



SAILA PIIPPO

Survey of Gynecological Problems
During Childhood and Early Adolescence
in an Academic Center



ACADEMIC DISSERTATION

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ACADEMIC DISSERTATION

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To all my girls

ABSTRACT

The purpose of this study was to analyze the occurrence of gynecological problems, and to describe the gynecological examinations and findings in young female patients up to 17 years of age, seen at a hospital level. The study was based on hospital patient material at tertiary referral level, especially at a consultation clinic for pediatric and adolescent gynecology at Tampere University Hospital.

The study involved 406 gynecological patients aged 4 months to 17 years. The unit for pediatric and adolescent gynecology was attended by 217 patients and they were treated by one gynecologist, 87 patients attended the gynecological outpatient clinic for adults and 89 patients were primarily examined at various hospital clinics. Thirteen of the patients were treated at major pediatric endocrinology centers in Finland.

The most common reasons for referral to hospital were abdominal pain (20%), endocrinological problems (18%), vulvar symptoms (17%) and suspected sexual abuse of children (17%). One third of the patients were referred directly to the gynecologist from primary care, and the rest of the patients came to consultation from other clinics inside the hospital. At the unit of pediatric gynecology vulvar inspection was the examination method used in 88% of the cases and an abnormal finding was documented in 40% of them. Vaginal inspection by speculum was carried out on 33%, sonography in 26% and microbiological samples were taken from 55% of the patients. Correct examination techniques and methods are essential in gynecological examination of children. Visualization of the vulva and the outer third of the vagina can usually be carried out without instruments. Sonography was an excellent noninvasive method to visualize the uterus and ovaries and it was also useful in the diagnosis of pubertal disorders and in follow-up of hormonal treatments. Diagnosis in most of our patients could be achieved by using noninvasive methods. A finding of normal gynecological anatomy was one of the most important conclusions among the patients examined.

Patients (n=68) examined primarily for problems in the vulvar area had often had long-standing symptoms, with a mean duration of 134 days (range 3 days to 3 years). Forty-eight patients had abnormal clinical findings in the examinations. An infectious etiology was found in 16 patients. An infectious etiology was not, however, found for 26 (38%) patients with both symptoms and abnormal clinical findings. All differential diagnostic possibilities in the

examination of vulvar complaints should be considered. Patients with nonspecific vulvar symptoms can be given symptomatic treatment and assurance of the benign nature of the condition.

A retrospective analysis over a 25-year period of patients (n=79) operated on because of an ovarian mass was carried out. Seven malignant tumors, 34 benign neoplasms and 26 functional cysts were found. In the 1990s preoperative sonography was carried out in 65% of cases. One ovary was removed from 32 patients and one ovary was resected in 37 cases. With proper preoperative work-up of abdominal pain and ovarian tumors in young females, unnecessary and too radical surgery could be avoided.

Percutaneous estradiol gel with gradually increasing doses was used for induction of puberty in 23 girls with Turner syndrome. Development of secondary sexual characteristics and uterine development progressed gradually during the study. All girls reached at least pubertal stage B4P4. With the gel the estrogen dose can be individually tailored to be similar to that in natural pubertal development. Efficacy of therapy can be evaluated by following the development of pubertal signs, sonographic measurement of uterine growth and endometrial thickness, and by assays of circulating estrogen and gonadotropin concentrations.

The girls examined in regard to suspected sexual abuse were mainly younger children, 55% of them under 7 years of age. No girls aged 15 or 16 years were referred for hospital examinations. Gynecological and/or psychiatric examinations showed evidence of sexual abuse in 31 (56%) cases. The gynecological and child psychiatric assessments agreed in 72% of the cases. Complicated cases of child sexual abuse with young victims, intrafamilial abuse and severe consequences were seen in our study. The older victims of sexual abuse did not seem to reach the services, and girls might have been left alone with their worries. Somatic evaluations, which are an essential part of the examination of child sex abuse victims, should be left to the experts because of the methodological difficulties and fairly small numbers of cases.

Pediatric gynecology is a small and not yet well known field where gynecology and pediatrics are combined. Female children in the pediatric age group constitute 10% of the population. Their need for special gynecological services is not well enough recognized.

The reproductive health of young females is an important aspect to be considered by all physicians working with young patients. Preventive

medicine and a conclusion of normal gynecological findings are important in pediatric gynecology. Tertiary referral level university hospitals should have a pediatric gynecologist to provide gynecological care for young patients in complicated cases, to educate students and physicians and to continue research in this field. Every level of the health care system is needed to provide adequate gynecological services for young females.

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ABBREVIATIONS

AFP	Alphafetoprotein
CA 12-5	Cancer antigen 12-5
CEA	Carcinoembryonic antigen
CEE	Conjugated equine estrogen
CT	Computerized tomography
DHEAS	Dehydroepiandrosterone sulfate
E1	Estrone
E2	17 β -estradiol
EE2	Ethinyl estradiol
E ₂ V	Estradiol valerate
FSH	Follicle-stimulating hormone
GH	Growth hormone
GnRH	Gonadotropin-releasing hormone
hCG	Human chorionic gonadotropin
HPV	Human papilloma virus
LH	Luteinizing hormone
MRI	Magnetic resonance imaging
SDS	Standard deviation score
SHBG	Sex hormone binding globuline
TS	Turner syndrome
US	Ultrasonography/ultrasonographic

LIST OF ORIGINAL PUBLICATIONS

The present thesis is based on the following original publications, which are referred to in the text by their Roman numerals.

- I Piippo SH, Lenko H, Laippala JP (1998): Experiences of special gynecological services for children and adolescents: a descriptive study. *Acta Paediatr* 87:805–808.
- II Piippo S, Lenko H, Vuento R (2000): Vulvar symptoms in paediatric and adolescent patients. *Acta Paediatr* 89:431–435.
- III Piippo S, Mustaniemi L, Lenko H, Aine R, Mäenpää J (1999): Surgery for ovarian masses during childhood and adolescence: A report of 79 cases. *J Pediatr Adolesc Gynecol* 12:223–227.
- IV Piippo S, Lenko H, Kainulainen P, Sipilä I (2004): Use of percutaneous estrogen gel for induction of puberty in girls with Turner syndrome. *J Clin Endocrinol Metab* 87:3241-7.
- V Piippo S, Luoma I, Rutanen M, Kaukonen P, Harsia A, Lenko H: Sexual abuse of girls: a study of 55 cases from the early and late 1990s. *J Pediatr Adolesc Gynecol*, submitted.

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INTRODUCTION

During the past few decades parents and physicians have become more aware of the fact that even prepubertal girls can have gynecological problems and need gynecological care. General practitioners, pediatricians, gynecologists, endocrinologists and urologists are facing the gynecological problems of young patients. Studies involving girls with a history of sexual assault have also helped us to understand the normal findings and variations in the genital anatomy during childhood and puberty. Gynecological sonography is an excellent tool in the evaluation of different anatomical and physiological conditions.

Despite their obvious health risks, associated with risk related behavior, adolescents have the lowest rate of gynecological office visits of any age group in the USA. Only 1% of 11- to 14-year-olds and 11% of 15- to 20-year-olds have had appointments with a gynecologist (Council of scientific affairs 1989). Shame or lack of knowledge, money or confidentiality are problems which make it difficult for a young girl to seek gynecological help.

According to population statistics, in 2001 Finland had 5 194 901 inhabitants, of whom 23% were under 19 years of age. There were ~580 000 females, 11% of the whole population, in this age group. The number of girls aged 0–6 years of age was ~200 000, prepubertal schoolgirls of 7–10 years of age numbered ~130 000 and pubertal girls aged 11–18 years numbered ~157 000. The healthcare system provides few and scattered services for the gynecological health of these young people.

General practitioners and pediatricians have very little training as regards conditions that affect the reproductive tract during childhood, since many of the conditions are rare. Pediatric surgeons do not generally have training in reproductive medicine, and reproductive aspects may not be sufficiently considered during surgical procedures. Most of the concepts and premises taught in general gynecology apply to the pediatric population. Caring for pediatric patients requires a thorough knowledge of embryology, development and growth, normal anatomy and special features of gynecological conditions appearing during childhood. The purpose of this study was to analyze the gynecological problems, gynecological examinations and findings in young female patients up to 17 years of age as seen at hospital level, especially at a consultation clinic for pediatric and adolescent gynecology.

REVIEW OF THE LITERATURE

This literature review summarizes the recent scientific knowledge concerning gynecological examination of children, especially pediatric vulval problems, ovarian tumors, delayed puberty and child sexual abuse. These are the areas covered by the original publications of the thesis. Even though gynecological sonography is an integral part of the diagnosis and follow up of precocious puberty it was not a main interest point in original studies and thus precocious puberty is not addressed in this literature review. Sexually transmitted diseases are covered as far as necessary in the examination of child sexual abuse. Menstrual disorders, contraception, pregnancy and abortions, the main interest points of adolescent gynecology are not discussed.

1. Interests in pediatric gynecology

Prior to the 1960s, pediatric gynecologists were mostly interested in gynecological tumors and the surgical challenges posed by congenital malformations. The history of congenital malformations and the surgical procedures associated with them are reported in ancient Greek and Roman literature (Edmonds 2002). A case of labial adhesion was described by Dewees (1825) as early as in 1825. From 1900 to 1950 many scientific articles dealt with issues of physical growth and development during childhood and adolescence. Stein and Leventhal (1935) described a syndrome of amenorrhea associated with bilateral polycystic ovaries, and Turner (1938) described a syndrome of infantilism, congenital webbed neck and cubitus valgus. The standards for staging of pubertal development were presented by Mashall and Tanner in 1969. In the 1960s the first textbooks on pediatric gynecology were published on both sides of the Atlantic; in 1960 Jack Dewhurst wrote his first textbook on pediatric malformations and their management. In 1968 he published his first textbook of pediatric and adolescent gynecology covering all fields of pediatric and adolescent gynecology.

In the 1960s the sexual revolution was witnessed and in the 1970s the literature focused increasingly on the consequences of sexual liberation, mainly among the young: issues of contraception, pregnancy, abortion and sexually transmitted diseases. In the 1980s it became increasingly apparent that pediatric and adolescent gynecology are very different subspecialties. Pediatric

gynecology deals mostly with more rare and specific problems of an individual child during childhood and the beginning of pubertal development: genital malformations including ambiguous genitalia, gynecological tumors of childhood, premenarcheal vulvovaginitis, disorders of growth and puberty and increasingly, sexual abuse of children. New interests concern the future fertility aspects of increasing numbers of severely chronically ill girls, for example cancer patients and organ transplantation survivors. A multidisciplinary team with pediatric endocrinologists, gynecologists, surgeons, child psychiatrists and psychologists is essential in the care of pediatric gynecological patients.

Adolescence is a period of physiological growth and development together with psychosocial maturation. Early adolescence (12–14 years) is a period of pubescent growth and maturation; youngsters retain concrete thinking and begin to separate from parents and identify with peers (Alderman et al. 1996). In mid-adolescence (15–17) thinking becomes more abstract, and risk-taking behavior increases with peer influence. Youngsters can imagine future consequences but cannot fully assess them. Concerns regarding body image affect health-related choices. Conflicts with parents are at a peak. In late adolescence (18–21) formal operational thinking develops, together with a fuller understanding of consequences of actions. The young person has developed a set of personal values that govern choices and they may accept parental values or develop their own.

Adolescent gynecology concentrates on problems, mostly in association with emerging sexuality, concerning all adolescents in every society throughout the world: menstrual disorders, sexually transmitted diseases, contraception, teenage pregnancy, abortion, and violence against women. The work is done on an individual level with patients, but the magnitude of these problems in different cultural environments worldwide emphasizes the importance of education, and efforts and decisions made on national and international levels.

In scientific interests, emphasis has recently been on publications concerning adolescent gynecology. A search of PubMed articles using the search terms “pediatric gynecology” and “adolescent gynecology” for articles in English concerning the age group 0–18 revealed many more articles on adolescent than on pediatric gynecology.

	1961–70	1971–80	1981–90	1991–2000	2001–2003
Pediatric	8	5	20	57	17
Adolescent	39	125	186	450	150

The search term “pediatric gynecology” in 2001–2003 revealed 17 articles, of which 13 dealt with pediatric gynecology. Two were bibliographies of the world literature on pediatric and adolescent gynecology, two dealt with congenital anomalies, one with tumors, three with vulvar symptoms and five with pediatric gynecology in general. Scientific interest in specific areas of pubertal development, and the treatment of pubertal disorders and various gynecological conditions is vast. However, many interesting questions in pediatric gynecology are still waiting for an answer.

2. Gynecological examination of children

Gynecological examination of children is still a taboo subject and can be a frightening experience for the patient, her guardian and even for the physician. Examination of the female genitalia is not routinely included in the health examination of girls. In the USA trained student observers rated 123 physical examinations of children under 10 years by pediatric house staff during health care maintenance visits. The physicians examined the ears, heart and abdomen in 97% of their subjects, regardless of sex. Female genitalia were examined in 39% and male genitalia in 84% of the children. A trend towards less frequent examination of genitalia in older children was also observed (Balk et al. 1982).

The first pelvic (or gynecologic) examinations are critical to the attitudes that a young girl will develop towards her genitals and reproductive health (Blake 1992). In a questionnaire study among Danish teenagers 32% of the girls gave a negative general evaluation of their first pelvic examination and 13% had found the examination very painful (Larsen et al. 1995). The negative experiences were associated with embarrassment, lack of control during the examination and insufficient knowledge of the examination. In a German study 169 girls up to 16 years of age, who had been examined at a pediatric and adolescent gynecological clinic, answered a questionnaire about anxiety and pain during the visit. Anxiety was reported by 52% of the girls and pain by 28% and there was positive correlation between anxiety and pain. The sex of the examiner had no influence on how the examination was experienced (Bodden-Heidrich et al. 2000). Children and teenagers should be given proper information and realistic expectations prior to their first pelvic examination. Gynecological examination of a child or an adolescent should never be forced.

2.1. Genital anatomy during childhood

The anatomical structures of the female genital tract develop during fetal life. Knowledge of embryological development is important for a physician to be able to understand structural anomalies of the female genitalia. In addition to natural growth the hormonal milieu is an important regulator of these changes. Genital anatomy undergoes many changes between infancy and adulthood: alterations in the size, shape and in the position of the organs continue postnatally until the end of puberty. In pediatric and adolescent gynecology it is of utmost importance to know the normal anatomy and

findings in the female genitals during growth and puberty. The typical gynecological conditions at different ages are related to the corresponding pubertal stage and genital anatomy.

2.1.1. Newborns

The gynecological anatomy varies according to age and the stage of pubertal development. The uterus is about 4 cm long and has no axial flexion. The cervix-corpora ratio is 3:1. In a newborn up to eight weeks of age the vulva and vagina are under the influence of placental estrogens. The labia majora are large and bulbous at birth and start to flatten a few days after birth. The mons pubis is a fatty pad and the vestibule is more anteriorly placed than it is in an adult woman. The labia minora are larger than in older children and close the vestibule. The clitoris is disproportionately large at this stage. The hymen of a newborn is thick and folded with a small opening (Berenson et al. 1991). The vagina is 4 cm long with acidic or neutral pH and lactobacilli as normal flora. In infants born prematurely the effect of estrogen on the genitals is even more prominent. The effect of maternal estrogens should completely disappear by 6–8 weeks after birth.

2.1.2. Infancy and childhood

In the period from eight weeks to seven years there is a quiescent phase and a girl is not normally exposed to significant amounts of sex steroids. There are no signs of pubertal development; no pubic hair or breast development. The uterus is small with a cervix-corpora ratio of 2:1. The vagina is 4–5 cm long with a thin, red epithelium, alkaline pH and mixed bacterial flora. The labia majora are flat and the labia minora small and thin, offering little or no protection to the vestibulum and vagina. The clitoris is small. The hymen is a thin membrane with even edges. There are three major hymenal configurations in prepubertal girls: annular, fimbriated and crescentic (Berenson et al. 1992). In an annular hymen the tissue appears smooth and circumscribes the vaginal introitus without folds and with an annular opening. In a fimbriated hymen there is more hymeneal tissue which folds around the vaginal opening. The crescentic hymen has minimal tissue visualized anteriorly and hymeneal tissue appears from 2 o'clock posteriorly around to 10 o'clock. Abnormal variations in hymenal configuration are imperforate, septate and microperforate hymens.

2.1.3. Early puberty

When GnRH pulse frequency accelerates, follicular development and estradiol production increase. The myometrium is growing and the cervix-corpora ratio is 1:1. The vagina elongates to 8 cm in length with a thicker mucosa and nonpathogenic mixed flora. Physiological leukorrhoea with an increasing estrogen effect starts at this age. The labia majora are filling out, the labia minora are becoming thicker and the hymen starts to become thicker and more folded. The development of pubertal signs follows a pattern described by Marshall and Tanner (1969). The mean age for breast budding, the sign of estrogen activity, for European girls is 10.7 years (Delemarre-van de Waal (2002)). In US the National Health and Nutrition Examination Survey from 1988-1994 studied pubertal development in a multiracial population. Mean age for the beginning of breast development, Tanner stage B2, was 9.7 years, and mean age of menarche 12.5 years (Lee et al. 2001).

2.1.4. Puberty

With advancing hormone secretion the genital anatomy changes further. Lengthening of the corpus is followed by an increase in the width and thickness of both the corpus and cervix.

By the end of puberty the cervix-corpora ratio is 1:2. Gradually the endometrium also starts to proliferate and menstruation starts (Krasnow et al. 1992). The vaginal flora changes and the vaginal epithelium increases in thickness, which provides better protection against infections. The vagina becomes more elastic. By Tanner stage III the hymen is obviously thicker and by stage V, folded and the vascular pattern disappears. At Tanner stage IV the labia minora become larger and more pigmented, offering better protection to the vestibulum and vaginal opening (Yordan et al. 1992).

2.2. Settings for examination

Patience during the examination, knowledge and clinical experience together with special instruments and examination techniques are the keys to successful gynecological examination of children (Gidwani 1987). Privacy, quiet, time and confidentiality are even more important than normally in the gynecologic examination of a child or an adolescent. Children have to be interviewed patiently to gain the confidence of both the child and her guardian. The

presence of a chaperone, often the girl's mother, is beneficial during the examination. Older children sometimes feel more relaxed without their parents present and their own opinion should be sought. Information about physical growth and pubertal development are always included in recording the history. A review of previous and current health, chronic diseases of childhood and congenital anomalies is important. The child's social background and family dynamics are also important to consider when we evaluate the relationships between different clinical symptoms and findings. The language and precise words used are very important, since children in particular use different names when they describe their anatomy and symptoms in the gynecological area (Blake 1992).

2.3. Examination techniques

An overall physical examination with evaluation of pubertal status is always included at the beginning of the clinical examination. It is important to emphasize to the child that she has control over the examination and that she will not be hurt in any way. It should also be explained to the girl why the examination is being performed and exactly what will happen, in a stepwise manner (Hairston 1997).

The best physical position for the examination of a child or an adolescent depends on the comfort of the child and maximal visualization for the physician. Small infants and young children are easily examined on their backs on their mother's lap (Capraro 1972). The thighs of the baby are flexed on her abdomen and the mother can hold them back. The child should be able to show and open the vulva herself and a mirror can be used to enable the child to see what is happening. The mother, holding a child, can be seated on a normal chair or can be in a semi-sitting position on the examination table. Older children usually feel comfortable on the examination table in a frog leg position or in a knee cheats position. In a questionnaire survey adolescents seemed most comfortable at their first pelvic examination when examined in a semi-sitting position (Seymore et al. 1986).

Visualization of the vulva is perhaps the most important part of the gynecological examination of children. For this, three techniques can be used; supine position with labial separation, supine position with labial traction, and the knee-chest position (Emans et al. 1980). In labial separation the labia majorae are pulled laterally. Better visualization of the vestibule and hymen

can be obtained by the labial traction method, when gentle traction is added while pulling the labia downwards. The knee-chest position (98%) and the supine traction method (96%) proved to be superior to the supine separation technique (86%) in opening the vaginal introitus in a study of 172 girls who were evaluated for sexual abuse (McCann 1990).

The vagina of a child is short and narrow, horizontally located and the fornices are not formed. The walls of the immature vagina are much less adaptable to manipulation than those of an adult and the tissues are easily hurt and irritated. With the supine traction method one third of the vagina can be visualized without instruments. In the examination of children complete visualization of the vagina is seldom needed but it is mandatory in patients with bleeding, suspicion of a genital tumor, an ectopic ureter or a foreign body. The introduction of any instrument to the introitus or in the vagina with the girl awake requires gentleness and is time-consuming. A technique introduced by Capraro (1972) consists of successively touching the girl's finger, inner thigh and labia with the instrument prior to its insertion into the vagina. The instruments and sampling equipment should be shown to the girl and she should be allowed to feel the instruments. When a young girl has enough estrogen to reach Tanner stage III breast development or to have passed menarche she normally has enough elasticity in the introital tissues to tolerate a carefully performed speculum and bimanual pelvic examination.

