

Endocrine Dysfunction in Erdheim-Chester Disease

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Disclosures

- Nothing to disclose

Objectives

- Overview of endocrine dysfunction in ECD
 - Diabetes insipidus
 - Partial and panhypopituitarism
 - Hypothalamic dysfunction
 - Hypothyroidism and thyroid nodules
 - Adrenal insufficiency
 - Premature ovarian insufficiency, infertility
 - Menopause and hormone replacement therapy
 - Hypogonadism
 - Osteoporosis
 - Diabetes mellitus
 - Obesity (peripheral and central)

Objectives

- How are hormones affected by ECD?
- What specific hormones are affected?
- What are the symptoms of hormone issues?
- How are hormone issues tested?
- How is hormone deficiency treated?
- How long do I have to stay on a treatment to stabilize?
- Why do many ECD patients have Diabetes Insipidus?
- What are some management techniques and treatments for DI?
- How do I know if I have DI?

Endocrinology & Metabolism

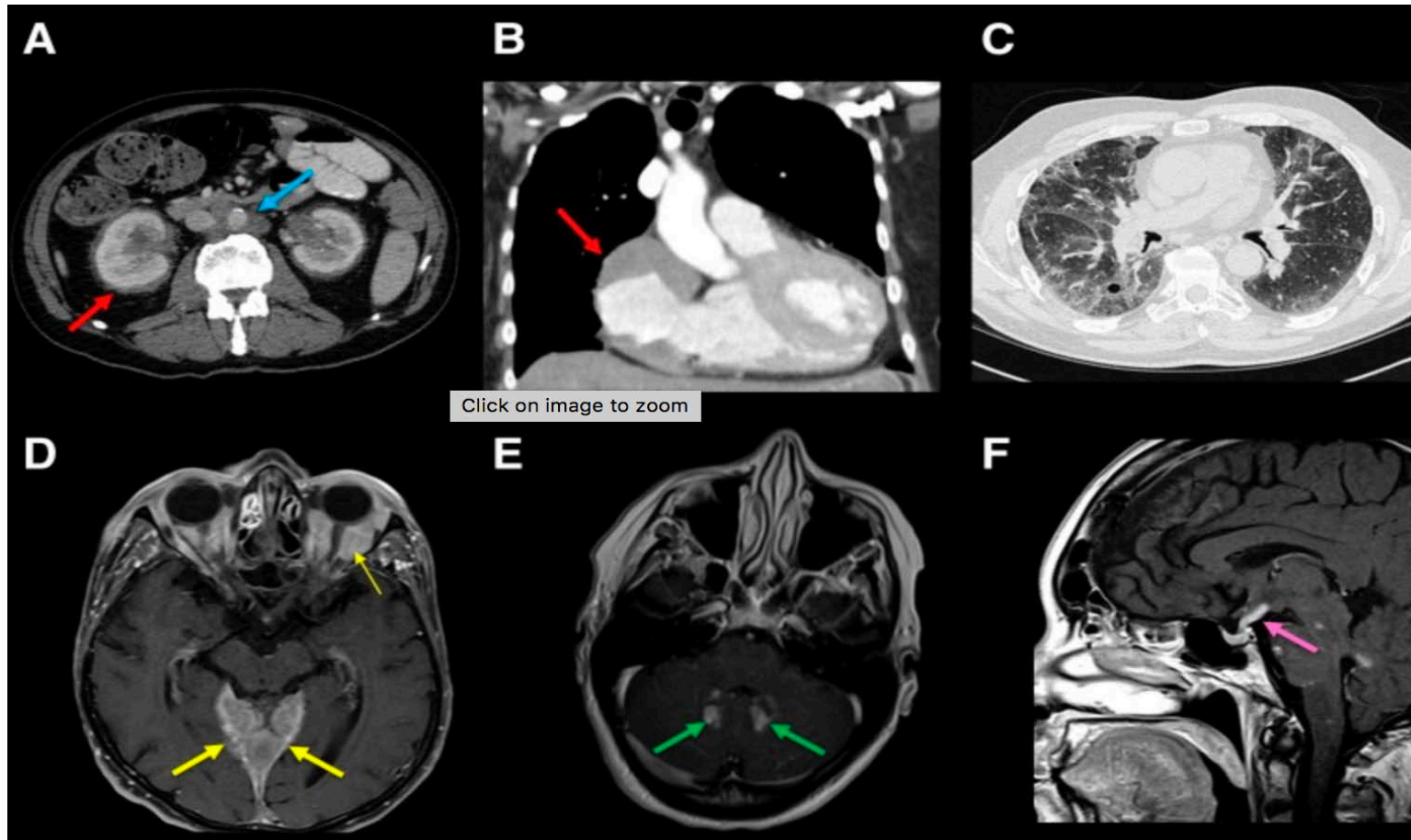
The screenshot shows the Hormone Health Network website. At the top, the logo for the Hormone Health Network is displayed, along with the text "International Resource Center" and "Pacientes y Cuidadores". Below this, there are three main navigation buttons: "HORMONES AND HEALTH", "DISEASES AND CONDITIONS", and "YOU AND YOUR ENDOCRINOLOGIST". To the right of these buttons is a search bar with the text "KEEP YOUR BODY IN BALANCE" and a search icon. Below the search bar is a "Select Language" dropdown menu.

