



HISTORY of PRESENTING ILLNESS

AMENORRHOEA in chicks
LOSS OF LIBIDO in dudes

- May or may not be **lactating uncontrollably**
- May or may not be vexed by **VISUAL PROBLEMS**

EXAMINATION:



Mainly interested in non-pituitary reasons for amenorrhoea
However; it only takes a moment to check for
BITEMPORAL HEMIANOPIA

FEMALE examination

Signs of Endocrinopathy

- Hirsutism
- Stigma of Cushing's disease
- Hypopituitaristic hypogonadism
- **THYROID DISEASE**

Genital exam

- Sexually transmitted pathogens eg. Chlamydia
- Anatomical defects
- Assess cervical os for patency

Rectal exam

Assess for pelvic inflammatory disease

MALE examination

Signs of Endocrinopathy

- (Hypogonadotropic Hypogonadism)
- Thyromegaly
 - Dermatologic changes in hair or fat
 - **THYROID DISEASE**

Genital exam

- Hypospadias
(Congenital defect of urethral meatus)
- **Assess testicular size**
 - Normal <20 cm or >4 cm
- Varicocele

Rectal exam

- Assess prostate gland for Nodules or swelling

ASK ABOUT THE DRUGS

Dopamine receptor antagonists

- phenothiazines
- butyrophenones
- thioxanthenes
- risperidone
- metoclopramide
- sulpiride
- pimozide

Dopamine-depleting agents, eg.

- methyl dopa
- reserpine

Others:

- Isoniazid
- Danazol
- Tricyclic antidepressants, monoamine antihypertensives, verapamil, estrogens, antiandrogens, cyproheptadine, opiates, H2-blockers [cimetidine], cocaine

Exam specifically for prolactin: try to express milk (demonstrate galactorrhoea)

INVESTIGATIONS:

!! PROLACTIN ASSAY!!

- **Must be a FASTING SAMPLE**
- After you have determined that there actually IS an increase in prolactin:
- **Beta-HCG**
- **TSH** (hypothyroidism)
- **LFTs** (cirrhosis?)
- **EUC** (chronic renal failure)
- **LH, FSH, Growth Hormone** (looking for panhypopituitarism)

Investigate for osteoporosis!

Low sex hormones → reduced bone formation

Then: If no obvious cause is identified or if a tumor is suspected, MRI should be performed. When the underlying cannot be determined and an MRI does not identify an adenoma, **idiopathic hyperprolactinemia** is diagnosed.

MANAGEMENT:

- **Fix the underlying problem**
 - **If none is found, give either**
 - **BROMOCRIPTINE**
 - **CABERGOLINE**
- Only needed twice weekly
 - **PERGOLIDE**
- Follow up:**
- **With fasting prolactin levels**
 - **With MRI to check on the mass**

DIFFERENTIALS of high prolactin

These conditions usually produce a prolactin level of less than 50 ng/mL.

- **Pregnancy** – is she post-partum?
- **Excessive exercise**
- **History of chest wall surgery or trauma**
- **Chronic renal failure**
- **Cirrhosis**
- **Postictal** patients also develop hyperprolactinemia within 1-2 hours after a seizure.
- **Hypothyroidism**
- **microadenomas** (more common in premenopausal women), which are smaller than 10 mm
- **macroadenomas** (more common in men and postmenopausal women), which are >10 mm.
- **Macroprolactinemia** is the apparent increase in serum prolactin without symptoms. In this condition, serum prolactin molecules can polymerize and subsequently bind to immunoglobulin G (IgG). This form of prolactin is unable to bind to prolactin receptors and exhibits no systemic response. In the asymptomatic patient with hyperprolactinemia, this condition should be considered. The discovery of macroprolactinemia could save the patient the inconvenience and cost of an in-depth evaluation for a microadenoma. If this condition is suspected, specific serum immunoassays must be performed to detect this form of prolactin. Women with macroprolactinemia are able to conceive. This condition generally requires no treatment.

