INTRODUCTION

Inability to predict the time of occurrence of spontaneous diureses in the nephrotic syndrome has retarded investigations of the physiologic changes which may precede, accompany, and follow these heartening but enigmatic events. It has been demonstrated recently that several agents (1-5) are capable of inducing diureses at a predictable time in a far higher percentage of trials than could be attributed to chance. Adrenocorticotropic hormone (ACTH) is one such agent, and the abrupt, profuse, and sustained diureses which may accompany or follow its administration are clinically similar to the dramatic diureses which occur spontaneously. Clinical observations on the effect of ACTH 4 on a group of children with the nephrotic syndrome is the subject of a separate report (6) in which the possible clinical significance of the results is also discussed. Serial physiologic measurements were made on selected patients before, during, and after administration of ACTH. These observations were directed toward an increased understanding of the syndrome itself and especially of the mechanism of diuresis rather than toward evaluation of possible relationships between the disease and pituitary or adrenocortical function. As an integral part of the approach, an attempt was made to disclose, if possible, consistent changes which might precede the onset of diuresis and, to this end, as many relevant physiologic measurements as practicable were made. These included: blood volume; discrete kidney functions; concentrations of electrolytes and nitrogenous constituents of serum; metabolic balances of electrolytes and nitrogen; serum lipid fractions; and urinary protein and sediment.

It has not been possible from any one or combination of changes to predict when diuresis would occur in relation to administration of ACTH. The most striking changes observed after the outset of diuresis were increases in plasma volume and unexpectedly large increases in glomerular filtration rate (GFR). These changes together with observations on other discrete kidney functions are described in the present paper. Observations on other measurements will be the subject of a subsequent report (7).

SUBJECTS AND METHODS

Observations were made on eight children with the nephrotic syndrome whose clinical status and course during ACTH administration is described in a separate report (6). Clinical data relevant to the observations presented here are included in Table I.

Various combinations of the following measurements
were made before, during, and after administration of ACTH: daily weight; plasma volume and hematocrit; clearances of inulin ($C_{\text{in}}$); endogenous creatinine ($C_{\text{cr}}$); thiosulfate ($C_{\text{THIO}}$) and p-aminohippurate ($C_{\text{PAH}}$); and maximum tubular excretion of PAH ($T_{\text{PAH}}$). In three children (I. C., K. N., J. S.), 24-hour clearances of endogenous creatinine ($C_{\text{cr}-\text{m}}$) were measured. These children were on low salt (20 meq. per day) but otherwise normal diets. Most of the time they were ambulatory and normally active.

Methods for inulin, p-aminohippurate, urea (8) and endogenous creatinine (9), in blood and urine, and the catheterization and infusion technique used for short-term simultaneous clearances have been described (8). Serum and urine thiosulfate concentrations were determined by the method of Newman, Gilman, and Phillips (10). $C_{\text{cr}-\text{m}}$ was calculated using 24-hour creatinine excretion and mid-point serum values interpolated from creatinine determinations made one to three days apart. Plasma volume was measured with T-1824 using a single 10-minute blood sample and the acetone extraction method of Chinard and Eder (11) for lipemic sera. Blood volume was calculated from plasma volume and hematocrit (12).

RESULTS

Changes observed in discrete kidney functions and plasma volume in relation to hormone administration are given in Table I. Data from B. B. and I. C. are shown graphically in Figures 1 and 2.

Glomerular filtration rate

The most striking changes observed during or following diureses associated with ACTH administration were marked increases in $C_{\text{in}}$. Such increases were observed on eight occasions in six of the eight children and were greatest in patients with low initial values. Thus increases in $C_{\text{in}}$ of 179, 211, 190, 50, and 256% above control values were observed respectively in I. C., K. N., B. B., M. L., and S. S. In B. B., this change in $C_{\text{in}}$ represents an increase from 35 to 133% of normal (Figure 1). In the three children whose initial values were within the normal range, measurements of $C_{\text{in}}$ showed no significant increase in two (J. S. and R. T.), but revealed an increase to the high value of 123% of normal in one (R. K.). Failure to observe an increase in $C_{\text{in}}$ following diuresis (as in I. C., February 1) may possibly be due to failure to make the measurement at the proper time as discussed later.

