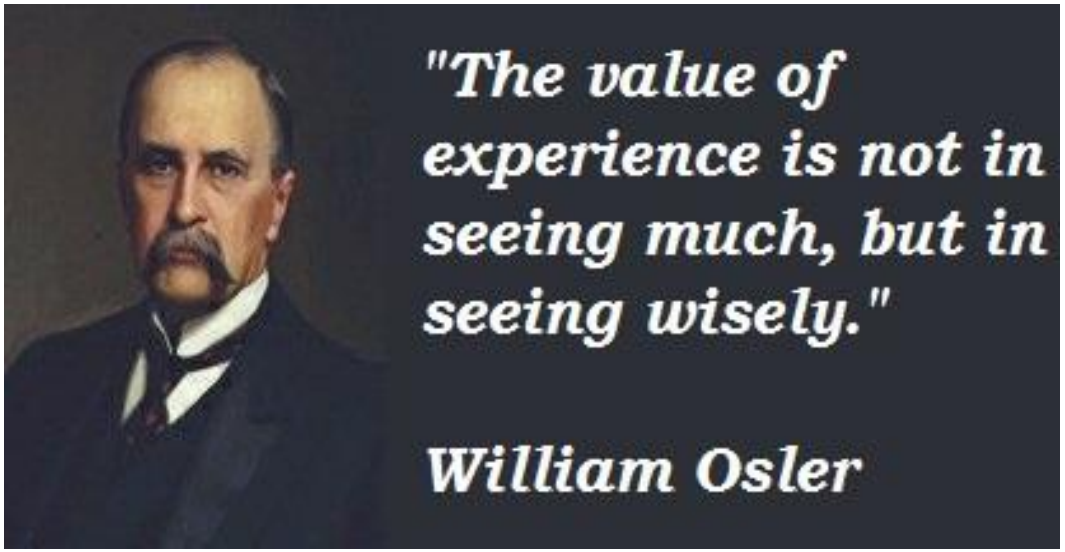
Masks in endocrinology



Dr. Ieva Ruža
Riga Stradins University
Riga Eastern Clinical University Hospital
8.02.2017.

Masked pathologies

- Nonspecific presentations of endocrine diseases
- Specific (endocrine) presentations of non-endocrine diseases (syndromes of ectopic hormone production)

Nonspecific presentations of endocrine diseases

(Davidson's Principles and Practice of Medicine, 2013)

- **Lethargy and depression** (hypothyroidism, diabetes mellitus, hyperparathyroidism, hypogonadism, adrenal insufficiency, Cushing's syndrome)
- **Weight gain** (hypothyroidism, Cushing's syndrome)
- **Weight loss** (thyrotoxicosis, diabetes mellitus, adrenal insufficiency)
- **Headache** (phaeochromocytoma, acromegaly, pituitary tumour)

Nonspecific presentations of endocrine diseases

(Davidson's Principles and Practice of Medicine, 2013)

- **Polyuria and polydipsia** (diabetes mellitus, diabetes insipidus, hyperparathyroidism, hypokalaemia)
- **Heat intolerance** (thyrotoxicosis, menopause)
- **Palpitations** (thyrotoxicosis, phaeochromocytoma)
- **Muscle weakness** (thyrotoxicosis, Cushing's syndrome, hypokalaemia, hyperparathyroidism, hypogonadism)
- **Coarsening of features** (acromegaly, hypothyroidism)

Anxiety?

