# Psychiatric overtones of Endocrinopathies: Unveiling the missing links


Dr Nalini Shah
Professor & Head
Department of Endocrinology
K E M Hospital
Mumbai, India


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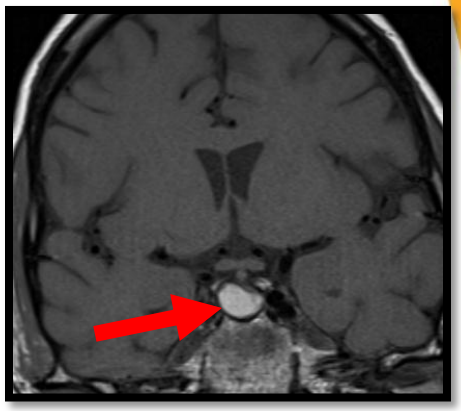
**Case 1**



Vomiting, headache

43 years/M, Lawyer
Symptomatic : 3 years
Easy fatigability,
Sadness,
Decreased interest in activities
Diffuse body aches, headache
**Left job**

**Na-108 mEq/L**

Hypocortisolism
Hypothyroidism
Hypogonadism

**Steroid, Thyroid and Testosterone supplements**

Sodium improved
Symptoms improved
**Patient resumed duty**

**Somatisation**

**Pan-hypopituitarism**

**Serum Sodium**

Started on T. Paroxitin

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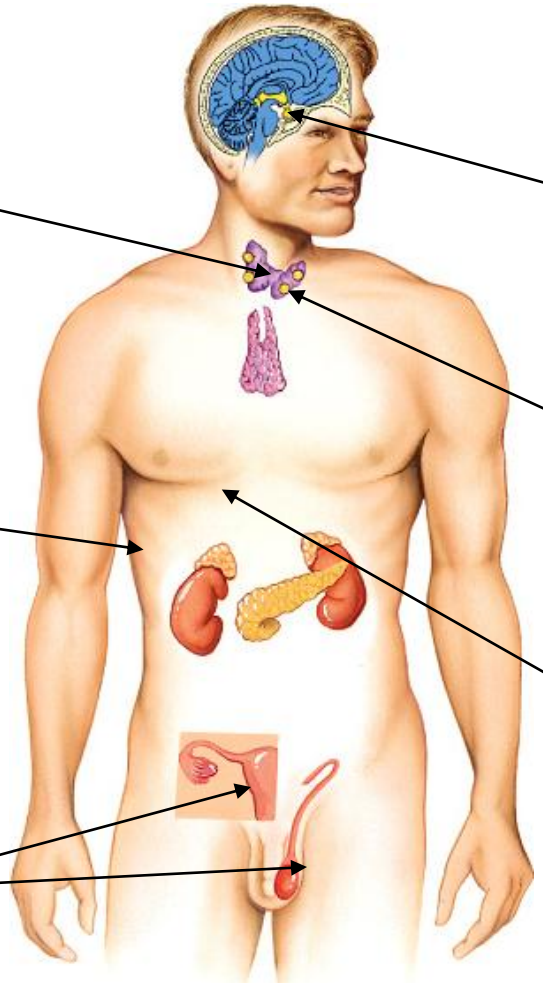
# Endocrinopathies linked with psychiatric manifestations

**Thyroid**
Hypothyroidism
Hyperthyroidism

**Pancreas**
Insulinoma
Metabolic syndrome

**Gonads**
Gender identity disorder
DSD

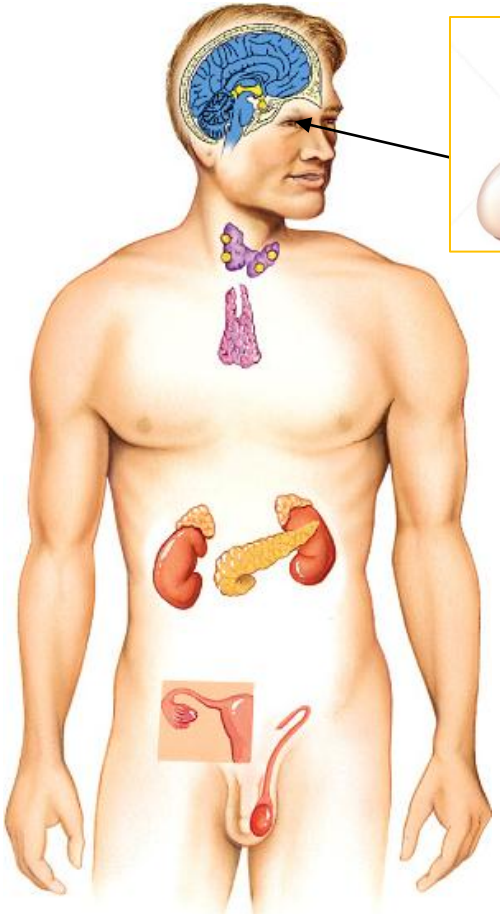


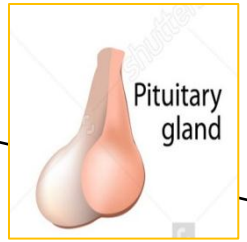
**Pituitary**
Cushing's disease
Prolactinoma
Hyponatremia
TSHoma
Gonadotropinoma

**Parathyroid**
Hyperparathyroidism

**Adrenal**
Pheochromocytoma
Addison's disease

# Endocrinopathies linked with psychiatric manifestations



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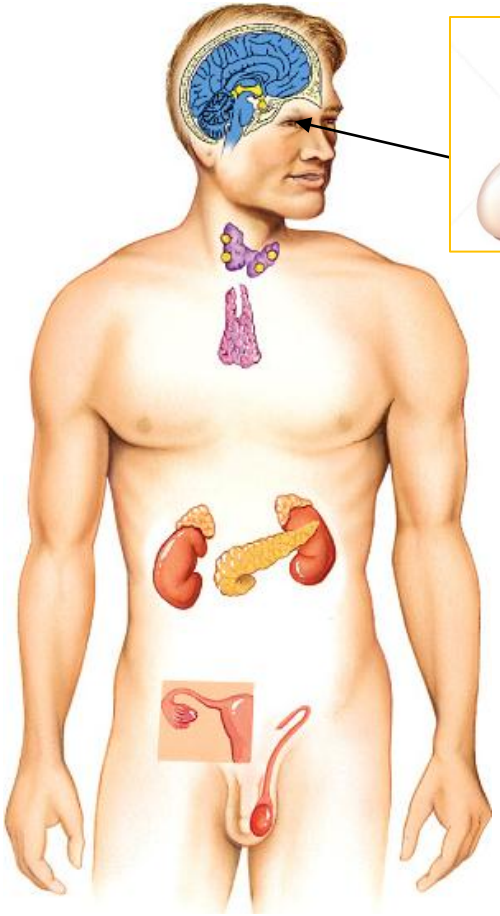
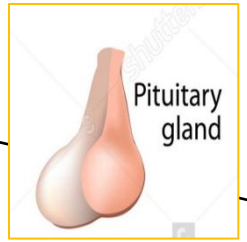
# Endocrinopathies linked with psychiatric manifestations



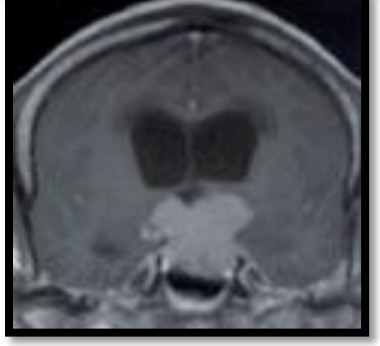



Pituitary
Cushing's disease
**Prolactinoma**
Hyponatremia
TSHoma
Gonadotropinoma

# Case 2

40 years/M
Symptomatic : 2 years
Delusion of persecution
Doubting wife of infidelity
Delusion of control

Ataxia
Urinary incontinence



**Serum prolactin: 6691 ng/ml (N<25)**

**Prolactinoma**

**Tablet Cabergoline**

**Worsening of psychiatric symptoms**

Cabergoline stopped
Arepriprazole started

**Trans-sphenoidal surgery**

**More common scenario..**

| | |
|---|---|
| FSH | 2.5 – 10 mIU/ml |
| LH | 2.5 – 10 mIU/ml |
| Testosterone | F – 0.2 – 0.8 ng/ml<br>M – 4.0 – 11 ng/ml |
| Prolactin 124 | 5.0 – 25 ng/ml |
| PTH | 11 – 67 pg/ml |
| ACTH | 0 – 46 pg/ml |
| Basal Cortisol | 5 – 25 µg/dl |
| Post Glucose GH | < 1 ng/ml |
| IGF1* | ng/ml |
| IGFBP3* | µg/ml |
| *Check normogram | |
| Comments: | |


**Antipsychotic drugs induced hyperprolactinemia**

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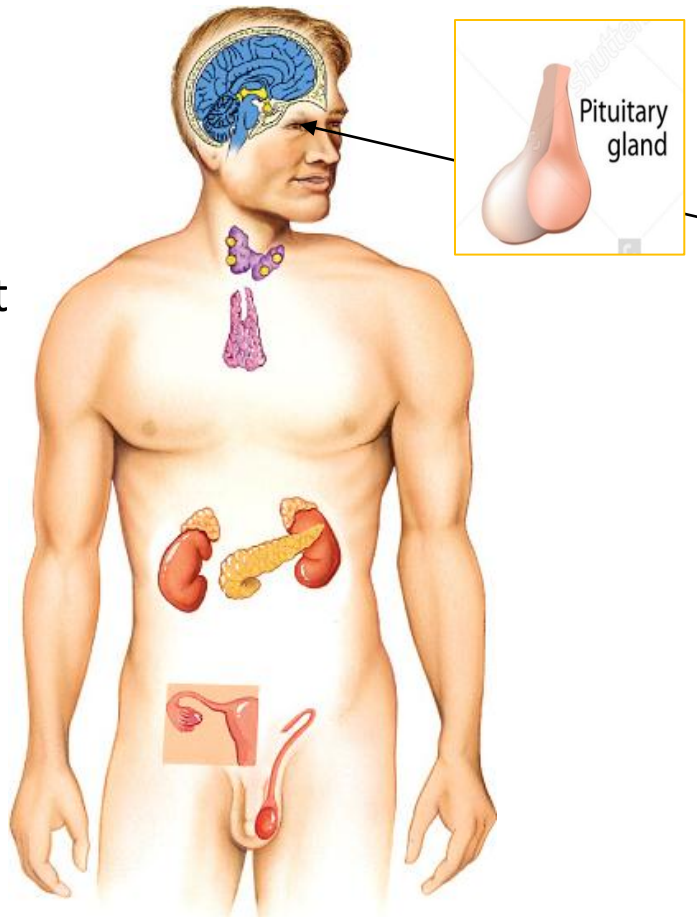
# Endocrinopathies linked with psychiatric manifestations

- Mass effect : psychotic manifestations
- Cabergoline can worsen psychosis
- Drugs are important cause of hyperprolactinemia