The main content area features a sidebar on the left with social media icons for Facebook, Twitter, Pinterest, and Google+, and a list of navigation links: "The Endocrine System", "Hormones", "Endocrine Disrupting Chemicals (EDCs)", "Steroid and Hormone Abuse", "Stress and Your Health", and "Peer Support Resources".

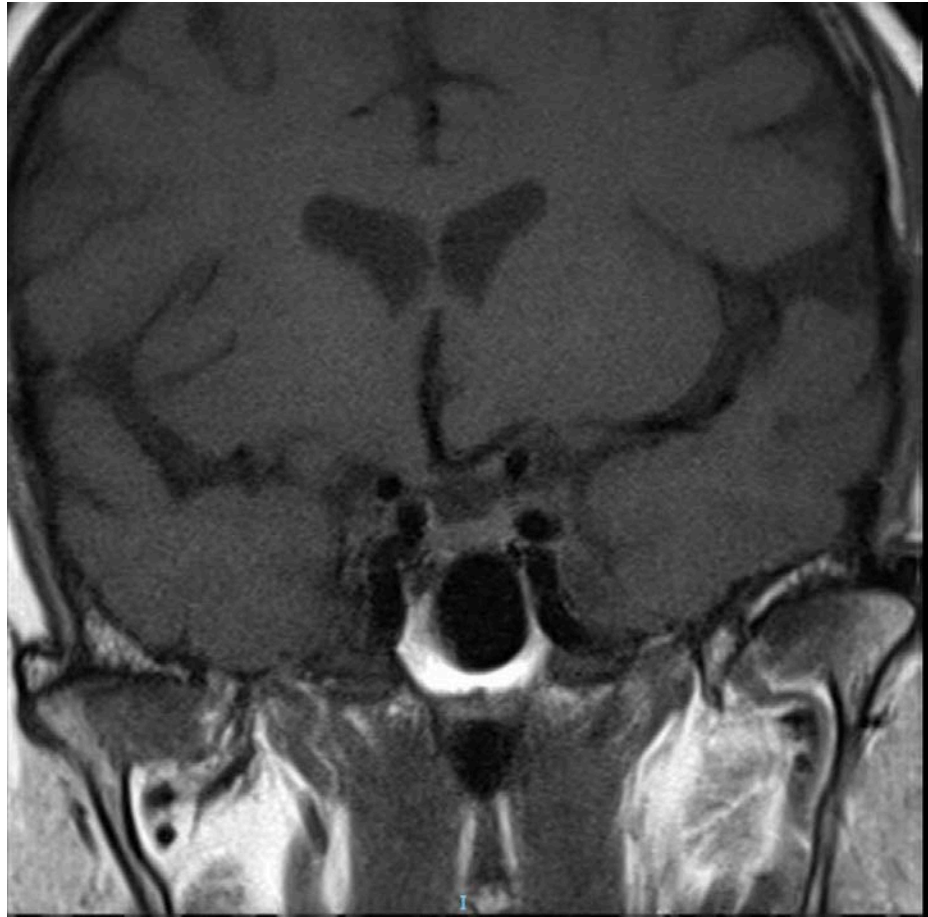
The main content area is titled "Download our Free App!". It includes a paragraph: "Virtually travel through the glands and organs of the endocrine system. The **Hormone Health Network's 3D Patient Education mobile application** uses the power of 3D visualization to explain the endocrine system and related conditions such as diabetes, thyroid disease, women's and men's health and many more. Users can virtually travel through the body with each hormone visualizing different endocrine disease states and conditions." Below this is another paragraph: "Features support use by clinicians to improve communication with their patients, including the ability to dissect, highlight, and share 3D models and other education materials from hormone.org with patients."

At the bottom of the main content area, there is a "FEATURED RESOURCE" section titled "Print Materials for Patients" with a shopping cart icon and an "ORDER" button. To the right of this is a video player for "Journey Through the Endocrine System ..." with "Watch later" and "Share" buttons.

Commonly affected organ systems



Pituitary Imaging





Juvianee I. Estrada-Veras et al. *Blood Advances* 2017.

