Physio.UGS

Physio10 Homeostasis

•Case Introduction: A 26-year-old woman increases her potassium intake from 80 to 160 mmol/day by eating more fruits and vegetables. After 2 weeks, her body adapts by increasing K^+ excretion, with only a small rise in plasma K^+. Sodium levels remain **un**affected.

•Daily K^+ Balance: Normal intake ≈ 100 mEq/day. Input must equal output قاعدة; the kidney is the main regulator of K^+ output.

	Potassium Excretion Rate	Sodium Excretion Rate	Plasma Aldosterone Concentration	Plasma Potassium Concentration
A)	↔	↔	↑	Large increase (>1 mmol/l)
B)	↔	↓	↑	Small increase (<1 mmol/l)
C)	↑ 2×	↔	↑	Small increase (<1 mmol/l)
D)	↑ 2×	↑	↓	Large increase (>1 mmol/l)
E)	↑ 2×	↑	↔	Large increase (>1 mmol/l)

K^+ Distribution in Body Compartments

•Intracellular: Major cation; ~3920 mEq in 28 L (140 mEq/L).

•Extracellular: ~59 mEq in 14 L (4.2 mEq/L).

•Clinical Importance: Small dietary changes can dramatically affect extracellular K^+, which must be kept within a narrow range to avoid serious consequences (e.g., arrhythmias).

Mechanisms Preventing K^+ Imbalance

•First Line of Defense: Rapid K^+ shift between intracellular and extracellular compartments.

•Second Line: Renal excretion adjusts more slowly, regulated by hormones.

Effects of K^+ Imbalance

- **Hyperkalemia >5.0**: Partial cell membrane depolarization, cardiac toxicity (ventricular fibrillation, asystole).عدم انتظام ضربات القلب
- **Hypokalemia <3.5**: Hyperpolarization, muscle weakness, fatigue, hypoventilation, delayed ventricular repolarization.

Regulation of K^+ Shifts Between Compartments لادخاله للخلايا

1. **Insulin**

Stimulates K^+ uptake into cells via Na^+/K^+-ATPase (especially after meals).

✓ بعد تناول الطعام (خاصة الغني بالبوتاسيوم)، يزداد إفراز الأنسولين،الأنسولين يحفز مضخة Na^+/K^+-ATPase التي تدخل K^+ إلى داخل الخلية مقابل إخراج Na^+، لمنع ارتفاع تركيز البوتاسيوم في الدم بعد الأكل

2. **Aldosterone**

•Stimulated by **hyperkalemia**. ↑

•Increases K^+ secretion and Na^+ reabsorption in kidneys (principal and intercalated cells).

3. **β-Adrenergic Receptors**

•Catecholamines stimulate K^+ uptake into cells.

✓ الكاتيكولامينات (مثل الأدرينالين) تحفّز مستقبلات β_2. هذا يُنشط Na^+/K^+-ATPase، فيُدخل K^+ إلى داخل الخلايا. يُستخدم أحيانًا كعلاج في حالات فرط بوتاسيوم الدم الحاد (مثل β_2-agonists).

Factors Leading to K^+ Release from Cells لإخراجه من الخلايا

- Cell Lysis: Damage or hypotonic solutions cause K^+ to leak out.

مثل اصابات شديدة،الانحلال الدموي،الحروق،تؤدي إلى تسرّب البوتاسيوم إلى الخارج

- Hypertonic ECF: Water leaves cells, increasing intracellular K^+, which diffuses out.

إذا كان السائل خارج الخلية يحتوي على كمية كبيرة من الأملاح (hypertonic): تخرج الماء من الخلايا،يزداد تركيز K^+ داخل الخلية فيبدأ K^+ بالخروج إلى الخارج بسبب فرق التركيز

- Strenuous Exercise: Can cause K^+ release; risk is higher if combined with dehydration or β-blockers.

العضلات تُطلق K^+ أثناء الانقباضات،هذا مؤقت، لكن إذا رافقه جفاف أو استخدام β-blockers يزيد خطرًا على القلب

- Decreased Na^+/K^+-ATPase Activity: Seen in **acidosis**, leading to extracellular K^+ accumulation.

Potassium Regulation: Internal and External

- Internal: Shifts between compartments (regulated by insulin, aldosterone, β-adrenergic activity, acid-base status). سريع
- External: Renal excretion بطيء (filtration, reabsorption(mostly proximal tubule), secretion).

Renal Handling of K^+

1. **Filtration**

Depends on plasma K^+ and GFR; not a major regulatory point.

2. **Reabsorption**

- Proximal Tubule: **~67%** (not regulated نسبة ثابتة~).
- Thick Ascending Loop: ~25-27% (not regulated).
- Intercalated Cells (Type **A**): K^+/H^+ ATPase (active in **hypo**kalemia ↓, insignificant in hyperkalemia).

3. **Secretion**

Late Distal Tubule & Collecting Ducts (Principal Cells): Main regulatory site, controlled by aldosterone.

تعتمد على:١ تركيز البوتاسيوم في الدم (كلما زاد، زاد الإفراز)،٢وجود الألدوستيرون: يُحفز مضخات Na^+/K^+ ATPase.،يزيد من نفاذية الغشاء لقنوات K^+،يؤدي إلى زيادة طرح البوتاسيوم في البول.

Control of K^+ Secretion in Cortical Collecting Tubule

- Extracellular K^+: Increases secretion.
- Aldosterone: Increases secretion.
- Sodium (volume) delivery: Increases secretion. ↑
- Acid-Base Status: Acidosis decreases, alkalosis increases K^+ secretion.

Mechanisms of K^+ Secretion (Principal Cells)

- Basolateral Na^+/K^+-ATPase: Maintains gradient. يدفعه للخروج مع البول
- Luminal Channels(apical slide): ENaC (Na^+ reabsorption), ROMK & BK (K^+ secretion).

✓ Renal Outer Medullary Potassium Channel (ROMK)
✓ Big Potassium Channel (BK)

Regulation Details

1. Effect of Extracellular K^+
   - **Directly** ↑ *increases* secretion by enhancing gradient & reducing backleak.
   - **Indirectly** ↑ *increases* secretion by stimulating aldosterone.
2. Aldosterone Feedback
   - High K^+ → Aldosterone release → Increased K^+ secretion → K^+ normalized → Aldosterone drops.
   - Disruption (e.g., Addison's disease) causes hyperkalemia.
3. Tubular Flow Rate

High flow rate (e.g., with diuretics) increases K^+ secretion by washing out K^+ in the lumen, maintaining the gradient.

4. Sodium Intake

High Na^+ intake ١increases flow (increasing K^+ secretion),but٢ suppresses aldosterone (decreasing K^+ secretion); net effect is usually balanced.

Clinical Perspectives

- ***Diuretics*:** Increase tubular flow, enhance K^+ secretion ↑, risk of hypokalemia.
- *Acid-Base Disorders:* Acidosis inhibits Na^+/K^+-ATPase, reduces K^+ secretion ↓ (risk of **hyper**kalemia). Alkalosis has the opposite effect.

Factor	Effect on K^+ Secretion/Excretion
↑ Extracellular K^+	↑ Secretion (direct & via aldosterone)
↑ Aldosterone	↑ Secretion
↑ Tubular Flow	↑ Secretion
↑ Na^+ Intake	Balanced (↑ flow vs ↓ aldosterone)
Acidosis	↓ Secretion
Alkalosis	↑ Secretion
Diuretics	↑ Secretion (risk of hypokalemia)

✓ K^+ homeostasis is tightly regulated by rapid cellular shifts and slower renal mechanisms.
✓ Aldosterone is the key hormone for renal K^+ excretion.
✓ Acid-base status, sodium intake, and flow rate all influence K^+ handling.
✓ Disturbances can cause serious clinical consequences, especially cardiac arrhythmias.

Part 2

Effects of Sodium Intake on Potassium Excretion

High Sodium Intake ↑

- Increases GFR: More sodium filtered, higher distal tubular flow.
- Reduces Proximal Na^+ Reabsorption: More fluid reaches distal tubule.
- Increases Potassium Secretion: Due to higher distal flow.
- Inhibits Aldosterone: Normally would decrease K^+ secretion.

Net Effect: The opposing effects (increased flow vs. decreased aldosterone) balance out, so overall potassium excretion remains unchanged.❗

***Low* Sodium Intake** ↓

- Increases Aldosterone: Stimulates K^+ secretion.
- Decreases GFR **&** Increases Proximal Reabsorption: Less distal flow, so K^+ secretion decreases.

Net Effect: Again… opposing effects balance, so potassium excretion remains unchanged❗

Effects of Acid-Base Status on Potassium Secretion

Acidosis

- Acute Acidosis: Decreases K^+ secretion ↓ (inhibits Na^+/K^+-ATPase, reduces K^+ permeability).
- Chronic Acidosis: Increases K^+ secretion ↑❗ (inhibits proximal Na^+ reabsorption, increases distal flow).

Alkalosis

- Increases Na^+/K^+-ATPase Activity: More K^+ enters cells, higher intracellular K^+.
- Increases K^+ Secretion and Excretion: Can lead to hypokalemia.

Causes of Potassium Imbalance❗

Hyperkalemia

- Renal Failure
- Decreased Distal Flow (heart failure, NSAIDs 💊, severe volume depletion)
- Decreased Aldosterone (adrenal insufficiency, K^+-sparing diuretics 💊)
- Metabolic Acidosis (mild effect)
- Diabetes (due to kidney disease, acidosis, insulin issues)

Hypokalemia

- Very Low K^+ Intake
- GI Loss (diarrhea)
- Metabolic Alkalosis
- Excess Insulin
- Increased Distal Flow (salt-wasting nephropathies, osmotic/loop diuretics)
- Excess Aldosterone

Clinical Question: Most serious hypokalemia is *caused by* excessive aldosterone secretion plus low sodium intake.

Calcium Regulation

Plasma Calcium

- Normal Level: ~2.4 mEq/L.
- **50% Ionized** (active),40% **protein-bound** غير نشط: mostly to albumin,10% complexed with anions:phosphate or citrate.

Parathyroid Hormone (PTH) يزيد إفرازه عند انخفاض الكالسيوم بالدم

•Kidneys: Increases distal Ca^{2+} reabsorption, decreases urinary loss.
•Bones: Stimulates bone resorption, releasing Ca^{2+}.
•GI Tract: Indirectly increases Ca^{2+} absorption via **vitamin D activation.**

Calcium Reabsorption in Nephron

•Proximal Tubule: Mostly paracellular (with water); some transcellular (via Ca^{2+} ATPase, Na^{+}/Ca^{2+} exchanger).
•Thick Ascending Limb: Predominantly paracellular.
•Distal Tubule: Also reabsorbs Ca^{2+}, regulated by PTH.

Integration of Renal Regulation of Body Fluids & Electrolytes:

•Excretion = Filtration - Reabsorption + Secretion
•Steady State: Fluid/electrolyte excretion matches intake.
•Osmolarity: Electrolyte osmolarity affects fluid volumes.