O-K, 27 y.o. woman

- 30 wks of pregnancy
- Hypertension (till 150/90)
- Treatment with methyldopa 250 mg bid
- USG – probable right side adrenal adenoma
- Observation, vaginal birth
- CT scan 1 month after the birth – right side adrenal non-adenoma (phaeochromocytoma?)
- Referral to endocrinologist

O-K, 27 y.o. woman

O-K, 27 y.o. woman

- 24h urine:
  - E – 134.7 mkg/24h [4-20]
  - NE – 957 mkg/24h [23-105]
  - Dopa – 336 mkg/24h [190-450]
  - VMA – 30.6 mg/24h [1-10]
- NSE – 14 ng/ml [<16.3], CEA – 0.7 ng/ml [<5]
- Chromogranin – 759 U/l [<100]
- Aldosterone, renin, ACTH, cortisol – normal
- **Diagnosis**: Right side phaeochromocytoma

Phaeochromocytoma and pregnancy

- 0.002% of all pregnancies
- Confusion with more prevalent forms of pregnancy-related hypertension
- **Plasma or urinary** metanephrines
- **MRI** – sensitivity of more than 90%
- Before **24 wks** – operate, later – wait till birth (possible CS with tumour removal)
- **Treatment** – alpha (phenoxybenzamine), then beta blockers

Lenders JWM, Eur J Endocrinol 2012, 166:143-150

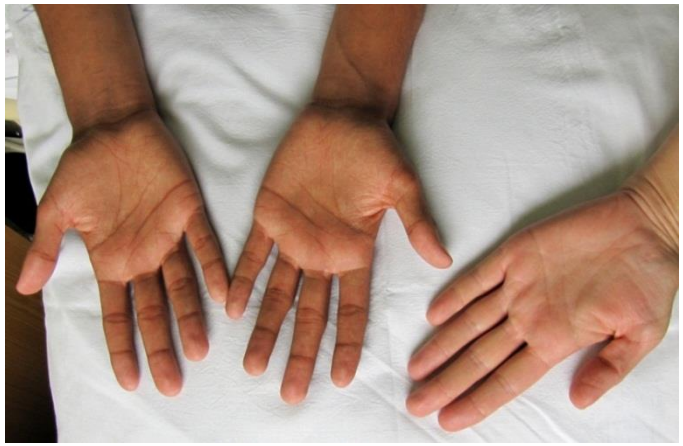
Anxiety

- Phaeochromocytoma (panic attacks!)
- Thyroid disorders
- Hypoglycaemia

Depression?

R-R, 19 y.o. man

- Depressed after mother's death 1 year ago
- Weight loss, fatigue, staying in bed
- After gastroenteritis collapsed on the street
- Admitted in regional hospital - dark palmar creases
- Transferred to endocrinology
- "Addicted to potato chips"



R-R, 19 y.o. man

- ACTH – 319.8 pg/ml [7.2-63.3]
- 8AM cortisol – 2.5 mkg/dl [3.7-19.4]
- Na – 113 mmol/l [135-145]
- Cl – 81.2 mmol/l [98-107]
- K – 5.3 mmol/l [3.5-5.1]
- Glucose – 4.97 mmol/l [3.8-6.1]
- Orthostatic hypotension [120/70 -> 70/50 mmHg]
- **Treatment**:
  - i/v -> p/o hydrocortisone
  - Fludrocortisone acetate
- **Diagnosis**: Primary adrenal insufficiency

Weight loss and fatigue

- “Severe fatigue was experienced by 41 % of the CAH patients, 42 % of the PAI patients, 50 % of the SAI patients and 42 % of the Cush-AI patients” (*Giebels V et al. J Endocrinol Invest 2014 Mar;37(3):293-301*.)
- **Endocrine** (Addison’s disease, hyperthyroidism, diabetes mellitus)
- **Non-endocrine reasons:**
  - **Systemic disease** (malignancy, malabsorption, cardiac, renal or liver failure, chronic respiratory disease)
  - **Infective** (TB, HIV, helminths)
  - **Psychiatric** (depression, anorexia nervosa)

Depression

- **Hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-adrenal (HPA) axes abnormalities observed in patients with depression** (*Musselman DL, Nemeroff CB. 1996*)

