

Physical and Chemical Changes of the Heart and Brain in Cushing's Disease

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Disclosures

▶ None

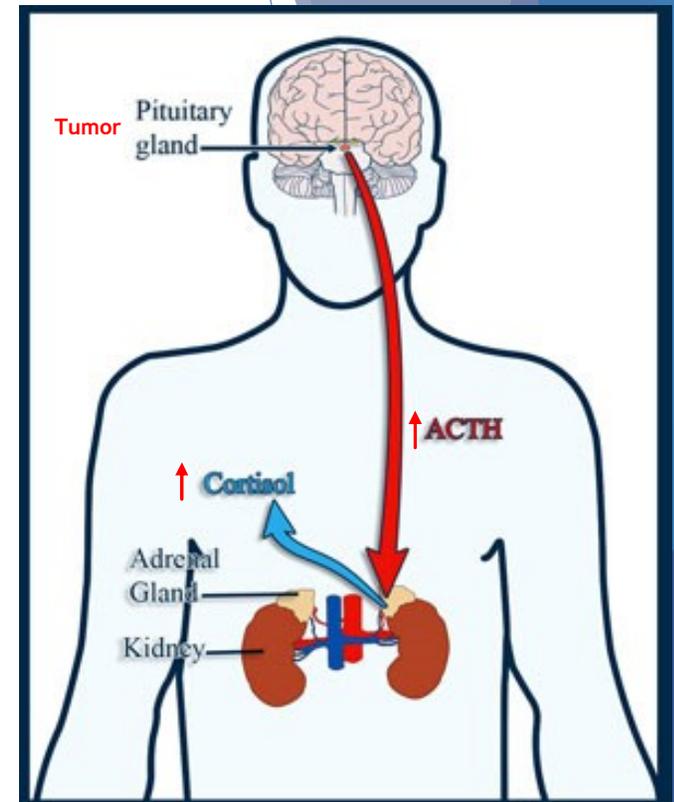
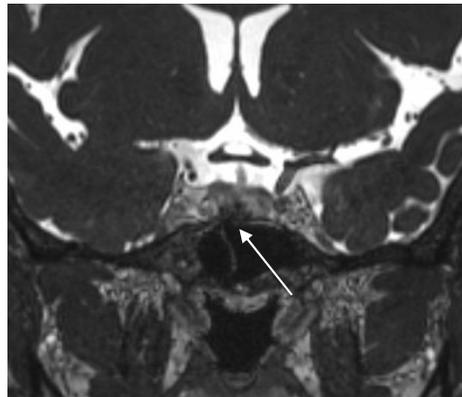
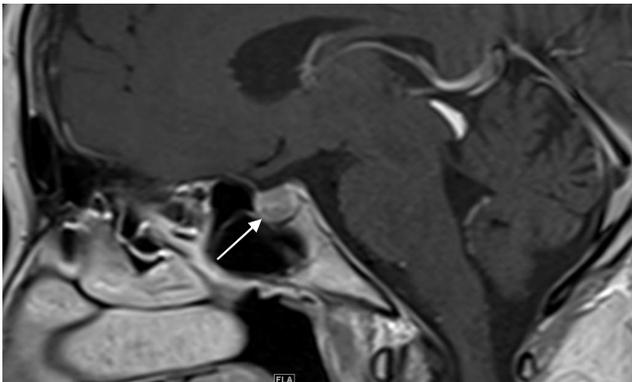


Outline

- ▶ Introduction and Clinical Presentation
- ▶ Cardiovascular Manifestations
- ▶ Brain Manifestations
- ▶ Effects of Treatment
- ▶ Long-term Prognosis

Introduction to Cushing's Disease

- ▶ Hypercortisolism
- ▶ ACTH secreting pituitary tumor - endogenous hypercortisolism
- ▶ Cushing's disease
 - ▶ Prevalence ~40:1,000,000 people^{1,2}
 - ▶ 9:1 female to male ratio¹
 - ▶ 80% of endogenous Cushing's syndrome³