Effect of Decreased GFR on Sodium & Creatinine Handling

Sodium

•Reduced GFR اخفاض الكمية المُرشّحة: Decreases sodium excretion initially.
•Compensatory Decrease in Reabsorption: Sodium excretion returns to normal as reabsorption adjusts.

Mechanisms:

- Tubuloglomerular Feedback: Macula densa senses low NaCl, triggers GFR increase.
- Glomerulotubular Balance: Reabsorption decreases in proportion to filtration, stabilizing excretion. يعني نسبة إعادة الامتصاص تتناسب مع كمية الترشيح. فإذا قل الترشيح، تقل إعادة الامتصاص بنفس النسبة، مما يحافظ على توازن الصوديوم

Creatinine

•Reduced GFR: Plasma creatinine rises يؤدي لتراكمه بالدم.
•Excretion Returns to Normal: Higher plasma creatinine increases filtered load, balancing excretion with production.

ارتفاع مستوى الكرياتينين في البلازما يزيد من الكمية المُرشّحة (filtered load) وهذا يُعيد طرح الكرياتينين ليتوازن تقريبًا مع معدل إنتاجه. أي أن طرح الكرياتينين يعود لمستواه الطبيعي رغم انخفاض GFR.

Effect of Decreased Tubular Reabsorption on Sodium Balance

•Initial Effect: Increased sodium excretion. عند نقصان إعادة الامتصاص (مثلاً بسبب ضرر أنبوبي)، فإن كمية الصوديوم المطروحة في البول تزداد.

•Compensatory Mechanism: Tubuloglomerular feedback reduces GFR, matching lower reabsorption.-> ↓ GFR-> مما يقلل كمية الصوديوم المُرشّحة من الأساس
Result: Sodium excretion stabilizes at near-normal levels. رغم الخلل الموجود

- ✓ Tubuloglomerular Feedback: Adjusts GFR in response to distal NaCl delivery.
- ✓ Glomerulotubular Balance: Matches reabsorption to filtration rate.
- ✓ Aldosterone and Flow Rate: Balance K^{+} excretion.
- ✓ PTH and Vitamin D: Regulate Ca^{2+} homeostasis

Physio11Acid-Base Balance

- Homeostasis: Balance between H^+ intake/production and removal is essential for physiological stability.
- Multiple Systems: Acid-base regulation involves not just the kidneys, but also chemical buffers and the lungs.

Mechanisms of Hydrogen Ion Regulation

Three Main Defenses:

- **Chemical Buffers:** Immediate, temporary action (bicarbonate, proteins, ammonia, phosphate).
- **Respiratory System:** Rapid (minutes), regulates CO_2 elimination.
- **Kidneys**: الأهمSlow (hours to days), most powerful, eliminates non-volatile acids الفوسفات, reabsorbs and generates HCO_3^-.

✓ **[H+]** is precisely regulated at **3–5 x 10^-8** moles/L (pH range **7.2 -7.4**)

Buffer Systems in the Body

- **Bicarbonate**: الأهمMain extracellular buffer, regulated by lungs (CO_2) and kidneys (HCO_3^-).
- **Phosphate**: Mainly intracellular and tubular buffer.
- **Ammonia**: Important in the renal tubules, especially during chronic acidosis. التخلص منH+
- **Proteins**(limited): Major intracellular buffers (**hemoglobin** in RBCs is especially significant). (60-70% of buffering is in the cells)

➢ **Buffer Effectiveness:** Depends on concentration and pKa proximity to physiological pH. A buffer is most effective when its pKa is close to the target pH of the fluid. The higher the concentration of its components, the better its buffering capacity. For example, plasma has a pH of about 7.4, so the ideal buffer would have a pka near that.
Although the **HCO3-** has a pka of 6.1 (not close to 7.4), it is still the most important ECF buffer because its components (CO2 and HCO3)) are tightly regulated by the lungs and kidneys, making it highly effective.

The **phosphate** buffer system has a pK of 6.8, which is not far from the normal pH of 7.4 in the body fluids, allows the system to operate near its maximum buffering power. However, its concentration in the extracellular fuid is low, at only about 8% of the concentration of the bicarbonate buffer. Therefore, the total buffering power of the phosphate system in the extracellular fluid is much less than that of the bicarbonate buffering system.—> توضيح

قرب قيمةpKaمنph

الـ pKa هي الرقم الذي يشير إلى الحموضة التي يعمل فيها النظام بشكل فعّال. كلما كانت pKa قريبة من pH السائل (مثل الدم pH = 7.4)، كان النظام أكثر فعالية في مقاومة التغيرات في الحموضة ,مثال: نظام الفوسفات (phosphate buffer) له pKa ≈ 6.8، وهو قريب من 7.4 ← لذلك يمكنه أن يعمل بكفاءة من حيث القيمة.

تركيز مكونات النظام :كلما كان تركيز الحمض والقاعدة المرافقة أعلى، كان النظام أكثر قدرة على منع تغيرات pH.مثال: نظام البيكربونات (HCO_3^- / CO_2): له pKa = 6.1 (ليست مثالية بالنسبة لـ 7.4)، لكن فعاليته عالية جدًا لأنه يوجد بتركيز عالٍ، والأهم: الرئتان والكليتان تتحكمان بشكل دقيق في CO_2 و HCO_3^-، مما يجعله نظامًا قويًا.

- ✓ الفوسفات له pKa أفضل (6.8 أقرب إلى 7.4 من 6.1)،لكن تركيزه في السائل خارج الخلوي منخفض (8% فقط من تركيز البيكربونات)،لذا قدرته الكلية على التوازن أقل من البيكربونات، رغم أن pKa أنسب. أفضل buffer هو الذي يجمع بين pKa قريبة من pH وتركيز عالٍ.

Importance of Buffer Systems

- **Hydrogen Ion Concentration:** Normal plasma **H^+** is extremely low(4 x 10^-8 mol/L) compared to daily acid production, highlighting the necessity of effective buffering and elimination.
- **Enzyme Activity:** **Small pH** changes can significantly affect cellular and enzymatic functions.

Bicarbonate Buffer System and Henderson-Hasselbalch Equation

$$pH = pK_a + \log([HCO_3^-] / (0.03 \times pCO_2))$$

- هذه المعادلة تربط بين تركيز البيكربونات (HCO_3^-) وضغط ثاني أكسيد الكربون (pCO_2) في تنظيم pH الدم.
- 0.03 هو معامل الذوبان لغاز CO_2 في البلازما (solubility coefficient)

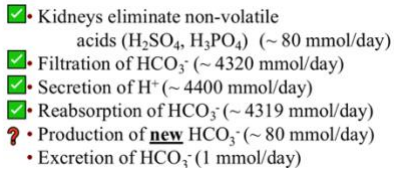
- Key Equation: where is the solubility coefficient of CO_2.
- Clinical Relevance: Changes in pCO_2 or HCO_3^- directly affect blood pH.
- Despite a pKa of 6.1 (not close to 7.4), the bicarbonate buffer is most effective due to active regulation by lungs and kidneys.

Respiratory Regulation of Acid-Base Balance دور الرئة

- Mechanism: Changes in ventilation adjust CO_2 (and thus H^+) levels.
- Increased ventilation [↑] → decreased [↓] CO_2 → decreased [↓] H^+ (**corrects acidosis**).
- Decreased ventilation → increased CO_2 → increased H^+ (**corrects alkalosis**).
- Correction Limit: Can correct **50–75%** of acid-base disturbances but cannot remove non-volatile acidsالفوسفوريك،الكبريتيك.

Renal Regulation of Acid-Base Balance دور الكلى

Role of Kidneys:



- Eliminate **non**-volatile acids (~80 mmol/day).
- Filter, reabsorb, and generate HCO_3^-.
- Secrete H^+ (~4400 mmol/day).
- Excrete HCO_3^- (1 mmol/day under normal conditions).
- Reabsorption: Most filtered HCO_3^- is reabsorbed; only a small fraction is excreted.
- Acidosis: Kidneys increase H^+ secretion, reabsorb/generate more HCO_3^-.
- Alkalosis: Kidneys decrease H^+ secretionامتصاص, excrete more HCO_3^-.

Segmental Handling of HCO_3^- and H^+ in the Nephron

- **Proximal Tubule:** Reabsorbs ~85% of filtered HCO_3^-.
- **Thick Ascending Limb:** Reabsorbs ~10%.
- **Distal Convoluted Tubule:** Handles the remainder. المتبقي

✓ **Rule** For ***each HCO_3^- reabsorbed, one H^+ is secreted.***

Mechanisms of HCO_3^- Reabsorption and H^+ Secretion

•Na^+/H^+ Counter-Transport: Driven by Na^+/K^+ ATPase, primarily in the proximal tubule and thick ascending limb.

Source of H^+: CO_2 diffuses into tubular cells, converted to H^+ and HCO_3^- by carbonic anhydrase. This mechanism, however, can establish a minimum pH of only about 6.7; as the Na+/H+ exchanger operates against a limited electrochemical gradient.

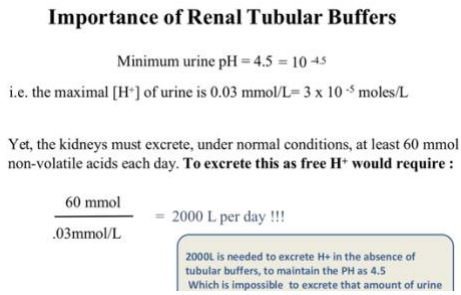
- HCO3 reabsorption and H' secretion in intercalatea cells of late distal and collecting tubules:

Type **A** intercalated cells contain hydrogen-ATPase and hydrogen- potassium-exchanger in the luminal membrane, to secret H+, H+/K+ exchanger is active when there is hypokalemia , while hydrogen-ATPase is always active

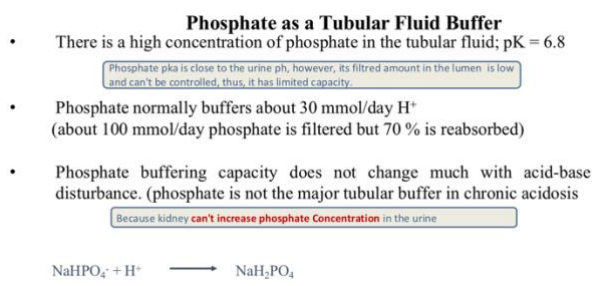
-The tubular fluid becomes highly acidic only in the collecting tubules and collecting ducts, where the urine pH can drop to as low as 4.5. This is possible because H+- ATPase can pump against an electrochemical gradient as great as 1000-fold.

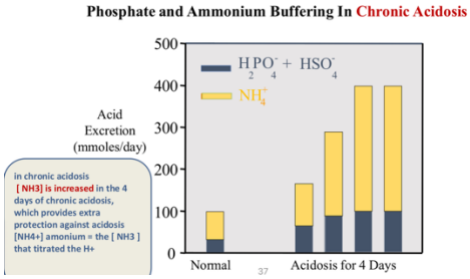
-The other difference is that HCO3- is reabsorbed by HCO3-/ Cl- exchanger

-same concept here each 1xH+ secreted is coupled with 1x HCO3- reabsorption the titration continues till all the filtered HCO3 is reabsorbed.