Diabetes insipidus (DI)

- Imbalance of water in the body: intense thirst even after drinking fluids (polydipsia), and excretion of large amounts of urine (polyuria; >4L per day)
- While the names diabetes insipidus and diabetes mellitus sound similar, they're not related
- Diagnosis: water deprivation test
- DI:
 - Central DI
 - Nephrogenic DI
 - Gestational DI
 - Primary polydipsia

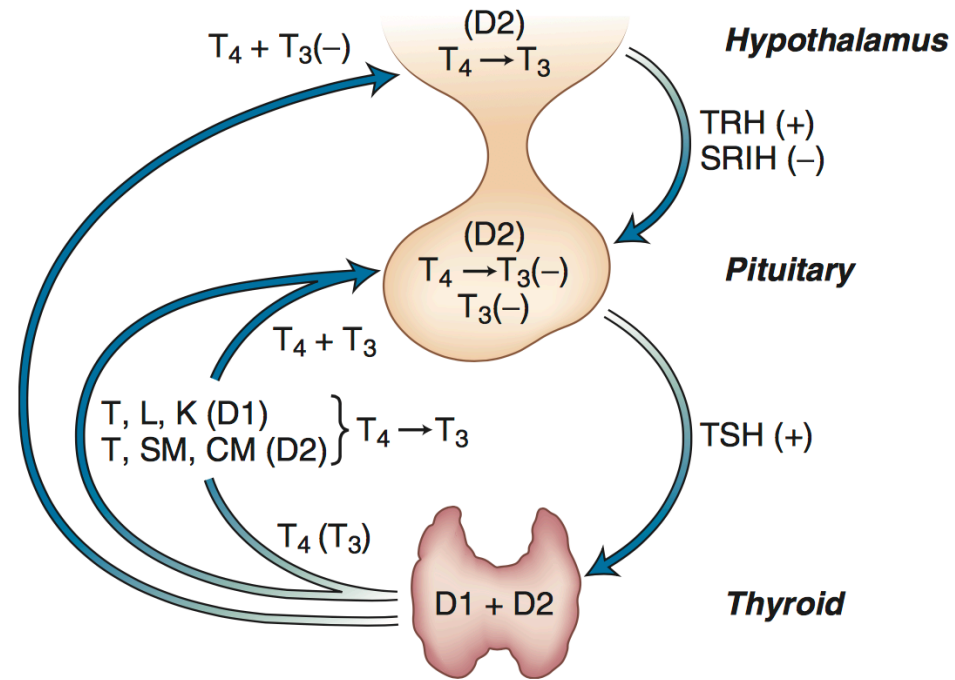
DI and ECD

- ~47% of patients, most patients have central DI
- Pituitary stalk thickening 25%
- Usual treatment is vasopressin (oral vs. intranasal), prevent dehydration, medical alert bracelet
- When desmopressin is prescribed, patients should be instructed to:
 - Avoid high fluid intake when the medication is ingested
 - Not ingest a higher than recommended dose
 - Promptly discontinue the medication and seek assessment if headache, nausea or vomiting develops

Panhypopituitarism

- Pituitary gland either fails to produce one or more of its hormones or doesn't produce enough of them
- Symptoms include:
 - Fatigue
 - Weight loss or obesity
 - Decreased sex drive
 - Sensitivity to cold or difficulty staying warm
 - Decreased appetite
 - Facial puffiness
 - Anemia
 - Infertility
 - Hot flashes, irregular or no periods, loss of pubic hair, and inability to produce milk for breast-feeding in women
 - Decreased facial or body hair in men
 - Short stature in children

Hypothyroidism



Hypothyroidism

Types of Hypothyroidism

Definitions

Primary Hypothyroidism

Biochemical diagnosis: TSH > RR (0.27-4.2 mIU/ml) with free thyroxine (fT4) < RR (0.9-1.7 ng/dl) on x2 repeated tests or TSH within RR on LT4

Subclinical Hypothyroidism

TSH > RR with normal fT4 x2

Overt hypothyroidism

TSH > RR and fT4 < RR with symptoms

Central hypothyroidism

fT4 < RR or low-normal levels in conjunction with a low, normal, or mildly elevated TSH

RR: reference range

LT4: levothyroxine therapy

NIH cohort

Baseline characteristics	Value
Age	54.3 ± 10.8 years
Sex	46 males (75%)
Mean time to diagnosis	4.2 years
Hypothyroidism- total	17 patients (28%)
Mean TSH (mIU/mL)	2.00 ±1.63 (0.27-4.20)
Mean free T4(ng/dL)	1.52 ±1.51 (0.9-1.7)

