ICE Student Online “Virtual” Case

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REQUIRED READING:
To access some of the resources below, please make sure to login to the library’s website first, in order for the links to load.

Note that some of the information presented in this case supports summarized information from:
First Aid for the USMLE Step 1 2014: pages 307, 309-310, 324, 329

Lecture Notes you might find helpful (see Endocrinology/Reproductive Sciences block schedule):
“Adrenal disorders” (1-hour lecture by Dr. Cryar), October 30

“Pituitary/Hypothalamic disorders” (lectures by Dr. Cryar), October 31

“Pathology Disorders of the Endocrine System” (2-hour lecture by Dr. Lopez), November 1st

Links and Review Articles:
Chief Complaint: “I am not having normal periods”

History of Present Illness:

Mrs. Brittany Davis is a 25-year-old Caucasian G2 P1011 woman who presents for her annual well-woman exam. She reports in the past 2 years that her periods have become much more irregular. She states that she has not had a period in over 6 months.

Prior to pregnancy, she had regular monthly menses every 28 days, lasting 5 days in duration. She gave birth to her child 3 years ago, and has been using condoms for contraception. She stopped breastfeeding her child over 2 years ago. Her periods resumed after she completed breastfeeding; however, they were irregularly spaced, coming every 1-4 months, until they ceased 6 months ago.

She states that in the past few months, she has noticed some white discharge from her breasts. She denies taking any new medications or having headaches or visual abnormalities. She denies any intermenstrual or post-coital bleeding, vaginal discharge, irritation, or dysuria.

Past Medical History:

Asthma, intermittent
Obstetrical History:

G2 P1011

1. Spontaneous vaginal delivery (SVD) - female infant, 7 pounds, 8 ounces. Delivery complicated by post-partum hemorrhage.
2. Spontaneous abortion (SAB) at approximately 10-weeks gestation. Dilation & Curettage (D&C) required, 1 year prior.

Gynecologic History:

1. Abnormal Pap smear - colposcopy and biopsy were normal, no excisional procedure, 2010
2. Last Pap smear - Negative for intraepithelial lesion (NIL), 2015

Health Maintenance:

She has not received a mammogram or colonoscopy due to age.

Past Surgical History:

1. Appendectomy
2. Dilatation & Curettage (D&C)

Allergies:

No known drug allergies

Medications:

1. Women’s multivitamin - 1 tab daily
2. Calcium carbonate with vitamin D - 600 mg/500 IU 1 tab twice a day
3. Albuterol - 90 mcg inhale 2 puffs every 4 hours as needed for shortness of breath

Family History:

Father – pancreatic mass, resected in 2013; patient isn’t sure of diagnosis

Brother – recurrent kidney stones (calcium oxalate)

Social History:

No tobacco, alcohol, or drug use. She works as a clerk in a department store. She has been married and monogamous with her husband for 5 years. They have a 3-year-old daughter. She eats a consistent diet of about 1800 calories per day and exercises for 30 min (usually walking with stroller) 3 times per week.
Review of Systems:

For pertinent positives and negatives, please see the HPI. All other systems are reviewed and are negative for pertinent findings.

Physical Examination:

Vital Signs: Temperature: 98.1°F (36.7°C), pulse: 83 beats/min, blood pressure: 108/64 mmHg, respiratory rate: 12/min. Oxygen saturation: 98% on room air, Weight: 125 lbs, Height: 5’4 inches.

General: Well-appearing young female, no acute distress. No hirsutism.

HEENT: PERRLA, EOMI, TM pearly grey, oropharynx clear, no lymphadenopathy. Thyroid non-palpable, no nodules.

Pulmonary: Lungs are clear to auscultation bilaterally, with no wheezes, rales, or rhonchi.

Cardiovascular: Regular rate and rhythm. No murmurs, rubs, or gallops.

Breasts: Symmetric bilaterally. No palpable masses or axillary lymphadenopathy. No erythema or retraction of the skin or nipples. Nipple discharge with gentle palpation noted bilaterally.


Skin: No visible or palpable rash.


Anus: Normal, without lesions, no hemorrhoids.

Neurologic: CN II-XII are intact. No focal neurologic deficits appreciated.

Psych: Mood and affect are appropriate.

Laboratory

In office urine pregnancy test – negative.

Studies:

Vaginal ultrasound was deferred.

**Question 1:** As you consider the potential diagnoses for Mrs. Davis, you first define amenorrhea. What is the difference between primary and secondary amenorrhea? Which does this patient have? *(Note: there may be different criteria for the definition of primary amenorrhea; use the above referenced article or another reputable resource).*

**Answer 1:** Primary amenorrhea – failure to menstruate by age 15 in the presence of normal growth and secondary sexual characteristics, or by age 13 if there is a complete absence of secondary sexual characteristics.

Alternate answer: failure to menstruate by age 16 (age 13 mean) in the presence of normal secondary sexual development (or age 14 without secondary sex characteristics).

Secondary amenorrhea – failure to menstruate after having previously normal menstruation. Absence of menses for more than 3 months in girls who previously had regular menstrual cycles or 6 months in women who had irregular cycles.

The patient’s presentation fits secondary amenorrhea.

**Question 2:** Utilizing the article above, what 5 aspects are used in the evaluation of a patient with amenorrhea, after pregnancy is excluded (hint, there are at least 3 laboratory tests that you can order).

**Answer 2:** History. Physical examination. FSH levels (note: would only order an FSH level after the more likely etiologies have been ruled out). Prolactin levels. TSH levels.

