What to do when your patient says

“I never got my period”

Evaluation and management of adolescent amenorrhea

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Faculty Disclosure

In the past 12 months, I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider (s) of commercial services discussed in this CME activity.

I do not intend to discuss an unapproved /investigative use of a commercial product/device in my presentation.
Educational Objectives

The participant should be able to summarize

• If your patient has not begun to menstruate, when should you intervene?
• What are the most likely diagnoses?
• How do you evaluate a girl for amenorrhea?
Primary Amenorrhea- *before menarche*
Secondary Amenorrhea- *after menarche*

- The prevalence of amenorrhea not due to pregnancy, lactation or menopause is approximately 3%-4%
- The majority of all causes of amenorrhea are accounted for by 4 conditions
  - Polycystic ovarian syndrome
  - Hypothalamic amenorrhea
  - Hyperprolactinemia
  - Ovarian failure
- World Health Organization
  - WHO Group I: no endogenous estrogen, nl /low FSH, nl PRL, no lesion in the hypothalamic pituitary
  - WHO Group II: estrogen, prolactin, FSH normal
  - WHO Group III: elevated FSH indicating gonadal failure
Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign

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The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/137/3/e20154480.full.html
Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign


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Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign

**ABSTRACT:** Despite variations worldwide and within the U.S. population, median age at menarche has remained relatively stable—between 12 years and 13 years—across well-nourished populations in developed countries. Environmental factors, including socioeconomic conditions, nutrition, and access to preventive health care, may influence the timing and progression of puberty. A number of medical conditions can cause abnormal uterine bleeding, characterized by unpredictable timing and variable amount of flow. Clinicians should educate girls and their caretakers (e.g., parents or guardians) about what to expect of a first menstrual period and the range for normal cycle length of subsequent menses. Identification of abnormal menstrual patterns in adolescence may improve early identification of potential health concerns for adulthood. It is important for clinicians to have an understanding of the menstrual patterns of adolescent girls, the ability to differentiate between normal and abnormal menstruation, and the skill to know how to evaluate the adolescent girl patient. By including an evaluation of the menstrual cycle as an additional vital sign, clinicians reinforce its importance in assessing overall health status for patients and caretakers.
Menstrual Abnormalities That Require Evaluation *Primary amenorrhea*

Menstrual periods that
- have not started within 3 years of thelarche
- At age 13, if no menses with complete absence of secondary sexual characteristics
- have not started by 14 years of age with signs of hirsutism
- Have not started by 14 years of age with a history or examination suggestive of excessive exercise or eating disorder
- Have not started by 15 years of age
Causes of primary amenorrhea “not ever starting a period”

1. Gonadal dysgenesis “ovary not working” – 43 percent
2. Absence of vagina and uterus – 15 percent
3. Physiological delay of puberty “late bloomer” – 14 percent
4. Polycystic ovary syndrome (PCOS) – 7 percent
5. Isolated gonadotropin-releasing hormone (GnRH) deficiency – 5 percent
6. Transverse vaginal septum – 3 percent
7. Weight loss/anorexia nervosa – 2 percent
8. Hypopituitarism – 2 percent
Evaluation of the patient

- **History**
  - Mother’s menarche/ any underlying systemic disease

- **Physical Examination**
  - Presence of breast development means previous estrogen action
  - Excess testosterone hirsutism
  - Assess the external and internal genitalia (anatomic defect)

- **Labs**
  - Exclude pregnancy
  - TSH r/o subclinical hypothyroidism

**Diagram:**
- **FSH**
  - Down: chronic anovulation, PCOS, functional hypothalamic amenorrhea
  - Up: Ovarian failure, Karyotype (Gonadal dysgenesis)
  - Anatomic Defect Mullerian Dysgenesis

- **Prolactin**
  - Up: Stress, Antipsychotic drug?, Prolactinoma
  - MRI of pituitary
Gonadal dysgenesis

- Can occur at any age (even in utero)
- Premature depletion of all ovarian oocytes and follicles
  - 45,X Turner syndrome most common
  - 46,XX If it occurs before sexual maturation there will be primary amenorrhea and incomplete breast development
  - 46, XY gonadal dysgenesis (Swyer syndrome)
    - 1:100,000 births
    - Female genitalia
    - The streak gonad does not secrete antimullerian hormone (AMH) resulting in persisting mullerian structures and a female phenotype-present at puberty with primary amenorrhea
    - Gonadal tumors occur in up to 25% of women with a Y chromosome
    - Unlike androgen insensitivity these gonads do not secrete hormones and should be removed at the time of diagnosis
Gonadal dysgenesis Turner syndrome