Buffering of secreted H+by filtered phosphate (NaHPO4) and generation of "new"HCO3-
However, once all the HCO3- has been reabsorbed and is no longer available to combine with H+, any excess H+ can combine with HPO4 = and other tubular buffers.
-After the H+ combines with HPO4= to form H2PO4-, it can be excreted as a sodium salt (NaH2PO4), carrying with it the excess H+.
-Note that a <u>new HCO3</u>- is returned to the blood for each NaHPO4 that reacts with a secreted Ht.





- ✓ Kidneys: Most powerful and final regulator, especially for non-volatile acids.
- ✓ Clinical Relevance: Understanding these mechanisms is crucial for diagnosing and managing acid-base disorders.
- ✓ HCO3- and CO2, are regulated respectively, by the kidneys and lungs

Physio12 Acid-Base Physiology

•In the kidneys, <u>filtered bicarbonate</u> (HCO_3^-) and <u>secreted hydrogen ions</u> (H^+) interact in the renal tubules-> <u>H^+ combines with filtered HCO_3^-</u>, <u>allowing HCO_3^- to be reabsorbed</u>.

•Only a <u>small amount of H^+</u> can be <u>excreted directly</u> *due to* urine pH limitations (cannot go below 4.5)-> <u>Excess H^+ binds to urinary buffers</u> such as <u>phosphate</u> ($NaHPO_4^-$) or <u>ammonia</u> (NH_3), resulting in the <u>generation of new HCO_3^-</u>, which is added to the blood.

- ✓ البيكربونات (HCO_3^-) تُرشّح من الدم إلى الأنابيب الكلوية، خلايا الكلية تفرز أيونات الهيدروجين (H^+) إلى داخل الأنابيب
- ✓ H^+يتفاعل مع HCO_3^-في الأنابيب، ويكوّنان ماء H_2Oوثاني أكسيد الكربون CO_2 <-ينتشر إلى داخل خلايا الأنابيب ويتحوّل مرة أخرى إلى HCO_3^-وH^+ <- HCO_3^-الناتجة تدخل إلى الدم، فيتم إعادة امتصاص البيكربونات بدلًا من فقدانها.

Production and Secretion of NH_4^+ and HCO_3^-

•In the proximal tubule, glutamine (from amino acid metabolism) is metabolized to produce ammonium (NH_4^+) and bicarbonate (HCO_3^-).

•NH_4^+ is secreted into the tubular lumen in exchange for sodium, and new HCO_3^- is transported into the interstitial fluid.

•Ammonia (NH_3) can also act as a buffer in the tubular lumen by binding H^+.

✓ This helps eliminate H^+ without excessively lowering urine pH, allowing continued acid excretion even under acidic conditions.

Buffering of H^+ Secretion by Ammonia in the Collecting Tubules

•In the collecting tubules, NH_3 buffers H^+ in the lumen, forming NH_4^+, which is excreted.

•This process allows H^+ to be buffered and new HCO_3^- to be added to the blood without loss of HCO_3^-.

Quantification of Renal Acid-Base Regulation

•Total **H^+** secretion is about **4320** mmol/day, matching the amount needed to reabsorb filtered HCO_3^-.

•Non-volatile acidsك الفوسفوريك (about **60** mEq/day) are excreted by titrating secreted H^+ with buffers like $NaHPO_4^-$ and NH_4^+.

•Titratable acid is measured by titrating urine with NaOH to pH 7.4, representing H^+ combined with phosphate and organic buffers.

•NH_4^+ excretion is calculated as urine flow rate × NH_4^+ in urine.

Titratable Acid❓ما المقصود ب

هو كمية أيونات الهيدروجين (H^+) التي تم إفرازها في البول وتم ربطها ب (buffers) مثل الفوسفات ($NaHPO_4^-$) أو مواد عضوية أخرى، هذه الأيونات لا تُطرح على شكل H^+ حر مباشر، بل تكون مرتبطة بعوازل داخل البول، مما يجعل البول غير شديد الحموضة.

4. حساب كمية NH_4^+ المطروحة في البول يتم باستخدام المعادلة:

NH_4^+ excretion = Urine flow rate × [NH_4^+ concentration in urine]

Net H^+ Excretion and Addition of New HCO_3^-

•Net H^+ excretion equals the amount of new HCO_3^- produced.

✓ Net H^+ excretion = titratable acid ($NaHPO_4^-$ + NH_4^+) – HCO_3^- excretion قيمة قليلة جدا.

Normally: 59 mmol/day net H^+ excretion (30 mmol/day titratable acid + 30 mmol/day NH_4^+ excretion – 1 mmol/day HCO_3^- excretion).

✓ يعني الكلى أخرجت ما يعادل 59 mmol من H^+ يوميًا، وأدخلت نفس الكمية من البيكربونات الجديدة إلى الدم❗

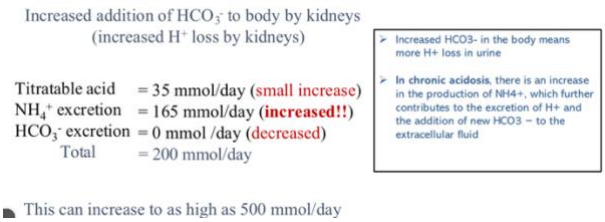
✓ الكلى لا تُخرج H^+ فقط، بل تنتج بيكربونات جديدة ($new\ HCO_3^-$) في نفس الوقت، الكمية الصافية من H^+ التي يتم إخراجها = كمية البيكربونات الجديدة التي تدخل إلى الدم.

Renal Compensation for Acid-Base Disturbances

•*Acidosis*: Kidneys increase H^+ excretion, HCO_3^- reabsorption, and production of new HCO_3^-.

•*Alkalosis*:العكس Kidneys decrease H^+ excretion, reduce HCO_3^- reabsorption, and increase HCO_3^- loss in urine.

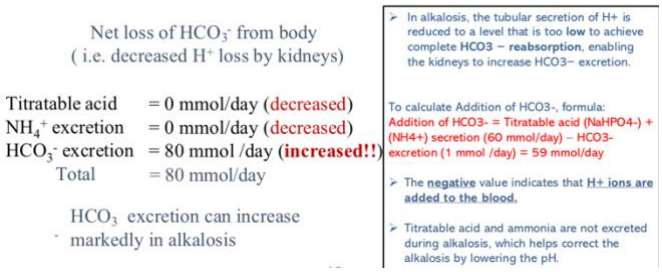
Renal Compensation During Acidosis



- In acidosis, especially chronic, NH_4^+ production and excretion increase substantially, leading to increased addition of new HCO_3^- to the extracellular fluid.

الكلية تقوم بزيادة إنتاج وإفراز NH_4^+ (الأمونيوم) بشكل كبير،هذا يسمح بإخراج H^+ الزائد عن طريق تحويله إلى NH_4^+ (الذي يُطرح في البول)،في الوقت نفسه، يتم إنتاج HCO_3^- جديد يدخل إلى الدم، مما يساعد على تصحيح الحموضة.

Renal Compensation During Alkalosis



- In alkalosis, HCO_3^- excretion increases because tubular H^+ secretion is reduced, resulting in incomplete HCO_3^- reabsorption and increased urinary loss of HCO_3^-.

Acid-Base Equations and Classification

- ❖ The Henderson-Hasselbalch equation is used to relate **pH**, HCO_3^-, and pCO_2.
- ❖ Acid-base disorders are classified as:

•Acidosis: **pH < 7.4** (can be metabolic الفشل الكلوي or respiratory)

•Alkalosis: **pH > 7.4** (can be metabolic مدرات البول or respiratory)

- Compensation involves the body adjusting the other component of the acid-base pair in the same direction as the disturbance.

✓ مثال: إذا كان الاضطراب(metabolic)، فإن الجسم يعدل التنفس (pCO_2) للتعويض. وإذا كان(respiratory)، فإن الكلى تعدّل HCO_3^- للتعويض❗

Renal Responses to Specific Disorders

•**Respiratory** Acidosis: Increased pCO_2 causes increased H^+ secretion and HCO_3^- reabsorption; kidneys add new HCO_3^- to offset pH drop.

السبب: ارتفاع pCO_2 في الدم (مثلاً بسبب نقص التنفس)بالتالي زيادة H^+ في الدم ← انخفاض pH

•**Metabolic** Acidosis: Decreased HCO_3^- leads to increased H^+ in tubular fluid; compensation includes increased ventilation (lowering pCO_2) and increased renal excretion of H^+ via NH_4^+ and $NaHPO_4^-$.

•**Respiratory** Alkalosis: Decreased pCO_2 leads to decreased H^+ secretion; excess filtered HCO_3^- is excreted, reducing plasma HCO_3^- and helping restore pH.

•**Metabolic** Alkalosis: Increased HCO_3^- in blood leads to increased filtration and excretion of HCO_3^-, with reduced H^+ secretion.

Clinical Calculation Examples

Example provided with patient urine data:

•Net acid excretion = titratable acid **+** NH_4^+ excretion **–** HCO_3^- excretion.

•In the example: (10 mmol + 15 mmol – 2 mmol) = 23 mmol/day.

✓ كمية H^+ الصافية التي تخلصت منها الكلية تساوي تقريبًا كمية البيكربونات الجديدة التي أضيفت إلى الجسم (تعويض مباشر للحموضة)

•Net acid excretion equals net rate of bicarbonate addition to the body.

Fundamental Equations and Concepts

- *Chemical Reactions:*
  CO_2 + H_2O ↔ H_2CO_3 ↔ **H^+ + HCO_3^-** أساس لتنظيم الحموضة بالجسم ph
- ***Henderson-Hasselbalch Equation:***

✓ **pH** = pK + log (HCO_3^-/ (0.03 × pCO_2))

Key Parameters:

pH, pCO_2 (partial pressure of CO_2), and HCO_3^- (bicarbonate)

Compensation Mechanisms

Metabolic Acidosis:

•↓ HCO_3^- (primary)

•Compensation: ↓ pCO_2 (via hyperventilation), ↑ renal HCO_3^- production

Respiratory Acidosis:

•↑ pCO_2 (primary)

•Compensation: ↑ renal HCO_3^- production

Metabolic Alkalosis:

•↑ HCO_3^- (primary)

•Compensation: ↑ pCO_2 (via hypoventilation), ↑ renal HCO_3^- excretion

Respiratory Alkalosis:

•↓ pCO_2 (primary)

•Compensation: ↑ renal HCO_3^- excretion

Clinical Approach to Acid-Base Disorders

Stepwise Diagnosis:

1.Assess pH (acidosis or alkalosis)

2.Assess pCO_2 and HCO_3^- (metabolic or respiratory origin)

3.Determine if compensation is present

Mixed Disorders 🔀**:**

•**Both** metabolic and respiratory components can be present (e.g., mixed acidosis or alkalosis)

Example Cases

Test	Normal	Decrease Value	Increase Value
pH	7.35-7.45	Acidosis	Alkalosis
PaCO2	35-45	Alkalosis	Acidosis
HCO3	22-26	Acidosis	Alkalosis
PaO2	80-100	Hypoxemia	O2 therapy
SaO2	95-100%	Hypoxemia	----------