Results

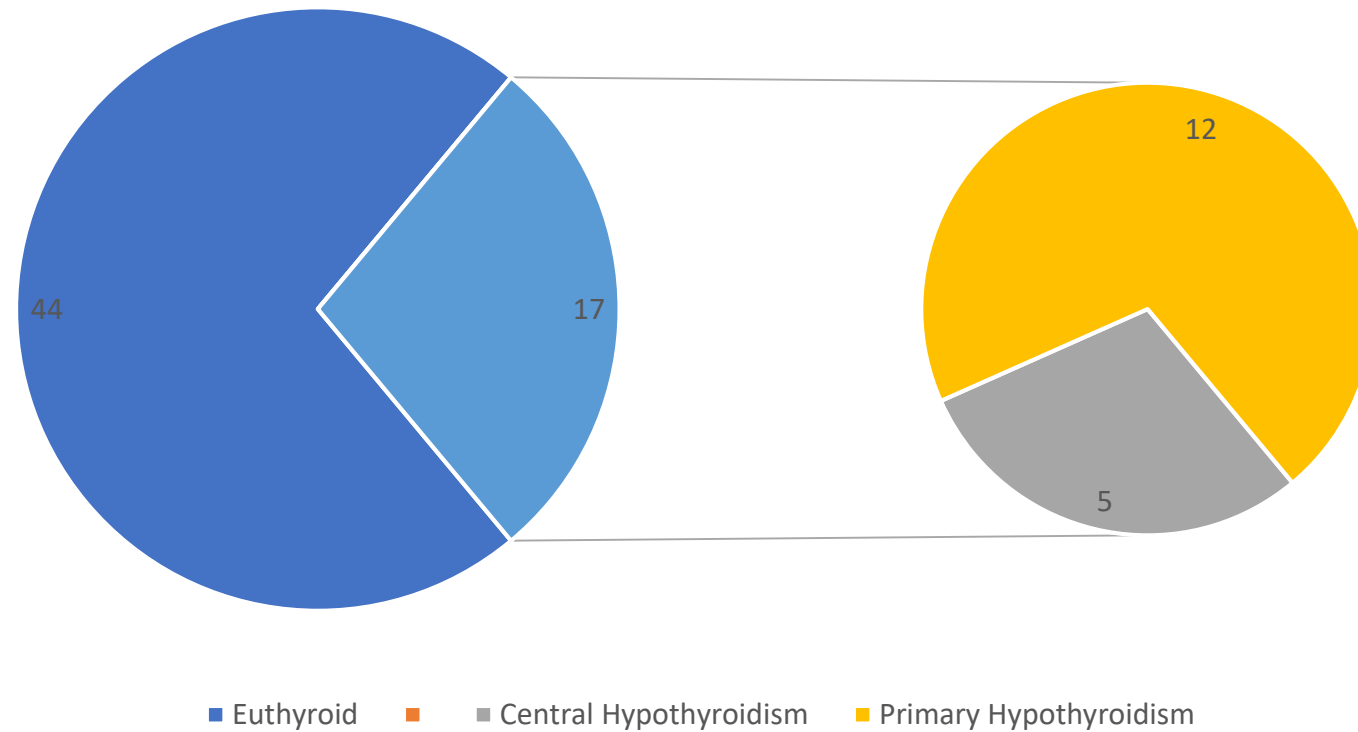
- The prevalence of hypothyroidism was higher than general population estimates (28% vs. 3.7%, $P < 0.05$)
- No subject presented with myxedema coma or thyrotoxicosis
- Fifteen patients had primary hypothyroidism
- Two patients had biochemical findings suggestive of central hypothyroidism (CH)
- Out of 2 patients suspected to have CH, one underwent additional dynamic testing

Results

- Seventeen subjects were on levothyroxine replacement
- Seven subjects suspected of primary hypothyroidism underwent TPO testing, out of which 4 had positive antibodies
- 3 subjects had primary hypothyroidism of unclear etiology with negative TPO
- The antibody status of 4 subjects suspected to have primary hypothyroidism was unknown
- Five subjects had a history or testing suggestive of central hypothyroidism
- One subject had total thyroidectomy for a benign tumor with mechanical symptoms

