Effects of cortisol on lipolysis and regional interstitial glycerol levels in humans

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Djurhuus, C. B., C. H. Gravholt, S. Nielsen, A. Mengel, J. S. Christiansen, O. E. Schmitz, and N. Møller. Effects of cortisol on lipolysis and regional interstitial glycerol levels in humans. Am J Physiol Endocrinol Metab 283: E172–E177, 2002; 10.1152/ajpendo.00544.2001.—Cortisol’s effects on lipid metabolism are controversial and may involve stimulation of both lipolysis and lipogenesis. This study was undertaken to define the role of physiological hypercortisolemia on systemic and regional lipolysis in humans. We investigated seven healthy young male volunteers after an overnight fast on two occasions by means of microdialysis and palmitate turnover in a placebo-controlled manner with a pancreatic pituitary clamp involving inhibition with somatostatin and substitution of growth hormone, glucagon, and insulin at basal levels. Hydrocortisone infusion increased circulating concentrations of cortisol (888 ± 12 vs. 245 ± 7 nmol/l). Interstitial glycerol concentrations rose in parallel in abdominal (327 ± 35 vs. 156 ± 30 μmol/l; P = 0.05) and femoral (178 ± 28 vs. 91 ± 22 μmol/l; P = 0.02) adipose tissue. Systemic [3H]palmitate turnover increased (165 ± 17 vs. 92 ± 24 μmol/min; P = 0.01). Levels of insulin, glucagon, and growth hormone were comparable. In conclusion, the present study unmistakenly shows that cortisol in physiological concentrations is a potent stimulus of lipolysis and that this effect prevails equally in both femoral and abdominal adipose tissue.

The potential role of cortisol in the regulation of lipid metabolism is a matter of debate. Whereas it is well established that glucocorticoids induce insulin resistance (2, 6) and promote proteolysis (13), studies in the field of intermediary lipid metabolism have yielded more conflicting results.

Recent in vitro studies have suggested that cortisol inhibits basal and catecholamine-stimulated lipolysis in cultured human adipocytes from abdominal tissue (23, 24), although these studies were long-term incubations carried out in the course of days rather than hours. On the other hand, in vivo experiments using [3H]palmitate infusion reported that high physiological levels of cortisol led to 60% increases in free fatty acid (FFA) concentrations and palmitate flux, an indicator of effective adipose tissue lipolysis, in humans (7). Partly in line with these findings, Samra et al. (30) observed increased circulating FFA concentrations and an increased systemic appearance rate for glycerol during hypercortisolemia but, concurrently, a decrease in FFA efflux from abdominal tissue. Taken together, these observations may be compatible with the notion that, although stimulating overall lipolysis at the whole body level, glucocorticoids may specifically inhibit abdominal lipolysis. This hypothesis gains further support from the clinical observation that patients with chronic hypercortisolemia secondary to Cushing’s syndrome are characterized by distinct abdominal obesity (19, 26, 35).

Microdialysis allows continuous monitoring of changes of concentrations of a variety of low molecular weight compounds from interstitial tissue to the microdialysate and, hence, estimation of regional concentrations in various tissues. The technique has been applied in a large number of studies in humans since it was first introduced (20).

The present study was undertaken to examine the effect of an acute physiological elevation of circulating cortisol concentrations on systemic and regional adipose tissue. In particular, we addressed the question of whether cortisol preferentially stimulates lower body adipose tissue lipolysis as opposed to abdominal lipolysis. To pursue this, we examined seven subjects with or without concomitant hydrocortisone infusion during infusion of somatostatin to prevent ensuing differences in hormone secretion, in particular alterations in insulinemia.

MATERIALS AND METHODS

Before the study, we performed a power analysis by use of an estimated 60% increase in serum FFA, found by Divertie et al. (7), and a power of 80%, α = 0.05. On the basis of this analysis, we included seven healthy young males [age 27 ± 2.5 SE (range 25–31); body mass index 24.0 ± 1.6 (range 19.6–23.4)].
Experimental protocol. The study was carried out as a single-blind, placebo-controlled, randomized trial.

