CASE VIGNETTE

“A woman born in 1967 presents with abdominal pain…”

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** Please do not open this packet until instructed to do so.**
Mrs. Ellen Anderson, a white architect born in 1967, is a new patient to your primary care office. She presents with a 3-day history of abdominal pain.

**Present Illness**
Mrs. Anderson tells you her pain is located in her right lower quadrant. It is constant, sharp, nonradiating, and intensifying. She rates its current severity as 8 on a scale of 10. When you ask whether the location of this pain has changed, she reports, “No.” She cannot cite any aggravating or ameliorating factors. She denies associated fever or chills, malaise, nausea, or vomiting. She denies noticing blood in her stools, change in stool color, or diarrhea. She does report constipation, with bowel movements every 2–3 days, but this has been her normal pattern for at least 10 years. Her last bowel movement was this morning; and her pain was not relieved with defecation. She denies noticing any abdominal or groin masses. She denies any abdominal skin infections or rashes. She also denies abdominal trauma, pain on urination, blood-tinged urine, or increased urinary urgency or frequency.

Mrs. Anderson’s last menstrual period was 8 weeks ago and was normal in timing and duration. Her menses typically occur every 28–30 days. She denies any known history of sexually transmitted diseases. She has been sexually monogamous with her husband of 10 years and had no previous sexual contacts. Neither she nor her husband uses contraception. She denies any unusual vaginal discharge or bleeding, vaginal itching, extreme menstrual cramping, pain with intercourse, or vulvar lesions.

Her sleep has been more fragmented than usual these past 3 days because she’s been waking frequently secondary to pain. She reports no loss of appetite nor recent weight change. She denies any recent travel within or outside the country.

She denies any history of gastrointestinal or gynecologic maladies; and she denies any history of appendectomy or other abdominal or pelvic surgery.

**Medical History**
Mrs. Anderson had chicken pox as a child and recalls being told she has “fibrocystic breasts” but denies any other significant medical history, including malignancies.

**Surgical History**
She had an uncomplicated tonsillectomy and adenoidectomy at 10 years old and has had no other surgeries. She denies any breast surgery or aspiration of breast cysts.
Gynecologic History
Mrs. Anderson has never been pregnant. She reached menarche at age 13 years and describes 4–5 days of mild-to-moderate flow with each cycle.

Social History
Mrs. Anderson states that she does not drink. She has never smoked or used illicit drugs. She lives with husband and denies any problems with anger or safety in the relationship. They have no pets.

Family History
Both of Mrs. Anderson’s parents are alive. Her mother, born in 1944, has IDDM but is otherwise healthy. Her father, born in 1938, is hypertensive, but is also otherwise healthy. Mrs. Anderson’s only sibling, a brother born in 1970, has no significant medical history. All of her grandparents are deceased, both grandfathers suffering heart attacks in their early 70s, her paternal grandmother succumbing to a cerebrovascular accident at age 66, and her maternal grandmother succumbing to unknown complications of diabetes.

Medications
Mrs. Anderson takes a multivitamin daily. She denies using any herbal remedies or other OTC medications.

Allergies
Mrs. Anderson has no known drug, food, latex, or other allergies.

Focused Review of Systems
Cardiac: Denies palpitations, syncope, dizziness, lightheadedness, chest pain.

Pulmonary: Denies shortness of breath, cough, hemoptysis, wheezing, dyspnea on exertion.

Endocrine: Reports increased breast tenderness and “lumpiness” over the past 2 weeks.

Denies heat or cold intolerance, dry skin, tremor, polydypsia/polyphagia/polyuria.

Musculoskeletal: Denies joint pain or stiffness, muscle aches or cramps, weakness, lower back or flank pain.
Neurologic: Does not need glasses for distance vision or reading. Denies recent vision, olfactory, or taste changes. Denies new onset weakness, coordination loss, neuralgias, or other sensory changes. Denies episodes of loss of consciousness with loss of bladder or bowel control. Denies severe or frequent headaches, with and without prior aura.

Psychological: Denies depression, anxiety, obsession with weight and exercise, difficulties with food, laxative abuse.