**Question 3:** Take a closer look at Tables 1-3 in the article. Organize the differential diagnosis in broad categories and eliminate the broad categories which do not fit in with this patient (for example primary vs. secondary amenorrhea causes). As you narrow your differential diagnosis, consider why some entities are unlikely in this patient, while others remain a possibility and warrant further work up. Fill in the table below for PCOS, High prolactin, Asherman syndrome and Sheehan syndrome (use examples 1 and 5 as guidance). **Answer 3:** see in red.

<table>
<thead>
<tr>
<th>Pertinent positives/negatives in History</th>
<th>Pertinent positives/negatives on physical exam</th>
<th>Likely: Yes or No</th>
<th>Useful tests/imaging/workup or further questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss/anorexia</td>
<td>Eats consistent diet of 1800 calories; no excessive exercise; no mention of weight loss</td>
<td>Stable BMI</td>
<td>No</td>
</tr>
<tr>
<td>2. PCOS</td>
<td>Previous successful pregnancy</td>
<td>No classic features of hirsutism etc.</td>
<td>No</td>
</tr>
<tr>
<td>---------</td>
<td>-------------------------------</td>
<td>--------------------------------------</td>
<td>----</td>
</tr>
<tr>
<td>3. High prolactin</td>
<td>Milky discharge from breasts</td>
<td>Bilateral nipple discharge</td>
<td>Yes</td>
</tr>
<tr>
<td>4. Asherman syndrome</td>
<td>D&amp;C (but more irregular periods not consistent with scar tissue development)</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>5. Ovarian tumor</td>
<td>No pelvic pain or complaints of ascites</td>
<td>Bimanual exam did not palpate mass, no ascites</td>
<td>No</td>
</tr>
<tr>
<td>6. Sheehan Syndrome</td>
<td>History of postpartum hemorrhage, but no mention of hypotension. Able to breastfeed baby (1st symptom of Sheehan is inability to produce milk)</td>
<td>Breast discharge would go against Sheehan</td>
<td>No</td>
</tr>
</tbody>
</table>

**Question 4:** Although Mrs. Davis reports no new medications, you wish to specifically ask her about medications that can lead to amenorrhea. Based on the hypothalamic-pituitary-ovarian axis, you consider different types of medications that could lead to amenorrhea. For each of the categories below, write a brief description of the mechanism of action, which would lead to amenorrhea. (Use the bolded category as an example)

1. **Oral Contraceptives (estradiol/progestin):** Mimic sex hormones, which decrease the pulse frequency of gonadotropin-releasing hormone (GnRH $\rightarrow$ decreases the secretion (FSH and LH) by the anterior pituitary $\rightarrow$ prevents follicle development $\rightarrow$ no ovulation)
2. **Antidepressants** (e.g. amitriptyline): Not fully understood, though several theories have been postulated, such as serotonin stimulation of GABAergic neurons and indirect modulation of prolactin release by serotonin.
3. **Mood stabilizers** (e.g. lithium, alprazolam, valproic acid): Stimulate GABA (inhibitory transmitter) (GABA $\rightarrow$ hypothalamus $\rightarrow$ inhibits hormone releasing hormones $\rightarrow$ inhibits normal hormone cascade)
4. Antipsychotics (e.g. haloperidol, risperidone) and GI meds (e.g. metoclopramide, cimetidine): Dopamine D2 receptor blockade (Prevent dopamine negative inhibition of prolactin → increase prolactin → inhibit FSH, LH)

Answer 4: See above in red.

You specifically review these medication/supplement exposures with the patient prior to ending the office visit. She confirms that she has not been on any of these medications. However, her husband does take lithium for bipolar disorder. She is agreeable to have laboratory work drawn this afternoon.

---Part B: --Information below available as soon as the above questions are answered-------------------------

Learning Objectives Part B:

1. Describe the usual clinical presentation of prolactinoma. Explain an appropriate approach to the diagnosis and treatment of a prolactinoma.
2. Define and understand the different multiple endocrine neoplasms (MEN) syndromes.

Laboratory Analysis:

Consider why each of the following laboratory values is important to the case. If you need laboratory reference values, consult the NBME Laboratory Values Sheet http://www.nbme.org/PDF/SubjectExams/LabReferenceValues.pdf

White blood cell count (WBC): 8,500/mm³
Hemoglobin: 14.1 g/dL
Hematocrit: 42.3%
Platelets: 210,000/mm³

Sodium: 140 mEq/L
Potassium: 3.6 mEq/L
Chloride: 85 mEq/L
Bicarbonate: 24 mEq/L
BUN: 14 mg/dL
Creatinine: 1.0 mg/dL
Calcium: 10.8 mg/dL - mild elevation

Beta-human chorionic gonadotropin (B-HCG): negative
Thyroid stimulating hormone (TSH): 2.1 µU/mL (normal)
Follicle stimulating hormone (FSH): 5 mIU/mL (normal)
Prolactin: 91 ng/mL (high)
You briefly consider the need to perform a progesterone challenge test. When the initial lab evaluation is normal, this test helps you determine if the patient has an appropriate response to progesterone withdrawal, by having withdrawal bleeding. For example, this test would help if you think her amenorrhea is caused by anovulation (PCOS) or you are trying to rule out Asherman syndrome or other structural causes. However, you decide it is not needed given the elevated prolactin level that would explain the reason for her amenorrhea. Instead, you would like to further investigate the elevated prolactin level.