The subjects were admitted to the research laboratory at 0700 (t = −150 min) after refraining from ingestion of food and beverages (other than tap water) and smoking during an overnight fast. Participants were instructed not to perform any physical exercise or ingest alcohol 1 day before the study and to consume a weight-maintaining carbohydrate-rich diet for 3 days before examination.

Upon arrival at the research laboratory, subjects were placed in a supine position in bed, wearing light hospital clothing in a room with ambient temperature of 22–24°C, and they remained in this position throughout the study. Two intravenous catheters (Venflon, Viggo, Helsingborg, Sweden) were inserted, one in the antecubital vein of the left arm and the other in a dorsal vein of the left hand. The latter was placed in a heated box at 65°C that allowed for arterialized blood samples to be drawn (1). Blood samples were drawn every 30 min and analyzed for plasma glucose (PG), FFA, glycerol, 3-hydroxybutyrate (3-OHB), alanine, cortisol, growth hormone, glucagon, insulin, and C-peptide.

At t = −120 min, infusion of somatostatin (330 μg/h, Ferring Pharmaceuticals), insulin (Actrapid, 0.08 mU·kg⁻¹·min⁻¹; Novo Nordisk, Bagsvaerd, Denmark), and growth hormone (GH, 2 ng·kg⁻¹·min⁻¹; Norditropin, Novo Nordisk) was commenced. Infusion of glucagon (Glucagen, 0.5 ng·kg⁻¹·min⁻¹; Novo Nordisk) was not added until t = −90 min to prevent transient hyperglycemia.

Euglycemia was intended, and isotonic glucose was infused to ensure PG >80 mg/dl.

At t = 0 min, an infusion in a randomized manner of either hydrocortisone sodium succinate (2 μg·kg⁻¹·min⁻¹ Solu-Cortef, Pharmacia Upjohn) or 0.09% NaCl was initiated and continued throughout the study (t = 360 min).

Microdialysis. After local analgesic of 0.25 ml lidocaine, a microdialysis catheter (CMA-60, CMA Stockholm, Sweden) was inserted at t = −150 min in the subcutaneous adipose tissue −5 cm dextrolateral of the umbilicus and in the right femoral subcutaneous adipose tissue. The microdialysis catheters have a molecular cut-off of 20 kDa and a membrane length of 30 mm.

Before insertion, the catheters were manually flushed with perfusion fluid (Ringer chloride, T1, CMA Stockholm; Na⁺ 147 mmol/l; K⁺ 1.4 mmol/l; Ca²⁺ 2.3 mmol/l; Cl⁻ 156 mmol/l, pH 6, and osmolality, 290 mosmol/kg) to allow for clearance of air bubbles from the microdialysis membranes. The microdialysis systems were perfused at a flow rate of 0.3 μl/min with the CMA-106 perfusion pump (CMA Stockholm). This flow rate was chosen to obtain −100% equilibrium of glycerol with the interstitial fluid (25). The observed change in interstitial glycerol concentration can be seen as an index of lipolysis (3, 12, 14).

Sampling of the interstitial fluid was commenced at t = −90 min to allow for 60 min of equilibration to minimize the influence of local edema and hemorrhage. The sampling was performed every 30 min and continued until t = 360 min.

Palmitate turnover. Systemic palmitate flux was measured at baseline and at the end of the hydrocortisone or saline infusion with the isotope dilution technique and steady-state equations. [9,10-³H]palmitate (Laegemiddelstyrelsen, Copenhagen, Denmark) was infused continuously at 0.3 μCi/min from −60 to 0 min and from 300 to 360 min. Blood samples for measurements of palmitate concentration and specific activity (SA) were drawn before the infusions and after 30, 40, 50, and 60 min of each infusion period. Plasma palmitate concentration and SA were determined by HPLC (21) by use of [³H₃]palmitate as internal standard (16). Systemic palmitate flux was calculated using the [9,10-³H]palmitate infusion rate divided by the steady-state palmitate SA.

Indirect calorimetry. Indirect calorimetry was performed with a ventilated hood (Deltatrac Metabolic Monitor; Datex, Helsinki, Finland) at 40 l/min. Energy expenditure, respiratory quotient, and 24-h excretion of urea were measured from the excretion rate of urea in urine collected during the entire study period, and glucose, protein, and lipid oxidation were calculated (8). Calibration of the system was performed by combustion of a known amount of 99.6% ethanol at regular intervals. Baseline calorimetry was performed at baseline after 30 min of rest and was carried out for 30 min. Stimulated calorimetry was initiated 30 min before the end of the experiment.