- 45,X oocyte loss is accelerated after 18 weeks in utero
- Well known phenotype
  - Short stature
  - Webbed neck
  - Low hair line
- Ovaries are replaced with fibrous tissue, no ovarian estrogen secretion
- External and internal genitals develop normally
- Mosaic karyotype
  - 45X, 46XX spontaneous puberty and menstruation
  - 45X, 46XY at risk for gonadoblastoma
Primary ovarian insufficiency (POI)

- Development of clinical menopause before age 40 years in women with normal karyotype
- Usually presents as secondary amenorrhea some present with primary amenorrhea

**Etiologies**
- Women carriers of fragile X premutation 16%
- Autoimmune abnormalities 40%
  - Most common autoimmune thyroiditis
  - More common in women with IDDM, myasthenia gravis, parathyroid disease
  - Autoimmune lymphocytic oophoritis associated with adrenal autoimmunity (Addison’s disease)
- Galactosemia
- FSH LH receptor mutations
- 17a-hydroxylase or 17,20-lyase deficiency
Primary Ovarian Insufficiency in Adolescents and Young Women

**ABSTRACT:** Primary ovarian insufficiency is the depletion or dysfunction of ovarian follicles with cessation of menses before age 40 years. There is no consensus on criteria to identify primary ovarian insufficiency in adolescents, and delay in diagnosis is common. Health care providers who make this clinical diagnosis should be mindful of the sensitive nature of this medical condition. Patients and their families should be counseled on the effect of the patient’s condition on future fertility, on the risk of comorbidities associated with primary ovarian insufficiency, and on the condition’s potential for genetic inheritance. Psychologic counseling also should be offered because impaired self-esteem and emotional distress have been reported after diagnosis of primary ovarian insufficiency. Once primary ovarian insufficiency is diagnosed, patients should be evaluated at least annually. The goals of hormonal therapy extend beyond simply symptom relief to levels that support bone, cardiovascular, and sexual health. Referrals to a reproductive endocrinology and infertility specialist should be made when desired by the patient and family to further discuss available reproductive treatments.
Diagnosis and Initial Evaluation of Primary Ovarian Insufficiency

- Menstrual irregularity for at least 3-4 consecutive months
- Negative pregnancy test
- FSH and estradiol levels (two random tests at least one month apart)
- Prolactin and TSH
- If diagnosis is confirmed
  - Karyotype
  - FMR1 premutation
  - Adrenal antibodies
    - 21-hydroxylase (CYP21) by immunoprecipitation or
    - Indirect immunofluorescence
  - Pelvic sonography
  - Bone mineral density
Recommendations for Women with POI

• This is a highly emotionally charged diagnosis impacting self-esteem, and causing emotional distress
• Remission may occur, but unlikely 5-10%
• Offer estrogen and progestin treatment to promote and maintain secondary sexual characteristics and reduce risk of osteoporosis
• Encourage to maintain lifestyle that optimizes cardiovascular and bone health
  • Weight bearing exercise
  • Adequate calcium and vitamin intake
  • Healthy diet to avoid obesity
  • Screen for cardiovascular disease
Recommendations for Adolescents with POI

• Offer psychological assistance to the patient and her family
  • This diagnosis is a strong shock
  • The girl can never be prepared
  • Feelings of anger, despair, loss of sense of femininity, sadness, depression are very common
  • Psychological support is recommended

• Deal with problems of estrogen deficiency
  • Aim to mimic normal pubertal development
  • Low dose estrogens
  • Gradually increasing to augment breast development
  • Avoid progestin until the breast mound and areola have developed
  • Protect bones, calcium, vitamin D, bone density testing

• Manage consequent infertility
  • 5-10% may have a chance at natural conception
  • In vitro fertilization of donor oocytes
  • Cryopreservation of ovarian tissue before depletion of oocytes
Elevated Prolactin Levels

- Hyperprolactinemia is associated with decreased estradiol concentrations and amenorrhea or oligomenorrhea
- R/O primary hypothyroidism
- MRI of pituitary
  - Prevalence of a pituitary tumor is 50%-60%
  - Poor correlation between tumor presence and prolactin level
- Treat with dopamine agonists or surgery
  - Cabergoline - blocks release of prolactin (2 X /week)
  - Bromocriptine
  - Transsphenoidal or transcranial surgery
- Medication which cause elevated prolactin
  - Psychiatric and gastrointestinal disorders
  - Phenothiazines, risperidone, SSRIs, metoclopramide, estrogens
Normal or Low FSH levels

