1.

bivalent ions from the derivation of (6), (7), and (8). It is obvious that serum sodium varies in the same direction as does $[HCO_3^-] + [Cl^-]$ (or Y).

Taking the partial derivative of P with respect to Y in (8), it is found that

$$\partial P/\partial Y = T[2 - \{\sqrt{Y/(Y+Z)} + \sqrt{(Y+Z)/Y}\}]. \quad (10)$$

It is obvious that $\partial P/\partial Y$ is always negative. In other words, an increase in Y always produces a decrease in P, and a decrease in Y always produces an increase in P.

It is to be noted then that, with all other factors remaining constant, a fall in serum sodium produces a rise in serum colloid osmotic pressure (Fig. 2). This is an

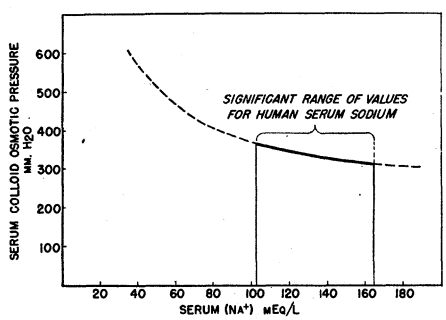

FIG. 2.

observation not previously emphasized and is a consequence of the Donnan equilibrium; it is discussed in more detail elsewhere (*11*). It is interesting in this connection that oral administration of isotonic sodium chloride has been shown to produce a fall in serum colloid osmotic pressure (*13*).

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Decreased "Hunger" but Increased Food Intake Resulting from Hypothalamic Lesions[1]

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A marked increase in food intake, hypothalamic hyperphagia, regularly follows bilateral lesions in the region of the ventromedian nuclei of the hypothalamus. There is no corresponding increase in energy output; the result is obesity. These effects have been produced experimentally in the rat, cat, dog, and monkey; they have been observed as one of the effects of basal brain tumors in man (Froelich's syndrome, or dystrophia adiposogenitalis), and of spontaneous degeneration of the ventromedian nuclei in the mouse.

The literature relating to this problem has been summarized elsewhere (*1, 6*), but since effects of lesions in this area are not generally known they will be listed briefly here. In the rat the diurnal cycle of food intake disappears, being replaced by a relatively constant level. Resection of most of the stomach does not appreciably reduce the hyperphagia. The increased food intake and rapid weight gain (dynamic phase) are not indefinitely maintained; a weight plateau is reached in about 2 months, with food intake gradually falling to a more normal level (static phase). However, after fasting to normal weight, these animals will again show a hyperphagia on return to an ad libitum diet.

Discrete bilateral electrolytic lesions made with the Horsley-Clarke stereotaxic instrument have ruled out direct involvement of the pituitary. In the rat these lesions also cause a marked upset in water balance, as demonstrated by delay in release of water loads, low ratio of water to food intake, and increased renal tubular reabsorption. An increased serum sodium in these animals suggests that a chronic state of relative

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