

# PHYSIOLOGY

Lecture 3

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# Prolactin

بسم الله نبدأ، رح نحكي بهذا التلخيص عن ثالث محاضرة للفسيو في جهاز الغدد والصم و الي بتحكي عن prolactin ، كالعادة رح تكون السلايدات باللون الأسود و الشرح باللون الازرق و أي معلومة خارجية باللون الأحمر

- A polypeptide hormone synthesized and secreted by lactotrophs in the anterior pituitary gland
- The lactotrophs account for approximately 15–20% of the cell population of the anterior pituitary gland,
- This increases dramatically in response to elevated estrogen levels, particularly during pregnancy.
- Prolactin levels are higher in females than in males, and the role of prolactin in male physiology is not completely understood.
- Plasma concentrations of prolactin are highest during sleep and lowest during the waking hours

اول ما تسمع كلمة prolactin بخطر عبالك الحليب كونه lactose موجود فيه و كونه المرأة بعد الحمل بترضع طفلها اكيد رح يكون اله دور كبير بعملية lactation اول اشئ نحكي عن تركيب prolactin،،، هو عبارة عن هرمون زيه زي اي هرمون بجسم الانسان و احنا منعرف انه الهرمونات بتكون بروتينات بالتالي بتتكون من polypeptide ذاكرين بالاناتومي لما اخذنا عن الخلايا الي بتكون ال pituitary حكيما ب anterior part عنا نصهم chromophilic و النص ال chromophobic ، اما عن chromophilic حكيما انه ما نسبته 35% بتكون acidophilic و الي بحوي على نوعين من الخلايا وحدة منهم اسمها lactotroph، و mammothroph و هذولة الخلايا همة المسؤولين عن انتاج ال prolactin

## Actions of prolactin

- Stimulates breast development of breast including growth and development of the mammary gland tissue and ductal proliferation
- These actions are enhanced by estrogen during pregnancy.
- Stimulates milk production in the breast by
  - 1- stimulates glucose and amino acid uptake by mammary gland cells
  - 2- synthesis of the milk proteins  $\beta$ -casein and  $\alpha$ -lactalbumin, the milk sugar lactose, and milk fats by the mammary epithelial cells
  - 3- Inhibits gonadotropin-releasing hormone (GnRH) during pregnancy leading to amenorrhea
  - 4- Inhibits spermatogenesis (by decreasing GnRH) when secreted in large amounts (Pituitary adenoma)
  - 5- modulates reproductive and parental behavior

❧ دور TRH :

في Nuclus موجودو ب hypothalamus اسمها para-ventricular nuclus بتفرز هرمون thyroid releasing hormon و الي بنتقل عن طريق portal circulation ما بين hypothalamus و pituitary حتى توصل anterior part و بتلاقي مستقبلات خاصة على lactotrophs و الي بدورها رح تحفز انتاج prolactin

❧ دور estrogen :

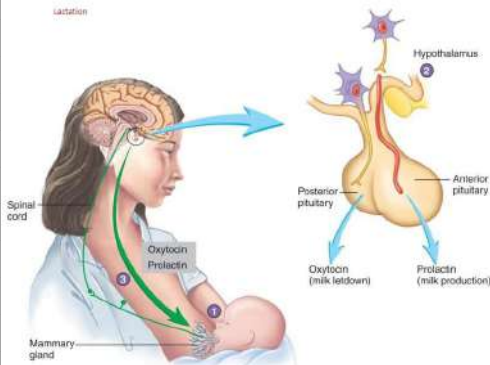
بينتج من ovaries و بزداد انتاجه اثناء و بعد فترة الحمل ، اله دورين في زيادة انتاج prolactin ،،، اول اشي بشكل مباشر عن طريق مستقبلات موجودة على lactotrophs ،،، ثاني اشي بشكل غير مباشر عن طريق تثبيط افراز dopamine من arcuate nuclei (رح نحكي بعد شوي ) و بالتالي تقليل prolactin inhibits factor

❧ دور dopamine:

بتم افراز prolactin inhibiting hormone والمعروف ب dopamine من arcuate الي بكون اساس عمله تثبيط انتاج prolactin من lactotrophs

❧ دور breast feeding :

