

## Mini-Review

# Lower Genital Tract Disease in Children and Adolescents—A review

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**Abstract.** Conditions affecting the lower genital tract of female children and adolescents are often significantly different than those seen in the adult. The purpose of this review is to provide an overview of vulvar, vaginal, and cervical conditions that may be encountered only rarely by the more generalized practitioner.

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**Key Words.** Vulvar diseases—Vulvar neoplasms—Cervix neoplasms—Vaginal neoplasms—Vaginal diseases—Vulvar diseases—Child—Adolescent

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### Introduction

Conditions affecting the lower genital tract in female children and adolescents are often significantly different than those seen in the adult. Visits to the physician's office because of such a complaint are a rarity in many practices, and often these patients receive care from highly specialized practitioners, often gynecologists, urologists, or pediatricians with a special interest in these conditions. The purpose of this review is to provide an overview of conditions that may be encountered only rarely by the more generalized practitioner. Gynecological examination techniques must be tailored to the age of the patient. Several review articles deal with examination techniques for both prepubertal children and adolescents.<sup>1–4</sup>

### Congenital Anomalies and Intersex Conditions

The first gynecologic examination a woman ever receives is actually at birth. The female infant should

be examined for appearance and patency of external genitalia, as well as undergoing palpation of the abdomen for masses. When ambiguous genitalia are detected during the newborn examination, the first effort must be directed at ruling out the potentially life threatening salt-losing form of congenital adrenal hyperplasia.<sup>5,6</sup> After that emergency has been ruled out, haste should be avoided. The American College of Obstetricians and Gynecologists (ACOG)<sup>7</sup> recommends that parents of a child with ambiguous genitalia be counseled that their child's genitalia are incompletely formed rather than assigning sex. A multidisciplinary approach is important for appropriate evaluation, and involves a detailed family history, physical examination, hormonal and genetic testing, and imaging studies. Surgical evaluation may be necessary as well. Rare clitoral neoplasms have been confused with ambiguous genitalia.<sup>8,9</sup>

Whether or not to surgically correct the genitalia of individuals with intersex conditions is a matter of great debate, with advocates on both sides, and is beyond the scope of this discussion. There are several reviews on the evaluation and management of these patients.<sup>6,10–15</sup>

### Normal Sexual Development

To understand the underlying mechanisms of congenital abnormalities of the lower genital tract, a brief review of normal sexual development is presented.<sup>16–23</sup> The primordial germ cells migrate from the yolk sac to the urogenital ridge via the hindgut in both sexes, about 3 weeks after fertilization. The mesothelium on the medial surface of the urogenital ridges becomes the gonads. There is evidence that the testis determining factor gene is the SRY gene.<sup>23</sup> This gene must express before differentiation of the urogenital ridge to form

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a testis occurs. The testis itself then induces further male differentiation. SRY may also cause undifferentiated cells to become Sertoli cells. Sertoli cells express the SOX 9 and SF-1 genes, leading to further male differentiation.

SF-1 is thought to activate the Müllerian Inhibiting Substance (MIS) gene. Sertoli cells produce MIS which causes regression of Müllerian structures (tubes, uterus, and vagina). If SRY doesn't express, the DAX1 gene expresses, leading to ovarian development. (SRY turns off DAX1). Leydig cells produce testosterone which leads to internal male development (epididymis, vas, seminal vesicles). 5-alpha reductase, present in external genital tissues and the urogenital sinus, converts testosterone to dihydrotestosterone. Dihydrotestosterone leads to external male development (penis, scrotum, prostate).

With development of the ovary, there is regression of the mesonephric (Wolffian) ducts and development of the structures of the paramesonephric (Müllerian) ducts. These paired ducts fuse, and give rise to the uterus, Fallopian tubes, and upper two thirds of the vagina.

