Menstrual disorders in adolescence: investigation and management

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Menstrual disorders in adolescence may present diagnostic and management challenges for the gynaecologist. This review will describe the common and uncommon menstrual disorders that may arise in early reproductive life, together with guidance on their investigation and management.

Key words: adolescence/amenorrhoea/dysfunctional uterine bleeding/menstruation/PCOS

Introduction

Adolescence is a time of enormous physical and psychological change for young women. Serious gynaecological pathology is rare in this age group, but menstrual disturbances are not uncommon and may add further disruption to this difficult phase for adolescents and their families.

It is likely that many adolescents with menstrual disturbances never present to their family doctor or gynaecologist. The American College of Obstetrics and Gynecology (ACOG, 1996) takes a proactive stance in adolescent health by recommending an initial visit to a gynaecologist for health guidance, screening and the provision of preventative services around the age of 13–15 years. This is an opportunity for clinicians to advise the adolescent on what is ‘normal’ for girls of her age regarding pubertal development, menarche and menstrual cyclicity and would not normally include a pelvic examination. This anticipatory guidance and information to young girls and their parents may help ease the transition from childhood through puberty and a healthy adolescence (Adams Hillard, 2002). Such guidelines do not exist in the UK and it is unlikely that an adolescent would encounter a gynaecologist without the clinical suggestion of pathology.

Effective history-taking from an adolescent requires particular skills and sensitivities. Adolescents may have difficulty raising issues of menstruation with their doctors (Malus et al., 1987) and may present with complaints of minor symptoms rather than their primary concerns (Patton, 1999). Neither the British nor Australian colleges of Obstetrics and Gynaecology recognize training in adolescent gynaecology as part of their core curriculum and there are no UK guidelines for the management and referral of specialized problems (Balen et al., 2002). Since the formation of the British Society of Paediatric and Adolescent Gynaecology, there is now a UK course for the management of adolescent gynaecological and intersex conditions. In 2003 the UK Royal College of Obstetricians and Gynaecologists (RCOG) has also approved a special training module in Paediatric and Adolescent Gynaecology. The ACOG has recently released a ‘tool kit’ designed to facilitate the inclusion of adolescents into a general ob-gyn practice (http://www.acog.org) which may be of use to practitioners in other countries treating adolescents.

Embarrassment about discussing menstruation, fear of disease and ignorance about available services are likely to mean that many problems are not discussed or present following maternal pressure. Alternatively, presentation with a menstrual disturbance may disguise other issues, such as those relating to contraception, pregnancy, sexually transmitted infection (STI) or even sexual assault, and the gynaecologist should ensure that the young woman is given the opportunity to raise other concerns. Adolescents do not access health services in the same manner as adults and effective services must recognize these patterns and plan accordingly. A recent survey of 248 obstetric and gynaecology units in the UK indicated that adolescents constitute up to 5% of new gynaecological referrals and, whilst it was recognized by most that adolescents had special needs, the majority did not provide specialized services (Balen et al., 2002).

Confidentiality is a primary ethical and professional duty for doctors, and a crucial issue in adolescent health care. In the USA, the ACOG, American Academy of Pediatrics and the American Medical Association have endorsed the principle of confidentiality in adolescent health care. In the UK and Australia the legal precedence of the Gillick case (Gillick versus West Norfolk and Wisbech Area Health Authority, UK) allows the practitioner to determine whether an adolescent has reached sufficient understanding and intelligence to be capable of making up her own mind on the matter requiring decision. Adolescents are unlikely to access sexual and reproductive health services unless they can be
assured of confidentiality (Rogstad et al., 2002), hence the gynaecologist should ensure that she maintains confidentiality and that the patient is assured of this.

Menarche

The menstrual cycle involves the coordination of many events by the hypothalamic–pituitary–ovarian axis and is readily influenced by physiological, pathological and psychological changes occurring during the reproductive lifespan. The age of menarche is determined by general health, genetic, socio-economic and nutritional factors. The mean age of menarche is typically between 12 and 13 years (Flug et al., 1984; World Health Organization, 1986; Herman-Giddens et al., 1997). The oft-quoted statement that there has been a decrease in the mean age of menarche in recent decades has not been substantiated by large population studies, either in the USA (Chumlea et al., 2003) or in the UK (Whincup et al., 2003). However, the UK study observed that almost one girl in eight reaches menarche while still at primary school. There appears to be a relationship between body weight and the onset of menarche, supported by earlier menarche seen in obese girls (World Health Organization, 1986).

Nutrition and body weight play an important role in pubertal development. Chronic disease, malnutrition, eating disorders and high levels of physical activity can delay menarche. The mechanism for this relationship has not been conclusively defined. Insulin has been suggested as a modulator of the tempo of pubertal development through regulation of insulin-like growth factor binding protein (IGFBP-1) and sex hormone binding globulin (SHBG; Ibanez et al., 1997). States of over-nutrition and obesity are associated with increased serum concentrations of insulin. Therefore if excessive nutritional intake persists during childhood, it is possible that hyperinsulinaemia resulting from obesity may lead to lower levels of IGFBP-1 and reduced SHBG concentrations, thus enhancing IGF-I and sex steroid bioavailability. Hyperandrogenism associated with PCOS may augment this situation. The converse would be true in states of malnutrition, where low levels of insulin would allow for the development of increased IGFBP-1 and SHBG levels. However, it is still unclear whether hyperinsulinaemia in childhood is a result of obesity, or if it is the cause of obesity. The role of genetic factors, which may determine insulin production and obesity risk in childhood, have also yet to be clearly explained.