2.4. Instruments and supplies

Most important and often sufficient are hands and eyes and a good light source. Magnification of the tissues of the vulvar area is also helpful. The speculums used for the examination of children and young adults come in different widths but should be long enough to enable examination of the whole vagina. To visualize the whole vagina a vaginoscope can be used for younger children and small speculums for older prepubertal and pubertal girls. A modern vaginoscope has a self-contained light source and a magnifying eyepiece. The speculums with the vaginoscope come in different sizes. Samples from the vagina can be obtained through the vaginoscope. Hysteroscopy can also be used for examination of the vagina in pediatric gynecology (Bacso 1994). Most often vaginoscopy in prepubertal girls has to be performed under anesthesia.

In addition to the special instruments mentioned above, supplies for cultures, wet mount slide preparations and Pap smears should be available. Saline solution is used to wet the cotton-tip applicators used in sampling. Appropriate culture media should be used for the culture of *Candida*, *Gardnerella vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and herpes simplex virus.

Chlamydia trachomatis infection can easily be diagnosed by ligase chain reaction from the first catch urine sample (Lee et al. 1995). Pap smears are informative in the evaluation of hormonal action and vaginal infections or possible tumors. Papilloma virus infections can be diagnosed by means of Pap smears and biopsies. The typing of the papilloma virus is important when diagnosing and treating papilloma virus infection during childhood and adolescence, since HPV-16- and HPV-18-like virus types lead to a higher risk of invasive cancers (Moscicki 1999). High-risk HPV testing can be part of the primary screening in association with cytology (Clavel et al. 2001).

In obtaining samples from prepubertal girls it is of utmost importance to remember that even gentle swabbing can cause discomfort. Samples from the vulva and anal area can be obtained with a moistened cotton-tip by gently rolling it on the skin or mucosa. Samples from the vagina can be taken blindly or by using a vaginoscope or small speculum. Pokorny and co-workers (1987) have introduced a method of obtaining samples from the vaginal vault using a vaginal aspirator.

2.5. Sonography

Ultrasonography is an excellent noninvasive method for evaluation of the pelvic structures of a child or a young adolescent. During growth and puberty the internal genital structures undergo changes in size and shape in a predictable fashion. Gonadotropin stimulation is believed to lead to enlargement of the ovaries and a multicystic ovarian appearance during puberty. Estrogen secretion results in uterine enlargement and produces an adult uterine configuration. Sonography is important in the diagnosis and treatment of pubertal disorders (Stanhope et al. 1985). In precocious puberty larger ovarian cysts appear, the size of the uterus increases and the possible presence of endometrium can be detected by sonography. Sonography is equally important in the assessment of lower abdominal pain, pelvic masses and ambiguous genitalia in children (Estroff 1997).

Sonography is well suited for young patients because their small size and lack of subcutaneous fat allow excellent spatial resolution. The examination is quick to perform, comfortable for the patient and no sedation is needed. Transabdominal imaging of the uterus and the ovaries, which requires a well-distended bladder, is used for pediatric and young adolescent subjects. A high frequency transducer should be used to optimize the resolution of small structures. Examinations of infants and young children can be performed with a 7.5 or 5 MHz transducer, whereas a 5 MHz or lower frequency transducer is used for older children and teenagers (Siegel 1991).

Transvaginal sonography provides better visualization of anatomic details and helps to elucidate unclear findings in transabdominal sonography (Bellah et al. 1991). The examination does not require a distended bladder and as it is performed at a closer distance the structural appearances can be better evaluated. In the USA, in an anonymous questionnaire to adolescent (14–20 years) and adult (21–61 years) patients, 26% of the respondents reported after the examination that transvaginal sonography had 'hurt a lot' and 50% reported that it had 'hurt a little'. Willingness to undergo further endovaginal examination increased with age (Bennett et al. 2000). Transvaginal sonography is not generally used in virginal young subjects, but current vaginal probes can be used transrectally (Estroff 1997). Transrectal scanning can be used in children and adolescents instead of transvaginal scanning. The images obtained are superior to transabdominal images and comparable to those obtained by transvaginal sonography (Timor-Tritsch et al. 2003).

2.5.1. Sonographic findings in the normal ovary

At birth the ovary is located within the superior margin of the broad ligament and is approximately 15 mm long, 3 mm wide and 2.5 mm thick (Haller et al. 1983). Ovarian volume is preferred as an indicator of ovarian size because of greater predictability. Volume in cubic centimeters can be calculated using the ellipse formula = length cm x height cm x width cm x 0.523 (Campbell et al. 1982). Ovarian volume has been shown to be stable and between 0.4–0.8 ml from birth until the age of five years. With the onset of puberty ovarian size increases progressively (Haber et al. 1994). In normal girls, uterine length, ovarian volume and circulating sex steroid concentrations correlate well with the Tanner stage (Cacciatori et al. 1991, Herter et al. 2002).

Orsini et al. (1984) studied age-related changes in ovarian size and morphology in 114 normal premenarcheal girls by means of sonography. At the age of six ovarian volume started to increase and more rapid growth was seen after the age of 9 years. A microcystic ovarian structure appeared at the age of 6–8 years in 20% of the girls and at 9–12 years in 30–50% of them. Macrocystic ovaries appeared at the age of 12. The uterus undergoes a regular increase in size and the cervix-corpora ratio changes progressively with advancing puberty (Orbak et al. 1998, Cacciatore et al. 1991).

Dysgenetic ovaries are usually not visible in sonography. The possibility of anticipating spontaneous puberty in 24 peripubertal Turner girls by sonography has been studied by Matarazzo et al. (1995). Nine girls with streak ovaries not identifiable in sonography did not develop any signs of spontaneous puberty. Six girls with normal ovarian volume above 0.7 ml and at least 6 cysts greater than 4 mm in diameter had spontaneous pubertal development. Four of nine girls with small ovaries and a few follicles of 2–4 mm in size showed signs of spontaneous puberty. Strong concordance existed between the sonographic appearance of the ovaries and gonadotropin secretion. In a comparison of 93 Turner syndrome girls with 190 healthy controls, matched by age and pubertal stage, the uterine volume and mean ovarian volume of prepubertal girls with Turner syndrome were significantly lower than those of the controls (Haber et al. 1999).

2.5.2. Sonographic findings in the normal uterus

Uterine shape and the dimension ratio between the corpus and cervix change throughout childhood and puberty. A uterine volume of 3.4 ml has been found in newborns (Haber et al. 1994). During the neonatal period the length of the uterus can be up to 4.6 cm and endometrium can be identified. Endometrial fluid has been found to be present in 25% of neonatal uteri (Nussbaum et al. 1986). Ultrasonography is an accurate method for the detection of neonatal uteri, for example in the determination of sex among infants with ambiguous genitalia. The uterus could be identified in 94% of normal female infants examined with covered external genitalia. Absence of a uterus was predicted in 98% of male infants (Kutteh et al. 1995).

After the neonatal period the uterus decreases in size after 3 months of age and shows little change until 7 years of age. The length of the uterus during this period is 2.5–3.3 cm, width 0.4–1.0 cm and cervical width 0.6–

1.0 cm (Ivarsson et al. 1983). After 7 years the uterus gradually increases in size. More dramatic growth of the uterus is seen during puberty. The fundus becomes larger than the cervix and the uterus becomes pear-shaped. In postpubertal girls the length of the uterus ranges between 5–8 cm and the maximum width is 1.6–3 cm. The start of menstruation can be anticipated by the appearance of the endometrium. After menarche the endometrium demonstrates a cyclical pattern of development each 28 days. Uterine volume is statistically significantly related to pubertal stage (Haber 1994). During the induction of puberty among girls with TS, using adequate estrogen doses, a uterine length of 5.8–8.6 cm, within the normal adult range, has been achieved (McDonnell et al. 2003).

3. Hormones and female sexual maturation

3.1. Gonadotropin-releasing hormone and gonadotropins

As a result of the function of the fetoplacental unit, fetuses have a rich steroidal milieu. Estrogen concentrations in fetal serum are very high. The newborn shows signs of this hormonal influence. Gonadotropin-releasing hormone, which is released by the hypothalamus in a pulsatile fashion, controls FSH and LH production from the pituitary gland and eventually estrogen production from the ovary. GnRH surges are apparent after birth until 4–6 months. Thereafter the levels are suppressed, although some secretion of bioactive gonadotropins at low levels takes place during childhood (Dunkel et al. 1990). Previously the gonadotropin regulating system was considered to be very sensitive to the negative feedback of small amounts of gonadal steroids during childhood (Grumbach et al. 1974). This theory has been called the gonadostat hypothesis. A new theory was based on the findings that agonal patients showed identical changes in gonadotropin secretion throughout infancy as gonadal patients (Conte et al. 1980). This indicates that a central inhibitory system restrains GnRH release and induces the quiescent phase in gonadotropin secretion.

Between 7–10 years is the awakening phase, with adrenal, pituitary and ovarian activity. As a result of withdrawal of the inhibitory effects mediated by the CNS, the hypothalamus begins to release GnRH with increasing frequency and amplitude in a pulsatile fashion, at first during the night and then gradually also during the day (Apter et al. 1993). Mean LH (24 h) concentrations increase 40-fold from prepuberty to late puberty. Mean FSH concentrations (24 h) increase only 3-fold, over the same period (Apter et al. 1993).

3.2. Estrogen and progesterone

Natural sources of estrogen include direct secretion by the gonads, and conversion of adrenal steroids in peripheral tissue. Estrogens, primarily 17 β -estradiol, but also estrone, are produced in the granulosa and theca luteal cells of the ovary. Additionally, androstenedione and testosterone are converted to estrogens by 17 β -hydroxysteroid dehydrogenase isoenzymes and aromatase in the gonads and in peripheral tissue (Labrie et al. 2000,

Simpson et al. 2001). Aromatase is expressed in fat, skin, osteoblasts, chondrocytes, vascular smooth muscle cells, endothelium and the central nervous system.

From the onset of puberty, pulsatile gonadotropin changes induce estrogen production in the ovary (Hansen et al. 1975). Estrogens are responsible for maturation of the female internal genitalia, and secondary sexual characteristics. Sexual hair growth, however, is primarily regulated by androgens. Menarche does not yet indicate full maturation of the neuroendocrine-ovarian axis. The first menstruation, in approximately 50% of cases, is a result of estrogen-withdrawal bleeding, and ovulatory cycles follow. Progesterone is a product of the theca luteal cells and is produced in measurable amounts after ovulation has started. Together with estrogen, progesterone causes the endometrium to involute and discharge and it also acts on the mammary glands.

Acceleration of growth during puberty is induced by increasing secretion of sex steroids. Estrogen receptors alpha and beta and androgen receptor are expressed in the human growth plate throughout pubertal development (Nilsson et al. 2003). Estrogens have an important role in the regulation of bone maturation and in the closure of epiphyseal plates in both sexes. A male with an inactivating mutation of estrogen receptors (ERs) was described in 1994 (Smith et al.). This 28-year-old man was 208 cm tall and had a bone age of 15 years. He had normal pubertal development, with no indication of accelerated pubertal growth. This case confirmed that estrogens are essential for epiphyseal closure also in males. Additionally, the report suggests that estrogens do not participate in the regulation of linear growth, but induce growth acceleration during puberty.

With ultra-sensitive bioassays, mean serum estradiol concentrations have been found to be significantly higher in prepubertal girls than boys (Klein et al. 1994, Paris et al. 2002). Estrogen exerts a biphasic effect on long bone growth: at low concentrations it induces growth, but at higher concentrations growth is inhibited (Moll et al. 1986). Growth stimulation is optimal at approximately 4 µg of estradiol per day (Rosenfield et al. 1998). One third of final bone mass is acquired during puberty. Estrogen is also critical to the attainment of normal bone mineral density in both sexes (Lorenzon et al. 1999).

3.3. Other hormonal factors influencing pubertal development

Leptin, a hormone derived from adipose tissue, plays a role in body composition. Since leptin levels rise throughout female puberty, there is an interest in its role. It has been suggested that leptin has a permissive role in the progression into puberty and the maintenance of normal hypothalamic-pituitary-gonadal function thereafter (Farooqi et al. 1999, Apter 2003).

Activins and inhibins are peptides that appear to participate in the regulation of FSH secretion. Inhibin B is produced by granulosa cells from small antral follicles under the feedback control of pituitary FSH secretion, and inhibin A by larger follicles and the corpus luteum (Crofton et al. 2002). During female puberty, the circulating inhibin B level increases from Tanner stage B1 through stage B3, suggesting high follicular activity before the development of ovulatory menstrual cycles, but serum inhibin A levels become measurable later in puberty, in agreement with the idea that inhibin A is mainly produced by the corpus luteum (Raivio et al. 2002). Anti-mullerian hormone also plays an important role in the regulation of ovarian follicle growth. Anti-mullerian hormone inhibits recruitment of primordial follicles into the pool of growing follicles and lowers FSH sensitivity of the follicles (Gruitjers et al. 2003)

4. Vulvar and vaginal diseases during childhood

Vulvovaginitis is the most common gynecological disorder in children. Gynecological problems that little girls have are often localized in the vagina or on the vulva and most often the diagnosis can be carried out by simple visual examination. Owing to the lack of estrogen the vaginal mucosa is thin and less resistant to infectious organisms and irritants. After puberty normal vaginal flora and the etiology of infections are the same as during adulthood.

4.1. Vulvovaginitis

Vulvovaginitis is inflammation of the vulvar and vaginal tissues. In children, the vulva is usually inflamed first with the vagina uninvolved, or secondarily affected (Farrington 1997). Anatomically the vulva of a young girl is unprotected, without labial fat pads or pubic hair. Vulvar skin is thin and vaginal mucosa atrophic. The vaginal cavity has a neutral pH and is warm and moist, which makes it excellent for bacterial proliferation. Poor hygiene is also considered to be one of the predisposing factors (Pierce 1992). The main symptoms of vulvovaginal infections are vaginal discharge (53%), erythema (15%) and pruritus (27%) (Koumantakis et al. 1997). Vaginal discomfort, urinary symptoms and an abnormal odor can also be present.

The majority of cases of pediatric vulvovaginitis does not have a specific etiology (Paradise et al. 1982, Jaquiery et al. 1999). An alteration in the flora of the vagina is thought to cause the vulvar and distal vaginal inflammation. Asymptomatic patients can be colonized with bacterioides species, group B streptococci, *Escherichia coli* and coagulase-positive staphylococcus (Paradise et al. 1982). The most common specific causes of childhood vulvovaginitis found in bacterial cultures are *Streptococcus pyogenes* and *Haemophilus influenzae*. *Candida*, *Gardnerella vaginalis* and sexually transmitted diseases usually appear after puberty. Threadworms are a common cause of vulvar symptoms.

In a prospective study of 200 girls aged 1–15 years examined in a pediatric emergency department because of genital complaints, the major causes of symptoms were found to be poor hygiene and threadworms. Threadworms were found in 43 patients. In bacterial cultures *Haemophilus influenzae* was found in 22 patients and streptococci in 17 patients. No trichomonas or

chlamydia infections were found. Significant bacteriuria was present in 20 cases. Specific local skin problems occurred in 28 patients (Pierce et al. 1992). In a retrospective study the clinical features and findings in bacterial cultures and microscopic examination of 80 prepubertal girls aged 2–12 years with vulvar complaints were analyzed. Vaginal secretion was obtained with a sterile catheter straight from the vagina. In 36% of cases pathogenic bacteria were isolated. In 59% of these cases the bacteria isolated were group A beta-hemolytic streptococci. No *Candida* was found in these patients (Stricker et al. 2003).

Cox, in the United Kingdom (1997), carried out a prospective laboratory-based survey of the infectious etiology of vulvovaginitis in young girls. Within a 19-month period 106 swabs from 104 patients were cultured for various bacteria. The most common pathogens found were group A streptococci in 19 cases and *Haemophilus influenzae* in 11 cases as the second most common infective cause of juvenile vulvovaginitis. *Candida* was isolated on nine occasions. The most common treatment used was empirical, topical clotrimazole cream. Antibiotics active against streptococcus were prescribed for 22% of the cases.

The etiology, clinical features and response to treatment of childhood vulvovaginitis in primary care were studied in a group general practice with 11 000 patients in the UK. Within a 70-month study period 42 patients from the study population were included. Specific bacteria were found in 10 cases: *Streptococcus pyogenes* in 7 cases, *Haemophilus influenzae* in 2 cases and *Staphylococcus aureus* in 1 case. No *Candida* was isolated. No evidence of sexual abuse or foreign bodies was found. Half of the patients had symptoms lasting over 10 days (Jones 1996).

The contribution of clinical and environmental factors and infections to the etiology of vulvovaginitis has been studied in Australia. Cases were 50 premenarcheal girls, aged over 2 years, from an emergency department, with vulvovaginal symptoms. Controls were 50 girls in the same age group undergoing minor surgery. No difference was found between the cases and controls in regard to hygiene practices, exposure to irritants or history of child sexual abuse. Normal vaginal flora included *Staphylococcus epidermidis*, diphtheroids and anaerobes. Most (80%) of the cases had no evidence of an infectious etiology. *Staphylococcus aureus* and group A streptococci were more commonly isolated from the cases. Infections were generally associated with vaginal discharge and vulvar inflammation (Jaquier et al. 1999).

Treatment options in cases of vulvovaginitis vary according to the etiology found. In cases of specific pathogens systemic antibiotic treatment can be prescribed. Candida infections can be treated with local or systemic antifungal medication (Stricker et al. 2003). In the majority of cases where the etiology is nonspecific various empirical treatments, improved hygiene, sitz baths, local estrogen therapy and topical creams are widely used. Nonspecific local symptoms usually disappear with advancing puberty and increasing local estrogen effect.

4.2. Sexually transmitted diseases

In the pediatric age group, before becoming sexually active, sexually transmitted diseases are rare and usually lead to the suspicion of sexual abuse. In the USA the prevalence of various sexually transmitted diseases was evaluated in 1538 children, aged 1–12 years, who were examined for sexual abuse. Gonorrhoea was found in 2.8%, human papillomavirus in 1.8%, *Chlamydia trachomatis* in 1.2%, syphilis in 0.1% and herpes in 0.1% (Ingram et al. 1992).

Acute *gonorrhoea* typically causes severe vaginitis but infection in the rectum and pharynx are frequently asymptomatic. The isolation of *Neisseria gonorrhoeae* from a prepubertal girl is probably the most convincing indicator of sexual abuse or activity. Since the infection is fairly rare the American Academy of Pediatrics has suggested that testing should be done only when the history or physical findings suggest the possibility of oral, genital or rectal contact or when epidemiologically indicated. Ingram et al. (1997) evaluated the culture results of 2898 girls examined over a 10-year period for sexual abuse. Cultures for *N. gonorrhoeae* were carried out in 2731 (94%) cases; 84 (3.1%) had positive cultures, 80 of whom had vaginal discharge. All these 84 girls could have been identified through selective screening criteria. Among a patient group from a pediatric emergency department, female patients at Tanner stage I–II with complaints of vaginal discharge or vulvar symptoms were studied. Among the 87 patients examined, 43 of them were symptomatic. Four girls had *N. gonorrhoeae* infection and 9 girls a streptococcus infection. Among the 44 asymptomatic girls no *N. gonorrhoeae* infections were found, and 3 had streptococcus infection (Shapiro et al 1999).

Infections caused by *Chlamydia trachomatis* are the most prevalent STDs among adults and sexually active adolescents. Infection in children can be

perinatally acquired. The risk of transmission from an infected mother to an infant is 50%. The infant can be infected at the conjunctiva, nasopharynx, rectum and vagina. The prevalence of *C. trachomatis* infection in sexually abused children is less than 5% (Schwarcz et al. 1990). In 2003 the National Institute of Health in Finland reported in females 8 cases of

Chlamydia trachomatis in the age group 0–4 years, none between 5–9 years, 49 cases in the age group 10–14 years and 2767 cases in the age group 15–19 years. Five cases of *N. gonorrhoeae* were reported during the same period in the age group 15–19 years. So far culture is the preferred method for diagnosis in children suspected of sexual abuse, but the urine-based ligase chain reaction is also specific and is more sensitive than culture for the detection of *C. trachomatis* and *N. gonorrhoeae* in children (Girardet et al. 2001).

Human papilloma virus infection is the most common viral sexually transmitted disease. Condylomata have been reported in 1–2% of sexually abused children and 50% to 60% of cases of genital warts in children reported in the literature appear to be the result of abuse (Schwarcz et al. 1990). The high rate of HPV DNA, 50%, detected in infants born to HPV-negative mothers suggests the possibility of horizontal transmission, besides sexual abuse, between infants and caregivers (Cason et al. 1995). Gutman et al. (1992) compared the presence of intravaginal HPV infection in 15 girls 11 years of age or younger with confirmed sexual abuse with findings in a non-abused control group. In vaginal wash samples HPV infection was found in 5 girls in the abused group but no cases were found among the non-abused subjects. Among 40 consecutive cases examined for suspected sexual abuse, sexual abuse was confirmed in 29 cases. None of the girls had genital warts or abnormal colposcopic findings, but HPV DNA was detected in 5 (16%) of the 31 girls with confirmed or suspected sexual abuse (Stevens-Simon et al. 2000).

