



Adolescent gynaecology: satisfying the needs for special patients

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Abstract

Introduction

Adolescent gynaecology requires special attention for understanding the dynamics of the adolescent's psychological and physiological circumstances. The first gynaecologic examination can be an important factor for establishing a long-term relationship. Creating a relaxing comfortable environment is essential for making the patient comfortable. As such, practitioners should be at ease discussing a variety of issues with adolescents, including eating disorders, substance abuse, house and school environment and dating violence. The practitioner should be familiar with the differential diagnosis, evaluation and management of diseases which are common in the adolescent period as amenorrhoea, dysfunctional uterine bleeding, pelvic pain, endometriosis and polycystic ovarian syndrome. Thus, recognition and prompt treatment of both diseases are advocated to prevent future fertility implications in a population with their entire fertility potential ahead of them.

Conclusion

Understanding these basic concepts is critical for complete care in a very important and unique age group. This review discusses adolescent gynaecology.

Introduction

Adolescent patients are always a challenge for a practitioner. First impact in the examination room for young girls may have a key role in their future health status. In this group, lack of self-consciousness about changes in their body makes the diagnosis more difficult. Referring for medical care usually delays during this period of their lives due to difficulties about defining pathological and physiological changes of youth.

As mentioned in several textbooks about adolescent gynaecology and reviews about this topic as the American College of Obstetricians and Gynecologists (ACOG) Committee Opinion in July 2010 first reproductive visit provides an excellent opportunity for the gynaecologist to start a patient-practitioner relationship, build trust and dispel myths and fears¹.

During the first visit, careful patient interview with and without parents should precede genital examination. Full body physical examination usually gives excellent clues even for reproductive problems, and also provides excellent settlement between the practitioner and the teenager. The aim of this review was to discuss how to satisfy the needs for special patients in adolescent gynaecology.

Discussion

History taking and physical examination

As recommended by the ACOG, the initial visit to the gynaecologist should occur between the ages of 13 and 15 years^{1,2}. Before starting the interview, confidentiality issues have to be explained to parents. By

this explanation, legal problems can be prevented and trust-based relationship between the adolescent and practitioner can be preserved. During this visit, important subjects of general health, such as immunisations including new aspects such as human papilloma virus (HPV) vaccination, risk prevention, tobacco and substance abuse, eating disorders such as obesity, anorexia and depression should be evaluated³. It is important to meet initially together with the teenager and her parents/guardian to explain the concept of confidentiality and privacy. For this purpose screening should begin with less sensitive issues such as safety (e.g. eating and sleeping habits and seat belt use) before addressing emotional and sexual issues⁴. A sexual history is an integral component of the gynaecologic visit. However if possible, sexual history and genital examination can be delayed for another meeting. If current interview is the 'one and only' chance for examination, the parent or guardian and teenager should be interviewed separately for sexual history. By this interviewing technique, trust-based relationship can be preserved, also hidden secrets in the depths of history can be enlightened.

Complete physical examination is important in adolescent examination. Body mass index, Tanner staging, breast development and other physical findings support the suspicions determined in the history. Asymptomatic patients who are not sexually active may delay their initial pelvic examination up to the age of 21 years⁵. Besides this predisposition, external genitalia should be inspected in all patients

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even if not sexually active. ACOG in their committee opinion in 2006 determined the indications for pelvic examination in the adolescent⁶. In this committee opinion, delayed puberty or precocious puberty, abnormal vaginal bleeding, pathological vaginal discharge, history of sexual intercourse, abdominal or pelvic pain and suspicion of outflow tract obstruction were defined as the indications for pelvic examination.

The use of models, diagrams and charts may provide a relief in the adolescent before examination by feeling the adolescent as an active part of examination.

Abnormal uterine bleeding

Menarche is a significant milestone in adolescent life. Progression from late childhood to sexually matured young women is branded by menarche. Abnormal menstruation affects 75% of females by late adolescence and it is the leading cause of physician visits among adolescents⁷. In the adolescent, anovulation, as a result of immaturity of the hypothalamic-pituitary-ovarian axis, is the leading cause of abnormal menstrual bleeding. In 2006, ACOG and the American Academy of Pediatrics published recommendations regarding the menstrual cycle as a 'vital sign'⁸. It may take up to 5 years postmenarche to establish regular ovulatory cycles⁹.

