Outflow tract disorders of the female genital tract

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Key content
• Congenital anomalies of the genital tract are uncommon.
• Embryological knowledge is essential in diagnosis and management.
• Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is best managed in tertiary centres by a multidisciplinary team.
• The more complex the obstructive disorder, the more specialist care is required.
• Ultrasound imaging is usually all that is required.

Learning objectives
• To understand the relationship between embryology and congenital abnormalities.
• To gain ability to recognise those problems that need specialist care.
• To understand the need for a holistic approach to care in MRKH syndrome.

Ethical issues
• Is failure to provide a multidisciplinary holistic approach acceptable medical care?

Keywords: adolescent dysmenorrhoea / amenorrhoea / embryology / MRKH

Introduction

Congenital abnormalities of the genital tract are uncommon and the general gynaecologist will only encounter these on rare occasions during their career. However, knowledge of the clinical presentation and management of these cases is extremely important in differentiating those patients whose care can be provided locally and those who need referral to a tertiary centre where appropriate management can be determined. Congenital abnormalities of the genital tract can be isolated, as in the case of an imperforate hymen, or more complex, involving the cervix, uterus and fallopian tubes and thus potentially affecting fertility and in some cases pregnancy may be impossible. Occasionally, congenital abnormalities of the genital tract may be associated with more complex syndromes and the importance of these relationships needs to be understood by those dealing with complex problems. Some patients who have these anomalies will find it extremely difficult to cope psychologically and may need a multidisciplinary team approach to manage their care. This is particularly pertinent as the majority of these patients are teenagers.

Embryology

A good understanding of the embryological development of the genital tract is fundamental in considering the complex clinical presentations in these conditions. The urogenital system develops from the intermediate mesothelium of the peritoneal cavity and the endoderm of the urogenital sinus (Figure 1). The ovaries are derived from the mesodermal epithelium lining of the posterior abdominal wall and primordial germ cells form by week 4, subsequently migrating into the developing ovary at week 6 and differentiate into oogonia. Both male and female fetuses initially have both a Wolffian (mesonephric) duct that lies medially and a Müllerian (paramesonephric) duct that lies laterally. The presence of a Y chromosome leads to male sex determination and in its absence and in the presence of two X chromosomes, the Wolffian ducts regress due to a lack of testosterone and the Müllerian ducts persist due to the absence of Müllerian inhibitory factor. The paramesonephric duct develops into the uterus and fallopian tubes whilst the vagina develops from the vaginal plate. The two Müllerian ducts fuse at the caudal end to form the body of the developing uterus and the unfused lateral arms form the fallopian tubes. The fused caudal portion extends cranially, eventually developing a central cavity, leading to development of the functional uterus.1

The development of the vagina has remained controversial but the current understanding based on the work of Drews6 suggests that the sinovaginal bulbs are the caudal ends of the Wolffian ducts and therefore the development of the vagina arises by the downward growth of a fusion of the lower part
of the Wolffian and Müllerian ducts. This has been suggested following work that shows that mitotic figures are only present in the lower end of the Wolffian duct. The solid vaginal plate extends caudally and eventually, by 20 weeks of gestation, cavitation has occurred, unifying the urogenital sinus that gives rise to the external genitalia with the uterus and cervix. It is therefore apparent that a number of uterine and vaginal anatomical abnormalities can arise based upon either failure of development of normal structures or malfusion of the paramesonephric duct and vaginal plate. In the unicorneate uterus it is likely that the failure of development of one of the Müllerian ducts leads to this maldevelopment.

Uterine duplication, i.e. uterus didelphus, bicornuate uterus and the septate uterus will all arise from varying degrees of fusion abnormalities of the two Müllerian ducts. Failure of the development of the cervix will cause cervical agenesis and in cases where both the Müllerian duct and Wolffian duct fail to migrate at their caudal ends, this will lead to failure of fusion with the vaginal plate and therefore absence of the vagina and failure of development of the uterus. Interestingly, in this condition known as the Mayer–Rokitansky–Küster–Hauser syndrome (MRKH), many patients have small underdeveloped anlage on the lateral pelvic side wall, which presumably derive from the Müllerian duct but if the Wolffian duct has regressed and not fused with the Müllerian duct then subsequent development may be impossible.