Results

Hypothyroidism in ECD

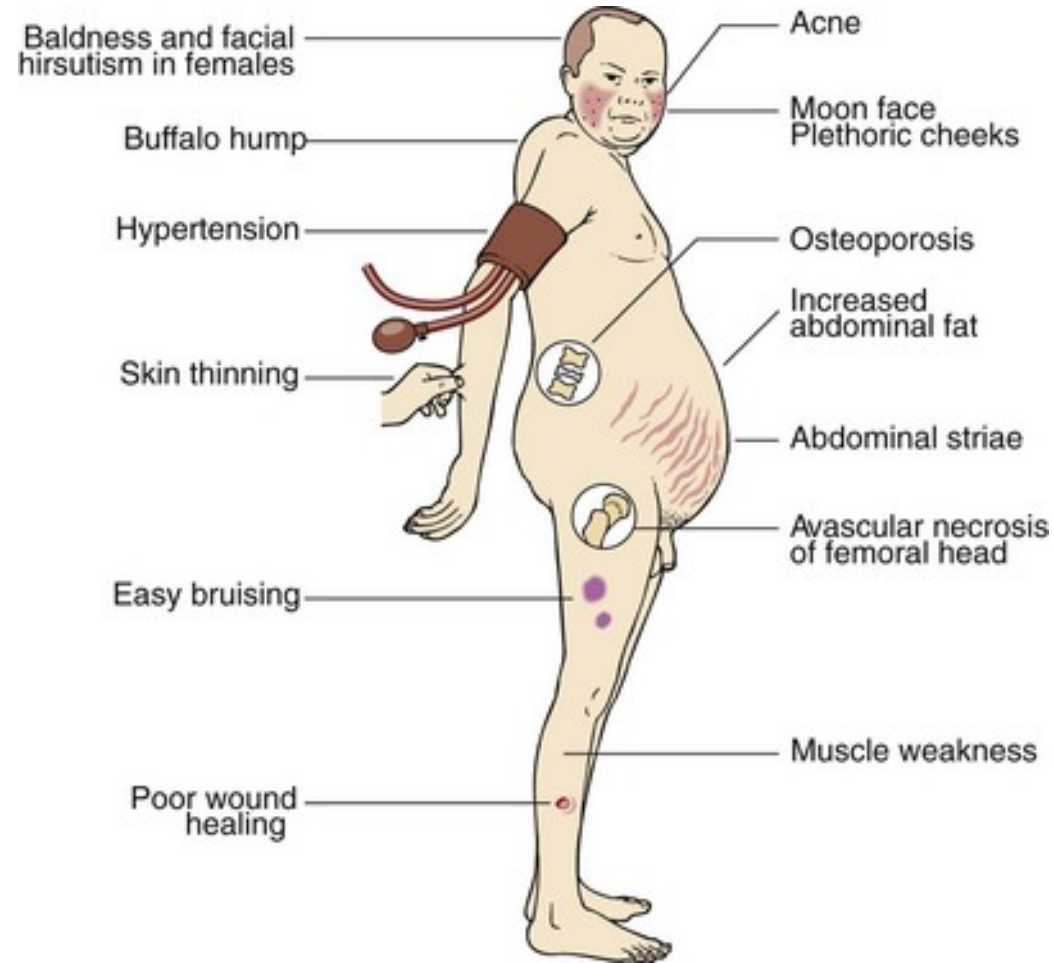


Adrenal insufficiency

- Body doesn't produce enough cortisol and/or aldosterone
- Primary (adrenal gland) vs. secondary (hypothalamus/pituitary)
- Primary is often referred to as Addison's disease
 - Extreme fatigue
 - Weight loss and decreased appetite
 - Darkening of your skin (hyperpigmentation)
 - Low blood pressure, even fainting
 - Salt craving
 - Low blood sugar (hypoglycemia)
 - Nausea, diarrhea or vomiting (gastrointestinal symptoms)
 - Abdominal pain
 - Muscle or joint pains
 - Irritability
 - Depression or other behavioral symptoms
 - Body hair loss or sexual dysfunction in women