### **Congenital Anomalies**

Anomalies of these structures relate to abnormalities of fusion and/or dissolution of the septum. The lower vagina is formed by the urogenital sinus, which grows upwards and meets with the lowermost portion of the paired fused paramesonephric ducts, and canalization occurs. The lower portion of the tract develops into squamous epithelium, and the upper portion into glandular epithelium. The meeting of the two epithelia forms the squamocolumnar junction which resides on the cervix, and plays an important role in the pathogenesis of cervical neoplasia. Anomalies associated with in utero exposure to diethylstilbestrol (DES) relate to interference with this portion of embryogenesis. Disruption by DES of mesenchyme can lead to a T-shaped uterus and cervical hoods/polyps, while interference with the normal migration of squamous epithelium can lead to adenosis, where there are islands of glandular epithelium in the vagina.

Congenital anomalies of the Müllerian system, if not detected during infancy, may present with primary amenorrhea or abnormal bleeding in adolescence. These anomalies can be divided conceptually into disorders of fusion, canalization, agenesis/dysgenesis/hypoplasia, or embryonic rests. More common Müllerian anomalies include hymenal abnormalities (imperforate, microperforate, and variants), vaginal agenesis (Mayer-Rokitansky-Küster-Hauser Syndrome), transverse vaginal septum (high, medium, or low), longitudinal septum (obstructive or nonobstructive), cervical

agenesis or hypoplasia, unicornuate uterus with or without rudimentary horn (which may have a communicating or noncommunicating endometrial cavity or no cavity), uterus didelphys or bicornuate uterus (complete or partial), septate uterus (complete or partial), and DES-related T-shaped uterus.

Müllerian anomalies may be associated with urinary tract anomalies, skeletal anomalies, inguinal hernia of adnexa, and occasionally congenital heart anomalies. A partially obstructing longitudinal septum is often associated with a uterus didelphys, and absent kidney on the side of the obstruction.<sup>24</sup>

Some patients with Müllerian anomalies may have abnormal menses due to obstructed blood flow if there is incomplete communication of the uterus, cervix, and vaginal outlet. Endometriosis can occur secondary to obstruction. Fertility issues related to endometriosis can arise. Outlet obstruction can present at birth w/ mucocolpos, or at menarche with hematocolpos, pain, urinary retention, and bowel symptoms in addition to primary amenorrhea. If endometriosis does not interfere, there is no decreased conception rate with uterine anomalies, but these women are prone to abnormal fetal presentation, preterm labor, and cervical malfunction. A septate vagina may obstruct tampon use or intercourse, and can be excised.<sup>25,26</sup>

### **Intersex Conditions**

In addition to ambiguous genitalia or primary amenorrhea, individuals with intersex conditions may initially present with an inguinal hernia which in a phenotypic female may contain a gonad or fallopian tube. A gonad may also be present in a labial mass, including a testis or ovotestis. These findings may be the initial ones leading to a complete evaluation for intersex conditions.

Up until recently, the classification of disorders of sexual differentiation was morphologic/gonadal; however, the molecular genetic basis of these disorders is now better understood, leading to a classification that takes these additional factors into account, with gonadal and genital anatomy, chromosomal findings, and specific male genetic metabolic defects evaluated.

### **Pseudohermaphroditism**

A complete classification and excellent discussion of intersex disorders is described by Robboy,<sup>16</sup> and a brief overview follows. Individuals with intersex conditions may have a normal or abnormal chromosomal constitution. For those with a normal chromosomal constitution, the presence of ovaries in the presence

of ambiguous genitalia constitutes female pseudohermaphroditism, while the presence of testes in chromosomally normal individuals with ambiguous genitalia constitutes male pseudohermaphroditism. Individuals with ambiguous genitalia and normal chromosomes may also have end organ defects, or defects of uncertain etiology. Conditions associated with an abnormal chromosomal composition may have infrequent or frequent ambiguous genitalia.

Female pseudohermaphrodites are XX females with ovaries who have had excess exposure to androgens in utero. This can be due to adrenogenital syndrome (congenital adrenal hyperplasia, or CAH), placental aromatase defect, which can lead to both maternal and fetal masculinization, maternal ingestion of progestins,<sup>27</sup> androgens, or a maternal virilizing tumor. Female pseudohermaphrodites show varying degrees of clitoral enlargement, and may have labioscrotal fusion. A common urogenital sinus with vagina and urethra may be present in some cases of CAH. If exposure to masculinizing hormones occurs early in fetal life, the effects can be severe, with the clitoris mimicking a penis with hypospadias.

