The Estimation of Protein in the Cerebrospinal Fluid Using the M.R.C. Photometer

J. G. ALEXANDER AND J. PARKES

From the Department of Pathology, Western General Hospital, Hull

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In the communication by Yeoman (1955) it is stated that the proportion of cerebrospinal fluid to 3% aqueous salicylsulphonic acid is one to three when used to determine the protein content in the M.R.C. photometer. This method has been studied by comparing results using his method and results obtained by the micro-Kjeldahl method (King, 1951) on the same specimens. Twenty specimens were examined in which the levels were representative of all levels found in practice, i.e., normal, moderate increase, and marked increase. The results showed that the M.R.C. photometer method was fairly accurate if 1 ml. of cerebrospinal fluid was added to 4 ml. (not 3 ml.) of 3% salicylsulphonic acid. One of us (J. G. A.) communicated with Dr. Yeoman and he agreed that the proportions should have been one to four and not one to three. It was found, however, that the true protein level (x) was slightly higher than the reading on the photometer (y), the two being related by the equation $x = \frac{16y + 20}{15}$

When the protein concentration exceeds 120 mg./100 ml. it is necessary to dilute the cerebrospinal fluid with water because the curve is no longer linear above this value. The use of saline as a diluent gives increased readings.

REFERENCES

- King, E. J. (1951). *Micro-Analysis in Medical Biochemistry*, 2nd ed., p. 46. Churchill, London.
 Yeoman, W. B. (1955). *J. clin. Path.*, **8**, 252.

The "Normal Range" of the Prothrombin Time Estimated by Quick's Method

G. I. C. INGRAM AND P. ARMITAGE

From the Louis Jenner Laboratory, St. Thomas's Hospital and Medical School, and the Medical Research Council's Statistical Research Unit, London School of Hygiene and Tropical Medicine

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Armitage and Ingram (1958) have recently investigated some errors affecting Quick's prothrombin time. They found that the differences between the prothrombin times of normal persons were much greater than could be explained by the experimental error of the method, and that it was possible to devise a simple rule of thumb to express the amount by which a given "control" plasma might be expected to differ from another normal plasma.

Prothrombin times were measured on 56 differing pairs of normal plasmas, with four replicate readings from each sample. The standard deviation of the difference between mean times for the paired subjects was about 9% of the average of the prothrombin times of the pair. Experimental error would have contributed only some 2% to this figure, or rather less than one-quarter of the total standard deviation. A reduction in the number of replicate readings made on the two samples will appreciably increase the contribution of experimental error, but will not greatly increase the total standard deviation, which can therefore be taken to be about 9% of the average prothrombin time, irrespective of the number of readings. Had only two replicate readings been obtained instead of four, the error contribution would have risen only to 3% of the average prothrombin time, or one-third of the total standard deviation, in the above experiments.

This means, for example, that in 95 cases out of 100 two normal prothrombin times will differ by less than about $2 \times 9\%$, or say *one-fifth* of their average (the rule is expressed in this way to be independent of the activity of the brain extract). In the control of anticoagulants, such small differences are clearly of no importance, but in the study of bleeding disorders and as a precautionary investigation, e.g., before needle biopsy of viscera, it may on occasion be useful to test borderline cases in this way.

It can usually be assumed that the patient's prothrombin time will differ materially from the control, if at all, only in one direction, e.g., it is often of no consequence if the patient's time is shorter than the control time. In this situation it may be said that only about once in 40 times, i.e., 2.5 times out of 100, should a normal prothrombin time exceed the control