Based on the laboratory results, you contact the patient and discuss your concern over the elevated prolactin. Before you proceed with further imaging, you repeat the prolactin level to ensure that this was not a lab error. The repeat prolactin level is 98 ng/mL, confirming the diagnosis of hyperprolactinemia. You order an MRI of the brain. You schedule an appointment to discuss the findings the afternoon after her MRI is performed.

**Studies:**

**MRI Image:**

![MRI Image](image)

**MRI Report:**

Small non-enhancing hypointense areas are seen in the region of pituitary gland on both sides, which could be possible small microadenomas. The lesion measures approximately 2.4 x 2.2 mm in size on right side and on left side is 2.6 x 2.1 mm in size.
Given the above information of an elevated prolactin and the imaging results, you consider the most likely diagnosis to be a prolactinoma. *(If you need to learn more about prolactinoma, see the following summary: Ferri, FF. Prolactinoma. In Ferri’s Clinical Advisor. 2016, 1028-1029)*

Consider what additional laboratory tests you would like to order?

As a rule of thumb, pituitary hormones should not be interpreted without measuring their target hormone. If considering pituitary dysfunction, order in pairs like TSH/FT4 or LH&FSH/estradiol. For instance, a low TSH is consistent with either hyperthyroidism or pituitary insufficiency, but the FT4 would be high in the former and low in the latter.

Additionally, hyperprolactinemia will suppress LH and FSH, so deficiencies of the gonadotropins is expected with hyperprolactinemia.

Also recommended is IGF-1 (somatotroph adenomas) and a 24-hour urinary free cortisol (corticotroph adenomas).

**Question 5:** Review the details of the patient’s H&P and the initial laboratory values. Could the diagnosis of prolactinoma be a part of a larger diagnosis? What complex diagnosis or syndrome should be considered when a pituitary adenoma is present? List the syndrome and its components (list at least 3 components). And what clues presented so far (hint: in the complete history) would support further consideration of this syndrome diagnosis? List at least 2 clues.

**Answer 5:**

Always consider MEN (multiple endocrine neoplasms) when the pituitary gland is involved

MEN1 (3Ps- **Pituitary, Pancreas, Parathyroid**)

Just FYI....

MEN 2a (medullary thyroid cancer, pheochromocytoma, parathyroid)

MEN 2b (medullary thyroid cancer, pheochromocytoma, Marfan/neuroma)

The patient’s family history is concerning for the possible diagnosis of multiple endocrine neoplasia (MEN) 1. As this is a genetic mutation, the combination of family history with her current prolactinoma diagnosis shows components of the MEN1 triad. Her father has had an unknown pancreatic mass removed. The presence of calcium oxalate stones in her brother raises the question of hypercalcemia from hyperparathyroidism. Slightly elevated calcium is seen in the patient’s labs; however, it is important to note that she is taking calcium supplements. A prudent physician would likely evaluate with a serum parathyroid hormone (PTH) level.
---Part C: --Information below available as soon as the above questions are answered-------------------------

Learning Objectives Part C:

1. Search for drug information in an online library resource to extract information to answer patient’s questions and concerns.

Patient information:

You discuss the different medication treatments for prolactinoma and decide with Mrs. Davis to begin Cabergoline. She will have a serum prolactin level drawn monthly. You explain that it is very rare for microadenomas to grow in size while on treatment. However, you tell her that if she begins to have vision changes and headaches, she must come in for evaluation (which would raise the concern for bitemporal hemianopsia from a large macro pituitary adenoma).

Cabergoline 0.25 mg po twice per week is initiated. This is then titrated in increments of 0.25 mg every 4 weeks, based on the prolactin level.

Additionally, the patient’s family history is concerning for the possible diagnosis of multiple endocrine neoplasia (MEN) 1. As this is a genetic mutation, the combination of family history with her current prolactinoma diagnosis shows components of the MEN1 triad. Her father has had an unknown pancreatic mass removed. The presence of calcium oxalate stones in her brother raises the question of hypercalcemia from hyperparathyroidism. Slightly elevated calcium is seen in the patient’s labs; however, it is important to note that she is taking calcium supplements. A prudent physician would likely evaluate with a serum parathyroid hormone (PTH) level.

Question 6: Two years from now, Mrs. Davis returns to your office and is interested in getting pregnant. She is currently taking the prescribed Cabergoline. What would you recommend for this situation? (Recommended resources: Epocrates, Lexicomp)

Answer 6: Pregnancy category B. Review the patient’s prolactin levels. If she is already pregnant, the medication should be discontinued.


What concerns do you have for this patient and how would you approach these issues? Discuss at least 2 issues that affect patients with prolactinoma.
Answer 7. Address fertility concerns as above. If she has difficulty conceiving, consider referral to a fertility specialist. Evaluate for signs of depression or anxiety (see more info below)

PROLACTINOMAS

Patients with prolactinomas present poor QoL as evaluated by different generic questionnaires. Gonadal dysfunction is one of the most important problems in these patients. In men, decreased libido, erectile dysfunction, and poor seminal fluid quality are frequent consequences of prolactin hypersecretion. In women, hyperprolactinemia causes amenorrhea, galactorrhea, vaginal dryness, dyspareunia, and decreased libido, which can lead to infertility. These reproductive dysfunctions have a great impact on the patient’s QoL, especially in women (Fig. 3). Mental health and psychological function measures have been described to be impaired in patients with prolactinoma. Altered personality profiles have been reported in these patients compared with the normal population. In particular, patients with prolactinoma presented minor extraversion, lesser novelty seeking, and increased shyness and neuroticism when compared with healthy controls. Moreover, women treated for microprolactinoma have been described as more vulnerable to anxiety and depression symptoms than control individuals.