In one study of adolescents hospitalised for menorrhagia and severe anaemia, 75% had anovulatory dysfunctional uterine bleeding and 25% had other causes of bleeding¹⁰. As already well investigated, persistence of irregular menses may be an indicator of other pathological conditions such as polycystic ovarian syndrome (PCOS), adrenal aetiologies (including Cushing's syndrome, late onset congenital adrenal hyperplasia and rare adrenal tumours), pregnancy-related issues (which should be considered in all cases), infections, trauma, structural lesions, suppression

of the hypothalamic-pituitary-ovarian axis (secondary to physical or emotional stress, eating disorders or weight loss from other causes) bleeding diatheses, stress, etc.

The evaluation of an adolescent with abnormal uterine bleeding should be initiated with a careful history¹¹. A menstrual calendar is often useful to document the exact bleeding pattern and can help in narrowing the differential diagnosis. Physical and gynaecological examinations with proper laboratory testing as human chorionic gonadotropin, thyroid-stimulating hormone, complete blood count, and platelet levels, prothrombin and partial thromboplastin time, liver function tests, and a von Willebrand (vW) disease panel including vW factor antigen, factor VIII and ristocetin cofactor activity levels can guide the physician in determining the cause of bleeding¹⁰. Specific causes of bleeding should be evaluated in the multidisciplinary approach.

For mild dysfunctional bleeding and haemoglobin level above 11 g/dL control within 2–3 months may be sufficient. More excessive bleeding needs iron supplements and combined oral contraceptives in therapy. In massive bleeding, if the haemoglobin level decreases below 9 g/dL hospitalisation may be required.

Progestins either cyclically or in depot form, for example, depomedroxyprogesterone acetate or gonadotropin-releasing hormone (GnRH) analogue treatment can be used as other treatment options in adolescents with abnormal uterine bleeding.

Polycystic ovarian syndrome and other hyperandrogenemic disorders

In 1935, Stein and Leventhal described, a syndrome within seven obese women who also had hirsutism. It is a common endocrine disorder that affects 4%–6% of the female population and is

characterised by increased androgens emanating from the ovary and possibly the adrenal gland¹².

In 2006, the Androgen Excess and PCOS Society suggested diagnostic criteria to all of¹³:

1. Excess androgen activity,
2. oligoovulation/anovulation and/or polycystic ovaries and
3. Other entities are excluded that would cause excess androgen activity.

Because of the high frequency of excess androgen activity-related symptoms and menstrual disorders in the adolescent period, exact diagnosis may not be possible until the end of puberty. The difficulty in defining the abnormal and physiological changes demonstration of hyperandrogenism is more important to secure the diagnosis. Tests to help clarify the diagnosis includes total testosterone, dehydroepiandrosterone sulphate (DHEAS) and 17-OH progesterone. Androstenedione may be added to monitor response to treatment, because this is the main androgen secreted by the ovary in PCOS¹⁴. Patients with PCOS are much more prone to developing the metabolic syndrome than those without PCOS. The metabolic syndrome is diagnosed by having at least three of the following findings:

1. increased abdominal fat mass (waist circumference more than 88 cm),
2. increased triglycerides (150 mg/dL or more),
3. decreased high-density lipoproteins (50 mg/dL or less),
4. increased blood pressure (130/85 mmHg or more) and
5. increased plasma glucose (100 mg/dL or more).

Education of patients with PCOS should be started in adolescence to avoid serious health problems in their future life. Long-term risks of metabolic syndrome such as diabetes and cardiovascular disease, current problems such as menstrual disorder, hirsutism, acne, obesity and related conditions require a multidisciplinary approach to the teenager.

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Menstrual irregularities in PCOS, mostly oligo or anovulation are a major risk factor for endometrial hyperplasia due to unopposed oestrogen. Weight loss seems to be the primary regulator of the menstrual cycles during treatment. Combined oral contraceptives help to maintain regular withdrawal bleeding, in addition to decreasing circulating androgen levels. Insulin sensitizers such as metformin can decrease peripheral insulin resistance which is one of the main factors in PCOS pathogenesis¹⁵.

Quantification of hirsutism is necessary in both treatment and follow-up of the adolescent. The Ferriman–Gallwey classification is the most widely used classification system. In the treatment of hirsutism anti-androgenic drugs such as spironolactone and flutamide is useful to prevent future hair growth. Electrolysis is generally used to remove existing hair. Combined oral contraceptives also aid in long-term management of hirsutism by decreasing levels of free testosterone.

The cosmetic implications of a hyperandrogenic state such as hirsutism and acne can gravely affect young women's self-esteem. Close attention should be paid to her psychological state during treatment which has satisfactory results in 6–12 months.

