VASOPRESSIN TEST: DIAGNOSTIC INACCURACY IN EVALUATION OF HYPOTHALAMIC-PITUITARY-ADRENOCORTICAL AXIS

By Seppo Leisti and Jaakko Perheentupa

ABSTRACT

An im vasopressin test was given to 141 children and adolescents, 52 with normal HPA axis and 89 with evident or suspected defect of the axis, and repeated in 36 cases, to establish criteria of a normal response, and to examine the accuracy and precision of the responses. Comparisons were made with the responses to the 2-h ACTH, insulin and 3-h metyrapone test.

The distributions of plasma cortisol levels and increments were positively skew, and a log transformation was made for appropriate statistical analysis. Maximal plasma cortisol level was positively and maximal increment negatively correlated with the basal level. In precision, the maximal level was superior to the maximal increment. Hence, a normal result was best defined by an area around the regression of maximal level on basal level in the normal series. The best single index of the response was the maximal level. A useful new method was introduced for quantitative comparison of plasma cortisol responses to different tests.

The vasopressin test result was frequently normal in patients who, according to repeated insulin tests were ACTH-deficient. Furthermore, the 10 patients with organic expansive hypothalamic lesions had a mean vasopressin response, that was greater relative to the insulin response than that of the reference series. However, 3 of 21 patients with organic non-expansive hypothalamic disease gave a subnormal vasopressin response but a normal insulin response. Moreover, in isolated GH deficiency and

Abbreviations and terms used in this paper: VT, vasopressin test; PIPD, per cent intra-pair difference. The term test result refers collectively to 2 parameters of plasma cortisol level during the test: basal level and maximal level (cf. Fig. 1).
after prednisone medication the mean vasopressin response was lower relative to the insulin response than in the reference series. Thus, this test is not reliable in screening for, or in anatomical diagnoses of ACTH deficiency.

Since 1965, vasopressin test (VT) has been used in testing for insufficiency of the hypothalamic-pituitary-adrenocortical (HPA) axis (Landon et al. 1965; Gwinup 1965a). It has been suggested to evoke ACTH secretion in hypothalamic hypopituitarism, thus providing a localization of the lesion (Landon et al. 1965; Bernard-Weil et al. 1967; Nieman et al. 1967; Rinne 1968; Binoux et al. 1971; Laurent de Angulo & van Gelderen 1972). This view has been challenged (Jenkins & Else 1968; Tucci et al. 1968; Carroll et al. 1969; Lundberg & Wide 1969; Toft et al. 1971). Other investigators have regarded VT as especially useful for the diagnosis of “incomplete” ACTH deficiency (Strott et al. 1967; Lundberg & Wide 1969; Barret et al. 1975).

We have comprehensively evaluated VT in a series of children suspected of deficient cortisol secretion and compared it with other tests of HPA function. Our results support the view that vasopressin stimulates ACTH secretion by a mechanism different from that of insulin and metyrapone. The VT often gave normal results in subjects with confirmed ACTH deficiency of supra- or extrasellar aetiology, but proved unreliable for such anatomical diagnoses.

**MATERIAL AND METHODS**

**The patients**

The series comprised a total of 141 subjects 1.7–23.2 years of age. Fifty-two of them (19 with familial short stature, 20 with delayed growth and maturation, 4 with a growth failure of pre-natal onset, 5 with a chromosome aberration and 4 with skeletal dysplasia) were shown to have normal secretion of GH, ACTH, TSH and ADH, and they form the reference series. We define ACTH and GH deficiencies as subnormal plasma cortisol and GH responses to repeated insulin tests (Editorial 1970, 1975). The secretion is called normal if the response was normal in at least one of the tests. Fifty-six of the subjects were hypopituitary. Eighteen had isolated idiopathic GH deficiency, which was hereditary in 3, and idiopathic in the others. Seven had GH deficiency of organic aetiology (breech presentation in 5 and craniopharyngeoma, and pre-optic glioma in 1) without ACTH deficiency, but with TSH deficiency in 3. Twenty subjects had ACTH and GH deficiencies of organic aetiology (breech presentation in 5, birth asphyxia in 2, craniopharyngeoma in 7, and neurofibromatosis, histiocytosis X, irradiated medulloblastoma, irradiated unclassified hypothalamic tumour, chromophobe adenoma and idiopathic hypopituitarism each in 1 patient. Seventeen of them were TSH deficient. Three were having cortisol substitution, 7.5–15 mg/m² daily; it was discontinued on the day preceding the test. Eleven subjects had, in repeated tests, subnormal cortisol, with normal GH responses to insulin. Five of them had cerebral gigantism, 3 an unknown organic brain disease with mental retardation, 2 a growth failure of pre-natal onset and 1 coeliac disease.
Eight subjects had autoimmune polyendocrinopathy–candidiasis syndrome (APECDS) (Blizzard & Gibbs 1968; Perheentupa & Hiekkala 1973). Five of them had adrenocortical failure of recent manifestation. Six subjects had primary hypothyroidism, unsubstituted before the investigation.