Treatment

The first-line treatment of prolactinomas, dopamine agonists, are able to reduce tumor size, normalize prolactin levels, and relieve symptoms in these patients, but impaired QoL may persist after successful treatment. Female patients with treated microprolactinoma showed lower scores in physical problems, vitality, emotional aspects, and social isolation compared with control individuals. These results were independent of prolactin levels, current or previous intake of dopamine agonists, and dosage or formulation of this treatment.

What you have learned from this case...

Mrs. Brittany Davis is a 25-year-old G2P1001 woman who presents with a history of irregular menses over the past 2 years, and cessation of menstruation, 6 months ago. Based on the chief complaint of amenorrhea, you start by defining primary and secondary amenorrhea and building the differential diagnosis for each category. You then learned how to evaluate a chief complaint of amenorrhea by first excluding pregnancy, followed by a thorough history and physical and multiple labs that will identify the most common causes of amenorrhea. As you narrow down your diagnosis to common causes, you utilize clues in the history and physical to consider why some entities are more or less likely. You also referred back to the hypothalamic-pituitary-ovarian axis (HPOA) to review several drugs and medications and their underlying mechanism of interference with the HPOA. As you narrow your diagnosis to one entity based on the history/physical, lab values and imaging studies, you consider a syndrome that contains your diagnosis. You also link this syndrome to other clues in the patient’s history. Finally, you become familiar with a treatment plan for the patient, as well as how the treatment would affect the patient’s ability to become pregnant in the future. Lastly, you learn about the quality of life for patients living with this disease and address two such issues.
STUDENTS IN THE WHITE SUBGROUPS: Please prepare a 4-5 sentence summary (~ 30 seconds to 1 minute) of this entire clinical case. This is often asked of students to do in the clinical setting after performing a full H&P. You will each present your summary at the live session.

Student Expectations

- Students are expected to arrive on time, in professional dress, white coat and badge.
- Students are expected to actively participate, show professional behavior such as appropriate listening skills and refraining from disrupting the session (please see the student evaluation rubric for more details).
- Students are expected to have prepared for the live session by reviewing the online “virtual” case and answering all the questions within each part, as well as reviewing the suggested lectures, and completing the required reading (see page 1-2, above) to prepare them for the live session.

ICE Assessment

- The CSIE ICE comprises 3% of the overall block grade in the following way:
  - 1.5% for completing all the questions from Parts A, B, C of the online “virtual” case
  - 1.5% from the student evaluation form (provided by you as the facilitator)

Live Session Facilitator Guide

General Timeline:

8:00-8:30 am - Facilitator Meeting with Content Expert to answer questions
8:30-10:20 am - Meet with your group
10:20-10:30 am - Release students, complete student evaluations and session feedback form
10:30-11:00 am - Faculty debriefing

Recommended timeline for the group activities

- Get started (5 minutes)
- Activity 1 (20 minutes): Online Virtual Case Summary Presentation and Debriefing
- Activity 2 (50-60 minutes): Practice Clinical Cases
- Activity 3 (20-30 minutes): High Yield Endo/Repro Disease Content
Get started (Start at 8:30 am: 5-10 minutes)

- Start the live session by introducing yourself.
- Meet the students and let them introduce themselves.
- Take this time to check attendance utilizing the provided student roster with their pictures/names. This will help in completing the student evaluation form for grading.
- If you are familiar with the students, take a few minutes to check in on them and how they are doing.
- Let the pre-designated student/students connect the computer to the AV system to log on and bring up the google doc forms to be used in the session.

Activity 1 – Online “Virtual” Case Summary and Debriefing (Start no later than 8:40 am: 20 minutes)

PART 1 – Online Virtual Case Summary (10 minutes)

Objective: To concisely present a clinical case, which is often done during rounds in the clinical setting.

Instructions:

- Ask each student in the “white” group to provide a 4-5 sentence summary (~ 30 seconds to 1 minute per student). This is often asked of students in the clinical setting after performing a full H&P. The summary should at least include the following:
  - Presenting symptoms
  - Important (pertinent) history and physical exam findings
  - Pertinent laboratory and other diagnostic test findings
  - Diagnosis
  - Treatment
  - Outcome

Example: Mrs. Davis is a 25 yo G2P1 female with amenorrhea (secondary) for 6 months. Labs revealed elevated prolactin and a microadenoma was found on MRI brain. She was treated with cabergoline, a dopamine agonist.

PART 2 – Online Virtual Case Debriefing (10 minutes or less)

Objective: Review, debrief, and reinforce the contents of the online virtual case.

Instructions:

- This is a brief review of the student online “virtual” case. Consider just opening it up to specific student questions rather than going through the entire case or every question. If there are no questions, move on to activity 2. If there are questions, please ask the “AV student” to bring up the case on eCampus (PDF) so you can review their question. The answers are in your Facilitator Guide PDF document (see also paper copy in your maroon folder).
Activity 2 – Clinical Cases (Start no later than 9:00 am: 50-60 minutes)

Objective: To use clinical clues from the presented clinical vignette to narrow the differential diagnosis. To use scientific data to make a diagnosis and recommend treatment for the identified condition.