✓ *Mixed Acidosis Example:*

- pH = 7.12, pCO_2 = 50, HCO_3^- = 18
- Diagnosis: Mixed acidosis (metabolic + respiratory)

  - لدينا عاملين يساهمان في انخفاض pH: ارتفاع pCO_2 (حماض تنفسي)، انخفاض HCO_3^- (حماض استقلابي)

✓ *Mixed Alkalosis Example:*

- pH = 7.60, pCO_2 = 30, HCO_3^- = 29
- Diagnosis: Mixed alkalosis (metabolic + respiratory)

  - كلا العاملين يؤديان إلى ارتفاع pH: انخفاض pCO_2 (قلاء تنفسي) ،ارتفاع HCO_3^- (قلاء استقلابي)

✓ *Case with Partial Compensation:*

- pH = 7.15, HCO_3^- = 8, pCO_2 = 24
- Diagnosis: Metabolic acidosis with partial respiratory compensation❗

  - توضيح: السبب الأساسي هو الحماض الاستقلابي بسبب انخفاض HCO_3^-، الجسم حاول التعويض عن طريق (hyperventilation)بالتالي ↓ pCO_2، لكن pH لا يزال منخفضًا ➜ التعويض غير كامل (partial compensation)

Causes of Acid-Base Disorders❓

Metabolic Acidosis:

- HCO_3^- loss or H^+ gain (e.g., diarrhea, renal tubular acidosis, diabetes, aspirin poisoning)

Respiratory Acidosis: غالبا مشكلة بالرئة

- CO_2 retention (e.g., brain damage, pneumonia, emphysema)

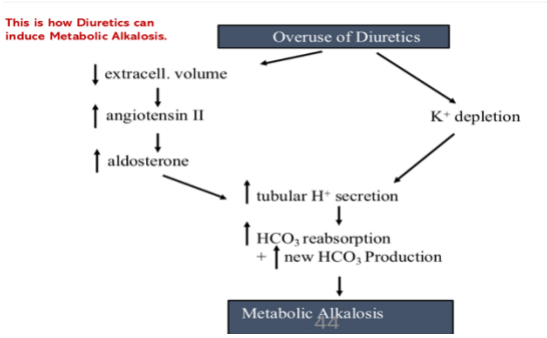
Metabolic Alkalosis:

- HCO_3^- gain or H^+ loss (e.g., vomiting, diuretics, aldosterone excess ،increased base intake (e.g. NaHC03)

(Diuretics: except carbonic anhydrase Inhibitors, because they cause acidosis)❗

Respiratory Alkalosis:

•CO_2 loss (e.g., high altitude, anxiety, pain)



	pH	HCO_3^-	CO_2
Metabolic acidosis	↓	↓	Norma
Metabolic alkalosis	↑	↑	Norma
Metabolic acidosis with respiratory compensation	↓	↓	↓
Metabolic alkalosis with respiratory compensation	↑	↑	↑

The Anion Gap

هو فرق الشحنات بين الأيونات الموجبة والسالبة في البلازما، ويُستخدم لتقييم نوع (Metabolic Acidosis)

•Anion Gap = Na^+ – (Cl^- + HCO_3^- السالبة)

•Normal range: **8–16** mEq/L

Clinical Use: Helps differentiate causes of metabolic acidosis:...

- *Increased Anion Gap:* Due to unmeasured anions (e.g. diabetes mellitus(ketoacidosis), lactic acidosis, salicylate poisoning(aspirin), methanol, starvation) -> (normal Cl-)
- *Normal Anion Gap* (increased Cl, Hyperchloremic): Due to direct HCO_3^- loss with compensatory ↑ Cl^- (e.g., diarrhea, renal tubular acidosis, Addison's disease, carbonic anhydrase inhibitors)

Practice Cases: Anion Gap Calculation

Example 1:

•pH = 7.25, HCO_3^- = 12, pCO_2 = 28, Cl^- = 102, Na^+ = 142

•Anion gap = 142 – (102 – 12)= 28 (high anion gap metabolic acidosis)

•Likely cause: Diabetes mellitus

Example 2:

•pH = 7.34, HCO_3^- = 15, pCO_2 = 29, Cl^- = 118, Na^+ = 142

•Anion gap = 142 – (118 – 15) = 9 (normal anion gap metabolic acidosis)

•Likely cause: Diarrhea

Table of Disorders

pH	HCO_3^-	PCO_2	Acid-Base Disorder ?
7.34	15	29	Metabolic acidosis
7.49	35	48	Metabolic alkalosis
7.34	31	60	Respiratory acidosis
7.62	20	20	Respiratory alkalosis
7.09	15	50	Acidosis: respiratory + metabolic

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- ✓ Compensation occurs via the lungs (for metabolic) or kidneys (for respiratory).
- ✓ Anion gap is crucial for diagnosing types of metabolic acidosis.
- ✓ Clinical cases require stepwise analysis: pH → pCO_2/HCO_3^- → compensation → anion gap.

Physio13Female Reproductive System

Two main functions:

•Preparing the body for conception and pregnancy.

•Supporting the period of pregnancy.

Female Reproductive Organs

•Main components: Ovaries, fallopian tubes, uterus (fundus, body, cervix), vagina, external genitalia, and mammary glands.

•Mammary glands are part of the reproductive system.

Anatomy Recap

- Ovaries: Site of ova (egg) development.
- Fallopian tubes: Connect ovaries to uterus, have fimbriae to catch the ovum.
- Uterus: Site of implantation and fetal development.
- Vagina and external genitalia.

Relationship of Uterine Tubes to Ovaries and Uterus

•Ovum is expelled from the ovary into the abdominal cavity, picked up by the fallopian tube, and transported to the uterus.

- Fertilization typically happens in the fallopian tube,Implantation occurs in the uterus.

Synchronization of Ovarian and Uterine Changes

•Ovarian and uterine cycles run in parallel.

•Ovaries prepare the ovum; uterus prepares for possible implantation.

Oogenesis (Egg Formation)

- Oogenesis: Generation of oocytes (eggs).
- Begins before birth, during embryonic development.
- **Primordial germ cells** migrate to the ovarian cortex, become **oogonia**, then **primordial follicles.**
- Primordial follicle = immature ovum (primary oocyte) surrounded by granulosa cells.
- At birth: 1–2 million primary oocytes as primordial follicles in ovaries.
- Primary oocytes are arrested in prophase I of meiosis until puberty.

Follicle Development and Atresia

- **No** development during childhood due to lack of hormonal stimulation.
- At puberty, hormonal axis activates; primary oocytes resume development.
- By puberty, only about 300,000–400,000 oocytes remain (from the original 1–2 million).

- Only 400–500 will mature and be ovulated during reproductive life; the rest degenerate (atresia) ضمور طبيعي لعدد من البويضات.

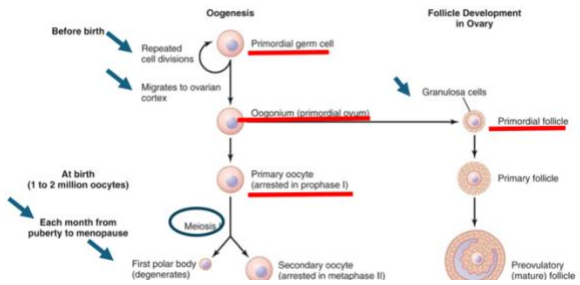
Hormonal Regulation of Oogenesis

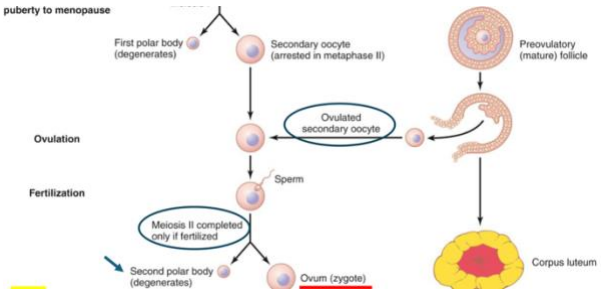
- Hypothalamus releases **GnRH** "Gonadotropin-Releasing Hormone" → stimulates anterior pituitary to release FSH and LH.
  - **FSH**: Stimulates follicle maturation and granulosa cell estrogen production.
  - **LH**: Stimulates theca cell androgen/progesterone production and triggers ovulation.
  - **Inhibin**: Secreted by granulosa cells, inhibits FSH release.
    - ✓ *Granulosa Cells Secrete:*

1. Estrogen:Stimulated by FSH (Follicle-Stimulating Hormone),Promotes growth of the uterine lining and regulates the menstrual cycle.
2. Inhibin:Inhibits FSH secretion from the anterior pituitary (negative feedback).
3. Progesterone:Secreted after ovulation, when the follicle becomes the corpus luteum, Prepares and maintains the uterine lining for possible implantation.
4. Aromatase Enzyme:Converts androgens (from theca cells) into estrogen.

Oocyte Maturation and Ovulation

- At puberty, primary oocyte completes first meiotic division → secondary oocyte + first polar body.
- Secondary oocyte is ovulated, arrested in metaphase II.
- Meiosis II completes **only** after fertilization, producing a mature ovum and second polar body.





Follicle Structure and Ovulation

- Mature (pre-ovulatory) follicle contains granulosa cells, theca cells, and an antrum filled with estrogen.
- **Ovulation**: Rupture of mature follicle, release of secondary oocyte.
- **Post-ovulation:** Ruptured follicle becomes corpus luteum (produces progesterone, important for luteal phase and early pregnancy).

- At birth, each ovum is surrounded by granulosa cells (primordial follicle).
- Granulosa cells nourish the ovum and secrete oocyte maturation-inhibiting factor, keeping it in meiotic arrest (prophase I).

- Basement membrane and stromal cells (later become theca cells) surround the follicle.

Follicular Development in the Ovary

- Each month, FSH stimulates 6–12 primordial follicles to mature.
- Only **one** follicle fully matures and ovulates; others undergo atresia.

Ovarian cycle phases:

- **Follicular** (pre-ovulatory) phase: Follicle maturation.
- **Ovulatory** phase: Ovulation occurs.
- **Luteal** (post-ovulatory) phase: Corpus luteum functions.

Female Hormonal System

- Puberty: Activation of hypothalamic-pituitary-ovarian axis.
- **Menarche**: **First menstrual cycle.** ages(11-15)
- Ovaries alternate ovulation each month, one month from the right ovary, the next from the left.
- Remaining follicles degenerate at menopause due to hormonal inhibition.
- FSH and LH are secreted in a monthly cycle, while GnRH is secreted in pulses every 90 minutes.

Key Points

- ✓ **No** new oocytes are formed after fetal development.
- ✓ Oocyte maturation is hormone-dependent.
- ✓ Only a small fraction of oocytes are ovulated; the rest undergo atresia.
- ✓ Corpus luteum supports early pregnancy *until* placenta takes over hormone production.

بعد الإباضة، يتحوّل الجسم المنفجر إلى الجسم الأصفر (Corpus luteum)، يُفرز هرمون البروجستيرون (وأيضًا بعض الإستروجين)، وهوأساسي لدعم بطانة الرحم وجعلها مناسبة لزرع الجنين،يحافظ على الحمل المبكر حتى تتكوّن المشيمة (Placenta)،بعد ذلك تبدأ المشيمة بإنتاج الهرمونات، ويبدأ الجسم الأصفر بالضمور.