Sexually transmitted diseases during adolescence are not discussed in this literature review.

4.3. Skin disorders

Besides infections, various skin conditions can cause vulvar symptoms in young girls. The spectrum and frequency of different skin conditions in girls with vulvar complaints was studied in 130 prepubertal girls in a dermatological clinic. Of these patients 33% had atopic or irritant dermatitis, 18% had lichen

sclerosus, 17% had psoriasis, 12% had vulvar lesions such as hemangiomas and nevi and 10% had streptococcal vulvovaginitis (Fischer et al. 2000).

4.5.1. Lichen sclerosus

Lichen sclerosus is a destructive inflammatory dermatosis, of autoimmune nature, involving the vulvar, prineal and perianal skin. It is characterized by white alterations in the vulvar area. Vesicles and papules occasionally occur and can become hemorrhagic. Lichen sclerosus is not an uncommon condition of the vulva at any age. Between 10 to 15% of all cases occur during childhood. In a series of 15 girls with lichen sclerosus between the ages of 18 months to 9 years dysuria, bleeding, itching and constipation were frequent complaints (Berth-Jones et al. 1991). The symptoms, findings, associated conditions and treatment of lichen sclerosus have been studied in 10 girls and one boy. Characteristic lesions were hypopigmented areas surrounding the vulva and anus; fissures and ulcers were also seen. Nine of the 11 patients reported difficulties with defecation, or anal symptoms. Vulvar and anal bleeding, perineal itching and painful urination were other symptoms reported (Loening-Baucke 1991).

In children a presumptive diagnosis can be made on the basis of the clinical appearance. A biopsy should be performed if the clinical presentation is unclear or if there is no improvement with treatment (Fivozinsky et al. 1998). Anogenital lichen sclerosus in girls can mimic sexual abuse and has led to false accusations and investigations for sexual abuse (Jenny et al. 1981). A high level of parent anxiety has been encountered prior to diagnosis regarding the differential diagnosis of child sexual abuse. Boys as well as men can be affected. The major symptom in males is phimosis.

Childhood lichen sclerosus on the vulva can be treated with 1% hydrocortisone ointment, which has not been a curative treatment but has improved the skin condition (Loening-Baucke 1991). The safety and efficacy of clobetasol proprionate 0.05%, a very potent corticosteroid, was demonstrated in the 1990s in the treatment of lichen sclerosus (Dalziel et al. 1991, Dalziel et al. 1993). Eleven patients aged 3–11 years, with clinically diagnosed lichen sclerosus not responsive to other therapies were treated with betamethasone dipropionate 0.05% ointment. After four months of treatment, nine girls had a completely normal vulva, and two had residual hypopigmentation but were asymptomatic. Three patients required

maintenance on hydrocortisone 1.0%. There were no cases of atrophy, stria formation or infection (Fischer et al. 1997).

A trend towards improvement of lichen sclerosus with increasing age has been recognized (Berth-Jones et al. 1991). The prognosis for lichen sclerosus in childhood is, however, poorly delineated. In follow-up of 36 patients with lichen sclerosus for 14 years, signs of the disease continued to manifest themselves, although many patients were asymptomatic (Ridley 1993). The course of vulvar lichen sclerosus after childhood has been studied among 21 women. Improvement of symptoms after puberty was reported by 16 patients, but 11 patients still required intermittent topical steroid therapy for their symptoms. One case of vulvar squamous cell carcinoma was diagnosed in a 32-year-old woman, which supports the need for long-term follow-up of these patients (Powell et al. 2002). Among adults, the results of retrospective studies suggest that 4–5% of women with lichen sclerosus develop squamous cell carcinoma of the vulva. It is not known whether effective treatment of prepubertal lichen sclerosus will alter the lifetime risk of vulvar squamous cell carcinoma.

4.3.2. Other skin conditions

Seborrheic dermatitis in the vulvar area is characterized by marked erythema. Symmetrical fissures between the labia majora and minora with seborrheic dermatitis have been described. Areas of seborrhea might be present in other areas of the body, such as behind the ears, in the scalp, or in the nasolabial folds. When isolated, seborrhea vulvitis is asymptotic. It is usually the pruritus and discomfort of secondary infections that bring the child to the physician. Systemic or topical antibiotics or topical antifungal agents are treatment options according to the severity of the symptoms and findings. Hydrocortisone cream 1% is beneficial after the secondary infection has resolved (Pokorny 1992).

Atopic dermatitis can also affect the vulvar area. Lesions can usually also be seen in other areas of the skin, particularly the flexural areas of elbows and knees. Treatment includes application of lubricant creams and occasional use of low potency topical steroids.

Psoriasis is a hereditary chronic inflammatory skin condition that affects 1–2% of the population. Vulvar lesions, which are pruritic, can occur. Genital involvement occurs in 44% of children with psoriasis (Weinrauch and Katz

1986). Vulvar psoriatic lesions should be treated with topical low- to mid-potency steroids.

Hemangiomas can also appear on the vulva. Capillary hemangiomas are flat and slightly elevated neoplasms composed of small blood vessels. Cavernous hemangiomas are composed of large thin-walled vessels and are more deeply located than capillary hemangiomas. They commonly develop during the first two months after birth and 80% regress before the age of five. Hemangiomas can be treated with sclerotherapy, cryotherapy or laser therapy (Ambros et al. 1992).

4.4. Labial adhesions

Labial adhesions are defined as partial or complete adherence of the labia minora. The fusion is usually in the midline and appears as a thin, pale and translucent streak. The etiology is thought to be related to low estrogen levels. Irritants may damage the surface of the thin squamous epithelium and as re-epithelialization occurs on both sides, the labia become fused. Most children with labial adhesions are asymptomatic; the symptoms occurring relate to urination and the accumulation of urine behind the fused labia. Ninety percent of cases present in girls less than 6 years old (Williams et al. 1986).

Leung et al. (1993) studied 9070 female infants retrospectively and none of them were reported to have had labial adhesions as newborns. An additional 1970 girls aged 7 days to 12 years were assessed prospectively for labial adhesions in a pediatric outpatient clinic. Thirty-five children were found to have labial adhesions, resulting in an incidence of 1.8%. Labial fusion was most common at the age of 13–23 months (3.3%) and all cases in this population were in girls aged 4 years or younger.

Labial adhesions are usually treated if symptoms are present. Partial adhesions are less likely to be symptomatic and require treatment. Adhesion can be treated with topical application of estrogen cream once or twice daily for two weeks or by mechanical separation (Christensen et al. 1971). Because of the risk of refusion, lubrication of the labia is needed also after the separation.

Muram (1999) studied treatment with topical estrogen, or office separation. Topical application of Premarin vaginal cream, containing 0.625 mg of conjugated estrogen per gram, was primarily used for all 259 girls with labial adhesions for 10–14 days. The fused labia separated in 121 patients,

using estrogen. Ninety-two of these patients had thin transparent adhesions. Mechanical separation in office settings was attempted in the remaining 138 patients. After application of xylocaine gel the separation was successful in 112 (81%) patients. Separation under general anesthesia was required in the last 26 patients. In another study 23 patients with labial agglutination not responsive to topical estrogen therapy were evaluated for manual separation. In 22 patients labial agglutination was separated under anesthesia, followed by topical estrogen for two weeks. There were nine recurrences, five of which were successfully treated with topical estrogen, but four required repeat manual separation (Bacon 2002).

5. Ovarian tumors

Neoplastic ovarian tumors in the pediatric age group are fairly rare, but often lethal if malignant. The clinical and pathological features of pediatric ovarian tumors differ from the features encountered in the tumors of adults. The surgical and medical management of ovarian malignancies in young patients is also different, because of the desirability of maintaining the patient's reproductive and menstrual capabilities.

Approximately 1% of all malignant neoplasms found in the age range of 0–17 years are ovarian in origin (Acosta et al. 1971). In an analysis of nine studies including 613 childhood ovarian tumors, 36% were non-neoplastic or physiologic, and 64% were true neoplasms, both benign and malignant (Breen et al. 1977). With the widespread use of sonography more functional tumors are certainly being diagnosed nowadays than before the late 1970s.

Ninety-one cases of ovarian masses presenting in patients below 18 years of age to the Children's Hospital of Philadelphia from 1979 to 1990 were reviewed retrospectively by Brown et al. (1993). Thirty-four tumors presented prior to 8 years of age, and 1 of them was malignant. Fifty-eight tumors presented after 8 years of age, and 18 (33%) of them were malignant. The most common benign tumors were simple cysts (22 cases), teratomas (25 cases) and ovarian torsion (13 cases). Malignant neoplasms included 14 germ cell tumors, 4 epithelial tumors and one leukemic infiltration. In this study 54 patients had preoperative sonography, which was 100% accurate in the diagnosis of an ovarian mass, but could not distinguish between benign and malignant tumors.

5.1. Clinical presentation

The symptomatology of juvenile ovarian tumors is related to the growth rate of the tumor, location, degree of malignancy, endocrine activity, age of the host and possible complications. The symptoms are often present for a fairly long time before the diagnosis is reached. As the ovary is an abdominal organ, most ovarian tumors will present in a prepubertal child as an abdominal mass and cause abdominal distension. The most common symptom caused by ovarian tumors is abdominal pain, which can be associated with nausea and vomiting. Endocrinologically active tumors can produce signs of precocious puberty or virilization.

Freud et al. (1999) studied 34 operatively treated ovarian tumors in children aged 0–17 years and found 18 non-neoplastic and 16 neoplastic tumors. The presenting symptom was abdominal pain in 50%, abdominal distension in 18% and precocious puberty in 18% of the patients.

A retrospective study carried out at Michigan Medical Center from 1980–1996 included 52 premenarcheal girls who had undergone ovarian surgery. Fifty percent of the patients were less than 1 year old. The presenting complaint in 31 patients included structural and/or endocrinological abnormalities and 21 patients presented with abdominal or systemic complaints (Quint et al. 1999).

Imai et al. (1994) analyzed 1938 patients aged below 18 years and remitted to a gynecological clinic for various reasons. Ovarian tumors were diagnosed in 114 patients. The most common symptom among all patients was abdominal pain. One-third of the girls with abdominal pain had an ovarian tumor and 106 patients (93%) with an ovarian tumor had abdominal pain. Fifty-five patients (48%) had germ cell tumors, 13 (11%) had epithelial tumors and 18 (16%) had stromal tumors.

5.2. Diagnosis of ovarian tumors in children

The diagnosis of ovarian lesions in pediatric and young adolescent patients is somewhat problematic. The incidence of ovarian lesions is low and the fairly unspecific symptoms are characteristic of other more common pathologic entities. Before the widespread use of sonography acute appendicitis was incorrectly predicted in 9–54% of pediatric patients with ovarian disease (Breen et al. 1977).

Physical examination should be performed with particular attention to sexual development, including Tanner stages. Pelvic examination, including rectal palpation, can reveal adnexal and pelvic pathology. Gynecological sonography is the method of choice in imaging the female pelvis. Ovarian cysts and follicles can be seen by ultrasonography in girls of all ages. During the neonatal period ovarian cysts and hydrometrocolpos account for approximately 15% of all abdominal masses and for the majority of pelvic masses (Kirks et al. 1981).

In children older than one year of age, pelvic masses of genital origin account for 3–4% of abdominal masses and 80% of these genital masses are ovarian in origin. Sonography was reliable in determining the site of origin

in 39 of 40 surgically treated pelvic masses and use of the method could suggest a specific diagnosis (Wu et al. 1987). Serial ultrasonographic scans of ovarian tumors in young girls can help to avoid unnecessary surgery. In a retrospective study of 64 cases of ovarian cysts and tumors diagnosed by ultrasonography over four years the incidence of surgery decreased from 18 operations in the first two years to 10 operations during the last two years. All children for whom abdominal surgery is considered should be examined by sonography preoperatively (Thind et al. 1989).

In addition to sonography, three-dimensional power Doppler ultrasonography, Magnetic Resonance Imaging and Computer Tomography can give useful information in the diagnosis of pelvic tumors and gynecological anomalies. In the diagnosis of uterine anomalies MRI showed a sensitivity and specificity of 100% in the classification of Müllerian duct anomalies and endovaginal sonography demonstrated a specificity of 100% and sensitivity of 80% (Pellerito et al. 1992). The comparative significance of preoperative Doppler and conventional ultrasonography, CT and MRI examinations in correlation with surgery and histopathological analysis in the diagnosis and staging of ovarian cancer has been studied in 280 women suspected of having ovarian cancer. In evaluation of an ovarian mass the accuracy of MRI (0.91) was higher than that of CT and significantly higher than that of Doppler US (0.78). As regards staging there was little variation in accuracy between US, CT and MRI (Kurtz et al. 1999). MR imaging is superior to CT in the differentiation of most dermoids, ovarian fibromas and endometriomas. In the differentiation of other benign and malignant ovarian tumors no superiority of MRI over CT has, however, been established (Hamm et al. 1999). In a series of 120 patients preoperative transvaginal color Doppler US and three-dimensional power Doppler US were carried out. In each of 11 ovarian malignancies, preoperative diagnosis by three-dimensional power Doppler US was confirmed by histopathology (Kurjak et al. 2000).

The first widely used monoclonal antibody in the study of ovarian cancer was that against CA 12-5. Circulating concentrations of CA 12-5 are elevated in 80% of all cases of nonmucinous ovarian cancers but also in 60% of cases of pancreatic carcinoma and 20–25% of cases of all other solid tumors (Schwartz, 1993). Levels of CA 12-5 have been found to correlate with regression, stability, and progression of epithelial ovarian cancer in 87–94% of instances (Canney et al. 1984). Since epithelial ovarian tumors are fairly rare among children and young adolescents CA 12-5 does not play as

important a role as among adults. Alpha-fetoprotein is an oncofetal antigen, a glycoprotein normally expressed by the fetus and re-expressed by endodermal sinus tumors, mixed germ cell tumors and immature teratomas. Fewer than 10% of epithelial ovarian carcinomas produce AFP (Horowitz et al. 1992). Human chorionic gonadotropin (hCG) is produced by trophoblastic cells; by normal human placental tissue as well as hydatidiform moles, placental site trophoblastic tumors, choriocarcinoma and embryonal ovarian carcinomas with trophoblastic differentiation. Carcinoembryonic antigen (CEA) is produced by epithelial and germ cell tumors. Circulating concentrations of CEA may also be markedly elevated in colon carcinoma patients and in cases of mucinous carcinomas (Horowitz et al. 1992).

5.3. Non-neoplastic functional tumors

Functional cysts are the most frequently observed cystic masses in the ovary accounting for 20–50% of ovarian tumors during childhood and adolescence (Kozlowski, 1999). They can present as follicular, corpus luteum or theca luteal cysts, all of which are usually benign and self-limiting, but the larger ones pose an increased risk of ovarian torsion. The size of these tumors is most often 2–4 cm but they may range up to 8 cm.

The diagnosis of ovarian cysts has become increasingly common. Ultrasonographic examination, which is often combined with gynecological examination, can lead to identification of clinically nonpalpable ovarian cysts (Schwatz, 1993). Ovarian cysts occurring during the fetal period are being diagnosed with increasing frequency by obstetric sonography. In a study of 21 000 pregnancies over a 5-year period, 2625 sonographically diagnosed ovarian cysts during the fetal period have been reported (Kirkinen et al. 1985). Follow-up by ultrasonography can be recommended as the primary treatment modality as regards neonatal ovarian cysts. In an Italian follow-up study, within a 13-year period 27 neonatal cysts were diagnosed *in utero*. Nine of these cysts were complicated by nonhomogeneous structures or septae, 8 showed complications soon after birth and 10 were simple cysts. One simple and four complicated cysts were operated on and 2 cysts were aspirated. Nineteen patients could be managed by means of observation only (Luzzatto et al. 2000).

A retrospective study on prepubertal ovarian cyst formation within a 5-year period among prepubertal girls aged 1–9 years concerned the results of

1818 ultrasonographic examinations. Ovarian cysts were identified in 99 cases. The incidence of small, clinically insignificant, unilocular cysts less than 10 mm in diameter in prepubertal females was 2–5%. Larger cysts of more than 20 mm in diameter were found in 17 patients, two of which were torsions with complex findings in the ultrasonographic examination. The results suggested that cysts smaller than 50 mm in diameter in prepubertal girls can be followed conservatively (Millar et al. 1993).

Surgically treated noninflammatory ovarian masses were reviewed in 140 patients aged less than 21 years from 1980 to 1998 in Kentucky. Ovarian cysts occurred in 57.9% of the patients, benign tumors in 30%, malignant tumors in 7.9% and torsional but normal ovaries in 4.3%. The age of the patient was found to be predictive of whether the operator was a surgeon or a gynecologist (Templeman et al. 2000). Qublan et al. (2000) examined the prevalence and outcome of simple ovarian cysts among 108 girls aged from 2 to 9 years. Among 183 ovaries imaged 65 simple ovarian cysts were seen, giving an incidence of 36%. A microcystic appearance (<9mm) was encountered in 83% and a macrocystic one (>9mm) in 17%. Eleven percent of the cysts persisted in the follow-up for more than 6 months, all macrocystic.

Ovarian torsion often gives a tumor-like image in sonography. Torsion is fairly rare but often results in removal of the torqued adnexae. A report on 12 children with 13 episodes of ovarian torsion included three neonates, six premenarcheal and three postmenarcheal girls. In all three neonates ultrasonography showed a complex abdominopelvic cyst. In five older patients ultrasonography showed a solid mass suggestive of torsion. Same-day surgery was performed but only one ovary was salvaged, owing to delays in diagnosis and treatment (Meyer et al. 1995). In an Israeli study, 8 patients aged 3–12 years with ovarian torsion were treated by means of laparoscopic detorsion. In follow-up with Doppler US imaging seven girls had normal appearing ovaries and one patient had a small ovary with no intraovarian blood flow (Pansky et al. 2000).

5.4. Neoplastic tumors

Because of the small number of cases a statistically significant age-related occurrence of specific types of ovarian neoplasm among children and adolescents cannot be estimated. Some age-related trends are evident, however. Germ cell tumors are predominant in all age groups, accounting

for approximately 60% of ovarian neoplasms in children and adolescents. Sex cord tumors are more common in younger children and epithelial tumors usually appear after the start of pubertal development (Breen et al. 1977). In a series of 353 ovarian neoplasms in patients under 20 years of age, 55% of the neoplasms were malignant. Germ cell tumors represented 58% of all the ovarian neoplasms. Epithelial tumors represented 19% in that series, none however, being found under the age of 9 years, and all epithelial tumors were benign. Gonadal stromal tumors, consisting of fibrothecomas, granulosa tumors and arrhenoblastomas, represented 18%; the rest were miscellaneous (Norris et al. 1972).

Although the incidence of ovarian neoplasms in the young female is low, the degree of malignancy is high when compared with ovarian tumors in adults. In an evaluation of 1309 ovarian neoplasms from all reported series from 1940–1975, 35% of the neoplasms were malignant and 65% were benign (Breen et al. 1977). In material collected from the major children's hospitals in Finland and Sweden between 1948–1969, 81 cases of ovarian tumors in children aged 0–14 years were found. Germ cell tumors represented the majority (60 cases). Epithelial tumors were diagnosed in 10 patients, sex cord tumors in 10 patients and one tumor was undifferentiated. Sex cord tumors were most frequent in the youngest age group (0–4 years) and epithelial tumors occurred mostly in the oldest (10–14 years) age group. The malignancy rate was 25% (Lindfors 1971).

5.4.1. Epithelial tumors

Tumors of epithelial origin represent 70–80% of adult ovarian tumors. In the first two decades of life the incidence of epithelial tumors varies from 4% to 13% (Hunt et al. 1979). The epithelial tumors presenting in the first two decades of life are usually of low malignant potential. In a 43-year review, from Toronto, of malignant ovarian tumors in children, 38 malignant tumors were found and only two of them were epithelial. Both patients were living 17 and 24 years later (Gibbon et al. 1992).

5.4.2. Sex cord tumors

Sex cord tumors include those with endocrinological potential such as granulosa, granulosa-theca, Sertoli-Leydig cell tumors (arrhenoblastomas) and thecomas. Endocrinologically active tumors can secrete estrogen and

result in precocious puberty, with elevated estrogen levels without gonadotropin activation. Fibromas and fibrosarcomas represent the endocrinologically inactive forms.

Pure granulosa cell tumors account for 26% and granulosa theca-cell tumors for 8% of stromal ovarian lesions during the first two decades. As these tumors are usually unilateral and well encapsulated, unilateral salpingo-oophorectomy is the treatment of choice. The course is benign in 70–95% of cases and the mortality rate low, 7% (Cronje et al. 1999). The stage at the time of diagnosis and mitotic activity of the tumor are prognostic factors related to survival (Sehouli et al. 2004).

A long posttreatment follow-up, up to 20 years, is recommended since granulosa cell tumors have late recurrences. Cronje et al. (1999) has reported a 17% recurrence rate after 10 years or more of follow up.