<https://www.newhealthadvisor.com/images/1HT08339/Cushings%20Disease.jpg>

Clinical Features

- ▶ Hypertension
- ▶ Hyperglycemia

Cardiac Changes

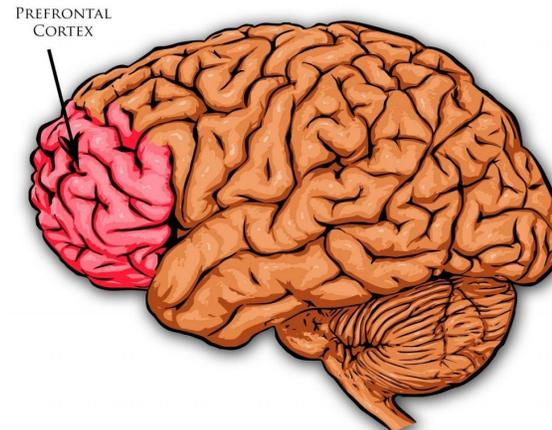
- ▶ Personality/Cognitive Changes

Brain Changes

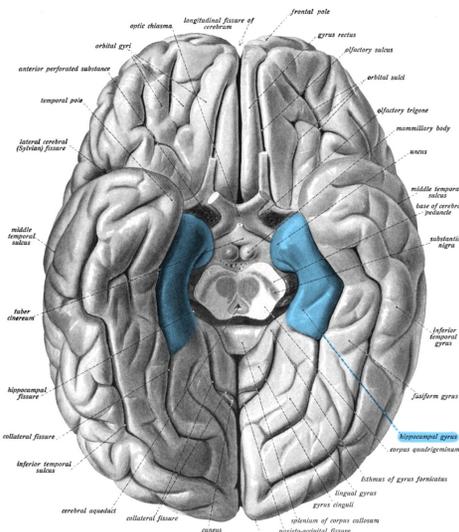
- ▶ Moon facies
- ▶ Hirsutism
- ▶ Buffalo Hump
- ▶ Purple Striae
- ▶ Osteoporosis
- ▶ Immune suppression

Brain Manifestations

- ▶ Cognitive Impairment⁸
 - ▶ Verbal skills
 - ▶ Learning skills
- ▶ Mood disorders⁸
 - ▶ Depression most common
 - ▶ Anxiety
 - ▶ Psychosis
- ▶ Memory Difficulty⁸



https://www.scienceabc.com/wp-content/uploads/2015/06/prefrontal_cortex.jpg



https://upload.wikimedia.org/wikipedia/commons/9/96/Sobo_1909_630_-_Parahippocampal_gyrus.png

Pathophysiology of cerebral changes

- ▶ Hippocampal atrophy⁸
 - ▶ Demonstrated in animal models and clinical studies
- ▶ Atrophy of prefrontal cortex⁸

Proposed mechanisms of atrophy⁸

- ▶ Decreased glucose utilization
- ▶ Increased excitatory amino acids/neurotransmitter
- ▶ Inhibition of long term potentiation
- ▶ Decreased neurogenesis

Reference 8:Patil CG, Lad SP, Katznelson L, Laws ER Jr. Brain atrophy and cognitive deficits in Cushing's disease. Neurosurg Focus. 2007;23(3):E11. Review. PubMed PMID: 17961025.