In an attempt to determine when changes in GFR occurred and to follow their course, 24-hour clearances of endogenous creatinine were measured. The ratio of $C_{\text{cr}}$: $C_{\text{in}}$ is irregularly greater than one in children with kidney disease (17). Consequently, repeated short term measurements of this ratio were made to relate changes in the 24-hour clearance to changes in GFR. Even though changes in this ratio were taken into account, $C_{\text{CR}-24}$ was interpreted only as reflecting changes in rather than as an absolute measure of GFR. Despite these reservations, changes in $C_{\text{CR}-24}$ were sufficiently large to demonstrate that GFR increased during the first 24 hours of diuresis, as shown in Figure 2. Additional impressions concerning changes in GFR during and following ACTH administration are gained from inspection of the data from I. C.$^7$

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$^6$ The frequency with which diuresis has been observed with ACTH in children with the nephrotic syndrome is reported separately (6). In this group of eight children, selected because measurements had been made both before and after ACTH, a diuresis failed to occur in only one of 14 courses. This failure occurred when only 50 mg. per day for three and one half days was given to a child (I. C.) who diuresed on three other occasions with larger dosages.

$^7$ Only a small fraction of the observed increases in $C_{\text{in}}$ could be related to increases in rate of urine flow during diuresis.
The decrease in C_{OB-24} seen during the first course of ACTH administration (January 4 to 16) has been observed in other patients and was often associated with a marked rise in serum nitrogen and endogenous creatinine. These changes suggest a temporary fall in GFR during ACTH administration. The low value for C_{IN} measured on February 28, one day after a three day course of ACTH which did not induce diuresis, lends support to this impression. The pattern of changes in C_{OB-24} in Figure 2 suggests that each diuresis was accompanied by an increase in GFR and followed by a decrease from the maximum value with subsequent stabilization at a value slightly or markedly above the control. It is possible that the fall in GFR may already have occurred when C_{IN} was measured on February 1, 1950, since re-accumulation of edema already had begun. Repeated responses to ACTH may, however, be as-

8 C_{OB}, measured simultaneously with C_{IN}, showed a comparable decrease at this time. Failure of C_{OB-N} to reflect this decrease may be partly explained by the inaccuracy of calculating clearances using mid-point values for serum creatinine concentrations interpolated from determinations made on fasting samples taken at intervals of several days (18). C_{OB-N} was consistently higher than C_{OB} which might be expected from the fact that the latter was always measured early in the day with the subject at rest and in a fasting state, whereas the former might be affected by such factors as eating and activity. associated, as shown in Figures 1 and 2, with a progressive increase in GFR to normal (I. C.) or even "supernormal" values (B. B.).

Changes of this order of magnitude in C_{IN} in children with diseased kidneys must raise the question of the validity of C_{IN} as a measure of GFR under these conditions. This question becomes especially pertinent in view of the consistent changes observed in three children (I. C., K. N., and B. B.) in the C_{OR}:C_{IN} ratio which decreased from a range of 1.5 to 1.9 before to a range of 1.0 to 1.4 after diuresis. However, the reasonably good agreement between C_{IN} and C_{THIO} (C_{THIO}: C_{IN} ratios ranging from 0.9 to 1.2) at both decreased and increased values of C_{IN} provides evidence that C_{IN} was a measure of GFR in these children. The changes observed in the C_{OR}:C_{IN} ratio are unexplained at present.

