



*Better health through
laboratory medicine.*

PEARLS OF LABORATORY MEDICINE

ACTH and Cortisol

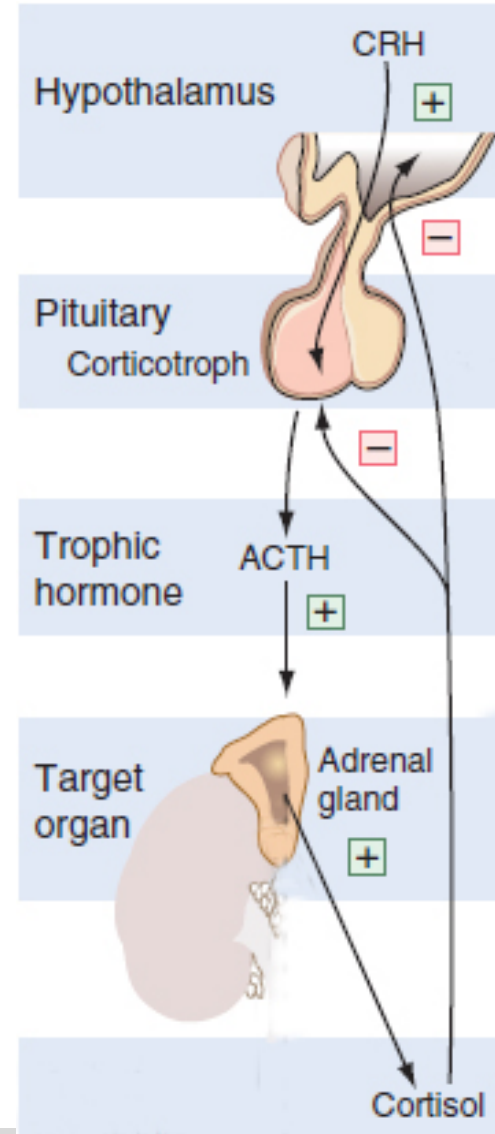
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The hypothalamic-pituitary-target organ axis



Cushing's Syndrome

- Striate rubrae
- Facial plethora
- Proximal muscle weakness
- Visceral fat accumulation
- Easy bruising
- Hypokalemia
- Weight gain
- Obesity
- Diabetes
- Hypertension



Causes of Cushing's Syndrome

- ACTH-Dependent Cushing's
 - Cushing's disease (=ACTH-producing pituitary adenoma)
 - Ectopic ACTH syndrome

- ACTH-Independent Cushing's
 - Adrenocortical adenoma
 - Adrenocortical carcinoma



Tests Used for the Diagnosis of Cushing's Syndrome

Clinical suspicion of Cushing's

Screening/confirmation of Diagnosis

- 1 mg dexamethasone overnight test
- 24-h urinary free cortisol excretion increased above normal (3x)
- Midnight plasma cortisol or salivary cortisol

If further confirmation needed

- Low dose dexamethasone test (plasma cortisol > 1.8 µg/dL after 0.5 mg dexamethasone q6h for 2 days)