1. What is your differential diagnosis (top eight candidates)?

2. What should your physical exam entail?

References 1–23
Physical Exam

General: Well-developed, well-nourished young woman in moderate distress, grimacing secondary to pain

Height: 5’6”

Weight: 135 pounds

Vital Signs: BP 140/90 (sitting) and 136/92 (standing), HR 98 (sitting) and 104 (standing), RR 16, T 99.0

Neck: Supple, no palpable masses or tender lymph nodes, thyroid symmetric and nonenlarged

Heart: Regular rate and rhythm; S₁S₂ audible; PMI nondisplaced; no murmurs, rubs or gallops

Lungs: Clear to auscultation with equal breath sounds bilaterally, no wheezing, rhonchi, or rales

Abdomen: Flat, soft, with normoactive bowel sounds in all four quadrants, no palpable masses or organomegaly; no visible lesions, ecchymoses, or rash, no dyesthesia to contact

Negative Murphy’s sign

Positive tenderness to light palpation and voluntary guarding of right lower quadrant

No rebound tenderness

No inguinal or femoral masses

Back: No costovertebral angle tenderness; no visible lesions, ecchymoses, or rash

Rectal: Heme-negative, normal sphincter tone, brown stool of soft consistency, no hemorrhoids or other perianal lesions

Appendix nontender
Pelvic: External labia well developed and appropriate for age; no lesions or anomalies

Vaginal mucosa pink and moist and without lesions or suspicious discharge

Exocervix with 2–3 mm firm circumferential rim at peripheral margin. Rim pale pink and moist, without lesions or suspicious discharge, and nonfriable. Cervix central to rim projects 1 cm into vaginal cavity, is pale pink and moist, without lesions or suspicious discharge, and nonfriable. (See photograph in the Handout on page 4.) No cervical motion tenderness

Uterus nontender, slightly softened, upper range of normal size

Right adnexa extremely tender to palpation with slight fullness

Left adnexa unremarkable and without palpable masses

Extremities: No clubbing, cyanosis, or edema

No rash or other lesions

3. What is your revised differential diagnosis (top four candidates)?

4. What laboratory test(s) would you like to perform and why?
Serum beta-HCG Pregnancy Test: Positive

Stat Complete Blood Count (CBC) with Differential: Pending

5. *What is your presumed diagnosis for Mrs. Anderson’s abdominal pain?*

6. *What is your next management step?*

References 24–33
You suspect Mrs. Anderson has an ectopic pregnancy and send her to the emergency department for evaluation. You also wonder whether her cervical lesion could somehow be related to the current situation or whether it’s an incidental finding. You decide to perform a Medline search later in the evening.

7. What study should be conducted to determine whether Mrs. Anderson has an ectopic pregnancy?

8. What are known risk factors for ectopic pregnancy?
The pelvic ultrasound in the emergency department reveals a 3x3 cm gestational sac in Mrs. Anderson’s right fallopian tube. Her CBC results are reassuringly normal.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>33.3</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>11.1</td>
</tr>
<tr>
<td>WBC</td>
<td>9,000</td>
</tr>
<tr>
<td>Platelets</td>
<td>140,000</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>39%</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>56%</td>
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<tr>
<td>Monocytes</td>
<td>3%</td>
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<tr>
<td>Basophils</td>
<td>1%</td>
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<tr>
<td>Eosinophils</td>
<td>1%</td>
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Laparoscopic surgery* is scheduled for that afternoon and proceeds without complication. Before discharge, the obstetrician talks with Mrs. Anderson about her cervical anomaly and its possible relation to exposure to diethylstilbestrol (DES) in utero. He tells her that follow-up on these findings is imperative.

*Mrs. Anderson is treated with a right-sided salpingectomy, although more commonly she would receive chemotherapy (Methotrexate) or laparoscopic salpingostomy, removing the ectopic pregnancy and preserving the tube.

9. What is your differential diagnosis for her cervical lesion?

References 34–39
One week later, Mrs. Anderson presents to your office for a follow-up visit. She is visibly distraught, commenting: “It’s the abnormality on my cervix that made me lose the pregnancy, right?” You reassure her that the lesion does not appear to be cancerous but resembles a pseudopolyp. Associated with her ectopic pregnancy it makes you suspect that she may have been exposed to diethylstilbestrol (DES) in utero, as the gynecologist told her at the time of her surgery.

“How have you ever heard of this medication? Usually it’s referred to as ‘DES.’”

“No, it doesn’t ring a bell. What is it?”

