**Cortisol**

|  |  |  |  |
| --- | --- | --- | --- |
| Test | Result | Unit for Result | Date of assessment |
| AM Cortisol 1  (“8 am”) (CPT Code 82533)] | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| \*\*PM Cortisol  (Addison's and circadian rhythm shift) | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| 24 Hour Urine Cortisol | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Salivary Cortisol2 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

1 If serum cortisol is used, a sufficiently narrow, early time window is recommended (eg, 8 AM, which may be drawn between 7:30 and 8:30 AM) to avoid divergent results

2More studies appear to have been done in the context of ME/CFS research using salivary cortisol than serum cortisol (based upon a PubMed search of “cortisol chronic fatigue syndrome”). Salivary cortisol measures may be collected multiple times a day and on multiple days. Based on Roberts et al. (2004), timing after awaking is important. Thus it is recommended that if a morning salivary cortisol is being collected, it should be a consistent time after waking (eg, 30 min or 60 min). Those wishing to include salivary cortisol measures are advised to review and implement, as appropriate, this and other quality measures presented by Powell et al (2013) Table 1. [Possibly: patients should be instructed regarding appropriate avoidance of food, water, gum, brushing teeth, smoking shortly before collection times.]

**Diabetes3**

|  |  |  |  |
| --- | --- | --- | --- |
| Test | Result | Unit for Result | Date of assessment |
| Glycosylated Hemoglobin (HgbA1C) | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Fasting glucose | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Oral glucose tolerance test (2 hour) | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

3 Note, if a test indicates that a patient has diabetes, a confirmatory test must generally be performed before assigning a diabetes diagnosis (if making a diagnosis is relevant to the study).

**Thyroid**

|  |  |  |  |
| --- | --- | --- | --- |
| Test | Result | Unit for Result | Date of assessment |
| Free T4 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Free T3 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| \*Thyroid-Stimulating Hormone (TSH) | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

**Sex hormones4**

|  |  |  |  |
| --- | --- | --- | --- |
| Test | Result | Unit for Result | Date of assessment |
| FSH | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| LH | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Estradiol | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Progesterone | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Testosterone, free5 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| DHEA-S | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

**4If labs are being drawn on menstruating females, study should determine how to standardize time in cycle. Otherwise status should be noted (eg, pregnancy, birth control type, post-menopausal, other)**

## 5Serum testosterone should be drawn in the morning at 8 AM (between 7:30 and 8:30 AM) due to significant diurnal effect (Brambilla et al, 2009). Generally speaking it may be advisable if other labs are drawn in morning as well, though diurnal effect appears to be less for some of these.

**Other**

|  |  |  |  |
| --- | --- | --- | --- |
| Test | Result | Unit for Result | Date of assessment |
| Plasma renin activity6 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Aldosterone6 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| ACTH | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| \*\*Fluid deprivation test with DDAVP7 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Prolactin | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

## 6 Study must specify whether patient is to be supine or sitting (standing is not recommended in ME/CFS studies) and time of day.

**7 Potentially important in ME/CFS studies, but no standard procedure is provided.**

## Pregnancy Test

Has a pregnancy test been completed**:** Yes No Not applicable

Pregnancy Test – N/A Reason: Post-Menopausal Surgically sterile Non-surgically sterile Male

Pregnancy Test - Date Performed: (mm/dd/yyyy)

Pregnancy Test Method: Blood Urine

Pregnancy Test – Result: Positive Negative

## GENERAL INSTRUCTIONS

Multiple studies have shown ME/CFS to be associated with alterations in neuroendocrine function. Laboratory tests may be used to study associations between alterations in neuroendocrine function and other factors, such as severity of illness or response to treatment. Laboratory tests may also be used to evaluate for comorbid endocrine conditions, or to determine an individual’s eligibility for a study (eg, ruling out uncontrolled hypothyroidism). Laboratory tests may also be used to determine an individual’s eligibility for a study.

Based on discretion of researcher, certain sex hormone measurements may be measured on male or female patients.

Important note: TSH is classified as a Core data element (i.e., required for all ME/CFS studies to collect). The remaining data elements are classified as Supplemental or Exploratory (i.e., non-Core) and should only be collected if the research team considers them appropriate for their study. The elements not identified by asterisks (\*) are supplemental.

\*Element is classified as Core

\*\*Element is classified as Exploratory

It is important that the study protocol documents detail if a local or central laboratory will perform the laboratory tests.

**SPECIFIC INSTRUCTIONS**

All tests are referring to venous blood draws unless otherwise specified.

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

* Lab panel – Choose the lab panel that was performed.
* Data and time specimen collected – Record the date (and time) the specimen was collected. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete data plus hours and minutes, etc). and in the format acceptable to the study database.
* Result – Record the numeric results or alpha-numeric results for each laboratory test.
* Unit for Result – Record the units the numeric results for each laboratory test are measured in.

**REFERENCES**

Brambilla DJ, Matsumoto AM, Araujo AB, McKinlay JB. The effect of diurnal variation on clinical measurement of serum testosterone and other sex hormone levels in men. J Clin Endocrinol Metab. 2009 Mar;94(3):907-13. doi: 10.1210/jc.2008-1902. Epub 2008 Dec 16.

Powell DJ, Liossi C, Moss-Morris R, Schlotz W. Unstimulated cortisol secretory activity in everyday life and its relationship with fatigue and chronic fatigue syndrome: a systematic review and subset meta-analysis. Psychoneuroendocrinology. 2013 Nov;38(11):2405-22.

Roberts AD, Wessely S, Chalder T, Papadopoulos A, Cleare AJ. Salivary cortisol response to awakening in chronic fatigue syndrome. Br J Psychiatry. 2004 Feb;184:136-41.