THE INSULIN TOLERANCE TEST 
AFTER PRE-TREATMENT WITH DEXAMETHASONE

By 

P. O. Osterman and L. Wide 

ABSTRACT

The plasma 11-hydroxycorticosteroid and serum GH responses to insulin-induced hypoglycaemia were studied in 25 healthy volunteers. The results of a control insulin tolerance test were compared with those of 2 similar tests which were performed after pre-treatment with dexamethasone 0.5 and 1.0 mg, respectively. The GH response to hypoglycaemia was significantly lower in women than in men in all 3 tests. In men, but not in women, the GH response was lower after pre-treatment with 1 mg dexamethasone than in the other 2 tests. The plasma 11-hydroxycorticosteroid response was significantly greater after pre-treatment with 0.5 mg dexamethasone than in the control test, and was at least as good after 1 mg dexamethasone. After pre-treatment with dexamethasone the subjects experienced less discomfort and a shorter duration of sweating than in the control insulin tolerance test. Pre-treatment with 1 mg dexamethasone also has other advantages. Thus, the basal plasma cortisol level is low and stable, which facilitates estimation of the magnitude of the cortisol response. Furthermore, information is obtained about the dexamethasone suppression response.

Determinations of the cortisol and somatotrophin (GH) responses to insulin-induced hypoglycaemia have been used as a test of the hypothalamo-pituitary function (Arner et al. 1962; Landon et al. 1963; Frantz & Rabkin 1964). The secretory patterns of the pituitary hormones are reflected by episodic fluctuations of the serum levels. The fasting, resting GH level in the morning usually is low. In contrast, most of the corticotrophin (ACTH) secretory bursts, giving
maximal plasma cortisol levels occur between 4 and 8 a.m. The cortisol level usually falls later in the morning, but fluctuations may occur. In the insulin tolerance test the fluctuating cortisol levels make determination of the basal level difficult. Furthermore, the plasma cortisol response to insulin-induced hypoglycaemia is influenced by the basal cortisol level. A high basal level is associated with a smaller response than a low level (Doar et al. 1970).

Small doses of dexamethasone administered at midnight effectively suppress the cortisol secretion the following morning (Nichols et al. 1965). It was the purpose of this study to see whether such suppression of the basal cortisol secretion was of any advantage when determining the cortisol response to insulin-induced hypoglycaemia and whether the insulin tolerance test could be combined with a commonly used dexamethasone suppression test (Nugent et al. 1965). The effect on the insulin tolerance test of pre-treatment with 0.5 mg and 1.0 mg dexamethasone was studied in 25 healthy volunteers. Several of the first tested volunteers claimed that they had less sweating after pre-treatment with dexamethasone. Fourteen of the volunteers therefore underwent a double-blind investigation and the duration of sweating, the subjective sensations during the test, the pulse rate, blood pressure and respiratory rate were recorded.

**MATERIALS AND METHODS**

**Control group**

Twenty-five healthy, non-obese volunteers, 15 women and 10 men, served as controls. Their mean age was 24 years (range 19-36). None of the subjects took any medicine during the study. The women had normal menstrual cycles and were not taking oral contraceptives. The tests were not performed on any particular day of the menstrual cycle. The subjects fasted after 9 p.m. the day before the test. They slept at home the night before the test and came to the Department of Neurology at 7 a.m. They then rested on a bed until the test was finished. A flexible venous cannula was inserted into a cubital vein. The cannula was kept patent with heparinized isotonic saline between sampling. In each case soluble insulin (Vitrum 40 U/ml) was injected intravenously at 8.00 a.m. in a dose of 0.15 U/kg b.w. Blood samples were drawn at 7.50, 8.00, 8.15, 8.30, 8.45, 9.00, 9.30 and 10.00 a.m. A 1-ml waste sample was discarded before each blood specimen was taken, to avoid contamination by the heparinized saline. Blood samples were taken for assay of 11-hydroxycorticosteroids in heparin plasma and of GH in serum. After centrifugation the plasma and serum were stored at −20°C until assayed. Blood samples for assay of blood glucose were kept in an ice bath during the time of the test and the determination was performed within one hour after completion of the test.