Adipose tissue blood flow. To ensure stable tissue perfusion conditions, subcutaneous adipose tissue perfusion was measured with the ¹³³Xe washout technique (17). Approximately 3 Mæ of ¹³³Xe were injected into the subcutaneous adipose tissue of the abdomen −5 cm sinistrolateral to the umbilicus. Disappearance of ¹³³Xe was continuously measured starting from 30 min after injection by use of a NaI detector (EG&G Ortec, Workingham, Berkshire, UK), as previously described (10). The tissue-to-blood partition coefficient was corrected for skinfold caliper as described by Bülow et al. (5).

Assays. PG was analyzed in duplicate with the glucose oxidase method (Beckman Coulter, Palo Alto, CA). Measurements were performed immediately to determine isotonic glucose infusion rate.

Serum GH was analyzed with a double monoclonal immunofluorometric assay (Delfia, Wallac Oy, Turku, Finland). Serum C-peptide and insulin were measured with an immunnoassay (Dako, Glostrup, Denmark). Plasma glucagon was measured by an in-house radioimmunoassay (22). Serum cortisol was measured with a solid-phase time-resolved fluorimmunoassay (Delfia, Wallac Oy).

Serum cortisol was determined by a colorimetric method with a commercial kit (Wako Pure Chemical Industries, Neuss, Germany).

Blood levels of alanine, glycerol, 3-OHB, and lactate were assayed with an automated fluorometric method (18).

Glycerol levels in the microdialysis dialysate were measured in duplicate by an automated spectrophotometric kinetic enzymatic analyzer (CMA 600, CMA, Solna, Sweden).

Statistical analysis. Results are expressed as time-averaged values during baseline (t = −150–0) and the stimulated period (t = 240–360 min). Statistical difference is based on comparison between the area under the curve (AUC) during baseline (t = −150–0) and that during the stimulated period (t = 240–360 min) unless otherwise specified.

AUC was calculated using ICUPlot version 1.0 (CMA Stockholm) with the trapezoid method. Statistical analysis was performed using SPSS for Windows version 10.0 (SPSS, Chicago, IL).

The Kolmogorov-Smirnov test of normal distribution of the data was performed, and depending on the outcome, a parametric (Student's t-test for paired samples) or Wilcoxon signed ranks test (for related samples) was used. P values <0.05 were considered significant.

RESULTS

Circulating hormones. During hydrocortisone sodium succinate infusion, serum cortisol rose to 888 ± 12 vs.
245 ± 7 nmol/l in the placebo situation (Fig. 1). Serum levels of insulin remained stable, ~30 pmol/l, in both experiments, as did plasma glucagon in the range of 40 ng/l. During infusion of somatostatin, serum C-peptide concentrations declined in both situations, but less so during hydrocortisone infusion (*P* = 0.03; Table 1). Comparable replacement levels of insulin and glucagon were recorded (Table 1): insulin [baseline (*P* = 0.60); stimulation (*P* = 0.76)] and glucagon [baseline (*P* = 0.50); stimulation (*P* = 0.74)].

Serum levels of GH were subtly increased before (*P* > 0.3; Table 2). Serum FFA increased from 0.320 ± 0.01 to 0.612 ± 0.01 mmol/l (AUC_difference *P* = 0.015).

**Interstitial glycerol concentrations.** In the abdominal subcutaneous adipose tissue, the interstitial glycerol increased to 327 ± 35 vs. 156 ± 30 μmol/l, corresponding to an average increase of 110% (AUC<sub>0.240–360</sub> difference *P* = 0.05; Table 3; Fig. 2). Femoral interstitial glycerol concentration increased to 178 ± 28 vs. 91 ± 22 μmol/l, equal to an increase of 96% (AUC<sub>0.240–360</sub> difference *P* = 0.02). No significant difference was found between the abdominal and femoral increases (*P* = 0.23).

**Palmitate metabolism.** Baseline palmitate fluxes (Fig. 3) were comparable in both situations (*P* = 0.24), whereas palmitate fluxes increased during hydrocortisone infusion (*P* = 0.01).