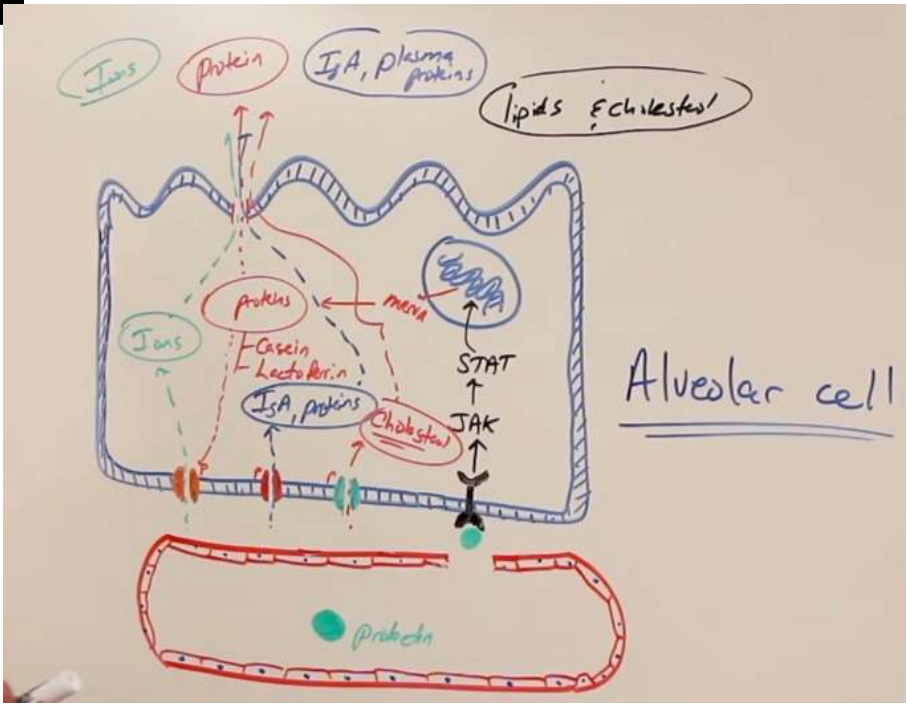
من النعم الي وضعها ربنا عز وجل في جسم المرأة حتى تلبى احتياجات الطفل بداية حياته ، جعل الرضاعة عامل تحفيز لتكوين prolactin عن طريقين ،،، الاول و المباشر على خلايا lactotrophs و بطريقة غير مباشرة بتحفيز انتاج TRH من para-ventricular nuclus بالإضافة الي دوره بتحفيز انتاج oxytocin من pos.pituitary و الي بزيد من انتاج الحليب



**بنصح و بشدة تحضروا نينجا نيرد ، بغطي  
جزء كبير من المحاضرة :  
<https://youtu.be/SN-bYAJQJ7Y>**

هسا حكيينا بالتفصيل كيف بنتج prolactin ،،، طيب لما يوصل ل alveolar cell الموجود في breast بتروح على مستقبلات خاصة عليها (تابعوا مع الصورة) و الي رح تعمل عدة تغييرات داخل الخلية منها :

اول اشي عن طريق تأثيرها على النواة و الجينات رح تحفز عدة بروتينات و مهمة للطفل مثل : milk proteins  $\beta$ -casein and  $\alpha$ -lactalbumin, the milk sugar lactose, and milk fats بعد هيك رح تأثر على عدة مستقبلات في basolateral surface و الي رح تسمح تدخل ions , Vitamin, IgA ,cholesterol, lipid و غيرها من المواد الضرورية للطفل ،،، مش بس هيك ، رح توقف تثبط افراز gonadotropin-releasing hormon و الي رح يعمل amenorrhea (انقطاع الحيض)



في حالات مرضية زي  
(Pituitary adenoma) رح تعمل  
على تقليل انتاج الحيوانات  
المنوية