Nineteen children were in relapse with the “minimal change” nephrotic syndrome (INS) (Churg et al. 1970). The test was given to them 1–8 days after the end of 6–28 days’ continuous prednisone medication (Abramowics et al. 1970) (60 mg/m² daily in 5 doses), again 4–6 days after the end of subsequent 4 weeks’ intermittent medication (40 mg/m² in 3 doses on Tuesdays, Wednesdays and Thursdays), and again after 0.5 year of continuing remission.

To establish its precision, the test was repeated in 36 subjects (20 reference, 14 hypopituitary, 1 hypothyroid, and 1 with APECDS). Seven such test pairs were done within 2–7 days, and 29 after intervals of 0.1–2.0 years.

Methods

Lysine-vasopressin (Lypressin, Sandoz AG, Basel) was given im in the early afternoon; 10 IU to children > 20 kg, and 5 IU to children < 20 kg. A basal blood sample and 2 samples at 0.5-h intervals after the injection were taken from a fingertip for determination of plasma cortisol. The children were ambulant, with a physician at hand on the ward during the test.

The other tests have been described elsewhere. The reference ranges of responses are 34.3–69.0 μg/100 ml for the 2-h plasma cortisol level in the ACTH test (Leisti & Perheentupa, in press), 25.7–53.6 μg/100 ml for the maximal cortisol level in the insulin test (Leisti & Perheentupa, unpublished data), and 4.7–22.8 μg/100 ml for the plasma 11-deoxycortisol level in the 3-h oral metyrapone test (Leisti 1977). Plasma cortisol was determined with a fluorimetric method (Leisti 1977). The distributions of cortisol levels and increments were positively skewed, and log transformation led to clearly more meaningful means and confidence limits (Gaddum 1945; Harris & DeMets 1972). Conventional statistical calculations were made by standard techniques (Armitage 1971).

The precisions of the parameters of VT were calculated from the distribution of intra-pair differences (PIPD) in the values of these parameters in repeated tests. The differences increased parallel to the values and were standardized by expressing them as percentages of the mean value. If the parameter had value a in the first test, and b in the second test, PIPD = 100 · (b−a)/(b+a). The precision is expressed as sd of the PIDS in a series of subjects.

Intra-individual dependence between different parameters of the test was calculated from the PIPDs of the test pairs (e.g., PIPDs of maximal cortisol levels versus PIPDs of basal levels), and inter-individual dependence from the values of the parameters in the first tests (e.g., maximal cortisol levels versus basal levels).

The plasma cortisol responses to the first VTs were compared with the plasma cortisol responses to insulin and ACTH in 2 ways. Firstly, a note was made of agreement or disagreement between the 2 responses as to normality/subnormality. Secondly, a quantitative analysis of the difference between the responses was made using the PIPD method (the response to insulin or ACTH was taken for b in the formula). The means of these PIPDs were calculated for the different series, and compared with a two-tailed Student’s t-test.