- **Adrenals:**
  - Addison's disease
- **Thyroid gland:**
  - Hashimoto's thyroiditis
  - Hypothyroidism
  - Grave's disease
  - Hyperthyroidism
- **Parathyroid gland:**
  - Hypoparathyroidism
- **Pituitary tumours**
- **Pancreas:**
  - Hypoglycaemia

K-T, 17 y.o. man

- **Suspected polymyositis:**
  - Malaise, sleepiness
  - Mild icterus
  - Limb muscle pain
  - Loss of appetite
  - Weight gain (+4 kg/6 months)

- Hospitalized in rheumatology
- Physical and mental development is consistent with his age
- Cold palms are noticed
- No previous drug use
- Mother denies family history of chronic, autoimmune or hereditary diseases

- Rheumatoid, autoimmune markers negative
- ECG, EchoCG - normal
- Chest X-ray – normal
- Abdominal USG – slight hepatomegaly
- Thyroid US – inhomogeneous structure

K-T, 17 y.o. man

- First blood tests:
  - mild anaemia (Hb – 10 g/dl)
  - ALAT – 87.8 U/l [5-55]
  - ASAT – 47.7 U/l [5-34]
  - Creatine phosphokinase (CPK) – 1415 U/l [26-270]
- EMG - bilateral symmetrical myopathy, distal polyneuropathy
- Neurologist – delayed tendon reflexes;

- …asks more tests...

K-T, 17 y.o. man

- …asks thyroid tests…

- TSH – 104 mIU/l [0.27-4.2]
- FT4 – 6 pmol/l [10-22]
- Anti-TPO – 180 IU/ml [0-35]
- **Diagnosis**: Chronic autoimmune thyroiditis with primary hypothyroidism and hypothyroid myopathy.

Madhu SV, et al. Myopathy presenting as a sole manifestation of hypothyroidism. J Assoc Physicians India. 2010;58:569-70.

Endocrine myopathies

- Sharma, Vikas et al. “Myopathies of Endocrine Disorders: A Prospective Clinical and Biochemical Study.” *Annals of Indian Academy of Neurology* 17.3 (2014): 298–302. *PMC*. Web. 15 Oct. 2015.

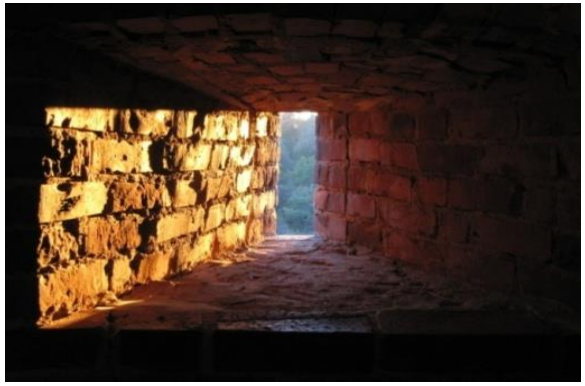
Type of disease	Number of patients
Hypothyroidism	10
Vitamin D deficiency	9
Hyperthyroidism	7
Steroid myopathy	6
Hyperparathyroidism	3
Pituitary disorder	2

Endocrine myopathies

- **Hypo**thyroidism >> Hyperthyroidism
- **Hyper**adrenalism >> Hypoadrenalism
  - Cushing's disease and syndrome!
- **Hyper**parathyroidism >>Hypoparathyroidism
- **Hypo**pituitarism >> Hyperpituitarism

Think about endocrine myopathy…

- Even in the absence of systemic findings, think of endocrine causes in case of:
  - pure muscle weakness
  - respiratory muscle weakness
  - new-onset psychosis or behavior disturbance
- Possibility of malignancy as the underlying etiology for any endocrinopathy
- Biochemistry – CPK
- EMG
- Treat underlying cause



N-A, 47 y.o. man

- **5 years** long history of progressing **shortening of height** (-18 cm), decreasing weight (-15 kg)
- 2 years long **fatigue** and extreme limb girdle and proximal lower limb **weakness**
- Progressive bone and joint pain
- Complete disability
- Huge **history of investigations** (parathyroid pathology, systemic disease, myeloma and malignancy excluded)
- The 3rd year – **hypophosphatemia found**, no success with cause
- Referral to endocrinology

