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Plasma Specific Gravity and Control of Fluid Administration in Artificial Fever.*

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Studies on plasma-specific gravity by Moore and Van Slyke revealed that a linear relationship exists between the total proteins and the specific gravity of plasma.[1] These observations were originally carried out on normal adult males and females, on patients with nephritis in varying degrees of edema and dehydrated individuals.

Table I represents a new classification derived from many of their original ranges, and the results of over 1,000 determinations by us in similar types of patients.[1, 2] The application of this table is thus made available to the control of fluid administration. We have been able to show that the relative amounts of dehydration and hydration can be accurately estimated by determination of plasma specific gravity. The need for estimation of adequate fluid balance in artificial fever therapy has long been wanting. The results of our observations illustrate that by this method one can accurately control the body fluid needs.

In over 50 normal adult males and females the plasma levels remained in the range of 1.0255-1.0288. The highest reading in dehydration thus far obtained was 1.0328 shortly after which the patient died. The lowest reading obtained was 1.0169 in a case of terminal nephritis.

The blood, 5 cc in amount, is obtained from the patient's ante-

TABLE I.†

Classification	Plasma Specific Gravity	Total Proteins
Dehydration	>1.0288	>7.5
Normal	1.0255-1.0288	6.3-7.5
Low Normal and Overhydration	1.0235-1.0255	5.6-6.3
Threshold Levels (at which edema may appear)	1.0227-1.0235	5.3-5.6
Edema	<1.0227	<5.3

† A problem now under investigation reveals that an important seasonal variation exists, which will be dealt with in a later paper.

* Appreciation is extended to Drs. Stafford L. Warren and Nathaniel Jones for their advice and cooperation in this investigation.

1 Moore, N. S., and Van Slyke, D. D., *J. Clin. Invest.*, 1930, **8**, 337.

2 Peters, J. P., and Van Slyke, D. D., *Quant. Clin. Chem.*, **1**, pp. 662, 682.

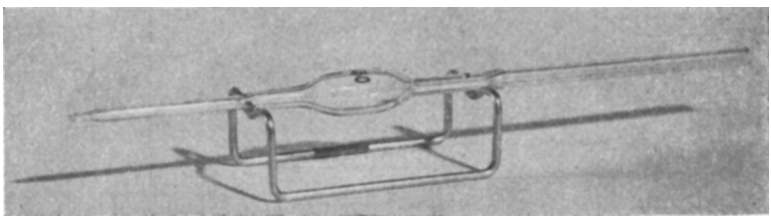

FIG. 1.
A 1 cc plasma pipette.

cubital vein without stasis to avoid increasing the plasma protein concentration.[3] This is delivered to a bottle containing a mixture of 4 mg of potassium oxalate and 6 mg of ammonium oxalate. This anticoagulant assures stability in the size of the red blood cells by eliminating fluid interchange and hemolysis. The blood is then centrifuged at 2200 revolutions per minute for 3 to 4 minutes.[4] Plasma rather than serum is used to include the weight of fibrinogen. These precautions thus reduce sources of error in blood collection.[5]

The method employed in this experiment is of the gravimetric type using special weighing pipettes.[6]

They much resemble blood pipettes and have volumes of 1 cc and 0.5 cc. Each has an outlet which measures .0002 cm^3 in diameter. The fluid once measured to the meniscus will remain there, since the narrow outlet becomes partly sealed by coagulation, and the fluid column immobilized by capillary adhesive forces as well. Once the level has been reached the pipettes may be inverted, tilted, and left for reasonably long periods of time without changes in weight or meniscus, since errors due to evaporation and mechanical loss are eliminated.

The plasma-filled pipette is then weighed and recorded to the fourth place. The temperature of the plasma is taken while the filled pipette is being weighed. The pipettes are cleaned and dried by suction with water and acetone, but not ether.

Calculations.

Formula:

$$\frac{\text{Weight of Plasma in Pipette} \pm \frac{\text{Capacity of Container in cc}}{2} \times \text{Temperature Factor}}{\text{Weight of Distilled Water in Pipette at } 20^\circ} =$$

Plasma Specific Gravity.

The temperature correction factor to be added for readings above 20°C and subtracted for readings below 20°C.

[3] Rowe, A. H., *J. Lab. and Clin. Med.*, 1915-1916, **1**, 485.

[4] Heller, V. G., and Paul, Henry, *J. Lab. and Clin. Med.*, 1934, **19**, 777.

[5] Peters, J. P., Eisenman, A. J., and Bulger, H. H., *J. Clin. Invest.*, 1925, **1**, 435.

[6] Pregl, *Wiener Klinische Wochenschrift*, 1925, **38**, 663.

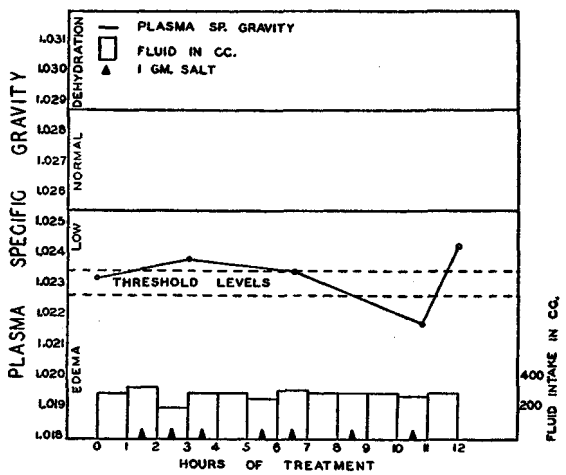

FIG. 2.

