

Measurement of "Extracellular Fluid Space" In Infants by Equilibration Technic Using Inulin and Sodium Ferrocyanide. (18761)

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"Extracellular fluid space" has been measured in adult man by Gaudino, *et al.*(1) and others(2) using inulin. These authors point out that inulin defines a smaller and probably more exact "extracellular space" than does thiocyanate, sucrose, mannitol, chloride, bromide, sulfate, and sodium. Levitt and Gaudino(3) in describing the method used in adults emphasize the need for complete urinary collection of the injected inulin in order to obtain reliable results. Using this technic 10 to 18 hours are required for the determination of the "extracellular space". To estimate the "extracellular fluid space" in sick infants it is desirable to employ a test which can be completed in a shorter period of time.

It would appear obvious that if one subtracted the amount of inulin excreted from the beginning of the injection to the end of equilibration period from the total amount given, the difference would represent the amount of inulin diffused throughout the "extracellular fluid space", and that from the estimation of the plasma level at this point one should be able to calculate the size of the "extracellular fluid space." Levitt and Gaudino(3) point out that this use of the equilibration period to estimate the inulin space would give unreliable results. This is not in agreement with the data presented below. The following data collected in 6 infants 9 days to 14 months of age with varying, severe congenital defects involving the central nervous system show a good correlation of "inulin" space when estimated both at the equilibration period and after collection of totally excreted

inulin, thus making the test more applicable in the study of sick infants. In a group of these infants, sodium ferrocyanide at low plasma levels (5.5 to 12 mg %) was used simultaneously to measure the "extracellular fluid space". At these levels of plasma ferrocyanide (Table I) we found no urinary evidence of renal toxicity. However, Miller and Winkler(4) found such evidence with the use of sodium ferrocyanide in adults. In most of their cases the plasma level of ferrocyanide was higher than those obtained in our infants. This substance was chosen because of its smaller molecular size and with the thought that it would reach equilibration more rapidly than does inulin and therefore shorten the time necessary to measure the "extracellular fluid space". It may, therefore, be a more effective agent in measuring this space in the presence of edema. However, its exact toxicity is not established(5).

Methods. A 5% glucose solution containing 1% inulin and .01% sodium ferrocyanide is given as a constant intravenous infusion at the rate of 0.75 to 1.0 cc per minute. Equilibration was defined as the period when a constant plasma level was obtained. In these studies at least 3 identical plasma levels over a period of 30 to 45 minutes indicated that equilibration had taken place. Equilibration in these small infants was usually obtained for inulin within 2 hours and for sodium ferrocyanide within 45 minutes. The infusion was discontinued at the end of the equilibration period. Inulin was determined by Harrison's (6) modification of the method of Hubbard and Loomis(7). The ferrocyanide method of

1. Gaudino, M., Schwartz, I. L., and Levitt, M. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1948, v68, 507.

2. Schwartz, I. L., Schachter, D., and Freinkel, N., *J. Clin. Invest.*, 1949, v28, 1117.

3. Levitt, M. F., and Gaudino, M., *Am. J. Med.*, 1950, v9, 208.

4. Miller, B. J., and Winkler, A., *J. Clin. Invest.*, 1936, v15, 489.

5. Stieglitz, E. J., and Knight, A. A., *J.A.M.A.*, 1934, v103, 1760.

6. Harrison, H. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1942, v49, 111.

COMPARATIVE TIME OF EQUILIBRATION OF INULIN AND SODIUM FERROCYANIDE

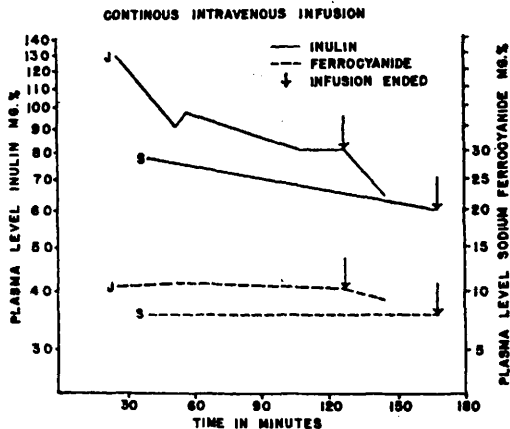


FIG. 1.

COMPARATIVE CLEARANCES OF INULIN AND SODIUM FERROCYANIDE

PATIENT	GLOMERULAR FILTRATION RATE CC./MIN. (UNCOR.)		RATIO Na FE / INULIN
	INULIN	Na FERROCY.	
J.			
PERIOD 1	5.5	4.7	0.85
" 2	5.1	4.3	0.84
" 3	4.7	3.9	0.83
S.			
PERIOD 1	7.7	6.4	0.83
" 2	7.8	6.4	0.82
" 3	6.1	5.1	0.83

FIG. 2.

of recovery of both inulin and ferrocyanide attests the validity of space estimation at the equilibration period. The close correlation of space estimation between these two periods for both substances would suggest that the renal "deadspace" in these infants is not a significant factor in estimating "extracellular fluid space".

Fig. 1 shows the relative rates at which inulin and ferrocyanide reach equilibration in

2 infants. The infusions were begun at zero-time and stopped at the time shown by the arrows on the graph. It is apparent that ferrocyanide reaches equilibrium much sooner than does inulin, which might have been expected from its smaller molecular weight, and that the "extracellular fluid space" could be determined more quickly using ferrocyanide than inulin.

Fig. 2 shows comparative rates of glomerular filtration when continuous infusions of inulin and ferrocyanide were given simultaneously in 2 of these infants. The plasma concentrations of arterial blood were used in calculating these clearance values. The inulin clearances are within normal values for the age group(9). The lower clearance values obtained with ferrocyanide, giving a ratio of Fe/In of 0.82 to 0.85, would indicate tubular reabsorption of ferrocyanide as was found in the adult by Miller and Winkler(4) who demonstrated that the ferrocyanide clearance was of the same order of magnitude as the urea clearance.

Summary. A close correlation of "extracellular fluid volume" as measured at equilibration and after collection of totally excreted inulin and sodium ferrocyanide was obtained in infants, thus shortening considerably the time needed for the determination. The ratios between the sodium ferrocyanide and inulin spaces were 0.96 to 1.04. Sodium ferrocyanide equilibrated in a much shorter time than did inulin. The comparative rate of glomerular filtration as measured by inulin and sodium ferrocyanide suggests tubular reabsorption of the latter substance in infants. No evidence of urinary disturbance was found in the infants given sodium ferrocyanide.

9. Rubin, M. I., Bruck, E., and Rapoport, M., *J. Clin. Invest.*, 1949, v28, 1144.

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