**Indirect calorimetry.** Lipid oxidation determined by indirect calorimetry showed no difference between baseline situations [518 ± 17 vs. 518 ± 33 kcal/24 h (*P* = 1.00; Table 4)], whereas a profound increase in lipid oxidation was found during hydrocortisone infusion [850 ± 31 vs. 564 ± 40 kcal/24 h (*P* = 0.02)].

### Table 1. Hormones

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Placebo</th>
<th>Cortisol</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin, pmol/l</td>
<td>Baseline 29.96 ± 1.14</td>
<td>31.06 ± 1.74</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>Stimulated 33.93 ± 1.50</td>
<td>31.93 ± 1.49</td>
<td>0.76</td>
</tr>
<tr>
<td>C-peptide, pmol/l</td>
<td>Baseline 205.60 ± 19.59</td>
<td>207.19 ± 20.71</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>Stimulated 40.74 ± 7.00</td>
<td>86.36 ± 11.49</td>
<td>0.03</td>
</tr>
<tr>
<td>GH, μg/l</td>
<td>Baseline 0.36 ± 0.04</td>
<td>0.62 ± 0.11</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Stimulated 0.54 ± 0.03</td>
<td>0.83 ± 0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>Glucagon, ng/l</td>
<td>Baseline 44.83 ± 7.44</td>
<td>40.54 ± 5.54</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Stimulated 29.19 ± 6.68</td>
<td>28.41 ± 6.67</td>
<td>0.74</td>
</tr>
</tbody>
</table>

Data are time-averaged values during baseline (*t* = −150–0 min) and stimulation (*t* = 240–360 min); paired analysis of area under the curve (AUC) during baseline and stimulation. GH, growth hormone.

### Table 2. Circulating metabolites

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Placebo</th>
<th>Cortisol</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine, μmol/l</td>
<td>Baseline 276 ± 14</td>
<td>246 ± 10</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>Stimulated 320 ± 15</td>
<td>270 ± 9</td>
<td>0.12</td>
</tr>
<tr>
<td>3-OHB, μmol/l</td>
<td>Baseline 40 ± 8</td>
<td>43 ± 8</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>Stimulated 44 ± 11</td>
<td>94 ± 10</td>
<td>0.29</td>
</tr>
<tr>
<td>Lactate, μmol/l</td>
<td>Baseline 619 ± 38</td>
<td>545 ± 22</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>Stimulated 680 ± 30</td>
<td>582 ± 20</td>
<td>0.08</td>
</tr>
<tr>
<td>Glycerol, μmol/l</td>
<td>Baseline 37 ± 3</td>
<td>37 ± 3</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Stimulated 34 ± 3</td>
<td>51 ± 3</td>
<td>0.03</td>
</tr>
<tr>
<td>[9,10-3H]palmitate, μmol/min</td>
<td>Baseline 81 ± 17</td>
<td>108 ± 33</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>Stimulated 92 ± 24</td>
<td>165 ± 17</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Data are time-averaged values during baseline (*t* = −150–0 min) and stimulation (*t* = 240–360 min); paired analysis of AUC during baseline and stimulation. 3-OHB, 3-hydroxybutyrate.
Glucose infusion rate and blood flow. Glucose infusion, measured as glucose infusion rate (mg/h) × h, was comparable: 21.45 ± 5.70 mg (saline) and 20.43 ± 6.03 mg (hydrocortisone; P = 0.93). Adipose tissue blood flow (ATBF) was equal during baseline [3.53 ± 0.52 ml/100 mg⁻¹·min⁻¹ (saline) vs. 3.3 ± 0.89 ml/100 mg⁻¹·min⁻¹ (hydrocortisone); P = 0.94] and during stimulation [4.29 ± 0.99 ml/100 mg⁻¹·min⁻¹ (saline) vs. 3.14 ± 0.53 ml/100 mg⁻¹·min⁻¹ (hydrocortisone); P = 0.45].