At puberty, normal secondary sexual characteristics and menses occur. As previously discussed, infants with the salt-losing form of 21-hydroxylase deficiency congenital adrenal hyperplasia must be identified early, as this is a life-threatening condition. Tumors are rare in female pseudohermaphrodites.

Male pseudohermaphrodites are XY individuals with testes who are undermasculinized. Male pseudohermaphroditism can occur in a variety of ways. Several gonadal defects can occur. These include testicular regression syndrome, where the phenotype is dependent on the gestational age of occurrence. Early destruction leads to absent internal genitals with external female genitals, whereas later destruction can lead to male external genitalia that range in appearance from infantile to nearly normal. Intermediate destruction leads to ambiguous genitalia with mixed Wolffian and Müllerian development. A rare cause of male pseudohermaphroditism is Leydig cell agenesis. The phenotype varies, and is usually female or ambiguous. Male pseudohermaphrodites may also have defects in testosterone synthesis or testosterone insufficiency due to various metabolic path derangements. In some forms of adrenogenital syndrome in males, individuals have ambiguous or female external genitals, with germ cells disappearing or decreasing within a few years of life.

These children, who have been raised as females, may first appear at puberty with lack of menses and virilization.

Male pseudohermaphrodites may also have a defect in the Müllerian inhibition system leading to persistent Müllerian ducts, also known as “hernia uteri inguinalis.” These individuals have normal external male

genitalia with unilateral or bilateral cryptorchidism, but also have an inguinal hernia containing an infantile uterus and fallopian tubes. Puberty occurs normally, but fertility is rare.

### **Intersex Conditions Associated with End Organ Defects**

Individuals with intersex conditions may also have an end organ defect. The most common is due to androgen receptor binding defects. The complete form, androgen insensitivity syndrome (AIS), is the most common, although partial forms with a variety of phenotypes exist.

AIS has an incidence of 1/20,000, and is transmitted as an x-linked recessive condition.<sup>16</sup> These children have an external female phenotype, and unless they present with an inguinal hernia or a labial mass containing a testis are often not diagnosed until puberty, presenting with primary amenorrhea. AIS patients have a short vagina, scant axillary and pubic hair and adolescent breast development. Testes are cryptorchid, and there is no epididymis, vas, seminal vesicles or prostate. There is usually no uterus, but occasional fallopian tube fragments have been identified. The testis is normal until about age 5. There is no spermatogenesis. Lesions include benign hamartomatous Sertoli nodules, and germ cell tumors, most commonly dysgerminoma. The risk of gonadal malignancy is low before age 25–30,<sup>28</sup> so patients have been allowed to pass through puberty before gonadectomy to permit development of secondary female sex characteristics.

Another form of end-organ defect is disordered testosterone metabolism due to 5-alpha reductase deficiency. This autosomal recessive condition leads to female or ambiguous genitalia in an XY individual. There may be a common urogenital sinus with the urethra and blind vagina entering it, and a small clitoris-like phallus. Testes are present in the inguinal canals or labia. No müllerian structures are present, and the Wolffian structures (vas, epididymis, and seminal vesicles) are normal. The testis is still capable of producing testosterone, and there is virilization at puberty. This can lead to major gender issues when an individual who has been raised as a female suddenly becomes masculinized. The condition is common in some geographic areas such as New Guinea, and in the Dominican Republic, and has been called a term that translates roughly into “Penis at 12.”<sup>16,29,30</sup>

Ambiguous genitals may also be due to uncertain defects in a variety of syndromes. An example of this is the Smith-Lemli-Opitz syndrome.

### Intersex Conditions with Abnormal Chromosomes

Abiguous genitalia may be frequent or infrequent in various intersex conditions with abnormal chromosomes due to additions, deletions or mosaics. Infrequent ambiguity is seen in individuals with Klinefelter Syndrome and Turner's Syndrome. Individuals with Turner's Syndrome have streak gonads, and germ cell tumors are rare if no Y material is present. This possibility must be actively excluded if virilization occurs, as the Y material may be cryptic. If the diagnosis is not made early, these children will present with primary amenorrhea.