- ✓ Granulosa cells provide nourishment and produce oocyte maturation inhibiting factor during childhood.

تنتج عامل تثبيط نضوج البويضة (Oocyte Maturation Inhibiting Factor):وهو يمنع البويضات من النضوج قبل سن البلوغ

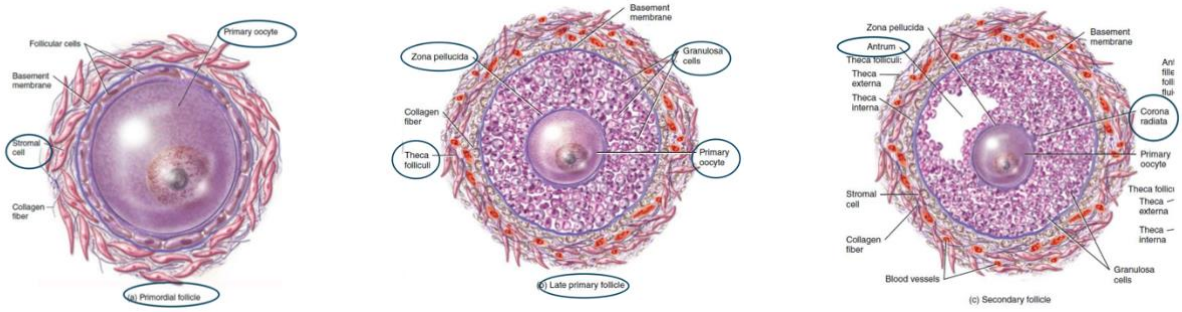
- ✓ Ovarian and endometrial cycles are synchronized for optimal fertility.

Hormonal Fluctuations During the Cycle

- The cycle averages 28 days (can vary).
- Early in the cycle, **FSH** is higher than LH, stimulating follicle growth.
- As ovulation nears(اليوم١٥) **LH** rises.

Types of Follicles and Their Development

- **Primary follicle:** Primary oocyte with several granulosa layers, zona pellucida المنطقة الشفافة, and differentiating stromal cells (theca folliculi).
- **Theca layers:** Theca interna (steroid hormone secretion) and theca externa (vascular capsule).
- **Secondary follicle:** Granulosa cells secrete follicular fluid (antrum forms); corona radiata forms.



Hormonal Feedback and Dominant Follicle Selection

- Granulosa cells produce estrogen (stimulated by FSH).
- High FSH + high estrogen = positive feedback❗, upregulating FSH and LH receptors on granulosa cells.
- **Only one** follicle becomes dominant (most sensitive to FSH/LH and highest estrogen output).
- Dominant follicle's estrogen and FSH suppress FSH, causing other follicles to degenerate (atresia)-> تُنتج أعلى كمية من الإستروجين.

هذا الإستروجين العالي يثبط FSH (تغذية راجعة سلبية لاحقًا)❗ مما يؤدي إلى ضمور باقي الجريبات (Atresia) وعدم نضوجها.

Vesicular (Graafian) Follicle and Final Maturation

- Early growth to antral stage is mainly FSH-driven.
- Estrogen and FSH promote more FSH and LH receptors, accelerating growth يجهزه للإباضه.
- LH and estrogen stimulate thecal cell proliferation and secretion. انتاج الهرمونات الستيرويدية

Ovulation

- About 8–12 follicles start to develop each cycle; **one** matures and ovulates on day 14.
- FSH is high early in the cycle, stimulating follicle maturation.
- Dominant follicle matures, produces high estrogen, and signals readiness for ovulation.
- LH surge ارتفاع مفاجيء (up to 10x baseline) occurs ~24 hours before ovulation, triggered by positive feedback from high estrogen.
- LH surge is essential for ovulation; FSH rises slightly.

- LH causes granulosa/theca cells to switch to progesterone production, prepping for ovulation and luteal phase.

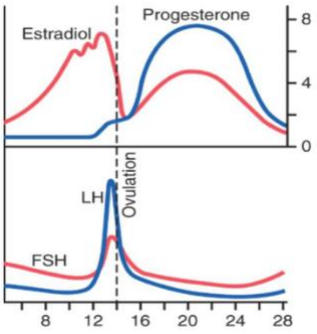
Mechanism of Ovulation

LH surge triggers:

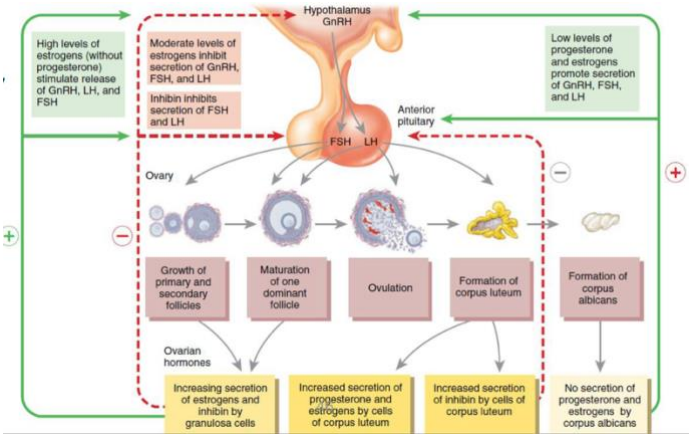
- Enzyme release from theca externa لاضعاف الجدار
- New blood vessel growth into follicular wall
- Follicle swelling and stigma degeneration تمزق
- Follicle rupture and ovum release-> تطلق البويضة الثانوية للخارج لتلتقطها أهداب فالوب

Steroid Hormone Synthesis

- LH stimulates granulosa/theca cells to produce steroid hormones from cholesterol (estrogen, progesterone, androgens).
- FSH stimulates granulosa cells to convert progesterone/androgens **to** estrogen (via aromatase).
- Early follicular phase: high FSH → high estrogen.
- As ovulation approaches, LH rises, estrogen peaks, and progesterone production begins. -> luteal phase



- ✓ Female reproductive hormonal control begins at puberty with GnRH, FSH, and LH.
- ✓ Follicular development is a competitive process; only one follicle ovulates per cycle.
- ✓ Hormonal feedback (positive and negative) regulates follicle selection, maturation, and ovulation.
- ✓ LH surge is essential for ovulation and transition to the luteal phase.



Physio14

The Luteal Phase and Corpus Luteum

- After ovulation, the remaining follicle in the ovary transforms into the **corpus luteum**, characterized by swelling, fat accumulation, and a yellow appearance.
- The corpus luteum is essential for progesterone production during the second (luteal) phase of the ovarian cycle.
- It remains functional for about two weeks, awaiting potential fertilization of the secondary oocyte. If fertilization occurs, progesterone maintains the pregnancy(انتاج المشيمة); if not, the corpus luteum degenerates into the **corpus albicans** (a white scar in the ovary).
- LH from the anterior pituitary maintains corpus luteum function; without fertilization, LH levels fall, leading to corpus luteum involution.

Hormonal Regulation and Feedback Mechanisms

- **Estradiol** is a primary form of estrogen.❗
- The cycle length varies, but the post-ovulatory (luteal) phase is consistently 14 days. Ovulation day can be estimated as: Cycle length – 14.
- FSH is responsible for follicle maturation in the first part of the cycle; an LH surge triggers ovulation.
- After ovulation, both FSH and LH levels decrease.↓
  - ❖ *Feedback mechanisms:*
- High estrogen, low progesterone: positive feedback (early cycle).

تحدث (قبل الإباضة)، الإستروجين يكون مرتفعًا، لكن البروجستيرون منخفضًا، هذا يحفز الدماغ (تحت المهاد والغدة النخامية) على: زيادة إفراز GnRH وبالتالي زيادة LH بشكل كبير

- High estrogen, high progesterone: negative feedback (luteal phase). تحدث (بعد الإباضة)،يكون كل من الإستروجين والبروجستيرون مرتفعَين (من الجسم الأصفر)،هذا يرسل إشارة للدماغ لتقليل إفراز GnRH → وبالتالي تنخفض FSH و LH ، النتيجة: يُمنع نضج جديدة، ويُعطى الرحم فرصة للاستعداد للحمل. follicles
- Low or moderate levels: feedback effects vary.

Gonadotropic Hormones and Ovarian Changes

- Ovarian changes during the sexual cycle depend entirely on FSH and LH.
- In childhood, low gonadotropin levels keep ovaries inactive.

- At puberty (age 9–12), increased FSH and LH initiate the first menstrual cycle (menarche, typically age 11–15).
- GnRH from the hypothalamus is released in pulses every 90 minutes, regulating FSH and LH secretion.
- FSH promotes growth of 6–12 primary follicles each month; estrogen is secreted during follicle growth.
- Two days before ovulation(48 hour), an LH surge triggers ovulation and initial progesterone secretion.
- Estrogen and progesterone from the corpus luteum provide negative feedback on FSH and LH.
- Inhibin from lutein cells further inhibits FSH.
- Low FSH and LH levels cause corpus luteum involutionإذا لم يحدث إخصاب للبويضة.

Monthly Endometrial Cycle and Menstruation

The endometrium (uterine lining) undergoes three phases:

1. **Menstruation**
2. **Proliferative phase**
3. **Secretory phase**

- The first day of bleeding marks the start of the menstrual cycle.
- Menstruation occurs if **no** fertilization happens: the corpus luteum involutes, estrogen and progesterone levels fall ↓, leading to endometrial necrosis and sloughing.
- Menstrual flow contains blood (50–150 mL), tissue fluid, mucus, and epithelial cells. Large numbers of leukocytes are released, reducing infection risk.
- Normally, menstrual blood does not clot due to fibrinolysin; heavy bleeding may occasionally result in clotting.

Factors Affecting Menstruation

- Duration and amount of bleeding vary due to genetics, environment, diet, family history, blood flow/pressure, and diseases.

Proliferative Phase (Estrogen Phase)

- Estrogen induces rapid proliferation of stromal and epithelial cells in the endometrium.
- The endometrial surface is re-epithelialized within 4–7 days after menstruation starts.
- Endometrial thickness increases to 3–5 mm by ovulation.
- After menstruation, only a thin stromal layer and deep glandular epithelial cells remain; original thickness is 1–2 mm. يتحضر لاستقبال بويضة مخصبة

Secretory Phase (Progestational Phase)

- Progesterone causes marked swelling and secretory development of the endometrium, increasing gland tortuosity and nutrient storage.
- Uterine “milk” (secretions) nourishes the early embryo before implantation.

- At the peak of this phase (about 1 week after ovulation), endometrial thickness reaches 5–6 mm.
- If fertilization does not occur, the corpus luteum degenerates, hormone levels drop, and the endometrium is shed.