**Pituitary**
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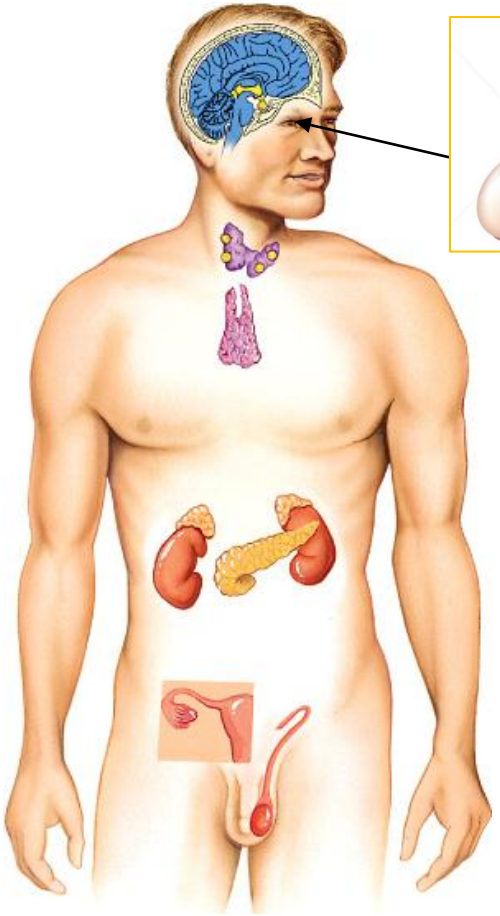
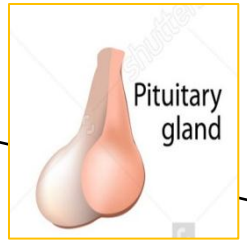
# Endocrinopathies linked with psychiatric manifestations






Pituitary
**Cushing's disease**
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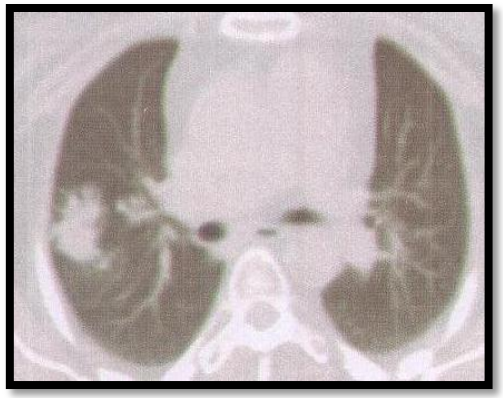
# Case 3

34 years/F
Irrelevant talk
Anger bursts
Delusion of control?
Suspicious nature
Delusion of reference

Facial mooning
Hirsutism
Amenorrhoea

Striae



| Biochemistry | | |
|---|---|---|
| Basal Cortisol | 72 µg/dl | 5-25 |
| Basal ACTH | 244 pg/ml | |
| 1 mg Dexamethasone suppressed cortisol | 26 µg/dl | <1.8 |

**ACTH secreting bronchial carcinoid**

Right upper lobectomy

**Cushings syndrome**

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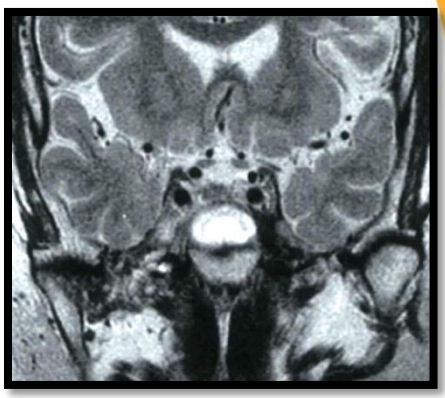
# Case 4

18 years/M,
Feeling low
Increase appetite and sleep
Difficulty in adjustment in new college
Feeling worthless
Decreased interaction with friends and family
Suicidal ideations

ODS cortisol : 18 µg/dl



MRI

**Cushings disease**

Under the treatment for depression

**Trans-sphenoidal surgery**

*Awaits radiation therapy*

# Endocrinopathies linked with psychiatric manifestations

- Psychiatric manifestations : wide spectrum
- Clinical clues: Important
- ODS cortisol : screening test

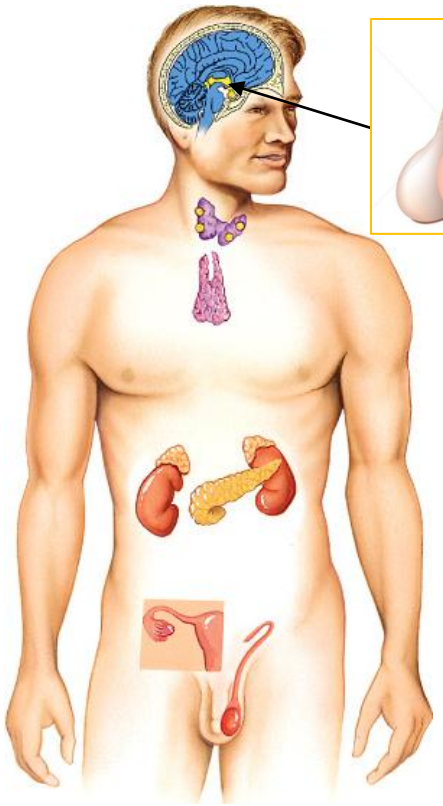
Mooning

Striae

Hyperpigmentation

Pedal edema

Fractures




Pituitary
**Cushing's disease**
Prolactinoma
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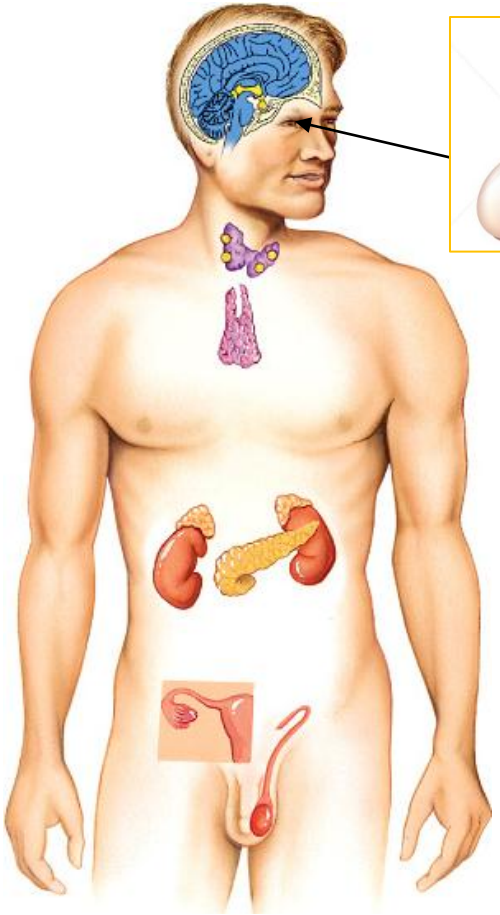
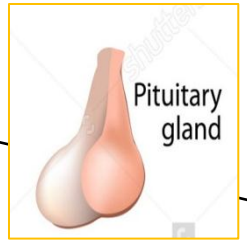
# Endocrinopathies linked with psychiatric manifestations






Pituitary
Cushing's disease
Prolactinoma
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**TSHoma**
**Gonadotropinoma**

Case 5

42 years/M, Driver,
Tremors and restlessness
Aggressive behaviour
Feeling of grandeur
Increased tendency to spend

Headache

Pituitary adenoma

Trans-sphenoidal surgery twice
Medical bridge therapy
Radiation therapy

Patient's symptoms improved
Resumed work

T4 and Testosterone normalised

| Hormonal profile | | |
|---|---|---|
| T3 | 23.8 pmol/L | 3.1-6.8 |
| T4 | 48.3 pmol/L | 12-22 |
| TSH | 31.64 uIU/L | 0.4-5 |
| FSH | 106 mIU/L | 2.5-10 |
| LH | 4.5 mIU/L | 2.5-10 |
| Testosterone | 11.9 ng/L | 4-11 |

Thyroid and Testosterone excess state

TSH and gonadotropin co-secreting pituitary tumor

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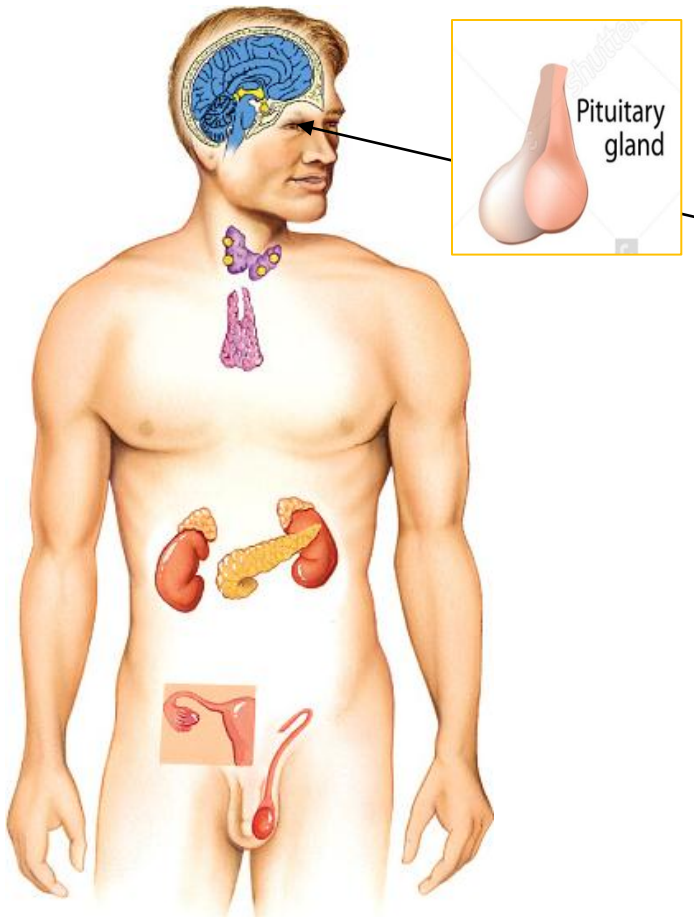
# Endocrinopathies linked with psychiatric manifestations

- Psychiatric manifestations: presenting feature




**Pituitary**
Cushing's disease
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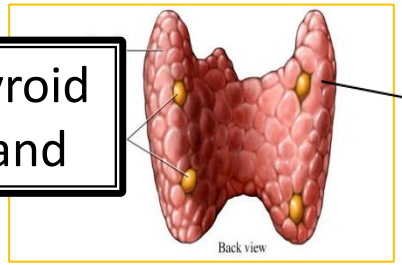
# Endocrinopathies linked with psychiatric manifestations