DISCUSSION

The aim of this study was to determine the effects of acute hydrocortisone sodium succinate and subsequent elevations of circulating cortisol on total and local FFA and glycerol mobilization in the postabsorptive state. In line with previous studies (6, 7), we found that cortisol increased serum FFA, serum glycerol, and whole body palmitate turnover, indicating increased systemic lipolysis. In addition, we observed that cortisol augmented lipid oxidation (assessed by indirect calorimetry) and led to proportionate increments in interstitial glycerol concentrations in abdominal and femoral adipose tissue, findings that to our knowledge are novel. On the whole, our results suggest that cortisol stimulates upper body and lower body subcutaneous adipose tissue lipolysis evenly and does not support the notion that glucocorticoids per se cause abdominal obesity by preferentially inhibiting regional upper body lipolysis. It should be emphasized that, with the present design, we accomplished cortisol concentrations in the high physiological range (32) in the presence of comparable levels of insulin and glucose.

In our study, we recorded insulin concentrations of 30 pmol/l, close to normal fasting levels of between 20 and 30 pmol/l, whereas the glucagon values of 40 ng/ml were decreased compared with normal fasting levels.

Table 3. Interstitial metabolites

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Cortisol</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal glycerol, µmol/l</td>
<td>Baseline</td>
<td>183 ± 32</td>
<td>233 ± 51</td>
</tr>
<tr>
<td></td>
<td>Stimulated</td>
<td>156 ± 30</td>
<td>327 ± 35</td>
</tr>
<tr>
<td>Femoral glycerol, µmol/l</td>
<td>Baseline</td>
<td>131 ± 47</td>
<td>139 ± 22</td>
</tr>
<tr>
<td></td>
<td>Stimulated</td>
<td>91 ± 22</td>
<td>178 ± 28</td>
</tr>
</tbody>
</table>

Data are time-averaged values during baseline (t = −150–0 min) and stimulation (t = 240–360 min); paired analysis of AUC during baseline and stimulation.

Table 4. Indirect calorimetry

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Cortisol</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid oxidation, kcal/24 h</td>
<td>Baseline</td>
<td>518 ± 17</td>
<td>518 ± 33</td>
</tr>
<tr>
<td></td>
<td>Stimulated</td>
<td>564 ± 40</td>
<td>850 ± 31</td>
</tr>
<tr>
<td>Protein oxidation, kcal/24 h</td>
<td>Baseline</td>
<td>574 ± 82</td>
<td>474 ± 26</td>
</tr>
<tr>
<td></td>
<td>Stimulated</td>
<td>814 ± 03</td>
<td>601 ± 02</td>
</tr>
<tr>
<td>RQ</td>
<td>Baseline</td>
<td>0.89 ± 01</td>
<td>0.88 ± 02</td>
</tr>
<tr>
<td></td>
<td>Stimulated</td>
<td>0.85 ± 03</td>
<td>0.81 ± 02</td>
</tr>
<tr>
<td>EE</td>
<td>Baseline</td>
<td>1,812 ± 124</td>
<td>1,785 ± 96</td>
</tr>
<tr>
<td></td>
<td>Stimulated</td>
<td>1,733 ± 105</td>
<td>1,185 ± 112</td>
</tr>
</tbody>
</table>

Results show indirect calorimetry during baseline and stimulation, a paired analysis. RQ, respiratory quotient; EE, energy expenditure.
levels of between 60 and 70 ng/ml (11). Thus a relative lack of glucagon may explain the need to administer small amounts of exogenous glucose temporarily at a rate of ~20 mg/h to maintain euglycemia; it is unlikely that the glucagon deficit has affected lipid metabolism, because glucagon has no detectable effect on lipolysis (10).

Circulating GH levels were minutely increased in our study. Although it is likely that glucocorticosteroids may interfere with GH secretion, the fact that GH levels were increased before cortisol administration suggests that the difference has been accidental rather than cortisol induced. GH has lipolytic effects (11), but it is unlikely that tiny GH elevations of 0.2–0.3 µg/l in the circulation have had any major impact on lipolysis.

Microdialysis measures flux-generating concentrations of a variety of compounds across a diminutive dialysis membrane and permits assessment of changes in interstitial concentrations of these compounds in various tissues (4, 14, 20, 28, 34). True (or “quasi-true”) equilibrium across the membrane is only accomplished with very low flow rates, as exploited in the present study (28). Under these circumstances, any increase in glycerol concentrations in the perfusate may be seen as a reflection of increased regional lipolysis, provided local blood flow and glycerol clearance are not altered.