Serum concentrations of leptin relate to body fat mass, and leptin appears to act on the hypothalamus to control caloric intake, decrease thermogenesis, increase levels of serum insulin, and increase pulsatility of GnRH (Mann and Plant, 2002), hence regulating the onset of puberty (Mantzoros et al., 1997). This may explain the observed relationships between body fat and ovarian maturation observed by Frisch and Revelle (1970). Homozygous mutation of the leptin receptor gene results in early-onset morbid obesity, and the absence of pubertal development in association with reduced growth hormone secretion (Clement et al., 1998). Menstrual bleeding lasts 2–7 days in 80–90% of adolescent girls (Flug et al., 1984). As a rule of thumb, changing three to six pads per day without soiling from oversaturated pads suggests a normal flow (Adams Hillard, 2002). Whilst adolescent menstrual cycles may initially be variable this does not mean that ‘anything goes’ and cycles tend to regulate over the first 2–3 years following menarche. Most cycles still range from 21 to 45 days, even in the first year after menarche, with an upper limit of normal (i.e. 2 SD) of 40–45 days (Southam and Richart, 1966; Flug et al., 1984; World Health Organization, 1986). By the third year after menarche, 60–80% of cycles are 21–34 days long, a pattern similar to that seen in adults (Wisdom and Kantero, 1971; Flug et al., 1984). Cycles >90 days represent the 95th percentile for length, even in the first gynaecological year. Thus consideration should be given to a gynaecological evaluation in girls whose cycles are longer than this interval, since amenorrhoea of this interval or longer may have important implications for long-term bone and cardiovascular health (Trelor et al., 1967).

Anovulation does not necessarily underlie prolonged or irregular cycles and some cycles are ovulatory with a long follicular phase (Venturoli et al., 1987). Early menarche is associated with early onset of ovulatory cycles. When menarche occurs at <12 years, 50% of cycles are ovulatory in the first year and virtually all by the fifth year. By contrast, it takes 8–12 years for all cycles to be ovulatory in girls with later onset of menarche (Vihko and Apter, 1984). This has important clinical implications for advising adolescents on the ‘normality’ of their menstrual pattern relative to their age at menarche and likely patterns in the future.

After menarche, pregnancy can occur. It is impossible and unwise to try to separate menarche from sexual health education in adolescent girls. Guidance about contraception and STI is essential, regardless of whether she is currently sexually active. The teenage birth rate in the UK is second only to that in the USA and a high percentage of adolescent pregnancies occurs in the initial months of sexual activity. Early menarche is associated with earlier age of sexual debut, increased rates of STI and cervical atypia and is hence an important indicator for continued risk behaviour regarding reproductive health (Andersson-Ellstrom et al., 1996). UK teenagers have high rates of STI (Creighton et al., 2002) and younger age is the strongest risk factor for Chlamydia trachomatis infection, across a broad range of populations (Burstein et al., 1998). Effective prevention strategies must include the younger adolescent population, ideally before they become sexually active.

Disorders of puberty

Precocious puberty

Well-described physical and anatomical changes of puberty, classified according to Tanner (1962) are evident from 9 to 13 years and follow the increase in adrenal androgens from 6 to 8 years. Precocious puberty has been defined by Marshall and Tanner (1969) as ‘Any secondary sex characteristic appearing in a girl before the age of 8 years (9 years for boys) or the onset of menstruation prior to 10 years of age’. The definition of lower limit for the onset of pubertal development in girls is controversial and pubertal growth may be occurring earlier than had previously been described, despite the age of menarche remaining constant. Racial variations are well established and pubertal development occurs earlier in girls from an Asian and Afro-Caribbean background than in white girls (Dutani and Brook, 1998; Chumlea, 2003). A US study of >17 000 girls suggests that pubertal development is seen in 15% of white girls aged under 8 years and 48% of black girls...
(Herman-Giddens et al., 1997), although the average age of menarche did not differ between these groups. Hence, US guidelines advise that investigation of breast or pubic hair development is justified in white girls aged <7 years and black girls <6 years (Kaplowitz and Oberfeld, 1999). Similar population figures for the UK are not available, hence the definition of precocious puberty remains unchanged.

Early signs of pubertal development are likely to cause alarm in parents and may lead to social and psychological difficulties for the girl aware that her body is becoming markedly different from that of her peers. In girls, 90% of cases are constitutional, secondary to premature release of gonadotrophins, without any organic lesion and puberty often proceeds slowly in these girls (Root, 2000).

In 10% of cases, precocious puberty is secondary to an intracranial lesion causing premature gonadotrophin release such as meningitis or cerebral tumour. The rare McCune–Albright syndrome (characterized by fibrous dysplasia of the skeletal system, cafe-au-lait spots, and endocrine dysfunction) is also associated with precocious puberty. In primary hypothyroidism increased circulating thyrotrophin-stimulating hormone and consequent increased thyroid-stimulating hormone may also elevate FSH and hence lead to premature ovarian activity (Duncan et al., 1998). Feminizing estrogen-secreting ovarian tumours are rare and the majority are benign. When precocious puberty presents under the age of 6 years an underlying disturbance affecting ovarian development is more likely. When these features occur closer to the time of normal puberty it is more likely that that problem is one of general advance of the maturational process (Adams Hillard, 2002).