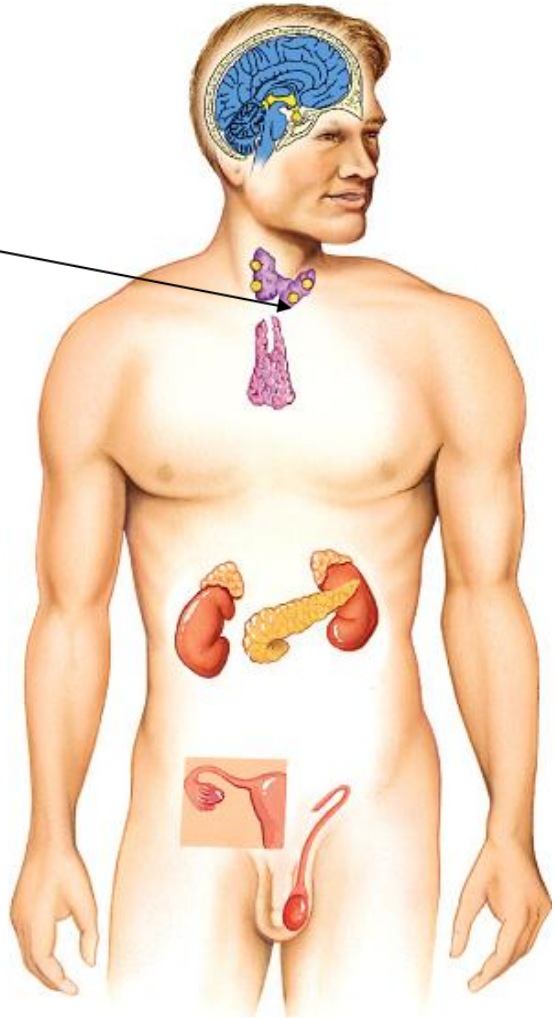
Thyroid gland




**Thyroid**

**Hypothyroidism**

Hyperthyroidism



# Case 6

32 years/F
Symptomatic : 2 years
Burning sensation with phonophobia
Increased irritability
Loss of interest
Swelling over face and whole body

| Thyroid function tests | |
|---|---|
| T3 ng/dl | 38.2 |
| T4 µ/dl | 1.3 |
| TSH mIU/ml | >150 |

Neurologist reference:
T. Amitriptyline.
Psychiatry reference

**Primary Hypothyroidism**

Started on T. Thyroxine 75 µg/day
Symptomatically better

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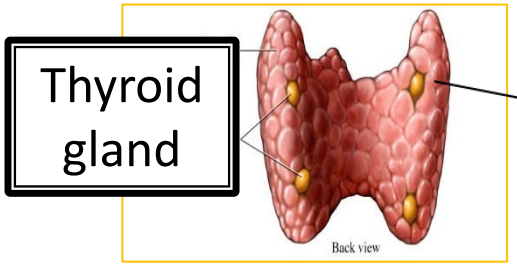
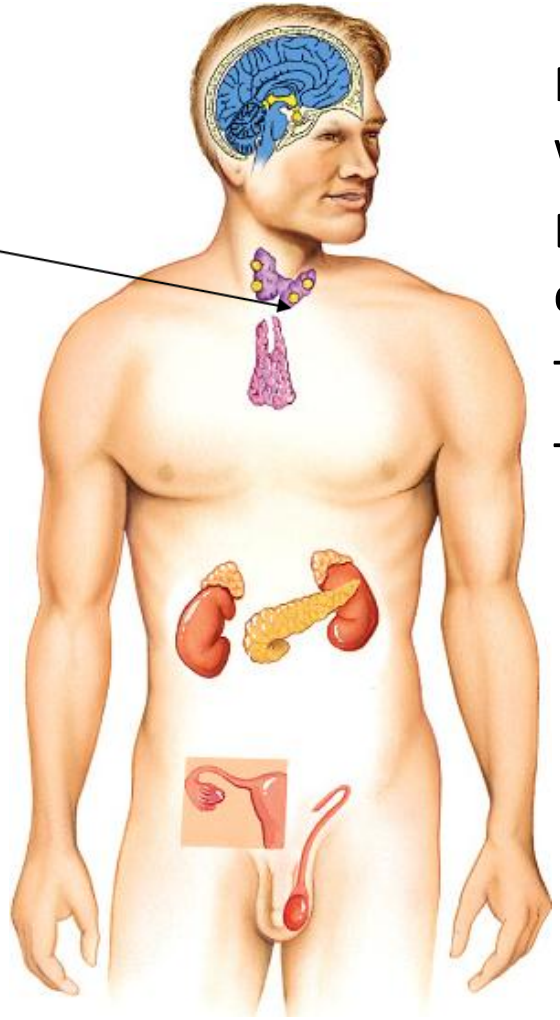
# Endocrinopathies linked with psychiatric manifestations




Thyroid
**Hypothyroidism**
Hyperthyroidism



Psychiatric manifestations: wide spectrum

Elderly : Depression, decreased cognition

Typical clinical clues

TSH : good screening test

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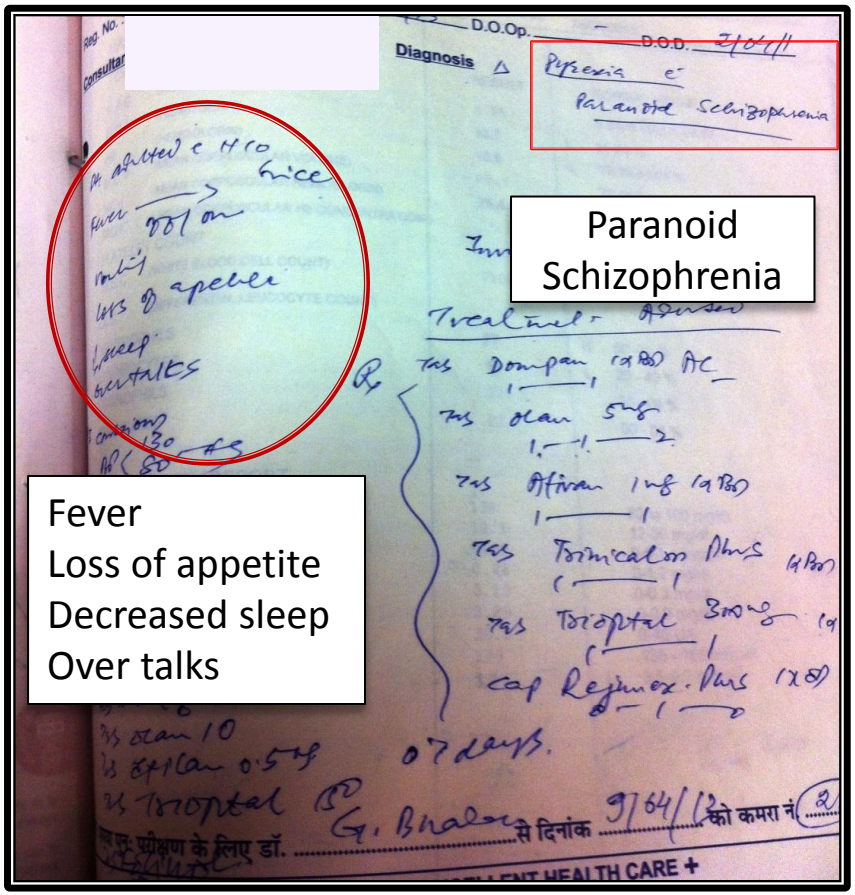
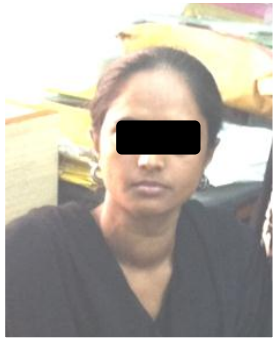
# Case 6

29 years/ Female




Paranoid Schizophrenia



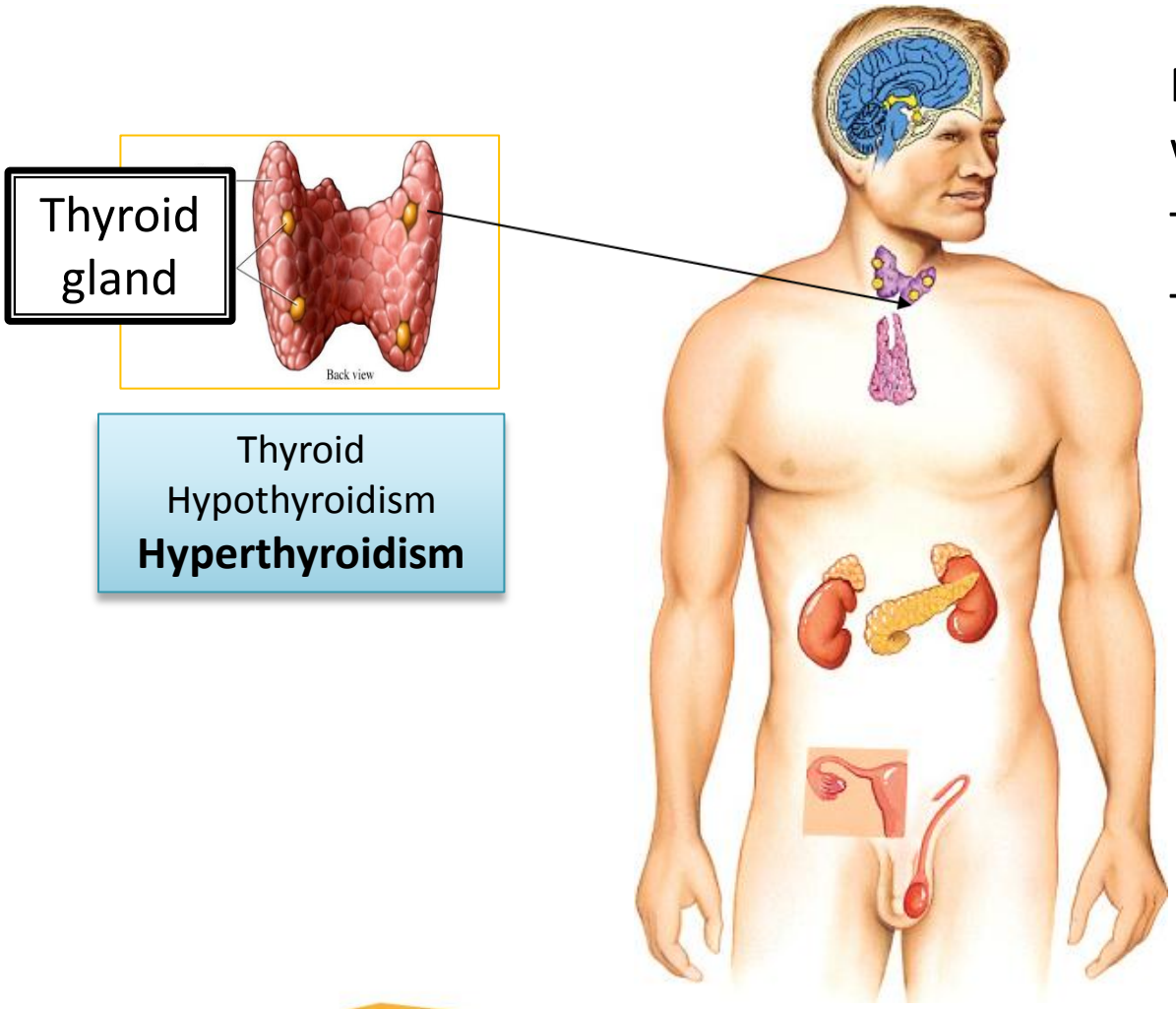
| Thyroid function tests | |
|---|---|
| T3 ng/dl | 239 |
| T4 µ/dl | 19 |
| TSH mIU/ml | <0.01 |