The term “normal” is used for values within the 95% confidence range of the reference series, and “subnormal” for values below that range.
Table 1.
Parameters of plasma cortisol in the vasopressin test: Statistics1) of the values in the reference series, precision2) in paired tests, and dependence on the basal levels.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (95% confidence interval)</th>
<th>Per cent intra-pair difference (PIPD)3)</th>
<th>Coefficient of correlation with basal levels5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cortisol, µg/100 ml</td>
<td>Mean ± sd</td>
<td>Inter-individual4)</td>
</tr>
<tr>
<td>Basal level</td>
<td>17.3 (9.1–33.2)</td>
<td>7.0 ± 21.6</td>
<td>0.38*</td>
</tr>
<tr>
<td>30-min level</td>
<td>41.5 (28.9–59.5)</td>
<td>– 4.2 ± 13.7</td>
<td>0.31*</td>
</tr>
<tr>
<td>60-min level</td>
<td>38.4 (23.6–62.7)</td>
<td>– 1.6 ± 11.6</td>
<td>0.33*</td>
</tr>
<tr>
<td>Maximal level6)</td>
<td>43.0 (29.6–62.3)</td>
<td>– 3.2 ± 11.7</td>
<td>–0.36*</td>
</tr>
<tr>
<td>30-min increment</td>
<td>22.7 (11.4–45.2)</td>
<td>–19.2 ± 33.9***</td>
<td>–0.36*</td>
</tr>
<tr>
<td>60-min increment</td>
<td>18.8 (5.6–62.5)</td>
<td>– 8.2 ± 39.7</td>
<td>–0.28*</td>
</tr>
<tr>
<td>Max. increment6)</td>
<td>24.1 (11.6–49.7)</td>
<td>–15.0 ± 30.7***</td>
<td>–0.36*</td>
</tr>
</tbody>
</table>

1) Calculated from log transformed data. 2) i.e. sd of the PIPDs. 3) Significance of the difference of mean PIPDs from zero, and of correlation coefficients: * P < 0.05, ** P < 0.01, *** P < 0.001. 4) Inter-individual: between the values of the first tests in the reference series. 5) Intra-individual: between PIPDs of test pairs. 6) Maximal level: the highest of the basal, 30 min and 60 min levels; maximal increment: maximal level minus basal level.

RESULTS

Side effects in VT. – Cutaneous vasoconstriction, slight abdominal pain, an urge to defaecate and, in some cases, nausea and vomiting, appeared within 5 min after the injection, and subsided within 10–30 min. Hypopituitary subjects tolerated the test quite as well as the reference subjects.

VT in the reference series (Table 1). – The level was maximal at 30 min in 31 subjects, and at 60 min in 17 subjects; 4 subjects had same level at both times.

Inter-individual variation in VT: interdependence between parameters (Table 1, Fig. 1). – The stimulated plasma cortisol levels showed a positive correlation with the basal level, and the increments negative correlation with the basal level. The increments had a high (P < 0.001) positive correlation with the stimulated levels (r = 0.69, 0.72 and 0.72 for the 30 min, 60 min and maximal values, respectively).
Log scale scatter diagrams for maximal levels and maximal increments of plasma cortisol against the basal levels in vasopressin tests of the 52 reference subjects. The diagonals are regression lines, and in the first diagram the identity (y = x) line. Areas of normal findings are formed by the 95% confidence limits for estimation of the dependent variable for given values of the basal level, and by the 95% confidence limits of the basal levels.

An analysis of the findings in the vasopressin test in patients with evident or suspected hypofunction of the HPA axis. The figures are log scale plots of the maximal cortisol levels against the basal levels. The area of normal findings (see Fig. 1) is indicated by the quadrangle, and the minimal normal values of the maximal increment (11.6 µg/100 ml) by the curved dashed line (disregarding the dependence of the increment on the basal level).

**HYPOPITUITARY** subjects with: isolated GH deficiency (●); combined and/or organic deficiency with normal cortisol and subnormal GH responses to insulin (△); combined and/or organic deficiency with subnormal cortisol and GH responses to insulin, without (□) or with (■) previous cortisol substitution; combined and/or organic deficiency with subnormal cortisol and normal GH responses to insulin (X).

**PREDNISONE MEDICATION:** children with idiopathic nephrotic syndrome, at the end of 6–28 days’ continuous prednisone medication (●), at the end of 4 weeks’ intermittent medication (△), and 0.5 year later in continuing remission (□).

**APECS:** children with autoimmune polyendocrinopathy-candidiasis syndrome (○).

**HYPOTHYROID:** subjects with primary hypothyroidism tested before the start of thyroxine substitution (X).
Intra-individual variation in VT: precision of parameters (Table 1). – The mean of the PIPDs were significantly different from 0 for 30-min and maximal increments, with a mean decrease in the values from the first to the second test. The maximal level was substantially more precise than either the basal level or the increment.

Intra-individual variation in VT: interdependence between parameters. – To assess how much of the intra-individual variation in the 3 parameters in repeated tests was mutually interdependent, the correlations between their PIPDs were analyzed (Table 1). The maximal level showed a positive correlation with the basal level. In contrast, the maximal increment showed a negative correlation with the basal level. The maximal levels and increments showed a positive correlation \( r = 0.49, P < 0.01 \).