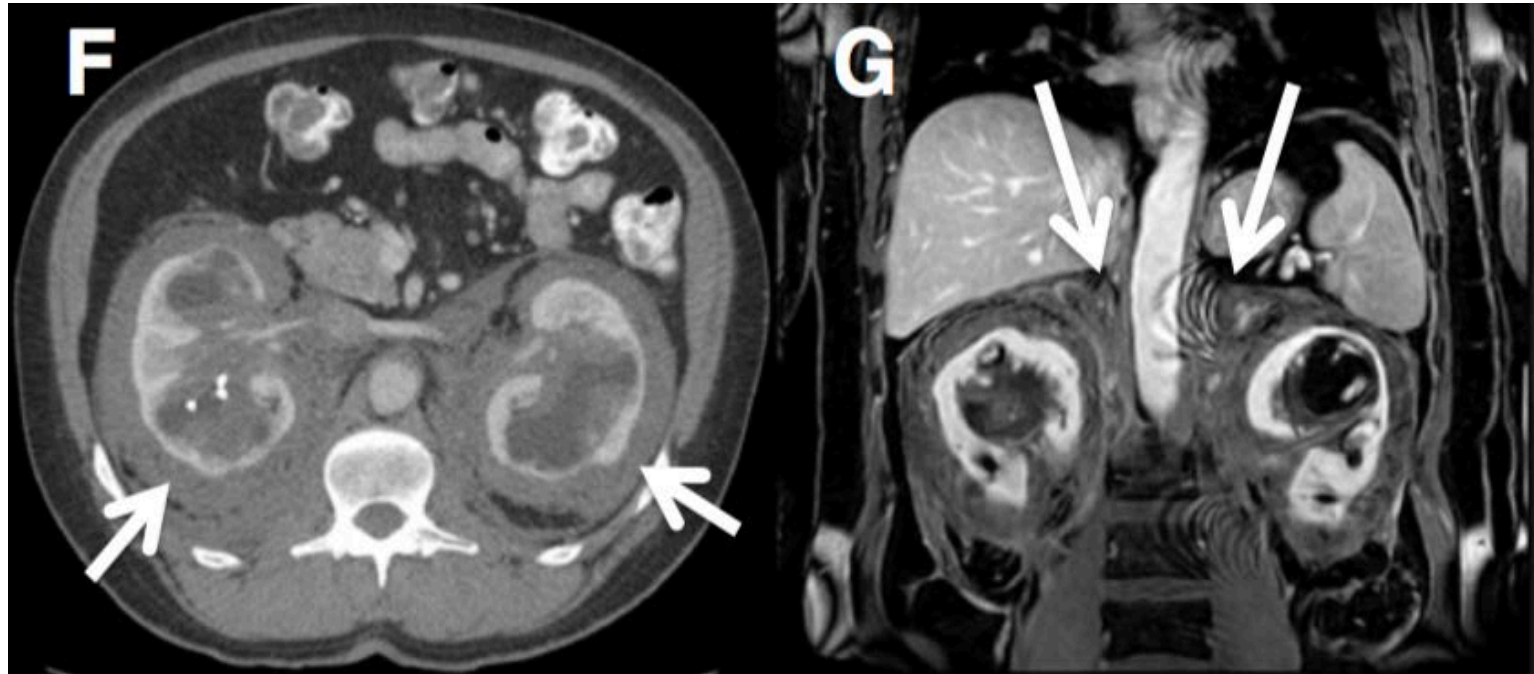
Steroid therapy leads to central adrenal insufficiency



Acute adrenal failure (addisonian crisis)

- Sometimes the signs and symptoms of adrenal insufficiency may appear suddenly: acute adrenal failure (addisonian crisis)
 - life-threatening shock
 - Severe weakness
 - Confusion
 - Pain in your lower back or legs
 - Severe abdominal pain, vomiting and diarrhea, leading to dehydration
 - Reduced consciousness or delirium
 - Low blood pressure
 - High potassium (hyperkalemia) and low sodium (hyponatremia)