Other intersex conditions with chromosomal abnormalities but infrequent genital ambiguity include the sex reversal syndromes. XX males are infertile, with near normal male phenotype, and atrophic testes. Most of these sporadically occurring individuals have a small amount of Y material on the paternal X chromosome due to a meiosis problem. There are also various heritable forms of the condition. Some forms of pure gonadal dysgenesis, with two streak gonads, fall into this category. XY females can occur in several syndromes, including Campomelic Dysplasia, where there is a mutation in SOX9, and due to a variety of nonsyndromic genetic conditions leading to loss or mutation of SRY. Testicular regression, androgen insufficiency or receptor defect, and 5-alpha reductase deficiency are also forms of XY sex reversal.

Individuals with abnormal chromosomes and frequent ambiguity include mixed gonadal dysgenesis (one testis and one streak), and true hermaphrodites, who possess both ovarian and testicular tissue. These individuals are at high risk for germ cell tumors, including gonadoblastoma, and dysgerminoma, with early onset, hence the haste to perform gonadectomy.

### Vulvar Disorders in Children and Adolescents

Female children and adolescents may present with a variety of vulvar complaints.<sup>31-33</sup> The most common presenting lower genital problem of a preadolescent child is vulvovaginitis.<sup>34</sup> Other presenting complaints that can bring a child to the gynecologist's office include bleeding and/or discharge.<sup>35</sup>

Evaluation of lower genital tract complaints in the child should take into account the hormonal milieu appropriate to the age of the child. Residual estrogen effect can be present up until about 2-3 years of age. After that age, until about 8 to 10 years, waning of the estrogen leads to an atrophic epithelium, which again starts to become estrogenized with the peripubertal years, usually from about 8-10 years.

Most cases of pediatric vulvovaginitis are of dermatologic origin, or may relate to atrophy and/or hygiene problems. Wiping front to back, cotton underwear in the daytime with none at night, and avoidance of tight leotards, prolonged contact with wet bathing suits, and irritants such as bubble baths will go a long way in dealing with this problem. A variety of specific conditions, including foreign bodies, pinworm, allergy, dermatitis, lichen sclerosus, and psoriasis may present as vulvovaginitis. Candidal diaper dermatitis can occur, but candidiasis in the estrogen poor prepubertal girl is rare.<sup>36</sup> Gonorrhea, trichomonas, and chlamydia may also present as vulvovaginitis in children, raising the question of sexual abuse. Presenting symptoms of vulvovaginitis include discharge, irritation or pruritus, burning on contact with urine, and vulvar redness or abnormal odor.<sup>36</sup> Bleeding may occasionally occur. Office evaluation including history, physical, and possible wet mount and cultures are part of the evaluation, and occasionally vaginocopy may be needed.<sup>35</sup> A scotch tape test for pinworms may be indicated. Local measures such as attention to hygiene and sitz baths take care of most cases; however, specific therapies may be indicated.

While the most common cause of vulvar symptomatology in the child is often a hygiene related vulvovaginitis, it should be remembered that a variety of dermatological conditions can affect the pediatric vulva, including lichen sclerosus, lichen planus, seborrheic dermatitis, atopic dermatitis, contact dermatitis, and psoriasis. A vaginal foreign body may cause a secondary vulvar irritation due to discharge. Other conditions affecting the vulva can be due to trauma, systemic illness, infections<sup>37</sup> including sexually transmitted diseases, and labial adhesions. Labial adhesions in the prepubertal girl are probably related to the relative atrophic state of the epithelium coupled with some local irritation or trauma. The adhesions can usually be separated but may require application of topical estrogen.<sup>38</sup>

Fischer<sup>39</sup> reviewed a series of 130 prepubertal girls with vulvar complaints. The mean age of the group was 5.8 years, and the presenting symptoms included itching, soreness, dysuria, or a lesion. 41 (33%) of the children had atopic/irritant dermatitis, 23 (18%) had lichen sclerosus, 21 (17%) psoriasis, 15 (12%) had benign lesions such as hemangiomas, nevi, or hymenal polyp, and 13 (10%) had streptococcal vulvovaginitis. Occasional cases of staphylococcal folliculitis, labial fusion, warts, molluscum, bullous pemphigoid, scabies, erythema annulare centrifugum, tinea, vitiligo, as well as vulvar presentations of systemic disease (varicella, staphylococcal scalded skin, Henoch-Schonlein purpura) were also seen.