**Hyperthyroidism**

Started on Tablet Neomercazole

T4 normalized
**Symptoms resolved**

# Endocrinopathies linked with psychiatric manifestations




Thyroid
Hypothyroidism
**Hyperthyroidism**

Psychiatric manifestations: wide spectrum

Typical clinical clues

TSH : good screening test

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# Thyro-stress

**Sanjay Kalra, Komal Verma[1], Yatan Pal Singh Balhara[2]**

Department of Endocrinology, Bharti Hospital, Karnal, Haryana, [1]Amity Institute of Behavioural and Allied Sciences, Amity University, Jaipur, Rajasthan, [2]Department of Psychiatry, National Drug Dependence Treatment Center, All India Institute of Medical Sciences, New Delhi, India

## Abstract

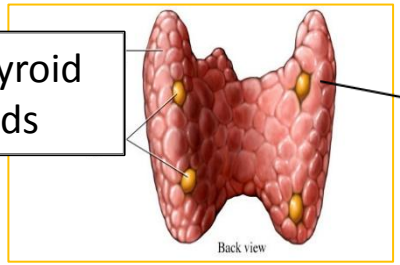
Our understanding of the biopsychosocial model of health, and its influence on chronic endocrine conditions, has improved over the past few decades. We can distinguish, for example, between diabetes distress and major depressive disorders in diabetes. Similar to diabetes distress, we suggest the existence of "thyrostress" in chronic thyroid disorders. Thyro-stress is defined as an emotional state, characterized by extreme apprehension, discomfort or dejection, caused by the challenges and demand of living with thyroid disorders such as hypothyroidism. This communication describes the etiology, clinical features, differential diagnosis, and management of thyro-stress.

# Wilson’s syndrome- ? Acceptable medical diagnosis

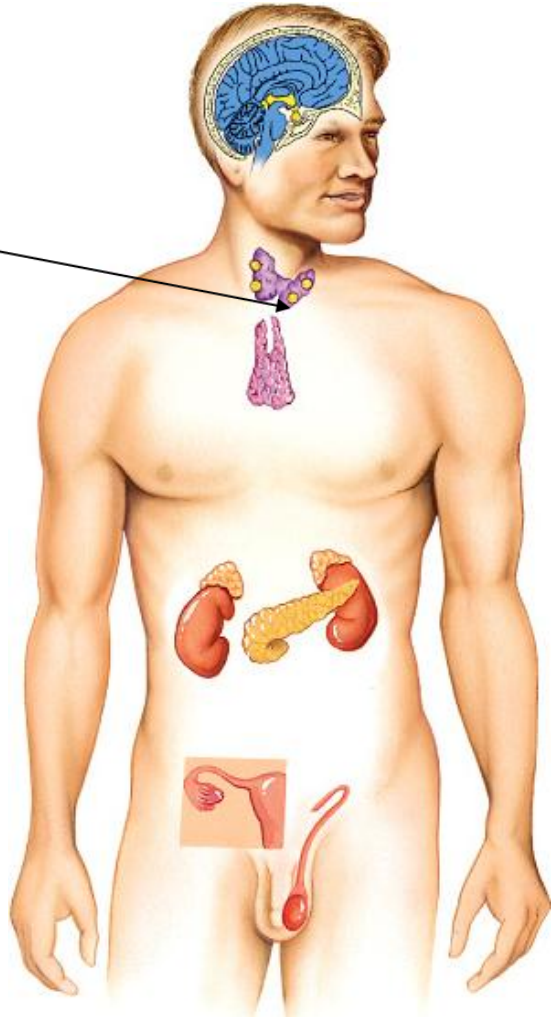
- Wilson's syndrome : Collection of nonspecific symptoms in people whose thyroid hormone levels are normal.
- Proponents : Mild form of hypothyroidism that responds to treatment with triiodothyronine (T-3).
- American Thyroid Association has found no scientific evidence supporting the existence of Wilson's syndrome.

# Endocrinopathies linked with psychiatric manifestations

Parathyroid glands




**Hyperparathyroidism**
Hypoparathyroidism



# Case 7

70 years/M
Symptomatic: 6 months
Easy fatigability
Loss of interest in surroundings
Decreased interaction with family
Increased sleep
Decreased appetite and constipation

Admission : Altered behaviour

**Serum calcium : 14.8 mg/dl**
**Serum phosphorus : 2.1 mg/dl**

Right inferior parathyroid adenoma

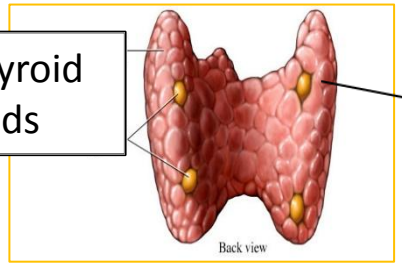
**Hyperparathyroidism**

Right Inferior Parathyroidectomy

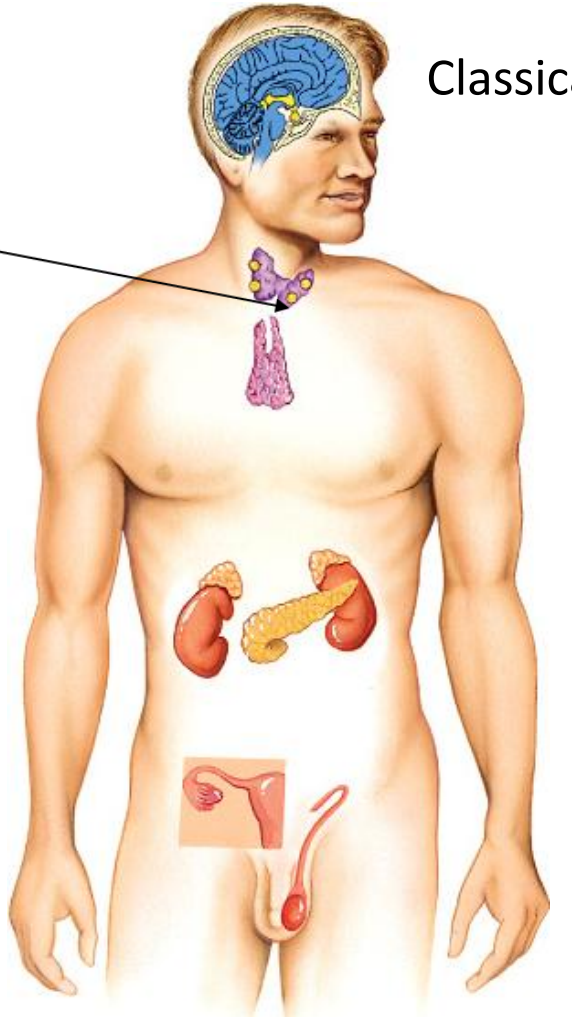
Symptoms improved completely

# Endocrinopathies linked with psychiatric manifestations

Parathyroid glands




**Hyperparathyroidism**
Hypoparathyroidism

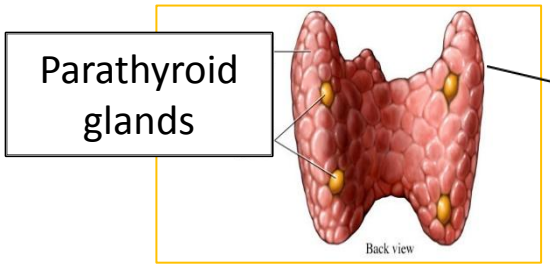


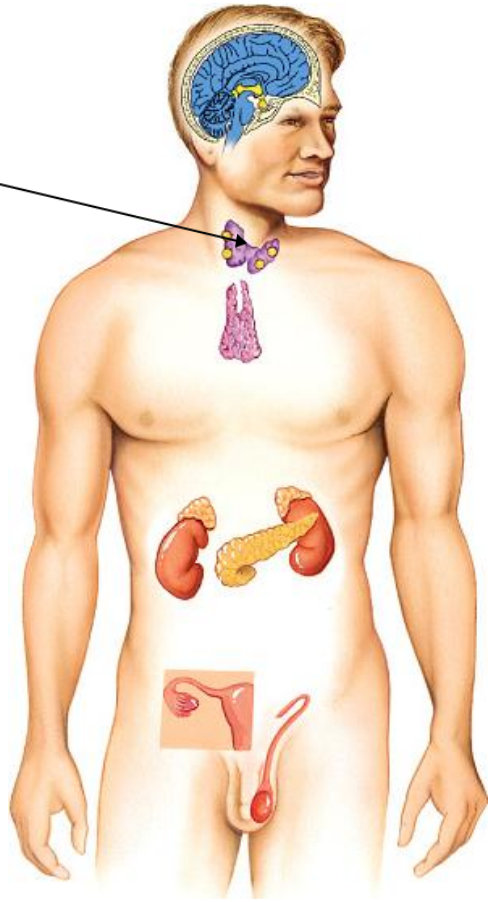
Classical description.

Bones, groans, moans & stones and psychiatric overtones

Simple screening test : Serum Calcium and phosphorus

# Endocrinopathies linked with psychiatric manifestations



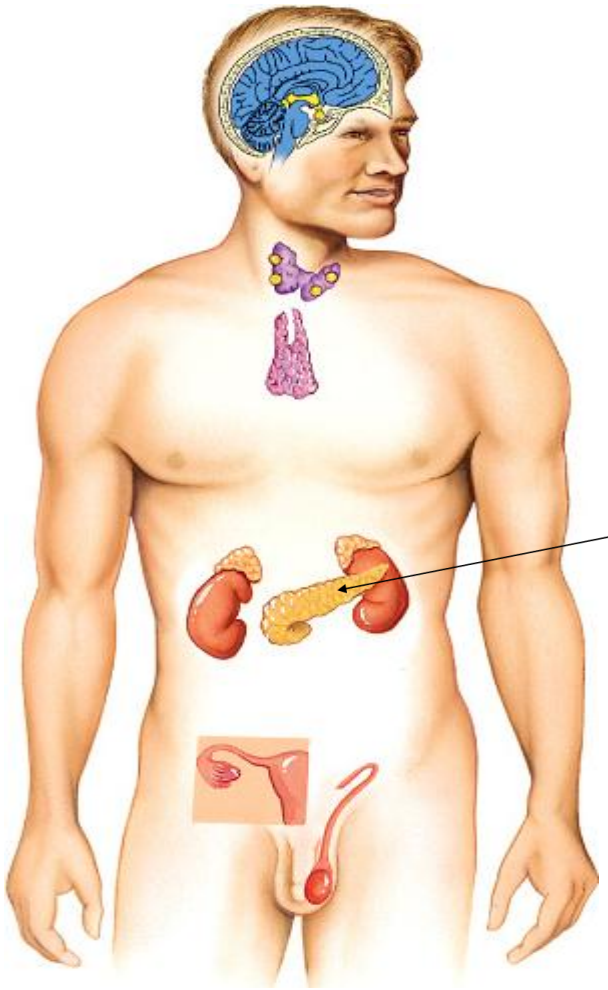
Hyperparathyroidism
**Hypoparathyroidism**

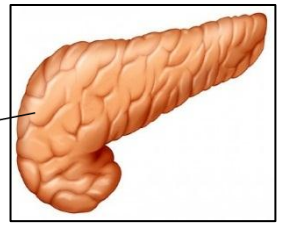
Depression : occasional presentation
Seizures, tetany, paresthesias
Dementia, Slowed mentation
Basal ganglia calcification


Low calcium, high phosphorus

Simple screening test :
Serum Calcium and phosphorus

# Endocrinopathies linked with psychiatric manifestations





**Pancreas**
**Insulinoma**
Diabetes/Metabolic syndrome

# Case 8

13 years old boy

Symptomatic : 2 years

Giddiness and altered behavior while going to tuitions

Increased irritability

Anxiety, palpitations, blank stares intermittently

**Episodes : aborted after eating**

**Random blood sugar : 51 mg/dl**

| 72 hrs fast test | |
|---|---|
| Critical sample sugar | 36.4mg/dl |
| Insulin | 9.6 (u IU/ml) |
| C- peptide | 1.65 ng/ml |
| B- hydroxybutyrate | Negative |

**Insulinoma**

Psychiatrist evaluation

EEG- Diffuse slowing in waveforms.