Thecomas are very rare before puberty and uncommon before the age of 30; they constitute only 4.8% of stromal ovarian neoplasms in young patients. All thecomas are endocrinologically active, whereas not all granulosa cell tumors are. Malignant transformation is rare and the treatment consists of unilateral salpingo-oophorectomy.

Arrhenoblastomas (androblastomas or Sertoli-Leydig cell tumors) are tumors originating from homologous testicular cells in the female gonad and are therefore histologically similar to tumors of Sertoli and Leydig cells. In children and adolescents 15% of ovarian stromal tumors are represented by arrhenoblastomas. Arrhenoblastomas are the most common masculinizing tumors of the ovary (Gallup et al. 1987).

Fibromas constitute 0.5–2% of all ovarian tumors found in infancy and childhood. Less than 10% of all ovarian fibromas are encountered in patients under the age of 30. Microscopically, fibromas are composed of bundles of spindle cells that produce collagen. Conservative treatment by resection of the fibroma is recommended for young patients.

5.4.3. Gonadoblastomas

Gonadoblastomas are rare tumors found almost exclusively in dysgenetic gonads. Presenting symptoms are primary amenorrhea and intersexuality. A female phenotype is present in 80% and the rest are phenotypic males with cryptorchidism, hypospadias and internal female sex organs. Treatment includes removal of the dysgenetic gonads. The nature of other treatments

depends on the type of germ cell tumor present; even if malignant components in the tumor are found, gonadoblastomas seldom behave in a clinically malignant manner (Breen et al. 1977).

5.4.4. Germ cell tumors

Germ cell tumors are, as previously stated, the most common ovarian tumors in patients less than 20 years of age. The degree of malignancy of the different types of germ cell tumor diminishes with advancing age and a trend for progressive histologic differentiation can be noted.

Mature teratoma is the most common ovarian neoplasm in children and accounts for 38% of pediatric ovarian neoplasms and 57% of pediatric germ cell tumors. Mature teratomas are often benign, but malignant transformation has been reported to occur in 1.4% of teratomas (Ayhan et al. 2000). The age range of occurrence is between 2–88 years. The mature cystic teratoma or dermoid cyst develops from totipotential cells and is composed of well-differentiated ectodermal, endodermal and mesodermal elements. Because mature teratomas are bilateral in 8–15% of patients, the contralateral ovary should be evaluated during operation (Horowitz et al. 1992). The treatment of choice is cystectomy, which can be performed by operative endoscopy (Shalev et al. 1998).

Immature teratomas are germ cell tumors which are limited to embryonal elements. At least one of the germ cell layers lacks full differentiation; most often the immature component is neuroepithelial (Farghaly 1992). Surgical therapy can be limited to unilateral salpingo-oophorectomy if no evidence of metastatic disease is present. High cure rates can be achieved with a conservative approach (Baranzelli et al. 2000) and platinum-based adjuvant therapy allows most women with ovarian germ cell malignancies to have conservative surgery without compromising survival (Tewari et al. 2000).

Dysgerminoma is the most common malignant germ cell neoplasm occurring in pure form. It accounts for 2–5% of ovarian malignancies. Ninety percent of patients with dysgerminomas are less than 30 years of age. Most patients with metastatic dysgerminoma can expect cure with maintenance of normal reproductive function when treated with conservative surgery and adjuvant chemotherapy (Brewer et al. 1999, Ayhan et al. 2000).

Embryonal carcinoma is a primitive tumor composed of undifferentiated germ cells and it accounts for 8% of all germ cell tumors. Embryonal carcinoma

is highly malignant and almost uniformly fatal. Choriocarcinomas and mixed germ cell tumors are other rare but usually fatal malignant forms of germ cell tumor present in children and adolescents (Breen et al. 1977).

5.5. Treatment considerations

The preservation of menstrual capacity and fertility are important to consider while treating ovarian tumors during childhood and adolescence. The extent of the surgical procedures as well as the operative methods used are of importance. Young women are frequently surgically explored for abdominal pain, often for possible appendicitis, and found to have a ruptured or bleeding follicle or corpus luteum cyst. Traditionally most of these cases have been managed by ovariectomy. However, most patients can be managed by ovarian cystectomy with preservation of ovarian tissue, if operation is even indicated (Bateman et al. 1991).

Ovarian tumors of borderline malignancy have low malignant potential and their conservative treatment is continuously evaluated. A retrospective review of 82 patients, under 40 years of age, with borderline ovarian tumors over a 25-year period was focused on fertility issues. Treatment was conservative in 39 patients and only 7 patients underwent treatment that compromised fertility. Fifteen of the patients in the study had delivered a total of 19 healthy children (Gotlieb et al. 1998). In the early clinical stages of ovarian cancer progression, the survival time was no different between women treated by means of conservative surgery compared with women treated by means of radical surgery. With conservative surgery the fertility of the patients could be preserved (Gonzalez-Lira et al. 1997).

In adults laparoscopy plays an important diagnostic and therapeutic role in the diagnosis and treatment of adnexal pathology. Few reports on ovarian procedures by laparoscopy in children are available. Laparoscopy is suitable for the diagnostic evaluation and treatment of benign ovarian processes. If malignancy is suspected, laparotomy is recommended, especially for prepubertal children. When laparoscopic surgery is performed for a benign process, every effort should be made to preserve bilateral ovarian function. If only laparotomy can save the ovary, then it is the procedure of choice. For persistent ovarian cysts cystectomy is preferable to cyst aspiration (Sharp 1997). Laparoscopic treatment of benign teratomas has been shown to be safe. Among 84 patients, laparoscopic cystectomy with preservation of ovarian

tissue was performed in 47 patients and oophorectomy in 37 patients (Shalev et al. 1998). In another study five child patients underwent laparoscopic oophorectomy, three patients because of torsion, one for teratoma and one for removal of streak ovaries. All recovered promptly after a hospital stay of two days (Davidoff et al. 1996). The shortened hospital stay, milder postoperative pain and better cosmetic result are so far the advantages of laparoscopic procedures. In an animal model laparoscopy was associated with a lower incidence of wound adhesion than laparotomy, but the potential for postoperative adhesions is also real after laparoscopic surgery (Jorgensen et al. 1995). Within a ten-year period (1984–1995) the incidence of complications related to laparoscopy in children was 1.8% in 430 laparoscopic procedures (Esposito et al. 1997).

6. Delayed puberty

Puberty is the stage of transition from the sexually immature to the potentially fertile stage during which secondary sexual characteristics appear. Delayed puberty is defined as the failure to manifest the initial signs of sexual maturation or failure to progress through puberty. Absence of telarche by 13.4 years of age or menarche by 15.5 years of age is considered to be delayed puberty (Traggiai et al. 2002). Menarche correlates better with skeletal age than with chronological age, height or weight (Rosenfield et al. 1993). The average bone age at the onset of breast development is approximately 10.75 years, and at menarche 13.0 years. Primary amenorrhea is one criterion of delayed puberty, but it can exist in some cases with full maturation of secondary sexual characteristics.

In a study by Sedlmyer et al. (2002) the etiology of delayed puberty in 232 subjects in a children's hospital in Boston, 74 of them female, was retrospectively evaluated. Constitutional delay of growth and maturation was the most common cause of delayed puberty, apparent in 30% of females. The second most common cause among females was hypergonadotropic hypogonadism, found in 26% of female patients. An underlying condition associated with hypogonadotropic hypogonadism was found in 19% and permanent hypogonadotropic hypogonadism was found in 20% of the girls studied.

6.1. Hypergonadotropic hypogonadism

Females with hypergonadotropic hypogonadism have significantly elevated circulating gonadotropin levels owing to ovarian failure. Turner syndrome (TS), with 45 XO karyotype, is the single most common cause of primary ovarian failure. The number of oocytes in the ovaries of fetuses with 45 XO karyotype in mid-gestation is normal, but thereafter an accelerated rate of apoptosis causes a drastic reduction in the number of follicles, resulting in a streak ovary (Singh et al. 1965). However the process of ovarian failure may occur over a longer period of time and there may be sufficient ovarian function to initiate spontaneous puberty (Weiss 1971). Some might go on to natural puberty, but only very few achieve spontaneous pregnancy. In an Italian study 16% of girls with TS had spontaneous puberty and menarche; the rest needed estrogen treatment at some phase of puberty (Pasquino et al. 1997).

Turner girls with signs of spontaneous pubertal development have been shown to have follicles in their ovarian cortical tissue (Hreinsson et al. 2002), which raises the possibility of future fertility through ovarian cryopreservation.

The second most common cause of primary ovarian failure with elevated circulating gonadotropin levels is physical or medical injury to the ovary. Most cancers of childhood require treatment with a variety of chemotherapeutic agents. Alkylating agents in particular can cause germ cell depletion in both sexes (Sklar 1999), however high doses used in preparation for bone marrow transplantation are required to cause ovarian failure. Antimetabolites and plant alkaloids appear to be safer for the ovary (Blumenfeld et al. 1999). The impact of radiotherapy on ovarian function depends greatly on the age of the girl, total dose of irradiation and the number of fractions given. Doses in excess of 20 Gy are needed for complete ovarian failure in most children and adolescents (Sklar 1999). Risk of ovarian failure seems to be higher when girls are treated during puberty (Legault et al 1999). Also cranial irradiation can cause disturbances of pubertal development. Among 188 long term survivors of acute lymphoblastic leukemia, girls who had received 18 Gy of cranial irradiation were at risk of having early menarche, whereas those who had received 24 Gy were at risk of late or absent menarche (Mills et al.1997).

Normalization of ovarian function is common, even in cases with severe hypergonadotropic hypogonadism, but may only occur after several years off chemotherapy (Wikström et al. 2003). Patients who are spared amenorrhea may be at risk of premature menopause. Regular assessment of ovarian function after chemotherapy-induced gonadal damage is necessary. In a recent advance, cryopreserved ovarian tissue from a 30-year-old with chemotherapy-induced menopause was planted beneath her skin 6 years after treatment. Ovarian function returned and *in vitro* fertilization treatment resulted in a fertilized oocyte, from 20 retrieved, which developed into a four-cell embryo (Oktay et al. 2004).

Spontaneous premature ovarian failure may also be caused by autoimmune oophoritis, which might be associated with thyroiditis, diabetes or polyendocrine failure. Other more rare causes of hypergonadotropic hypogonadism are resistance to gonadotropin action, mutations of FSH and LH receptors and other genetic conditions (Timmreck et al. 2003).

6.2. Hypogonadotropic hypogonadism and constitutional delay

Congenital hypogonadotropic hypogonadism can be an isolated defect or it can be associated with other cerebral, hypothalamic or pituitary dysfunctions. Kallman syndrome, olfactory genital dysplasia, accounts for approximately half of the cases of isolated gonadotropin deficiency (Crowley 1992). Tumors, trauma, autoimmune hypophysitis, degenerative disorders, radiation and chronic illnesses are causes of acquired hypogonadotropic hypogonadism. Anorexia nervosa and athlete amenorrhea are very common cause of hypogonadism in adolescents. Anorexia nervosa is a complex hypothalamic disorder due to undernutrition.

Constitutional delay of puberty is diagnosed among 6% to 30% of females evaluated because of pubertal delay (Timmreck et al. 2003, Sedlmeyer 2002). Girls with constitutional delay often have familial predisposition of delayed puberty. These girls are usually lean, shorter than their peers and their bone age lags behind. Diagnosis is carried out by way of exclusion, with systemic diseases taken into account.

6.3. Primary amenorrhea with normal estrogen production

Absence of menses with normal development of sexual characteristics can be a result of anatomic abnormalities or disturbances of hormonal balance at hypothalamic or ovarian levels. An imperforate hymen and vaginal or uterine aplasia are rare causes of primary amenorrhea. Evaluation of the anatomy by inspection of the vulvar and vaginal area, and gynecological sonography, are always part of the examination when primary amenorrhea is evaluated. It is preferable to initiate an evaluation when abnormalities become apparent and not wait until a young woman differs significantly from her peers (Timmreck et al. 2003).

Psychogenic amenorrhea is a result of severe psychological stress, most often, however, causing secondary amenorrhea. Pregnancy, disturbances of thyroid function and hyperprolactinemia should also be considered in the differential diagnosis. Polycystic ovary syndrome affects 5% to 10% of reproductive aged women. The diagnosis includes ovarian hyperandrogenism and anovulation together with obesity and hirsutism. Sometimes this condition manifests itself as primary amenorrhea (Pfeifer et al. 2003).

6.4. Diagnosis of delayed puberty

Examinations of primary amenorrhea include clinical and laboratory assessments. The actions of estrogens and androgens in girls are evaluated by staging breast development and the development of hair in axillary and pubic areas according to Tanner. Determination of bone age is always included in evaluations of growth and pubertal development. Ovarian activity, uterine development and genital anatomy can be assessed by means of gynecological sonography.

In girls, assay of basal serum levels of estradiol, FSH, LH, TSH and prolactin is most often the first biochemical evaluation of hypothalamo-pituitary-ovarian function. Basal FSH levels are, however, very often of little independent value, except in primary ovarian failure. Serum FSH and LH concentrations are nowadays measured in our institution using time-resolved fluoroimmunoassays, both assays having an analytical sensitivity of 0.10 IU/l. The value of a single sample, however, is problematic because of the pulsatile secretion and diurnal fluctuations in gonadotropin secretion within and between individuals at different stages of puberty (Apter et al. 1993).

A GnRH test might be helpful in differentiation between constitutional delay and hypogonadotropic hypogonadism. A bolus of GnRH given intravenously tests the capacity of the pituitary to release FSH and LH. During puberty the release of gonadotropins increases, particularly that of LH, a fact that might be useful in the diagnosis of constitutional delay (Muller 2003). Delayed puberty can be considered to be a variation of normal when a GnRH bolus elicits a response in LH level above 7 IU/l (Goodpasture et al. 1993). One third of hypogonadic girls can, however, have clear responses in GnRH tests. A subnormal response supports the diagnosis of hypogonadotropic hypogonadism.

The estrogen of primary interest during pubertal development is 17 β -estradiol. In our institution serum estradiol concentrations are measured using a fluoroimmunoassay with an analytical sensitivity of 0.02 nmol/l (Sjöblom et al. 1990). Levels of estradiol vary considerably during childhood and adolescence, which makes a single measurement of this hormone rarely informative. Levels of estradiol should always be interpreted in relation to pubertal development, menstrual cycle, gonadotropins and sonographic findings.

6.5. Treatment of delayed puberty

After a diagnosis of delayed puberty or absent menses is made the options for treatment can be considered. In constitutional delay the best option most often is good information and expectation. Sometimes, however, a wish for hormonal replacement might be accepted, since physical immaturity might prolong psychological immaturity and cause further problems.

This review concentrates on pubertal induction in girls with hypergonadotropic hypogonadism by means of estrogen. The development of secondary sexual characteristics and the maturation of female identity during the induction of puberty are essential for girls with hypogonadism. Sufficient uterine growth and development of the endometrium, with menstrual periods, are important for possible future fertility (Brook 1999). Estrogen is important, even at low levels, for the onset of pubertal growth; at higher levels estrogen enhances epiphyseal maturation (Grumbach 2000).

The most common feature of Turner syndrome, already present during childhood, is decreased growth velocity. Treatment of the short stature by means of growth hormone (GH) is nowadays a standard treatment in many countries. The timing and dosage of GH treatment and initiation of the induction of puberty, together with the estrogen doses used, are critical to the final height. Analysis of different studies on girls with TS has revealed predictive factors for growth where GH therapy is concerned. The greatest benefit of GH therapy is achieved in the youngest girls, with higher GH doses, and the onset of puberty should not be before 13–14 years (Ranke et al. 1995). The number of years of GH therapy prior to the initiation of estrogen treatment has been the most important factor determining final height (Chernausek 2000). Early started estrogen substitution therapy may also have a positive effect on the final height (Reiter et al. 2000). Addition of low dose estrogen to GH treatment has been shown to improve bone deposition and calcium metabolism in girls with TS (Beckett et al. 1999).

6.5.1. Estrogens

Both natural and synthetic estrogens have been used in hormone replacement therapy. Natural estrogens include estrone (E1), 17 β -estradiol (E2) and estriol. Orally administered estradiol is clinically ineffective because of extensive metabolism in the liver. Use of the percutaneous route of administration has made it possible to use estradiol in estrogen treatment.

Conjugated equine estrogen (CEE), mainly used in the US, is a mixture of ten different estrogens, none of which are estradiol precursors (Ansbacher 2001). The clinical efficacy of CEE is likely to be the result of the combined effect of each estrogen in the blend (Bhavnani 1998). Conjugates of natural estrogens are E1 sulfate and the ester estradiol valerate (E2V). Estradiol valerate is commonly used in postmenopausal hormone replacement therapy in Europe. Ethinyl estradiol (EE2) is a synthetic analogue of estradiol used in contraceptive pills.

The route of estrogen administration is important to consider. Estrogen given orally reaches the systemic circulation only after absorption into the portal venous system and metabolism by the liver (Hirai et al. 1981). Most of the estradiol administered orally is converted to less potent estrone during first pass metabolism. Estradiol can, however, successfully be used transdermally using patches or gel. Oral estrogens increase production of hepatic proteins such as sex hormone-binding globulin (SHBG) and corticosteroid-binding globulin (Mashchak et al. 1982). With transdermal administration of estrogen, an equivalent increase in serum SHBG levels does not take place (Stomati et al. 1996). An increase of circulating SHBG concentrations with oral estrogens may reduce the availability of free estrogen, which affects the individual dose-response of different kinds of estrogen treatment (Levitz et al. 1997). Equivalent doses of different estrogens are 2 mg E2V = 0.625 mg CEE = 1.5 mg E2 (transdermal) = 5 µg EE2. (Information from Orion pharma.)

6.5.2. Induction of puberty

The aim of pubertal induction by estrogen in hypogonadic girls is to achieve physical and psychological development, which mimics the natural tempo of spontaneous puberty. The development of secondary sexual characteristics, and the maturation of female identity during the induction of puberty are essential for such girls. The induction of puberty has traditionally been achieved mainly by using oral estrogens (Brook 1999), followed by the addition of progestin after 1–2 years. Progestin is added to the treatment to induce menstrual bleeding and to protect the subject from endometrial hyperplasia and cancer. Recently the effect of estrogen on final height has been studied, and low dose estrogen regimens have become more common (Reiter et al. 2000). Rosenfield et al. (1998) found that using very low doses

of systemic estradiol, starting with 0.2 mg of depot estradiol before the age of 15 to induce puberty in girls with TS who are also treated with GH, can result in increased final height.

During the past decade transdermal estradiol patches and percutaneous estradiol gel have become available for the treatment of postmenopausal women. Administration of estrogen replacement by the percutaneous route may have less deleterious effects on hepatic metabolism than oral estrogen, and could be useful, for example, in girls with previous cancer treatments or TS (Jospe et al. 1995). Transdermal estradiol patches have successfully been used in the induction of puberty.

Cisternino et al. (1991) used 25 ug and 50 ug patches, with cyclic medroxyprogesterone acetate for 10 days each month after six months of treatment up to 3 years of treatment. Plasma E2 levels rose to normal pubertal levels, and pubertal development progressed without side effects. It has also been possible to mimic the pubertal fluctuation of estradiol concentrations by use of estradiol patches overnight, starting with doses of 3.1–6.2 ug of estradiol per 24 h (Ankarberg-Lindgren et al. 2001).

7. Sexual abuse of children

7.1. Definition

Child sexual abuse occurs when a child is engaged in sexual activities that the child cannot comprehend, for which the child is developmentally unprepared and cannot give consent, and/or that violate the law and social taboos of society (Kempe 1978). The sexual activities may include all forms of oral-genital, genital or anal contact or non-touching abuse such as exhibitionism, voyeurism and child pornography.

7.2. Epidemiology

Sexual abuse of children is considered to have been present in most cultures during the history of mankind. The prevalence of child sexual abuse in many countries during the 20th century has remained the same, but the number of reported cases increased after the 1980s. Sexual abuse in the studies has been defined: girls younger than 14 years of age having sexual contact with an adult at least 5 years older. In interviews of 5940 women from 48 US states in the 1940s, Kinsey et al. (1953) reported a prevalence of 12% of sexual abuse during childhood. In a study from the 1970s with very thorough interviews in San Francisco area among undefined population a prevalence of 28% was reported (Russel et al. 1983). In a literature survey from the 1980s the prevalence of child sexual abuse in the USA was 10–12% (Feldman et al. 1991). Studies in the USA have suggested that approximately 1% of children experience some form of sexual abuse each year, resulting in the sexual victimization of 12–25% of girls and 8–10% of boys by age 18 (National study on the incidence of child abuse and neglect, 1988).

As studied in 21 different countries, the prevalence of child sexual abuse ranges from 7% to 36% for women and from 3% to 29% for men (Finkelhor 1994). Comparisons between different studies and countries are difficult because of cultural and definitional differences. Retrospective design, small and incompletely described samples, lack of a comparison group, and questionnaires without demonstrated validity or reliability are methodological difficulties in studies of child sexual abuse (Browne et al. 1986). Certain risk groups for sexual abuse, mentally ill, retarded or handicapped girls, are often not included in these studies.