### Conditions Confused with Sexual Abuse

While it is critical to be aware of potential sexual abuse and investigate it, sometimes lack of familiarity



with the presenting signs of some of these vulvovaginal conditions can lead to an erroneous diagnosis of abuse, and one should be aware for example that lichen sclerosus can be associated with vulvar purpura, and the child with LS may have blood-filled blisters from minimal straddle activity such as riding a tricycle.<sup>38</sup>

Bays<sup>40</sup> has described a variety of conditions which may be mistaken for abuse. These include a congenital pit near the fourchette, straddle injury, and perianal streptococcal cellulitis. There may be erythema and excoriations due to diaper dermatitis, poor hygiene, candida, pinworm, or irritants such as bubble bath. Increased perianal pigmentation can be seen in non-abused children. Bruises may occur in Ehler's-Danlos, some hematologic disorders, hypersensitivity vasculitis, purpura fulminans, and meningitis with disseminated intravascular coagulopathy. Mongolian spots can appear bruise like. Phytodermatitis should not be mistaken for a burn or bruising. This condition can be seen when plant psoralens, present in the juice of figs, limes, lemons, parsnips or celery come into contact with skin with subsequent sun exposure. Lichen sclerosus, lichen planus, seborrheic, atopic and contact dermatitis, psoriasis, and lichen simplex chronicus may all present with pain, bleeding, or fissures. Congenital conditions such as failure of fusion of the posterior fourchette, and irregularities of the anal verge, or anal skin tags, and anal changes due to Crohn's disease, hemolytic uremic syndrome, lichen sclerosus, rectal tumor, neurogenic patulous anus, severe/chronic constipation w/megacolon, and nonabuse-related rectal prolapse may also be confused with abuse. Urethral conditions such as caruncle, prolapse, hemangioma, papilloma, polyp, and prolapsed ureterocele should likewise be ruled out. Of particular concern are infections that can be both sexually and nonsexually transmitted, such as herpes or condyloma accuminatum.

Human papillomavirus-related lesions in girls always raise the issue of abuse, although this is not thought to be true in all cases,<sup>41,42</sup> and the histologic changes in a biopsied lesion may be indeterminant. Sonnex et al<sup>43</sup> demonstrated human papillomavirus (HPV) DNA on fingers of adults with condyloma, concluding that not all HPV is sexually transmitted. Possible alternative routes include vertical and horizontal mother to child transmission. Smith et al<sup>44</sup> reported on 11 children, average age 2.3 years, with a clinical diagnosis of condyloma accuminatum which were excised. All 11 were positive for HPV DNA, but only nine were diagnosed by microscopy. The authors suggested consideration of HPV typing in these cases. Condyloma and genital HPV infection are rare but can occur in infants and nonabused children. There is an estimated 2% incidence of condyloma and 33% incidence of HPV DNA in abused children.<sup>41</sup> By adolescence, HPV DNA can be present in 13–38% of

sexually active adolescents, with a 3% condyloma rate, and there may also be abnormal cytology.<sup>41</sup> A variety of other conditions of the anogenital region may appear as warts including molluscum contagiosum, nevi, pseudoverrucous papules, condyloma lata, Bowenoid papulosis, Crohn's disease, Darier's disease, neurofibromatosis, Langerhan's cell histiocytosis, granular cell tumor, and syringoma.<sup>45</sup>

Quint et al<sup>46</sup> have classified vulvar lesions in adolescents by lesion type into solid, cystic, ulcerative, or infectious. Solid lesions include acrochordons (skin tags), nevi, molluscum contagiosum, condyloma accuminatum, vulvar intraepithelial neoplasia, and the nonneoplastic epithelial disorders, including lichen sclerosus and squamous cell hyperplasia. Lichen sclerosus, while generally thought of as a disease of the elderly, also occurs in prepubertal girls.<sup>47–49</sup> The lesion shows a "keyhole" distribution around the vaginal and anal orifices, with whitening and thinning of the epithelium. The lesion often improves symptomatically at puberty but may persist without symptoms. Long-term risk of malignancy is unknown; however, there was a report of a case of development of squamous cell carcinoma in a 32-year-old woman after resolution during puberty of childhood LS.<sup>49</sup>