In each case 3 insulin tolerance tests were performed. At 11 p.m. the day before the test the subject took dexamethasone (Dexacortal®) in a dose of 1.0 mg (1.0-dexamethasone-insulin tolerance test = 1.0-DEX-ITT) or 0.5 mg (0.5-dexamethasone-insulin tolerance test = 0.5-DEX-ITT) or no drug (11 subjects) or placebo (14 subjects) (control insulin tolerance test = ITT). The 3 tests were usually performed within 1 week in the same subject. Following the 1.0-DEX-ITT an interval of 2 days was allowed to elapse before any other test was performed.

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Several of the first examined 11 subjects claimed that they had less discomfort and less sweating during the dexamethasone-insulin tolerance tests than during the control test. One possible explanation for this might be that stress was more intense during the control test, which was performed as the first test in 10 of the 11 subjects. Accordingly, the subjects were more familiar with the test procedure during the dexamethasone-insulin tolerance tests. To test these subjective experiences the next 14 volunteers underwent a double-blind investigation. Dexamethasone 1.0 mg and 0.5 mg and placebo respectively, were administered in capsules of identical appearance. The capsules were taken at 11 p.m. the evening before the test. The sequence of placebo and dexamethasone 0.5 and 1.0 mg was randomized. A nurse who did not know which of the 3 tests was being performed supervised the subject and recorded the duration of sweating and the subjective sensations (such as hunger, drowsiness, feebleness, irritability) during the test. The pulse rate, blood pressure and respiratory rate were recorded at the blood sampling times and every 5 min from 8.25 to 9 a.m. In these 14 subjects the ITT was the first test 5 times, the 0.5-DEX-ITT was the first one 4 times and the 1.0-DEX-ITT was the first one 5 times.

**Chemical methods**

Blood glucose was determined by a glucose oxidase method (Hjelm & de Verdier 1963).

The concentration of non-conjugated 11-hydroxycorticosteroids in plasma was determined by a fluorimetric method according to Mattingly (1962). The precision (intra-assay variation) and the between-assay variation expressed as coefficient of variation (c. v.) were 3 and 8 per cent respectively.

The GH concentration in serum was assayed by the radioimmunosorobent technique described by Wide et al. (1967), in its recently described modification where the antibodies are indirectly coupled to the solid phase (Wide et al. 1973). The antibodies were rabbit-anti-human-GH coupled to human GH on CNBr-activated ultrafine Sephadex particles. The GH preparation used for immunization and for labelling with $^{125}$I was obtained from AB Kabi, Stockholm, and had been purified according to Roos et al. (1963). This preparation was also used as a laboratory standard. The sera were assayed in 0.1 ml aliquots in duplicate with incubation for 24 h at room temperature. The sensitivity was 0.2 ng/ml and the intra-assay variation (c. v.) for values between 0.6 and 10 ng/ml was around 6 per cent. The corresponding figure for between-assay variation was 10 per cent.

**Statistical methods**

The basal levels of blood glucose, plasma 11-hydroxycorticosteroids and serum GH were determined as the mean of the levels at 7.50 and 8.00 a.m.

The fall in blood glucose was determined in each test as the difference between the basal level and the lowest recorded level during the test. The fall in per cent of the basal level was also calculated.

The level of plasma 11-hydroxycorticosteroids was usually highest at 9.00 or 9.30 a.m. The increase in plasma 11-hydroxycorticosteroids was therefore determined in each test as the difference between the basal level and the mean of the levels at 9.00 and 9.30 a.m.

The time of the maximal serum level of GHI varied considerably more than the time of the maximal plasma level of 11-hydroxycorticosteroids. The measured maximal
increase in serum level of GH during the test also varied considerably between different subjects (range 2.6–51.2 ng/ml). The increase in GH secretion in each test was therefore estimated planimetrically and expressed in area units (1 area unit = 1 \( \frac{\text{ng} \cdot \text{min}}{\text{ml}} \)).