Rarely, anomalous puberty may arise when there is inappropriate hormonal secretion with virilization. Causes include gonadal dysgenesis with a functioning tumour, congenital adrenal hyperplasia and adrenal tumours. Precocious adrenarche has been associated with an increased risk of subsequent insulin resistance and hyperandrogenism/PCOS (Ibanez et al., 2000; Pathomvanich et al., 2000).

The causes of precocious puberty are summarized in Table I. In assessing precocious puberty, the child’s previous growth and development as well as timing and sequence of physical milestones should be considered. This assessment might be most appropriately performed by a paediatrician. It is important that parents and girls are aware that menarche is likely to occur in the 2 years following initial pubertal development. Bone maturation is accelerated in precocious puberty, leading to premature epiphyseal closure and curtailed stature. Pituitary suppression with GnRH agonists is frequently indicated to delay puberty. Therapy with GnRH agonists does not substantially affect adult height in girls who enter puberty between ages 6 and 8 years (Leger et al., 2000; Root, 2000).

### Delayed puberty

Delayed puberty is defined as absence of onset of puberty by >2 SD later than the average age, i.e. >14 years in females. Delayed puberty may be idiopathic/familial or due to a number of general conditions resulting in undernutrition. Absence of puberty may also be due to gonadal failure (elevated gonadotrophin levels), or due to impairment of gonadotrophin secretion.

Although some cases of delayed puberty in girls may be due to constitutional delay and require only reassurance, the patient requires review within 6 months, at which point investigation is likely to be indicated. Delayed puberty due to chronic disease may respond to improved control of the associated condition. Eating disorders such as anorexia nervosa and bulimia affect 0.5–1% of young women in developed countries with long-term mortality rates approaching 20% (Tamburrino and McGinnis, 2002). The classic triad of presenting symptoms is weight loss >15% of ideal body weight, behavioural changes and amenorrhoea (secondary or primary). Delayed puberty associated with low body mass index (BMI) should be carefully questioned about eating disorders, as amenorrhoea may precede significant weight loss. Bulimia is associated with irregular menstruation and can occur in girls of normal weight. Intense exercise, such as long-distance running, ballet, rowing, long-distance cycling and gymnastics, is associated with delayed menarche in young girls, and with amenorrhoea in older women (Frisch et al., 1981). These ‘endurance’ sports are associated with lower bodyweight and percentage fat. The extent to which menarche is ‘delayed’ is related to the age at which participation in the sport begins, and to the intensity of training. Promotion of very thin women as ‘ideal’ role models through media and fashion has contributed to an increase in dieting in adolescent girls. In addition, there are future implications for ovarian function, fertility and sexuality and psychological support may be required at an early stage.

When chromosomal or structural abnormalities are suspected, or premature ovarian failure, the patient should be referred directly to a tertiary referral centre offering tailored services for young women, preferably with the results of preliminary investigations.

Gonadal failure presenting as delayed puberty requires specialist assessment and management. Clinicians should be aware that several studies indicate long delays in both recognition of premature ovarian failure as abnormal and

### Table I. Causes of precocious puberty

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
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</thead>
<tbody>
<tr>
<td>Gonadotrophin dependent (‘true’ or ‘central’ precocious puberty)</td>
<td>Idiopathic (family history, overweight/obese)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Inappropriate hormonal secretion with virilization.</td>
</tr>
<tr>
<td>Intracranial lesions (tumours, hydrocephalus, irradiation, trauma)</td>
<td>Gonadotrophin secreting tumours</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Variants</td>
</tr>
<tr>
<td>Premature thelarche (and thelarche variant)</td>
<td>Adrenarche</td>
</tr>
<tr>
<td>Gonadotrophin independent</td>
<td>Congenital adrenal hyperplasia</td>
</tr>
<tr>
<td>Sex steroid secreting tumours (adrenal or ovarian)</td>
<td>McCune–Albright syndrome</td>
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<tr>
<td>Exogenous estrogen ingestion/administration e.g. child ingesting oral contraceptive pills</td>
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Intersex disorders

It is imperative that intersex conditions are managed in centres by a multi-disciplinary team that includes paediatric surgeons, urologists (often paediatric and adult), plastic surgeons, endocrinologists, specialist nurses, psychologists and also the gynaecologist—whose role is to help co-ordinate the transition from childhood through adolescence and then womanhood and help with issues relating to sexual function and sexual identity, endocrinology and fertility. It is during the difficult time of adolescence that the patient usually first realizes that there are serious problems and it is often the specialist gynaecologist who helps her to understand the diagnosis and requirements for management. The support of a skilled nurse and clinical psychologist is invaluable at this time. The Department of Health in the UK is currently reviewing the national provision of services for the management of intersex. Those units that have the skills to manage intersex conditions usually also have the appropriate facilities to treat complex anatomical anomalies of the Müllerian tract (for example cervical and vaginal agenesis).

Disorders of sexual development may result in ambiguous genitalia or anomalies of the internal genital tract and may be due to genetic defects, abnormalities of steroidogenesis and dysynchrony during organogenesis. Age of presentation will depend upon the degree of dysfunction caused. Ambiguous genitalia occur in ~1:30 000 newborns. Issues concerning genital surgery for intersex are controversial and data on long-term outcomes are lacking. However, the effects on sexual function of surgical removal of parts of the clitoris are largely unknown. A recent UK study by Minto et al. (2003) of 39 adults with intersex conditions and ambiguous genitalia and found markedly increased rates of sexual dysfunction in those who had undergone genital surgery compared with those who had not had surgery. These risks should be discussed when counselling parents regarding genital surgery in infants or children, and provide further evidence that delaying surgery until individuals can make their own decision is preferable when possible.