Cystic lesions include inclusion cysts, which can be seen after trauma or childbirth, Bartholin's cysts, and mesonephric duct cysts (Gartner's duct cysts), which are residual Wolffian remnants. Anterolateral mesonephric duct cysts can protrude through the introitus. The cysts are thin-walled. The differential diagnosis includes imperforate hymen, which can be distinguished by lack of ability to pass a probe.<sup>50</sup> Because clinical decision-making can be challenging, surgery should not be undertaken prior to a complete evaluation and anatomic assessment, and strong consideration should be given to referring these patients to clinicians who have experience in making these judgments. Ulcers can be seen with sexually transmitted diseases such as chancroid, lymphogranuloma venereum, herpes, and syphilis, or may reflect other conditions such as Behçet's Syndrome,<sup>51</sup> Crohn's disease, pemphigus, and pemphigoid. Crohn's disease can manifest on the vulva as erythema and edema, progressing to slit-like cutaneous ulcers, which may become secondarily infected.<sup>52,53</sup> In Behçet's disease, the presence of oral or ocular findings should suggest the diagnosis, which requires at least three of the following to confirm it; recurrent aphthous ulcers of mouth/genitalia, uveitis, cutaneous vasculitis, synovitis, or meningoencephalitis. The ulcers are painful, and of nonspecific histology.<sup>53,54</sup> Pyogenic and infectious conditions include folliculitis which may be related to depilatory efforts, furuncles or carbuncles due to staphylococcus, hidradenitis suppurativa, tinea, psoriasis, and allergic reactions.

A variety of tumor-like lesions of the vulvovaginal region may also be seen.<sup>55</sup> Hydrocolpos, due to a transverse vaginal septum or imperforate hymen, may present early on as a vulvovaginal or an abdominal mass or may not present until hematocolpos develops at menarche. Other mass lesions include hymeneal cyst or tag, teratoma, lipoma, rhabdomyoma, fibroma, lymphangioma, granular cell tumor, neurofibromatosis, schwannoma, hemangioma, paraurethral cysts, urethral prolapse, congenital hydrocele, Bartholin's cyst, Langerhan's cell histiocytosis, granular cell tumor, and syringoma. Hymeneal cysts usually resolve spontaneously, and rarely need excision.<sup>56-58</sup> Lowry et al<sup>55</sup> described a case of a vulvar hamartoma with a variety of mesenchymal elements in an 8-year-old girl. Conditions in the differential diagnosis of a vulvar mass include gonadal remnant (possibly testis), inguinal hernia, cyst of the canal of Nuck, as well as benign and rare malignant tumors. A cyst of the canal of Nuck can develop where the peritoneum that invests the round ligament as it inserts into the labia majora develops a cyst. Aggressive angiomyxoma, a locally aggressive lesion, has been reported in an 11-year-old.<sup>59</sup> Malignant vulvar neoplasms described in children include squamous cell carcinoma, adenocarcinoma, malignant melanoma, sarcoma botryoides (embryonal rhabdomyosarcoma), and yolk sac tumor.<sup>55,60,61</sup>

Urethral prolapse is a vulvovaginal condition seen in children as well as postmenopausal women.<sup>62,63</sup> It is most common in prepubertal African-American girls and postmenopausal Caucasian women. It may be noticed after increased intraabdominal pressure subsequent to crying, cough, or constipation. It appears as an inflamed edematous bleeding mass at the introitus. The peak pediatric age group is 5-9 years. It presents with painless bleeding or staining of underwear, dysuria, or vulvar pain. Occasionally voiding is obstructed. Treatment is usually nonsurgical, with saline compresses or sitz baths and reduction with catheter placement and topical estrogen/antibiotic creams. Excision is occasionally performed. Differential diagnosis includes bladder prolapse, ureterocele prolapse, paraurethral cyst, ectopic ureter, polyps, papilloma, imperforate hymen, genital prolapse, and rhabdomyosarcoma. Prolapsed ureterocele is more common in Caucasian girls, and can be seen as a smooth mass protruding through the urethra, with circumferential exit of urine. This is in distinction to the donut with hole (meatus) appearance of urethral prolapse. A paraurethral cyst tends to be smaller, with deviation of the urethral orifice and an eccentric urinary stream.<sup>64</sup>