طبعا كل ما سبق بيأثر بشكل  
كبير على حالة الشخص و على  
reproductive cycle

### Physiologic effects of prolactin and its regulation dopamine

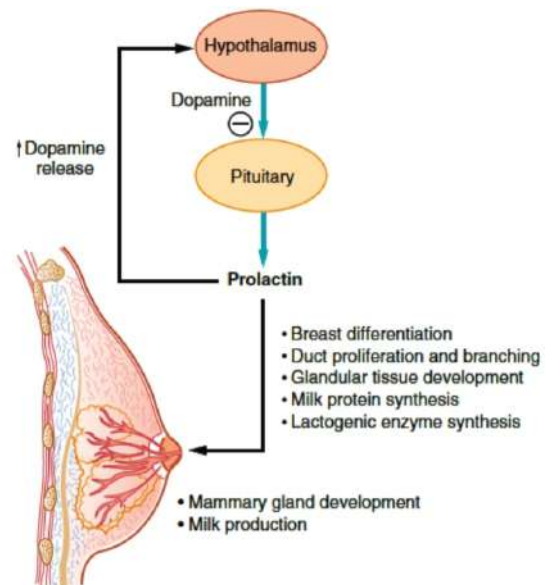
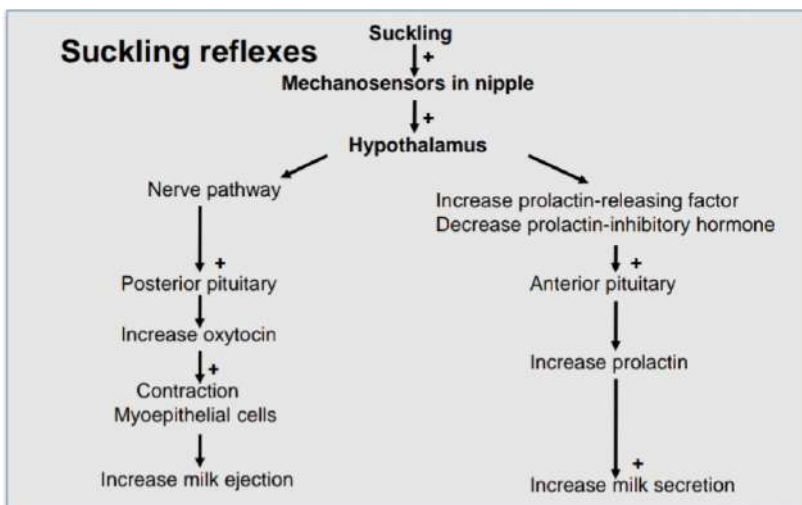
Prolactin release is predominantly under negative feedback control by hypothalamic dopamine.

Suckling stimulates the release of prolactin by releasing the tonic inhibition of dopamine.

Prolactin inhibits its own release by stimulating dopamine(feed back regulation)

The release of prolactin in response to suckling is neuroendocrine reflex

تكلما فوق عن الشغلات الي بتأثر على prolactin سواء بالتحفيز او التثبيط



## Control of prolactin secretion

- Prolactin release is predominantly under tonic inhibition by dopamine derived from dopaminergic (D2) neurons of the hypothalamus.
- D2 inhibition of lactotroph release of prolactin is mediated by D2 Gai protein-coupled receptors.
- Prolactin release is affected by :
  - 1-suckling of breast during lactation increase prolactin secretion
  - 2- increased levels of ovarian steroid hormones, primarily estrogen.
- This surge in prolactin release in response to a suckling stimulus is mediated by a decrease in the amount of dopamine released at the median eminence, relieving the lactotroph from tonic inhibition.
- Estrogen stimulates growth of the lactotrophs during pregnancy as well as prolactin gene expression and release.
- TRH has identified as potential prolactin-releasing factors

### Regulation of Prolactin Secretion

#### Factors that Increase Prolactin Secretion

- Estrogen (pregnancy)
- Breast-feeding
- Sleep
- Stress
- TRH

#### Factors that Decrease Prolactin Secretion

- Dopamine
- Bromocriptine (dopamine agonist)
- Somatostatin
- Prolactin by negative feedback
- Placental progesterone during pregnancy

## Mechanism of prolactin on breast and mammary glands

- The effects of prolactin on the breast and mammary gland are mediated by a cytokine cell membrane receptor
- Hormone receptor binding that stimulates the Janus kinase (JAK) and signal transducer and activator of transcription (STAT) pathway
- Commonly known as the JAK/STAT signaling pathway

بعد ما انتج prolactin ينتقل للدم حتى يوصل لل breast بيرتبط مع receptor اسمه cytokine cell membrane receptor والي بنقل الاشارة الى Janus kinase (JAK) والي بنقل اشارة الى transducer and activator of transcription (STAT) pathway و الي بحفز تكوين البروتينات

اكتشفوا العلماء اثناء الحمل و نتيجة افراز progesterone من placenta رح تنافس Prolactin و تقلل من تأثيرها و بالتالي ما بيتكون الحليب

مش حكينا فوق انه لما ينتج prolactin بعمل تثبيط لل GnRH هذا و على المدى البعيد رح يوقف انتاج البيوضات لانه اوقف انتاج كل من FSH , LH من Ant. pituitary بالإضافة لوجود تثبيط GnRH فمممكن اعتبار brest feeding احد موانع الحمل ، غالبا

- Progesterone produced by the placenta during pregnancy interferes with prolactin binding to the receptors on the alveolar cells within the breast, thereby directly suppressing milk production during pregnancy
- High levels of prolactin during lactation and as lactation continues, suppresses ovulation because prolactin inhibits GnRH secretion by the hypothalamus and FSH and LH secretion by the anterior pituitary.
- Although not 100% effective, breastfeeding is a method of contraception and family spacing in some regions of the world.

