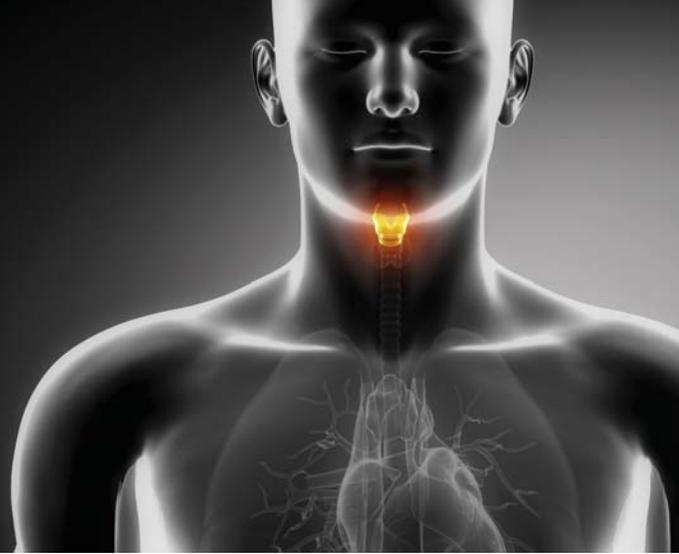


# Hot and Bothered: A Case of Endocrine Disease

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## Part I – A Well-Baby Exam

Robert handled three-month-old Hayden's carrier and held open the door for his wife, Carrie.

"Any particular concerns about Hayden today?" asked Dr. O'Dell as they entered the examination room.

As she lifted Hayden from the carrier, Carrie said, "I don't think that Hayden is growing as fast as James did. And she might be running a slight fever."

Dr. O'Dell examined Hayden and checked her computer files. "Hayden's temperature is somewhat elevated, her skin is damp and her pulse is higher than I'd like."

She tilted the screen so both parents could see. "From this graph it appears that Hayden is falling behind her expected weight curve. Are you still breast-feeding her? Breast-fed babies tend to have slightly lower body weights."

"We shifted to formula after the first month, so that makes two months on formula now," replied Carrie.

"Does she eat well?"

"No problem with that. She's always hungry," Carrie answered, as Hayden pumped small fists in the air and screeched in agreement. "And fussy."

Robert added, "I'm worried about Carrie, too. She has some of the same symptoms as Hayden. And she's not sleeping well either."

Carrie smiled tiredly, pushing back a strand of hair. "Hot and bothered seems to be my middle name these days."

"Demands of a new baby can be exhausting, as you know. Some irritability can be expected," Dr. O'Dell glanced at Robert, "especially if you aren't getting enough sleep."

"Robert helps out," Carrie said quickly. "Lots of things bug me right now, that's all. I'm sure it's nothing."

"But it's got to be something," insisted Robert. "Carrie's always complaining about how warm the house is, and she's lost weight."

"Robert!"

"Carrie, I'm worried!"

Dr. O'Dell shifted from Hayden to examining Carrie. After collecting her vital signs, Dr. O'Dell manipulated the glands in Carrie's throat area and frowned. "You do seem to share several of Hayden's symptoms, like her elevated body temperature and rapid pulse, but I'm more concerned about this thyroid enlargement. How much do you know about the thyroid gland and how it operates?"

Both parents shook their heads, as Hayden gurgled.

“Hayden wants to know too,” Carrie said, trying to lighten the mood.

Dr. O’Dell smiled. “You know how much I like my patients to have background knowledge, but the thyroid situation is pretty complicated. I’ll just stick to the main points today to get you up to speed. Okay?”

At their nods, she continued. “The regulation of the system starts when the hypothalamus in the brain releases TRH, or thyrotropin-releasing hormone. This TRH acts on the pituitary, causing that gland in turn to release thyroid-stimulating hormone. With me so far?”

“You mean this all starts in the brain, not in her throat?” Robert protested.

“Yes, the brain is an important player in hormonal control. For today, let’s concentrate on the pituitary and the thyroid. The TSH released from the pituitary acts on the thyroid to help that gland release thyroid hormone, known as thyroxin, into the bloodstream. If your thyroid is overactive or enlarges around your throat, it produces too much thyroxin, and that can cause increased metabolism. A simple blood test for these hormones will help rule out thyroid problems.”