Neurology evaluation

**Surgical enucleation**

***Symptoms improved***

# Case 9

34 years old male, Newspaper Editor
Multiple episodes of well documented hypoglycemia
Anxious to get evaluated

| 72 hrs fast test | |
|---|---|
| Critical sample sugar | 54 mg/dl |
| Insulin | 98 uIU/ml |
| C- peptide | 0.49 ng/ml |

CT scan- No evidence of insulinoma

Ga DOTATATE scan- No evidence of SSTR expression

EUS- Multiple hypoechoic nodules in pancreatic parenchyma

***Posted for surgery…***

| 72 hrs fast test : repeated | |
|---|---|
| Critical sample sugar | 34 mg/dl |
| Insulin | 47 uIU/ml |
| C- peptide | 0.35 ng/ml |

***Self injection of Insulin ..***

**Manchausen Syndrome**

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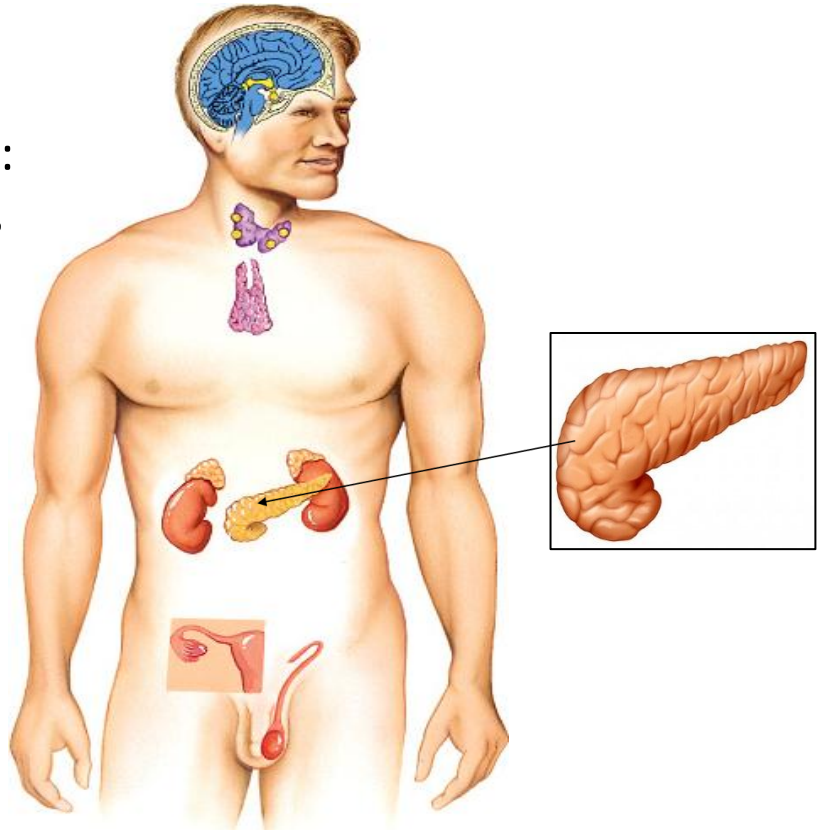
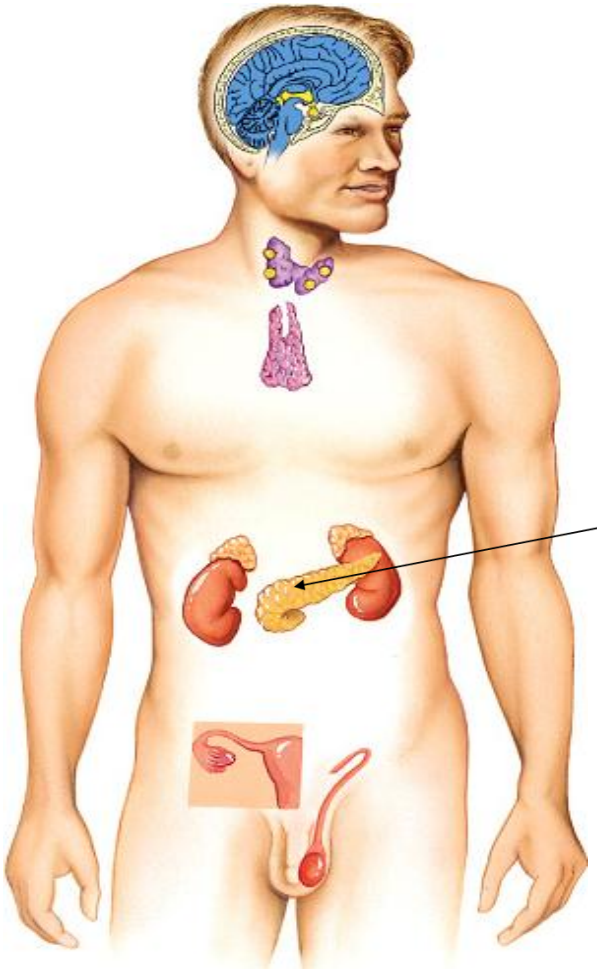
# Endocrinopathies linked with psychiatric manifestations

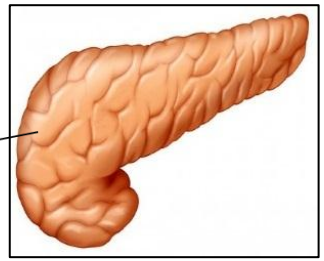
- Hypoglycemia: Neuro-cognitive manifestations
- Recognition is important: life threatening episodes
- Surgery is curative
- Malingering: occasional



Pancreas
**Insulinoma**
Diabetes/Metabolic syndrome

# Endocrinopathies linked with psychiatric manifestations





Pancreas
Insulinoma
**Diabetes/Metabolic syndrome**

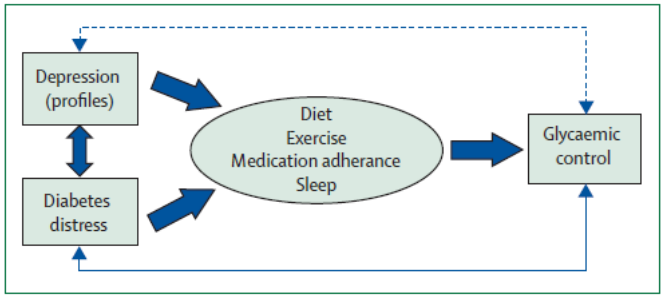
# Endocrinopathies linked with psychiatric manifestations