The prevalence and context of child sexual abuse in Finland was studied in 1990 by means of questionnaires completed by about 9000 15-year-olds. Six to eight percent of the girls and one to three percent of the boys reported experiences that could be classified as sexual abuse. Among girls who reported sexual experiences, 1.5% had been 5–6 years old and 15.5% between 7–10 years at the time of the first sexual experience with an adult (Sariola et al. 1994).

7.3. Consequences of child sexual abuse

Attempts to diagnose child sexual abuse and to treat the victims are based on the assumption that sexual abuse of children has adverse lifelong consequences. In a case-control study of sexually abused children 5 years after presentation of the abuse, the victimized children were found to have more disturbed behavior, lower self esteem, were more depressed and were more anxious than the controls (Swanston et al. 1997). The abused children also had significantly higher levels of bingeing, self-injury and suicide attempts. Besides sexual abuse, the pre-existing, longstanding adverse psychosocial circumstances, often present among sexually abused children, contribute importantly to the problematic behavior and school performance observed (Paradise et al. 1994).

Early onset of sexual abuse is associated with poorer prognosis. Among 499 youths treated in 1987–1992 at a tertiary care public sector psychiatric hospital, 80% of the 78 patients who had been sexually abused during early childhood (0–3 years of age) had hypersexual, exposing and victimizing sexual behavior (McClellan et al. 1996).

The relationship between physical and sexual abuse before the age of 18 and psychosocial functioning in mid-adolescence (age 15) and early adulthood (age 21) was investigated in a 17-year longitudinal study beginning at age 5 at registration at a public kindergarten in Boston (Silverman et al. 1996). At the age of 21, in a private face-to-face interview, nearly 11% of the 375 participants reported physical or sexual abuse before 18 years of age. The abused subjects demonstrated significant impairment in functioning. At the age of 15 years 88% of the female sex abuse victims had had suicidal ideation, 38% aggressive behavior and 38% somatic complaints. At the age of 21 70% of the abused and 27% of the nonabused women had had one or more DSM-III-R disorders. Does this need to be defined? In the abused group 44%

showed alcohol abuse/dependence, 35% had symptoms of post-traumatic stress disorder, 9% showed antisocial behavior and 26% had had suicide attempts.

In a longitudinal cohort study of 1000 New Zealand children up to the age of 16, retrospective reports of child sexual abuse before age 16 were obtained at age 18 in personal private interviews (Fergusson et al. 1996 a.) Of these, 10.4% (17.3% of the females) reported experiences of child sexual abuse before the age of 16. A relationship between the extent of abuse and the risk of psychiatric disorder was found (Fergusson et al. 1996 b.). Major depression, anxiety disorders, conduct disorders and substance abuse were significantly more common among the sex abuse victims. The highest prevalence of psychiatric disorders was among girls with more severe (intercourse) forms of abuse. These results persisted when they were adjusted for childhood family and related factors.

In Australia the psychological adjustment of 103 young people presenting at two hospitals in Sydney because of sexual abuse was compared with that of a similar group of nonabused young people. Nine years after the incident 49 of the abused young people and 68 nonabused controls were interviewed and assessed. The sexually abused young people performed more poorly on tests of depression, self-esteem, anxiety, behavior and despair. They were also more likely to have a history of self-induced vomiting, smoking and drug use (Swanston et al. 2003).

7.4. Physical examination

7.4.1. Patient history

The history obtained during interview with a child is a very important part of the medical evaluation in cases of suspected child sexual abuse. The quality of interviews of children with suspected sexual abuse is the focus of great concern (De Jong 1998). In legal thinking, every time a clinician talks to a child – taking a medical history, during examination and treatment or psychotherapy – a professional interviews the child. The evaluators must be careful to ask open-ended questions. However, during the physical examination relevant questions can be asked. The child might spontaneously give additional information during examination of the mouth, genitalia and anus. Statements made by the child during the examination are considered to be reliable evidence in US courts (Myers 1986). Specific interviews

regarding disclosure are best left to professionals familiar with special interview techniques (American professional society on the abuse of children 1995, Taskinen 2003).

7.4.2. Physical and gynecological examination

Children and young adolescents suspected of having experienced sexual abuse should be somatically examined. Usually the child can be prepared for the examination and be examined when he or she feels ready for it. Only if the abuse has happened within 72 hours and/or acute somatic changes and forensic material can be expected to be found should the examination be done immediately. In adult rape victims the best chance to recover seminal evidence is less than 50%, with far lower chances after 24 hours (Ferris et al. 1998).

In pediatric examination the health of a girl and possible signs of maltreatment are evaluated. Special attention is paid to the mouth and breasts. Growth parameters and pubertal development of the child are evaluated. In girls genital examination includes inspection of the medial aspects of the thighs, labia majora and minora, clitoris, urethra, periurethral tissue, hymen, hymeneal opening, fossa navicularis, posterior fourchette and anal area (American Academy of Pediatrics, 1999).

Time and patience are more important than ever during the examination of children with suspected sexual abuse. The mother, a nurse or some other secure chaperone for the child is usually present. The child should be told about the different steps taken during the examination. The same examination positions as in other situations can be used according to the age and level of cooperation of the child. A multi-method approach to the examination of the child's genitalia can be used (McCann et al. 1990). The child is examined by means of three different techniques: supine labial separation technique, a supine labial traction method and in a prone knee-chest position. The supine labial separation technique provides an excellent view of the vestibule and perineum without distorting the tissues, but the edges of the hymen might fail to separate in many prepubertal girls. The supine labial traction method is more successful in opening the vaginal introitus. The prone knee-chest position is the most successful method in separating the edges of the hymen and it allows the posterior part of the hymen to stretch out under its own weight (Emans et al. 1980). The location of findings in the introitus and at

the hymeneal edges can be described in a clockwise order seen by the examiner with the patient supine.

7.5. Physical findings

In the female child and adolescent, injuries to the genital area resulting from sexual abuse are usually located posteriorly in the perineum, fossa navicularis and between the 4 and 8 o'clock positions on the hymen with the patient supine (Berenson 1998). The significance of a notch or a cleft on the hymeneal rim depends on both the location and extent of the defect. Superior and lateral notches that do not extend to the vestibule have been observed in 35% of newborn girls (Berenson et al. 1991). Injury of the posterior hymen without damage to the surrounding structures can be indicative of penetrating trauma, such as attempted vaginal intercourse (Pokorny et al. 1992). Notches located between 5 and 7 o'clock on the inferior portion of the hymen are considered to be diagnostic of prior trauma or abuse according to studies on both nonabused and abused subjects (Berenson et al. 1992). In the examination of patients and evaluation of findings the healing pattern of anogenital injuries is an important factor. The healing of anogenital trauma was followed in a prospective 10-year study of 94 children, 13 boys and 81 girls (Heppenstall-Heger et al. 2003). The children were followed until the injuries had healed, and anatomic changes in coloscopy remained in 15 patients with hymenal wounds, in 6 cases after surgical repair of the posterior fourchette and in 2 cases of anal scarring.

In most sexually abused children and young adolescents the physical findings are often subtle or absent altogether (Muram 1989, Adams et al. 1994). Some forms of abuse do not cause injuries and no physical evidence of abuse can be found (Bays et al. 1993). Even in girls in whom sexual abuse has been documented, somatic evaluation fails to reveal specific findings in 50–90% of victims (Muram 1989, McCann et al. 1992). It is very important to differentiate normal anatomic variations and nonsexually related conditions from findings in sexual abuse (Berenson 1995, McCann et al. 1990). Adams and Knudson (1996) examined 204 girls aged 9 to 17 years at Tanner stages 3, 4 and 5 who all reported a history of penile vaginal penetration. Abnormal genital findings were documented in only 32% of these girls. Findings were more common when the girls reported bleeding (50%) or when the examination occurred within 72 hours of the last episode of abuse (69%). In

a study of 157 children with anogenital symptoms but without disclosure or suspicion of sexual abuse 15% of the children had examination findings suggestive, probable or definite as regards abuse (Kellog et al. 1998).

Anal findings are uncommon in girls reporting sexual abuse. Rectal tissue is elastic and positive findings on physical examination after reported anal penetration are rare. Rectal findings that are considered consistent with injuries from sexual abuse include fresh or healing tears located off the midline or extending externally beyond the rectal folds. Rectal tags located off the midline and dilatation of the rectal sphincters may also refer to recent penetrating trauma (Britton et al. 1997).

Colposcopy can be used to obtain more detailed information about the external genitalia and to document the findings. A colposcope is a binocular magnification system that contains several different strength lenses and a light source. A camera or video for recording the findings can be attached to a colposcope. An additional green filter can be used to assist in the detection of scars, vascular changes or other unusual lesions (McCann 1993). Teixeira (1981) introduced use of a colposcope to the evaluation of suspected sexual abuse. There has been debate concerning whether an examiner using a colposcope can detect and interpret changes better than an individual using the unaided eye (Muram et al. 1989).

The utility of colposcopic photographs has been evaluated to assess their use for peer review, second opinion and court testimony. Roberts and Moran (1995) had two teams evaluating colposcopic photographs of 70 girls and found levels of 93% and 94% of inter-observer and intra-observer reliability. Photographs of 189 girls referred for evaluation for possible sexual abuse in Kentucky were sent to four expert evaluators independently. The reviewers' accuracy for the entire set of photographs was uniformly high (93–95%). Accuracy rates were significantly lower for prepubertal girls (83–90%) and for girls with signs of abuse (58–88%) (Muram et al. 1999). Diagnostic accuracy is better with an increased number of examinations and with the use of a colposcope. A colposcope allows one to obtain adequate photographs, which is strongly recommended during each assessment for possible sexual abuse (Muram 2001).

7.6. Documentation and conclusions

There is often discrepancy between the child's history, conclusions in the psychiatric and somatic examinations, and the ruling of the court. In Sweden,

Table 1. Classification of Anogenital Findings in Suspected Sexual Abuse

Class 1: Normal Found in newborns
Periurethral or vestibular bands
Longitudinal intravaginal ridges or columns
Hymeneal tags, bumps or mounds
Hymeneal cleft in the anterior part of the hymeneal rim, above the 3 to 9-o'clock line
Estrogen changes
Linea vestibularis

Class 2: Nonspecific Findings that may result from sexual abuse, depending on timing of examination, but may also be normal variants.
Perianal skin tags or increased pigmentation
Diastases ani without folds or wrinkles
Erythema of vestibular or perianal tissues
Increased vascularity in the vestibule
Labial adhesions
Hymeneal rim that appears narrow, but is > 1 mm wide
Vaginal discharge
Lesions of condyloma accuminata in child < 2 y old.
Anal fissures
Anal dilatation, with stool in the rectal vault
Venous congestion in perianal tissues

Class 3: Suspicious

Findings that have rarely been described in nonabused children, but have been noted in children with documented abuse and would prompt the examiner to investigate carefully the possibility of abuse.

Enlarged hymeneal opening, with measurements >2 SDs above mean for age and examination method.

Hymeneal notch/cleft/partial transection located on or below 3 to 9 o'clock line (patient supine)

Acute abrasions, lacerations or bruising of labia or perihymeneal tissue, with no history of injury

Apparent condyloma accuminata in child > 2 years old

Distorted anal folds, with irregular appearance and possible edema

Immediate anal dilatation of > 20 mm, with no stool visible or palpable

Class 4: Suggestive of abuse or penetration

Findings or combination of findings that can only reasonably be explained by postulating abuse or penetrating injury of some type.

Combination of 2 or more suspicious genital findings or 2 or more suspicious anal findings

Scar or fresh laceration of posterior fourchette, not involving the hymen

Perianal scar

Class 5: Clear evidence of blunt force or penetrating trauma

Findings that can have no explanation other than trauma to hymen or perianal tissues

Complete hymeneal transection (healed): hymen has been torn so that there is no measurable hymeneal tissue remaining between vaginal and vestibular walls

Areas, more extensive than transections, where there is complete absence of hymeneal tissue below the 3 to 9 o'clock line (patient supine)

Acute laceration of the hymen, which may extend into the vagina and/or posterior fourchette

Ecchymosis or bruising of the hymen

Perianal lacerations extending deep to the external anal sphincter

in child sexual abuse cases in one daycare center, the court's ruling was based solely on the defendant's confession. Agreement between the children's psychiatric evaluations and child reports was high, but there were large discrepancies between the results of child psychiatric evaluations and the court rulings. Thirty children from one day-care center were included in the police investigations, sexual abuse of 15 children in was reported, but the perpetrator was convicted only for the 6 cases to which he confessed (Lindblad et al. 2000).

An immediate examination and forensic evidence collection in cases of child sexual abuse has been recommended when the abuse has occurred within 72 hours or when there is bleeding or acute injury (American Academy of Pediatrics 1999). Very often the physical examination is delayed and no forensic material can be expected to be found. In a retrospective study, 273 children under 10 years of age were evaluated in a hospital emergency department in Philadelphia, Pennsylvania, for sexual abuse. Some form of forensic evidence was identified in 25% of the children, all of whom were examined within 44 hours of the assault. Sixty-four percent of the evidence was found on clothing and linen. After 24 hours, all evidence, with the exception of one pubic hair, was recovered from clothing and linen. According to this study, systematic swabbing of the child's body is unnecessary after 24 hours. Clothing and linen should be pursued for analysis (Christian et al. 2000).

A diagnosis of child sexual abuse is drawn from the child psychiatric and physical examinations and from the child's history. Physical examination alone is infrequently diagnostic in the absence of a history and/or specific laboratory findings (American Academy of Pediatrics 1999). The child is examined as regards general physical health and special attention is paid to the erogenic and anogenital areas. All findings, including normal ones, are documented. Drawings and colposcopic photographs are helpful. Classification of anogenital findings in child sexual abuse by Adams and Knudson (1996) and the principles of assessing the likelihood of child sexual abuse are presented in Tables 1 and 2. These guidelines help the examiner to achieve better objectivity.

Table 2. Overall assessment of likelihood of abuse

Class 1: No evidence of abuse

Normal results of examination, no history, no behavioral changes, no witnessed abuse.
Nonspecific findings with another known or likely explanation, and no history of abuse or behavior changes.
Child considered at risk for sexual abuse, but gives no history and has only nonspecific behavior changes.
Physical findings of injury consistent with history of accidental injury, which is clear or believable.

Class 2: Possible abuse

Class 1 or 2 findings in combination with marked behavior changes, especially sexualized behaviors, but child unable to give history of abuse.
Presence of condyloma in a child < 2 years old, or herpes type 1 genital lesions without history of abuse, and with otherwise normal results of examination.
Child has made a statement, but it is not sufficiently detailed or is not consistent
Class 3 findings with no disclosure of abuse

Class 3: Probable abuse

Child gives a clear, consistent, and detailed description of being molested, with or without physical findings.
Class 4 findings in a child with or without a history of abuse, and with no history of accidental penetrating injury.
Positive culture for
Chlamydia Trachomatis from genital area in a prepubertal child > 2 years.
Positive culture for herpes simplex type 2 from genital lesions.
Confirmed condyloma accuminata, when lesions first appeared in a child > 2 years old.
Trichomonas infection, diagnosed by wet mount or culture.

Class 4: Definite evidence of abuse or sexual contact

Class 5 physical findings with no history of accident.
Finding sperm or seminal fluid in or on a child's body.
Pregnancy.
Positive, confirmed cultures for *Neisseria gonorrhoeae* from genital, anal, or pharyngeal source.
Evidence of syphilis acquired after birth (i.e., not perinatally acquired).
Witnessed abuse, or cases where photographs or videotapes show child being abused.
Human immunodeficiency virus infection, with no documented means of transmission other than sexual contact.

AIMS OF THE STUDY

The purpose of this study was to analyze the gynecological problems, gynecological examinations and findings in young female patients up to 17 years of age as seen at a hospital level, especially at a consultation clinic of pediatric and adolescent gynecology. The most common problems were further elucidated. The specific aims were:

1. To study the occurrence of gynecological problems present during childhood and early adolescence in hospital patient material (I, II and V).
2. To evaluate the symptomatology and possible infectious etiology of vulvar symptoms among children and young adolescents (II).
3. To evaluate the clinical practice of preoperative work-up and the outcomes of operatively treated ovarian masses in girls up to 17 years of age (III).
4. To evaluate the use of percutaneous estradiol gel in the induction of puberty in hypogonadal girls with TS and the use of sonography in follow-up of the treatment (IV).
5. To elucidate the findings in somatic (especially gynecological) examination of girls suspected of having suffered sexual abuse. To evaluate to what extent a gynecologist and a child psychiatric team agree in their assessments of child sexual abuse. To report the psychosocial outcomes and court rulings in cases of child sexual abuse (I, V). The two time periods evaluated represent different levels of professional learning.

Anomalies of the female genital tract and precocious puberty are important issues in pediatric and adolescent gynecology, but they are not included in this study. Sexually transmitted diseases in a wider perspective, contraception and teenage pregnancies, the major gynecological concerns of older adolescent girls, are not discussed in this study either.

PATIENTS AND METHODS

1. Patients

The Department of Obstetrics and Gynecology at Tampere University Hospital has had an outpatient consultation clinic for pediatric and adolescent gynecology since 1988. The services have been targeted at girls up to 16 years of age needing gynecological evaluation. This special unit has functioned weekly with 4 to 7 patient visits. Contraception services and treatment of

Table 3. The study material and the design of studies I–V.

Study	Study I	Study II	Study III	Study IV	Study V
Number of patients	204	68	79	23	55
Objectives	To study the gynecological problems of girls <16 years of age who visited a special unit compared with girls examined at adult settings.	To evaluate the symptoms and infectious etiology of vulvar complaints of girls <17 years of age.	To evaluate the pre-operative work-up operative treatment of ovarian tumor on girls <18 years of age during 1971–1995.	Study the use of percutaneous estradiol gel for induction of puberty.	Describe characteristics of girl <17 years old examined for suspected sexual abuse. Agreement between gynecological and psychiatric conclusions.
Design	Retrospective	Prospective	Retrospective	Prospective open multi-center study	Retrospective
Main outcome measures	Nature of symptoms, Examination methods, Clinical findings, Laboratory findings	Vulvar symptoms. Clinical findings, Micro-biological findings	Pre-operative examinations, Symptoms, Histology, Operative procedure	Pubertal development, Side effects, Safety	Case characteristics, Gynecological findings, Psychiatric findings, Consequences

sexually transmitted diseases among adolescents have mainly been provided by community health care centers. Adolescents seeking abortion have been treated at the adult gynecological clinic.

During the study Tampere University Hospital has served as a secondary referral center for a population of 193 000 people living in the city and 255 000 in the surrounding communities. Of these ca. 450 000 people, 89 000 are 16 years of age or younger, approximately half of them females. As a tertiary referral center the hospital served a population of 1.3 million people. At that time the gynecological outpatient clinic had approximately 11 000 patient visits annually.

A summary of the materials and methods used in the original publications is presented in Table 3.

Patients in studies I, II, III and V were examined and/or treated at Tampere University Hospital, Finland. Patients from all five major pediatric endocrinology centers in Finland participated in study IV.

2. Methods

2.1 Clinical examinations

The patients in Studies I, II and V attended the unit of pediatric and adolescent gynecology, and were examined by a single gynecologist with experience in pediatric and adolescent gynecology. The gynecological examination included a careful and thorough inspection of the vulva, vaginal introitus, hymen and anal region, using a good light source, and colposcopic examination was carried out if needed. Labial separation and labial traction methods were used to visualize the vulvar area. The outer third of the vagina in children can most often be examined without instruments, and the whole vagina was inspected by vaginoscopy or with the help of a small speculum if indicated by symptoms or clinical findings. Examination with the aid of a speculum was routinely carried out only among girls who reported intercourse. Anesthesia was used if immediate examination or vaginoscopy was needed for a prepubertal child and the child was too fearful to cooperate in examinations. Rectal or vaginal bimanual palpation was carried out when clinically indicated. Photographic documentation was available. Sonography was included in the examination with great ease. Simultaneous examination by a pediatrician, included in the evaluation of child sexual abuse, consisted of inspection for signs of maltreatment, and examination of the mouth, throat, breasts and abdomen. The 79 patients operated upon because of ovarian tumors (Study III) and 87 patients in 1989–91 (Study I) were examined in normal settings in the Departments of Gynecology, Surgery or Pediatrics.

2.2. Microbiological diagnostics

Microbiological samples from the patients in Study I were collected if indicated by symptoms or findings. In patients examined for vulvar symptoms (Study II) microbiological samples were taken for culture of bacteria, *Mycoplasma*, *Ureaplasma* and *Candida*, and Gram stain and Pap smear samples were obtained from the vulva and vagina from all patients irrespective of their symptoms and clinical findings when this was possible without causing too much discomfort. Gram staining was carried out in order to look for leukocytes, clue cells and various bacteria. In cases of suspected sexual abuse (Studies I and V) a Pap smear and swabs for culture of *Candida*, *Trichomonas*

vaginalis, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* were taken from the vaginal introitus and/or the vagina and rectum if it could be done without causing too much discomfort to the child. These samples were always obtained if the interval between suspected sexual abuse and the examination was less than three days or if sampling was indicated because of local symptoms. Samples for the detection of sperm, other forensic DNA material and acid phosphatase were obtained if indicated. In premenarcheal patients the sampling devices, Q-tips for example, were always moistened in saline before touching the mucosae.