- Hypothalamic amenorrhea-inconsistent GnRH
  - Levels of estradiol are low
- PCOS persistent rapid increased GnRH, excessive LH synthesis, hyperandrogenism, impaired follicle maturation
  - Obesity
  - Androgenization
  - Levels of estradiol normal
- Progesterone challenge test
  - Withdrawal bleeding correlates poorly with estrogen status
  - Test delays diagnostic process
  - 20% of women with oligomenorrhea or amenorrhea with estrogen present have no withdrawal bleeding
  - Withdrawal bleeding occurs in 40% of women with amenorrhea due to stress, weight loss, exercise, or hyperprolactinemia where estrogen is reduced and in up to 50% of women with ovarian failure
Hypothalamic amenorrhea

• Functional disorders of the hypothalamus or higher centers are the most common reason for chronic anovulation
• Psychogenic stress, weight changes, undernutrition, excessive exercise
• Women involved in competitive sports have a 3 fold higher risk of primary or secondary amenorrhea (highest long distance runners)
• Chronic debilitating diseases, uncontrolled juvenile diabetes, end-stage renal disease, malignancy, acquired immune deficiency syndrome, malabsorption
• Isolated gonadotropin deficiency (Kallman syndrome)
  • Anosmia
  • Amenorrhea, low FSH/LH due to GnRH deficiency

Absence of all or part of the uterus and vagina in the presence of otherwise normal female sexual characteristics

Mullerian agenesis (MRKH)
- Vagina may be short or absent
- Normal female testosterone
- Normal ovaries
- Associated with urogenital and skeletal malformations
- Incidence 1:2500-5000

Complete Androgen Insensitivity
- Vagina may be short or absent
- Normal male range testosterone
- Family history
- Absent pubic hair
- 46, XY karyotype
- Incidence 1:60,000
Absence of all or part of the uterus and vagina in the presence of otherwise normal female sexual characteristics

- Mullerian agenesis 1:5000
- Complete Androgen Insensitivity 1:60,000
- Imperforate hymen 1:1000
- Transverse vaginal septum 1:80,000
- Isolated vaginal agenesis
- Isolated uterine agenesis
- Postpartum endometritis or operative curettage for postpartum hemorrhage cause intrauterine synechiae

Cryptomenorrhea
- Cyclic pain
- Accumulation of blood behind obstruction
- Endometriosis
- Pelvic adhesions
Internal and external structures

- Failure of Müllerian duct development which leads to poorly developed uterus, cervix, and upper vagina
- Fallopian tubes are frequently normal but may be hypoplastic/aplastic or malformed
- Normal 46, XX karyotype
- Ovaries are structurally and functionally normal
- Vulva, labia majora, labia minora, clitoris are all normal
MRKH has many variations

- **Type 1 isolated** OMIM* 277000- blockage or defect in the caudal part of the vagina and uterus, with normal fallopian tubes, ovaries and renal system (44%)
- **Type 2** (56%) asymmetric hypoplasia of one or two buds, with or without dysplasia of fallopian tubes, renal defects (40%-60%),
- **MURCS association**- Mullerian duct aplasia, Renal dysplasia, Cervical Somite anomalies 16% of MRKH Type 2
  - Renal dysplasia-unilateral renal agenesis (23-28%), renal ectopia (17%), renal hypoplasia (4%), horseshoe kidney
  - Skeletal-affect spine less frequently face, and limb extremities
  - Heart and hearing malformations less common

OMIM Online Mendelian Inheritance in Man
Müllerian agenesis

- 7 to 10 percent of women have a normal but obstructed or rudimentary uterus with functional endometrium