In the present study, we observed comparable increments in interstitial glycerol concentrations in femoral and abdominal adipose tissue during cortisol exposure. This observation is at variance with previous suggestions that cortisol may inhibit lipolysis in cultured abdominal adipocytes in vitro (23, 24) and diminish FFA efflux from abdominal adipose tissue in vivo (30).

In this context, it should be considered that any change in regional blood flow could alter the flux-generating concentration gradients across the dialysis catheter. We did not, however, observe any change in ATBF during cortisol exposure. This finding is in line with the study of Samra et al. (30). In addition, we utilized a low perfusion rate in our study, meaning that the results were obtained at quasi-equilibrium and that any change in relative recovery has been of minor importance.

Furthermore, a concomitant increase in the rate of lipolysis and of reesterification of FFA to triacylglycerol in abdominal adipocytes could lead to an increased glycerol release and a decreased or unchanged FFA release. Still, the study of Samra et al. (30) failed to observe any indications that the ratio of FFA to glycerol in efferent subcutaneous blood changed during cortisol exposure.

The prevailing concentrations of glucose and, hence, insulin in the circulation are evidently crucial; it is well described that lipolysis is exquisitely sensitive to minute changes in insulinemia (15, 29). With the present design, we accomplished virtually identical levels of insulin and glucose by infusing somatostatin (to inhibit endogenous insulin secretion) and glucose to maintain euglycemia. In some previous studies (30), a distinct possibility was raised that minute elevations in circulating glucose and insulin concentrations might have inhibited lipolysis in some regions.

It should be highlighted that our results, including the observation of stimulated abdominal adipose tissue lipolysis, represent the direct and acute effects of cortisol. With prolonged elevation of circulating glucocorticoid levels, insulin resistance and subsequent hyperinsulinemia evolve, and it is indeed conceivable that the combination of hypercortisolism and hyperinsulinemia may preferentially inhibit upper body lipolysis, as suggested in the studies by Samra et al. (30).

Furthermore, it should be noted that the arteriovenous difference study by Samra et al. (30) employed a hydrocortisone infusion of 11 h, and our study had a duration of merely 6 h. Additionally, supraphysiologic levels of cortisol were obtained (1,500 nmol/l) in the former study, whereas we accomplished cortisol levels comparable to severe stress (~800 nmol/l).

As discussed elsewhere, microdialysis and the arteriovenous technique developed by Frayn et al. (9) and exploited in the study of Samra et al. (30) are two distinct methods with complementary applications in the study of adipose tissue metabolism (4, 33). For instance, the arteriovenous technique includes substantial components of skin metabolism and intravascular lipoprotein lipase (LPL) activity; in regard to quantitative measurements of flux rates, both methods are hampered by inability to measure blood flow rates in the relevant tissue compartments (4, 33). Theoretically, it is thus possible that some of the findings in studies employing arteriovenous techniques could relate to changes in either the activity or the effectiveness of LPL.

Alternative mechanisms whereby cortisol could promote deposition of upper body fat include specific stimulation of lipogenesis. Finally, it is a vexing question how cortisol affects visceral adipose tissue. This lipid pool is not readily accessible, and it is possible that cortisol specifically may inhibit lipolysis in the region.

The intracellular mechanisms behind the metabolic effects of glucocorticoids are uncertain. Cortisol acts at the intracellular glucocorticoid receptors that are present in significant numbers in adipocytes (25, 27). Studies in human and rat adipocytes have suggested that glucocorticoids may stimulate both LPL and hormone-sensitive lipase (HSL) activity (24, 31). On the other hand, the study of Samra et al. (30) indicated inhibition of HSL in adipose tissue. The apparent discrepancy could relate to minute elevations of circulating insulin concentrations in the latter study, the rate of lipolysis being extremely sensitive to insulin.

In conclusion, our results clearly suggest that cortisol in physiological concentrations stimulates whole body lipolysis and that this effect is caused by proportionate stimulation of femoral and abdominal subcutaneous adipose tissue. To what extent these events may be modulated by ensuing hyperinsulinemia remains uncertain.

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REFERENCES