**Effective renal plasma flow (C_{PAH})**

Significant and consistent increases in C_{PAH} were observed to accompany increases in C_{IN} during diureses occurring with ACTH. However, increases in C_{PAH} were consistently less than those in C_{IN} so that in the six children (I. C., K. N., B. B., R. K., M. L., and S. S.) who showed an increase in C_{IN} the C_{IN}:C_{PAH} ratio increased from a range of 0.10 to 0.17 before to a range of 0.22 to 0.32 after diuresis. Whether these changes
| Subject | Date       | Hormone administration | Weight | CIN | CCR | CTHIO | CP | TM | CN/C | CN/CR | CTHIO/TM | Plasma volume | Blood volume | Hematocrit | Comment                                                                 |
|---------|------------|------------------------|--------|-----|-----|--------|----|----|------|-------|----------|----------------|--------------|--------------|------------|---------------------------------------------------------------|
| I.C.    | 12/7/49    |                        | 23.4   | 11.9| 18.0| 12.0   | 77.9| ---| 0.15 | 1.5  | 1.0      |                |              |             |            | Duration of disease—7 mos.                                      |
|         | 2/12       |                        | 24.4   | --- | 18.0|        |     | --- | ---   | ---   | ---      |                |              |             |            | Constant edema since onset with no spontaneous diuresis.       |
| Ht. 96.0 cm. | 12/16-21   | Cortisone 335 mg. (6d) | 24.7-25.2 | --- | --- |        |     | --- | 0.15 | 1.5  | 1.0      |                |              |             |            | Diuresis 15th day after start of therapy (1/19). Minimum weight following diuresis. Outset of reaccumulation of edema. Maximum weight. No diuresis. Diuresis 13th day after start of therapy (3/21). Minimum weight following diuresis. Outset of reaccumulation of edema. Diuresis 15th day after start of therapy (5/26). In apparent clinical remission 12/1/50. |
| Wt. 15.2 kg. | 1/4/50     | ACTH 1000 mg. (13d)   | 21.4-20.9 | --- | --- |        |     | --- | ---   | ---   | ---      |                |              |             |            | Duration of disease—10 mos.                                      |
|         | 1/19       |                        | 20.3   | --- |     |        |     | --- |       | ---   | ---      |                |              |             |            | Constant edema since onset with no spontaneous diuresis.       |
| S.A. 0.62 M² | 1/4-16     | ACTH 350 mg. (3d)     | 18.5-19.1 | --- | --- |        |     | --- |       | ---   | ---      |                |              |             |            | Duration of disease—10 mos.                                      |
|         | 1/24-27    |                        | 19.3   | 10.1| 18.6| 70.9   | --- | --- | 0.14 | 1.8  | ---      | 663            | 1074         | 40.0        |            | Constant edema since onset with no spontaneous diuresis.       |
|         | 5/11-24    | ACTH 687.5 mg. (14d)  | 17.2-20.7 | --- | --- |        |     | --- |       | ---   | ---      | 645            | 904          | 30.0        |            | Duration of disease—10 mos.                                      |
|         | 5/24       |                        | 20.7   | 38.2| 37.5| 33.2   | 106 | --- | 0.36 | 1.0  | ---      |                |              |             |            | Constant edema since onset with no spontaneous diuresis.       |
|         | 5/26       |                        | 20.1   | --- |     |        |     | --- |       | ---   | ---      |                |              |             |            | Duration of disease—10 mos.                                      |
|         | 11/16      |                        | 17.5   | --- |     |        |     | --- |       | ---   | ---      |                |              |             |            | Constant edema since onset with no spontaneous diuresis.       |

Expected normal value

\[
\text{Expected normal value} = \frac{\text{Surface area of child (M²)}}{1.73M²} \times \text{normal adult value corrected to 1.73M².}
\]