Amenorrhoea

Amenorrhoea is defined as the absence of menstrual period, which is common in adolescent period. Finding the underlying cause of amenorrhoea presents a diagnostic challenge and requires an understanding of normal menstrual function during pubertal years. Primary amenorrhoea is commonly defined in textbooks as the absence of menstrual cycle until the age of 16, normative age distributions for United States indicate that the 95th percentile for menarche is 14.5 years¹⁶. Secondary amenorrhoea is defined as the

absence of three or more consecutive menstrual periods in patients with regular menses. In adolescents who have never had regular cycles for 6–12 months may be allowed before pursuing evaluation of amenorrhoea. The initial approach in differential diagnosis of amenorrhoea is excluding the presence of pregnancy. Low incidence of using contraceptive methods in adolescents increases the risk of pregnancy. Moreover, denial of sexual activity makes the diagnosis more challenging.

In primary amenorrheic adolescents, development of secondary sex characteristics, height and body mass index should be noted. Serum gonadotropin levels (follicular-stimulating hormone, FSH, and luteinising hormone, LH) and oestrogen are key laboratory indicators in defining the possible cause of primary amenorrhoea. High FSH, LH and low oestrogen levels indicate hypergonadotropic hypogonadism. It indicates failure of the ovary to produce oestrogen despite adequate stimulation by the pituitary gland. The most common cause of hypergonadotropic hypogonadism in an adolescent is Turner syndrome¹⁷. Turner syndrome is defined by elevated gonadotropin levels, delayed puberty and 45,XO karyotype. It affects 1:500 females. All adolescents with primary amenorrhoea, delayed puberty and high serum gonadotropin levels should have chromosomal analyses performed. Other causes of hypergonadotropic hypogonadism include trauma, infection, radiation, chemotherapy and congenital adrenal hyperplasia.

Hypogonadotropic hypogonadism is a more common cause of amenorrhoea in adolescents. The most common cause of hypogonadotropic hypogonadism is constitutional delay of hypotalamo-hypophyseal-ovarian axis. Anorexia nervosa (AN), exercised induced amenorrhoea, systemic diseases, Kallman syndrome (deficiency of GnRH) and panhypopituitarism are other less

common causes of hypogonadotropic hypogonadism.

Eugonadotropic amenorrhoea occurs in adolescents with normal secondary sex characteristics and primary amenorrhoea. In this category of amenorrhoea, serum FSH, LH and oestrogen levels are within normal range. Imperforated hymen presents with cyclic abdominal pain in an increasing manner. Rokitansky–Koster–Hauser–Mayer syndrome accounts for 15% of cases of primary amenorrhoea in adolescent¹⁸. In this syndrome, karyotype is 46,XX, phenotype is female and the uterus is absent.

Hyperandrogenism is the key feature in the management of secondary amenorrhoea. Hirsutism, cliteromegaly and acne are findings of hyperandrogenism in physical examination. PCOS is the most common cause of hirsutism and menstrual irregularities in adolescents¹². Hyperandrogenism can also be a sign of adrenal or ovarian malignancy. Proper imaging studies should be performed in adolescents when highly elevated testosterone and DHEAS levels are encountered, to exclude malignancies.

The evaluation of adolescents with secondary amenorrhoea and no physical signs of hirsutism or virilisation begin with the measurement of serum gonadotropin levels. High levels indicate ovarian failure. Normal or low levels should be evaluated with serum prolactin, thyroid-stimulating hormone and progesterone challenge test. Elevations in serum prolactin levels can be an indicator of hypophyseal microadenoma or primary hypothyroidism. A withdrawal bleed within a week of completing a 5-day course of medroxyprogesterone acetate, 10 mg daily, indicates anovulation. On the other hand, absence of withdrawal bleeding indicates severe hypoestrogenism or severe endometrial damage.

Menarche is an important event during adolescents. Normality or irregularity of menses provides important information to health

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professionals about adolescents' physical condition. Menstrual disorders should be carefully evaluated and effectively diagnosed in this population for both physical and psychological health.

Endometriosis

Endometriosis is simply defined as the presence of glands and stroma outside the uterus. There are many questions about pathophysiology of the disease in adult women and these issues are magnified when dealing with adolescents. Estimating the prevalence of endometriosis is difficult. Goldstein et al.¹⁹ reported endometriotic lesions in 47% of girls undergoing laparoscopy for chronic pelvic pain with 58% of these girls having minimal disease in 1980. Endometriosis in the adolescents has been extensively reviewed by Dovey and Sanfilippo²⁰. In this review, the authors mentioned that the onset of symptoms before the age of 20 years, with an average time lapse between the onset of symptoms to diagnosis is 9 years. The youngest adolescents with endometriosis is reported in an pre-menarchal 11-year-old girl which reminds us that endometriosis must be in the differential for any young patient being evaluated for chronic pelvic pain²¹.