Functions of Ovarian Sex Hormones

Estrogens (mainly estradiol):

- Promote proliferation and growth of secondary sexual characteristics (breasts, hips, external genitalia).
- Transform female sex organs from child to adult form.
- Change vaginal epithelium to a stratified type, increasing resistance to trauma and infection.
- Cause endometrial proliferation استعدادا للحمل.
- In the breast: stimulate stromal tissue growth, ductal system development, and fat deposition (but not milk production).
- On the skeleton: inhibit osteoclastic activity, stimulate bone growth, and cause early epiphyseal closure (growth cessationوقف الطول بعد البلوغ). After menopause, decreased estrogen leads to osteoporosis.
- Slightly increase protein deposition, metabolic rate, and fat deposition in subcutaneous tissues.

Progestins (mainly progesterone):

- Prepare the uterus for pregnancy and the breasts for lactation.-> by stimulating development of milk-producing glands (though actual milk production requires prolactin after birth).
  - Promote secretory changes and increased thickness in the endometrium.
  - Enhance glandular development and nutrient storage for potential embryo nourishment.

Physio15the male reproductive system

Anatomy of the Male Genital System

- **Gonads** (Testes): Site of sperm production.
- **Ductal System:** Includes epididymis, vas deferens, and urethra for sperm transport.
- **Accessory Glands:** Seminal vesicles, prostate, and bulbourethral glands secrete fluids supporting sperm.

Testis Structure

- Contains lobules filled with seminiferous tubules (sperm production site).

Seminiferous tubules house:

- **Sertoli cells** (support spermatogenesis)
- **Spermatogenic cells** (spermatogonia → spermatozoa)
- **Leydig cells** (outside tubules) produce testosterone.

Male Sex Hormones

- Testosterone: **Main** male sex hormone, produced by **Leydig cells.**

- Other hormones: Dihydrotestosterone, estrogens (formed from testosterone by Sertoli cells).❗

Hormonal Regulation

•Hypothalamus: Releases **GnRH**" Gonadotropin-releasing"(pulsatile, every 1-3 hours).

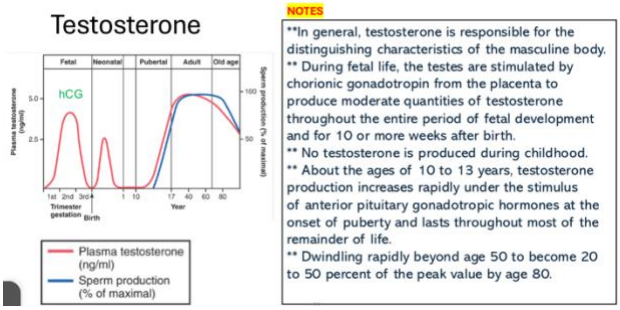
•Anterior Pituitary: Releases **LH**"Luteinizing Hormone" (stimulates Leydig cells for testosterone) and **FSH**"Follicle-Stimulating Hormone"(stimulates Sertoli cells for spermatogenesis).

•Negative Feedback❗: Testosterone inhibits GnRH, LH, and FSH. Sertoli cells produce **inhibin** to further inhibit FSH. للحفاظ على توازن مستويات الهرمونات

Testosterone: Life Span and Function

Testosterone Levels Over Life

1. Fetal Life: **High** due to placental hCG; crucial for male differentiation (SRY gene activation).
2. Early Neonatal: Needed for testicular descent.استقرارها بالمكان الطبيعي
3. Childhood: **No** testosterone production. مستوياته منخفضة
4. Puberty: Testosterone surges↑↑ for secondary sexual characteristics.
5. Adulthood: Peak levels. اعلى مستوى
6. Old Age: Declines↓ but never reaches zero.



Functions During Fetal Development

- SRY gene triggers testes formation and testosterone secretion.
- Testosterone leads to penis and scrotum development, testicular descent.

Adult Primary & Secondary Sexual Characteristics

1. Genital growth: Penis, scrotum, testis enlarge.
2. Body hair: Pubic, facial, and other body hair increases. Bellow the eyebrow -> Growth
3. Baldnessالصلع: Linked to genetics and androgens↑.Above the eyebrow
4. Voice: Larynx enlarges, voice deepens.
5. Skin: Thickens, acne may develop.
6. Muscle: Protein synthesis and muscle mass increase.
7. Bone: Bone matrix and calcium retention increase.
8. Metabolism: Basal metabolic rate rises↑ (~15%).

9. Red Blood Cells: Count increases ↑ (15-20%).
10. Electrolyte/Water Balance: Sodium reabsorption ↑ increases in kidneys.

➢ **Spermatogenesis**

- Before Puberty: Primordial germ cells migrate to testes, become dormant spermatogonia. خلايا خامدة
- At Puberty: Spermatogenesis begins, continues throughout life.
  - **Type A spermatogonia:** Stem cells (self-renew).
  - **Type B spermatogonia:** Enter meiosis, become primary spermatocytes.
  - Primary spermatocytes: Undergo meiosis I → secondary spermatocytes.
  - Secondary spermatocytes: Undergo meiosis II → 4 spermatids (2 X, 2 Y).
  - Spermatids: Mature into spermatozoa via spermiogenesis (**no** division, just maturation).

Duration: ~74 days from spermatogonium to mature spermatozoa.

Spermiogenesis

- **Head**: Contains condensed nucleus, acrosome (with enzymes for ovum penetration). •

- On the outside of the anterior two-thirds of the head is a thick cap called the acrosome that is formed mainly from the Golgi apparatus.
-The acrosome contains several enzymes similar to those found in lysosomes of the typical cell, including hyaluronidase (which can digest proteoglycan filaments of tissues) and powerful proteolytic enzymes proteases (which can digest proteins). These enzymes play important roles in allowing the sperm to enter the ovum and fertilize it.

- **Body**: Packed with mitochondria for energy.
- **Tail**: Propels sperm.

Sperm Transport and Fertilization

Sperm travel through male and female reproductive tracts to reach the ampulla of the fallopian tube for fertilization.

Hormonal Control of Spermatogenesis

1. Testosterone: Essential for germ cell growth/division.
2. LH: Stimulates Leydig cells to produce testosterone.
3. FSH: Acts on Sertoli cells for spermatid maturation.
4. Estrogens: Produced by Sertoli cells (from testosterone); important for libido and sperm maturation.
5. Growth Hormone: Supports early spermatogonial division; deficiency leads to infertility.

✓ rate of spermatogenesis is constant and cannot be accelerated by hormones such as gonadotropins(LH,FSH) or androgens(testo.).

Effect of Temperature on Spermatogenesis

- *Testicular Temperature:* Spermatogenesis is highly sensitive to temperature. The testes are located in the scrotum to maintain a temperature about 2°C below core body temperature, which is essential for sperm production.
- *Descent of Testes:* Testes must descend into the scrotum during fetal life; failure (cryptorchidism) may require surgery if not corrected naturally.

- *Scrotal Reflexes:* On cold days, the scrotum contracts to pull the testes closer to the body, maintaining the temperature difference; the scrotum acts as a controlled cooling mechanism.
- *Sperm Lifespan:* Sperm can live weeks in male ducts, but only 24-48 hours after ejaculation at body temperature; can be preserved for years when frozen يتم حفظهم بالتجميد.

Maturation of Sperm in the Epididymis

- *Immature Sperm:* Sperm formed in seminiferous tubules are non-motile.
- *Epididymal Maturation:* Over 18-24 hours in the epididymis, sperm acquire motility but remain **in**active due to inhibitory proteins until ejaculation.

➢ **Semen Composition**

Sources:

- Vas deferens fluid and sperm (~**10%)**
- Seminal vesicle fluid (~**60%**): Rich in fructose, citric acid, prostaglandins, and fibrinogen.
- Prostate gland fluid (~**30%**): Milky, contains calcium, citrate, phosphate, clotting enzyme, profibrinolysin; slightly alkaline.
- Bulbourethral glands: Small amounts of mucus.
- Prostaglandins: Aid fertilization by making cervical mucus more receptive and stimulating uterine contractions to move sperm toward the ovaries.

✓ Alkalinity: Prostatic fluid neutralizes acidic seminal(6-6.5) and vaginal fluids(3.5-4.0), optimizing sperm motility (semen pH ~7.5).

Accessory Sex Glands and Semen Environment

- Sperm Motility: Sperm need tails and mitochondria for movement and require a supportive, alkaline environment.
- Seminal Vesicles: Produce slightly acidic, nutrient-rich fluid (fructose, citric acid).
- Prostate Gland: Produces alkaline secretion to protect sperm.
- Bulbourethral Glands: Secrete mucoid fluid.

✓ pH Importance: Acidic environments in male urethra and female tract inactivate sperm; alkaline semen is essential for activity.

✓ Prostaglandins: Stimulate vas deferens contractions and backward peristalsis in female reproductive tract, aiding sperm movement toward the ovum.

Differences Between Oogenesis and Spermatogenesis

Timing:

- **Oogenesis**: Begins before birth, all mitotic proliferation occurs in fetal life.

- **Spermatogenesis**: Begins at puberty, continues throughout life.

Meiotic Divisions:

- Oogenesis: One mature ovum **+** polar bodies per primary oocyte.
- Spermatogenesis: Four mature spermatozoa per primary spermatocyte.

Completion:

- Oogenesis: Second meiotic division only upon fertilization.
- Spermatogenesis: Spermatids undergo further differentiation (spermiogenesis).

Cytoplasm:

- Oogenesis: **Un**even, most goes to ovum.لدعم الجنين
- Spermatogenesis: Even, little cytoplasm in sperm.

FEATURE	OOGENESIS (FEMALE)	SPERMATOGENESIS (MALE)
Timing of Onset	Begins **before birth** – oogonia form during fetal life	Begins **at puberty** – spermatogonia start dividing after puberty
First Meiotic Division	Primary oocyte completes meiosis I at **puberty**, forming a **secondary oocyte** + **first polar body**	Primary spermatocyte completes meiosis I, forming **two secondary spermatocytes**
Second Meiotic Division	Occurs **only if fertilization happens**; results in an **ovum** + **second polar body**	Secondary spermatocytes complete meiosis II to form **four spermatids**
Number of Gametes per Cell	**One ovum** (functional) + **polar bodies** (non-functional)	**Four spermatozoa** (all functional)
Cytoplasm Distribution	**Uneven** – most cytoplasm goes to the ovum	**Even** – equal division among four spermatids, but they have **little cytoplasm**
Post-meiotic Maturation	Ovum is already mature after meiosis and fertilization	Spermatids undergo **spermiogenesis** to become mature spermatozoa

Male Sexual Act

•Reflex Mechanisms: Integrated in sacral and lumbar spinal cord; initiated by psychic or physical stimulation (usually both).

Penile Erection – Parasympathetic Role

•Nerve Pathway: Parasympathetic impulses from sacral region via pelvic nerves.

•Neurotransmitters: Release acetylcholine and nitric oxide (NO), activating guanylyl cyclase, increasing cGMP.

•*Effect:* cGMP relaxes penile arteries and smooth muscle, increasing blood flow and causing erection (corpora cavernosa and corpus spongiosum fill with blood).

•*Result:* Penis becomes hard and elongated (erection).

Emission and Ejaculation – Sympathetic Role

- *Emission داخلي*: Sympathetic impulses (**T12-L2**) cause contraction of vas deferens, ampulla, prostate, and seminal vesicles, expelling sperm and fluids into the internal urethra.
- *Ejaculation خارجي*: Filling of urethra with semen triggers sensory signals, causing rhythmic contractions that expel semen (ejaculation).