Sensitivity is paramount in dealing with young women found to have genetic or hormonal abnormalities with profound implications for their future sexual and reproductive health. The physician...
Progestogens are not required because the uterus is absent. Exogenous estrogen should then be prescribed.

Structural disorders of the reproductive tract during embryological development (Müllerian disorders) are usually associated with normal ovarian development and therefore do not require sex steroid therapy, but for those with an absent vagina an artificial vagina needs to be developed when the young woman is ‘appropriately mature’ to understand the diagnosis and the options regarding intervention. Surgical ‘neo vaginas’ are now rarely advised since vaginal dilators provide excellent results and are now first line therapy for vaginal agenesis (ACOG, 2002). The renal tract should be imaged in those with Müllerian abnormalities to rule out an associated structural variation.

Women with Mayer–Rokitansky–Kuster–Hauser syndrome (MRKH or Rokitansky syndrome) have a 46,XX genotype and a normal female phenotype with spontaneous development of secondary sexual characteristics, as ovarian tissue is present and functions normally. The Müllerian ducts have failed to fuse and so there is vaginal agenesis. The incidence is ~1:5000 female births and may be associated with renal tract anomalies (15–40%) or anomalies of the skeletal system (10–20%). The external genitalia have a normal appearance, but the vagina is short and blind-ending, such that either surgery or gradual dilation is necessary to achieve a capacity appropriate for normal sexual function. Hormone treatment is not required as ovarian estrogen output is normal. Indeed ovulation occurs and ovarian stimulation followed by oocyte retrieval can be performed in order to achieve a ‘biological’ pregnancy via surrogacy.

The vaginal dimple can vary in length from just a slight depression between the labia to up to 5–6 cm. Vaginal dilators, made of plastic or glass, are used first to stretch the vaginal skin and the patient is encouraged to apply pressure for 15 min twice daily with successive sizes of dilator. An adequately sized vagina is usually formed by 6 months but this may take longer and long-term use of dilators may be required—depending upon the frequency of sexual intercourse.

The diagnosis of Rokitansky syndrome can usually be made without the need for a laparoscopy. Sometimes, however, an ultrasound scan will reveal the presence of a uterine remnant (anlagan) which is usually small and hardly ever of sufficient size to function normally. If there is active endometrial tissue within the uterine anlagan the patient may experience cyclical}

...
Fusion abnormalities of the vagina

Longitudinal fusion abnormalities may lead to a complete septum that may be associated with two complete uterine horns with two cervices or a partial septum causing a unilateral obstruction. Excision is required both to prevent retention of uterine secretions and to permit sexual intercourse.

Transverse fusion abnormalities usually present with primary amenorrhoea and require careful assessment before surgery. The commonest presentation is of cyclical lower abdominal pain and a visible haematocolpos with a bulging purple/blue hymen. The surgery required is a simple incision. Delayed diagnosis may lead to haematometra and consequent increased risk of endometriosis (secondary to retrograde menstruation). A transverse vaginal septum due to failure of fusion or canalisation between the Müllerian tube and sinovaginal bulb may present similarly but is associated with a pink bulge at the introitus as the septum is thicker. Great care must be taken during surgery to prevent annular constriction rings and the procedure should only be performed in dedicated centres by experienced surgeons.

Primary amenorrhoea

The failure to menstruate by the age of 16 years in the presence of normal secondary sexual development, or 14 years in the absence of secondary sexual characteristics, warrants investigation. This distinction helps to differentiate reproductive tract anomalies from gonadal quiescence and gonadal failure. Primary amenorrhoea may be a result of congenital abnormalities in the development of ovaries, genital tract or external genitalia or a disturbance of the normal endocrinological events of puberty. Overall it is estimated that endocrine disorders account for ~40% of the causes of primary amenorrhoea, the remaining 60% having developmental abnormalities. For an excellent review of this topic see http://www.emedicine.com/med/topic117.htm and for a summary see Table III.

Secondary amenorrhoea

Secondary amenorrhoea is the absence of menstruation, which may be temporary or permanent and of >6 months duration, although 6 months is largely an arbitrary definition and amenorrhoea should be considered within its clinical context. Any cause of secondary amenorrhoea may also cause primary amenorrhoea. PCOS and pregnancy may both present with secondary amenorrhoea in early reproductive life. A prolonged hypoestrogenic state carries the risk of bone demineralization, osteoporosis and fracture. Therefore, secondary amenorrhoea associated with low estrogen levels requires estrogen supplementation to maintain bone density. The causes of secondary amenorrhoea are summarized in Table IV.