2.3. Ovarian tumors

Information concerning surgical treatment of ovarian tumors in girls aged 17 years or less covered a period of 25 years. The following data were recorded: presenting symptoms, preoperative diagnostic work-up, preoperative sonography, and details of operations, histological diagnosis, and later gynecological and obstetric outcome.

2.4. Induction of puberty

The patients in Study IV received percutaneous estrogen therapy, consisting of estradiol in hydro-alcoholic gel. Increasing doses of estradiol gel were applied once daily on the skin of the lower trunk or thighs. The estradiol doses were: 0.1 mg for the first year, 0.2 mg for the second, 0.5 mg for the third, 1.0 mg for the fourth and 1.5 mg for the fifth year. The total duration of the study treatment was five years. Starting from the third year a progestin test with 10 mg of medroxyprogesterone acetate daily for 10 days to induce menstrual bleeding was performed every six months. After a positive test result cyclic monthly progestin administration using the above dosage was started.

The efficacy of treatment in Study IV was assessed by following pubertal development, growth and hormonal parameters. Height, weight, skeletal age and pubertal status (according to Tanner) were evaluated every six months. Heights were analyzed as standard deviation scores. Serum E2, FSH and LH concentrations were measured at every yearly visit. To evaluate absorption of the medication a serum estrogen profile was obtained yearly: estradiol was not administered during the previous evening and estradiol concentrations

were measured next morning before administration and 2 and 4 hours after administration of the medication. Annual assessment also included a GnRH test, and assay of DHEAS and testosterone.

Serum estradiol concentrations were measured using a fluoroimmunoassay, with an analytical sensitivity of 0.02 nmol/l. Serum FSH and LH concentrations were measured using a time-resolved fluoroimmunoassay, both assays had the analytical sensitivity of 0.10 IU/l.

Abdominal ultrasonography was carried out in Study IV at baseline and every 6 months after one year of therapy to follow uterine growth and endometrial development by a gynecologist or roentgenologist in respective study centers. Blood pressure, hematological data, liver enzymes, fasting cholesterol, HDL cholesterol and triglycerides were investigated to evaluate the safety of the medication.

2.5. Examination of suspected child sexual abuse

Data on gynecological, physical and psychiatric evaluations and follow-up as well as information about abusive event of patients in study V was gathered from medical records. The two time periods evaluated represent different levels of professional learning. Conclusions regarding the probability of sexual abuse in relation to the gynecological findings in 1989–91 were based on information from the literature. At that time, the diameter of the hymenal opening, for example, was considered to be a diagnostic criterion of child sexual abuse. During the later period, conclusions from the physical and genital findings were made using the guidelines presented by Adams et al. (1996). Additionally, all patients with negative somatic findings but with the conclusions of child psychiatric evaluation being suggestive or clearly evident of sexual abuse were concluded to have experienced sexual abuse.

Study II was a prospective study. Information for Studies I, III and V was collected retrospectively from hospital medical records. At the special unit of pediatric and adolescent gynecology all patient information was originally recorded in the medical records with further scientific purposes in mind. The child psychiatrist who had been examining the child and was familiar with the case collected the data and conclusions concerning child psychiatric evaluations. Study IV was an uncontrolled open prospective study. Statistical analyses in Studies I and III were carried out using SPSS statistical

software. The statistical analyses for study IV were performed with SAS® for Windows software.

Approval from the Ethics Committee of Tampere University Hospital was obtained for Studies I, II, III and V. The ethics boards of each of the hospitals participating approved Study IV.

RESULTS

1. Patients and gynecological examinations

The study included a total of 406 gynecological patients aged 4 months to 17 years. Most (314) patients were examined and treated because of various gynecological symptoms and problems between January 1989 and December 1997 at the Department of Obstetrics and Gynecology, Tampere University Hospital. Some (217) of them (Studies I, II, and V) were seen at the special unit for pediatric and adolescent gynecology, 87 (Study I) patients were seen in normal gynecological outpatient settings and 79 (Study III) were seen in various hospital clinics. Twenty-three patients were included in both Studies I and V. Ten patients from Study IV were treated at Tampere University Hospital and the remaining 13 patients at four other major university hospitals in Finland.

The numbers of patients and their age distribution (Studies I, II, III and V) are given in Table 4. Patients are divided in age groups: Four months–1 year, 2–6 years, 7–10 years, 11–13 years, 14–15 years and 16–17 years. The age of the patients in Study IV at enrollment ranged from 10.7 to 17.7 years, the median being 13.6 years. Studies II and V included mostly prepubertal children, as patients in their teens and early adolescence are represented in Studies I, III and IV.

Table 4. Age distribution of patients in studies I, II, III and V.

	Patients n=	Age					
		0-1 yrs	2-6 yrs	7-10 yrs	11-13 yrs	14-15 yrs	16-17 yrs
Study I	204	13	24	24	48	95	-
Study II	68	2	34	18	7	5	2
Study III	79	1	0	4	9	29	36
Study V*	55	5	25	14	9	2	-
All	406	21	83	60	73	131	38
% of all		5 %	20 %	15 %	18 %	33 %	9 %

* study III includes 23 patients also included in study I

Table 5. Origin of referral to consultation.

	Study I ^a Special clinic n =	Study I ^a Adult clinic n =	Study II ^b n =	Study III ^c n =	Study V ^e n =	All n(%)
Primary care						
Public health care center	7	30	21	23	11	92 (23)
Private practitioner	6	9	11	11	4	41 (10)
Hospital						
Pediatric clinic	84	21	26	5	13	149 (36)
Child psychiatric clinic	10	3	5	0	22	40 (10)
Surgical clinic	6	17	1	27	0	51 (13)
Other hospital clinic	1	3	0	2	2	8 (2)
No remittance	2	3	0	4	3	12 (3)
Other	1	1	4	7	0	13 (3)
All	117	87	68	79	55	

a= Experiences of special gynecological services for children and adolescents

b= Vulvar symptoms in pediatric and adolescent patient

c= Surgery for ovarian masses during childhood and adolescence

d= Use of percutaneous estradiol gel for induction of puberty

e= Sexual abuse of girls

Table 6. Reasons for referral to the hospital

	Study I ^a		Study II ^b		Study III ^c		Study IV ^d		Study V ^e		All	
	Special clinic	Adult clinic	n	n	n	n	n	n	n	n	n	% of all
Menstrual disorder, vaginal bleeding	10	7	4	3	0	0	1	25	6			
Endocrinological problems	31	21	0	3	23	0	78	18				
Vulvovaginitis, vulvar symptoms	27	9	35	0	0	4	75	17				
Genital anomaly, synechia	6	1	9	0	0	1	17	4				
Sexual abuse suspicion	21	2	14	0	0	37	74	17				
Abortion	2	22	0	0	0	0	24	5				
Contraception	3	0	0	0	0	0	3	1				
Abdominal pain	13	22	1	51	0	0	87	20				
Abdominal tumor, swelling	0	0	0	20	0	0	20	5				
Urinary symptoms	0	0	3	1	0	3	7	2				
Psychiatric problems	0	0	0	0	0	8	8	2				
Diverse	4	3	2	1	0	1	11	3				
	117	87	68	79	23	55	429	100				

a= Experiences of special gynecological services for children and adolescents

b= Vulvar symptoms in pediatric and adolescent patient

c= Surgery for ovarian masses during childhood and adolescence

d= Use of percutaneous estradiol gel for induction of puberty

e= Sexual abuse of girls

Primary care remitted 33% of the patients to gynecological evaluation (Studies I, II, III and V). Sixty-one percent of the patients came to the gynecological consultation clinic from other clinics in Tampere University Hospital, 36% from the Department of Pediatrics (Table 5).

Reasons for referral to hospital examination and eventual gynecological consultation are presented in Table 6. Abdominal pain and abdominal swelling were the most common reasons for the examinations, in 20% of all patients. Endocrinological symptoms were the reason for referral in 18%, suspected sexual abuse was the reason in 17% and vulvar symptoms were the reason in 17% of all patients.

A concomitant chronic disease was present in 97 (30%) gynecological patients in Studies I, II and V. The most common chronic diseases were congenital malformations (10 patients), asthma and allergy (11 patients), pubertal disorder (12 patients), neurological disease (10 patients) and mental retardation (5 patients).

Examinations performed on patients included in Studies I, II and V are presented in Table 7. Vulvar inspection was performed in 88% of the patients. Microbiological samples were obtained from 55% and a Pap smear from 38% of the patients. The vagina was visualized with the aid of a speculum or by vaginoscopy in 38% of the patients. The internal genitalia were examined by sonography in 26% of the patients. . Sonography was often used in the follow-up of hormonal treatments. Fifty-seven percent of all patients had some abnormal finding in any of the examinations and in the rest of the patients all findings were normal. Abnormal findings were most often obtained in colposcopy (in 67% of the examinations), in vaginoscopy (53%) and in vulvar inspection (40%).

Table 7 . Examinations and abnormal findings *

Method	Study I special clinic n = 117		Study I adult clinic n = 87		Study II Study V All n = 68		Study V All n = 55		n = 327	
	Examinations (% of total)	Abn. finding (% of tests)	Examinations (% of total)	Abn. finding (% of tests)	Examinations (% of total)	Abn. finding (% of tests)	Examinations (% of total)	Abn. finding (% of tests)	Examinations (% of total)	Abn. finding (% of tests)
Vulvar inspection	82 (70)	28 (34)	85 (98)	13 (15)	68 (100)	42 (62)	54 (98)	33 (61)	289 (88)	116 (40)
Vaginal inspection with speculum	24 (32)	2 (8)	68 (78)	10 (15)	9 (13)	1 (11)	8 (15)	0	109 (33)	13 (12)
Vaginosis	5 (4)	5 (60)	1 (1)	0	9 (13)	4 (44)	2 (4)	2 (100)	17 (5)	9 (53)
Colposcopy	0	0	0	0	2 (5)	1 (50)	4 (7)	3 (75)	6 (2)	4 (67)
Vaginal palpation	23 (20)	2 (9)	69 (79)	12 (17)	3 (4)	1 (33)	3 (5)	0	98 (30)	15 (15)
Rectal palpation	18 (15)	0 (0)	16 (18)	3 (19)	14 (21)	0 (0)	3 (5)	0	51 (16)	3 (6)
Sonography	37 (32)	3 (8)	36 (41)	18 (50)	8 (12)	0 (0)	3 (5)	0	84 (26)	21 (25)
Microbiology	44 (38)	3 (7)	37 (43)	6 (16)	61 (90)	21 (34)	38 (69)	7 (18)	180 (55)	37 (21)
Pap smear	46 (40)	3 (7)	40 (46)	10 (25)	22 (32)	6 (27)	15 (27)	3 (20)	123 (38)	22 (18)
Any method	115 (98)	47 (48)	85 (98)	52 (63)	68 (100)	48 (71)	55 (100)	36 (65)	321 (98)	183 (57)

* any one patient may have more than one abnormal finding

2. Vulvar symptoms and microbiological examinations (Studies I, II and V)

Vulvar symptoms were the second most common reason for gynecological examination of the patients included in Study I. Eighteen percent of all patients included in Study I were examined because of vulvar symptoms. In Study II vulvar problems among 68 consecutive patients who had symptoms or signs of vulvar irritation or infection were further elucidated. Local genital symptoms or urinary symptoms were reported in 25 (45%) patients examined for suspected sexual abuse (Study V): 14 patients had local symptoms such as itching and burning, 6 patients had bloody discharge, two had condylomas and three had urinary symptoms. Sexual abuse was considered in 13 patients with vulvar symptoms in study II.

Patients examined primarily for problems in the vulvar area (Study II) had often had long-standing symptoms. The mean duration of symptoms was 134 days (range 3 days to 3 years), i.e. 19 weeks, with a median duration of 60 days. Nineteen (41%) of these patients had had symptoms for one to six months before referral and 9 (20%) patients had had symptoms for over 6 months. Only seven (10%) patients were examined within a week of the beginning of the symptoms.

Table 8. Vulvar symptoms and microbiological findings (Studies I,II,V)

	Study I Group 1	Group 2	Study II	Study V
Number of patients	117	87	68	55
Vulvar symptoms	27	9	62	25
Microbiological findings			Result(samples)	Result(samples)
Streptococci	0	0	11 (56)	0 (22)
Candida	2	1	4 (59)	1 (27)
Chlamydia	1	4	0 (26)	1 (28)
Gonococcus	0	0	0 (23)	0 (30)
Abnormal Pap smear	3	10	6 (22)	2 (15)

Of the patients evaluated for vulvar symptoms (Study II), 48 patients (71%) had abnormal clinical findings, i.e. redness, leukorrhea and/or labial synechiae in the gynecological examination (Table 7). Most abnormal findings were identified in vulvar inspection. The microbiological and Pap smear findings (Studies I, II and V) are presented in Table 8. No microbiological etiology was found among 26 (38%) patients with both symptoms and abnormal clinical findings included in Study II.

3. Ovarian tumors during childhood and adolescence (Study III)

Abdominal pain was the reason for hospital remittance in 20 % of all patients in the study (Table 3).

Abdominal pain was the presenting symptom among 71% of the patients with operatively treated ovarian tumors (Study III). Forty-four of the 79 patients included in Study III were primarily examined by a gynecologist, 30 by a surgeon and 5 by a pediatrician. Surgeons and pediatricians consulted a gynecologist 17 times preoperatively and 19 times during the operation. Thirty-eight patients underwent preoperative sonography. In the 1970s sonography was carried out in 15% of the patients, and during the last five years of the study in 65% of the patients examined. Sonographic findings agreed with surgical findings in 100% of cases during the 1970s, in 83% during the 1980s, and in 71% of cases during the 1990s.

The interval between the appearance of symptoms and the time of treatment varied from emergency treatment to a period of more than six months. Eighteen (23%) of the patients were operated on within 24 hours of the beginning of the symptoms, 10 (13%) within 2–3 days, 15 (19%) within 4–7 days, 15 (19%) within 1–4 weeks, 16 (20%) within 1–6 months and the remaining 5 (6%) after an observation period of at least six months.

Of all operatively treated ovarian tumors 7 (9%) were malignant neoplasias, 34 (43%) were benign neoplasias and 26 (33%) were functional cysts, half of which were histologically verified. Eight patients (10%) had ovarian torsion, and four patients (5%) were operated on because of a suspected ovarian mass, while they actually had other gynecological

conditions. Two of the patients also had appendicitis. Fifty-two (66%) operations were performed by a gynecologist and 27 (36%) by a surgeon. Thirty-seven (47%) of the operations were emergency procedures, 10 of them because of a neoplasm. Two of these girls had a malignant tumor, 18 patients had functional cysts, 4 had adnexal torsion and 5 patients had other adnexal conditions. Twenty-three of the emergency operations were performed by a surgeon and 14 by a gynecologist. Fourteen of the patients operated on in emergency conditions by a surgeon had a functional cyst.

Among the 7 malignant tumors there were 3 mucinous cystadenocarcinomas (one with a low malignant potential), 1 sarcoma, 1 small cell carcinoma, 1 arrhenoblastoma and 1 juvenile granulosa cell tumor. All malignant neoplasms were operated on by a gynecologist; the primary operation was either unilateral oophorectomy or salpingo-oophorectomy. In the cases of benign neoplasms, oophorectomy or salpingo-oophorectomy was performed in 19 cases and ovarian resection in 15. Twenty-nine of the 34 patients with benign neoplasms were operated on by a gynecologist. In the eight cases of ovarian torsion, removal of the ovary or tuba was necessary. Twenty-six patients had a functional ovarian cyst and 13 of them were histologically verified. More conservative techniques were used to treat functional cysts, i.e., ovarian resection, suturation, or puncture. Surgical procedures on the contralateral ovary were performed in 13 patients with benign tumors, in 11 cases by a gynecologist. Incidental appendectomy was performed on 33 patients; of the 27 patients operated on by a surgeon, 23 underwent appendectomy.

4. Induction of puberty (Study IV)

Use of estradiol gel by patients with TS for pubertal induction was easy and compliance was good. Use of medication was 100% in all but the 6-month (94.4%) and 4.5-year (93.1%) visits.

The treatment was effective. The pubertal stage advanced gradually along with the increasing estrogen doses. Of these girls, 79% reached B5 and 58% reached P5 stages. All girls reached at least stage B4P4. Breast development progressed gradually and symmetrically during the whole study. The mean

serum estradiol concentration at baseline was 0.022 nmol/l and it increased steadily to 0.162 nmol/l at five years of treatment. At the same time the mean serum baseline FSH concentration decreased from 77.4 IU/l to 19.2 IU/l after five years and the mean serum baseline LH concentration decreased from 20.6 IU/l to 6.6 IU/l. The concentrations of FSH and LH after stimulation with GnRH decreased as the study progressed and estrogen doses were increased. With estrogen doses of 1 mg and 1.5 mg there were, however, only slight elevations in FSH and LH concentrations in the GnRH tests. Absorption of estradiol from the gel was observed in the estrogen profile as a rise in concentrations after application of the gel. Individually, the estrogen concentrations were very variable. An elevation of mean serum DHEAS values from 4.67 mmol/l to 6.53 mmol/l over the five-year period was observed. Serum mean testosterone levels remained constantly low, ranging between 0.59 and 0.86 nmol/l during the study.

Abdominal ultrasonographic data were obtained from 18 girls. Mean uterine length increased from 33 (15–66) mm (mean + range) at baseline to 67 (48–91) mm at five years of therapy. Mean uterine volume increased from 5.5 (1.7–12.6) ml at one year of treatment to 31.5 ml (8.2–82.8) ml at five years. Mean endometrial thickness increased gradually to 3.9–2.8 mm at 4–5 years of therapy. The maximum endometrial thickness measured during the study was 11 mm. Regular menstrual periods were induced with progestins, according to the protocol, between 2.5 and 3.5 years of treatment in 19 cases. In three cases regular progestins were started at 6 months because of spontaneous bleeding and in one case it was at 1.25 years.

Mild skin irritation after application of the medication was reported four times during the study. Spontaneous menstrual bleeding or spotting before the use of cyclic progestins was reported by 11 girls. During the cyclic estrogen/progesterone therapy 9 episodes of irregular bleeding were reported by five subjects. Two girls had transient amenorrhea and two had menorrhagia. Two girls left the study prematurely at 3.5 years. One did not like the gel and changed to another form of estrogen treatment, and the other girl moved abroad. As regards serious adverse events in the treatment, one subject developed anorexia nervosa and recovered from it, one girl with menorrhagia was diagnosed as having von Willebrand disease and one girl was diagnosed as having aortic aneurysm associated with TS.

5. Examination of cases of suspected child sexual abuse (Studies I and V)

The study included 55 girls, 24 examined in 1989–91, and 31 in 1995–97. The examinations for child sexual abuse were initiated in 21/55 (38%) patients when the girl herself reported the abuse to a carer. In 19/55 (35%) cases the girl's mother was the first adult who noticed or who was confided in about the suspected sexual abuse. Other adults who primarily became aware of possible child sexual abuse were social workers or day care personnel in 10 (18%) cases, friends or relatives in 6 (11%) and the primary care physician in 8 (15%) cases.

Somatic evaluation for suspected sexual abuse was carried out in 36 (65%) cases merely because of suspicion of sexual abuse. In 1989–91 50% of the patients were initially remitted to hospital evaluations with undefined somatic or psychiatric symptoms and the question of possible sexual abuse was raised during the examination. In 1995–97 77% of the patients were remitted to the evaluation because of suspected child sexual abuse and only 23% with other complaints.

In 58% of all patients in study V the suspected offender was the child's biological father. In 16% of cases the perpetrator was someone outside the child's family. The type of sexual abuse suspected was genital fondling in 36% of all cases. Intercourse or attempted intercourse was reported in 18% of patients, all among those assessed as having evidence of sexual abuse. Among girls with no gynecological or psychiatric evidence of sexual abuse the precise nature of the sexual involvement could not be given in 59% of cases.

In the pediatric examination, signs, mainly bruises, possibly referring to physical abuse were observed in 10 patients. In the pediatric and/or gynecological examinations a total of 22 (40%) patients were concluded likely to have been sexually abused according to the somatic findings. Fifteen patients had changes in the hymenal structure and 7 patients had diagnostic findings in the vulva or anal region, such as a dilated anal opening and scarring of the vulva or anal region, and large anal fissures.

The results of the child psychiatric evaluations showed evidence of sexual abuse in 29 patients. A gynecological and a child psychiatric evaluation were both carried out in 42 cases. Thirty-one patients were concluded to have

evidence of sexual abuse according to the results of the gynecological and/or psychiatric examinations. The assessments in gynecological and child psychiatric examinations agreed in 72% of those cases where both examinations were carried out (Table 9). No child psychiatric evaluation was carried out in 12 cases. In 4 of these cases the gynecological examination led to a somatic diagnosis not related to sexual abuse; one case of bacterial vulvitis, one of atopic dermatitis, one of fetal alcoholic syndrome, and one neglected child. In five cases, the gynecological examination failed to reveal any abnormal findings.