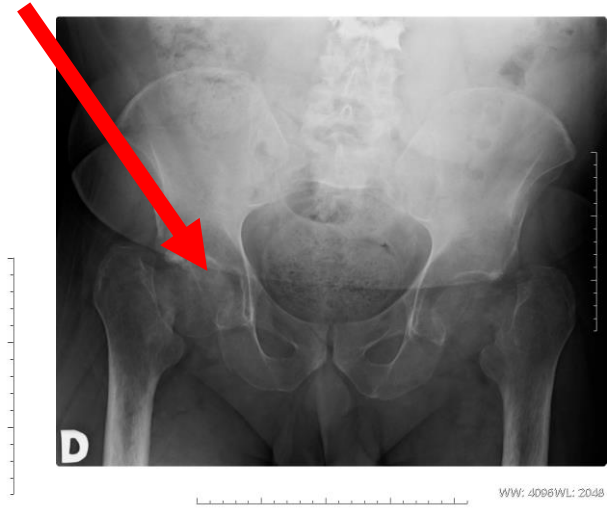
	Sep-2009	Feb-2010
Ca [plasma]	2.4 [2.1-2.6mM/l]	2.48
Ca [24h urine]	250 mg [100-300mg]	142 mg
P [plasma]	0.4 / 0.37 [0.8-1.6mM/l]	0.51/ 0.48
P [24h urine]	1.06 [0.4-1.3g] !	0.94
PTH	93.6 [12-72pg/ml]	137
AP	342 [50-136U/l]	

N-A, 47 y.o. man

- In 5 months – previous complaints persist
- Additional observation - **right upper leg mass** (previously not observed, “old thing”)