Examination and investigation of amenorrhoea in adolescence

Taking a gynaecological history from an adolescent should include questions about sexual activity and risk-taking behaviour. However, pregnancy should be ruled out with laboratory testing in cases of oligoamenorrhoea or amenorrhoea even if sexual activity is denied, since adolescence may feel unable to confide in a clinician about this (Adams Hillard, 2002).
Table V. The investigation of amenorrhoea

<table>
<thead>
<tr>
<th>Method</th>
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<tbody>
<tr>
<td>History</td>
</tr>
<tr>
<td>Physical examination</td>
</tr>
<tr>
<td>Note body mass index, pubertal development,</td>
</tr>
<tr>
<td>Stigmata of PCOS and other endocrine disease</td>
</tr>
<tr>
<td>Acne and hirsutism</td>
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<tr>
<td>Endocrine assessment</td>
</tr>
<tr>
<td>Pregnancy test if suspected</td>
</tr>
<tr>
<td>FSH, LH, prolactin, thyroid function tests</td>
</tr>
<tr>
<td>Testosterone (if stigmata of PCOS)</td>
</tr>
<tr>
<td>Further endocrinology only if above do not provide diagnosis</td>
</tr>
<tr>
<td>Ultrasound</td>
</tr>
<tr>
<td>MRI if suggestion of complex anatomical problem</td>
</tr>
<tr>
<td>Pituitary/hypothalamic imaging</td>
</tr>
<tr>
<td>As indicated clinically</td>
</tr>
<tr>
<td>Bone mineral densitometry</td>
</tr>
<tr>
<td>If hypoestrogenic</td>
</tr>
<tr>
<td>Karyotype</td>
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<tr>
<td>If premature ovarian failure</td>
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</table>

PCOS = polycystic ovary syndrome.

The need for a bimanual examination in a young woman who has never been sexually active should be carefully considered. The majority of adolescents can be assessed using an examination of the external genitalia and imaging studies such as ultrasound if needed. However, a cooperative adolescent, even if never sexually active, can often be evaluated with a single finger bimanual examination, allowing her mother to be present if the patient wishes. Examination may identify a blind ending or absent vagina or haematocolpos, and the visualization of the cervix. Transabdominal ultrasound may indicate whether the uterus and ovaries are present. In the USA, magnetic resonance imaging is the primary investigation of preference and can provide information additional to ultrasound. Examination under anaesthesia (EUA) is the final step in diagnosis which might rarely need to be combined with laparoscopy, for example in complicated Müllerian abnormalities (Letterie et al., 1995).

A transabdominal ultrasound examination of the pelvis is an excellent non-invasive method of obtaining valuable information in these patients. An examination under anaesthetic is sometimes indicated for cases of intersex with primary amenorrhoea; it is rarely required in cases of secondary amenorrhoea.

The investigative techniques for amenorrhoea are listed in Table V. Signs of hyperandrogenism (acne, hirsutism, alopecia) are suggestive of the polycystic ovary syndrome (PCOS, see below). Hyperandrogenism must be distinguished from virilization, where high circulating androgen levels are associated with deepening of the voice, increase in muscle bulk and cliteromegaly.

A baseline assessment of the endocrine status should include measurement of serum prolactin and gonadotrophin concentrations and an assessment of thyroid function. Elevated gonadotrophin (FSH and LH) concentrations indicate ovarian failure whilst suppressed levels suggest hypogonadotrophic hypogonadism. Hyperprolactinaemia due to prolactinoma may present with

Menstrual disorders in adolescence

Premature ovarian failure

Premature ovarian failure may present as primary or secondary amenorrhoea in adolescents. Karyotyping is indicated to exclude Turner’s syndrome (45X, or 46XX/45X mosaic) or other sex chromosome mosaicsisms. Thyroid-stimulating hormone, fasting glucose and adrenal antibodies should be checked and repeated annually, due to the association with autoimmune disease in those with a normal karyotype. Idiopathic familial POF is also well recognized and may be associated with a mutation of the inhibin gene (Marozzi et al., 2002). Ovarian antibodies are rarely useful. Measurement of bone mineral density is indicated in amenorrhoeic women who are estrogen deficient. A total of 8% of bone mass is lost in the first year after menopause and thereafter between 1 and 2% (Luisetto et al., 1993). The vertebral bone is more sensitive to estrogen deficiency and vertebral fractures tend to occur in a younger age group (50–60 years) than fractures at the femoral neck (>70 years). For review see Bakalov and Nelson (2001). Dual-energy X-ray absorptiometry (DEXA) is valuable in predicting patients at risk of fracture. However, DEXA scans of adolescents require normal values for this population that may not be routinely included with the scanner software (http://www-stat-class.stanford.edu/pediatric-bones/).

Oligomenorrhoea

Oligomenorrhoea may be defined as menses occurring less frequently than every 35 days. The commonest cause of oligomenorrhoea is PCOS and other causes include either temporary disturbances of menstrual cycle control, body weight (obesity or underweight) and hyperprolactinaemia as well as developing causes of secondary amenorrhoea.
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**PCOS in adolescence**

PCOS appears to underlie irregular menses in up to one-third of girls (Venturoli et al., 1986). Menarche is not usually delayed, but bleeding is then persistently irregular. In adolescents, PCOS can present with primary or secondary amenorrhoea, acne, hirsutism or merely irregular periods, as set out in Table IV.

Ovarian dysfunction leads to the main signs and symptoms of the PCOS and the ovary is influenced by external factors, in particular the gonadotrophins and insulin, which are themselves dependent upon both genetic and environmental influences. Approximately 20–33% of women of reproductive age will have polycystic ovaries on ultrasound scan (Polson et al., 1988; Michelmore et al., 1999); while perhaps 75–80% of these will have symptoms consistent with the diagnosis of PCOS. Menstrual disturbance is likely to be the main issue for adolescents with PCOS but the established long-term risks of obesity, subfertility and diabetes as well as the possible risks of endometrial hyperplasia and carcinoma (Hardiman et al., 2003) and cardiovascular disease (recently reviewed by Rajkowha et al., 2000) and breast cancer (Balen, 2001) require consideration. Obesity also compounds the clinical manifestations of PCOS and weight loss may lead to symptom improvement.