Classification

There is no universally accepted classification of congenital abnormalities of the genital tract. In 1988 the American Fertility Society (AFS) produced a standard form of classification (Figure 2) but this form is largely focused on vertical fusion defects. Acien et al. have subsequently published clinical embryological classifications in an attempt to link development with clinical presentation. For the clinician who sees these anomalies rarely, the latter classification is overly complex, and the AFS system will probably serve most clinical situations.

Incidence

The incidence of congenital anomalies of the genital tract is difficult to determine as many women with anomalies are not diagnosed if they are not symptomatic. The incidence is influenced by the study group and in fertile women with normal reproductive outcome, the incidence ranges from 2–4%. These abnormalities are primarily abnormalities of uterine fusion with septate uteri constituting 90% of cases, bicornuate uteri 5%, and the didelphic uterus 5%, when the abnormality is detected.

Development abnormalities

MRKH syndrome (uterovaginal agenesis)

The incidence of this condition is thought to be approximately 1:5000 female births or 1:10 000 of the population. This is based on a single study from Finland and does not allow similar predictions for other populations. Patients with MRKH syndrome present in their teenage years with primary amenorrhoea in the presence of normal secondary sexual characteristics. These patients have normal ovaries and therefore puberty occurs at the normal time and in the normal sequence. However, the absence of a uterus and vagina means there is no menstruation. Approximately 40% of patients with MRKH syndrome will have associated renal
tract abnormalities and an absent kidney is found in approximately 12%. There are other associated anomalies at a significantly lower incidence, for example, spinal abnormalities and long limb abnormalities, and some 3% of patients may have some degree of hearing loss. A molecular genetic understanding of the aetiology of this condition remains unresolved but it is likely that there is some polygenic multifactorial inheritance. Affected siblings have been documented as has the presence of MRKH in discordant monozygotic twins. Of interest is that in the offspring to MRKH patients who have conceived using surrogacy, there is yet to be any case of a child with MRKH syndrome. The diagnosis is usually made clinically when examination reveals the presence of secondary sexual characteristics in association with a normal hormone profile and genital examination reveals an absent or a blind vagina. Imaging confirms the diagnosis but laparoscopy is unnecessary.

Management of these patients requires attention to two distinct areas: first, management of the congenital anomaly itself, in order to allow the patients to become sexually active, and second, the management of the psychological impact of this condition. It is now very well established that without suitable psychological support, many patients will fail the anatomical treatment and be unable to come to terms with their congenital abnormality. In the largest series published in the world, 245 patients were managed conservatively and with the use of a combination of psychology and the nonsurgical management of Müllerian agenesis, success rates in achieving functional sexual intercourse were 95%. The management to create the vagina involves the use of vaginal dilators as the treatment of first choice and this has been supported by a policy statement from the American College of Obstetricians and Gynaecologists. The technique involves passive dilatation of the vaginal dimple using graduated dilators. There are many designs of dilators available and no particular design excels over others but the results achieved are significantly different when patients are psychologically prepared to undergo the treatment regimen. A study carried out by Nadarajah et al. showed that in 60 patients followed up for 5 years, over 90% had a totally satisfactory sexual experience. Some 25% of patients complained that they had either poor lubrication or dyspareunia but this did not interfere with their enjoyment of sexual intercourse. A surgical approach is rarely required but there have been a wide range of surgical procedures suggested with success rates ranging from 80–90%.

### Obstructive outflow tract disorders of the vagina

Perturbations of the normal embryological development of the vagina may lead to a number of conditions that result in obstruction to menstrual flow and depending on the fusion abnormality, may present with primary amenorrhoea and cyclical pain or dysmenorrhoea alone. Management of these cases is dependent upon the level of obstruction and both the anatomical and functional success becomes increasingly poor with higher obstructions.