10. What is diethylstilbestrol (DES)? When was it used?

11. What were and are DES’s indications for use? Was it an effective agent for its initial indication?

12. What is DES’s mechanism of action?

References 40–55

Caveats to consider when assessing a patient’s health risks from DES exposure

- Most people who were exposed to DES have not experienced negative health consequences.
- These case materials represent the state of DES research at the time of development, and interpret current studies at that time for clinical practice.
- Research on DES is ongoing, and some animal studies have identified health effects that might yet occur.
Many facts and findings you have gleaned from Mrs. Anderson’s history and physical exam and from her present illness suggest DES exposure before birth. You believe she needs to know more about the consequences of DES exposure before you give her further advice.

13. What are DES’s associated adverse effects in women exposed in utero (DES Daughters)?

14. What are the treatment options and prognosis of clear cell adenocarcinoma (CCA)?

References 56–100
Case Vignette

You begin to explain, “This was a medication given to pregnant women between 1938 and 1971 to help prevent miscarriages…”

“Oh wait—I actually wanted to ask you about that. My mother had a number of miscarriages before she had my brother and me. While pregnant with each of us, she was given something to prevent her from having another miscarriage. Is it still available? Could you prescribe it for me? Obviously it worked.”

Mrs. Anderson does not recall the name of the medication her mother took during her pregnancies but offers to ask her mother later in the day. She adds: “What about my mother? If she did indeed take DES, is she at any risk for anything?”

15. What are the adverse effects in women prescribed DES while pregnant?

References 101–109
You answer, “Well, we’ve seen a modest increase in the risk for breast cancer. To put it in perspective for you, having a mother or sister who had breast cancer about doubles a woman’s chance of developing breast cancer. Having been prescribed DES has a much smaller effect on a risk—instead of multiplying the usual risk by 2, it seems to multiply the risk by 1.3.”

Mrs. Anderson comments that her brother, too, has been trying to have a child for many years unsuccessfully but hasn’t pursued the matter further.

16. **What are the adverse effects of DES in men exposed in utero (DES Sons)?**

References 110–130
“If I’m able to have children, will I be able to carry the pregnancy?” Mrs. Anderson asks you.

17. **What is the impact of DES on the third generation (the offspring of DES Daughters and Sons)?**

References 131–138
Mrs. Anderson is concerned that she and her family might have to have tests and might require intense screening by a specialist in DES exposure.

18. What are the current screening recommendations for DES Daughters?

19. What are the current screening recommendations for women prescribed DES while pregnant?

20. What are the current screening recommendations for DES Sons?

21. When should a primary care provider refer a DES Daughter to a specialist with DES experience? What services should the obstetrician/gynecologist provide?

References 126–145
You recommend that Mrs. Anderson see Dr. Adams, an obstetrician/gynecologist who specializes in the care of DES patients. “She will be able to determine whether your cervical lesion is DES-related. As I said, my suspicion is this is the case. Dr. Adams also will be able to assist you with several fertility options. I’ll send her a copy of the information you told me today and that will help expedite matters.”

“Here’s some more information about DES,” you state. “On this sheet are a list of several self-help organizations, support groups, and other useful resources. Please contact any of them if you have any questions or concerns. And please feel free to call me any time with any questions.”

“Thank you. I’ll call Dr. Adams.”

“You’re welcome. Again, please don’t hesitate to call. I’m glad you came back in.”

**22. What DES advocacy and information resources are available to patients and health care providers?**

**23. What research on DES is being conducted?**
Epilogue
Mrs. Anderson calls you later that evening to tell you her mother is not sure whether she was prescribed DES. You suggest that Mrs. Anderson assist her mother in tracking down this information by contacting the family physician who may have prescribed the medication. He might no longer be practicing, you acknowledge, but the office still should have access to her mother’s medical records.

One month later, Mrs. Anderson calls to confirm that her mother was prescribed desPlex throughout her pregnancies with both herself and her brother.

Several months later you receive a letter from Dr. Adams in which she describes the results of Mrs. Anderson’s formal fertility work-up. A hysterosalpingogram indicated that Mrs. Anderson has almost complete stenosis of her left fallopian tube, in addition to the complete obstruction of her right fallopian tube (which was removed earlier in surgery). Her uterus appears to be of normal morphology on the basis of this study. Dr. Adams has recommended in vitro fertilization to Mrs. Anderson. Mrs. Anderson is considering this option; but has not yet made a final decision.