•*Orgasm and Resolution:* Emission and ejaculation together constitute orgasm; after, sexual excitement rapidly ceases (resolution phase).

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Entry of the Ovum into the Fallopian Tube

- Ovulation releases the secondary oocyte into the abdominal cavity, which is quickly swept into the fimbriated end of a fallopian tube by cilia activated by estrogen.
- A slow fluid current and ciliary motion guide the ovum toward the uterus, with a 98% success rate.

Fertilization of the Ovum

- Fertilization typically occurs at the ampulla of the fallopian tube.
- Sperm transport is aided by uterine and tubal contractions (stimulated by prostaglandins in seminal fluid and oxytocin released during female orgasm).
- The sperm must penetrate the corona radiata and zona pellucida of the oocyte

Capacitation of Spermatozoa

- Sperm leaving the epididymis are not immediately capable of fertilization due to inhibitory factors from male genital ducts.

In the female tract, sperm undergo "capacitation" (1–10 hours), involving:

- Removal of inhibitory factors.
- Loss of excess cholesterol, weakening the acrosome membrane.
- Increased permeability to calcium ions, enhancing flagellar movement and enabling acrosome enzyme release.

Acrosome Reaction and Penetration

- The acrosome contains hyaluronidase (breaks down hyaluronic acid) and proteolytic enzymes (digest proteins), allowing sperm to penetrate the granulosa cells and zona pellucida.
- The sperm binds to receptor proteins on the zona pellucida, releases enzymes, and creates a pathway to the oocyte.
- The sperm and oocyte membranes fuse, combining their genetic material to form a zygote with 23 paired chromosomes.

Prevention of Polyspermy

- After the first sperm enters, calcium influx triggers cortical granule release, which modifies the zona pellucida to prevent further sperm entry.

Transport of the Fertilized Ovum

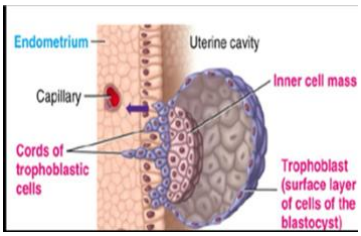
- The zygote remains in the fallopian tube for 3–5 days, nourished by tubal secretions, and undergoes several cell divisions to form a blastocyst (~100 cells).
- Progesterone relaxes the isthmus of the tube, and ciliary action moves the blastocyst toward the uterus.

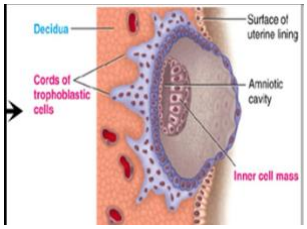
Implantation of the Blastocyst

- The blastocyst stays in the uterine cavity for 1–3 days before implanting (5–7 days after ovulation).
- It initially receives nutrition from "uterine milk" (endometrial secretions).
- Trophoblast cells on the blastocyst surface secrete proteolytic enzymes to digest and invade the endometrium, facilitating implantation.

Placental Development

- Trophoblast and adjacent cells proliferate to form the placenta and pregnancy membranesالتي تحيط بالجنين للحماية ك الكيس الأمنيوسي.
- Blood capillaries grow within trophoblastic cords; maternal blood sinuses develop around them, forming placental villi تسمح بتبادل المواد بين الأم و الجنين.
- By 21 days post-fertilization, fetal heart pumps blood into these capillaries.





Placental Circulation

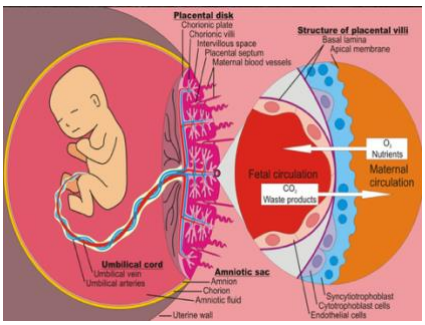
- Fetal blood flows through two umbilical arteries into villous capillaries, then returns via a single umbilical vein.
- Maternal blood from uterine arteries fills sinuses surrounding the villi and returns via uterine veins.

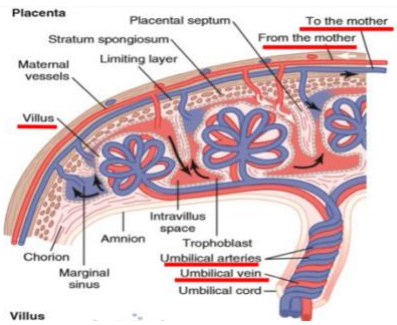
Early Nutrition of the Embryo

- For the first week after implantation, the embryo relies on the decidua (endometrial cells) for nutrition.
- The placenta begins providing nutrients after about 16 days post-fertilization, as its permeability and surface area increase with development.

Functions of the Placenta

- Respiration: Oxygen diffuses from maternal to fetal blood.
- Nutrition: Glucose and other nutrients are transferred (facilitated diffusion).
- Excretion: Waste products are removed from fetal blood.
- Endocrine: Secretes hormones essential for pregnancy.
- Protection: Acts as a partial barrier to some pathogens and substances.



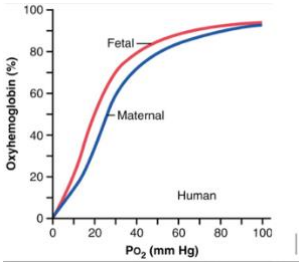


Oxygen Diffusion and Fetal Hemoglobin

- .Maternal blood PO_2 in placental sinuses: ~50 mm Hg; fetal blood after oxygenation: ~30 mm Hg (20 mm Hg gradient).

الفرق بين القيمتين (Gradient) هو 20 ملم زئبقي، وهذا الفرق يكفي لنقل الأكسجين من دم الأم إلى دم الجنين عبر المشيمة

- Fetal hemoglobin has a higher affinity for oxygen (**left-shifted dissociation curve**) and higher concentration (about 50% more than maternal hemoglobin).



- The **Bohr effect** enhances oxygen transfer as fetal blood clears CO_2 into maternal blood, increasing its oxygen affinity.

أثناء تبادل الغازات، يقوم دم الجنين بالتخلص من ثاني أكسيد الكربون (CO_2) إلى دم الأم، انخفاض CO_2 في دم الجنين يؤدي إلى زيادة ارتباط الهيموغلوبين بالأكسجين،في المقابل زيادة CO_2 في دم الأم تقلل من قابلية هيموغلوبين الأم للأكسجين، مما يدفع الأكسجين للانتقال إلى دم الجنين بسهولة أكبر❗

Hormonal Factors in Pregnancy

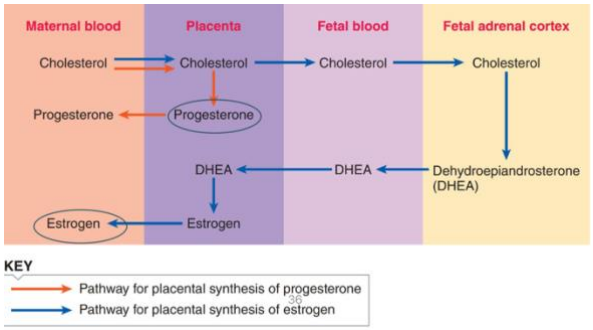
The placenta produces large amounts of:

- **Human Chorionic Gonadotropin (hCG):** Synthesized by trophoblasts, detectable 8–9 days after ovulation, peaks at 10–12 weeks, then declines. Maintains the corpus luteum, which secretes estrogen and progesterone, and stimulates fetal testes to produce testosterone في حال كان الجنين ذكراً.

يمكن اكتشافه في الدم أو البول بعد 8–9 أيام من الإباضة، وهو أساس اختبارات الحمل، يصل إلى ذروته في الأسبوع 10–12 من الحمل، ثم يبدأ في الانخفاض التدريجي

- **Estrogens:** Produced by syncytial trophoblasts from DHEA"Dehydroepiandrosterone "(from fetal/maternal adrenals). Promote uterine, breast, and genital enlargement and relax pelvic ligaments for labor.

- **Progesterone:** Initially from the corpus luteum, later mainly from the placenta❗. Essential for decidual cell development (nutrition), decreases uterine contractility فيساعد على تثبيت الحمل, increases secretions for embryo nutrition, and prepares breasts for lactation بالاضافه ل دور الاستروجين.



Physio17

Response of the Mother's Body to Pregnancy

Weight Gain

- Average gain: 10–15 kg, mostly in last two trimesters.
- Components: fetus (~3.5 kg), amniotic fluid, placenta, uterine/breast enlargement, increased blood/extracellular fluid, fat accumulation.
- Extra fluid is excreted after birth.

Increased Appetite

- Due to fetal nutrient demand and hormonal changes.
- Without dietary control, weight gain can be excessive.

Metabolism During Pregnancy

- Basal metabolic rate increases by ~15% in latter half.
- Higher energy needed for muscle activity; mother may feel overheated.

Endocrine Changes

- Pituitary Gland: Enlarges by 50%; increased ACTH" Adrenocorticotropic Hormone", TSH "Thyroid-Stimulating Hormone", prolactin. FSH/LH suppressed by placental hormones.

- Adrenal Glands: Increased glucocorticoid and aldosterone secretion.
- Thyroid Gland: Enlarged; more T4 produced.
- Parathyroid Glands: Enlarge to enhance calcium absorption for fetal bone development, even more so during lactation.

Nutrition During Pregnancy

- Mother often does not absorb enough protein, calcium, phosphates, iron in late pregnancy.
- Body stores these nutrients in advance.
- Key supplements: iron (prevents anemia), vitamin D (for calcium absorption), folic acid, vitamin K (for baby's clotting factors).

Maternal Circulation and Cardiac Output

- Blood flow through placenta increases.
- Maternal cardiac output rises 30–40% by week 27.
- Cardiac output drops slightly in last 8 weeks, despite high uterine blood flow.

Blood Volume

- Increases by ~30% before term due to aldosterone/estrogen and kidney fluid retention.
- Bone marrow produces more red blood cells.
- Extra blood provides safety during delivery (only ~350 ml lost at birth).

Respiratory Changes

- Oxygen use increases by ~20%.

- Increased minute ventilation and respiratory rate due to higher metabolic rate and progesterone effects.
  - Minute Ventilation = Respiratory Rate × Tidal Volume

خلال الحمل، تحدث: زيادة في عدد مرات التنفس (Respiratory Rate). وزيادة في حجم النفس الواحد (Tidal Volume)بالتالي زيادة فيMV (بنسبة تصل إلى 30–50%)

Renal Function

- Increased urination from higher fluid intake and excretory load.
- Enhanced reabsorption of sodium, chloride, water.
- Renal blood flow and filtration rate increase due to relaxin.

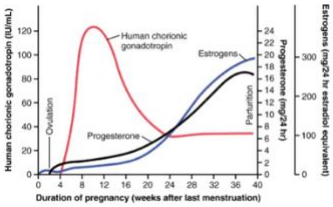
Labor:

Uterine Excitability Near Term

Uterus becomes more excitable due to hormonal and mechanical changes, leading to labor (parturition).