Vaginal agenesis with rudimentary uterine horns

Vaginal agenesis with agenesis of the cervix

## MRKHK associated anomalies and frequencies

<table>
<thead>
<tr>
<th>Renal</th>
<th>30-40%</th>
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<tbody>
<tr>
<td>Unilateral renal agenesis (50%)</td>
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<td>Ectopia one or both kidneys</td>
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<td>Renal hypoplasia</td>
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<td>Horseshoe kidney</td>
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<td>Hydronephrosis</td>
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<thead>
<tr>
<th>Auditory</th>
<th>10-25%</th>
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<tr>
<td>Middle ear malformations (stapedial ankylosis)</td>
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<td>Sensorineural defects</td>
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<td><strong>Adysplasia</strong> of the auditory meatus</td>
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<table>
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<tr>
<th>Skeletal</th>
<th>30-40% spine</th>
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<tr>
<td>Scoliosis</td>
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<td>Isolated vertebral anomalies</td>
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<td>Klippel Feil association</td>
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<tr>
<td>Sprengel’s deformity</td>
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<tr>
<td>Rib malformation or agenesis</td>
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<td>Spina bifida</td>
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<th>Skeletal</th>
<th>16% Face and limb</th>
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<tr>
<td>Brachymesophalangy</td>
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<td>Ectrodactyly</td>
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<td>Duplicated thumb</td>
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<td>Absent radius</td>
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<td>Atrio-digital dysplasia</td>
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<td>Facial asymmetry</td>
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**Recommendations for Adolescents with MRKH**

- **Offer psychological assistance to the patient and her family**
  - This diagnosis is a strong shock
  - The girl can never be prepared
  - Feelings of anger, despair, loss of sense of femininity, sadness, depression are very common
  - Psychological support is recommended

- **Discuss options to create neovagina**
  - Only when the girl is ready
  - Dilators versus surgery

- **Options for fertility and family building**
  - Their ovaries are normal
  - Ovarian follicle retrieval + fertilization = embryo (Surrogate uterus)
  - Adoption
  - Uterine transplant
Evaluation of the young woman with MRKH

- History
- Physical exam
- Transabdominal ultrasound
- If cyclic abdomen/pelvic pain
  - MRI to assess if there is any functioning endometrium
  - Laparoscopy
  - If there is functional tissue the small rudimentary horns without associated cervix and vagina of the uterus may be removed
- Evaluate for other associated anomalies
  - US for renal agenesis or pelvic kidney
  - Scoliosis
  - Hearing impairment
Management of the woman with MRKH

• Psychosocial counseling to discuss the functional and emotional effects for this condition
• For young woman discuss with parents and get input on when the patient is ready to hear specific details
• Healthy sexual relationships are possible
• Future fertility options—this girl is fertile
• KEY: encourage the family to have open discussions and support their daughter
Creating and lengthening the vagina

• Surgical and non-surgical methods
• When is the best time?
• Is this a personal decision or a parent’s decision?
• Wait until adolescent or even adulthood when the patient has reached physical and psychological maturity and can participate in the decision making
• Increases compliance with vaginal dilator therapy whether used as a primary treatment or post operative adjuvant treatment to prevent vaginal stenosis
• There is a lack of long-term outcome data
• There is no comparison of surgical or non-surgical techniques
• The main objective is not just to create a passageway for penetration but to facilitate enjoyable sexual intercourse
Vaginal dilator therapy

- Vaginal molds or dilators increasing width and length.
- Apply gentle pressure on the vaginal dimple for 30 minutes daily.
- Gradually and progressively stretch the vagina with time.
- Healthy non-scarred vaginal dimple which is amenable to stretching.
- Most important, must have a motivated individual.
- Vaginal dilation is a non-invasive and inexpensive method.
- Success rate 90%.
- First line treatment for vaginal agenesis.
- Recommended by ACOG.
“Non surgical creation of the neovagina should be the first-line approach”
Going beyond the physical concerns of MRKH

- Lack of long-term outcome studies
- Change the emphasis from the physical aspects to how individuals adjust
- A young woman’s sense of well-being and quality of life are impacted
- There is a need to help young women cope with the psychological impact
- Critical time periods
  - diagnosis
  - treatment for a neovagina
  - relationships with men
  - creation of a family
Going beyond the physical concerns of MRKH

- How do you talk about MRKH
- Who do you tell and when
- How do your friends and partners respond
- A woman with MRKH may be unable to bear children, but she is fertile, she is able to have conceive a biological child, but will need a surrogate carrier
- Successful parenthood
- Individual adjustment and coping mechanisms to handle stress of diagnosis
  - Working toward life goals
  - avoidance, resignation, and minimization
  - how a women’s level of knowledge about her condition affected her ability to cope with it
Information management

- Disclosure includes physicians informing patients about their diagnosis.
- Disclosure also includes patients and parents sharing information with family members and the wider community.
- Talking about a condition that involves the genitals and sexuality can be difficult for many adolescents and adults.
- To whom, when, and how to best disclose information about the condition.
- How much information is useful to patients and appropriate for others to know?
- How should the news of the condition be delivered and by whom?
New treatments