### Disorders of prolactin secretion

الامراض هاي رح ناخذ عنها بالتفصيل بالباثو ان شاء الله

#### ⊙ Hyposecretion ( Prolactin deficiency )

- Infarction of pituitary ( Sheehan's syndrome)
- Drugs Dopamine agonist

غالبا يكون بالمرأة بعد انتهاء الحمل

#### ⊙ Hypersecretion : Caused by

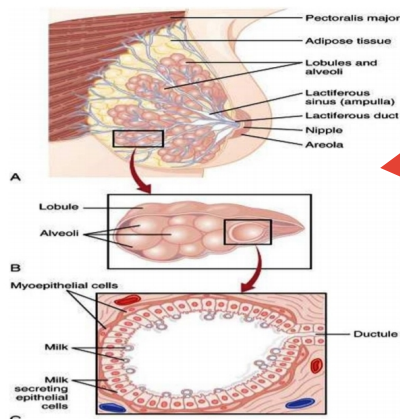
- 1- Hypothalamic damage (due to loss of the tonic "inhibitory" control by dopamine)
- 2- a hormone-producing pituitary adenoma
- 3- Prolactinomas are the most common tumors of pituitary gland... Usually benign neoplasm.

#### ☆ Patients with a prolactinoma present with :

- A- elevated levels of prolactin (hyperprolactinemia)
- B- excessive secretion of milk (galactorrhea)
- C- reproductive dysfunction including loss of libido , amenorrhea
- D- In males, prolactinomas may cause infertility by producing hypogonadism due to inhibition of GnRH. can be treated with bromocriptine, which reduces prolactin secretion by acting as a dopamine agonist.

بآخر سلايد الدكتور ما قراها او شرحها ، بس حتى هي عبارة عن case بتعطينا فكرة كيف ممكن تيجي اسئلة USMLE و بس مطلوب منا نقرأها

The mammary gland.



الدكتور ذكر أهم الاسماء و ضاف انه contraction of of myoepithelial cell by oxytocin

## CLINICAL CORRELATION CASE A

- A mother of two school-age children still in her reproductive years consults her physician because she has had no menstrual periods for the past 6 months. A pregnancy test is negative, and she is not taking any medications. She also complains of problems with her peripheral (temporal) vision and has also noted milky discharge from her nipples. A magnetic resonance image (MRI) scan of the brain reveals a pituitary mass.
- On physical examination, she is afebrile and has a normal blood pressure. Laboratory values are within normal ranges for serum glucose, Na<sup>+</sup> and K<sup>+</sup>. Increased levels of prolactin are measured, with normal levels of all other pituitary hormones. She is diagnosed as having a prolactinoma.
- Prolactinomas account for 50% of functioning pituitary tumors and are more frequent in females than in males.
- Tumor size is correlated with prolactin levels.
- Women present with amenorrhea (lack of menses), galactorrhea (milk discharge from nipples), and infertility.
- Large tumors extending caudal to the pituitary are associated with visual defects due to compression of the optic chiasm.
- In males, presentation is impotence, loss of libido, and infertility as well as headaches
- Administration of dopamine agonists to reduce prolactin production
- Tumors that do not shrink in size with medical treatment may require focused radiation therapy and/or surgical removal.

## Extra Questions

For milk to flow from the nipple of the mother into the mouth of the nursing infant, what must occur?

- A) Myoepithelial cells must relax
- B) Prolactin levels must fall
- C) Oxytocin secretion from the posterior pituitary must take place
- D) The baby's mouth must develop a strong negative pressure over the nipple
- E) All the above

Answer: C

Which anterior pituitary hormone plays a major role in the regulation of a nonendocrine target gland?

- A) ACTH
- B) TSH
- C) Prolactin
- D) FSH
- E) LH

Answer : C