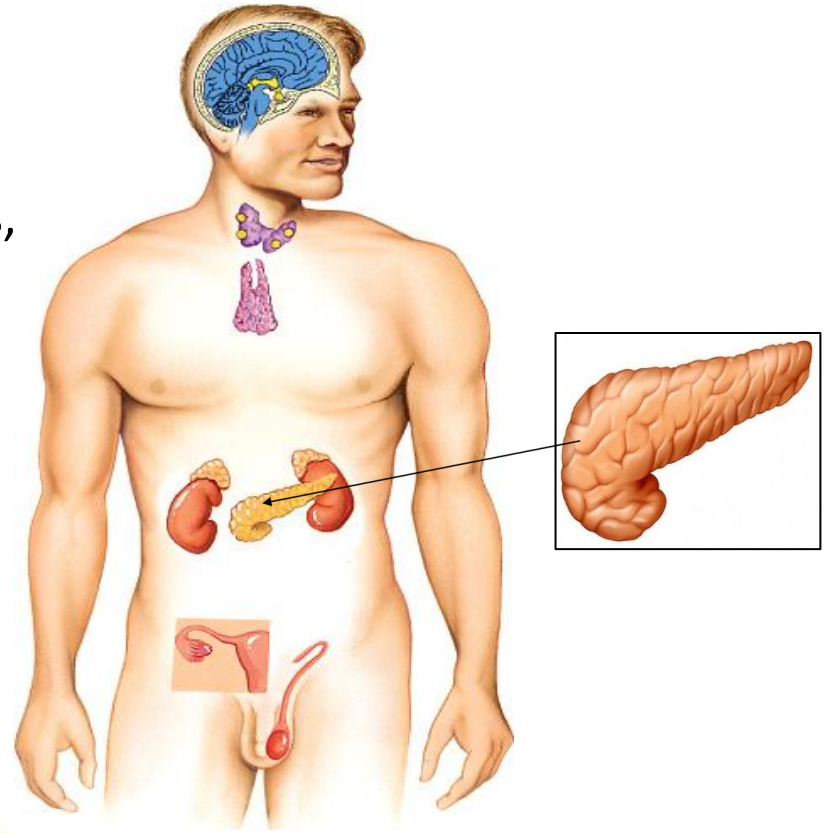
**Depression and diabetes 1**

**Constructs of depression and distress in diabetes: time for an appraisal**

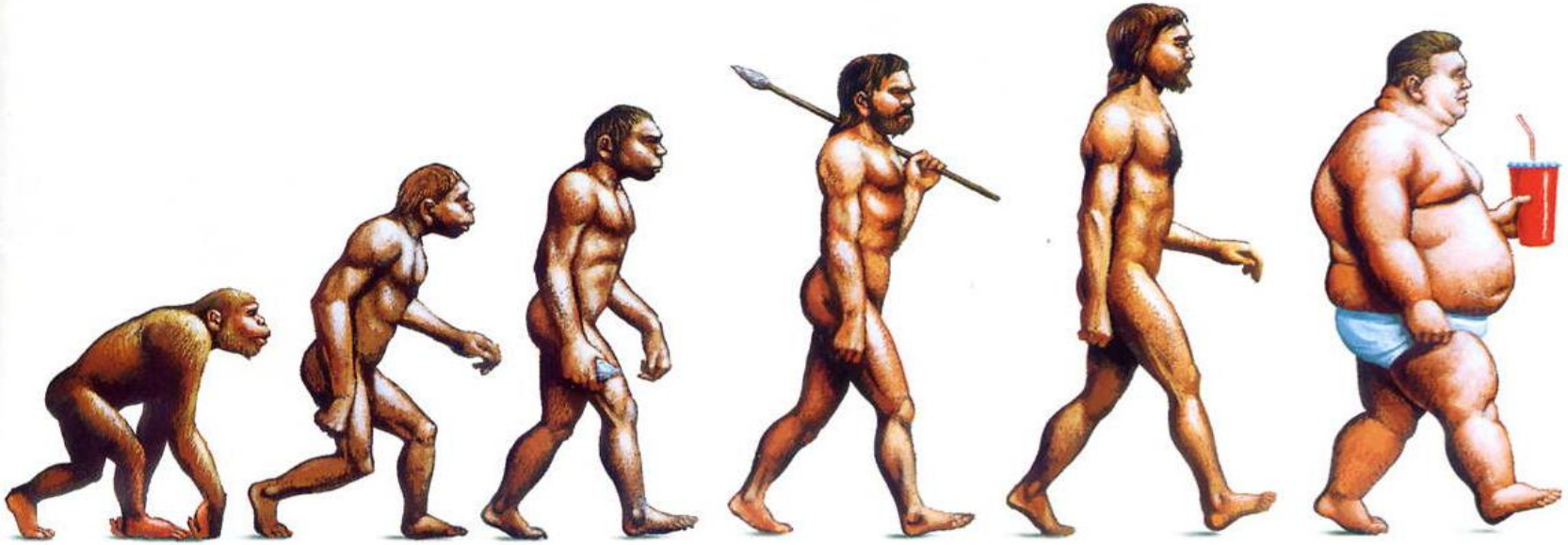
*Frank J Snoek, Marijke A Bremmer, Norbert Hermanns*

- Depression : ~20% of patients with Diabetes
- Diabetes-distress: Worries, concerns, and fears of DM patients 10-30% patients with diabetes



Pancreas
Insulinoma
**Diabetes/Metabolic syndrome**



Cover Illustration, *The Economist*, 2002

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# Obesity : Common scenario

**BMI : 40.2kg/m2**
**HBA1c : 10.8%**

## Is Obesity a Psychiatric Disorder?

If so, the majority of the U.S. population might benefit from psychiatric care

Posted Jun 24, 2014

**Neurobiology of food addiction**

Daniel M. Blumenthal[a] and Mark S. Gold[b]

**Current Opinion in Clinical Nutrition and Metabolic Care** 2010, 13:359–365

Food and drugs (of abuse) act on same central neuro-biological pathways

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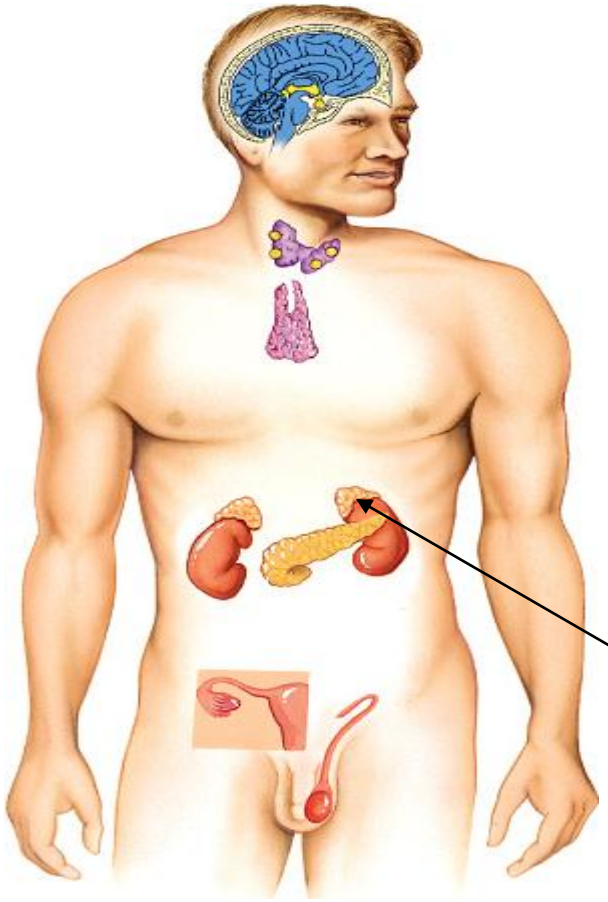
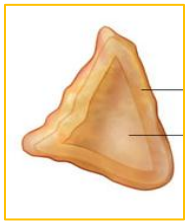
# Endocrinopathies linked with psychiatric manifestations



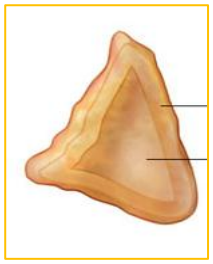


Adrenal

**Pheochromocytoma**

Addisons disease

Pheochromocytoma



**Adrenal gland**



## The Protean Manifestations of Pheochromocytoma

Horm Metab Res 2009; 41: 658–663

**Table 1** Conditions that may suggest pheochromocytoma (those italicized may have elevated plasma and urine catecholamines and their metabolites)

| | |
|---|---|
| 1 Anxiety, *panic attacks* with labile blood pressure | 14 *Factitiously-produced hypertension* |
| 2 Migraine | 15 Cushing's Syndrome |
| 3 Paroxysmal atrial tachycardia | 16 *Postural tachycardia syndrome (POTS)* |
| 4 Hyperdynamic β-adrenergic circulatory state | 17 *Acute infectious disease* |
| 5 Preeclampsia (*eclampsia with convulsions*) | 18 *Autonomic hyperreflexia* |
| 6 *Unexplained shock* | 19 Hyperthyroidism |
| 7 *Unexplained multisystem organ failure and lactic acidosis* | 20 Menopause |
| 8 Cardiomyopathy (*with failure*) | 21 Hyperglycemia without Diabetes |
| 9 *Baroreflex failure* | 22 *Acrodynia ("Pink Disease" – mercury poisoning)* |

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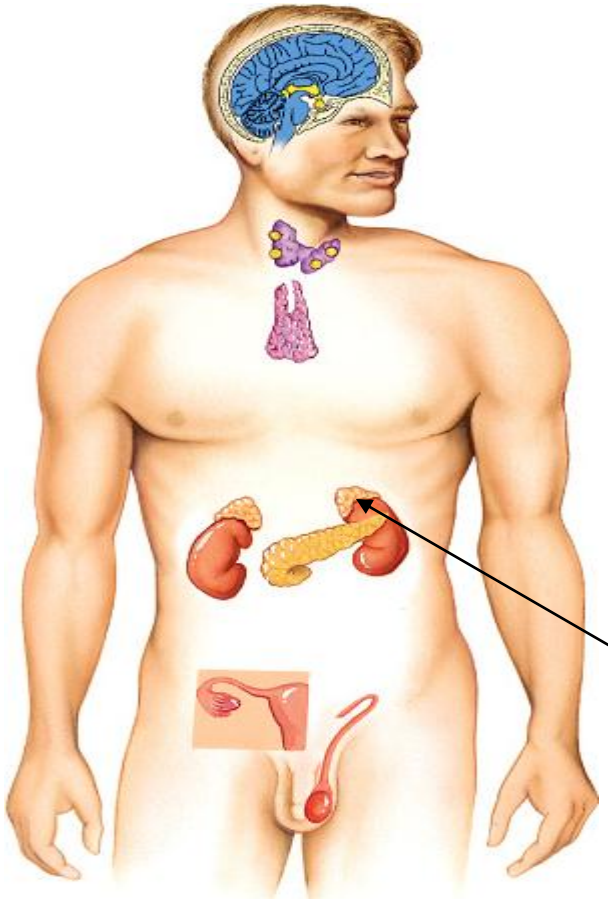
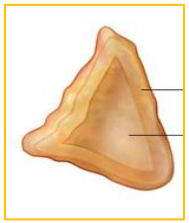
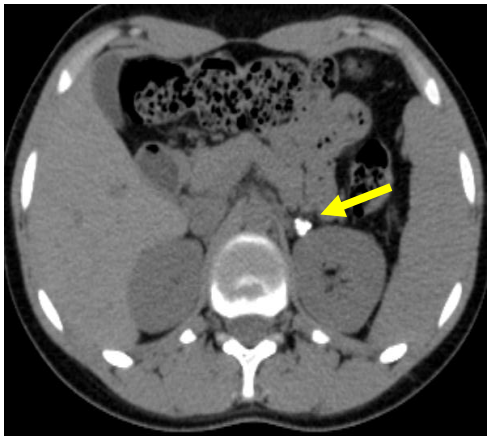
# Endocrinopathies linked with psychiatric manifestations

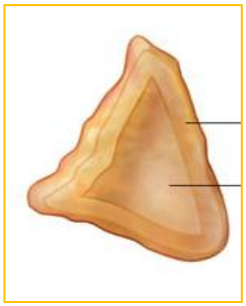




Adrenal
Pheochromocytoma
**Addisons disease**



Adrenal Tuberculosis

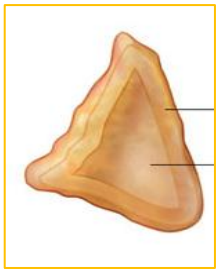


**Adrenal gland**

34 years/F
Symptomatic : 3 years
Generalised weakness
Loss of appetite
Aches and pain
Low energy levels

**ACTH : 1069 pg/ml**
**Basal cortisol : 3.8 µg/dl**

**Adrenal insufficiency : Addisons disease**



**Adrenal gland**

# Adrenal Fatigue

GOGLE

adrenal fatigue

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Vishwa Wellness

Mens wellness
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Vishwa Wellness


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Himalaya Herbal Healthcare, ...
₹ 1,262.51
iHerb.com


Jarrow Formulas Adrenal ...
₹ 2,900
Amazon India

### What Are The Symptoms Of Adrenal Fatigue? - Adrenal Fatigue Solution

https://adrenalfatiguesolution.com/adrenal-fatigue-symptoms/

**Adrenal Fatigue** can cause symptoms like tiredness, an inability to handle stress, low blood sugar, a weakened immune system and cravings for salty foods.

Supplements For Adrenal ... · This book shows you how to ... · Recipes

### Adrenal fatigue: What causes it? - Mayo Clinic

www.mayoclinic.org/diseases-conditions/addisons.../adrenal-fatigue/faq-20057906

**Adrenal fatigue** is a term applied to a collection of nonspecific symptoms, such as body aches, fatigue, nervousness, sleep disturbances and digestive problems.

### Adrenal Fatigue Syndrome: Your Body Knows Something That You Do ...

https://www.drlam.com/articles/adrenal_fatigue.asp

★★★★★ Rating: 5 - Review by Judy D.

Dragged down by **Adrenal Fatigue**? Do you feel tired? Does day to day life seem to drain you? Read this expert in-depth article and start your recovery today!

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BMC Endocr Disord. 2016 Aug 24;16(1):48. doi: 10.1186/s12902-016-0128-4.

# Adrenal fatigue does not exist: a systematic review.

Cadegiani FA[1], Kater CE[2].