PCOS may first manifest in adolescence but its origins are likely to be much earlier. PCOS is associated with increased weight gain during puberty (Balen and Dunger, 1995). Genetic study of PCOS has identified links with insulin secretion and action as well as increased ovarian androgen secretion). Association has been reported with common allelic variation at the variable number of tandem repeat locus (VNTR) in the promoter region of the insulin gene (Waterworth et al., 1997). This locus has been variably associated with the risk of obesity, insulin resistance and type 2 diabetes. The identified association has been with the class III/III genotype, particularly in women who have anovulatory cycles and are hyperinsulinaemic (Waterworth et al., 1997; Michelmore et al., 2001).

**Management of PCOS in adolescence**

The clinical management of young women with PCOS should be focused on her individual problems. Obesity worsens both symptomatology and the endocrine profile and so obese girls (BMI >25 kg/m²) should be encouraged to lose weight, and they should also have a test of fasting glucose tolerance (e.g. 2 h GTT) and fasting insulin to assess the glucose:insulin ratio. Impaired glucose tolerance has been seen in up to one-third of adolescents with PCOS (Palmert et al., 2002).

Hyperandrogenism and hirsutism are distressing symptoms for young women and the clinician should be aware that cosmetic measures may disguise the extent of the problem. Optimally treatment combines cosmetic and medical therapies. Medical regimens stop further progression of hirsutism and slow the rate of hair growth. However, drug therapies may take 6–9 months or longer before any benefit is perceived and so laser, electrolysis, waxing and bleaching may be helpful in the interim. Medical therapy is aimed at slowing the rate of hair growth whilst cosmetic treatments attempt to remove existing hair. Laser therapy works best in women with dark hair on fair skin, but is expensive and not permanent (despite claims to the contrary). Electrolysis is the only permanent method of hair removal and should be delayed until androgens are effectively suppressed.

Hyperandrogenism can be treated by a combination of an estrogen (such as ethinylestradiol, or a combined contraceptive pill), and the anti-androgen cyproterone acetate (CPA, 50–100 mg). Estrogens lower circulating androgens by a combination of a slight inhibition of gonadotrophin secretion and gonadotrophin-sensitive ovarian steroid production and by an increase in hepatic production of sex hormone-binding globulin resulting in lower free testosterone. The CPA is taken for the first 10 days of a cycle (the ‘reversed sequential’ method) and the estrogen for the first 21 days. After a gap of exactly 7 days, during which menstruation usually occurs, the regimen is repeated. As an alternative, the preparation Diane® (Schering UK) contains ethinylestradiol in combination with CPA, although at a lower dose (2 mg). CPA acts as a competitive inhibitor at the androgen receptor. CPA can rarely cause liver damage and liver function should be checked after 6 months and then annually. Combined oral contraceptive pills (COCP) have the added advantage of providing effective contraception for adolescents, given the high rates of unintended pregnancy in this group. If contraception is needed, counselling should include the information that COCP will not protect against STI and additional barrier contraception is advised. However, the COCP has the disadvantage of increasing insulin resistance (Morin-Papunen et al., 2000). However, this effect on insulin sensitivity has not been observed with the norgestimate-containing OCP in non-obese PCOS subjects (Cibula et al., 2002).

Spironolactone, a potassium sparing diuretic, has anti-androgenic properties and is useful in women for whom the oral contraceptive pill is contra-indicated (e.g. because of hypertension). Spironolactone, at a dose of 50–200 mg daily, may result in erratic menstrual bleeding and should be combined with reliable contraception. A new COCP, Yasmin® (Shering UK), contains the progestogen, drospirenone, which is a derivative of spironolactone, with potential anti-androgenic properties and benefits for women with PCOS.

Although diet is the first line treatment for improving insulin sensitivity in overweight adolescents with PCOS, insulin-sensitizing agents, such as metformin, are becoming increasingly popular in the management of PCOS as they act directly on insulin resistance and help correct both metabolic and endocrine problems. Although initial studies suggest an improvement in menstrual regularity in PCOS, the role of insulin-sensitizing medications in adolescents with PCOS is unclear. Primary prevention of diabetes mellitus and cardiovascular disease by lifestyle modification, including regular exercise and a balanced diet, is particularly important in adolescents, who have the opportunity to establish healthy habits before entering adulthood. The findings of diabetes prevention trials suggest that these interventions may be more efficacious than pharmacological therapy (Legro, 2002;
Kauffman et al., 2002; Kiess et al., 2003). However, the implications of PCOS for long-term health remain unclear, and, although mortality rates have not conclusively been shown to be elevated in PCOS patients, concerns exist that women with this syndrome cluster risk factors for premature morbidity and mortality (Wild, 2002).

Management of amenorrhoea

The general principle of treatment is to replace estrogen when hypoestrogenaemia is demonstrated in order to prevent the consequences of long-term estrogen deficiency. Even short-term estrogen deficiency leads to bone loss, increasing the risk of osteoporosis. More prolonged deficiency may also increase cardiovascular risk. When a uterus is present, progestogens should also be given to avoid endometrial hyperplasia. Longitudinal studies are needed to determine the optimum replacement needed for young hypoestrogenic women such as those with Turner’s syndrome. In these patients, growth hormone supplements may also be used to increase stature.