Since there is no evidence that a sex difference in renal functions exists in children before puberty, a single normal adult value for each discrete function was used to calculate expected normal values for both boys and girls. These values were arbitrarily taken as the average of mean values for normal men and women (15). Per unit of surface area, values for discrete kidney functions for children of this age are expected to be within the normal adult range (16). Day on which weight loss of 0.2 kg. or greater was first observed and which was followed by continued loss of body weight.
| Subject | Date   | Hormone administration | Weight | C_IN | CCR | C_THIO | C_PAH | T_MPAH | C_IN/ C_PAH | C_CR/ C_IN | C_THIO/ C_IN | C_PAH/ T_MPAH | Plasma volume | Blood volume | Hematocrit | Comment                                                                 |
|---------|--------|------------------------|--------|------|-----|--------|-------|--------|-------------|-------------|--------------|--------------|---------------|----------------|--------------|------------|---------------------------------------------------------------|
| B. B.   | 3/16/50 | ACTH 740 mg. (9d)      | 19.0  | 14.0 | 28.1| 16.2  | 148   | 0.09   | 2.0         | 1.2         |              |              | ml.           | ml.          | %           | Duration of disease—7 mos.                                    |
|         | 3/17   |                        |        |      |     |       |       |        |             |             |              |              |               |              |            | Constant edema since onset with no spontaneous diuresis.       |
|         | 3/17-26 | ACTH 893.8 mg. (25d)   | 18.4  | 15.0 |     |       |       | 0.26   | 1.0         |             |              |              | ml.           | ml.          |            | Diuresis 11th day after start of therapy (3/28).               |
|         | 4/1    |                        |        |      |     |       |       |        |             |             |              |              |               |              |            | Minimum weight following diuresis.                             |
|         | 4/21   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          | 25.6        | Maximum weight.                                                 |
|         | 6/12   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Diuresis 10th day after start of therapy (5/1).                 |
|         | 11/2   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Minimum weight following diuresis.                             |
|         |        | Expected normal value  | 40.5  | 207  |     |       |       | 0.20   |             |             |              |              | ml.           | ml.          |            | in apparent clinical remission 5/9–10/1.                        |
|         |        |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Reaccumulation of edema 10/1/50.                               |
|         |        |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | 13 days ACTH therapy (525 mg.) resulted in diuresis.            |
| J. S.   | 3/29   | ACTH 625 mg. (6jd)     | 15.6  | 15.0 |     |       |       | 0.22   | 1.1         |             |              |              | ml.           | ml.          |            | Duration of disease—2.5 mos.                                   |
|         | 4/11   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | One spontaneous diuresis 4 weeks after onset.                   |
|         | 4/14-20|                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Minimal edema at start of therapy.                             |
|         | 4/21   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Diuresis 8th day after start of therapy (4/22).                 |
|         | 4/22   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Minimum weight following diuresis.                             |
|         | 4/24   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Moderate intermittent peripheral edema 12/1/50.                 |
|         | 5/1    |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            |                                                                 |
| R. K.   | 7/10/50 | ACTH 500 mg. (11d)     | 27.6  | 27.8 |     |       |       | 0.24   | 1.2         |             |              |              | ml.           | ml.          |            | Duration of disease—11 mos.                                    |
|         | 7/11   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | One diuresis in March 1950 following paracentesis.             |
|         | 7/12   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Reaccumulation of edema 4 months later.                         |
|         | 7/12-22|                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Diuresis 11th day after start of therapy (7/23).                |
|         | 7/23   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Minimum weight following diuresis.                             |
|         | 7/27   |                        |        |      |     |       |       |        |             |             |              |              | ml.           | ml.          |            | Reaccumulation of edema and spontaneous diuresis in October and again in November. |
### TABLE I—Continued