Author information

**Erratum in**

Erratum to: Adrenal fatigue does not exist: a systematic review. [BMC Endocr Disord. 2016]

## Abstract

**BACKGROUND:** The term "adrenal fatigue" ("AF") has been used by some doctors, healthcare providers, and the general media to describe an alleged condition caused by chronic exposure to stressful situations. Despite this, "AF" has not been recognized by any Endocrinology society, who claim there is no hard evidence for the existence. The aim of this systematic review is to verify whether there is substantiation for "AF".

**METHODS:** A systematic search was performed at PUBMED, MEDLINE (Ebsco) and Cochrane databases, from the beginning of the data until April 22nd, 2016. Searched key words were: "adrenal" + "fatigue", "adrenal" + "burnout", "adrenal" + "exhaustion", "hypoadrenia", "burnout" + "cortisol", "fatigue" + "cortisol", "clinical" + "burnout", "cortisol" + "vitality", "adrenal" + "vitality", and "cortisol" + "exhaustion". Eligibility criteria were: (1) articles written in English, (2) cortisol profile and fatigue or energy status as the primary outcome, (3) performed tests for evaluating the adrenal axis, (4) absence of influence of corticosteroid therapy, and (5) absence of confounding diseases. Type of questionnaire to distinct fatigued subjects, population studied, tests performed of selected studies were analyzed.

**RESULTS:** From 3,470 articles found, 58 studies fulfilled the criteria: 33 were carried in healthy individuals, and 25 in symptomatic patients. The most assessed exams were "Direct Awakening Cortisol" (n = 29), "Cortisol Awakening Response" (n = 27) and "Salivary Cortisol Rhythm" (n = 26).

**DISCUSSION:** We found an almost systematic finding of conflicting results derived from most of the studies methods utilized, regardless of the validation and the quality of performed tests. Some limitations of the review include: (1) heterogeneity of the study design; (2) the descriptive nature of most studies; (3) the poor quality assessment of fatigue; (4) the use of an unsubstantiated methodology in terms of cortisol assessment (not endorsed by endocrinologists); (5) false premises leading to an incorrect sequence of research direction; and, (6) inappropriate/invalid conclusions regarding causality and association between different information.

**CONCLUSION:** This systematic review proves that there is no substantiation that "adrenal fatigue" is an actual medical condition. Therefore, adrenal fatigue is still a myth.

Myth vs Fact

# Adrenal Fatigue

This fact sheet was created to address myths about adrenal fatigue and to provide facts on its relation to true medical diseases.

Hormone Health NETWORK®

ENDOCRINE SOCIETY

"Adrenal fatigue" is not a real medical condition. There are no scientific facts to support the theory that long-term mental, emotional, or physical stress drains the adrenal glands and causes many common symptoms.

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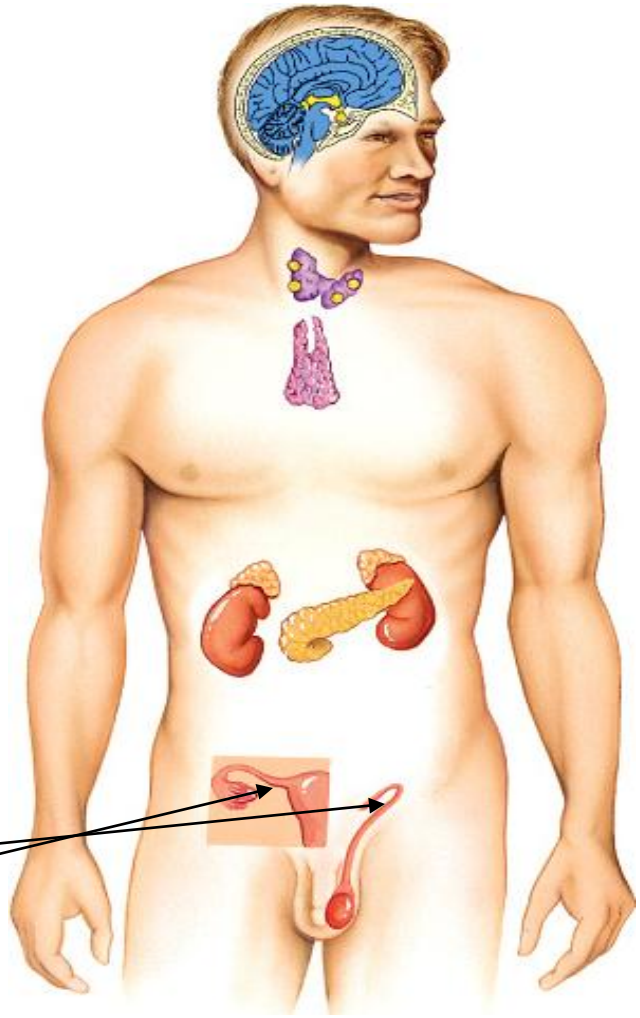
# Endocrinopathies linked with psychiatric manifestations



Gonads

**Gender Identity disorder**

DSD

# Gender Identity Disorder

**Case 10**

28 years old, reared as female

Well till 10 years of age

**11 years**: Internal mental discomfort- could not define it
Felt discomfort sitting up with girls and using female washroom

**12 years**: More comfortable with boys.
Developed liking for her female friend

**12 years – 18 years-** Feelings got stronger

Consulted a plastic surgeon for gender re-assignment surgery
Endocrinology referral

***Internal and external genitalia : Female***
***Hormonal profile : Female***

Psychiatry reference

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**Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline**

World Professional Association of Transgender Health's "Standards of Care" guidelines recommend that the diagnosis be made by a Mental Health Professional

**Table 1. Diagnostic Criteria for Gender Identity Disorder.***

- Strong and persistent cross-sex identification (not merely a desire for any perceived cultural advantages of being the other sex)
  - Children (at least four criteria must be met)
    - Repeatedly stated desire to be a member of the other sex or insistence on actually being a member of the other sex
    - In boys, preference for cross-dressing or simulating female attire; in girls, insistence on wearing only stereotypically masculine clothing
    - Strong and persistent preferences for cross-sex roles in make-believe play or persistent fantasies of being a member of the other sex
    - Intense desire to participate in the stereotypical games and pastimes of the other sex
    - Strong preference for playmates of the other sex
  - Adolescents and adults (at least one criterion must be met)
    - Stated desire to be of the other sex
    - Frequent attempts to pass as the other sex
    - Desire to live or be treated as the other sex lives or is treated
    - Conviction of having the typical feelings and reactions of the other sex
- Discomfort with original sex or sense of inappropriateness in the role of that sex
  - Children (at least one criterion must be met)
    - In boys, assertion that penis or testes are disgusting or will disappear, assertion that it would be better not to have a penis, or aversion to rough-and-tumble play and rejection of male stereotypical toys, games, and activities; in girls, rejection of urinating in a sitting position, assertion that she has or will have a penis, assertion that she does not want to have breasts or menstruate, or marked aversion to normative feminine clothing
  - Adolescents and adults (at least one criterion must be met)
    - Preoccupation with getting rid of primary and secondary sex characteristics (e.g., request for hormones, surgery, or other procedures to physically alter sexual characteristics and simulate the other sex) or belief in having been born with the wrong sex
- No concurrent physical intersex condition
- Clinically significant distress or impairment in social, occupational, or other important areas of functioning

* These criteria were adapted from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) (fourth edition, text revision).[4]

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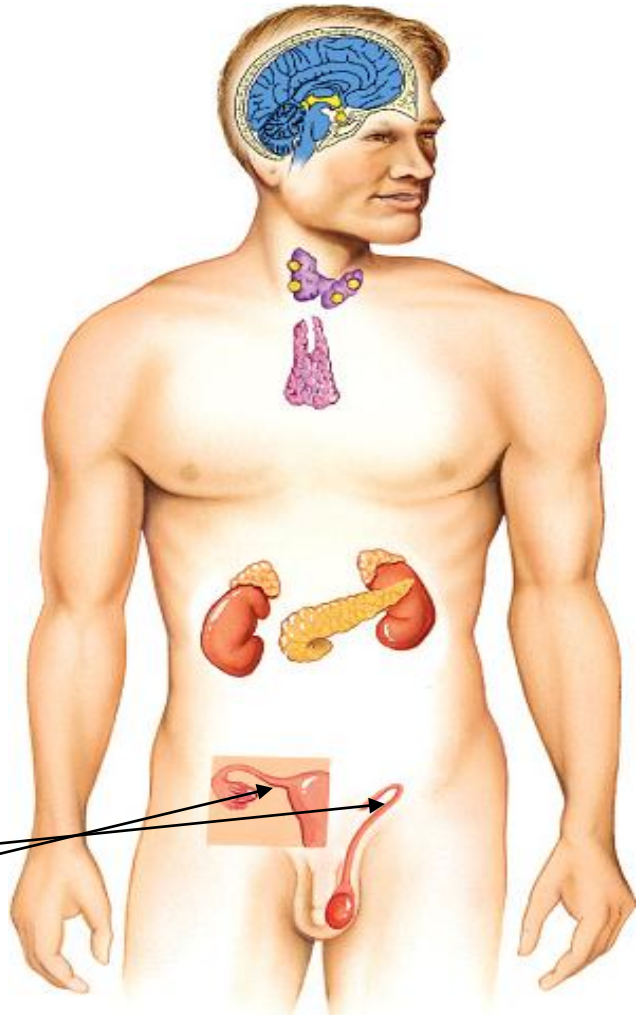
# Endocrinopathies linked with psychiatric manifestations



Gonads
Gender Identity disorder
**DSD**

# Disorder of sexual development

**Case 11**

19 years old, reared as female
Ambiguity since birth (Both gonads in labioscrotal fold)

