A 4-year-old girl was transferred to our hospital for evaluation of abdominal pain. Two days prior to transfer, she developed fever, abdominal pain, and one episode of emesis and loose stool. She was seen at an outside emergency department, where a diagnosis of gastroenteritis was made. Eighteen hours later, she returned to the same emergency department having developed worsening abdominal pain such that she would not move.

Her medical history was remarkable for bilateral ear tags for which no evaluation had been performed. Review of systems and family history were unremarkable.

On physical exam at the outside emergency department, she was lying very still on the bed, refusing to flex her abdomen when her father lifted her up. She cried when approached by physicians. Her growth percentiles were in the 25th percentile. Her pulse was 180 beats per minute, respiratory rate was 28 breaths per minute, blood pressure was 128/62 mm Hg, and temperature was 38.5° C. A head, eyes, ears, nose, and throat (HEENT) exam was unremarkable. There was no significant adenopathy. Her lungs were clear. She was tachycardic with normal rate and rhythm and no murmurs. Her abdomen was distended and rigid with rebound tenderness in all four quadrants. Any movement caused significant abdominal pain. Neurologic exam was unremarkable.

On laboratory evaluation, her white blood cell count was 18,000/mm³ with 83% neutrophils, and her platelet count was 240,000/mm³. Her electrolytes were normal.

Robert Listernick, MD, moderator: Seems easy, she has appendicitis.

Sally Reynolds, MD, pediatric emergency department physician: Nothing about appendicitis is easy, particularly when trying to establish the diagnosis in a timely fashion in young children. For example, many toddlers who ultimately are diagnosed with appendicitis may present with the chief complaint of diarrhea. The younger the children, the more likely that they will have a perforation by the time the diagnosis is made. In addition, the language barrier in an urban population can be a huge impediment to timely diagnosis of appendicitis. We definitely see an excess of Hispanic children with perforations, many of whom had been interviewed with interpreters at the initial visit.

Jennifer Trainor, MD, pediatric emergency department physician: When we looked at our data, we found that Hispanic children with appendicitis either did not complain of right lower quadrant pain or did not have right lower quadrant pain on exam. They seemed to have higher pain thresholds.

Dr. Reynolds: Although some physicians believe it is lupus, emergency room physicians believe that appendicitis is “the great imitator.”

Dr. Listernick: Have newer imaging modalities helped lower perforation rates?

Dr. Trainor: In children with suspected appendicitis, guidelines have suggested ultrasonography as the first diagnostic test.
visualized. For inconclusive studies or in those situations in which the differential diagnosis is broader, computed tomography (CT) is recommended.

Timothy Lautz, MD, pediatric surgeon: While by no means 100%, I have been impressed at how the pain disappears in response to intravenous fluids in those children who are ultimately found not to have appendicitis.

Marybeth Browne, MD, pediatric surgeon: I would also point out that in many children whose symptom complex has been present for more than 3 or 4 days, we often recommend a CT scan to make sure there has been no perforation and abscess formation.

Dr. Listernick: If the clinical suspicion is appendicitis, does the child go to the operating room immediately, even in the middle of the night?

Dr. Browne: Although it’s dependent on surgeon availability, many will wait until the morning to operate. There have been multiple studies that have shown that there’s no increase in perforation rate or hospital length of stay if an operation is performed within 12 hours of presentation. We start intravenous antibiotics immediately that treat the disease. In fact, not that I’m advocating it at all, there have been some studies purporting to demonstrate the non-operative management of acute appendicitis using intravenous antibiotics.

Marleta Reynolds, MD, pediatric surgeon: To be clear, over the years these clinical algorithms have changed as more evidence has been accumulated, and we’ve increasingly tried to limit radiation exposure. If it’s very clear that the child has appendicitis based on the history and exam, no imaging is done, antibiotics are started, and the child goes to the operating room. If there’s a question as to whether or not the child has appendicitis, an ultrasound is obtained. If the ultrasound is negative and there’s still some clinical suspicion, the child will be admitted to the hospital and observed overnight. The attending will see the child in the morning and make a determination as to whether a CT scan would be worthwhile.

She received intravenous ceftriaxone and metronidazole and went directly to the operating room from the emergency department.

Dr. Listernick: OK, let’s look at the outside studies. To be clear, all the imaging was performed elsewhere.

James Donaldson, MD, pediatric radiologist: The ultrasound demonstrated a thick-walled, inflamed, non-compressible, blind-ending tubelike structure with a cross-sectional diameter of 13 mm (normal size is < 6 mm). Doppler imaging showed increased vascular flow around its periphery. These are all the classic findings of acute appendicitis.

Dr. Trainer: We should also point out that the sensitivity and specificity of ultrasonography is extremely center-dependent. A multicenter study showed that in those hospitals where ultrasonography is used to diagnose appendicitis in at least 90% of cases, its sensitivity rate was 78%. However, the sensitivity declined dramatically in those centers where it was used less often; at centers that used it 50% of the time, the sensitivity was 52%, and at the four centers that used it only 9% of the time, the sensitivity was only 35%.

Dr. Donaldson: If you really want to get into an argument, I’ll point out that some centers are beginning to perform magnetic resonance imaging on children to diagnose appendicitis. They’ve developed some very fast sequences (< 5 minutes) that don’t require sedation of the children; the sensitivity and specificity were found to be very high. The obvious disadvantage is the cost.

