CASE: A 15-year-old girl presented to her pediatrician with primary amenorrhea. She was worried because all of her friends had begun menstruating. Her pediatrician saw an abnormal vaginal opening and referred the patient to a gynecologist.

The patient reported thelarche at age 11 and adrenarche at age 12. She denied vaginal spotting, unusual drainage, and either cyclical or noncyclical abdominal pain. She was otherwise healthy and on no medications. She denied (when asked in private) any sexual activity. Her family history was negative for any gynecological issues.

Physical examination revealed Tanner stage 4 breasts and a normal abdominal examination without any discomfort or palpable masses. She refused a pelvic examination because the last time it was very uncomfortable. An abdominal ultrasound examination performed in the office revealed a small uterus and normal ovaries. Follicle-stimulating hormone and estradiol levels were in the normal postpubertal range.

Her gynecologist suspected outflow obstruction, either imperforate hymen or transverse vaginal septum and took the patient to the operating room. After making the initial incision into the hymenal region, no fluid collection was identified, and indeed, no vaginal canal could be found. The surgery was terminated, and the patient was then referred to a tertiary care center.

QUESTIONS FOR THE ADOLESCENT GYNECOLOGIST
What is the differential diagnosis at this point?
It has been established in the operating room that this patient probably does not have a lower vagina. The differential diagnosis of vaginal agenesis includes:
• Congenital absence of the uterus and vagina (known as müllerian aplasia, müllerian agenesis, or Mayer-Rokitansky-Kuster-Hauser syndrome [MRKH]; to be consistent with the American College of Obstetricians and Gynecologists [ACOG] terminology, we will refer to this entity as müllerian aplasia)
• Androgen insensitivity disorder (formerly called testicular feminization)
• Congenital absence of the lower part of the vagina

Table 1 summarizes some differences between müllerian aplasia and androgen insensitivity disorder, the 2 most common etiologies for vaginal agenesis.

How common is müllerian aplasia?
This is a rare condition (1 in 5,000) defined by complete or partial agenesis of the vagina and uterus and possible associated renal (30–40%), skeletal (10–12%), and other abnormalities (auditory, cardiac) (5–16%). Most patients will have a rudimentary uterine bulb without functioning endometrium (Fig. 1), but 2–7% of patients with müllerian aplasia have functioning endometrium, in which case the uterine remnants may need to be removed laparoscopically for pain management. Patients have normal 46,XX chromosomes and regular ovarian function. The cause of the syndrome remains unclear. Müllerian aplasia is the second most common cause of primary amenorrhea (following gonadal dysgenesis; for example Turner’s syndrome).

Would you have recommended that the gynecologist that initially cared for the patient do any other studies before proceeding to the operating room?
This patient would have been better served with additional testing than an immediate trip to the operating room. Patients with an obstructive anomaly usually present much sooner after thelarche because the usual time span between thelarche and menarche is approximately 2–2.5 years. As soon as several cycles of menstrual blood have accumulated in the obstructed
Because this patient presented 4 years after thelarche, one would have expected her to have menstruated for approximately 1–2 years. If she had an obstruction in her outflow tract, as was presumed, she would have had a large fluid-filled vagina and/or uterus and abdominal pain. Since the clinical presentation in this case (primary amenorrhea without any pain or mass on ultrasonography) did not fit the diagnosis made by ultrasonography, further evaluation of the anatomy should be done before proceeding to the operating room. Magnetic resonance imaging (MRI) is considered the gold standard for determining congenital anomalies. In addition, an obstruction is often a diagnosis that can be made clinically. A patient with an imperforate hymen has a bulging hymen that is clearly distinguishable (Fig. 2). A patient with müllerian aplasia and/or a transverse vaginal septum will usually have a normal hymen and a dimple or shallow vagina after that (Fig. 3). If there is a higher obstruction, a rectal examination can help distinguish the two.

What further evaluation do you recommend at this point?

Once the diagnosis of müllerian aplasia is made, the patient needs an evaluation of her kidneys (by MRI or excretory urogram) and spine (by X-rays). If abnormalities are found in this initial evaluation, we recommend expanding the evaluation to include auditory and cardiac tests. Although cardiac anomalies are thought to be uncommon in this syndrome, a recent review of 25 women with müllerian aplasia found that 16% had cardiac defects. In the patient presented, MRI revealed a pelvic kidney, but no uterus.