Hormonal Factors Increasing Uterine Contractility

- Estrogen/Progesterone Ratio: Estrogen rises relative to progesterone, increasing uterine contractility and gap junctions in muscle يسهل انتقال الإشارات وتناسق الانقباضات.



- Oxytocin: More receptors, higher secretion during labor; positive feedback from cervical stretch.
- Fetal Hormones: Fetal pituitary (oxytocin), adrenal (cortisol), and prostaglandins from membranes all stimulate contractions.

Mechanical Factors

- Uterine Stretch: Increases contractility.
- Cervical Stretch/Irritation: Induces labor via reflexes and myogenic signals.

عند اقتراب الولادة، يبدأ رأس الجنين بالضغط على عنق الرحم هذا الضغط يسبب تمدّد ميكانيكي لعنق الرحم، تنشيط ردود فعل عصبية (reflexes) من خلال الأعصاب الحسية، إفراز مزيد من الأوكسيتوسين (→ تغذية راجعة إيجابية → ↑ الانقباضات)،تحفيز إشارات عضلية ذاتية (myogenic signals) تُسهّل الانقباضات.

- ✓ Twins or multiples: Born earlier due to increased stretch.

Positive Feedback in Labor

Cervical stretching triggers stronger uterine contractions, which further stretch the cervix, increasing oxytocin ↑ release and contractility until birth.

Abdominal Muscle Contractions

Strong uterine contractions cause pain, triggering abdominal muscle reflexes that aid in expelling the baby.

Stages of Labor

1. First Stage: Onset of labor to full cervical dilation~10cm.
2. Second Stage: Full dilation to birth of baby.
3. Third Stage: Birth of baby to delivery of placenta.
4. Fourth Stage: Delivery of placenta to stabilization (~6 hours postpartum).

✓ Intermittent contractions مهمة are crucial to prevent fetal hypoxia.

✓ تعطي فرصة للجنين للحصول على الأكسجين بين الانقباضات،لو كانت الانقباضات مستمرة بلا توقف، قد يحدث نقص أكسجين للجنين.

Separation and Delivery of the Placenta

- Placenta separates, opening sinuses and causing bleeding (~350 ml).
- Uterine contraction and vasoconstrictor prostaglandins minimize blood loss.

Labor Pain

- Early: Uterine muscle hypoxiaبسبب الانقباضات المتكررة.
- Second stage: Stretching/tearing of cervix, perineum, vaginal canal.

Lactation:

Breast Development

- Begins at puberty (estrogen-driven).
- During pregnancy: Estrogen, growth hormone, prolactin, glucocorticoids, insulin stimulate ductal and stromal growth.
- Progesterone: Needed for lobule-alveolar development and secretory function.

Prolactin and Milk Production

- Prolactin rises 10–20x during pregnancy, but milk secretion is inhibited by estrogen/progesterone.
- Colostrum (pre-milk secretion) produced around delivery; transitions to milk in 1–7 days post-birth.
- Milk production requires background secretion of growth hormone, cortisol, parathyroid hormone, and insulin.

Prolactin After Birth

- Basal prolactin returns to normal after a few weeks.
- Suckling triggers surges in prolactin, maintaining milk production.
- Without nursing, milk production ceases in ~1 week.

عملية الرضاعة (Suckling) تحفّز دفعة جديدة من البرولاكتين، مما يحافظ على استمرار إنتاج الحليب،إذا توقفت يتوقف انتاجه

Suppression of Ovarian Cycles

- Nursing delays return of ovulation/menstruation. ك وسيلة طبيعية لمنع الحمل هذه الفترة
- Suckling inhibits GnRH, suppressing FSH and LH.

Milk Ejection ("Let-Down") Reflex

- Suckling sends sensory impulses to hypothalamus, promoting oxytocin release.
- Oxytocin causes myoepithelial cells to contract, expressing milk into ducts.
- Milk flows 30 seconds to 1 minute after suckling begins.

Physio18Abnormalities in the Reproductive System

Abnormal Spermatogenesis and Male Fertility

Sterility العقم

•Causes: Destruction of seminiferous tubular epithelium by diseases (e.g., bilateral orchitis from mumps), congenital degeneration, excessive testicular temperature من الأسباب عدم نزولها للمكان الطبيعي, x-ray exposure❗.

✓ Excessive temperature of testes (usually temporary).

•Leydig cells often continue testosterone production even if germinal epithelium is destroyed.

Cryptorchidism

•Definition: Failure of testes to descend into the scrotum at birth.

A testis that remains in the abdominal cavity throughout life is incapable of forming sperm.

- Consequences: Undescended testes cannot form sperm; tubular epithelium degenerates حيث الحرارة تؤذي الخلايا.
- Causes: Insufficient fetal testosteroneفي الفترة الجنينية.
- Treatment: Surgical correction.

➢ Effect of Sperm Count on Fertility

- Normal ejaculate: ~3.5 ml, Each 1 ml of semen usually contains around 120 million sperm.
- The normal range is 35 million to 200 million sperm/ml.
- Infertility likely if sperm count <20 million/ml.
- A normal ejaculation (3.5 ml × 120 million sperm/ml) contains an average of around 400 million sperm.❗

✓ انخفاض العدد وحده لا يعني دائمًا العقم، لكن يزيد احتماله❗.

Effect of Sperm Morphology and Motility on Fertility

Infertility can occur with normal sperm count ❗if many sperm are abnormally shaped (e.g., two heads, abnormal tails) or nonmotile.

Factor	Impact on Fertility
Low sperm count (<20 million/mL)	↑ Risk of infertility
Abnormal sperm shape	↓ Fertilization ability
Poor motility	↓ Sperm reach the egg
Cryptorchidism	Damaged sperm-producing cells

Abnormalities of Male Sexual Function

Prostate Gland and Its Abnormalities

- Growth at puberty, stationary until age 50(20-50 yrs), then involutes. تبدأ بالضمور
- Benign prostatic hypertrophy (BPH) can cause urinary obstruction.
- Prostate cancer: 2-3% of male deaths, growth stimulated by testosterone, slowed by estrogen therapy or removal of testes.

Hypogonadism in the Male

•Congenital/Testicular Failure in Fetus: No male characteristics develop; female organs form.

•**Pre**pubertal Loss (Eunuchism): Infantile sex organs, weak muscles, childlike voice, no male hair pattern, increased height due to delayed epiphyseal closure.

- ✓ no loss of hair on the head
- ✓ no masculine hair distribution on the face

•**Post**pubertal Castration: Regression of sexual organs but not to a childlike state, loss of masculine features, decreased sexual desire, loss of the thick masculine bones, loss of masculine hair production

- ✓ primarily because the semen-forming organs degenerate and there has been a loss of the testosterone-driven psychic desire(not lost).

Testicular Tumors and Hypergonadism

•Leydig Cell Tumors: Excessive testosterone ↑, (100* of testosterone) rapid growth, early epiphyseal closure in children.-> قصر

•Germinal Epithelium Tumors (Teratomas): Contain various tissues, may secrete **hCG** or estrogen. يسبب أعراض أنثوية أحيانا

- ✓ more common than interstitial Leydig cell tumors❗

Erectile Dysfunction (Impotence)

•*Causes*: Neurological problems, such as trauma to the parasympathetic nerves from prostate surgery, low testosterone, drugs (nicotine, alcohol, antidepressants), vascular disease (hypertension, diabetes, atherosclerosis).

- ✓ In men older than 40 years

•*Treatment*: **PDE-5 inhibitors**(phosphodiesterase-5)(sildenafil (Viagra), vardenafil (Levitra), tadalafil (Cialis)) enhance cyclic GMP, promoting vasodilation and erection.

Abnormalities of Ovarian Secretion

Hypogonadism-Reduced Ovarian Secretion

•Congenital or **Pre**pubertal Failure: Female eunuchism, no secondary sexual characteristics, infantile organs, prolonged bone growth.❗

•**Post**pubertal Ovarian Loss: Regression of sexual organs, atrophy of breasts, thinning of pubic hair, similar changes after menopause.

Female Sterility

•Causes: Abnormal genital function or ova development.

•Most common: Failure to ovulate❗ (due to low gonadotropins or abnormal ovaries).

Anovulatory Cycles

- Often occur at puberty or before menopause due to insufficient LH surge❗.
- No corpus luteum or progesterone, cycle shortened.

Ovulation Detection كشف حدوث الإباضة

•Urine pregnanediol (progesterone metabolite) or body temperature charting (progesterone raises temperature by ~0.5°F at ovulation).

•Absence of progesterone effects indicates anovulatory cycles.

تحليل البول لوجود مادة Pregnanediol (ناتج استقلاب البروجستيرون),أو قياس درجة حرارة الجسم يوميًا: ترتفع بحوالي 0.5 درجة فهرنهايت بعد الإباضة بسبب تأثير البروجستيرون، عدم وجود هذه الزيادة يشير إلى دورة بدون إباضة.

- *Treatment of Anovulation:* Human chorionic gonadotropin (**hCG**) can induce ovulation but may cause multiple births حمل متعدد if overstimulated.

Polycystic Ovarian Syndrome (PCOS) متلازمة تكيس المبايض

small sacs of fluid develop along the outer edge of the ovary. These are called cysts. The small fluid-filled cysts contain immature eggs. These are called follicles. The follicles fail to regularly release eggs.

•Hormonal disorder with multiple ovarian cysts, irregular periods, excess androgens (hirsutism شعر زائد), and insulin resistance.

•*Symptoms*: Irregular cycles, hirsutism, polycystic ovaries.

•*Treatment*: Lifestyle changes, hormonal therapy(combination pills and progestins pills), metformin(to improve insulin sensitivity) .

Pregnancy Complications:

Preeclampsia عادة بالنصف الثاني من الحمل

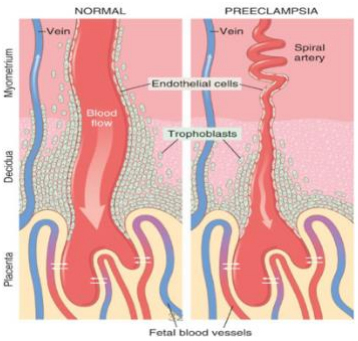
•Pregnancy-induced hypertension, proteinuria, edema (excess salt and water retention), weight gain, arterial spasm.

•*Causes*: Possible hormonal excess (placental or adrenal), autoimmunity, or insufficient placental blood supply

leading to endothelial dysfunction and increased inflammatory cytokines (TNF-a and IL-6)

✓ the acute symptoms usually disappear within a few days after birth of the baby.

•*Pathology*: Failure of spiral artery remodeling, reduced placental blood flow, maternal hypertension بسبب تضيق الأوعية , and organ dysfunction.



Eclampsia

•Severe form of preeclampsia with widespread vascular spasm, seizures, coma, renal and liver dysfunction, extreme hypertension, high mortality.

•*Treatment*: Vasodilators and immediate delivery reduce mortality. الولادة قبل الموعد هو الحل لتقليل خطر الوفاة

تمّ بحمد الله، وفّقكم الله واذكرونا بدعواتكم

By: Ayah Freihat