**Early childhood** : Played with girls

**11- 15 years**: Internal mental discomfort- Felt like boy (facial hair appeared)
Felt attracted towards females

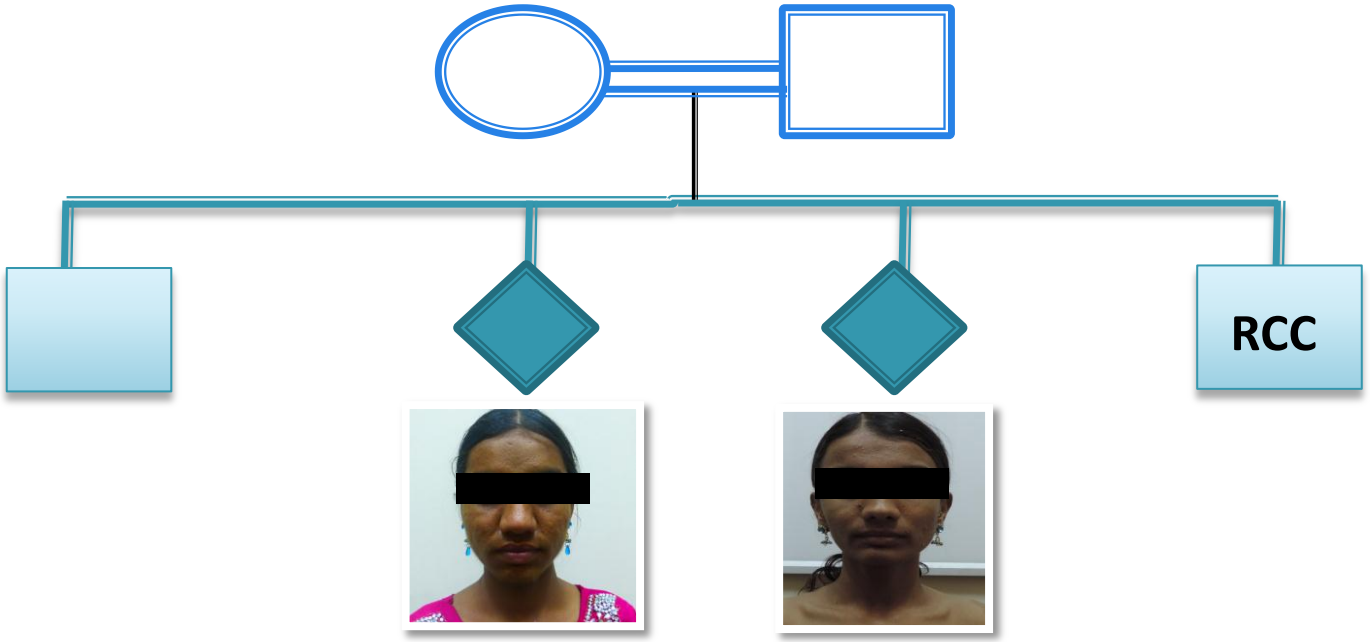
**15-18 years**: Masturbation and ejaculation started
Un-mangeable physical attraction towards females
Suicidal ideation

**18 years-** Sought medical concern for sex change

Endocrinology referral

***Internal and external genitalia : Male (Ambiguity)***
***Hormonal profile : Male***

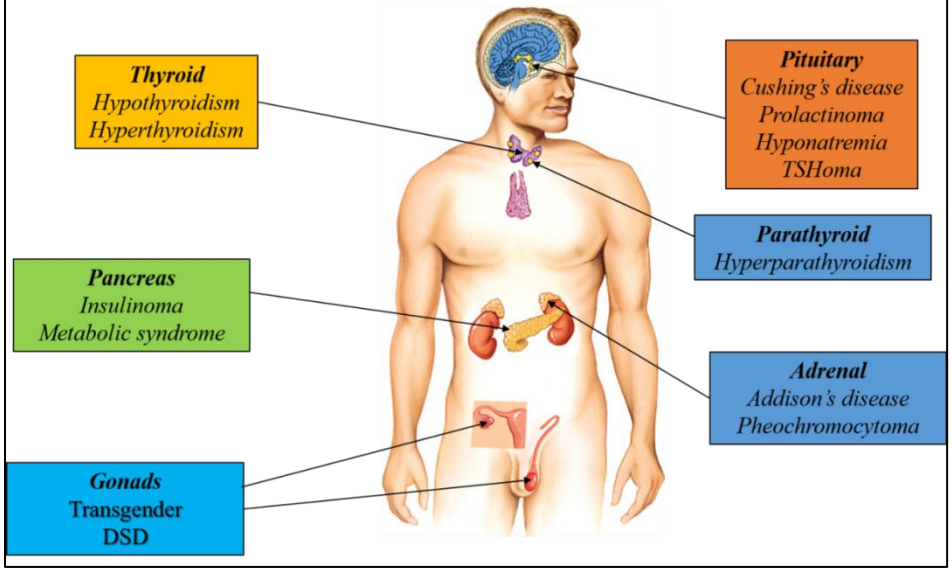
# Family history



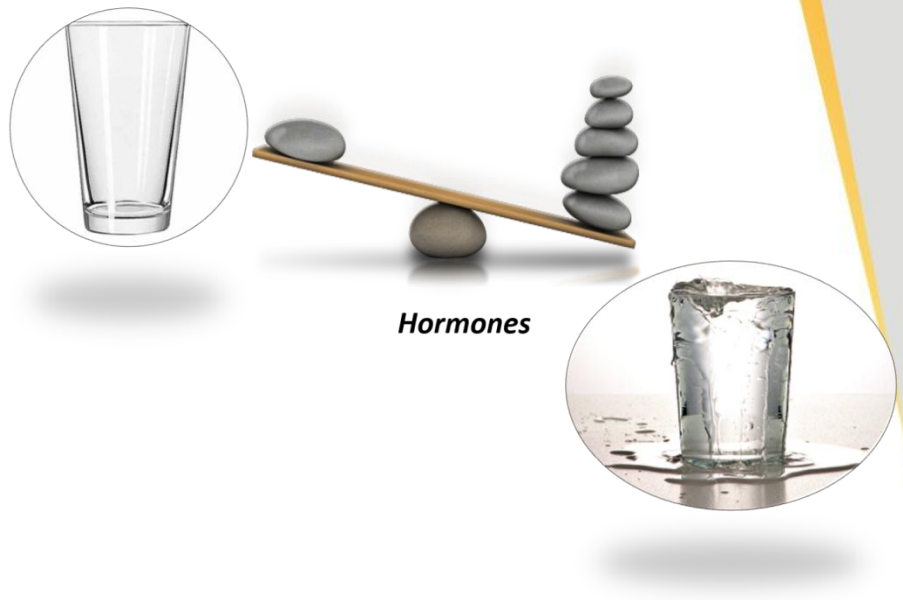

| Desired sex: | Male | Female |
|---|---|---|

***Role of Psychiatrist :*** ***Management of psychiatric co-morbidities***
***Discernment of deep gender identity***

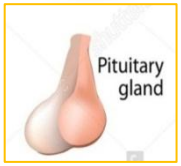
## Endocrinopathies linked with psychiatric manifestations




## Endocrine disorders : A perspective



# Distress of appearance: Stature




Growth hormone

Growth hormone deficiency : Short stature

Growth hormone excess : Tall stature

# Distress of pubertal development

24 years old male

Delayed Puberty


*Pubertal development*

3 years old child

Early Puberty

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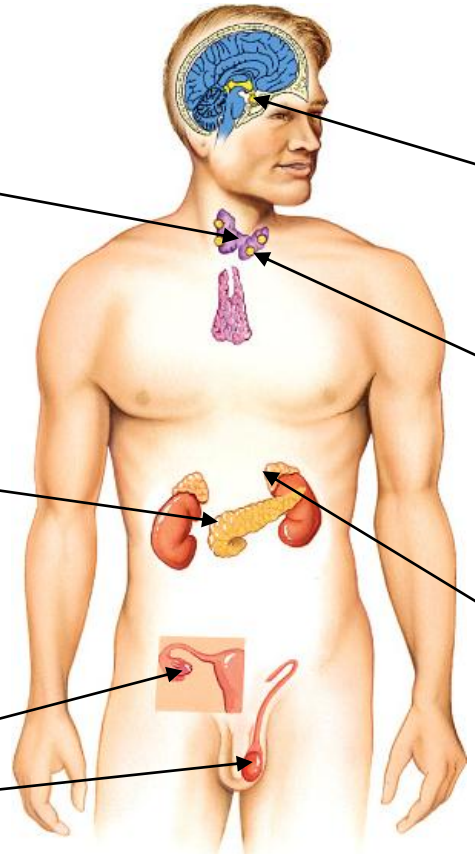
# Endocrinopathies linked with psychiatric manifestations



**Thyroid**
Hypothyroidism
Hyperthyroidism

**TSH**

**Pituitary**
Cushing's disease
Prolactinoma
Hyponatremia
TSHoma
Gonadotropinoma

**Prolactin**
**Sodium**
**ODS Cortisol**

**Parathyroid**
Hyperparathyroidism

**Calcium**
**Phosphorus**

**Pancreas**
Insulinoma
Metabolic syndrome

**Blood sugars**

**Adrenal**
Pheochromocytoma
Addison's disease

**Metanephrines**
**Basal cortisol**
**ACTH**

**Gonads**
Gender identity disorder
DSD

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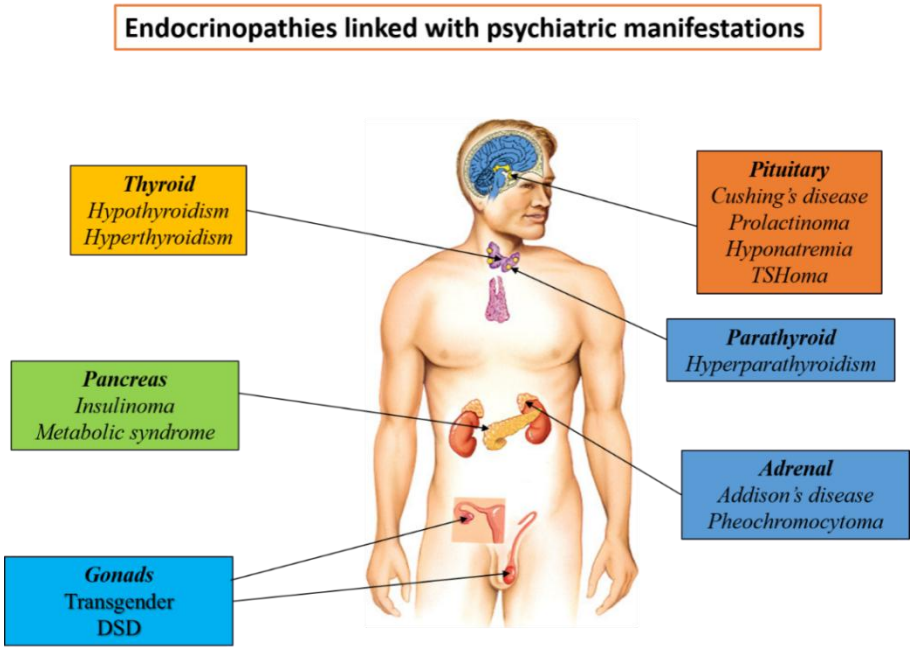
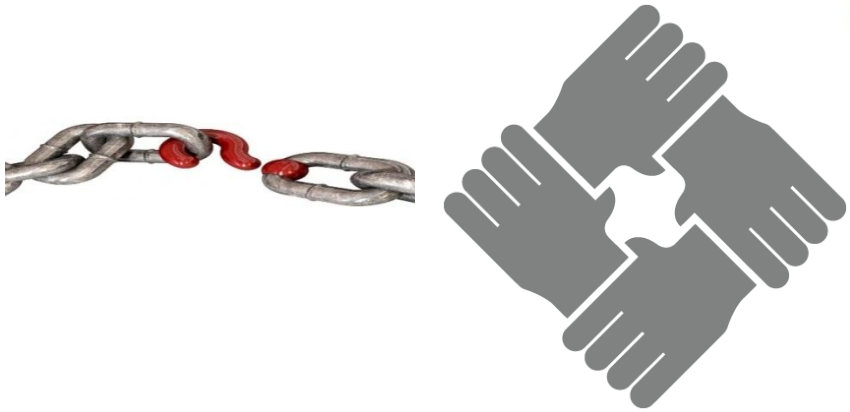
# Conclusion



Team work : key to link up the missing link