Instructions:

1) Divide students into 4 groups of similar size.
2) Each group will work on 2 cases plus a bonus case (all groups will have the same bonus case).
3) Project Activity 2 Handouts A-D in Google docs.
4) Allow the groups 10-15 minutes to work through the cases and answer the provided questions. Encourage them to use online resources.
5) Rotate between groups and guide them if they are struggling (using the answers provided to you).
6) Regroup and go through answers, allowing all four groups to present their work (allow each group to present their two cases, e.g.: group A presents cases 1-2, group B presents cases 3-4, group C presents cases 5-6; group D presents cases 7-8).
7) Briefly discuss the bonus case with them as a large group, highlighting key points.
8) Allow 45-50 minutes for presentation and discussion of the cases.

Group A Cases (Case 1 and 2 plus Bonus case below)

Case 1
Mrs. Katrina Watts is a 35-year-old woman who has complained of nervousness, weakness, and palpitations with exertion for the past 6 months. Recently, she noticed excessive sweating and wanted to sleep with fewer blankets than her husband. She had maintained a normal weight of 120 pounds but was eating twice as much as she did 1 year ago. Menstrual periods have been regular but there was less bleeding.

Vital signs: HR 92/minute and BP 130/60 mmHg. She appears anxious, with smooth, warm, and moist skin. Physical exam shows a fine tremor, a bounding cardiac apical impulse, a pulmonic flow murmur, and she cannot rise from a deep knee bend without aid. Her eyes are not prominent, and she has no focal skin thickening.

Laboratory studies:
Total T4: 15.6 µg/dL (N=4.5-12.5), Total T3: 250 ng/dL (N=80-160), and TSH: 0.1 µU/mL (N=0.2-3.5).

Ultrasound:
The thyroid gland contained 3 nodules, 2 on the right and one on the left with a total gland size of 60 grams (3 times normal size), all nodules being of firm consistency and there was no lymphadenopathy.
Questions:

1. Signs or symptoms of hyper or hypothyroidism? List the signs and symptoms.
2. Laboratory evidence of hyper or hypothyroidism? (explain)
3. What is the most likely cause?
4. What additional test would be helpful to confirm diagnosis?
5. What are the treatment options?

Answers:

1. Hyperthyroid. Anxious, warm, smooth skin, fine tremor, bounding apical impulse, pulmonic flow murmur
2. High total T4/T3 and low TSH
3. Toxic multinodular goiter
4. A thyroid scan to verify the autonomy of the thyroid nodules. Needs fine needle aspiration (FNA) evaluation of thyroid nodules larger than 1 cm or with suspicious ultrasound features prior to radiiodine treatment if none of the nodules show hyperactivity on the thyroid scan.
5. Radioactive iodine or surgery with antithyroid drug pretreatment (notes from Dr. Cryar: iodine is infrequently used as pretreatment. It must be timed properly because the patient may have break through of the Wolff-Chaikoff effect after a few weeks and patients with autonomously functioning nodules may have the Jod-Basedow phenomenon resulting in hyperthyroidism.)

Case 2
Mr. Ted Bran is a 35-year-old man who presents to the clinic because of 6 months of fatigue and weakness. He often feels lightheaded when he first gets out of bed in the morning or stands suddenly. Review of symptoms is positive for frequent headaches, nausea, and vomiting. Orthostatic blood pressures show a blood pressure of 125/75 mmHg seated and 105/60 mmHg standing. Physical exam reveals hyperpigmentation of the skin.

Laboratory results:
Na 126 mEq/L
K 5.2 mEq/L
Cl 97 mEq/L
HCO3 19 mEq/L
AM Cortisol 4.3 mcg/dl

Questions:

1. What are the important clues in the brief HPI?
2. What do the laboratory tests reveal?
3. What is the likely diagnosis?
4. What are some etiologies of this disease?
5. How would you confirm the diagnosis?
6. How is it treated?
Answers:
1. Middle aged male, weakness/fatigue, orthostatic hypotension, and hyperpigmentation
2. Hyponatremia, hyperkalemia, low serum cortisol
3. Addison disease
4. Most cases are idiopathic or autoimmune related. Other causes include: DIC, Waterhouse-Friderichsen syndrome (hemorrhagic necrosis of the adrenal gland, classically due to meningococcemia), granulomatous disease such as TB, HIV infections, neoplasm, trauma.
5. Use the Cosyntropin stimulation test (ACTH stimulation test) to confirm diagnosis and to differentiate primary from secondary causes.
6. Hydrocortisone or prednisone, fludrocortisone. Stress dosing during current illness and surgery to avoid adrenal crisis.

Group B Cases (Case 3 and 4 plus Bonus case below)

Case 3
Mrs. Nancy Liu is a 67-year-old woman who presents to the clinic with a 1-month history of constipation. She also is experiencing vague diffuse abdominal pain, nausea and vomiting. Her only other complaint is diffuse bone pain over the last month which she attributed to “just getting old.” Her physical exam shows diffuse abdominal tenderness.

Laboratory results:
Na 140 mEq/L
K 4.0 mEq/L
Cl 110 mEq/L
HCO3 26 mEq/L
BUN 20 mg/dl
Creatinine 1.2 mg/dl
Albumin 4.0
Calcium 12.3 mg/dl
Phosphate 2.0 mg/dl
PTH 100 pg/ml

Questions:
1. What are the important clues in the brief HPI?
2. What do the laboratory tests reveal?
3. What is the likely diagnosis?
4. How is it treated?