This patient was a 37-year-old woman with general paresis treated for 12 hours at 41.5°C. The plasma levels remained in the overhydration range and for several hours during treatment gross edema was present. A total of 3550 cc of water and 7 g of salt were used.

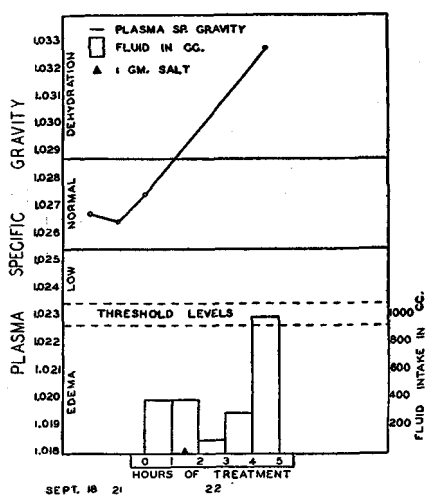

FIG. 3.

This patient was a 45-year-old man treated for general paresis at 41.5°C. Since his fluids were poorly stored, the dehydration factor constituted the major problem here. Just after the temperature reached 41.5°C, the patient's condition became critical with ensuing collapse, and coma, after which he expired. A total of 2100 cc of water and 1 g of salt was used.

The weight of the dry, clean pipette is subtracted, in the above formula, from the plasma-filled pipette. Since the volume is stationary, only plasma need be weighed, except for necessary periodic restand-

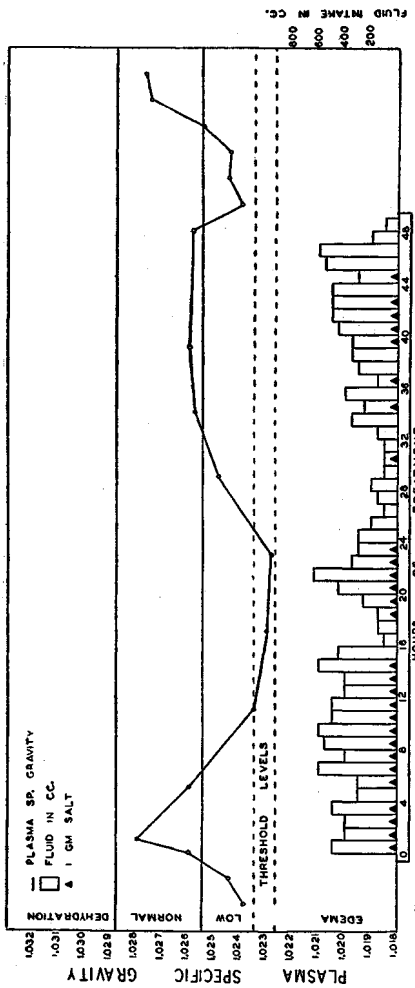

Fig. 4.

This case represents a 23-year-old man, treated for 48 hours at 39.5°C for infectious arthritis. Fluid and salt administrations were increased and decreased at various intervals as indicated. Dehydration never became a factor in this controlled case. Early signs of overhydration and edema between the twentieth and twenty-fourth hour were signals for reduction of fluids and salts. From this period on normal ranges were entered and maintained with a maximum of comfort for the patient. General condition excellent at the end of treatment.

ardizations with distilled water to check changes following cleaning processes.

The capacity of the pipette can be obtained directly from the weight of distilled water as recorded in Landolt and Börnstein's Tabellen.[7] The temperature factor is obtained from the graph in Peters and Van Slyke,[7] which corrects to 20°C in terms of which all values are expressed. The total protein content of plasma may then be computed from the specific gravity by the formula:

[7] Total Protein/100 cc plasma = (343 × (Sp.gr. — 1.007).

This method has been selected because of its simplicity and greater

[7] Peters, J. P., and Van Slyke, D. D., *Quant. Clin. Chem.*, **2** Methods, pp. 5, 690, 691.

accuracy. As compared with Kagan's[8] modification of Barbour and Hamilton's[9] falling drop method for the determination of plasma specific gravity, we have found that an entire series of determinations can be done with greater accuracy and rapidity. This method eliminates the use of nomograms, except for temperature correction, and the chance of error in timing of drops and controlling of standards.

This method of estimating body fluid status has been applied successfully to patients during artificial fever therapy. Figs. 2 and 3 reveal situations which were encountered before specific gravity was routinely measured and the fluid administration regulated by its interpretation. The data from Figs. 2 and 3 represent the extremes of a series of cases during the fall of 1938. No analyses or interpretations of the first few cases were made until a sufficient number had been obtained. Thus fluid regulation was not controlled in these early cases by this gravimetric method. Fig. 4 is that of a prolonged 48-hour treatment and indicates how well adequate hydration can be controlled by repeated determinations. In this case an endeavor was made to keep the specific gravity as nearly as possible at 1.0255.

Conclusions. 1. The use of special gravimetric pipettes introduces a new, rapid and accurate method for determining plasma specific gravity. 2. The measurement of specific gravity in artificial fever assures proper regulation of body fluid balance and eliminates the dangers of dehydration and over-hydration during the course of treatment. Many of the hazards of this form of therapy are thus reduced when proper levels are maintained or, in difficult situations, the treatment is stopped.

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[8] Kagan, B. M., *J. Clin. Invest.*, 1938, **17**, 369.

[9] Barbour, H. G., and Hamilton, W. F., *J. Biol. Chem.*, 1926, **69**, 625.