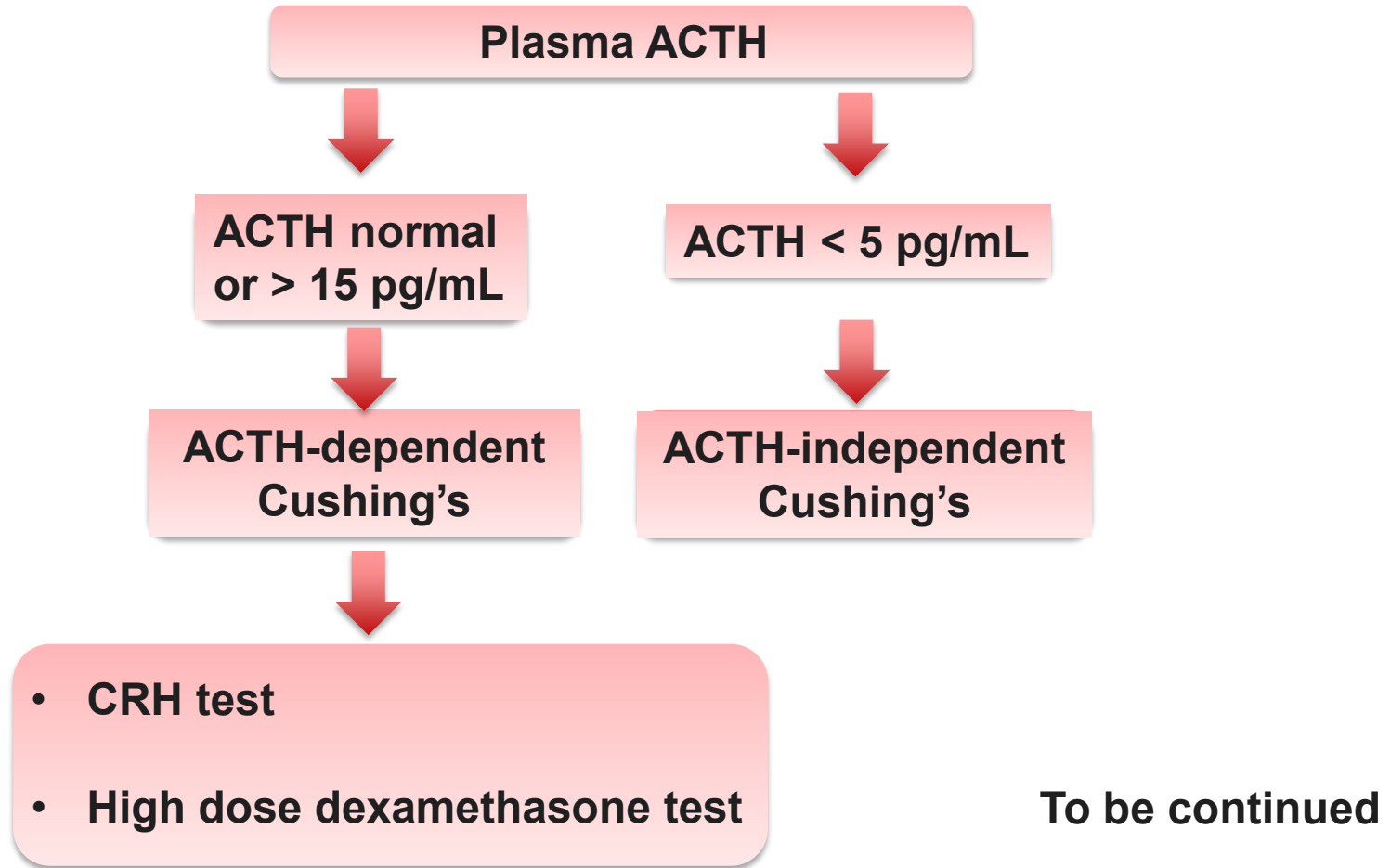
Normal results

Abnormal results

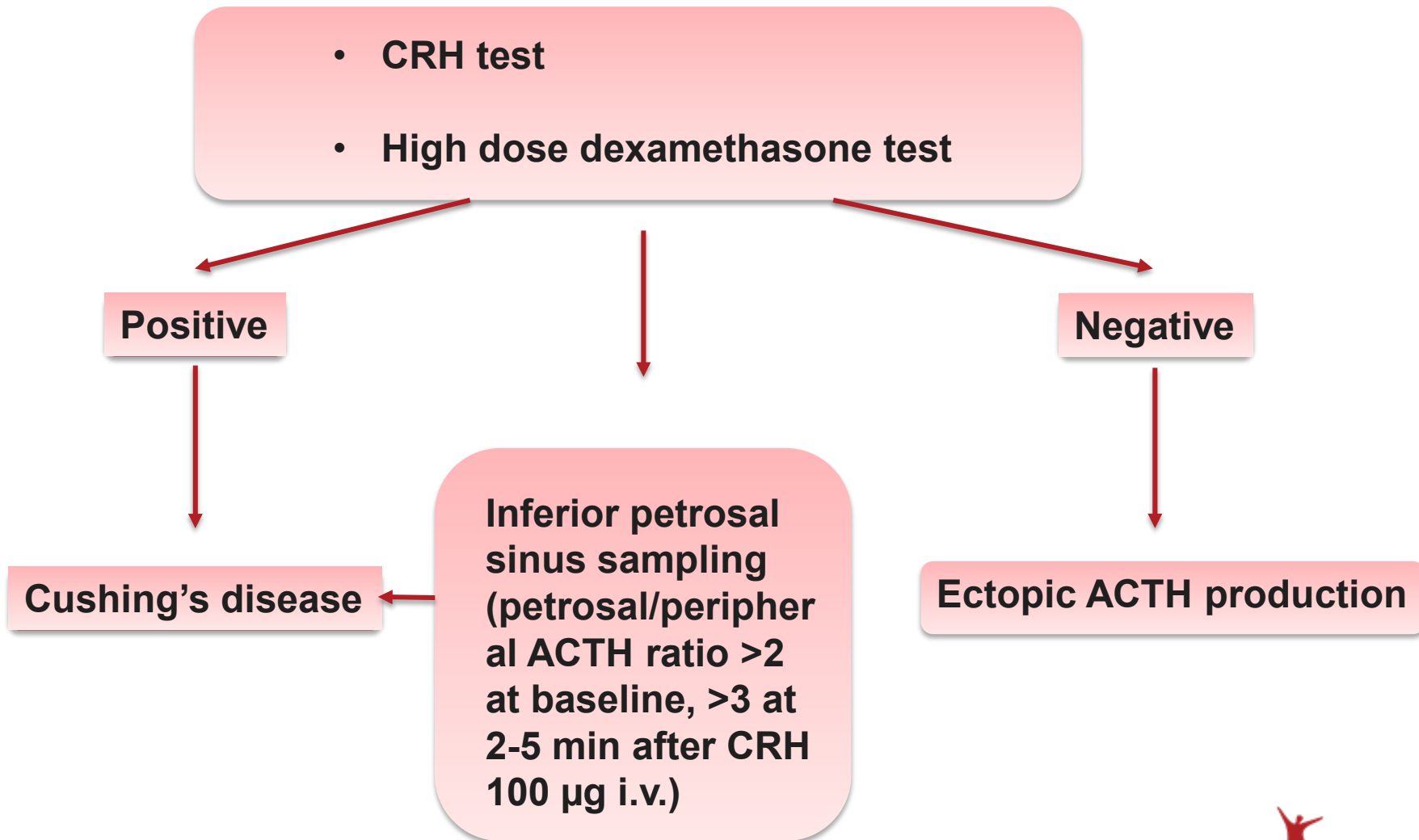
Differential diagnosis



Tests Used for the Differential Diagnosis



Tests Used for the Differential Diagnosis (Continued)



Adrenal Insufficiency

- Primary adrenal insufficiency (Addison's disease)
 - Autoimmune adrenalitis
 - Tuberculosis
 - Granulomatous disorders
 - Metastatic disease
 - Adrenal hemorrhage
 - HIV
 - Acquired immuno-deficiency syndrome
 - Infection



Adrenal Insufficiency

- Secondary adrenal insufficiency
 - Pituitary tumors
 - Pituitary irradiation
 - Pituitary hemorrhage
 - Long-term steroid therapy



Tests for the Diagnosis of Adrenal Insufficiency

- Basal hormone measurements
- ACTH stimulation test
- Corticotropin-releasing hormone test



ACTH Measurements

- Prechilled EDTA lavender-top tube, on ice, kept frozen at -20°C until time of analysis
- Competitive binding radioimmunoassays (RIAs)
- Immunoassays that measure the concentration of ACTH are more common
 - Intact ACTH (1-39)
 - N-terminal ACTH fragments (1-24)
 - ACTH precursors
- Chemiluminescent method



Cortisol Measurements

- Serum cortisol measurement
 - 90% of circulating cortisol bound to protein, mostly bound to albumin and the glycoprotein transcortin (cortisol-binding globulin [CBG])
 - 10% is unbound, free hormone, active
 - Radioimmunoassay (RIA) and chemiluminescent methods, high-performance liquid chromatography (HPLC) with tandem mass spectrometry (LC-MS)
- Urinary free cortisol measurement
 - LC-MS
- Salivary cortisol
 - LC-MS



References

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Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

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