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| Subject | Date | Hormone administration | Weight (kg) | CIN (ml per min) | CCR (ml per min) | CTHIO (ml per min) | CPAH (mg per min) | TMPAH (mg per min) | Cl/Cr | CCR/CIN | CTHIO/CIN | CPAH/TMPAH | Plasma volume | Blood volume | Hematocrit | Comment |
|---------|------|------------------------|-------------|------------------|-----------------|-------------------|------------------|------------------|-------|--------|----------|------------|--------------|-------------|------------|----------|---------|
| R. T.   | 1/4/50 | Cortisone 1300 mg. (17d) | 17.5        | 49.4             | -               | -                 | -                | -                | 31.3  | -      | -        | 1.6        | -            | -            | -          | Duration of disease—4 mos. Constant edema since onset with no spontaneous diuresis.
| M. Age 5 yrs. | 1/6-22 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis following Cortisone.
| Ht. 91.5 cm. | 1/16 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
| Wt. 14.1 kg. | 2/20 | Cortisone 575 mg. (8d) | 16.8        | 37.5             | -               | -                 | -                | -                | 34.7  | 0.30   | -        | 1.1        | -            | -            | -          | Diuresis 13th day after start of therapy (4/11). Minimum weight following diuresis.
| S.A. 0.58M² | 3/1-8 | DCA 40 mg. | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | A second course of ACTH therapy (5/22-6/6 920 mg.) induced no diuresis. Generalized edema continues 8/17/50.
|                               | 3/29 | ACTH 880 mg. (11d) | 22.5        | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 4/10 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 4/11 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 4/15 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 5/8  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 5/26 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 6/7  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
| Expected normal value         |      |                        |             |                  |                 |                   |                  |                  |       |        |          |            |              |              |            | No manifest edema 8/17/50.
| M. L.                          | 3/2/50 | ACTH 800 mg. (10d) | 21.4        | 44.2             | -               | -                 | -                | -                | 28.2  | 0.22   | -        | 1.6        | -            | -            | -          | Duration of disease—1 mo. Constant edema with no spontaneous diuresis.
| M. Age 5 yrs.                  | 3/4   | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 3/6-13 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 3/14  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 3/15  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 3/20  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
|                               | 5/22  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis.
| Expected normal value         |      |                        |             |                  |                 |                   |                  |                  |       |        |          |            |              |              |            | No manifest edema 8/17/50.
| S. S.                          | 2/27/50 | Cortisone 400 mg. (7d) | 15.0        | 29.0             | -               | -                 | -                | -                | 16.0  | 0.12   | -        | 1.8        | -            | -            | -          | Duration of disease—15 mos. Constant edema since onset with no spontaneous diuresis.
| M. Age 3.5 yrs.                | 3/2-8  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis after Cortisone.
|                               | 3/9   | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | Diuresis 8th day after start of therapy (4/4). Minimum weight.
| Ht. 94.0 cm.                  | 3/22  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No manifest edema 8/17/50.
| Wt. 14.5 kg.                  | 3/23  | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No manifest edema 8/17/50.
| S.A. 0.60M²                   | 3/27  | ACTH 1040 mg. (13d) | 15.0        | 41.3             | -               | -                 | -                | -                | 40.0  | 0.21   | -        | 3.0        | -            | -            | -          | Duration of disease—15 mos. Constant edema since onset with no spontaneous diuresis.
|                               | 3/23-4/8 | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No diuresis after Cortisone.
|                               | 4/4   | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | Diuresis 8th day after start of therapy (4/4). Minimum weight.
|                               | 4/6   | -                       | -           | -                | -               | -                 | -                | -                | -     | -      | -        | -          | -            | -            | -          | No manifest edema 8/17/50.
in the $C_{IN}:C_{PAH}$ ratio are associated with vascular changes or alterations in the permeability of the glomerular membrane cannot be assessed at present.

**Maximum tubular excretion of PAH**

Increases in $T_{MPAH}$ accompanied increases in $C_{IN}$ in two children (M. L. and S. S.) in whom it was measured before and during diuresis. The changes in $T_{MPAH}$ were less than those in $C_{IN}$ so that the $C_{IN}:T_{MPAH}$ ratios increased from initially low values before to higher values. In the remaining child in whom repeated measurements of $T_{MPAH}$ were made, no change in $C_{IN}$ was observed and the changes in $T_{MPAH}$ were irregular.

**Plasma and blood volume**

Increases in plasma volume during or after diuresis were observed in four out of five children in whom such observations were made. The changes in I. C., K. N., B. B., and J. S. were 29, 17, 26, and 11% respectively, above the control values. Corresponding increases in blood volume in I. C., K. N., and J. S. were observed but the changes were proportionately less because of decreases in hematocrit values. Failure to observe an increase in plasma volume in R. K. may possibly be explained again by a failure to make the measurement at the proper time.