LIPOMA

Pseudofractures

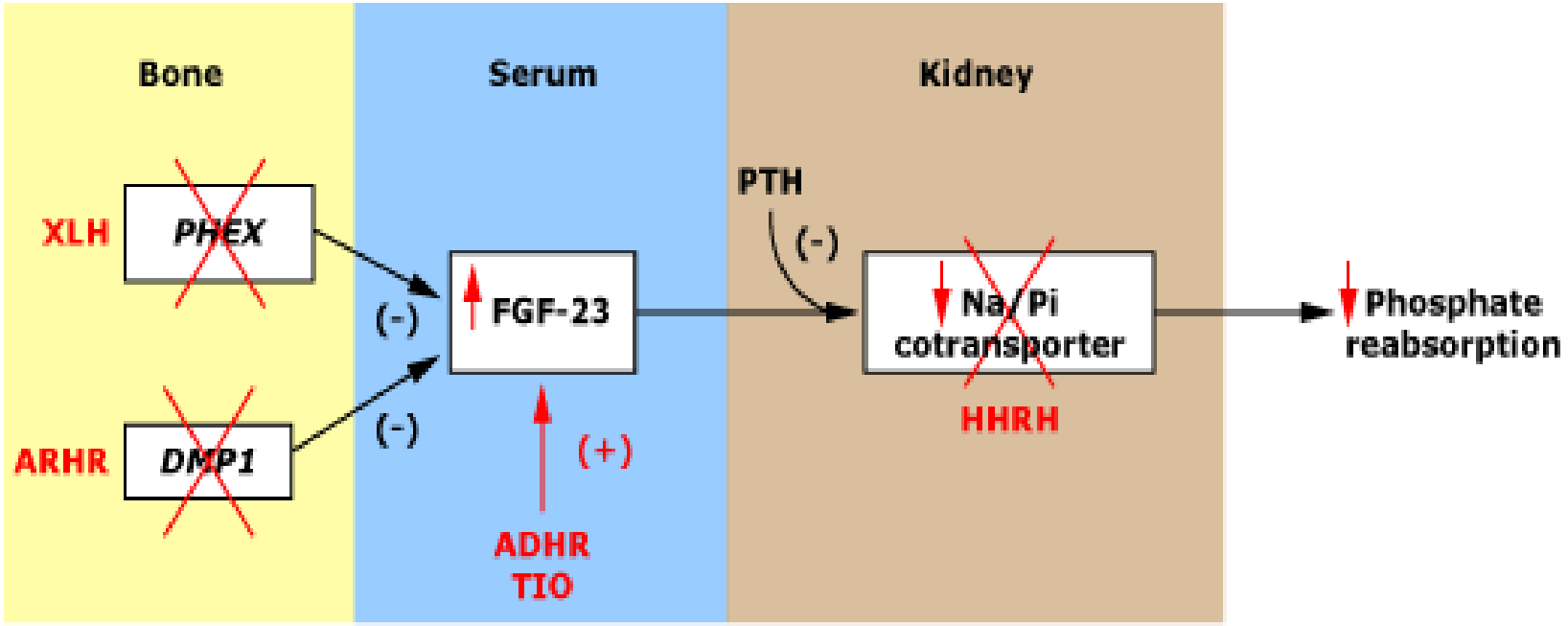


N-A, 47 y.o. man

- Case consulted in Dallas, USA – **tumour-induced hypophosphataemia suspected** (FGF-23?)
- Tertiary hyperparathyroidism
- **Operated (2 in 1)**, no malignancy (giant-cell tumour??), «biochemically» healthy

- **Diagnosis**: Secondary tumour-induced renal phosphate wasting with severe hypophosphataemia

Pathogenesis of osteomalacia



Source: UpToDate, 2011

Syncopes?

V-I, 59 y.o. woman

- 6 months ago – first-time **generalized seizure** followed by unconsciousness
- **Brain CT** – changes consistent with **Fahr's syndrome** – diffuse symmetrical parenchymal calcifications (basal ganglia, subcortical regions of cerebral white matter and cerebellum)
- …one test is needed…

V-I, 59 y.o. woman

- **No Ca testing done!**
- No cognitive, behavioural or substantial motor changes
- Episodic numbness for 7 years
- 3 months ago - **sudden fall with unconsciousness**, hospitalized in neurosurgery department, more detailed investigation done -> **hypocalcaemia**
- Referral to endocrinologist

V-I, 59 y.o. woman

	Mar-2008	May-2008	Nov-2009	Aug-2010	Nov-2010	Dec-2011
Ca [plasma] [2.2-2.6 mM/l]	1.06	1.65	1.87	1.71	1.97	1.86
Ca [24h urine] [2.5-7.5 mM/l]		1.14	3.27			6.3
P [plasma] [0.74-1.52 mM/l]	2.41	2.43	2.11	2.36	1.94	1.67
P [24h urine] [11-42 mM/l]		20.8	15.7			37.46
PTH [1.3-6.8 pM/l]	<0.32	<0.32	<0.32			<0.32
Creatine kinase (CK) [21-215 U/l]	1373 / 2698	192				

- **Diagnosis**: Idiopathic calcification of basal ganglia (Fahr's syndrome). Primary hypoparathyroidism.

Borrowed from: Hegde AN et al. RadioGraphics January-February 2011;31(1):5-30

Syncopes?

- Not only heart and sugar...
- Always **check electrolytes** – calcium and sodium!

Pancreatitis?