The Physiological Effects of Prolactin and Consequences of its Deficit or Excess

RELEASE

All these factors can stimulate release, usually by direct action on the dopamine-releasing parts of the hypothalamus

- **Estrogens** especially high levels at the end of pregnancy, used to prepare the mammary glands
- **TRH** (Thyrotropin-Releasing Hormone); Hence HYPOTHYROIDISM can cause high prolactin!
- **Suckling** (spinal reflex arc)
- **GnRH** probably acts on lactotrophs themselves
- **VIP** (vasoactive intestinal peptide)

Freeman et al.
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EXTRAPITUITARY SITES OF PROLACTIN SYNTHESIS:

- Hypothalamus (on its own!) - Adrenal glands
- Placenta, amnion, uterus - Fatty tissue (?...)
- Mammary glands ...Influence via leptin)
- Lymphocytes (??)

ALSO: **Inhibited by**
THYROXIN and
SOMATOSTATIN

INHIBITION HYPOTHALAMUS

Exerts a **CONTINUOUS TONIC INHIBITION** via **DOPAMINE D 2 receptor**. A dysfunctional hypothalamus will result in hyperprolactinaemia

METACLOPRAMIDE
= **D2 ANTAGONIST**
= stimulates prolactin release

BROMOCRYPTINE
= **D2 AGONIST**
= inhibits prolactin release

D2

In the Anterior Pituitary...

ACIDOPHILE LACTOTROPH CELL
Cleaves a prohormone and produces

PROLACTIN

Highest level at night

Half life: 20min

FEEDBACK

Drop in prolactin: echoed by a drop of dopamine activity in the hypothalamus.

FEEDBACK

Prolactin can inhibit its own secretion by acting on the hypothalamus

Genes encoding prolactin, growth hormone, and placental lactogen evolved from a common ancestral gene by gene duplication. The divergence of the prolactin and growth hormone lineages occurred about 400 million years ago.

Membrane-anchored receptor appertaining to the class 1 cytokine receptor superfamily

Tissues:

tyrosine phosphorylation of several cellular proteins, including the receptor itself and Janus Kinase 2 (JAK-2)

Signal transduction via various kinases:

The active phosphorylated receptor activates cascades of enzymes which bring about gene transcription and protein synthesis of all sorts

DEFICIT

USUALLY: 2ndry to hypopituitarism
OR: postpartum pituitary necrosis (Sheehan syndrome)
Or... MEDICATIONS!!
Plus... Anorexia and nicotine...

- **Menstrual disorders**
- **Inadequate lactation**
- **delayed puberty**
- **infertility / subfertility**
- the rare "**Purpueal Alactogenesis**"
- **BITEMPORAL HEMIANOPIA** from a non-secretory pituitary tumour, causing a pan-hypopituitaristic picture

EXCESS

Galactorrhea due to excess
Oligomenorrhea,
Amenorrhea
Infertility,

- generally result from prolactin suppression of gonadotropin-releasing hormone (GnRH).
- **MALES** may complain of a loss of sexual interest, infertility or hypogonadism.

Plus always theres the visual field defects.

Osmoregulation:

- decreases the transport of sodium and increases the transport of potassium across mammary epithelial cells
- inhibits water transport into human amnion
- acts on the proximal convoluted tubule of the renal nephron to promote sodium, potassium, and water retention

supports ANGIOGENESIS...

BUT prolactin breakdown products INHIBIT angiogenesis...

CHIEF FUNCTION: LACTOGENESIS

prolactin stimulates uptake of some amino acids, the synthesis of the milk proteins casein and a-lactalbumin, uptake of glucose, and synthesis of the milk sugar lactose as well as milk fats.

MAMMOGENESIS

Stimulates growth and differentiation of mammary ductal epithelium, in parallel with estrogen / progesterone

REPRODUCTIVE EFFECTS:

Maintains progesterone activity: thus

- **enhances implantation**
- **inhibits ovulation**
- plus, increases female sexual receptivity, enhances parenting behaviour

IMMUNE EFFECTS:

T-lymphocyte activation by IL-2 requires prolactin
Also required for mitogen-stimulated lymphocyte proliferation