**DISCUSSION**

Prompt increases above initially reduced rates of glomerular filtration are commonly seen during the early stages of acute nephritis in children. On the other hand, reduced clearances in children with the nephrotic syndrome of several months' duration have been interpreted as indicating a less reversible process. The rapid increases in glomerular filtration rate reported here in children who had reduced kidney function and who were given ACTH demonstrate, therefore, a potentiality for improvement in function beyond that commonly considered possible in children with the nephrotic syndrome.

There is no evidence and it is not implied that these results are peculiar to diureses induced by ACTH. Although the magnitude of the changes was somewhat greater than those previously reported with other agents (1, 4, 19), it is entirely possible and probable that quantitatively similar changes may accompany spontaneous or induced diureses.

The results described have no bearing on the question of whether pituitary or adrenal cortical hormones have any direct relationship to the nephrotic syndrome. They do indicate that ACTH administration may induce repeated diureses at predictable times permitting serial measurements of changes which may accompany and be involved in the mechanism of diuresis. Thus large increases in glomerular filtration rate and significant increases in plasma volume were observed during diureses in these children. These observations lend support to the concept (20) that increases in plasma volume and in glomerular filtration rate accompany and may be involved in the mechanism of diuresis in children with the nephrotic syndrome.

**SUMMARY**

Profuse, sustained diureses occurring at predictable times in a high percentage of trials during or following administration of ACTH to children with the nephrotic syndrome permitted observations on changes which may accompany and be involved in the mechanism of diuresis. Serial measurements of discrete kidney functions and plasma volume are reported before, during and after 13 such diureses in eight children. The results indicate:

1. In five children with initially reduced rates of glomerular filtration, increases in inulin clearances ranging from 50 to 256% above control values were observed during or following diureses on five out of six occasions. In three observations on three children with rates of glomerular filtration initially within the normal range, an increase of 54% was observed in one. Thus in nine observations where inulin clearances were measured before and after the outset of diuresis, significant increases were observed in six.

2. Daily 24-hour creatinine clearances, measured in one of the three instances in which no marked increase in inulin clearance was observed after diuresis, suggest that glomerular filtration rate did increase during diuresis. In addition, the 24-hour clearances suggest that a marked increase in glomerular filtration rate during diuresis may be followed by a decrease from the maximum
value, but with subsequent stabilization at a value slightly or markedly above the control. Repeated responses in children with reduced function may then be associated with a progressive increase to normal or even "supernormal" values.

3. A consistent decrease in the endogenous creatinine: inulin clearance ratio was observed as glomerular filtration rate increased. However, clearances of thiocyanate and inulin showed reasonably good agreement at both high and low rates of glomerular filtration.

4. Clearances and maximum tubular excretion of p-aminobiphosphate increased during diuresis but proportionately less than inulin clearances. Consequently, increases in the \( C_N:CP_{PAH} \) and the \( C_N:TM_{PAH} \) ratios were observed as rates of glomerular filtration increased.

5. In four of five observations on five children, increases in plasma volume (T-1824) ranging from 11 to 29% above control values were observed during diureses.

CONCLUSIONS

1. Diureses occurring during or following administration of ACTH to children with the nephrotic syndrome are usually associated with marked improvement in kidney function. Repeated diureses in children with initially reduced function may be associated with progressive increases in rates of glomerular filtration to normal values. These observations demonstrate a potentiality for improvement in function beyond that commonly considered possible in the nephrotic syndrome of many months' duration. It is believed that these changes are not peculiar to diureses associated with ACTH administration but may accompany spontaneous or other types of induced diureses.

2. The changes observed in plasma volume and glomerular filtration rate support the concept that increases in plasma volume and glomerular filtration rate are associated with the mechanism of diuresis in children with the nephrotic syndrome.

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REFERENCES