An example of a calculated area is shown in Fig. 1. In studies of patients it is desirable that the number of blood samples are reduced as much as possible. In almost all tests the GH levels had already decreased at 10 a.m. Only the values at 7.50, 8.00, 8.30, 8.45, 9.00 and 9.30 a.m. were therefore used in the planimetric calculation for establishing tolerance limits of the GH increase.

The values for increase of GH and 11-hydroxycorticosteroids were converted to common logarithms for the calculation of mean values and tolerance limits. By using the logarithms an observed positive skewness was largely eliminated, resulting in a distribution closer to normal for the respective variables. For calculating one-sided tolerance limits statistical tables (Owen 1962) were used. The results were evaluated by Student's \( t \)-test for paired and unpaired observations.

**RESULTS**

In 3 tests (1 ITT in a woman, and 1 0.5-DEX-ITT in a woman and a man) the basal GH level was very high, 13–17 ng/ml. These tests were the first test performed in the respective subjects. In the following 2 tests in each subject the basal GH level was only 0.2–3.2 ng/ml. The high basal GH level in the first tests were probably due to stress caused by the unfamiliar test procedure. None of the results from these 3 tests were used in the statistical calculations.
Mean blood glucose levels (combined values for women and men) in the control-insulin tolerance test (□—□), 0.5-dexamethasone-insulin tolerance test (▼——▼) and 1.0-dexamethasone-insulin tolerance test (○——○). Range of standard errors of the mean (SEM): 1.4–3.4 mg/100 ml.

**Blood glucose**

The blood glucose fell to less than 40 mg/100 ml in all tests but 3 (range 13–46 mg/100 ml). The fall in per cent of the basal level exceeded 50 per cent in all tests. In the ITT as well as in the 0.5-DEX-ITT and 1.0-DEX-ITT there were no significant differences in the mean basal blood glucose levels between women and men, whereas the mean minimal blood glucose levels were lower in women (25.1, 24.4, 26.6 mg/100 ml, respectively) than in men (27.5, 29.8, 30.8 mg/100 ml, respectively). The difference was, however, significant ($P < 0.05$) only in the 0.5-DEX-ITT. The mean fall in mg/100 ml blood and in per cent of the basal level showed no significant sex difference in any of the 3 tests.
Table 1.
The results of the control-insulin tolerance test (ITT), 0.5-dexamethasone-insulin tolerance test (0.5-DEX-ITT) and 1.0-dexamethasone-insulin tolerance test (1.0-DEX-ITT) in 25 control subjects. The values for blood glucose and 11-hydroxycorticosteroids are given as combined values for both sexes, the values for GH are given for each sex separately.

<table>
<thead>
<tr>
<th>Test</th>
<th>Blood glucose</th>
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<th>Growth hormone</th>
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<td></td>
<td>Basal level</td>
<td>Minimal level</td>
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<td></td>
<td>mg/100 ml</td>
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<td></td>
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<tr>
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<td>84.5</td>
<td>26.1</td>
<td>23.7</td>
<td>9.4</td>
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<td>Conf. lim.</td>
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<td>23.4–28.8</td>
<td>20.7–26.7</td>
<td>7.7–11.5</td>
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<tr>
<td>Range</td>
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<td>13–36</td>
<td>12.8–43.2</td>
<td>3.6–25.4</td>
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<td>0.5-DEX-ITT</td>
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<tr>
<td>M</td>
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<td>26.7</td>
<td>11.6</td>
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<td>Conf. lim.</td>
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<td>23.9–29.5</td>
<td>9.4–13.8</td>
<td>13.1–17.7</td>
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<td>13–42</td>
<td>4.7–21.4</td>
<td>6.4–24.8</td>
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<tr>
<td>Range</td>
<td>65–113</td>
<td>17–46</td>
<td>4.0–12.2</td>
<td>3.0–23.4</td>
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Abbreviations: M = mean value; geometric mean when used for mean increase of 11-hydroxycorticosteroids and GH; arithmetic mean when used for mean basal levels and mean minimal blood glucose levels. Conf. lim. = 95 per cent confidence limits of mean.
Mean plasma 11-hydroxycorticosteroid levels (combined values for women and men) in the control-insulin tolerance test (■—■), 0.5-dexamethasone-insulin tolerance test (▼——▼) and 1.0-dexamethasone-insulin tolerance test (●——●). The vertical lines represent ± 1 SEM.