Diagnostic accuracy of VT (Fig. 2). – Of the 25 hypopituitary subjects with normal cortisol responses to insulin, only 15 gave normal results. Of the 31 subjects with a subnormal cortisol response to insulin, 17 gave normal results. Of the total of 24 hypopituitary subjects with a subnormal result, 16 had a normal increment \( \geq 11.6 \text{ g/100 ml} \). The subject who had a chromophobe adenoma removed (the only hypopituitary subject with intrasellar aetiology) had a slightly subnormal basal level with normal maximal level and increment.

At the end of the continuous prednisone medication tests gave subnormal results in all 10 subjects, and in 8 the increment was subnormal. At the end of intermittent medication 11 of 17 subjects gave subnormal test results, and in 7 the increments were also subnormal. Half a year after the medication, 2 of 9 subjects gave subnormal results, but all had normal increments. Among the total of 23 subjects with subnormal test results, 8 had a normal increment.

Of the 8 subjects with APECS the result was normal in 2. These 2 also had normal response to ACTH test. One of the others had a normal increment. Of the 6 subjects with primary hypothyroidism, 4 had normal results.

VT compared with other HPA tests (Fig. 3). – For these comparisons, the maximal cortisol level was used as an index of the response to VT. In the reference series, a significant inter-individual correlation of the response was present between VT and the ACTH test \( r = 0.66, P < 0.001 \), between VT and the insulin test \( r = 0.58, P < 0.001 \) and between VT and the 3-h metyrapone test \( r = 0.34, P < 0.05 \).

To tests the hypothesis that VT distinguishes between hypothalamic and pituitary lesions, our subjects with hypothalamic hypopituitarism were classified according to the nature of the lesion (Table 2, group b and c). In cases of discrepancy with the insulin test in subjects with organic non-expansive or expansive extrasellar hypopituitarism the number of normal responses was
Comparison between plasma cortisol responses to the vasopressin test and other test in 52 reference subjects (○) and in subjects with evident or suspected hypopituitarism. The normal limits are indicated with quadrangles. The (dashed) diagonals give the 90% confidence limits for the per cent intra-pair differences between the 2 responses in reference subjects. For groups and symbols see Fig. 2.

higher for VT. But most of the subjects with idiopathic GH deficiency, and those tested at the end of intermittent prednisone medication had the reverse response pattern. In cases of discrepancy with the metyrapone test after intermittent prednisone, VT response was predominantly subnormal. This was also true in the comparison with the ACTH test after intermittent prednisone and in idiopathic GH deficiency.

In comparison with the PIPD method (Table 2) a mean PIPD greater than in the reference series would indicate that cortisol secretion was stimulated by
Table 2.  
Comparisons of the response to the vasopressin test\(^1\) with the response to the ACTH\(^2\), insulin\(^1\) and 3-h metyrapone tests\(^3\). Columns A: frequencies of discrepant (subnormal-normal/normal-subnormal) responses pairs. Columns B: means ± SEM of the per cent intra-pair differences between the two responses.

