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Equation for osmotic pressure of serum protein (fractions)

The colloid or protein osmotic pressure (II) is a function of protein molality (linear) and of Donnan and other effects. Albumin is the major osmotic protein, but also globulins influence II. Equations based on concentrations of albumin and nonalbumin (globulin concentration + fibrinogen concentration) protein approximate II better than albumin alone. Globulins have a wide range of molecular weights, and a 1956 diagram indicated that II of globulin fractions decreased in the order α1-, α2-, β-, and γ-globulin. The molecular weight of the serum protein fractions had been extrapolated, so van’t Hoff’s law and nonlinear regression analysis of the curves permitted expression of the diagram as an equation: II = x_{alb} (0.338C_{tot} + 0.00339C_{glob}) + x_{α1} (0.518C_{tot} + 0.0107C_{α1}) + x_{α2} (0.203C_{tot} + 0.00155C_{α2}) + x_{p1} (0.187C_{tot} + 0.000577C_{p1}) + x_{p2} (0.161C_{tot} + 0.000223C_{p2}), where II = osmotic pressure of serum (fractions). The late Arthur C. Guyton published a diagram (4) on (MW) of the molecules (1). The diagram initiated this discussion (5). Two versions were almost consistently slightly lower than computed "Ott" and readings from Ott’s curves. The result is in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

RESULTS

The result is

\[ \Pi_{\text{serum}} \cdot \text{"Ott", } 2°C \cdot \text{cmH}_2\text{O} = x_{alb} (0.518C_{\text{tot}} + 0.0107C_{\text{glob}}) + x_{α1} (0.338C_{\text{tot}} + 0.00339C_{α1}) + x_{α2} (0.203C_{\text{tot}} + 0.00155C_{α2}) + x_{p1} (0.187C_{\text{tot}} + 0.000577C_{p1}) + x_{p2} (0.161C_{\text{tot}} + 0.000223C_{p2}) \]

in which II = osmotic pressure of serum at 2°C (in cmH2O); and x_{alb}, x_{α1}, x_{α2}, x_{p1}, and x_{p2} are the fractions of albumin, α1-, α2-, β-, and γ-globulin, respectively. At one and the same concentration of fractions, II_{"Ott"} decreases in the order α1-globulin, albumin, α2-globulin, β-globulin, and γ-globulin.

Fibrinogen has a higher MW than IgG and should influence II less than γ-globulin, but, as part of plasma total protein, C_{fratio} contributes to II of other proteins (Fig. 1). The error induced by relying on serum instead of plasma should, however, with few

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Clinical errors could be avoided by computing $\Pi_{\text{osm, Ott}}$ at fractionation of serum, a routine investigation. I restrict myself to a few examples of possible implications of $\Pi_{\text{osm, Ott}}$.

Filtration of fluid from plasma driven by capillary pressure ($P_c$) minus tissue pressure ($P_t$; $P_c - P_t = \Delta P$) is rather effectively opposed by $\Pi_1$ minus tissue pressure ($\Delta \Pi_1$) at capillary endothelial small pores, and increase of $\Pi_1$ tends to increase the volume of plasma (3–5). In acute phase reactions, $\Pi_{\text{osm, Ott}}$ increases because many reactants are $\alpha_1$- and $\alpha_2$-globulins (1).

The present author is less competent than Guyton’s (4) followers to evaluate the influence of increase of plasma volume on cardiac output, etc.

In humans, $C_{\text{alb}}$ and concentration of $\gamma$-globulin correlate with their catabolism (3, 7), which takes place outside plasma, and high $\Pi_1$ is believed to downregulate hepatic albumin synthesis (3). Increase of $C_{\text{glob}}$ may be followed by decrease of $C_{\text{alb}}$ in states (3) generally associated with acute phase reactions, but $\Pi_1$ was calculated by an equation based on $C_{\text{tot}}$ and $C_{\text{alb}}$ (3). Might $\Pi_{\text{osm, Ott}}$ (Table 1) add theoretical credibility to findings that indicate autoregulation of $\Pi_1$, also by plasma protein extravasation and catabolism and prove helpful in making decisions about colloid substitution therapy?

The findings in humans could be explained by the fact that there are, in addition to small endothelial pores, very sparse pores so large that they permit passage of most plasma proteins (2, 7) and in which flow is opposed very weakly by $\Delta \Pi$. Increase of $\Pi_1$ and $P_c$ (isogravimetry) and reabsorption by $\Delta \Pi$ of low-protein fluid through small pores have been suggested to enhance large-pore protein convection (Ref. 3 in Ref. 2). In this or other experimental studies on protein transfer familiar to me, little attention is paid to change of $P_c$ at capillary pulsation.