Answers:
1. Elderly woman, constipation with associated symptoms, bone pain
2. Hypercalcemia, low phosphorus, elevated PTH, normal renal function
3. Primary hyperparathyroidism (80% due to PTH-producing parathyroid adenoma)
4. Acute severe forms – hydration, loop diuretics to increase calcium excretion. Also calcitonin and bisphosphonates. Long term treatment – parathyroidectomy (cure rates 96-98%)

Case 4
Ms. Jenny Fredrick is a 19-year-old woman who presents to the ED with three days of fever, abdominal pain, and vaginal discharge. She is sexually active but does not always use protection. She has been with her current partner for 1 month. Her last menstrual period ended 5 days ago. Vitals reveal T 101.4 °F, heart rate 92/min, respiratory rate 12/min, blood pressure 110/70 mmHg. On physical examination she has diffusely tender abdomen without rebound or guarding. She has cervical motion tenderness and right-sided adnexal tenderness.

Laboratory results:
CBC – WBC 17,000/mm³
U/A – 10 WBC/hpf, nitrates negative
Beta-HCG – negative
Vaginal saline wet mount – pH 4.5, WBCs >10 per HPF, no clue cells, no trichomonads, and KOH wet mount negative for budding yeast or hyphae.

Questions:
1. What are the important clues in the brief HPI?
2. What do the laboratory tests reveal?
3. What is the likely diagnosis? How can this be confirmed?
4. How is it treated?

Answers:
1. Adolescent female, sexually active, abdominal pain, vaginal discharge, fever, cervical motion tenderness
2. Leukocytosis, pyuria (likely sterile), leukorrhea
3. Pelvic inflammatory disease, PCR for Chlamydia and N. gonorrhea (first catch urine or cervical swab)
4. Uncomplicated PID – outpatient management with IM Ceftiriaone plus doxycycline +/- metronidazole (CDC gives multiple other regimens). Hospitalize for IV ABX if severely ill, pregnant, concern for tubo-ovarian abscess, unable to take oral medications. Surgery indicated for tubo-ovarian abscess.

Group C Cases (Case 5 and 6 plus Bonus case below)

Case 5
Mrs. Carla Williams is a 24-year-old nulligravid woman who presents to the clinic with menstrual problems. She reports that her periods are irregular and widely spaced. Menarche was at age 14 and have never been regular. During the past year she has had 3 complete menses, once going 6 months between periods. She is sexually active and uses condoms for contraception. Vitals this visit are temp 98.6 °F, heart rate 80/min, blood pressure 140/85 mmHg. She is 165 cm (5’4’’) tall and weighs 83 kg (190
lb). Her exam shows facial acne with a few dark hairs on the upper lip and chin. Hyperpigmentation noted over neck and axillae. Speculum and bimanual exam are normal.

Laboratory results:
Pregnancy test – negative  
FSH – normal  
LH – elevated  
TSH – normal  
Prolactin – normal  
Chemistry and lipid panel normal.  
Fasting insulin 36 µU/ml (5-20 µU/ml)  
Fasting blood sugar 130 mg/dl (70-100 mg/dl)  
Total testosterone 78 ng/dl (8-60 ng/dl)  
Free testosterone 30 pg/ml (0.06-1.08 pg/ml)  
17OH-progesterone 92 ng/dl (<200 ng/dl)  
DHEAS 340 ug/dl (44-332 ug/dl)  

Pelvic Ultrasound – bilateral enlarged ovaries with multiple peripheral small follicles and increased stromal echogenicity

Questions:  
1. What are the important clues in the brief HPI?  
2. What do the laboratory tests reveal?  
3. What is the likely diagnosis?  
4. How is it treated?

Answers:  
1. Young adult, irregular periods, obese, acne, acanthosis, hirsute, hypertensive  
2. Elevated LH, elevated fasting insulin and glucose, elevated testosterone and DHEAS, US with string of pearls signs as seen with PCOS  
3. Polycystic ovarian syndrome (PCOS)  
4. OCPs – to regulate cycles and halt excess androgen production  
a. Metformin and weight reduction to help with insulin resistance  
b. Clomiphene can be used for ovulation induction, if fertility is desired

Case 6
Mrs. Christina Walters is a 32-year-old woman who presents to the clinic with 6 months of weight gain. She has amenorrhea and is frustrated by excessive facial hair growth. She has had no recent changes in her diet and is on no medications. Her vital signs show a temp 98.6 °F, heart rate 80/min respiratory rate 12/min, blood pressure 148/90 mmHg. Physical exam reveals a well-developed hirsute female with truncal obesity, abdominal striae, and peripheral edema. She struggles to rise from a chair during her neurologic exam.
Laboratory results:
Na 140 mEq/L
K 3.4 mEq/L
Cl 92 mEq/L
HCO3 25 mEq/L
Glucose 225 mg/dl
Urinary free cortisol (UFC) level 410 mcg/24 hour

Questions:
1. What are the important clues in the brief HPI?
2. What do the laboratory tests reveal?
3. What is the likely diagnosis? What additional testing would be helpful? What are some etiologies of this disease?
4. How is it treated?