Management of dysfunctional uterine bleeding in adolescence

The term ‘dysfunctional uterine bleeding’ (DUB) is taken to mean ‘excessively heavy, prolonged or frequent bleeding of uterine origin, which is not due to pregnancy or to recognizable pelvic or systemic disease’(Fraser, 1985). Ovarian cycles associated with bleeding may be ovulatory or anovulatory, and the condition may be acute or chronic. In later reproductive life, DUB is regular and ovulatory in ~80% of cases, but in adolescence and early reproductive life, anovulatory DUB with irregular cycles is relatively common, up to 50% of cycles in the first year of menarche.

Young women presenting with ovulatory DUB are occasionally found to have underlying coagulopathies. If there is a family history of coagulopathy or a history of heavy bleeding at surgery or tooth extraction, it is worth discussing with a haematologist which special investigations may be indicated and how the blood should be collected. In the majority of cases, no significant underlying pathology will be found and reassurance of the patient and her parents is the most appropriate management.

General physical examination should search for evidence of pelvic and systemic pathology that may account for heavy and/or irregular bleeding. Investigations may include abdominal ultrasound scan and, if necessary, examination under anaesthesia. An estimation of circulatory haemoglobin levels should be performed on all females complaining of menorrhagia. Immune thrombocytopenia purpura (ITP) may also present with menorrhagia in the adolescent (associated with bruising, petechiae and mucosal bleeding) requiring specialist haematological assessment (Bevan et al., 2001). The incidence of these disorders in the UK has not been reviewed recently, but a 9 year audit of paediatric cases in the USA from 1971 to 1980 revealed that a primary coagulation disorder was found in almost 20% of 59 patients admitted to a children’s hospital for acute menorrhagia, where genital tract pathology had been excluded. One-quarter of those with severe menorrhagia (haemoglobin <10 g/100 ml), one-third of those requiring transfusion, and one-half of those presenting at menarche had such an underlying disorder (Claessens et al., 1981). Red blood cell indices and serum ferritin levels may be indicated if there is iron deficiency anaemia. In anovulatory DUB, serum LH and FSH changes may indicate PCOS or a premature perimenopausal state. Transabdominal ultrasound and serum androgens will provide additional information in the diagnosis of PCOS. If there is irregular and acute bleeding, complications of pregnancy should be excluded.

Management of DUB

Management of DUB in the adolescent is medical in almost all circumstances. Modern low-dose oral contraceptive pills can be safely prescribed to most young women, provided that they are not known to have contraindicating factors. The combined oral contraceptive pill has been shown by objective measurement to reduce menstrual blood loss in ovulatory and anovulatory DUB (Nilsson et al., 1971).

In the treatment of anovulatory DUB, progestogens may be suitable for women who are unable or unwilling to take estrogen-
advantages.

all progestogen preparations and the main reason why women

Irregular 'breakthrough' bleeding is the main unwanted effect of

(rare) intrauterine pathology if a general anaesthetic is planned.

Hysteroscopy at the same time may also be indicated to exclude

should consider insertion of the device under general anaesthetic.

management of refractory DUB in young women but the physician

provides reversible contraception. The Mirena has a place in the

anovulatory DUB (Anderson and Rybo, 1990). The system also

is a highly effective long-term treatment for both ovulatory and

system (IUS) releasing 20 \( \mu g \) of levonorgestrel/day (LNG-IUS 20)

intrauterine implant

containing compounds. Oral progestogens are only effective if
given for \( \geq 21 \) out of 28 days and low-dose luteal phase
progestogens are not an effective treatment for menorrhagia
(Lethaby et al., 2000).

In the adolescent with anovulatory DUB, cyclical oral
progestogens may be required until spontaneous regular ovulation
occurs.

The disadvantages of oral progestogen regimens for DUB
include the need for long-term oral medication and the possibility
of unwanted 'pre-menstrual symptoms' including: bloating, edema, headache, depression and reduced libido; androgenic
effects (depending on the progestogen used), such as acne and
hirsutism; irregular breakthrough bleeding and a change in
carbohydrate tolerance and lipid balance. The contraceptive
depot preparation of medroxyprogesterone acetate (such as
Depo-Provera\textsuperscript{\textregistered}) will induce amenorrhoea in 50% of users at 1
year. For those who can accept the 15–20% rate of irregular or
prolonged breakthrough bleeding, this may provide a safe and
effective treatment regimen. The Mirena\textsuperscript{\textregistered} intrauterine implant
system (IUS) releasing 20 \( \mu g \) of levonorgestrel/day (LNG-IUS 20)
is a highly effective long-term treatment for both ovulatory and
anovulatory DUB (Anderson and Rybo, 1990). The system also
provides reversible contraception. The Mirena has a place in the
management of refractory DUB in young women but the physician
should consider insertion of the device under general anaesthetic.
Hysteroscopy at the same time may also be indicated to exclude
(rare) intrauterine pathology if a general anaesthetic is planned.
Irregular 'breakthrough' bleeding is the main unwanted effect of
all progestogen preparations and the main reason why women
choose to discontinue these preparations, despite their other
advantages.