A major distinction between adolescents and adults in the development of endometriosis is its association with Müllerian anomalies. Non-obstructive Müllerian anomalies do not seem to be associated with an increased incidence of endometriosis.

ACOG recommends proceeding with laparoscopy in adolescents with persistent dysmenorrhoea who do not respond to oral contraceptive pills (OCP) and non-steroidal anti-inflammatory drug therapy²². The literature does not yet confirm that post-operative medical treatment should be routinely prescribed or that intervening in the adolescent population prevents disease progression or

long-term sequel such as adult infertility²³.

Endometriosis is a disturbing situation of a young woman in pain and a physician who needs to make a diagnosis and manage the symptoms. Laparoscopic excision of visible lesions remains the gold standard for establishing the diagnosis and long-term control of the symptoms in adolescents. Medical treatment and complementary therapies are often required in the management of disease.

Ovarian cysts

Adolescence is an age group in which, development of both simple and complex cysts is quite common. Conservative management (observation or organ sparing surgery) is essential to preserve the reproductive potential of the teenager.

Asymptomatic simple cysts smaller than 6 cm on ultrasound examination can be observed with or without administration of OCPs. Use of OCPs for 2–3 months to prevent recurrence but not to treat the presenting cyst can be the choice of treatment. Complicated cysts, cysts larger than 10 cm do not resolve despite the expectant management requires laparoscopic investigation²⁴.

Adnexal masses with solid components in the adolescent period usually mature teratoma in origin. Observation of these kinds of cysts less than 5 cm in diameter is a feasible option. Risk of torsion of the including ovary and a 1%–2% risk for malignancy is present in expectant management. If the ovarian torsion has occurred, conservative untwisting of the ovary rather than unilateral oophorectomy should be performed. Removing the lesion which caused the ovary to become twisted is advocated, in order to decrease the risk of a repeat event, but this is not always easy as oedema of the ovary may not allow the underlying cause to be identifiable²⁵.

Malignant tumours of the ovary in adolescents are germ cells and sex

cord origin in common. Evaluation should include advanced imaging studies such as computerised tomography, Doppler ultrasound imaging and tumour markers (AFP, LDH, HCG, CEA and CA125). If the tumour markers are abnormal and malignancy is suspected, then a unilateral salpingo-oophorectomy and appropriate staging is performed. It is preferable to subject the patient to a second procedure after the final pathology specimens are reviewed than to perform an unnecessary ablative procedure.

Sexually transmitted disease

Biologic, cognitive, social, and behavioural developmental circumstances contribute to adolescent sexually transmitted disease (STD) susceptibility²⁶. Biologically, adolescent females are more susceptible to STDs compared with males and older females. Adolescents' cognitive stage of development may render them at risk for STDs. Young adolescents are concrete thinkers who are less able to think abstractly, conceptualise or determine long-term consequences of their actions. Multiple barriers prevent adolescents from seeking STD care. Lack of health insurance and inability to pay for services are barriers to care²⁷. In addition, adolescents may be uncomfortable seeking services at facilities that are not 'teen friendly'²⁶.

Chlamydia and gonorrhoea frequently present as an asymptomatic infection in females. In addition, many chlamydia infected males do not offer a classic urethritis history. Adolescents infected with *Neisseria gonorrhoeae* often are coinfecting with *Chlamydia trachomatis*. Because the cost of a chlamydia treatment course can be less expensive than the cost of chlamydia testing, the Centers of Disease Control and Prevention (CDC) has recommended empirically treating gonorrhoea-test positive persons for both gonorrhoea and chlamydia²⁸. Recommended

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treatment regimen is ceftriaxone 125 mg im single dose (alternatively cefixime 400 mg po single dose) for *N. gonorrhoeae* and doxycycline 100 mg po twice daily for 7 days (alternatively azitromycine 1 g po single dose) for *C. trachomatis*²⁹.

Trichomoniasis is an STD that is caused by a pathogenic, flagellated single-celled parasitic protozoan, *Trichomonas vaginalis*. In females, trichomoniasis classically presents with an irritating, profuse, yellow-green vaginal discharge with vulvovaginal itching and discomfort. In males, trichomoniasis is usually asymptomatic with fewer organisms and less inflammation²⁶. The recommended treatment regimen remains metronidazole 2 g orally in a single dose²⁸.