Genital prolapse is often associated with other anomalies, neurologic defects, and lower skeletal or spinal abnormalities.<sup>2</sup> Bladder extrophy and the presence of a cloaca require the input of physicians with particular expertise.

While some of vulvar disorders seen in adolescents are similar to adults, some are unique. Schroeder<sup>53</sup> points out that adolescents may present with hypertrophy of the labia minora. This may be symptomatic, or may become a cosmetic concern, in which case, excision can be considered. Postoperative edema may necessitate a Foley catheter.

As the world continually becomes smaller, practitioners in the United States may encounter girls who present with dysmenorrhea and vaginal dilatation due to female circumcision, still practiced in some African countries.<sup>65</sup>

### Vaginal Bleeding in Children

Vaginal bleeding in a newborn may be due to withdrawal of maternal hormones. The differential diagnosis of vaginal bleeding in a child includes urethral prolapse, vulvovaginal infections, including those due to enteric flora, shigella, or beta-hemolytic streptococci, condyloma accuminatum, trauma, foreign bodies, endocrinopathies, neoplasia (local or ovarian with hormonal production), and sexual abuse.<sup>66</sup> Scratching due to dermatoses may also bleed. A thorough history is critical. Tumors and tumor like lesions such as vulvar hemangiomas, uterine arteriovenous malformations,<sup>67</sup> sarcoma botryoides, and vaginal yolk sac tumor may also present with bleeding. Rare cervical lesions may also bleed. A rare cause in the U.S., but a common cause in the tropics, is a leech swimming into the vagina from swimming in a river or pond.<sup>68</sup> Uterine neoplasms usually seen in adults have appeared as sporadic reports, including endometrial carcinomas and malignant mixed Müllerian tumors. Of 52 cases of vaginal bleeding in girls 10 years or under reviewed by Hill et al,<sup>69</sup> 54% were due to a local lesion, 11% had malignant genital tumors, 21% of the children presented with precocious pubertal signs, and in 25%, no diagnosis was made.

### Other Vaginal Conditions

Vaginal polyps that must be distinguished from sarcoma botryoides were described by Norris and Taylor.<sup>70</sup> While most of these cases were in adults, there were two cases in infants, present at birth. The infant cases lacked the cytologic atypia of the adult cases, but were clinically suspected to be sarcoma botryoides because of significant edema, and in fact one case was described as having grapelike masses protruding from the introitus. Unlike sarcoma botryoides, these polyps do not have skeletal muscle differentiation with rhabdomyoblasts. Ulbright et al<sup>71</sup> described an intramural vaginal papilloma, basing their

theory of Müllerian rather than mesonephric histogenesis on electron microscopy. Sarcoma botryoides of the vagina is usually seen in girls under 5 years of age. Prognosis is much better than before, with more effective chemotherapy, and less radical surgery than the prior exenterations.<sup>72</sup>

Other rare reported conditions have included vaginal adhesions in Stevens-Johnson syndrome,<sup>73</sup> vaginal stones in disabled children,<sup>74</sup> and pyocolpos secondary to infected hydrocolpos.<sup>75</sup> Blair et al<sup>76</sup> described superficial ulcerations and thrombophlebitis with bacteria on the mucosal surface and systemic phlebitis and capillaritis in a 15-year-old with toxic shock syndrome.