Answers:
1. Middle aged woman, weight gain, amenorrhea, hirsutism, hypertension, truncal obesity, striae, peripheral edema, proximal muscle weakness
2. Hyperglycemia, markedly elevated urinary free cortisol (UFC)
3. Cushing syndrome
   a. 24 hour UFC, Dexamethasone suppression test, midnight plasma or salivary cortisol, serum ACTH level.
   b. High ACTH – pituitary adenoma or an ectopic ACTH-producing neoplasm (ACTH-dependent Cushing’s)
   c. Low ACTH – Adrenal tumor/hyperplasia or exogenous glucocorticoid administration (ACTH-independent Cushing’s)
4. Treatment
   a. ACTH independent – surgical removal of adrenal tumor
   b. ACTH dependent – removal of pituitary corticotroph tumor
   c. Non-resectable tumors or severe disease awaiting surgery: Ketoconazole (inhibits glucocorticoid production), metyrapone (inhibits cortisol formation in adrenal pathway), and aminogluthethimide (inhibits the synthesis of steroids)

Group D Cases (Case 7 and 8 plus Bonus case below)

Case 7
Mrs. Carman Rodriguez is a 26-year-old woman who presents to the emergency department with intense lower abdominal pain. She also complains of lower back pain and nausea. No fever is reported. She has had several previous visits to the ER during the last year with similar complaints. She started her menstrual period yesterday. She is married with no children. She has been trying to get pregnant for the last 2 years. Her older sister has a similar history. Abdominal exam reveals a diffusely tender lower abdomen. Pelvic exam reveals fixed retroversion of the uterus.
Laboratory results:
CBC – normal WBC
U/A and urine culture – hematuria (felt to be menstrual in origin) and negative
Serum pregnancy test – negative
GC/Chlamydial testing – negative

Ultrasound (US) of Pelvis:
Adnexal mass of complex echogenicity, internal echoes consistent with blood

Questions:
1. What are the important clues in the brief HPI?
2. What do the laboratory tests reveal?
3. What is the likely diagnosis?
4. How can this be confirmed?
5. How is it treated?

Answers:
1. Young adult female, recurrent abdominal pain during periods, infertile, family history
2. Normal labs (no signs of infection, not pregnant), US consistent with endometriosis or hemorrhagic cyst
3. Endometriosis
4. Laparoscopy with biopsy proven histology is standard for dx of endometriosis
5. Medical – alleviate symptoms - NSAIDs, and suppress menstrual cycles - OCPs, medroxyprogesterone (induces pseudopregnancy), androgen derivatives, or gonadotropin releasing hormone agonist (induces pseudomenopause). Surgical – for refractory cases may include laparoscopic laser vaporization, cauterization or excision, ovarian cystectomy for endometrioma, hysterectomy

Case 8
Mrs. Charis Gold is a 34-year-old African American G0 woman who presents for her annual gynecological exam. She reports increasing fatigue over the past year and thinks her periods are heavier and more painful than before. Ibuprofen helps with the pain. She is generally healthy and take hydrochlorothiazide for hypertension. Onset of menarche was at age 9, and she denies previous problems with periods. Vital signs include a heart rate of 105 bpm and BP 120/78 mmHg. She appears tired and pale. Cardiac, lung, and abdominal exams are normal. On pelvic exam, there is no discharge or cervical motion tenderness. Her uterus feels enlarged to 12 week size and misshapen.

Laboratory results:
Hgb 8.7 g/dl, HCT 27%, MCV 72
Serum ferritin - low
Urine pregnancy test – negative

Questions:
1. What are the important clues in the brief HPI?
2. What do the laboratory tests reveal?
3. What is the likely diagnosis? How can this be confirmed?
4. How is it treated?

Answers:
1. Adult, African American woman, fatigue, menorrhagia and dysmenorrhea, pale, uterine enlargement (mass)
2. Microcytic anemia – iron deficiency
3. Uterine leiomyomata (fibroid), Pelvic US, saline hysterosonography (submucosa myoma missed on US), MRI (highly accurate in size, location, and # of leiomyomas), hysteroscopy – (identification and removal of submucosa leiomyomas)

Bonus Case (same bonus case for all groups)
You receive notice that a 1-week-old male infant in your practice named Jeremy Smith has an elevated TSH level on the first newborn screen. You contact the family immediately and ask them to come in that day. The parents report that the baby is doing well since discharge from the nursery with no concerns from the parents.

Physical Exam:
Infant has regained birthweight and has a normal physical exam.

Laboratory studies:
Texas Newborn Screen

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Screening Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino acid disorders</td>
<td>Normal</td>
</tr>
<tr>
<td>Organic acid disorders</td>
<td>Normal</td>
</tr>
<tr>
<td>Galactosemia</td>
<td>Normal</td>
</tr>
<tr>
<td>Biotinidase deficiency</td>
<td>Normal</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Abnormal, high TSH</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia (CAH)</td>
<td>Normal</td>
</tr>
<tr>
<td>Hemoglobinopathies</td>
<td>Normal</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Normal</td>
</tr>
<tr>
<td>SCID</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Questions:
1. While most infants with congenital hypothyroidism have normal exams at birth, what signs/symptoms should alert the physician to the condition?
2. What are the laboratory test(s) to obtain immediately?

3. Why is early diagnosis and treatment so important?

4. What is the treatment and how is it administered?

Bonus Case Answers:
1. Signs and symptoms: decreased activity (the good baby that doesn’t cry but sleeps), poor feeding and weight gain, small stature, jaundice, decreased stooling or constipation, hypotonia, hoarse and cry. Physical findings: coarse facial features, macroglossia, large fontanelles, umbilical hernia, mottled-cool-dry skin, developmental delay, pallor, myxedema, and goiter.