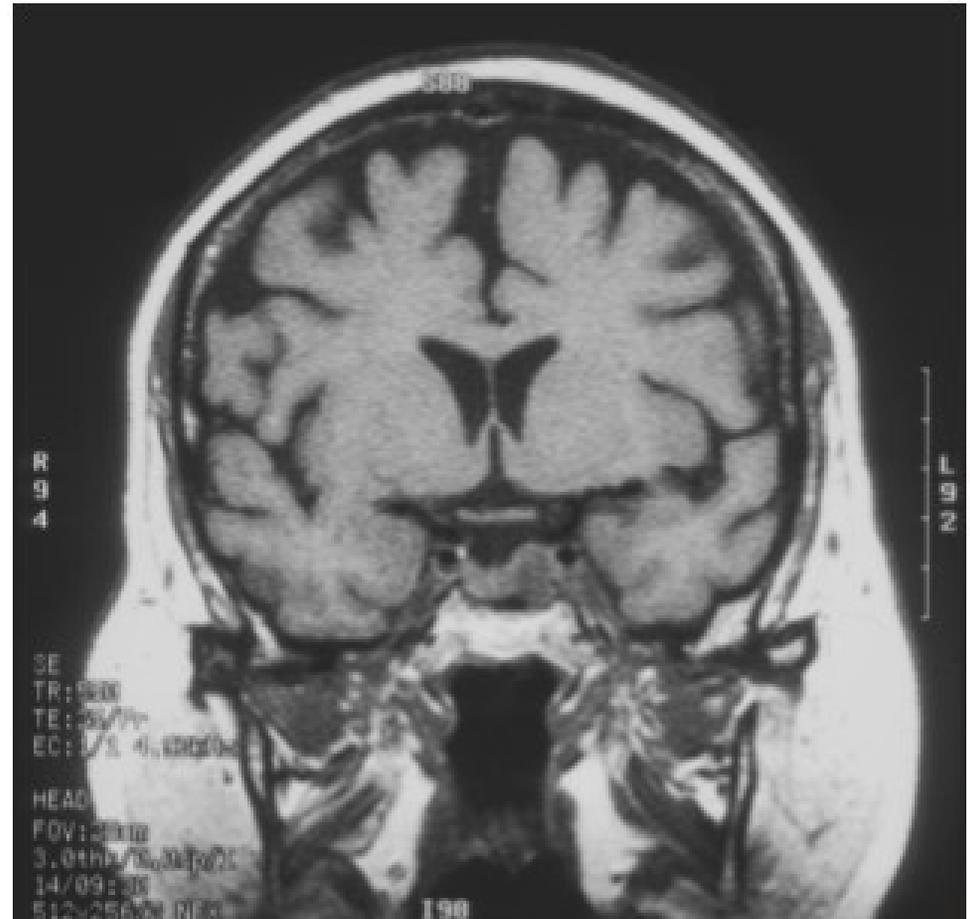


FIG. 1. Magnetic resonance image showing brain atrophy in a 32-year-old woman with Cushing's disease.

Duration of Steroid Exposure & Onset of deficits

- ▶ Clinically : 2- 6 months ----Changes in brain and hippocampus -cerebral cortical atrophy within 6 mths
- ▶ Supported by animal (primate) studies

Cardiovascular Manifestations

▶ Metabolic Syndrome⁴

- ▶ Visceral Obesity
- ▶ Hypertension
- ▶ Elevated Fasting glucose
- ▶ Dyslipidemia

Results in

- Insulin Resistance
- Diabetes
- Impaired Glucose Tolerance
- Cardiovascular disease (atherosclerosis; CAD; CHF and Stroke)