Follow-up information from the medical records was available for 33 patients. There were 13 instances of an adverse psychiatric or psychosocial outcome among the 23 patients with gynecological or psychiatric evidence of sexual abuse, and one instance among the 10 patients with no evidence of abuse. A serious mental illness, requiring in-patient hospital treatment, developed in three of the patients with gynecological and psychiatric evidence of sexual abuse. One of the girls with no evidence of sexual abuse was also later hospitalized as a result of psychiatric problems. Additionally, five girls with evidence of abuse have had serious behavioral difficulties during adolescence. One sexually abused patient and one perpetrating father have committed suicide and deaths of four other parents have been recorded. All criminal proceedings took place during the later study period. There were no criminal proceedings connected to the patients with no gynecological or child psychiatric evidence of sexual abuse. In six cases of child sexual abuse, five suspected perpetrators were tried and sentenced.

Table 9. The association between the conclusions in the gynecological and psychiatric examinations

		Child psychiatric conclusion			All
		Abused	Non-abused	Not examined	
Gynecological conclusion	Abused	19	2	0	21
	Non-abused	9	12	12	33
	Not examined	1	0	0	1
All		29	14	12	55

DISCUSSION

1. Pediatric gynecology

The beginning of modern pediatric and adolescent gynecology can be traced to well over a century ago. The most frequently encountered subjects of pediatric gynecology in English-language medical journals at the end of the 19th century were vaginal atresia and associated anomalies and gynecological tumors (Yordan et al. 1997). Vulvovaginitis and teenage pregnancies were additional issues dealt with during the first half of the 20th century. As awareness and understanding of child sexual abuse increased during the early 1960s in the US and in the 1980s in Scandinavia it has become evident that pediatric patients have many different kinds of gynecological problems. Advances in the understanding of pubertal endocrinology have improved the diagnostics and treatments of patients with pubertal disorders and genetic syndromes.

Caring for pediatric patients in gynecological practice requires a thorough knowledge of embryology, normal growth and development during puberty and changes in gynecological anatomy throughout childhood and adolescence. Besides that correct examination techniques and knowledge of the nature and course of different gynecological problems of girls are required. Simple examination and visualization of genitals is often sufficient for diagnosis. Gynecological ultrasonography is a well-tolerated noninvasive method for visualization of the internal genitalia and ovaries for diagnostic purposes. Additionally, sonography is an excellent tool in the follow-up of the effects of endocrinological therapies. Laparoscopy may further improve the diagnosis and treatment of pediatric gynecological problems, but child patients present significant challenges, since pediatric anatomy and pathophysiology is often different from that of adults (Sharp 1997). A pediatric gynecologist always has to work in close cooperation with pediatricians, pediatric endocrinologists, pediatric surgeons, general practitioners, child psychiatrists, psychologists and social workers.

2. Hospital consultation services

To meet the new challenges, the Department of Obstetrics and Gynecology at Tampere University Hospital founded a special outpatient consultation unit of pediatric and adolescent gynecology in 1988. This unit has provided special consultation services in this emerging field. Originally the purpose was to consult the pediatric endocrinologist in the treatment of pubertal disorders. At the same time examinations of children with suspected sexual abuse were beginning to be carried out and pediatricians recognized that many different gynecological problems of girls needed specialist consultations. To gather knowledge and clinical experience the patients of the special unit have mainly been examined and treated by only one gynecologist. Additionally, residents interested in this field have been trained.

The results of this study at the special hospital outpatient unit give a picture of the occurrence and nature of different gynecological problems during childhood and early adolescence. The patients in this study represent only a small proportion of the female children and young adolescents living in the hospital referral area, and thus the incidences of gynecological problems in the population cannot be given. Different age groups are, however, equally represented, which is important since children of different ages have different kinds of gynecological problems. In our study child sexual abuse and vulvar symptoms were typical problems among the younger children and abdominal pain, pubertal disorders and problems related to menstruation were common among young adolescents.

Sixty-one percent of the patients included in the study were remitted for gynecological consultation from other clinics inside the hospital, about half of them from the Department of Pediatrics. A smaller number of patients (33%) were remitted directly from primary care. This led to some overrepresentation in the material of complicated cases. Physicians working at hospital level were perhaps more aware of and ready to address the issues concerning the gynecological health of girls and the aspects of future fertility of girls with chronic diseases. Pediatricians were also more aware of the gynecological services available.

Gynecologic problems of girls are still taboo and are not addressed during annual health controls (Hairston 1997). It is very likely that Finnish parents, school nurses and physicians do not easily recognize gynecological problems of children and young adolescents. A long interval between the beginning of

symptoms and the diagnosis and treatment of symptomatic bacterial vulvitis of patients in this study is one sign of this phenomenon. All physicians treating young females should have knowledge of normal anatomy, development and growth during childhood. They should also be familiar with the basic examination and treatment methods of the most common gynecological problems during childhood and early adolescence. Pediatric gynecologists are needed to examine and treat the more complicated cases, to gather the clinical experience and information and to educate other gynecologists, pediatricians and general practitioners.

3. Gynecological examination

Information on the patient's previous health is very important in the evaluation of gynecological problems during childhood and adolescence, especially in cases of endocrinological abnormalities and child sexual abuse. Gynecological problems are often related to and integrated with other health conditions of the youth and also her social environment. Information gathered on development, growth, puberty and chronic illnesses is very important.

The first gynecological or pelvic examinations are critical to the attitudes that a young woman will develop towards her genitals and reproductive health (Blake 1992). Visualization of the vagina is seldom obligatory in the gynecological examination of children. In the present study, vulvar inspection, including inspection of the outer 1/3 of the vagina, and vaginal discharges, was carried out among 88% of the patients at the outpatient clinic. This examination revealed an abnormal result in 40% of the cases. Noninvasive examination methods together with ultrasonography established the diagnosis in 83% of the patients in the special unit in the present study (Study I). In our study the whole vagina was visualized in 38% of girls, which is equivalent to the proportion of post pubertal girls in our study. Examination under anesthesia was very seldom needed.

When a young girl is examined gynecologically it is important to explain the reasons for the examination, the procedures needed and the steps taken, both to the mother and the girl, before and during the process. According to our experience the necessary examinations and sampling can be carried out without causing discomfort. Assurance of this can be given to the girl and

her guardian when the details of the examination are discussed beforehand.

Evaluation and findings of normal gynecological anatomy were one of the most important conclusions among patients examined. Fifty-two percent of patients examined at the special unit and 43% of all patients in the study had normal findings in the examinations. Very often the purpose of gynecological examination of children is to verify normal vulvar anatomy and presence of uterus with inspection and sonography or to follow pubertal development.

4. Ultrasonography

In pediatrics, ultrasonography plays an important role in clinical evaluation of the pelvis, particularly in the assessment of pelvic masses, lower abdominal pain, ambiguous genitalia and pubertal disorders (Kutteh 1995).

In the present study, among patients operated on for an ovarian tumor, 34 (43%) had a benign neoplasm and 38 (48%) a functional tumor. Sonography was included in preoperative examinations in only 15% of patients in the 1970s and in 65% in the 1990s. Surgery for functional lesions seems to have been too extensive. Sonography is the initial examination of choice for evaluating patients with suspected gynecological masses (Siegel et al. 1992). Based on the present study I suggest that a sonographic examination of the pelvis should always be included in the examination of acute abdominal pain of girls in early puberty and in adolescence in order to differentiate appendicitis, gynecological conditions and other reasons for symptoms. Unnecessary and too radical surgery could thus be avoided, as functional ovarian tumors could be diagnosed and most often treated by expectation.

Changes in uterine and ovarian growth and morphology can easily be followed by sonography in accordance with pubertal development and hormonal changes (Orbak 1998). Among patients visiting the unit of pediatric gynecology, 48 (20%) were examined by ultrasonography and abnormal results were found in only 3 patients. In our practice of pediatric and adolescent gynecology, sonography has been shown to be an invaluable tool for the evaluation of gynecological anatomy and in the diagnosis and follow-up of pubertal disorders.

In the present study sonography was used to follow up the medical treatment of patients with precocious puberty, and the induction of puberty among girls with hypogonadism. Uterine growth and endometrial status were followed bi-annually during the induction of puberty. The response to estrogen treatment could be reliably followed and uterine measurements correlated with increasing estrogen doses and serum estrogen concentrations. Since serum estrogen concentrations have great individual variation, sonographic measurements of uterus and endometrium are an excellent tool to evaluate the long-term response to estrogen treatment. Based on the results of the present study and the clinical experience gathered since 1988 a sonographic evaluation of pelvic structures is nowadays included in the examination of most of our young gynecological patients.

5. Vulvitis and vaginitis

Vulvar and vaginal symptoms are perhaps the most common gynecological complaints among prepubertal girls. Vulvovaginitis is the term used by clinicians for these complaints. The problems can often be divided into those on the outside vulvar area and those inside the vagina. Vulvitis causes pruritus, burning and erythema on the outside. Etiologies of vulvar complaints vary in different studies according to the examiners' viewpoints.

Various etiological reasons for vulvar symptoms described in the literature were also seen in our study: infections, labial synechia, dermatological conditions, foreign bodies, vulvar traumas, condylomas and sexual abuse. A microbiological etiology was found in 31% of the patients with vulvar complaints (Study II). In other patient groups in the present study the incidence of microbiological findings varied among the patients sampled from 7% (Study I, special unit) to 18% (Study V). *Streptococcus pyogenes* infections were always symptomatic and were the most common bacterial infection present among our patients. *Candida* infections were present both before and after the start of puberty. *Gardnerella vaginalis* was detected only among pubertal girls.

According to our findings 69% of patients with vulvar complaints had other than infectious etiologies and 37% of patients with abnormal clinical findings in vulvar inspection had normal microbiological culture results. In order to provide proper treatment for the patients, vulvar conditions should

always be evaluated and all diagnostic alternatives considered. Infections can be diagnosed by cultures of bacteria and *Candida* and treated accordingly. According to our findings swab samples can be obtained from any of the symptomatic areas, vulva or vagina. Extensive sampling, which is unpleasant for the child, is not needed.

The primary examination of girls with vulvar symptoms can be carried out by a general practitioner or a pediatrician. Complicated cases should however be referred to a pediatric gynecologist without delay. After infections, dermatological and other medical conditions have been ruled out there is basis to inform the girl and her parents about the benign nature of the condition. For the nonspecific vulvar symptoms of unknown etiology possibly related to atrophic mucosae, hygiene and local creams are the basic treatment principles. Mild steroids can be used locally to reduce symptoms. Short-term local estrogen therapy may sometimes be helpful in improving the mucosa, for example in cases of labial synechia. According to our clinical experience, prepubertal vulvar symptoms most often vanish with advancing puberty as the estrogen effect becomes apparent.

6. Ovarian tumors

The actual incidence of ovarian masses during childhood and adolescence has probably not changed over the years. The use of sonography has, however, led to the detection of many cysts and masses that previously would have gone undetected. Fortunately, only 1% of ovarian tumors during childhood and adolescence are malignant. Neoplasms are more likely to be germ cell rather than epithelial in origin. Functional non-neoplastic cysts are more frequent after pubertal development has started.

According to previous studies, 64% of ovarian masses encountered in children and adolescents are neoplastic while 36% of masses are non-neoplastic or physiologic (Breen et al 1977). Thirty-five percent of these neoplasms were malignant. In the present study benign neoplasms constituted 43%, functional cysts 33% and ovarian torsions 10% of the cases. Nine percent of all operatively treated ovarian tumors were malignant, and malignancy rate of the neoplasms was 16%, which agrees with the results of previous studies.

An operation was performed as an emergency procedure in 47% of the cases. The large proportion of emergency operations and operative treatment of functional tumors can be strongly criticized. The importance of preoperative gynecological examination with sonography, evaluation of hormonal levels and tumor markers was poorly recognized. Functional ovarian cysts seldom need operative treatment, and even if they do, an observation period of several months before operation can be recommended. Frequent use of sonography helps to avoid unnecessary surgery.

All operative procedures on the ovary, including laparoscopy, can have adverse effects on the future fertility of the girl. The surgical procedures for benign neoplasms and functional cysts in this study were quite extensive. In the treatment of benign neoplasms, the ovary was completely removed in 19 patients, in case of functional tumor one ovary was resected in 12 instances. The operative approach to adnexal surgery has certainly changed after the period when this patient material was collected. In the future, gynecologists and pediatric surgeons should pay continuous attention to the use of proper preoperative work-up and conservative fertility sparing operative techniques in the management of ovarian masses in all females of fertile age.

7. Induction of puberty

The main target of estrogen replacement therapy in hypogonadic girls has been to induce puberty and feminization sufficiently early without reducing adult height (Ranke et al. 1995). Many of the previous studies concerning growth during pubertal induction have concluded that estrogen has a negative effect on growth. This certainly is due to the fairly high estrogen doses used. Chernausek (2000) used for example a starting dose of 0.3 mg of CEE, starting between 12-15 years of age, for six months after which the dose was increased to 0.625 mg. Growth stimulation is optimal at approximately 4mg/day of estradiol (Rosenfield et al. 1998) and higher doses enhance the closure of epiphyseal plates. The use of very low estrogen dose at the beginning of pubertal induction with slow gradual increase of doses, similar to natural puberty, as in our study, may provide better attainment of optimal final height without unnecessary delay in the earliest signs of puberty.

According to our results the use of percutaneous estradiol gel provides an easy, safe and effective means to induce puberty in girls with hypogonadism. Acceptance of the treatment was excellent and according to safety parameters and adverse events the use of percutaneous estradiol was safe for the patients.

The steady increase of mean serum estradiol concentrations proved the efficacy of percutaneous estradiol therapy for the induction of puberty. Circulating estradiol concentrations within and between individual subjects showed great variation and cannot alone be used in the follow-up of treatment. The very small increases in mean FSH and LH concentrations in GnRH tests with the 1.0 mg and 1.5 mg doses of estradiol indicate that for some of the subjects smaller doses would have been sufficient. Declines in the basal and stimulated FSH and LH concentrations with increasing estradiol doses are useful in measuring the efficacy of estradiol therapy.

Percutaneous estradiol therapy resulted in excellent gradual development of secondary sexual characteristics and uterine growth. After five years of treatment all girls had reached Tanner stage B4P4, 65% of them had reached Tanner stage B5, and 48% Tanner stage P5. Achieving normal adult uterine size is important if infertility treatments (embryo transfer) are considered during later life. Endometrial thickness was within the normal range during the menstrual cycle, which indicates endometrial safety of the treatment.

Fluctuation of estradiol concentrations over twenty-four hours might have a positive effect as regards the natural development of puberty (Ankarberg-Lindgren et al. 2001). Such an effect could be achieved in our study by means of percutaneous application of the gel in the evenings in an easier and more cost effective way than the intermittent use of estradiol patches suggested in the above study. The use of estradiol gel facilitates the adjustment of the dosage by changing the concentration of the gel and amount of medication applied. Estradiol gel is one of the best options among products available on the market for individual and flexible adjustment of estrogen dosage.

Percutaneous estrogen has become standard practice for pubertal induction in our clinic. After this study even more attention has been paid to the very low starting dose and the slow gradual increase of doses during the therapy under close follow up of growth and bone maturation. During the use of growth hormone, estradiol concentrations are kept very low, with only a slight decline in FSH concentrations. With estradiol gel the doses used can be individually adjusted according to pubertal stages, growth, bone-age, gynecological ultrasonographic data and circulating FSH concentrations.

8. Gynecological evaluation of suspected sexual abuse of a child

Child sexual abuse is a significant problem in pediatric and adolescent gynecology. The prevalence of child sexual abuse among girls younger than 14 years is approximated to be 10–12 % (Feldman et al. 1992). The possibility of sexual abuse has to be considered in the differential diagnosis of many gynecological, pediatric and child psychiatric conditions. In order to be objective the examiner has to have a very systematic approach in the somatic examination and document all findings. The physicians performing these examinations need wide clinical experience of the normal and abnormal findings and knowledge of their clinical significance. The model procedure in our special unit, in which a team of an experienced gynecologist, pediatrician or a forensic pathologist examines all victims of suspected child sexual abuse, can be recommended. Suggestion for a schedule of the evaluation in cases of suspected child sexual abuse is presented in Table 10.

Suspicion of child sexual abuse always profoundly affects the child and her family. That is why there should always be evidence and knowledge before the suspicion is expressed. When suspicion is raised every case should be assessed. It is important to find out if an incidence of sexual abuse has taken place and provide treatment for the girl and her family. It is, however, equally important to find out if the suspicion is unfounded and tell this to the girl and her carers. Fifty-one girls (13%) in the present study were examined because of sexual abuse. Twenty-four (47%) of these girls were assessed as having somatic findings suggestive, suspicious or clearly evident of child sexual abuse. Anogenital findings among our patients were fairly common when compared with other studies. This could mean that the cases seen were severe and that there were not many false suspicions or false alarms. The conclusions of somatic and child psychiatric assessments agreed in 72% of the cases when both evaluations were carried out. Their reliability justified the medical, legal and social measures taken on behalf of the child, family and society. I think that somatic examination is an important part of the examination of sexual abuse cases. These examinations should however be concentrated to physicians with special experience on this field. When an examination is done properly, it can even contribute to the therapeutic process, as the young patient is informed about the usually normal genital findings.

Table 10. Schedule of evaluation procedures in suspected child sexual abuse

1. Suspicion of sexual abuse

- a. Child tells about the event
- b. Childs' behavior or symptoms raise the suspicion
- c. Suspicion by an adult person
- d. Suspicion based on social investigations
- e. Investigations of pedofile cases
- f. Perpetrator makes a confession

2. Gathering of social and medical information

- a. Interview of the child
- b. Interview of the parents
- c. Interview of other adults
- d. Gathering of social information
- e. Conclusion of present information
- f. Possible further examinations

3. Medical evaluation

- a. Child psychiatric examination
- b. Pediatric examination
 1. Physical well-being
 2. Signs of maltreatment
- c. Gynecological examination
 1. Inspection of erogenic areas
 2. Inspection of vulva and introitus
 3. Inspection of hymen
 4. Inspection of vagina (when needed)
 5. Documentation of findings, photographs
6. Sampling for health and forensic purposes, optional
 - * forensic samples, if less than 72 hours from event
 - * STD , HIV, hepatitis
 - * Pap-smear
 - * Detection of sperm and DNA material
 - * Blood sample for DNA

4. Criminal examinations, often simultaneously with medical examinations

5. Disclosure of the possibility of sexual abuse

6. Treatment and child protection measures

7. Concluding statements to authorities by request

Sexual abuse during childhood has far-reaching consequences for a young girl's life. The patients in our study represent the most severe cases of child sexual abuse. Fifty-five percent of our patients were under 7 years of age, sexual abuse was often intrafamilial (67%) and the forms of abuse were genital fondling or intercourse (54%). Severe social and psychological outcomes were very common among our patients with a disclosure of child sexual abuse, which agrees with previous studies.

An important finding in this study is that only two girls aged 14-15 years and no girls aged 15-16 years in Study V were examined because of suspected sexual abuse. However girls aged 14 to 16 years have reported 70 % of the experiences of sexual abuse encountered in an epidemiological study in Finland (Sariola et al. 1994). Girls of this age group in our hospital area did not reach our services as well as the younger ones. Sexual abuse and violence experienced by teen-age girls might easily be interpreted to be a personal problem of the girl, bad behavior, and wrong friends or consequence of the use of alcohol. Girls are left alone with their worries and guilt or perhaps given a prescription for contraceptive pills. Health personnel, schools and parents should notice the clear difference between teen-age dating and sexual violence. Young victims of rape or any kind of sexual violence should have organized and targeted medical and psychiatric services provided for them. Parents, schools and healthcare should give a clear message about young persons' rights to physical and sexual integrity by educating young girls and boys.

SUMMARY AND CONCLUSIONS

This study describes and evaluates gynecological problems during childhood and early adolescence, based on a great deal of patient material from a special consultation unit of pediatric and adolescent gynecology at a university hospital. Gynecological examination of children requires knowledge of normal growth and development of children during childhood and puberty, normal findings and variations in genital anatomy at different ages, diagnosis and treatments of gynecological problems, and good examination skills and techniques. To be able to treat these patients, close cooperation is needed between gynecologists, pediatricians, pediatric endocrinologists, pediatric surgeons, child and adolescent psychiatrists, psychologists and social workers.

This study involved 406 gynecological patients aged between 4 months to 17 years. They represent a population of 45 000 females aged 16 or under living in the secondary referral area of the hospital. Even though the number of young females studied is small, different age groups up to 16 years are equally represented. Typical problems among the prepubertal girls were vulvar symptoms and suspected sexual abuse. Abdominal pain, pubertal disorders and problems related to menstruation were common problems during early puberty. The small number of patients seen at the special unit leads us to suspect that many girls did not receive the advice and help they would have needed with their gynecological problems. Pediatric gynecologists are needed to study the problems of the pediatric age group; they can discuss the most problematic cases together with pediatricians and educate other health professionals and parents.