Vaginal organs, engineered from the patient’s own cells can be created as a viable option for vaginal reconstruction *The Lancet, Volume 384, Issue 9940, 26 July–1 August 2014, Pages 329-336*

Tissue-engineered autologous vaginal organs in patients: a pilot cohort study

Atlantida M Raya-Rivera, Diego Espuelos, Reyna Fierro-Pastone, Esther López-Baygues, Pedro Valencia, Ricardo Ordieres-Flares, Shay Soker, James J Yeo, Anthony Atala

Summary

Background Several disorders might require vaginal reconstruction, such as congenital abnormalities, injury, or cancer. Reconstructive techniques for which non-vaginal tissue is used can be associated with complications. We assessed the use of engineered vaginal organs in four patients with vaginal aplasia caused by Mayer-Rokitansky-Küster-Hauser syndrome (MRKH).

Methods We invited to participate four consecutive patients who presented over a 3-year period with congenital vaginal aplasia due to MRKH. Patients were aged 13–18 years. We obtained a vulvar biopsy of autologous tissue from every patient. We cultured, expanded, and seeded epithelial and muscle cells onto biodegradable scaffolds. The organs were constructed and allowed to mature in an incubator in a facility approved for human-tissue manufacturing. We used a perineal approach to surgically implant these organs. We recorded history, physical examination, vaginoscopy, serial tissue biopsies, MRI, and self-administered Female Sexual Function Index questionnaire results for all patients, with a follow-up of up to 8 years.

Findings We noted no long-term postoperative surgical complications. Yearly serial biopsies showed a tri-layered structure, consisting of an epithelial cell-lined lumen surrounded by matrix and muscle, with expected components of vaginal tissue present. Immunohistochemical analysis confirmed the presence of phenotypically normal smooth muscle and epithelia. The MRBs, which showed the extent of the vaginal aplasia before surgery, showed the engineered organs and the absence of abnormalities after surgery, which was confirmed with yearly vaginoscopy. A validated self-administered Female Sexual Function Index questionnaire showed variables in the normal range in all areas tested, such as desire, arousal, lubrication, orgasm, satisfaction, and painless intercourse.

Interpretation Vaginal organs, engineered from the patient’s own cells and implanted, showed normal structural and functional variables with a follow-up of up to 8 years. These technologies could be useful in patients requiring vaginal reconstruction.
New Treatments


Living Donor Uterus Transplant and Surrogacy Ethical Analysis According to the Principle of Equipoise.
Testa G¹, Koon EG², Johansson L³.

Author information

Abstract
The uterus is the most recent addition to the list of organs that can be successfully transplanted in humans. This paper analyzes living donor uterus transplantation according to the ethical principle of equipoise. A comparison is made between living donor uterus transplantation and gestational surrogate motherhood. Both are solutions to absolute uterine infertility that allow the transfer of genetic material from intended parents to a child. The analysis concludes that living donor uterus transplantation does not violate the ethical principle of equipoise and should be considered an ethically acceptable solution to absolute uterine infertility. This article is protected by copyright. All rights reserved.
New treatments

Full Text

Uterus transplantation: From animal models through the first heart beating pregnancy to the first human live birth

Womens Health (Lond Engl) July 2016 12: 442-449,

Other women’s wombs: uterus transplants and gestational surrogacy

John A. Robertson

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ABSTRACT

The birth of a child after uterus transplant from a living donor in Sweden in October, 2013 has spurred reproductive and transplant physicians in Europe and North America to investigate whether uterus transplants, from living or cadaveric donors, will be a safe and effective therapy for women with uterine insufficiency. While progress with uterus transplant depends on medical factors, there are also important ethical and legal concerns. Uterus transplant is essential for women without access to surrogacy. It may also be sought by infertile women who dislike surrogacy. This article examines medical, ethical, legal, and policy issues that arise with womb transplant, including the role of surrogacy policies that make them necessary. The conclusion is that there is a clear ethical path for either surrogacy or uterus transplant to be used by women with uterine insufficiency.

KEYWORDS: uterus transplants, surrogacy, law, eutocogenesis, gametogenesis, organ donation

Womens Health
One uterus bridging three generations: first live birth after mother-to-daughter uterus transplantation

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Objective: To determine whether a uterus from the mother of a woman with absolute uterine factor infertility can be transplanted to daughter and carry a pregnancy with delivery of a healthy child.