2. TSH, free T4, also repeat newborn screen

3. Delayed diagnosis and treatment can result in severe developmental delays (average IQ 76 in pre newborn screen era, untreated patients lose an average of 1-2 IQ points per month until age 2, 40% of untreated patients require special education in school). Optimal diagnosis is within 10-13 days and normalization of thyroid hormone blood levels by age 3 weeks.

4. Levothyroxine 10-15 mcg/kg/day, crushed in a spoon dissolved in small amount of breast milk or water and given immediately via syringe.

Activity 3 – High Yield Endo/Repro – Label the Axis [Start by 9:50 to 10:00 am: 20-30 minutes]

Objective: To describe and understand the physiology of the hypothalamic-pituitary axis and its role in disease (pathophysiology).

Instructions:
- Divide into four groups A thru D
- Each group will complete the diagram of the assigned portion of hypothalamic-pituitary axis.
- Each group will be given one drug and one disease related to the axis. For each drug or disease they will look up the mechanism of action and determine how this would manipulate the HPA and add it to the diagram.
- Regroup and have each group share their answers.

Group A HP-Adrenal Axis

Instructions:
1) Label the hormones (text boxes) to complete the Adrenal Axis
2) For each drug or disease look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease - Addison Disease
   b) Drug - Corticosteroid
Group A HP-Adrenal Axis Answers

1) Label the hormones (text boxes) to complete the Adrenal Axis
   A. Corticotropin releasing hormone (CRH)
   B. Adrenocorticotropic Hormone (ACTH)
   C. Cortisol
2) For each drug or disease, look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease - Addison Disease
      - Addison disease (primary adrenal insufficiency) \(\rightarrow\) decreased cortisol production
        \(\rightarrow\) increased ACTH \(\rightarrow\) ACTH contains melanocyte-stimulating hormone \(\rightarrow\) tan
   b) Drug – Corticosteroid
      - Corticosteroids (prednisone) \(\rightarrow\) inhibit ACTH and CRH production \(\rightarrow\) decreased cortisol production
      - Removing oral steroids abruptly can cause adrenal crisis since the adrenals have not been stimulated to make (or cannot make) cortisol and ACTH is low from oral steroids
Group B HP-Thyroid Axis

Instructions:
1) Label the hormones (text boxes) to complete the Thyroid Axis
2) For each drug or disease look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease – Graves’ Disease
   b) Drug – Levothyroxine
Group B HP-Thyroid Axis Answers

1) Label the hormones (text boxes) to complete the Thyroid Axis
   A. Thyrotropin Releasing Hormone (TRH)
   B. Thyroid Stimulating Hormone (TSH)
   C. Thyroid hormones - T4, T3

2) For each drug or disease look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease – Graves’ Disease
      • Graves’ disease (Hyperthyroidism) $\rightarrow$ high T3, T4 $\rightarrow$ negative feedback to hypothalamus and pituitary $\rightarrow$ decreased TSH production
   b) Drug – Levothyroxine
      • Levothyroxine (in patient with hypothyroidism [high TSH]) $\rightarrow$ mimics T3, T4 $\rightarrow$ decreases TSH
Group C HP-Gonadal Axis

Instructions:
1) Label the hormones (text boxes) to complete the Gonadal Axis
2) For each drug or disease look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease – Menopause
b) Drug – Oral contraceptives (estradiol/progesterone)

Group C HP-Gonadal Axis Answers

1) Label the hormones (text boxes) to complete the Gonadal Axis
   A. Gonadotropin releasing hormone (GnRH)
   B. Follicle stimulating hormone (FSH) and luteinizing hormone (LH)
   C. Estradiol
   D. Testosterone

- Development/maintenance of reproductive tissues
- Maintaining oocytes
- Masulinization
- Sperm produc
- Muscle growth
- Aggression
2) For each drug or disease look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease – Menopause
      • Menopause \(\rightarrow\) decreased estrogen \(\rightarrow\) less negative feedback \(\rightarrow\) FSH increases
   b) Drug – Oral contraceptives (estradiol/progesterone)
      • Oral contraceptives (estradiol/progesterone) \(\rightarrow\) negative feedback on LH, FSH
        \(\rightarrow\) prevents LH surge \(\rightarrow\) no ovulation
Group D Growth Hormone and Prolactin Secretion

Instructions:
1) Label the hormones (text boxes) to complete the Growth Hormone and Prolactin pathways
2) For each drug or disease look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease – Acromegaly
   b) Drug – Cabergoline
Group D Growth Hormone and Prolactin Excretion Answers

1) Label the hormones (text boxes) to complete the Growth Hormone and Prolactin pathways
   A. Somatostatin
   B. Growth Hormone Releasing Hormone (GHRH)
   C. Growth Hormone (GH)
   D. Insulin-like growth factor 1 (IGF-1)
E. Dopamine
F. Prolactin

2) For each drug or disease look up the mechanism of action and determine how this would manipulate the HPA. Add to the diagram.
   a) Disease – Acromegaly
      • Acromegaly (GH adenoma) \(\rightarrow\) increased GH \(\rightarrow\) increased IGF-1 \(\rightarrow\) excessive non-linear bone growth
      • Can’t easily measure GH so IGF-1 measured
   b) Drug – Cabergoline
      • Cabergoline (D2 agonist) \(\rightarrow\) mimics dopamine \(\rightarrow\) inhibits prolactin
      • Treatment selected for the patient in the student case with a diagnosis of prolactinoma