### Vaginal Discharge

The differential diagnosis of a vaginal discharge in a child includes infection, including secondary to bowel flora (often from wiping back to front or other hygienic issues), STD, enterobius vermicularis (pinworm), or foreign body.<sup>38</sup> As discussed previously, vulvar symptoms may be the presenting complaint. Hemorrhagic vaginitis, most often preceded by a history of watery diarrhea, suggests vaginal contamination by bowel flora, such as shigella, or streptococcus, among others.<sup>67</sup>

### Cervical Disease in Children and Adolescents

The prevalence of HPV infection in sexually active adolescents is high, with estimates of about 13–38%.<sup>41</sup> Although cancer risk is low,<sup>77</sup> Pap smear abnormalities are frequent. Diller et al<sup>78</sup> studied 1664 patients aged 16 years or less, and found a dysplasia rate of 0.78%, all mild to moderate, with none worse, as well as increased rates of Trichomonas infection compared to adults.

The risk of HPV infection of the cervix is thought to be greater in adolescents due to the developmental biology of the area. With adolescence and estrogenization of the genital tract begins the process of squamous metaplasia. The squamocolumnar junction is located in adolescence on the outer portion of the cervix (the portio vaginalis). The columnar epithelium at this age is visible on the exocervix, and is called ectropion. This more vulnerable columnar epithelium undergoes squamous metaplasia in an ascending manner, from caudal to cranial, resulting in the squamocolumnar junction moving upward over the course of reproductive life. It is often high up in the canal in postmenopausal women. The area between the original squamocolumnar junction and the current squamocolumnar junction is termed the transformation zone or T-zone, and this rapidly proliferating area is the site of cervical intraepithelial and invasive abnormalities.

Metaplasia and the development of the T-zone is associated with sexual activity, and possibly related to inflammation such as chlamydia, or herpes. Adolescent susceptibility to cervical abnormalities due to HPV may be related to this developing squamous metaplasia, or to differences in estrogen and progesterone levels, or cell types in the T-zone in adolescents compared to adults.<sup>79</sup> Most infections resolve spontaneously; however, a small percent persist. The rate of cervical intraepithelial neoplasia in adolescents with atypical squamous cells (ASC) on pap smear is similar to that of adults.<sup>80</sup>

Sexually active adolescents should undergo pap smear screening starting three years after onset of intercourse, but not later than age 21, according to ACOG. In liquid-based cytology specimens, reflex testing of ASC pap smears for high risk HPV types using hybrid capture technology is employed by many laboratories. Recommendations for adolescents with abnormal pap smears have been developed by consensus, and may be viewed on the ASCCP website, [www.asccp.org](http://www.asccp.org).

Unusual benign cervical lesions have been described. Cervical papillomas have been reported in children.<sup>81</sup> Smith and Quint<sup>82</sup> described a 4-year-old with a recurrent cervical Müllerian papilloma. This rare childhood lesion can also occur in the vagina. Recurrence is rare in what is felt to be a benign condition usually treated with local excision. Most patients present with a sanguinous vaginal discharge. The immunoprofile of Smith's case was more consistent with a Müllerian than mesonephric origin.

Invasive cervical cancer is rare in children and adolescents. Older reports suggested that these were all adenocarcinomas of mesonephric origin; however, other neoplasms have rarely occurred.<sup>50</sup> Gupta<sup>83</sup> reported on a mesonephric adenocarcinoma of the cervix in a 1.5-year-old girl. Dekel<sup>84</sup> reported a cervical squamous cell carcinoma in a 15-year-old. There have been rare case reports of endometrioid carcinoma,<sup>85</sup> clear cell carcinoma associated with hemihypertrophy,<sup>86</sup> alveolar soft part sarcoma,<sup>87</sup> malignant mixed mesodermal tumor,<sup>88</sup> immature teratoma,<sup>89</sup> and Wilms' tumor of the cervix.<sup>90</sup> Unusual cervical lesions both benign and malignant can protrude through the introitus, including giant polyp.<sup>91</sup> Sarcoma botryoides, a vaginal lesion in the young child, is more likely to present as a cervical lesion in the adolescent.<sup>92,93</sup> Of interest is Dargent's experience with radical trachelectomy, a uterine sparing procedure for cervical carcinoma.<sup>94</sup>

Female children and adolescents can present with a wide variety of lower genital tract conditions unique to these age groups. Generalists who see these patients should be familiar with the scope of these conditions, with liberal referral to those with special expertise in the area.



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