#### Imperforate hymen

The hymen is a thin membrane that occurs at the junction of the sinovaginal bulb with the urogenital sinus and is usually

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**Figure 2.** American Fertility Society classification of congenital abnormalities of the genital tract. Reprinted from: *Journal of Pediatric Surgery* 41(5), Gholoum S, Puligandla P, Hui T et al. Management and outcome of patients with combined vaginal septum, bicornuate uterus, and ipsilateral renal agenesis (Herlyn–Werner–Wunderlich syndrome). p987, ©2006, with permission from Elsevier
perforated during fetal life. Failure of this perforation leads to the membrane remaining intact and as puberty begins, menstrual blood collects behind the membrane and the vagina begins to distend. This is often painless initially and only when the vagina becomes sufficiently distended does a haematocolpos result and cause discomfort. Occasionally, if the mass is sufficiently large, it may affect micturition and defaecation, and may be palpable abdominally. Inspection of the vulva reveals a membrane that is blue in appearance with the darkened blood transilluminating through the thin membrane. A differential diagnosis of a transverse vaginal septum must always be considered but the appearances here are totally different with the septum being pink, although bulging, because the septum is so much thicker. Surgical treatment involves a cruciate incision to relieve the obstruction and the remaining quadrants of the hymen may be left in situ or may be excised. Following surgery, the haematocolpos will completely drain within 3–5 days and usually with no sequelae to this condition whatsoever especially in cases presenting early.

Transverse vaginal septum
The incidence of this is unclear but probably not greater than 1:30 000–50 000. The septae may occur anywhere along the length of the vagina although they are classified as upper, mid and lower, with the upper septae accounting for 46%, 30–40% in the mid vagina, and 15–20% in the lower (Figure 3). The presenting symptoms are usually increasing cyclical abdominal pain and the absence of menstruation. It is not uncommon for the diagnosis to be missed for several months. Only when a clinically palpable mass is discovered does the possibility of an obstructed outflow tract disorder arise and ultrasound imaging will confirm the presence of a haematocolpos and occasionally a small haematometra. If there has been sufficient time lapse between the onset of menarche and the diagnosis, a haematosalpinx can also occur. The surgical management of this condition requires the excision of the septal defect in its entirety and subsequently an end-to-end anastomosis of the upper and lower vagina. It is imperative that dissection occurs laterally to excise all of the septal tissue or the risk of stenosis will occur. A firm vaginal mould should be inserted through the site of the anastomosis for a minimum of 10 days and thereafter the patient should be instructed in the use of vaginal dilators for 2–3 months to ensure that stenosis does not occur and that a functional result will ensue. Excellent results are normally obtained for lower and middle septal defects but for higher septal defects, the results are less encouraging. When the upper vaginal portion is short, there is a risk of damage to the bladder or the rectum and great care has to be taken during the procedure. When these higher septal defects are resected, a mould may need to remain in situ for 3–6 months to obtain the best results.

However, one of the difficulties with these patients is the age of presentation and often they can be as young as 12 or 13 years when the cooperation with the use of either moulds or dilators is difficult to ensure. This means that in some cases, patients may return some years later and although they have been able to obtain menstrual drainage, and use tampons, the ability to have sexual intercourse may be difficult due to stenosis. At this stage, a further procedure can be carried out in order to remove the stenotic area and attempt re-anastomosis but this should only be done if the patient is capable of maintaining a regimen of using vaginal dilators. Pregnancy success in patients with this type of disorder vary with the level of obstruction and Rock et al. reported a pregnancy rate of 100% in patients with lower third obstruction, 40% in middle third and only 20% in the upper third and the likely explanation for this is the incidence of endometriosis at the time of the obstructive problem which may cause architectural damage to the pelvis. However, IVF is appropriate in this patient group but it should be emphasised that other than those patients with a lower third anastomosis, delivery should be by caesarean section. Patients with lower third problems can be allowed to have a vaginal delivery but care must be taken in ensuring the use of an episiotomy to prevent lateral damage during head descent.