### Table 1. $\Pi_{\text{osm, Ott}}$ at 37°C, in cm H$_2$O, computed from albumin concentration and concentrations (g/l) of globulin fractions, and their sum $C_{\text{tot}}$

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<th>$C_{\alpha_2}$</th>
<th>$C_P$</th>
<th>$C_\gamma$</th>
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*First line shows a clinical average distribution of fractions. Second and third lines show influence of change (in bold) of fraction concentration. $C_{\text{alb}}$, $C_{\alpha_1}$, $C_{\alpha_2}$, $C_P$, $C_\gamma$, and $C_{\text{tot}}$: concentration of albumin, $\alpha_1$-globulin, $\alpha_2$-globulin, $\beta$-globulin, $\gamma$-globulin, and total protein, respectively; $\Pi_{\text{osm, Ott}}$, protein osmotic pressure computed by the equation.

### Fig. 1. Computed protein osmotic pressure at 2°C ($\Pi_{\text{osm, Ott}}$) of solutions of albumin (alb) and globulin fractions ($\alpha_1$, $\alpha_2$, $\beta$, and $\gamma$). The dashed line represents the van’t Hoff part of $\alpha_1$-globulin $\Pi$. When serum $\Pi_1$ is calculated from these diagrams (4, 6), $\Pi_1$ of each fraction is read at the total protein of the sample, that $\Pi$ is multiplied by the percentual (or fractional) concentration of the component, and the sum of the 5 pressures is calculated $\Pi_1$ of the sample (6).

exceptions, be smaller than that caused by omission of the effect of low-MW globulin fractions.

Does $\Pi_{\text{osm, Ott}}$ reflect Ott’s (6) diagram adequately? At $C_{\text{fraction}} > 55$ g/l, Ott’s curves for $\alpha_1$-globulin and albumin seem straight, in contrast to the curves in Guyton’s modified (how?) version (4) of Ott’s diagram. If Ott’s curves were drawn by hand, it may be difficult to find equations that fit them exactly.

The difference between $\Pi_{\text{osm, Ott}}$ of serum fractions and readings from Ott’s (6) diagram was small. Computed $\Pi_{\text{osm, Ott}}$ may agree fairly well with Ott’s data.

Ott’s maximum $\pm 6.7\%$ difference between calculated and measured $\Pi_1$ was reduced to $\pm 4.5\%$ after exclusion of anabuminic and nephrotic sera (6). At strong increase of high ($\alpha_2$- and $\beta$-lipoproteins, IgM) or low (monoclonal Ig heavy chains) MW globulins, the equation over- and underestimates, respectively, measured $\Pi_1$ (6, 7). If Ott’s data are checked, it may be worthwhile to pay attention to the influence of acidosis (5) on fraction $\Pi_1$.

Colloid osmometry has little place in clinical routine. The fact that $C_{\text{alb}}$ is the main determinant of $\Pi_1$ in disease has led to the view (textbooks of clinical chemistry) that $C_{\text{alb}}$ reflects change of $\Pi_1$ in disease. Because of the second-power terms, increase of $C_{\text{glob}}$ (any globulin) increases the osmotic effect of $C_{\text{alb}}$ by increasing $C_{\text{tot}}$ (Fig. 1). In this respect, equations based on $C_{\text{tot}}$ and $C_{\text{alb}}$ (2) are correct. Neither approach indicates that $C_{\text{alb}}$ may be low, despite (because of?) high $\Pi_1$; both ignore the effect of low-MW globulins (Table 1).
of maximal vasodilatation (4), and tissue II and protein catabolism. I have come across no attempts to copy, in intact laboratory animals, human diseases (1, 2) preceded by increase of \( \gamma \)-globulin concentration and associated with increase of \( \alpha \)-globulin concentration and decrease of \( \text{C}{\text{a}}_{\text{lb}} \).

What is relevant may be change of \( \Pi_{\text{Ort}} \) from the individual’s average in health. In Ott’s clinical series, a \( \Pi_{52^\circ \text{C}} > 40 \text{ cmH}_2\text{O} \) was, however, high (6). Methods for determination of protein are changing, but the changes of \( \text{C}{\text{ fraction}} \) in Table 1 are small compared with many met in clinical work. The clinical value of \( \Pi_{\text{Ort}} \) remains to be established.

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REFERENCES