I-K, 47 y.o. woman

- Recurrent episodes of pancreatitis
- Conservative treatment
- **No alcohol** use; **gall bladder pathology excluded**, **diabetes excluded,** no smoker, no POC or other drug use
- **…**
- Two most common “endocrine” reasons for pancreatitis are…

I-K, 47 y.o. woman

- New GP notices high lipid values
- Referral to endocrinologist

I-K, 47 y.o. woman

	Mar-2008	Oct-2008	Mar-2009	Oct-2009 (*)	Oct-2015
Triglycerides [<2 mmol/l]	**35.65**	**21.26**	**40.19**	**32**	**76.48!**
Cholesterol [<5 mmol/l]		**8.82**	**11.58**	**9.29**	**6.8**
LDL [<3 mmol/l]		**0.31**	**UND!**	**UND!**	**2.8**
HDL [>1.1 mmol/l]		**0.7**	**0.9**	**0.71**	**0.36**

I-K, 47 y.o. woman

- **Standing plasma test ("Refrigerator test") –** VLDL production, possible chylomicrons
- **Ophthalmologist** – retinal blood vessels with "light reflex", retinal lipaemia

(picture) Yuan et al. ***CMAJ*** 2007; 176 (8): 1113

I-K, 47 y.o. woman

- **Diagnosis**: Excessive **primary** familial hypertriglyceridaemia and hypercholesterolaemia with prevalent production of **VLDL** and **chylomicrons** (class V by Fredrickson). Recurrent pancreatitis exacerbations (in history)

- **Treatment**:
  - diet!
  - fenofibrate
  - plasmapheresis

Pancreatitis

- Elevated pancreatitis risk if TG >11.3 mM/l (1000 mg/dl)
- **Hypertriglyceridaemia => hyperviscosity => impaired capillary circulation => pancreatic ischaemia => inflammatory reaction**
- Treatment target – to keep TG < 5.65 mM/l (500 mg/dl)

- N.B. Check for hypercalcaemia!

Diarrhoea

- Hyperthyroidism (goiter)
- Carcinoid syndrome (flushing)
- Zollinger-Ellison syndrome (peptic ulcer)
- Vipoma (watery diarrhoea, hypokalaemia)
- Medullary thyroid cancer

Table 2. Selected Endocrine Paraneoplastic Syndromes.

Clinical Presentation	Hormone	Most Common Responsible Tumors
Cushing's syndrome	Corticotropin or corticotropin-releasing hormone	Small-cell carcinoma of the lung, carcinoid tumors, medullary thyroid carcinoma, pheochromocytoma
Hypercalcemia	Parathyroid hormone–related peptide	Squamous-cell carcinoma of the lung, skin, head and neck; renal carcinoma; carcinoid tumors
	1,25-Dihydroxycholecalciferol	Lymphomas
Acromegaly	Growth hormone	Carcinoma of the lung, lymphoma
	Growth hormone–releasing hormone	Small-cell carcinomas, carcinoid, pancreatic endocrine tumors
Gynecomastia	Human chorionic gonadotropin	Carcinomas of the lung, bladder, or kidney
Hyponatremia	Arginine vasopressin	Small-cell carcinoma of the lung, carcinomas of the head and neck
Hypoglycemia	Insulin-like growth factors	Epithelial and mesenchymal tumors, hepatocellular carcinoma
Hypertension	Renin	Wilms' tumor; sarcomas; carcinomas of the lung, ovary, liver, pancreas
Zollinger–Ellison syndrome	Gastrin	Pancreatic endocrine tumors, ovarian cancers
Polycythemia	Erythropoietin	Leiomyoma, renal-cell carcinoma, hepatocellular carcinoma

McMahon GT et al, N Engl J Med 2010; 362:156-166

Hyperprolactinaemia – additional causes

- Pregnancy
- Hypothyroidism
- Drugs (antidepressants, antipsychotics etc.)
- Stress
- Physical exertion
- Anterior chest wall and nipple stimulation
- Sex
- Renal failure
- Cirrhosis

Other common associations

- Atrial fibrillation – hyperthyroidism
- Anaemia – hypothyroidism
- Hydrothorax – hypothyroidism
- Polyuria – diabetes mellitus, diabetes insipidus

- N.B.! Diabetes mellitus can mask pain and any septic complications

ESIM
EUROPEAN SCHOOL OF INTERNAL MEDICINE

Thank you!