Design: Part of an observational study.

Setting: University teaching hospital.

Patient(s): Twenty-eight-year-old woman with uterine agenesis, her male partner, and her 50-year-old mother.

Intervention(s): In vitro fertilization with embryo cryopreservation before live donor uterus transplantation (UTx). Induction immunosuppression. Embryo transfer 12 months after UTx, pregnancy controls, delivery, and hysterectomy.
New treatments

First human uterine transplant in the United States occurred on February 24, 2016. Unfortunately, the uterus was removed on postoperative day 12 due to a severe infection of the graft, which infiltrated the vasculature of the uterus and caused disruption of one of the two arterial anastomoses.

Deceased Donor Uterine Transplantation
Innovation and Adaptation
Rebecca L. Flyckt, MD, Ruth M. Farrell, MD, MA, Uma C. Perni, MD, MPhil, Andreas G. Tzakis, MD, PhD, and Tommaso Falcone, MD

This commentary endeavors to share our practical experience in developing and implementing the first uterine transplant clinical trial in the United States. Uterine transplant is a promising novel treatment for uterine factor infertility. After reported successful live births after uterine transplant in Sweden, research teams around the world are either embarking on or are considering the development of uterine transplant protocols. Our observations on the applied rather than theoretical aspects of uterine transplantation research in human subjects are detailed in this article. Important among these considerations are composing a broad and experienced multidisciplinary team as well as performing adequate preclinical preparations, including ideally animal studies and practice organ procurements. Ethical preparation is tantamount to clinical preparation for the complexities inherent in uterine transplant, and our a nonfunctional or surgically absent uterus. After extensive research and preparation, the first clinical trial of uterine transplantation in the United States for the treatment of uterine factor infertility was approved at Cleveland Clinic in September 2015. The protocol is internally funded to perform 10 uterine transplants in women with uterine factor infertility; there are no medical charges assessed to research members for participation in the trial.

International interest in uterine transplant research has been stimulated by the groundbreaking success of Dr. Mats Brannstrom and the Swedish uterine transplant team, which published a report of the first live birth after uterine transplant involving living donors in February 2015. Additional live births from this group have now been described. Several academic centers in the United States are either embark-
# Common causes of primary amenorrhea

<table>
<thead>
<tr>
<th>With breast development 30%</th>
<th>Without breast development 70%</th>
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<tbody>
<tr>
<td>• Mullerian agenesis 10%</td>
<td>High FSH 40%</td>
</tr>
<tr>
<td>• Androgen insensitivity 9%</td>
<td>• 46XX 15%</td>
</tr>
<tr>
<td>• Imperforate hymen 1-2%</td>
<td>• 46XY 5%</td>
</tr>
<tr>
<td>• Vaginal septum 1-2%</td>
<td>• Abnormal 20%</td>
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<tr>
<td>• Constitutional delay 8%</td>
<td>Low FSH 30%</td>
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<tr>
<td></td>
<td>• Constitutional delay 10%</td>
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<td></td>
<td>• Prolactinomas 5%</td>
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<td>• Kallman syndrome 2%</td>
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<tr>
<td></td>
<td>• Other CNS 3%</td>
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<td></td>
<td>• Stress, wt loss, anorexia 3%</td>
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<td></td>
<td>• PCOS 3%</td>
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<td></td>
<td>• CAH 1%</td>
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Patient 1

• Clinical presentation of patient with pituitary disease misdiagnosed as MRKH with clandestine uterus
• (great learning case)
Pituitary causes of amenorrhea

- Prolactinoma
- Other pituitary tumors
- Nonfunctional tumor (craniopharyngioma)
- Metastatic tumor
- Space-occupying lesion
- Empty sella

- Arterial aneurysm
- Pituitary necrosis
- Postpartum pituitary necrosis (Sheehan)
- Panhypopituitarism
- Systemic inflammatory disease
- Sarcoidosis
- Hemochromatosis
Patient 2

- Clinical presentation of patient misdiagnosed with chronic constipation with cryptomenorrhea and outflow obstruction
Patient 3

- Clinical presentation of patient with auditory deficit and primary amenorrhea with clandestine uterus and Perrault syndrome
Patient 4

- Clinical presentation of patient with MRKH personal comments of patient and mother re: journey
Patient 5

• Clinical presentation of a Division I athlete with POI
Patient 5

• Clinical presentation of HS track star (mother diagnosed with breast cancer during pregnancy, died when patient was 9 years old) who presents with sacral fracture