Encasement of adrenal glands in ECD

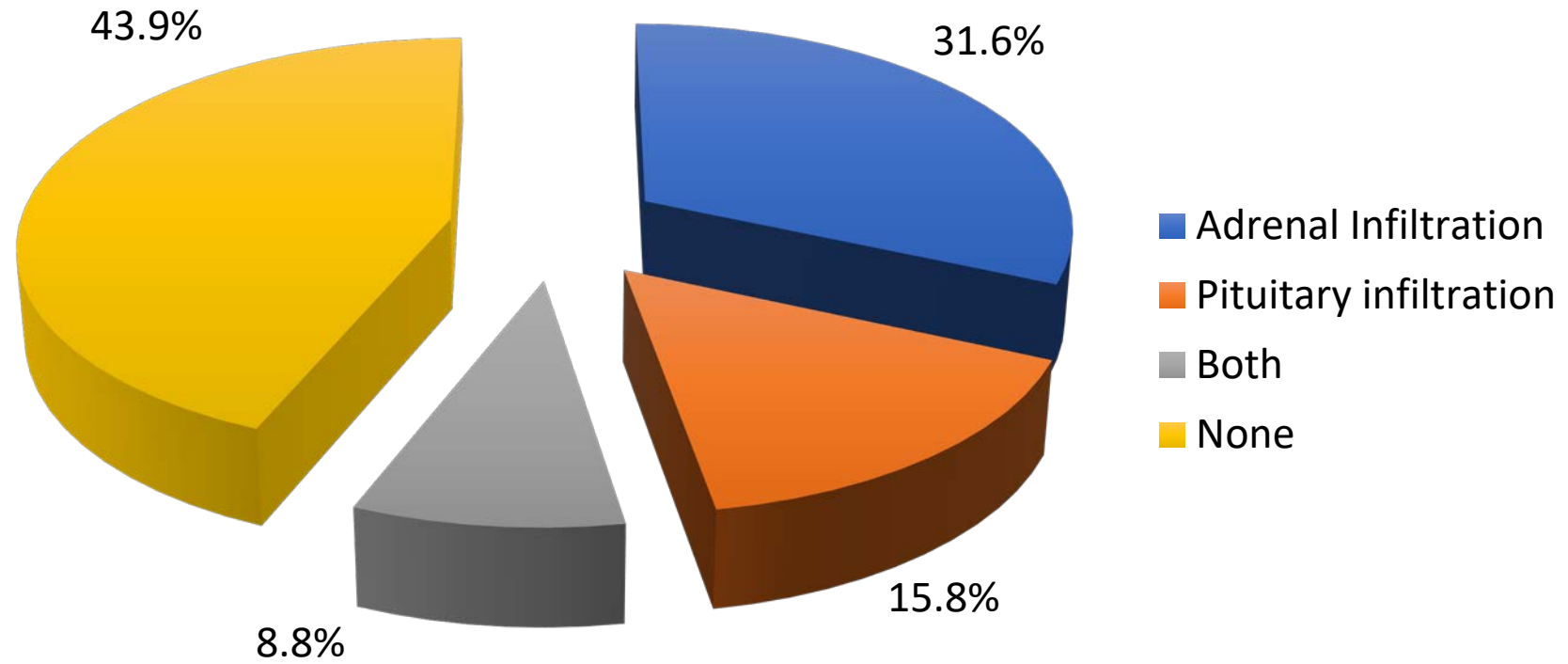


Juvanee I. Estrada-Veras et al. *Blood Advances* 2017.

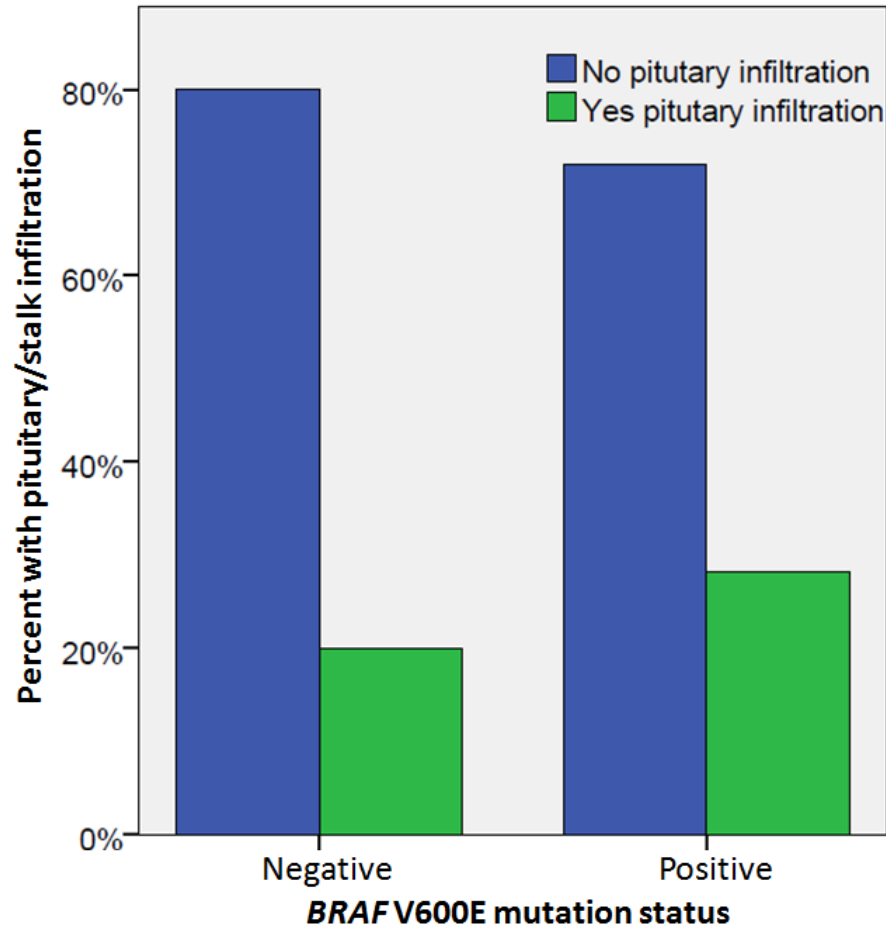
NIH cohort

Age (yrs)	54.3 ±10.8
Age at presentation (yrs)	46 (16-74)
Mean time to diagnosis (yrs)	4.2
Sex	46 males (75%)
BMI (Kg/m²)	29.6 ±5.9
<i>BRAF</i> V600E status	
Positive	56.1% (32/57)
Not tested	4.9% (3/61)
Inconclusive	1.7% (1/58)
Adrenal Infiltration	31.6% (18/57)
Pituitary/stalk Infiltration	15.8% (9/57)
Adrenal and Pituitary/stalk Infiltration	8.8% (5/57)
No infiltration	43.9% (25/57)