The mean blood glucose levels (combined values for women and men) are shown in Fig. 2 and Table 1. In the 1.0-DEX-ITT the basal level and the blood glucose levels at 9, 9.30 and 10 a.m. were significantly higher ($P < 0.02$) than in the 0.5-DEX-ITT and in the ITT. The mean minimal blood glucose levels, however, did not differ significantly between the different types of test, and neither did the mean fall in mg/100 ml blood or in per cent of the basal level.

**Plasma 11-hydroxycorticosteroids**

There were no significant differences in the plasma 11-hydroxycorticosteroid levels in the 3 tests between women and men. The mean plasma 11-hydroxycorticosteroid levels (combined values for women and men) are shown in Fig. 3...
and Table 1. In the ITT the basal level was significantly higher \( (P < 0.001) \) than in the 0.5-DEX-ITT and in the latter it was significantly higher \( (P < 0.001) \) than in the 1.0-DEX-ITT. When the basal plasma 11-hydroxycorticosteroid level was lower than 12.1 \( \mu g/100 \) ml and at least 4.9 \( \mu g/100 \) ml lower than the control basal plasma 11-hydroxycorticosteroid level the suppression response to 1.0 mg dexamethasone was considered normal. This corresponds for each of the two criteria to a tolerance limit below and above which, respectively, at least 97.5 per cent of the normal population lies, with confidence 95 per cent.

The increase in plasma 11-hydroxycorticosteroids was significantly lower \( (P < 0.001) \) in the ITT than in the 0.5-DEX-ITT. The increase in the 1.0-DEX-ITT was also significantly lower \( (P < 0.05) \) than in the 0.5-DEX-ITT and did not differ significantly from the increase in the ITT. For each type of test a lower tolerance limit for the increase in plasma 11-hydroxycorticosteroids was calculated, such that at least 97.5 per cent of the normal population has a greater increase than the limit level with confidence 95 per cent. Accordingly, the increase in plasma 11-hydroxycorticosteroids was considered normal when it was \( > 2.6, > 5.8 \) and \( > 3.4 \) \( \mu g/100 \) ml in the ITT, 0.5-DEX-ITT and 1.0-DEX-ITT respectively.

**Fig. 4.**
Mean GH levels for women and men in the control-insulin tolerance test. The vertical lines represent \( \pm 1 \) SEM.
Mean GH levels for women and men in the 0.5-dexamethasone-insulin tolerance test. The vertical lines represent ± 1 SEM.

**Serum GH**

The mean serum GH levels for women and men are presented in Figs. 4, 5 and 6 and Table 1. In all 3 tests the basal serum GH levels were significantly higher (ITT: \( P < 0.005 \), 0.5-DEX-ITT: \( P < 0.05 \), 1.0-DEX-ITT: \( P < 0.001 \)) in women than in men. Neither in women nor in men did the basal serum GH levels differ significantly between the 3 tests. In women the mean basal serum GH level was significantly lower (\( P < 0.025 \)) in the third test in succession (1.4 ng/ml) than in the first and second tests (3.1 and 2.8 ng/ml, respectively). In men there were no significant differences in the basal serum GH levels between the first, second or third tests in succession (0.92, 0.92, 0.37 ng/ml). In 12 tests, all in women, the serum GH level fell by 0.4–5 ng/ml from the basal level during the first 30 min of the test. In each case this fall was followed by a normal increase in the GH level. Six of the 12 tests were the first of the 3 tests performed, 5 were the second and 1 was the third. In these 12 tests the lowest recorded serum GH level was used as the basal level for the planimetric estimation of the increase which occurred after 8.30 a.m.
In all 3 tests the increase in serum GH levels was significantly lower (ITT: $P < 0.005$, 0.5-DEX-ITT: $P < 0.02$, 1.0-DEX-ITT: $P < 0.05$) in women than in men. In men the increase in serum GH level was significantly lower in the 1.0-DEX-ITT than in the 0.5-DEX-ITT ($P < 0.02$) and in the ITT ($P < 0.05$). In women the increase did not differ significantly between the 3 tests. For each sex and type of test a lower tolerance limit for the increase in serum GH was calculated, such that at least 97.5 per cent of the normal population has a greater increase than the limit level, with confidence 95 per cent. Accordingly, the increase in serum GH was considered normal in women when it was $> 32$, $> 53$ and $> 64$ area units in the ITT, 0.5-DEX-ITT and 1.0-DEX-ITT, respectively. The corresponding figures for men were 274, 400 and 136 area units respectively.

