EMBRYOLOGIC BASIS OF FEMALE CONGENITAL TRACT MALFORMATIONS

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Congenital uterine anomalies and reproductive outcome.
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The direct cause of genital malformations is unknown.

Sometimes:

- MURCS association
- Pulmonary hypoplasia, hereditary renal adysplasia, and Rokitansky syndrome (Figure).
- Others

- Multifactorial, poligenic, familiar mechanisms

Pulmonary hypoplasia

Index case

Renal agenesis

Family pedigree
The embryological development and the chain of anatomical events leading to malformation are better known

- Cases with double uterus associated with an obstructed hemivagina and ipsilateral renal agenesis.
Acién P.
Embryological observations on the female genital tract.
Hum Reprod 7:437-445, 1992
All cases of unilateral renal agenesis are associated either:

1. With **agenesis of all derivatives of the ipsilateral urogenital ridge** (generally with *unicornuate uterus* on the contralateral side) or

2. With **distal mesonephric anomalies** (generally with ipsilateral blind hemivagina) and uterine duplicity (*didelphys or bicornuate uterus*)
Embryological bases: GONADS

- Fifth week of pregnancy
- Wolff’s body
- Urogenital ridge
- Somatic cells/ germ cells
- Teloferon. Fibronectin
- Primary sexual cords/ secondary

Moore and Persaud. The developing human. Fifth ed
FORMATION AND DIFFERENTIATION OF THE GONADS

- Undifferentiated gonads
- Aorta
- Adrenal
- Células germinales
- Conducto mesonefrico
- Intestino
- Undifferentiated gonads
- Cresta gonadal
- Cresta urogenital
- Cavidad peritoneal
- 6 Semanas
TESTIS DIFFERENTIATION

Chromosome Y and TDF/SRY gene

GONADA INDIFFERENCIADA

Chromosome Y and TDF/SRY gene

Mesonephric duct

Paramesonephric or Müller’s duct
INTERNAL GENITALS AND URINARY SYSTEM
Development of the urinary system

- Metanephrogenic mass
- KIDNEY

Paramesonephric ducts
- Uterine primordium
- Müller tubercle
- Wolffian ducts
- Urogenital sinus
- Ureteral bud
- Inductor function of the mesonephric duct
EMBRYOLOGY OF THE VAGINA

G. Bok and U. Drews, J Embryol exp Morph 73, 275-95, 1983

**Fig. 9. Hypothesis of the embryological development of the human vagina.** MD, paramesonephric or Müllerian duct; WD, mesonephric or Wolffian duct; MT, Müllerian tubercle; US, urogenital sinus; UB, ureteral bud; U, ureter.
Sanchez-Ferrer et al, Hum Reprod 21;1623-28, 2006
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Acién P. Embryological observations on the female genital tract. Hum Reprod 7;437-445, 1992

Fig. 9. Hypothesis of the embryological development of the human vagina. MD, paramesonephric or Müllerian duct; WD, mesonephric or Wolffian duct; MT, Müllerian tubercle; US, urogenital sinus; UB, ureteral bud; U, ureter.
Advanced development of the female genital tract

Differentiation of the external genitals
Blind hemivagina
Blind Hemi vagina

Mesonephric and Paramesonephric remnants

Mü ep

Wolff ep
1. Cylindrical epithelium
2. Squamous metaplasia
3. Junction
4. Atretic cervix and possible mesonephric duct

Acién et al,
In summary:

1. The appropriate development, fusion and reabsorption of the separating wall between both Müllerian ducts is induced by the Wolffian ducts placed at both sides and which act as guide elements.

2. The fused Müllerian ducts form the uterus until the external cervical os. Mesonephric ducts enlarge caudally, form the sinuvaginal bulbs, incorporate the Müller tubercle’s cells and give rise to the vaginal plate. By metaplastic induction or by epidermization from the sinus, the vagina is covered by a squamous epithelium.

3. Since the ureteral bud sprouts from the opening in the Wolffian duct, the absence or distal injury of one of these ducts will give rise to a renal agenesis and blind or ipsilateral athretic hemivagina and uterine anomaly (fusion or reabsorption defect) due to a failure in the inducing function of the injured mesonephric duct.
Clinical-embryological classification of the female genital malformations

1. **Agenesis or hypoplasia** of a whole **urogenital ridge**

2. **Mesonephric anomalies**, with absence of the Wolffian duct opening to the urogenital sinus and of the sprouting ureteral bud.
   a) With large hematocolpos in the blind vagina.
   b) With Gartner’s pseudocyst in the anterolateral wall of the permeable vagina.
   c) With partial reabsorption of the intervaginal septum.
   d) With complete unilateral vaginal or cervico-vaginal agenesis.

3. **Isolated müllerian anomalies**, can affect:
   a) **Müllerian ducts**: uterine and or tubal anomalies, sometimes segmentary (**UTERINE ANOMALIES, ASRM classification**). Other Müllnerian anomalies
   b) **Müllerian tubercle**: vaginal (or cervico-vaginal) agenesis or atresia, and segmentary atresias as the transverse vaginal septum.
   c) **Both** Müllerian tubercle and ducts (**Rokitansky syndrome, uni or bilateral**)

4. **Anomalies of the urogenital sinus** (**hymen, cloacal anomalies**)

5. **Malformative combinations**
Malformative combinations

Acién et al,
Hum Reprod 19:2377-84, 2004
Clinical-embryological classification of the female genital malformations

4. Isolated Müllerian anomalies:

a) Müllerian ducts:
Uterine and or tubal anomalies, sometimes segmentary

(UTERINE ANOMALIES, ASRM classification).

Other Müllerian anomalies:

- Müllerian anomalies “without a classification”: from the didelphys-unicollis uterus to the bicervical uterus with or without septate vagina (Fertil Steril [2008, March 24, epub] 2009; 91:2369-75): discrepancy in the fusion and resorption processes between both uterine segments (superior and inferior) corresponding to the converging and diverging portions of the Müllerian ducts.

- Segmentary defects.

- Affectation or absence of affectation of the Müllerian tubercle
Classifying Müllerian anomalies

Acién et al
Fertil Steril 2009;91:2369-75
Diagram of fusion and/or resorption defects independent in the superior and inferior uterine segments:
(A) Fusion defect of the superior uterine segment without defects in the cervix or vagina;
(B) Fusion defect in the superior uterine segment and a resorption defect in the inferior segment and vagina;
(C) Resorption defect in the superior uterine segment and a fusion defect in the inferior uterine segment, generally with septate vagina;
(D) Resorption defects in the inferior uterine segment (cervix) and in the vagina, with normal development of the uterus (superior uterine segment).
Segmentary atresias in Müllerian malformations
OTHERS ANOMALIES FROM:

Mesonephric remnants

GARTNER CYSTS

Müllerian remnants

ACCESORY UTERINE HORNs or APPENDICES
THANK YOU VERY MUCH
FOR YOUR ATTENTION!