Given that the patient had normal follicle-stimulating hormone and estradiol levels and a normal uterus on ultrasound examination, why did she have no cyclical pain or fluid collection?

The diagnosis in this case was not correct. The office ultrasonogram was misinterpreted. On occasion, these patients can have a pelvic kidney, which may be mistaken for

### Table 1. Characteristics That Differentiate Müllerian Aplasia and Androgen Insensitivity Disorder

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<th>Müllerian Aplasia</th>
<th>Androgen Insensitivity Disorder</th>
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<tbody>
<tr>
<td>Karyotype</td>
<td>46,XX</td>
<td>46,XY</td>
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<tr>
<td>Gonads</td>
<td>Ovaries</td>
<td>Testes</td>
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<tr>
<td>Pubic/axillary hair</td>
<td>Normal</td>
<td>Sparse or absent</td>
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<tr>
<td>Breast development</td>
<td>Normal</td>
<td>Normal</td>
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<td>Testosterone levels</td>
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What are treatment options for this patient? If surgery is done, when should it occur?

The treatment options are either vaginal dilation or surgery. Most adolescent gynecologists, as well as the ACOG Committee on Adolescent Health Care, recommend dilation as a first-line treatment in the motivated patient.3 The choice of when to proceed with the creation of a vagina is a personal choice. Because most women with müllerian aplasia do not have functioning endometrium and therefore have no pain, many are just presumed to be “late bloomers” and do not see a doctor until age 15 or 16.

After the correct diagnosis is established, counseling with the girl and her parents is very important. There are 2 parts to this decision: When to create the vagina and what kind of vaginal creation?

The decision about when to proceed is very personal. Often the psychological impact of this diagnosis is traumatic, and the patient needs time to adjust. Some girls have a potential sexual partner and want to start immediately, some opt to wait until they have a partner, and others want to be as “normal” as possible and start treatment quickly, so that when they want to have vaginal intercourse, they can. We emphasize that it takes effort and persistence to create a vagina and that the correct timing is only when the patient is ready for it. The most important message to the patient is that there is no quick fix for this problem because all treatment entities need life-long attention. It is particularly important that the patient and her family understand that surgical options also demand aftercare, in the form of wearing some kind of soft mold, to prevent scarring and strictures. The McIndoe procedure has been the most commonly used in the United States and has extensive long-term follow-up, with success rates of 83–

Fig. 3. Patient with müllerian aplasia. The vaginal introitus appears superficially normal, and the vaginal agenesis is not obviously seen. (Catheter is in the urethra.) Quint. Primary Amenorrhea. Obstet Gynecol 2006.
92%. The skin scar from the graft site remains a problem for some patients. Reported long-term outcomes of the other procedures vary; overall success rates are reported around 90%, with some smaller series reporting lower rates. There is no consensus concerning the best procedure, and in choosing a procedure the experience of the surgeon is often the determining factor.

What fertility issues does this young woman face?
Because she does not have a uterus, her only option for fertility is in vitro fertilization surrogacy. Several studies have looked at this and found it to be successful, with a nearly 50% live birth rate and with no increase in congenital anomalies in the offspring. Another option is adoption.

Are women with müllerian aplasia more likely to have psychologic impairment than others?
The most difficult aspect of a müllerian aplasia diagnosis is usually the accompanying prognosis and realization of infertility, which can be very traumatic for the patient and her parents. The entire family often needs time to adjust to this before addressing the vaginal issues. Psychological counseling may be indicated. A multidisciplinary approach is now used in many places, and group programs are set up in many European centers. Without adequate psychological preparation, the chances of having a successful outcome and a balanced, well-adjusted patient are greatly reduced.

When should the primary care provider consider referral to a specialist?
This depends to a large extent on the type of practice the primary provider has. Because most providers see very few such patients, except in cases of obvious imperforate hymen, it may be wise to refer most cases of primary amenorrhea. This is particularly the case when an anatomical problem is likely. Patients should not be taken to the operating room until all endocrine and imaging results have been obtained and a clear diagnosis has been established. A treatment plan can then be developed that is acceptable to the patient.

Editor’s Note
The authors found this informational Web site very helpful for patients: http://www.MRKH.org.

REFERENCES