There was no significant correlation in any type of test between the fall in blood glucose or the minimal blood glucose levels and the increase in plasma 11-hydroxycorticosteroids or in serum GH. Nor was there any correlation between the increase in 11-hydroxycorticosteroids and the increase in GH.

Fig. 6.
Mean GH levels for women and men in the 1.0-dexamethasone-insulin tolerance test.
The vertical lines represent $\pm 1 \text{ SEM.}$
Control group studied with a double-blind technique

In these 14 subjects the mean duration of sweating was significantly greater ($P < 0.02$) in the ITT (29.4 min) than in the 0.5-DEX-ITT (16.5 min) and significantly greater ($P < 0.005$) in the ITT than in the 1.0-DEX-ITT (12.0 min). The difference between the 2 dexamethasone-insulin tolerance tests was not significant. The duration of sweating did not differ significantly between the first (21.8 min), second (19.7 min) or third tests (16.9 min) in succession. There was no significant correlation between the duration of sweating and the blood glucose response (determined as the fall in blood glucose or the minimal blood glucose level) in any of the types of test.

The mean increases in pulse rate, systolic blood pressure and respiratory rate did not differ significantly in the 3 tests.

Six of the 14 subjects considered the ITT more unpleasant than any of the DEX-ITT’s. Not one claimed the reverse. Some subjects found excessive perspiration in the ITT more unpleasant, others considered drowsiness or feebleness or irritability in the ITT more unpleasant than in the DEX-ITT’s.

DISCUSSION

A fall in blood glucose to less than 50 per cent of the basal fasting level and to less than about 40 mg/100 ml is generally considered to be adequate to stimulate a pituitary hormonal (ACTH, GH, prolactin) response. In the present study adequate hypoglycaemia was achieved in all volunteers by the administration of insulin 0.15 U/kg b. w. Women showed lower minimal blood glucose levels than men, and this is in accordance with the observation by Greenwood et al. (1966). In this context the finding by Frantz & Rabkin (1965) that oestrogen induced a significant decline in the basal blood glucose level in men also deserves to be mentioned. The fall in blood glucose in the present study, however, did not differ between women and men and the observed minor difference in the minimal blood glucose levels probably is too small to explain any difference in pituitary hormone (GH) response between the two sexes.