Both parents were silent for a moment, thinking over what they’d learned.

Robert took Carrie’s hand. “But this is easy to fix, right Doctor?”

Dr. O’Dell patted Carrie’s arm. “Most cases have straightforward treatments.”

A blood sample was taken from both Carrie and Hayden, and a follow-up visit was scheduled for a week later.

### Questions

1. What symptoms (in Carrie and Hayden) most clearly relate to an increase in metabolic rate?
2. Diagram the thyroid–pituitary relationship for a normal individual. Include the glands and several cells within each gland. High thyroxin levels are known to feed back to the pituitary, causing a reduction of TSH levels. Add this feedback loop to your diagram. Make sure you recognize the important role of the hypothalamus, even though it is not the focus of the case.
  - a. Is the thyroxin feedback loop described above a positive or a negative feedback loop?
  - b. Draw/label the cell receptors on the thyroid (and on the pituitary) necessary for feedback control.
3. Examine your thyroid-pituitary diagram. Remember that TSH is released at a constant, moderate level in order to maintain normal thyroxin levels in the blood.
  - a. What would be the immediate result of high TSH level on thyroxin level?
  - b. How would the feedback mechanism function to restore homeostasis after high TSH levels? Include receptor details.
  - c. What would be the immediate result of low TSH level on thyroxin level?
  - d. How would the feedback mechanism function to restore homeostasis after low TSH levels? Include receptor details.
  - e. Summarize: Which of the two gland systems is considered to be “on” until it is turned “off”?

## Part II – The Follow-up Visit

“I have some interesting results to show you,” Dr. O’Dell said as Carrie and Robert brought Hayden into the examination room. “Carrie, I didn’t know that you participated in the study that Dr. Rasam, our endocrinologist, ran a few years ago.”

“I wasn’t sick,” Carrie answered. “They asked for healthy volunteers, and they took a blood sample, but I wasn’t chosen for the actual study.” She sounded disappointed.

Dr. O’Dell smiled. “Dr. Rasam said they were overwhelmed by volunteers, so they couldn’t use everyone. Luckily, your initial results were still in the database, so I was able to compare your recent data with the previous test. That will help us see any trends in the data over time. Take a look,” she said as she swiveled the screen to show Carrie’s results:

	<i>Carrie 2 years ago</i>	<i>Carrie currently</i>	<i>Normal values</i>
<i>Thyroid hormone (thyroxin)</i>	6.0 ug/dL	19.5 ug/dL	4.5–12.5 ug/dL
<i>Thyroid stimulating-hormone (TSH)</i>	1.03 mIU/L	0.1 mIU/L	0.3–3.04 mIU/L

### Questions

1. Characterize Carrie’s thyroid hormone and TSH levels over time.
2. Return to your thyroid-pituitary diagram.
  - a. Assuming that TSH is the only factor involved, predict what TSH level (low, high) would be necessary to maintain her current thyroxin level.
  - b. Consider Carrie’s values (as high or low) in your diagram. What inconsistency is revealed by these data?
  - c. Is Carrie’s feedback system functioning normally? Explain.

## Part III – Additional Testing

Dr. O'Dell continued. "Low TSH levels should result in low thyroxin levels, not the reverse. Something seems to be stimulating the thyroid in the absence of TSH. When I saw your results, I spoke to Dr. Rasam and he suggested a special ELISA test on the blood sample I collected from you. The ELISA result indicates that Carrie shows early signs of Graves disease."

Both Carrie and Robert looked confused.

"Carrie, a subset of your immune system antibodies is mistakenly attacking your thyroid gland, causing an increase in hormone production. Common symptoms include insomnia, anxiety, fatigue, heat sensitivity, weight loss, and increased sweating. Your hair might get brittle, and your menstrual cycle might change."

Carrie nodded. "I've had all those symptoms."

"But this Graves disease can be cured, right?" asked Robert, holding Carrie's hand tightly.