Pelvic inflammatory disease (PID) is a clinical syndrome caused by the spread of microorganisms from the lower genital tract to the upper genital tract²⁶. PID is a polymicrobial infection where multiple pathogens are involved. Sexually transmitted organisms, particularly *C. trachomatis* and *N. gonorrhoeae* are often implicated³⁰. Of all cases of PID, roughly two-thirds involve either *N. gonorrhoeae* or *C. trachomatis*, and most are associated with bacterial vaginosis-associated microflora in the upper genital tract³¹. PID can manifest with various clinical presentations ranging from asymptomatic to severe peritonitis and tubo-ovarian abscess (TOA) formation. PID is a serious consequence of STDs and an important cause of infertility, ectopic pregnancy and chronic pelvic pain. Clinicians must decide between outpatient and inpatient therapy when selecting a treatment regimen. The CDC offers the following suggestions for hospitalisation: inability to exclude surgical emergencies (i.e. appendicitis), pregnancy, failure to respond to outpatient oral therapy, inability to tolerate oral therapy (i.e. severe nausea/vomiting), the presence of severe illness (i.e. high

fever and peritonitis) and the presence of a TOA³². If an outpatient regimen is chosen, it is imperative that follow-up occurs in 48e72 h to ensure clinical improvement.

HPV infections remain the most common STD in developed countries³³. The greatest risk factors for infection are young age and sexual activity, with highest rates of infection in adolescents and women less than 25 years of age³⁴. The majority of HPV infections are transient and asymptomatic, with the immune system clearing the large majority of infections in immune-competent individuals. In the small percentage of women who fail to clear these infections, persistent infection (sometimes with multiple subtypes) and/or new infections can predispose to the development of high-grade cancer precursor lesions and cervical cancer²⁹. Focusing on the cervix, the majority of infections and subsequent corresponding cytological abnormalities are transient and of minimal significance (low-grade squamous intraepithelial lesions) in terms of oncogenic potential. A smaller percentage of adolescents will have persistent infections with higher risk subtypes and manifest high-grade cytological abnormalities. One of the most exciting and promising developments in modern medicine with regard to both STD and cancer prevention relates to the new highly effective HPV vaccines. The HPV vaccine trials that were conducted enrolled young sexually active women, mostly between the age of 16 and 23 years, and efficacy was highest among the previously non-exposed individuals. Given this, young girls, adolescent and young women (age 9–26) are the FDA-approved target populations for the quadrivalent HPV vaccine.

Anorexia nervosa

Because the menstrual disturbances are the common symptoms in AN, gynaecologists frequently come into

contact with girls suffering from eating disorders. The prevalence of AN among women in late adolescents and early adulthood is estimated to be between 0.5% and 1.0%³⁵. AN is a debilitating illness in which multiple physiologic, life-threatening disturbances are present. Puberty itself is a risk factor for AN. Hormonal and psychological changes in the maturing body, stressful developments in peer relationships and self-esteem issues can play a role in the development of AN. Assessment of AN requires understanding the context of the development of the patient; the mental, emotional and physical status of the patient, and the structure and functioning of the family system³⁶.

In the pathogenesis of AN, increase in the activity of corticotropin-releasing hormone (CRH) and Adreno-cortico tropic hormone (ACTH) inhibits the pulsatile release of GnRH and LH. FSH is usually normal. Ovarian functions are impaired due to hormonal changes. These hormonal changes results irregularities in menstrual cycle.

The gynaecologist should refer the young girl to a psychologist or a psychiatrist with experience in the field of eating. Treatment in AN should focus on acknowledgement of the disease and motivations to enhance weight restoration. Resumption of menses is usually considered a strong indicator of recovery from AN, but it is well known that about one-third of weight-restored subjects remain amenorrhoeic³⁷. A recent clinical effectiveness study, the Treatment Outcome for Child and Adolescent Anorexia Nervosa (TOuCAN) trial revealed no clear advantage of inpatient treatment, with an indication of a potentially worse outcome in the inpatient group³⁸.

Conclusion

Adolescence is a unique period of time in human development, a transition between childhood and adulthood. Thus, adolescent patients require special attention. Physicians,



especially general practitioners should be familiar to the common problems of adolescents mentioned above.

Abbreviations list

ACOG, American College of Obstetricians and Gynecologists; AN, AN, anorexia nervosa; FSH, follicular-stimulating hormone; GnRH, gonadotropin-releasing hormone; HPV, human papilloma virus; LH, luteinizing hormone; OCP, oral contraceptive pills; PCOS, polycystic ovarian syndrome; vW, von Willebrand.

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