Unger et al. (1965) found that the fasting GH levels were significantly higher in women than in men. Frantz & Rabkin (1965) demonstrated that the fasting GH levels of men and women at the time of waking in the morning did not differ but after normal activity for 1–3 h the fasting GH level rose markedly in women. After administration of oestrogen to men a similar rise in the fasting GH level was induced by physical activity. The results of the present study are in accordance with those previously reported in ambulatory subjects. The basal serum GH levels were significantly higher in women. Emotional stress probably also contributed to the higher basal serum GH levels in women. In women the mean basal GH level was significantly lower in the
third test in succession than in the first or second test. In 12 tests in women
(11 performed as the first or second test, 1 as the third test in succession), the
serum GH level fell by 0.4–5 ng/ml from the basal level during the first 30 min
of the test. These results indicate that the standardization of the preliminaries
of the test was not quite effective for establishment of basal serum levels of GH.
To our knowledge the present finding that the GH response to insulin hypo-
glycaemia was lower in women than in men has not been reported previously.
From a study of the GH response to insulin hypoglycaemia by Frantz & Rabkin
(1964, Table 1) it can be calculated that the mean GH increase in men was
49.8 ng/ml and in women 32.4 ng/ml. There were, however, only 6 subjects of
each sex and the difference is not quite significant. Greenwood et al. (1966)
did not find any statistically significant differences in GH response to insulin
hypoglycaemia between 11 women and 11 men, but the data concerning the
GH responses are given only as combined values for both sexes. In most other
reports there are either too few subjects of each sex to allow for statistical
calculations or the values are not given for each sex separately. The higher
basal GH levels in women may be related to the lower GH response found in
this sex. It is possible that the pituitary capacity for GH response is diminished
if the hypoglycaemia has been preceded by a period of increased GH secretion
cau sed by physical and emotional stress. Support for this concept is found in
some previous studies on the GH response to arginine and insulin-induced
hypoglycaemia (Frohman et al. 1967; Merimee et al. 1969). Whether this is the
sole explanation for the differences in GH responses between the two sexes is
uncertain. In women the GH secretion is influenced by changes in the concen-
tration of the ovarian steroid hormones (Yen et al. 1970; Merimee & Fineberg
1971; Hansen & Weeke 1974). In the present investigation the insulin tolerance
tests were not performed on any particular day of the menstrual cycle. The GH
responses in women were less consistent than in men. In some the response was
as good as in the men, while in others rather low responses were achieved. This
may reflect the varying effect of the ovarian steroid hormones during different
phases of the menstrual cycle.

No correlation was found between the blood glucose response and the increase
in plasma 11-hydroxycorticosteroids or serum GH, nor between the increase in
11-hydroxycorticosteroids and in serum GH. These results are in accordance
with several other studies (Carroll et al. 1969; Donald 1971; Cacciari et al.
1975) but at variance with those of Greenwood et al. (1966). The explanation
for this is probably that the latter investigators performed more than one test
in each control subject and studied the individual response to various dose
levels of insulin. Their results indicate that in each individual there is a corre-
lation between the blood glucose response and the increases in plasma 11-
hydroxycorticosteroids and serum GH. The inter-individual variations in the
present study, however, are too great to allow such a correlation to be detected.
It is well established that the ACTH as well as the GH response to insulin hypoglycaemia can be suppressed by prior administration of dexamethasone (Hartog et al. 1964; Frantz & Rabkin 1964; Wynn 1967; Nakagawa et al. 1969). The inhibitory effect of glucocorticosteroids on ACTH and GH release is probably dependent on both the dose administered and the duration of administration (Werder et al. 1971). Thus, Copinschi et al. (1975) found that acute pre-treatment with 1 mg dexamethasone the evening before the test did not significantly reduce the GH and cortisol responses to insulin-induced hypoglycaemia. Likewise, Moses & Miller (1969) did not find any suppression of the plasma 17-hydroxycorticosteroid and GH responses to insulin hypoglycaemia in subjects who were acutely pre-treated with a low dosage of dexamethasone (0.75 mg at 11 p.m. the evening before the test and 0.50 mg the morning of the test). Moses & Miller (1969) also suggested that dexamethasone pre-treatment should be used in insulin tolerance tests to "allow a patient with suspected hypopituitarism to be tested for ACTH and growth hormone reserves while being protected from adrenal insufficiency by steroids".

