

URINARY-FREE CORTISOLS (UFC) & 17-HYDROXYCORTICOSTEROIDS (17OHS)

Dr. Friedman uses urinary measurements of cortisol called urinary-free cortisols (UFC) and 17-hydroxy-corticosteroids (17OHS) to evaluate cortisol status in patients either suspected of having Cushing's syndrome or to monitor cortisol replacement dosing. Urinary-free cortisol measures only free cortisol in the urine. For the urine to excrete cortisol, it gets filtered by the kidney and gets reabsorbed. There is also an enzyme called 11beta-hydroxysteroid dehydrogenase that interconverts cortisol and inactive cortisone. Cortisol has to exceed the ability of this enzyme to convert it to cortisone as well as to exceed the ability of the kidney to reabsorb cortisol in order for it to appear in the urine. Additionally, cortisol is bound to a protein to cortisol-binding globulin (CBG) that limits the amount of free cortisol that is in the plasma. Only the free cortisol in the plasma can be excreted into the urine. As cortisol production rates increase, the amount of free cortisol in the urine, as measured by UFC, only increases slightly until a threshold is exceeded at which time the amount of urinary-free cortisol increases more rapidly. Therefore, with mildly increased cortisol production rates, such as in mild Cushing's syndrome, the amount of urinary-free cortisol may only be mildly elevated. However, with high cortisol production as in more classic Cushing's syndrome, urinary-free cortisol goes up more dramatically.

The 17-hydroxy-corticosteroids (17OHS) measures cortisol, some cortisol precursors, and some cortisol metabolites. They have to have a hydroxy group at the 17 position of the cortisol ring. This was one of the first assays used to determine cortisol production rate and was discovered in 1958 by Dr. Liddle at Vanderbilt. This test was widely used to assess cortisol production in patients with Cushing's syndrome; however, the urinary-free cortisol is a newer test and has somewhat replaced the 17-hydroxysteroids. The 17OHS test can pick up more mild productions of cortisol and is more linear with increased cortisol production rates as opposed to the urinary-free cortisol that is more exponential. For this reason, sometimes the 17OHS test can pick up mildly elevated increased cortisol production as mild Cushing's syndrome while the urinary-free cortisol is normal.

Many patients with adrenal insufficiency, either because they are cured of Cushing's syndrome and have postoperative cortisol deficiency, have had their adrenals removed, or have low cortisol due to pituitary dysfunction, are receiving cortisol replacement. Dr. Friedman desires to measure whether the cortisol replacement is accurate. To determine this, he has found the 17OHS assay is probably the best determination of cortisol replacement. The 17OHS assay in most laboratories have a range between 2 mg and 6 mg

per 24 hours. The 17OHS may also be corrected for creatinine because patients that are bigger and have a higher creatinine secretion along with their higher 17OHS production. The range for the 17OHS corrected for creatinine is 1.6 mg to 3.6 mg. Dr. Friedman has found that 17OHSs in the upper range of normal usually indicates proper cortisol replacement. A 17OHSs in the lower range of normal might indicated inadequate cortisol replacement, and a 17-hydroxycorticosteroids above the normal range indicates overreplacement. The UFC can also be examined, but usually the UFC measures the cortisol in the urine within the first hour after taking the pill. It is therefore falsely high because during that first hour, it exceeds the kidneys' threshold to reabsorb it as well as the threshold of cortisol-binding globulin and therefore, it is often high while the 17-hydroxysteroids are normal. This would indicate proper replacement. The amount of cortisol in the urine as measured by UFC *after* the first hour or so of taking a cortisol pill is usually quite low.

For most patients, Dr. Friedman measures both the UFC and 17OHS both to diagnose Cushing's syndrome and to monitor replacement. To obtain more information about Dr. Friedman, go to his website at www.goodhormonehealth.com.