<table>
<thead>
<tr>
<th>Patients</th>
<th>No. of cases</th>
<th>Vasopressin test/ ACTH test (A)</th>
<th>Vasopressin test/ insulin test (A)</th>
<th>Vasopressin test/3-h metyrapone test (A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference series</td>
<td>52</td>
<td>0/0 - 5.7 ± 1.0</td>
<td>0/0 - 7.1 ± 1.2</td>
<td>0/1</td>
</tr>
<tr>
<td>Hypopituitary patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Idiopathic isolated GH deficiency</td>
<td>18</td>
<td>3/0 -13.4 ± 3.0*</td>
<td>3/0 - 2.4 ± 2.8**</td>
<td>2/1</td>
</tr>
<tr>
<td>b. Organic, non-expansive aetiology(^5)</td>
<td>21</td>
<td>5/4 -11.6 ± 3.7</td>
<td>3/10 15.3 ± 4.4</td>
<td>3/4</td>
</tr>
<tr>
<td>c. Organic, expansive extrasellar aetiology(^6)</td>
<td>10</td>
<td>2/2 - 4.4 ± 3.5</td>
<td>0/4 20.9 ± 4.8**</td>
<td>0/2</td>
</tr>
<tr>
<td>Patients with pregnisone medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. At end of continuous medication</td>
<td>10</td>
<td>0/0 -36.8 ± 11.8*</td>
<td>0/0 -14.6 ± 12.0</td>
<td>0/0</td>
</tr>
<tr>
<td>b. At end of intermittent medication</td>
<td>17</td>
<td>5/0 -19.6 ± 5.1**</td>
<td>5/0 - 5.2 ± 5.4*</td>
<td>8/1</td>
</tr>
<tr>
<td>c. After 0.5-year remission</td>
<td>9</td>
<td>1/0 - 8.6 ± 2.6</td>
<td>1/0 4.6 ± 2.2</td>
<td>2/0</td>
</tr>
<tr>
<td>APECS patient</td>
<td>8</td>
<td>1/0 - 2.9 ± 4.1</td>
<td>1/0 3.6 ± 3.4</td>
<td>0/0</td>
</tr>
<tr>
<td>Hypothyroid patients</td>
<td>6</td>
<td>1/2 -12.5 ± 9.7</td>
<td>0/2 10.0 ± 10.0</td>
<td>1/0</td>
</tr>
</tbody>
</table>

1) Parameter = maximal cortisol level. 2) Parameter = 2-h cortisol level. 3) Parameter = 3-h plasma deoxycortisol level. 4) Significance for the difference from the reference series: * \(P < 0.05\), ** \(P < 0.01\). 5) Includes cases due to breech presentation, birth asphyxia, organic brain disease with mental retardation, and cerebral gigantism; excludes combined deficiency of unknown aetiology. 6) Includes cases due to craniofaryngioma, pre-optic glioma, histiocytosis X, neurofibromatosis, radiated medulloblastoma, and an unclassified hypothalamic tumour; excludes subjects with cortisol substitution.

vasopressin more than by the other test in the patient group as compared with the reference series. In comparison with the insulin test, this was true for the subjects with hypopituitarism due to an expansive extrasellar lesion. But in idiopathic GH deficiency and after intermittent prednisone the mean PIPD was significantly smaller between VT and the insulin test, and between VT and the ACTH test. Even at the end of continuous prednisone medication the mean
PIPD between VT and the ACTH test was significantly smaller. The subjects with organic non-expansive hypothalamic disease did not differ from our reference series.

DISCUSSION

In our reference series, parameters of response correlated both inter- and intra-individually with the basal cortisol level. The inter-individual correlation has been observed for the increment (Knebusch 1967; Barret et al. 1975), but not applied in establishing the criteria of a normal response. Such dependence was originally established by Birke et al. (1958) for the response to the 8-h ACTH test, and we have observed similar inter-individual correlations in the 2-h ACTH test (Leisti & Perheentupa 1977a) and the 5-day metyrapone test (Leisti & Perheentupa 1977). Therefore, the basal level should be made one element of the criteria of a normal finding (Fig. 1). However, this technique is cumbersome for comparisons between different tests, and for that purpose we used the maximal cortisol level, as it was the best single index of the response.

Various parameters have been proposed for setting the criteria of a normal response to VTs (im and iv), such as minimum absolute increment (Landon et al. 1965; Bernard-Weil et al. 1967; Bethge et al. 1967; Knebusch 1967; Neiman et al. 1967; Jenkins & Else 1968; Karp et al. 1968; Rinne 1968; Tucci et al. 1968; Jacobs & Nabarro 1969; Laron et al. 1969; Lundberg & Wide 1969; Binoux et al. 1971; Toft et al. 1971), minimum per cent increment (van der Wal et al. 1965; Rochiccioli et al. 1971), minima for increment and maximal level (Jasani et al. 1967; Carroll et al. 1969; Shenkin et al. 1970; James & Landon 1971), minima for increment or maximal level (Feurle et al. 1970; Laurent de Angulo & van Gelderen 1972), minima for basal and maximal level (Strott et al. 1967), minima for basal level and increment and maximal level (Gwinnup 1965a; Brostoff et al. 1968), and minimum for difference of the highest and lowest cortisol concentration (Zurbrügg & Joss 1970). This variability tends to cause confusion in comparison between different series. We consider the increment to be of little value. It is highly dependent on the basal cortisol level which fluctuated markedly in children. That probably explains why, in precision, the increment is inferior to the maximal level. Using the latter as index of response, VT in our series was similar (11.7%) in precision to the 2-h ACTH test (8.1%) (Leisti & Perheentupa, in press) and the insulin test (10.6%) (Leisti & Perheentupa, unpublished data). The importance and application of our measure of precision is discussed elsewhere (Leisti & Perheentupa, in press).