The usefulness of dexamethasone pre-treatment in insulin tolerance tests is further illustrated by the results of the present investigation. After pre-treatment with 0.5 mg dexamethasone the evening before the test the plasma 11-hydroxycorticosteroid response to insulin hypoglycaemia was even greater than in the control tests. After pre-treatment with 1.0 mg dexamethasone the response was lower than after pre-treatment with 0.5 mg but still as good as in the control tests. The lower plasma 11-hydroxycorticosteroid response in the 1.0-DEX-ITT compared with that in the 0.5-DEX-ITT could be due to differences in the duration of hypoglycaemia (Landon et al. 1963). The blood glucose levels were significantly higher at 9, 9.30 and 10 a.m. in the 1.0-DEX-ITT. This might also contribute to the lower GH response in men in the 1.0-DEX-ITT compared with those in the ITT and the 0.5-DEX-ITT. However, the mean minimal blood glucose levels and the mean fall in blood glucose did not differ between the different types of test. This may indicate that a greater inhibitory effect on ACTH and GH release by dexamethasone 1.0 mg as compared with 0.5 mg contributed to lower 11-hydroxycorticosteroid and GH responses in the 1.0-DEX-ITT than in the 0.5-DEX-ITT.

Cortisol is secreted episodically and in subjects with a "normal" sleep-waking cycle maximal plasma cortisol levels are found between 4 and 8 a.m. (Weitzman et al. 1971). In several studies the insulin tolerance tests have been started at 10 a.m. in order "to minimize the effect of diurnal variation in plasma cortisol" (Landon et al. 1963). The plasma cortisol response to insulin-induced hypoglycaemia is higher in the evening than in the morning (Takebe et al. 1969; Ichikawa et al. 1972). A high basal cortisol level in the morning is associated with a smaller response than a low level (Doar et al. 1970). After pre-treatment with 1 mg dexamethasone the fasting basal plasma cortisol level is low and
stable. It is then also convenient to begin the test at 8 a.m. in order to shorten the duration of fasting in the morning.

In a well-known single dose dexamethasone suppression test 1 mg dexamethasone is given between 11 and 12 p.m. and the plasma cortisol concentration is determined at 8 a.m. the following morning (Nugent et al. 1965). This test is commonly used for the diagnosis of Cushing’s syndrome. Pathological results of dexamethasone suppression tests have also been reported in patients with chromophobe adenomas and in acromegals (Asfeldt 1969; Faglia et al. 1973). When the test is used for the diagnosis of Cushing’s syndrome it is appropriate to determine a tolerance limit below which the plasma cortisol level is suppressed in normal subjects. In patients with hypothalamo-pituitary disorders there is often both a pathological circadian plasma cortisol rhythm and a pathologically low plasma cortisol level (Osterman et al. 1973). In these patients it is more convenient to determine the suppression response as the decrease in the plasma cortisol level at 8 a.m. after pre-treatment with 1 mg dexamethasone compared with the control level. In the present study a decrease in the plasma 11-hydroxycorticosteroid level by more than 4.9 μg/100 ml was considered normal.

An advantage of the dexamethasone-insulin tolerance tests was that the subjects experienced less discomfort and a shorter duration of sweating in comparison with the control insulin tolerance test. The explanation for this is unknown. The reason might be a shorter duration of hypoglycaemia, but this seems unlikely. There was no correlation between the blood glucose response and the duration of sweating in the tests. Furthermore, the beneficial effect of dexamethasone was almost as good with 0.5 mg as with 1.0 mg and there was no essential difference between the blood glucose curves in the ITT and the 0.5-DEX-ITT. It is noteworthy that signs indicating adrenergic stimulation during the test (increase in pulse rate, blood pressure and respiratory rate) did not differ between the 3 tests. Another difference between the latter signs and sweating was that the increases in pulse rate, blood pressure and respiratory rate were maximal at about 8.30 a.m., whereas sweating usually started 5–15 min later.

In conclusion, the results of the present investigation show that pre-treatment with 1 mg dexamethasone the evening before an insulin tolerance test is advantageous. The fasting basal plasma cortisol level is low and stable, which facilitates estimation of the magnitude of the cortisol response. The time at which the test is performed in the morning will probably influence the cortisol response less than in the ordinary insulin tolerance test. The cortisol response is at least as great as in the ordinary insulin tolerance test. Furthermore, information is obtained about the dexamethasone suppression response. The test subjects experience less discomfort and a shorter duration of sweating.
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