**Menstrual disturbances in PCOS**

In obese girls with PCOS, weight loss may lead to resumption
of ovulation (Kiddy \textit{et al.}, 1992). Cyclical progestogen
treatment for 10 days every 6 weeks will generally lead to
withdrawal bleeding and prevent hyperplasia. The COCP is an
alternative method of producing a regular withdrawal bleed,
but concerns about effects on insulin resistance must be
considered (see above).

**Menstrual disorders in adolescents with intellectual disability**

Historically there has been a tendency to aim for amenorrhoea
in institutionalized women with intellectual disability, using
continuous progestogens or by surgery. This has arisen from
concerns about the ability of a young intellectually disabled
woman to cope with menstruation and the risks of sexual abuse
and unplanned pregnancy. Common menstrual disorders in this
group include dysmenorrhoea (or behavioural changes thought
to reflect pain), amenorrhoea associated with delayed puberty
or secondary to low weight, menorrhagia and cyclic exacerbation
of conditions such as epilepsy (Grover, 2002).

**Endometriosis and pelvic pain**

Dysmenorrhoea is a common gynaecological complaint among
adolescent girls. Traditional teaching has distinguished primary
(or spasmodic) and secondary dysmenorrhoea, but there is
little objective evidence that these are distinct conditions
with differing pathologies. It is likely that many cases of
dermatosis in young women have been put down to
'spasmodic' dysmenorrhoea and persistent, disruptive and
severe dysmenorrhoea unresponsive to non-steroidal anti-
inflammatory drugs (NSAID) and COCP warrants investiga-
tion and treatment. Endometriosis may also present with non-
cyclic pain, bowel and urinary symptoms.

The differential diagnosis of chronic pelvic pain in the
adolescent (>6 months) is extensive (see Table VII). History
should include questioning about bowel symptoms suggestive
of irritable bowel syndrome or inflammatory bowel disease as
well as a social and sexual history.

Pelvic examination may be helpful if the young woman is
sexually active, and may reveal uterosacral tenderness or
nodularity suggestive of endometriosis, or cervical excitation
suggestive of infection. Pelvic ultrasound is more sensitive for
ovarian pathology. It is reasonable to offer an empirical 3
month trial of COCP, taken continuously for dysmenorrhoea.
Failure to respond to this therapy and persistent gynaecological
symptoms is an indication for laparoscopy. The patient’s
consent should be obtained before laparoscopy to excise visible
endometriosis.

**Table VII. Differential diagnosis of dysmenorrhoea and pelvic pain in adolescence (data derived from Quint, 2002)**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclical, or associated with bowel and bladder symptoms, dyspareunia if sexually active</td>
<td>Uterus and ovaries</td>
</tr>
<tr>
<td>Related to bowel motions, associated with bloating</td>
<td>Gastrointestinal tract</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Genitourinary system</td>
</tr>
<tr>
<td>Associated with back pain</td>
<td>Musculoskeletal system</td>
</tr>
<tr>
<td>Variable pattern</td>
<td>Psychosocial</td>
</tr>
</tbody>
</table>

*IBS* = irritable bowel syndrome.
Endometrial ablation has been reported as an option for managing heavy and irregular bleeding in this population (Wingfield et al., 1994) but little is known about the medium to long-term efficacy of this treatment in young women. In addition, since endometrial ablation does not guarantee contraception and subsequent pregnancy is associated with very poor fetal outcome, tubal ligation is usually recommended at the same time. In a case series of >100 adolescents with significant intellectual disability and moderate to high support needs requiring specialist advice for menstrual disorders, Grover (2002) encountered only two young women requiring hysterectomy or endometrial ablation for menstrual disorders. Alternative management included providing information about menstrual hygiene training, and improvement of family support services including respite care. The capacity of women with disabilities, even those with high support needs, to gain additional skills in their personal menstrual management may often be underestimated (Griffin et al., 1994). Effective medical managements for menstrual disorder in intellectually disabled girls and women were essentially the same as those for non-disabled women and included NSAID for dysmenorrhea and COCP or DMPA for menorrhagia. Surgery was only performed as a ‘last resort’. Since this study the Mirena (Schering, UK) intrauterine system has become widely available. It is likely that Mirena will have a major impact on menstrual management in this population, and may obviate the need for surgery with its attendant risks and loss of reproductive potential in these vulnerable women. Mirena has demonstrated an 86% reduction in menstrual blood loss at 3 months and a 97% reduction at 12 months in women with ovulatory dysfunctional uterine bleeding (Anderson and Rybo, 1990), which continues over a 5 year period. Nearly 50% of Mirena users experience amenorrhoea during 3 years of use (Baldaszi et al., 2003). Menstrual blood loss is also reduced in anovulatory bleeding. The system also acts as a highly effective and reversible contraceptive. Insertion under general anaesthetic may be preferable in women with intellectual disability.

Summary

Adolescent menstrual disorders are relatively common and it is unclear who these young women present to and what information is provided to them. The issues of when to talk, how to talk and what to say to young girls and their families regarding the processes of early maturation and menstruation are unresolved. These discussions will inevitably stray into issues of self-confidence, body image and sexuality and it is possible that many gynaecologists may not feel sufficiently comfortable or experienced in these areas. Those adolescents who do attend the gynaecologist will often attend with a mother or friend and sensitivity in dealing with even minor disorders is paramount. Referral to specialized centres for rarer but serious endocrine or structural abnormalities is necessary. Liaison with paediatricians or psychosexual counsellors may also be required.

References

Fraser, I.S. (1985) The dysfunctional uterus: dysmenorrhea and dysfunctional