The diagnostic accuracy of VT was poor. Among our 31 patients who, according to a repeatedly subnormal insulin response, were ACTH-deficient, the VT result was abnormal in 14 only. This kind of discordance has been taken as evidence that vasopressin has a direct action on the pituitary gland, and so
could be employed in ACTH deficiency, to distinguish between hypothalamic and pituitary ACTH deficiency. In the literature we found 26 cases of hypothalamic disease in which the insulin test and VT results had been compared. In 11 the response pattern was normal vasopressin-subnormal insulin, by the writers’ own criteria (Landon et al. 1965; Bethge et al. 1967; Nieman et al. 1967; Jacobs & Nabarro 1969; Laron et al. 1969; Zurbrügg & Joss 1970; Laurent de Angulo & van Gelderen 1972; Barret et al. 1975). However, 3 patients had the reverse pattern. In our series the reverse pattern was observed in 6 hypopituitary patients with hypothalamic disease. Our subjects with hypopituitarism due to an expansive hypothalamic lesion had stronger mean cortisol responses to vasopressin relative to insulin than the reference subjects. However, the reverse was true for the subjects with idiopathic GH deficiency. We can offer no explanation for these findings, and are unaware of any similar experimental studies.

Of 44 previously reported cases of hypothalamic hypopituitarism with comparison of the results of VT and metyrapone test (Landon et al. 1965; Bernard-Weil et al. 1967; Nieman et al. 1967; Jacobs & Nabarro 1969; Laron et al. 1969; Lundberg & Wide 1969; Binoux et al. 1971; Toft et al. 1971; Laurent de Angulo & van Gelderen 1972; Barret et al. 1975; Leisti & Perheentupa 1977), the pattern was normal vasopressin – subnormal metyrapone in 19 patients and the reverse in 3. In our series of 37 hypopituitary subjects the corresponding figures were 7 and 5. This does not support Landon’s original suggestion that a normal response to vasopressin associated with abnormal response to insulin and/or metyrapone is diagnostic of hypothalamic ACTH deficiency.

Pituitary ACTH deficiency, on the other hand, should, according to Landon, be associated with subnormal responses to all HPA tests, including VT. In our only subject with intrasellar hypopituitarism the responses were normal to vasopressin and ACTH but subnormal to insulin. Of the total of 49 previously reported patients with intrasellar disease (Landon et al. 1965; Bethge et al. 1967; Nieman et al. 1967; Jenkins & Else 1968; Jacobs & Nabarro 1969; Binoux et al. 1971), 10 had the pattern normal vasopressin – subnormal insulin and 3 the reverse. Of the 119 similar patients (Landon et al. 1965; Bernard-Weil et al. 1967; Nieman et al. 1967; Strott et al. 1967; Jenkins & Else 1968; Rinne 1968; Tucci et al. 1968; Jacobs & Nabarro 1969; Lundberg & Wide 1969; Binoux et al. 1971; Toft et al. 1971; Barret et al. 1975) 17 had the pattern normal vasopressin – subnormal metyrapone and 23 the reverse. We conclude, as have others (Jenkins & Else 1968; Tucci et al. 1968; Carroll et al. 1969; Lundberg & Wide 1969; Toft et al. 1971), that an anatomical diagnosis can not be based on the response pattern. For screening of ACTH deficiency VT should in our opinion be replaced by the 2-h ACTH test (Leisti & Perheentupa, in press).

Concerning HPA suppression after glucocorticoid medication (Clayton et al. 1965; Gwinup 1965b), Jasani et al. (1967) suggested that in cases of discordant
responses it was VT that was normal, rather than the insulin or metyrapone test. Other investigators have disagreed (Tucci et al. 1968; Shenkin et al. 1970). Our patients at the end of prednisone treatment had lower mean cortisol responses to vasopressin relative to insulin than the reference series.

REFERENCES

Gwinup G.: Metabolism 14 (1965b) 1282.
Leisti S.: Clin. Endocr. 6 (1977) 305.

Received on June 16th, 1977.