"It's treatable, yes, but this autoimmunity is a lifelong problem that has to be carefully managed to avoid symptoms such as eye swelling or bulging often seen in Graves patients, as well as other complications."

### Questions

- Consider the immunological involvement in this case, and the time frame over which it has occurred.
  - Which antibody (Ig) class was produced first in this sequence of events?
  - Which class is most likely involved in an ongoing autoimmunity situation?
- Return to your thyroid-pituitary diagram. Explain the consequences to both thyroxin and TSH levels:
  - if the auto-antibodies are against the thyroxin molecule.
  - if the auto-antibodies are against the TSH molecule.
- Does either scenario in Question 2 above fit Carrie's hormone data?
- Anti-receptor antibodies can block hormone entry or stimulate the receptor (like original hormone). Use your diagram to explain the consequences to both thyroxin and TSH levels if the auto-antibodies:
  - block the thyroxin receptors on the pituitary.
  - stimulate the thyroxin receptors on the pituitary.
  - block the TSH receptors on the thyroid.
  - stimulate the TSH receptors on the thyroid.
- Does any scenario in Question 4 fit Carrie's hormone data? What must be the problem in Graves disease?
- Identify the type of hypersensitivity (by name and number) that Carrie is experiencing.

## Part IV – Treatment Options

Carrie was silent for a moment as she touched her daughter’s hair. “What about Hayden?” she asked. “Does our daughter have this too?”

Dr. O’Dell pulled out another sheet of lab results. “Hayden’s thyroxin levels were at the high end of normal during her newborn blood screen. Did anyone suggest a follow-up blood test?”

“No,” answered Robert. “They said everything was fine.”

“I’m afraid Hayden also has a problem, but one I hope is relatively easy to solve. Here’s the data.”

	<i>Hayden (newborn)</i>	<i>Hayden (3 mos.)</i>	<i>Normal values</i>
<i>Thyroid hormone (thyroxin)</i>	15.0 ug/dL	22.2 ug/dL	6–15 ug/dL
<i>Thyroid stimulating-hormone (TSH)</i>	Not performed	0.3 mIU/L	0.3–3.04 mIU/L

### Questions

- Which values for Hayden (of those given) are abnormal or borderline?
- Given Carrie’s diagnosis, what is the most likely source/cause of Hayden’s problem?
- How did the “active agent” enter Hayden? Give two possible routes.
- If Carrie had continued to breast feed, how would that have affected Hayden’s problem?
- For Hayden, Dr. O’Dell suggests three months of a low dose anti-thyroid medication (such as methimazole) that will reduce her thyroxin production. Regular blood tests to monitor both thyroxin and TSH levels will be continued during this time.
  - Why is short-term therapy (of several months duration) likely to work?
  - Hayden’s treatments would end about 6 months after her birth. Why is that number significant?
  - Will long-term therapy (years or lifetime) be needed? Why or why not?
  - Graves disease may have a heritable component. What future testing would you suggest for Hayden?
- Will this same therapy work for Carrie? What will happen as treatment progresses?
  - What about general immunosuppression as a treatment? Name a potential consequence.
- Dr. O’Dell explains that Carrie may need to have treatments with a short-lived radioactive isotope of iodine that will accumulate in her thyroid gland along with the normal iodine concentrating there.
  - What will these treatments accomplish?
  - What will happen to antibody levels as a result? List the players and the general sequence of events.
  - Why would thyroid hormone pills be prescribed after treatment is completed?
  - Surgical removal of the thyroid gland (thyroidectomy) is rarely used to treat this problem. What would it accomplish here? Name a potential danger of this surgery (think anatomically).
- Could Carrie’s problem be solved by a thyroid transplant from a matching donor? Explain.
- Autoimmunities are relatively uncommon. What usually happens to autoimmune antibody-producing clones during development?

## Final Outcome

Carrie elected to have the radioactive iodine treatment, rather than surgery. Her thyroid size and hormone level was monitored as the treatment progressed. Her thyroxin levels are now maintained by daily synthetic hormone medication. By six months of age, Hayden's metabolism, weight, and hormone levels are within normal ranges. Her hormone levels will be checked at regular intervals in the future, just in case Hayden inherited genes that might affect this system.



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