Longitudinal vaginal septum
As can be seen in Figure 4, longitudinal fusion defects may occur in the presence of two hemi-uteri and two hemi-cervices. Embryologically, each cervix fuses with the urogenital sinus to develop into two hemi-vaginas. The
septum that divides these may be partial or complete and patients usually present with either difficulty with inserting tampons or discomfort during intercourse. They may not present at all until pregnancy when it is an incidental finding. Excision of the vaginal septum is usually advisable both to improve the chance of achieving a pregnancy in those who are trying to conceive but also to avoid difficulties that may arise during childbirth. Excision is straightforward and can be carried out by sharp dissection, diathermy or laser.

If one of the hemi-vaginas fails to completely canalise, a blind vaginal cavity results and at the time of puberty when menstruation begins, menses from the unobstructed vagina are found to flow normally, whereas the obstructed hemi-vagina accumulates menstrual fluid. This can create a confusing clinical situation which often leads to late diagnosis. However, eventually a clinically palpable mass should lead the clinician to suspect outflow tract disorder. Dysmenorrhoea can be quite severe and patients are sometimes admitted as emergencies. The surgical management of these conditions involves careful excision of the vaginal septum in its entirety but care has to be taken because this type of septum can be very thick. It is ill-advised to drain a hemi-vagina as a temporary means as this may result in ascending infection, septicaemia and a life-threatening situation. It is imperative therefore that these procedures are carried out by surgeons whose skills allow them to do this surgery effectively and that the operation performed is curative. The results of surgery in these circumstances are excellent and dyspareunia is rarely a problem. It is important to inform the patients that their uterus didelphus remains and therefore obstetric complications need to be explained.
Uterine anomalies
From an outflow tract perspective, the only uterine anomaly that may cause a problem is the presence of a rudimentary horn. In this circumstance, the caudal ends of the Müllerian duct fail to fuse and a unicornuate uterus with an adjacent or attached uterine horn may result. This horn is functional and therefore at the time of the onset of menses, the endometrium within the horn will shed and therefore create a haematometra, with retrograde menstruation and severe dysmenorrhoea. In girls with dysmenorrhoea that is unresolved through normal medication, an ultrasound scan should be performed to identify whether or not there is a rudimentary horn present. When these are non-communicating, the horn needs to be removed surgically and the uterus reconstructed. If this is carried out meticulously, reproductive performance is the same as with a unicornuate uterus. Occasionally, these horns may be communicating, in which case they are usually asymptomatic. However, if diagnosed prior to pregnancy, they should be removed because a pregnancy in a communicating horn can lead to uterine rupture and maternal fatality.

Imaging
The choice of imaging to diagnose a congenital abnormality depends on the skills of the operator involved. In the vast majority of cases, ultrasound scanning is sufficient as long as the ultrasonographer or radiologist is familiar with congenital abnormalities (Figure 5). In situations where the anatomical structure is in doubt, an MRI scan can be carried out to delineate the congenital abnormality (Figure 6). For uterine anomalies, hysterosalpingography or hysterosonography can be used to outline the uterine cavity and detect any abnormalities.

Management philosophy
Congenital malformations of the genital tract in teenage and adult women generate understandable anxiety with regard to sexuality, sexual function and reproduction. The issues are complex psychologically as well as gynaecologically and evidence presented above illustrates superior outcome for patients treated in a multidisciplinary, holistic manner. Centres that try to manage these patients without an experienced team of health professionals are not giving their patients the best care, and as such, pose an ethical question about the appropriateness of their approach. Gynaecologists, like all doctors, must have the patient’s best interests at the forefront of their decisions with regard to best practice.

Conclusion
Congenital malformations of the genital tract are rare but obstetricians and gynaecologists must be aware of them as they can affect obstetric outcome and fertility if the diagnosis is delayed (Figure 7). Simple obstructive outflow tract disorders, such as an imperforate hymen, can be treated very effectively by the general gynaecologist but more complex obstructive disorders need the approach of tertiary surgeons to obtain optimum results. Patients with MRKH syndrome are best managed in tertiary centres where a multidisciplinary team approach can achieve outstanding results without the need for surgical intervention.

Conflict of interest
None declared.
References