Dr. Listernick: Moving forward, this child clearly needed to go to the operating room based on her physical examination. She received intravenous ceftriaxone and metronidazole and went directly to the operating room from the emergency department. She underwent laparoscopic appendectomy with the intraoperative findings of an inflamed, engorged appendix.

During the case she remained persistently tachycardic. She had coarse breath sounds bilaterally. At the end of the case, following removal of the endotracheal tube, she had inspiratory stridor and increased work of breathing that did not respond to racemic epinephrine. A nasal trumpet was placed and the decision was made to transfer her to the intensive care unit.

On arrival, her blood pressure was 117/62 mm Hg, pulse 153 beats per minute, and temperature was 38°C. She had a nasal trumpet in place. Lungs were clear. She was tachycardic with regular rhythm and no murmur. Pulses were symmetric and strong. Abdomen was mildly distended and tender to palpation without hepatosplenomegaly, and she had soft hypoactive bowel sounds.

Dr. Listernick: Is this child septic?

Matthew Friedman, MD, pediatric intensive care physician: We need to be careful with the terminology we use. Systemic inflammatory response syndrome (SIRS) is an inflammatory state characterized by fever (or hypothermia), tachycardia, tachypnea, and
either leukopenia or leukocytosis. Sepsis is SIRS in the setting of infection. This child certainly has SIRS, perhaps from an infection to be determined.

**Dr. Trainor:** For what it’s worth, I know that the emergency department physicians were worried about this child from the start. Despite the peritoneal signs, she looked sicker than they would have expected. Her tachycardia was persistent and unresponsive to fluid therapy and narcotics. She was thought to be in compensated shock.

**Dr. Listernick:** Well, on admission to the intensive care unit postoperatively, PL-2 Zoe Shapleigh noted a goiter. Free T4 was > 7.5 ng/dL (normal, 0.97-1.67 ng/dL) and thyroid-stimulating hormone (TSH) was totally suppressed at < 0.1 uIU/mL.

When I was in medical school, the endocrinologist used to talk about “spiking a goiter.” The T4 result would come back as undetectable and the next day the physical exam would note a previously unmentioned goiter. I don’t think pediatricians are used to looking for thyromegaly.

**Donald Zimmerman, MD, pediatric endocrinologist:** The first thing I do in my clinic is choke the kid.

**Dr. Listernick:** I’ve heard that. Why wasn’t this child sicker intraoperatively with this degree of hyperthyroidism?

**Dr. Zimmerman:** I can only speculate but here’s an interesting theory. This child had a contrast-enhanced computed tomography scan that Dr. Donaldson didn’t show. The most effective treatment to block release of thyroxine from the thyroid gland is iodine. She received a big bolus in the form of iodinated contrast, which may have prevented thyroid storm.

**Dr. Listernick:** If the diagnosis of hyperthyroidism had been suspected before the necessary surgery, what would you have recommended?

**Dr. Zimmerman:** There isn’t a satisfying definition of “thyroid storm,” and thyroid hormone levels are not higher in thyroid storm than they are in people without thyroid storm. I probably would have given this child a slug of iodine in the form of cold iodine or Lugol’s solution, as well as a beta blocker.

**Dr. Listernick:** Is there a differential diagnosis here?

**Dr. Zimmerman:** Not really. She has Graves’ disease. On closer examination, she had mild exophthalmos. Ultimately, her level of thyroid stimulating immunoglobulin was quite high. For completeness, the only other condition that produces exophthalmos and hyperthyroidism is an activating mutation of the TSH receptor. Proptosis in these infants is due to premature synostosis of the skull bones rather than infiltrative Graves’ ophthalmopathy.

**Dr. Listernick:** And the differential diagnosis of hyperthyroidism without the presence of exophthalmos?

**Dr. Zimmerman:** Besides Graves’ disease, a fairly common etiology is sub-acute thyroiditis. The thyroid gland has an episode of intense inflammation due to anti-thyroid antibodies and releases all its preformed thyroxine, leading to hyperthyroidism. Following this episode, the patient becomes hypothyroid, the pituitary kicks in, TSH is secreted, and the patient becomes euthyroid again. So these patients may have normal T4 levels and mildly elevated TSH. In retrospect, our patient had symptoms of hyperthyroidism (nervousness, poor sleep, episodes of sweating) for 4 months.

**Dr. Listernick:** What are the treatment options?

**Dr. Zimmerman:** First, we gave her cold iodine to prevent secretion...
of preformed thyroid hormone and block its production by inhibiting organification, the inclusion of iodine into thyroglobulin. Next, we started therapy with a beta blocker. One of the most important actions of thyroid hormone is to increase the number of beta adrenergic receptors; individuals with hyperthyroidism are so tachycardic because they’re hypersensitive to normal levels of circulating adrenaline.

Dr. Listernick: So these measures deal with the acute symptoms. What about long-term management?

Dr. Zimmerman: This could be a very long discussion. The three possible treatments include: 1) surgery, 2) radioiodine therapy, and 3) antithyroid medication. Each comes with a unique set of risks and benefits. Radioiodine therapy has the theoretical risk of inducing malignancy, particularly if given to a young child.