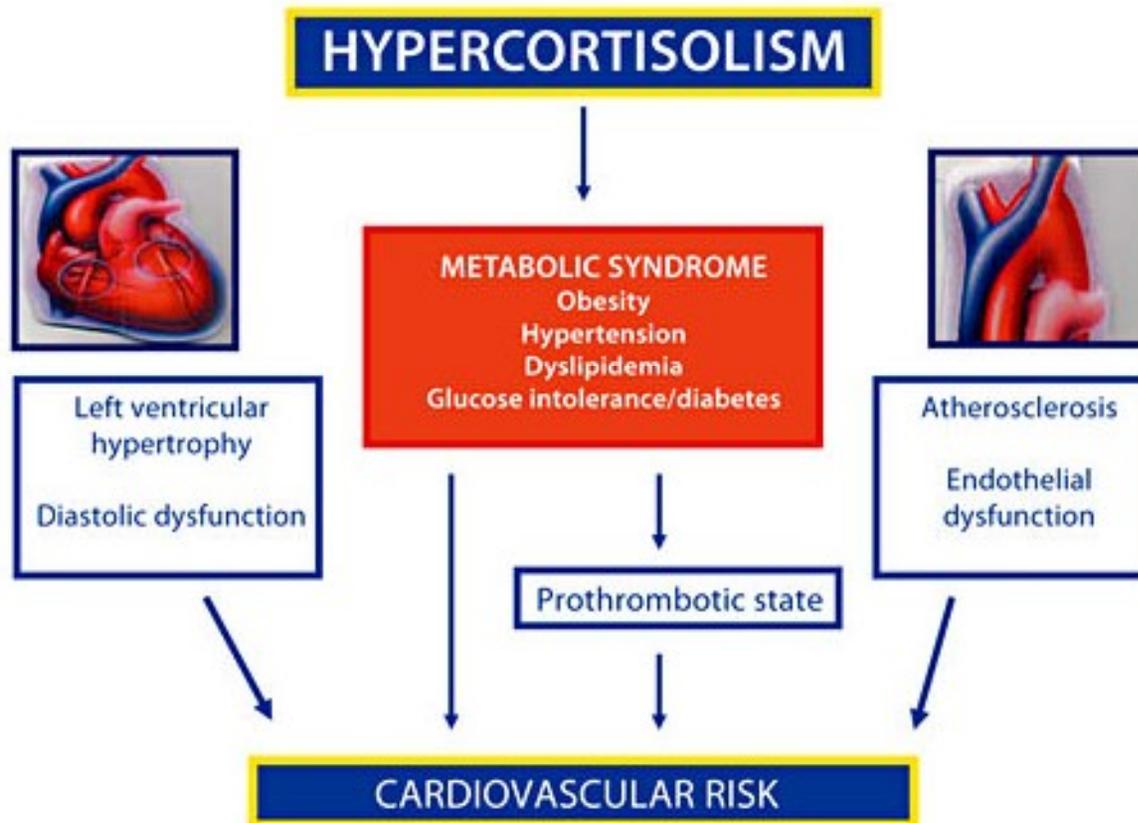
Mortality - double general population⁵

- Strokes
- Myocardial Infarction
- Uncontrolled diabetes mellitus
- Infections

Pathophysiology of cardiovascular risk in Cushing's

- ▶ Cardiac Remodeling⁶
 - ▶ Up to 70% with abnormal left ventricular mass parameters on echo
 - ▶ Concentric hypertrophy 42%
 - ▶ Concentric remodeline 23%
- ▶ Arterial atherosclerosis⁷
 - ▶ Contributes to systemic hypertension and CAD
- ▶ Prothrombotic state⁷
 - ▶ Thromboembolic events, especially after surgery
 - ▶ Hyperhomocysteinemia

Pathophysiology of cardiovascular risk in Cushing's



Reference 7: De Leo M, Pivonello R, Auriemma RS, Cozzolino A, Vitale P, Simeoli C, De Martino MC, Lombardi G, Colao A. Cardiovascular disease in Cushing's syndrome: heart versus vasculature. *Neuroendocrinology*. 2010;92 Suppl 1:50-4. doi: 10.1159/000318566. Epub 2010 Sep 10. Review. PubMed PMID: 20829618.

Long term prognosis

- ▶ Cardiac effects if complete remission⁴
 - ▶ Evidence that cardiac remodeling occurs and may return to normal size⁷
 - ▶ Cardiovascular morbidity improves but does not return to baseline
- ▶ Mortality⁴
 - ▶ May return to general population risk if remission
 - ▶ Can be up to 5X higher than general population if residual/recurrence
- ▶ Cerebral Effects⁸
 - ▶ May see reversal up to 10% of cerebral atrophy with remission
 - ▶ Improvements in memory with decrease cortisol levels
- ▶ Age
 - ▶ Younger patients regain and sustain improvement in cognitive function quicker than older patients

Conclusions

- ▶ Cushing's disease remains a difficult disease to treat with significant cerebrovascular and brain effects
- ▶ Complete surgical resection is best treatment
- ▶ Partial reversal of morbidity and mortality effects is possible with remission

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Questions?