Results

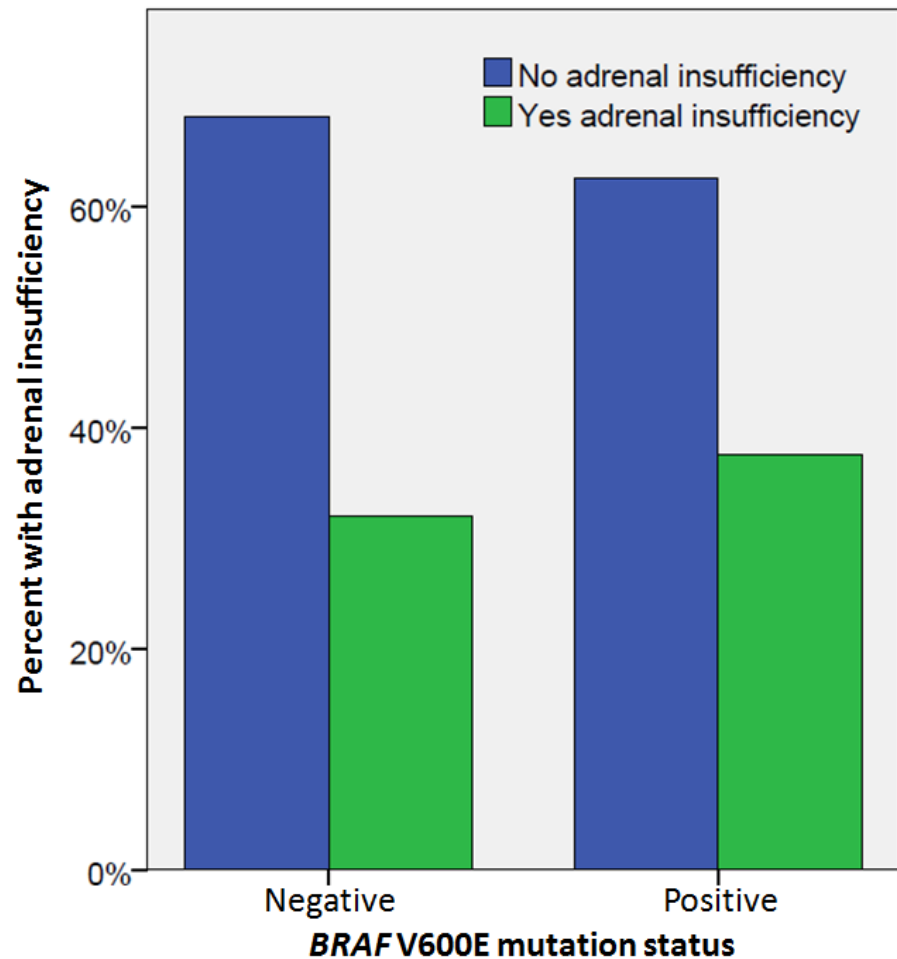


Comparable rates for pituitary/stalk infiltration by *BRAF* V600E status



- 28.1% vs. 20%
- OR 1.6 (95% CI 0.5-5.4, P=0.5)

Comparable rates for AI by *BRAF* V600E status



- 37.5% vs. 32%
- OR 1.3 (95% CI 0.4-3.8, P=0.7)

AI conclusions

- Infiltrative processes of the HPA axis in patients with ECD tend to favor the adrenal glands in *BRAF*-positive patients, without influencing the rates of AI
- Every patient with ECD needs to be evaluated for AI, regardless of *BRAF* status or HPA axis infiltration
- There is a poor biochemical-radiological concordance in ECD
- ECD patients with AI are at significant risk of morbidity and mortality during an adrenal crisis.
- Patients and their caregivers should receive ongoing education about how to manage steroid dosing during illness, and all ECD patients with AI should wear medical identification jewelry.

Patient education

NIH Clinical Center Patient Education Materials Managing Adrenal Insufficiency

What are the adrenal glands?

Your body has two adrenal glands. Each gland is located above a kidney. The adrenal glands secrete many hormones needed for the body's normal functioning. Two of these hormones are cortisol and aldosterone. Cortisol helps the body use sugar and protein for energy and enables the body to recover from infections and stresses (for example: surgery and illness). Aldosterone maintains the right amount of sodium (salt), potassium, and water in the body.

- Surgical removal of the adrenals

Temporary AI is caused by some medications, infections, and/or surgeries. Causes of temporary AI include the following:

- Transsphenoidal surgery for Cushing's disease that removes a tumor from the pituitary gland
- Removal of a tumor causing the adrenal glands to make too much

Stress dosing kit and medical identification jewelry



When should I seek an Endocrinologist to test or treat the deficiencies?

- At all times!

Endocrine related information

- The Endocrine Society: www.endocrine.org
- Hormone Health Network: <https://www.hormone.org>
- Mayo Clinic: www.mayoclinic.org
- NIH: fady.hannah-shmouni@nih.gov

Thank You

- We appreciate the cooperation of the ECD patients and of the Erdheim-Chester Disease Global Alliance
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