Our experience shows that with good cooperation from the patient the vulvar area and outer third of the vagina could be visualized without instruments in 88% of cases. The vagina can be examined without anesthesia with a vaginoscope or with the aid of a very narrow speculum, beginning at school age. According to our results diagnosis in most of our patients could be achieved by noninvasive methods. The findings and evaluation of normal gynecological anatomy are very important parts of diagnostics in pediatric gynecology.

Vulvar complaints are the most common gynecological problems among prepubertal girls. A microbiological etiology was found among 31% of our patients with vulvar problems, the most common pathogen being *Streptococcus pyogenes*. Infections can be diagnosed by means of microbiological cultures

and treated accordingly. No microbiological etiology was found in 38% of patients with abnormal clinical findings and symptoms. Dermatological conditions and the possibility of sexual abuse are important issues to consider in differential diagnosis. According to our clinical experience vulvar symptoms of childhood usually disappear with advancing puberty.

Sonography is an excellent noninvasive method to visualize the uterus and ovaries. In this study it was used in the diagnosis of pubertal disorders and in the follow-up of hormonal treatments. Sonography was also used in the evaluation of gynecological anatomy. The importance of gynecological sonography in examinations of abdominal pain and ovarian masses in young females has not been well enough recognized, according to our findings. Good preoperative work-up in these cases would have reduced the number of unnecessary operations or contributed positively to the operation. Sonography was an excellent tool in the follow-up of pubertal induction by estrogen gel.

Many patients were referred to a gynecologist by a pediatrician because of endocrinological problems, most typically in cases of precocious or delayed puberty. Delayed puberty or amenorrhea is encountered in various syndromes, after chemotherapy and in anorexia nervosa. The use of percutaneous estradiol gel provided a safe, individual and well-accepted treatment for the induction of puberty in such girls. In delayed puberty secondary sexual characteristics and uterine growth proceeded gradually during the treatment, mimicking natural pubertal development. The efficacy of the therapy could be followed by means of development of pubertal signs, ultrasonographic measurement of uterine growth and endometrial thickness, and circulating gonadotropin concentrations.

Severe cases of child sexual abuse were represented in this study. Fifty-five percent of our patients were under 7 years of age and sexual abuse was intrafamilial in 67% of cases. There were 13 instances of an adverse psychiatric or psychosocial outcome among the 23 patients with gynecological or psychiatric evidence of sexual abuse. The sexual abuse of small children seems to be a different phenomenon than the abuse of teenage girls. Sexual abuse of pubertal girls was perhaps not recognized and the older victims of sexual abuse did not reach the services. A gynecologist/pediatrician team was found to be of benefit in performing the examinations. The importance of a systematic approach during the examination and in the documentation of findings emerged in the retrospective analysis of our patients. Somatic evaluation of sexual abuse cases among children and adolescents should be left to experts

because of the methodological difficulties and the fairly small numbers of cases. A somatic examination performed correctly can also contribute to the therapeutic process.

IMPLEMENTATION

This study has covered the most common gynecological problems in the pediatric age group and presented a way to approach these problems. Pediatric gynecology combines gynecological knowledge and skills to pediatrics and reproductive endocrinology. Documentation of normal gynecological findings and preventive health care are important parts of pediatric gynecology. Gynecological anatomy and maturation during growth and pubertal development are important fields of interest shared with pediatric endocrinologists and oncologists. Vulvar problems and child sexual abuse are mutual concerns with general pediatricians, child psychiatrists and forensic pathologists. Operative interests are shared with pediatric surgeons treating anomalies and gynecological tumor. Gynecological concerns of adolescent girls, contraception, and symptoms related to menstruation, sexually transmitted diseases etc are parts of the work shared with general practitioners.

It is important for all physicians working with young patients to consider the future reproductive health of the young females. Basic knowledge of gynecology during childhood and adolescence and the nature of pediatric gynecological examination should be included in the clinical training given by medical faculties. Girls in the pediatric age group constitute 10% of the population. Their need for a special kind of gynecological service is poorly recognized. Tertiary referral level university hospitals should have a pediatric gynecologist to provide gynecological care for young patients in complicated cases in close co-operation with other specialities, as well as educate students, other physicians and continue research on this field. At secondary referral level and in primary care, education on pediatric and adolescent gynecology should be provided to physicians with special interest in this field. Every level of health care system is needed to provide their part of the gynecological services for young females.

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ORIGINAL PUBLICATIONS

Experiences of special gynaecological services for children and adolescents: a descriptive study

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Gynaecological examination of girls during childhood is undertaken somewhat infrequently. These genital examinations should not be taboo or a frightening experience for the girl, for her parents or for the physician. Studies of children suspected of sexual abuse have paid attention to the wide variety of gynaecological conditions already present in childhood. In 1988 we founded a special gynaecological outpatient clinic for girls under 16 y of age at a university hospital to develop the special knowledge and skills needed in children's gynaecology. In this gynaecological clinic for children and adolescents we were able to gain and offer expert knowledge of the problems of this age group. In this special clinic for children, gynaecological examination by special techniques and sonography led to a diagnosis in 71% of the patients without any instrumentation. Children and adolescent girls in need of special gynaecological care should be recognized specifically. Particular attention should be paid to the gynaecological care of victims of child sexual abuse and mentally or physically handicapped girls. In good co-operation with the girl, a gynaecological examination can become a positive experience during the development of female identity. □ *Gynaecological examination, gynaecology in childhood, sexual abuse*

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For many physicians and parents, gynaecology before puberty has not existed. Traditionally, any gynaecological problems of children are resolved by the paediatrician, although routine paediatric examination seldom includes examination of the female genitalia (1). The increased awareness of child sexual abuse has, however, increased the frequency and need of such examinations. It has also become apparent that there is a wide variety of gynaecological conditions requiring attention in prepubertal patients (2–4). Taken together, there is increasing awareness by physicians and parents to listen, note and examine the gynaecological complaints of prepubertal and adolescent girls. The gynaecological examination of this patient group requires special knowledge and skills on the part of the physician in performing the gynaecological examination and sonography (5).

In 1988, the Department of Gynaecology in The Tampere University Hospital, Finland, established a gynaecological outpatient clinic for girls aged ≤ 15 y. The purpose was to concentrate all children's gynaecological problems to the supervision of one gynaecologist. We sought to create a suitable atmosphere for the examination of children and to increase our knowledge and understanding of this group of patients. In this paper we describe the experiences we have gained at this clinic in relation to the experiences at respective adult gynaecological clinic treating girls under 16 y of age.

Subjects and methods

The Tampere University Hospital is a tertiary referral and teaching hospital which serves a population of 1.3 million inhabitants. The gynaecological outpatient clinic is attended by 11 000 patient visits yearly.

The study period was from January 1989 to December 1991. Information on all girls under 16 y of age who visited the gynaecological outpatient clinic was collected retrospectively from the hospital medical records. The reason for the visit, the examination techniques used, any clinical and laboratory findings and the diagnosis and treatments were recorded, together with the information on the patients' previous physical and mental health. The data from the first visit of each patient were used in the analysis.

The patients were divided into two groups. Group 1 comprised 117 girls treated as patients at the special clinic for children and adolescents; Group 2 consisted of 87 girls treated at the adult gynaecological clinic. The physicians in primary care and hospital clinics had been informed, that there were consultation services available at the special clinic once a week. The girls visited the special clinic if the referring physician or the head of the outpatient clinic considered her to be in need of special services. If no such need was recognized or if the consultation was urgent the patient was seen in the normal adult gynaecological outpatient clinic. The characteristics of the two groups

Table 1. Indications for gynaecological examination in Groups 1 and 2.

Age (y)	0-1		2-6		7-10		11-13		14-15		All	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Menstrual disorders	-	-	-	-	-	-	4	3	6	4	10	7
Endocrinological problems	4	1	4	1	11	3	3	4	9	12	31	21
Local genital symptoms	2	-	9	-	4	-	10	2	2	7	27	9
Suspected sexual abuse	3	-	7	2	5	-	5	-	1	-	21	2
Contraception	-	-	-	-	-	-	1	-	2	-	3	-
Pregnancy, abortion	-	-	-	-	-	-	-	-	2	22	2	22
Abdominal pain	-	-	-	-	-	-	5	7	8	15	13	22
Suspected genital anomaly	3	-	1	-	1	-	1	-	-	1	6	1
Other	-	-	-	-	-	-	2	-	2	3	4	3
All	12	1	21	3	21	3	31	16	26	64	117	87

were evaluated to examine the benefits of providing special services for children and adolescents.

Results

During the 3-y study period, 204 girls under the age of 16 y visited the gynaecological outpatient clinic. They made 357 visits during this period—1% of all visits to the outpatient clinic during the period in question.

Girls of all ages were equally represented in Group 1, whereas most of the girls in Group 2 were in their teens. In Group 1 47% of the girls were under 11 y, whereas in Group 2 only 8% of the girls were prepubertal. The median age in Group 1 (117 girls) was 10.3 y and in Group 2 (87 girls) 14.9 y.

In Group 1, 101 girls (87%) were referred for gynaecological examination from another clinic in the same hospital; 84 from the Department of Paediatrics, 10 from the Department of Child Psychiatry and the remaining 7 patients from other departments. In Group 2, 68% (57) of the girls were referred to the gynaecological outpatient clinic from primary care and 24% (20) from other clinics of the hospital.

The most common reasons for the gynaecological examination in Group 1 were consultations for pubertal development, local genital symptoms and suspicion of sexual abuse. The girls in Group 2 were most commonly seeking abortion, had endocrinological problems or abdominal pain (Table 1). A total of 31% of all girls had some pre-existing chronic disease (Table 2). Chronic diseases were more common in Group 1 than in Group 2. Of the patients in Groups 1 and 2, 25 and 13%, respectively, had previously been referred for consultation at the child psychiatric clinic or to a psychologist.

In Group 1 the gynaecological examination did not automatically include the examination of the vagina with a speculum. Inspection of the genitalia and sonography were most often sufficient for the diagnosis and visualization of the vagina with speculum was needed in 24% of the patients (Table 3). In Group 2, 68% of the patients underwent a routine gynaecological examination with

instruments. Vaginoscopy was performed on 5 girls in Group 1 and on one girl in Group 2, in 5 cases under anaesthesia. There were three abnormal findings in vaginoscopy, all in Group 1: ectopic ureter, vaginal foreign body and bacterial vaginitis.

Thirty-seven percent of the patients in both groups underwent sonography, usually by the trans-abdominal technique. In Group 1, sonography was usually required to evaluate the uterus or the hormonal activity of the ovaries, or to exclude tumours. In Group 2 sonography was usually employed to diagnose pregnancy or pregnancy disorders. Diagnostic sonographic findings were more common in Group 2.

There were 10 patients who were referred to the hospital because of urgent medical needs in Group 1 and 18 in Group 2. The average number of visits per patient for an urgent problem was 1.3 in Group 1 and 1.8 in Group 2. None of the patients in Group 1, but 8 of the 18 patients in Group 2, needed operative treatment. Problems were encountered in six of the eight patients operated on, owing to the inexperience of the initial examiner. The need for a sonography in combination with the gynaecological examination was not initially recognized and control visits were scheduled late. Due to these factors in two cases operative treatment of large symptomatic ovarian tumours

Table 2. Chronic diseases in childhood gynaecological patients.

Disease	Group one (n = 117)	Group two (n = 87)
Diabetes	4	1
Problems in pubertal development	6	4
Neurologic disease	5	3
Malignant disease	3	0
Mental symptoms	4	2
Endocrinological disorders	3	2
Congenital malformations	4	3
Asthma and allergy	6	2
Eating disorders	0	2
Others	7	2
All	42	21

* One patient may have several chronic diseases.

Table 3. Examinations made of children, with normal and abnormal findings (%).

	Group 1 (n = 117)			Group 2 (n = 87)		
	Normal	Abnormal	Not made	Normal	Abnormal	Not made
Inspection	54	28	18	72	13	15
Speculum	22	2	76	58	10	32
Vaginoscopy	2	3	95	1	0	99
Rectal palpation	18	0	82	13	3	84
Vaginal palpation	21	2	77	47	12	41
Ultrasound	34	3	63	18	18	64
Microbiology	41	3	56	31	6	63
Pap smear	42	3	55	30	10	60
Any finding	51	47	2	44	52	4

*One of 5 vaginoscopies was performed without anaesthesia.

was delayed and one patient was operated on twice because an imperforate hymen was diagnosed only after a laparotomy. In three patients the diagnosis of appendicitis was problematic.

The diagnoses among the patients in Group 1 were: precocious puberty 16, vulvitis 17 and other genital conditions 8, suspected child sexual abuse 15, menstrual disorders 12 and normal findings 21. In Group 2 the most common diagnoses were: early pregnancy (seeking abortion) 20, pregnancy disorders 3, sexually transmitted diseases 9, neoplasias 5 and normal findings 11.

Altogether 23 girls were examined on account of suspected sexual abuse, only two of whom were from Group 2. Seventeen of these girls were under 10 years of age. On physical examination somatic findings (changes in the hymen or in the vulvar area or sexually transmitted diseases) strongly suggestive of sexual abuse were found in 8 girls. Two more girls had changes possibly indicative of abuse, (vulvar irritation, anal scarring or decreased tonus of the anal sphincter). Of these 23 patients 18 underwent psychiatric examination. Seven of these patients were diagnosed to have been subjected to sexual abuse. In 9 patients the psychiatric diagnosis remained unclear but suggestive of abuse. In two patients the psychiatric examination excluded sexual abuse. Five patients were not considered to need psychiatric evaluation since in the gynaecological examination a somatic condition causing their symptoms was found. The behaviour of eight patients during the gynaecological examination was recognized as unusual for their age; two girls were psychotic, four girls were so afraid that no examination was possible at the first visit and two girls seemed to be unusually relaxed and easy to examine. In five of these girls evincing abnormal behaviour during paediatric and gynaecological examination psychiatric examination confirmed the sexual abuse and in three the results were suggestive.

Thirty-one percent of patients in Group 1 and 13% in Group 2 visited the gynaecologist mainly for diagnostic purposes, such as evaluation of ovarian activity or suspected precocious puberty, and were treated in the referring clinic. In Group 1, 10% had local vulvar treatment and 4% received systemic antibiotic treatment by the gynaecologist. In Group

2, 21% of the patients underwent legal induced abortion and 13% other operative treatments. Five patients in Group 2 and 1 patient in Group 1 underwent laparotomy. Eighteen percent of the patients in Group 1 and 26% in Group 2 attended a subsequent control visit at the gynaecological outpatient clinic.

Discussion

This paper describes the gynaecological problems in childhood and early adolescence seen at a tertiary level referral hospital. The range of gynaecological problems in childhood and adolescence is wide. The primary health care system in Finland provides good services through general practitioners in child health care centres and schools. Hospital paediatricians who were aware of the availability of gynaecological services for children referred 72% of the patients to the special clinic. Almost half of the girls visiting the special clinic had a pre-existing health problem but the gynaecological problem was, in many cases unrelated to their primary condition. The gynaecological complaints of the girls in Group 1 represent the typical problems in this age group. The small number of girls remitted direct from primary care to the special clinic would lead one to suspect that there must be a considerable need for gynaecological care for children and adolescents which is not yet satisfied.

Children and adolescents would benefit from special services by an experienced children's gynaecologist. An experienced child gynaecologist can often arrive at a diagnosis in this age group only by inspection of the vulva, sonography and laboratory tests. With appropriate gynaecological examination techniques the whole vulvar area and at least one-third of the vagina can be visualized without instruments in 98% of prepubertal girls (6). The uterus and ovaries can be visualized by sonography. In this study, instrumentation was needed to examine 29% of the patients in Group 1. In Group 2 the figure was 68% and only 10% yielded an abnormal finding in this examination. Instruments may be used in the examination at later visits as the patient matures.

According to our findings, the need for special gynaecological care was better recognized for prepubertal patients than for adolescents. The patients in Group 2 who were examined as urgent cases, all adolescents, clearly needed special care. The doctors on duty did not know the problems of this age group well enough, and this caused extra visits, delays in diagnosis and treatment problems. Special examination techniques and the right environment are also of utmost importance for the adolescents. Adolescents themselves prefer to consult a female doctor (7).

Very special attention is also called for in the treatment of victims of child sexual abuse and severely physically or mentally handicapped girls. The physician examining children, possibly sexually abused, with genital symptoms must be familiar with the normal and abnormal findings in different age groups in order to make a correct diagnosis and to avoid mistakes. The examiner must also be able to communicate with children who have emotional traumas. In our clinic a paediatrician and the child gynaecologist together examine girls with suspected sexual abuse. Gynaecological examination, if appropriately undertaken, can be a therapeutic experience and may help a young girl to build up her female identity.

Children's gynaecological complaints have long been underestimated and overlooked, but are real. Organized special services make it possible for gynaecologists to acquire further knowledge and better skills in this new

field. Modern sonography is an excellent non-invasive tool in child gynaecology. Gynaecologists should be encouraged to acquire the knowledge and skills essential in the gynaecological examination and care of children and adolescents. Paediatricians, family physicians and parents should also be encouraged to listen to their children complaints and seek help for them when it is needed.

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Vulvar symptoms in paediatric and adolescent patients

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Vulvovaginal symptoms in children and young adolescents are not yet very well understood, nor is the actual incidence known. This study evaluates the character and possible infectious aetiology of vulvar symptoms of females aged up to 16 y. The signs, symptoms and bacteriological findings of 68 consecutive cases were studied. The study was conducted in the University Hospital of Tampere at a special gynaecological consultation clinic for children and adolescents. Sixty-eight patients were included in the study: 48 girls (71%) were prepubertal, at Tanner stage MIP1, 26 patients were 2–4-y-old and 15 were 5–7-y-old. The duration of symptoms was known for 46 patients: 41% had had symptoms for >1 mo and 20% for >6 mo. Forty-eight patients had abnormal clinical findings on examination and 16 (33%) of them had an infectious aetiology. *Streptococcus pyogenes* infection was identified in 11 (16%) patients, all of whom had symptoms. *Candida* was identified in 6 (9%) patients. No infectious aetiology was found among 26 patients who had symptoms and abnormal clinical findings. Vulvovaginal symptoms during childhood are more common among younger children (<7 y). In 67% of patients no infectious aetiology could be found. Samples for microbiological culture should be taken from symptomatic patients and symptomatic areas. Cultures of *Candida* and bacteria are necessary but usually sufficient. If a microbiological aetiology is established, treatment can be assigned accordingly.

Patients with vulvar symptoms and findings but with an unclear aetiology need support and advice on proper hygiene and can intermittently use mild corticosteroids locally.

Key words: Childhood, genital findings, sexual abuse, vaginitis, vulvitis

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Vulvovaginal symptoms and signs of vulvar inflammation are among the most common reasons for gynaecological concern in prepubertal girls. At a gynaecological outpatient clinic for children and adolescents 23% of the patients were seen because of local genital symptoms (1). After the neonatal period the effect of maternal oestrogens wanes and disappears and the mucosa at the vulvar area becomes atrophic and sensitive to irritants and microbial pathogens. Before puberty the vulva is anatomically unprotected, since there are no labia minora or pubic hair and the labia majora are flat.

Vulvovaginal symptoms can be caused by local irritants, foreign bodies and bacterial infections. Poor hygiene is considered to be one of the major causes of vulvar symptoms (2). *Streptococcus pyogenes*, *Haemophilus influenzae* and *Candida* are pathogens which can cause symptomatic vulvitis in periadolescent girls (3–6). There is an apparent lack of knowledge of how to examine and treat vulvar problems during childhood (2). However, such knowledge is clearly important for appropriate care of young girls and also in the examination of children with a history of sexual abuse.

This study aimed to elucidate the role of an infectious

aetiology of vulvar problems of children and adolescents. The symptoms, clinical evaluation and aetiology are described of vulvar complaints among girls aged 16 and under, in 68 consecutive cases referred for consultation to a university clinic.

Patients and methods

All patients aged 16 or younger referred to the unit of Pediatric and Adolescent Gynecology at Tampere University Hospital because of problems in the vulvar area during a 30-mo period from April 1992 to September 1994 were included. Tampere University Hospital serves a population of 460 000 as a secondary referral centre and 1.3 million inhabitants as a tertiary referral centre. The Department of Obstetrics and Gynecology has a special consultation clinic for children and adolescents under 16 y of age. This clinic functions 1 afternoon weekly with 4–7 visits wk⁻¹ and 200 visits y⁻¹. The patients at this clinic are referred either from other hospital clinics (87%) or from primary care (13%) (1).

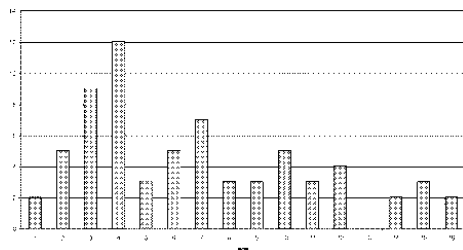


Fig. 1. Age distribution of patients ($n = 68$).

Sixty-eight patients entered the study: 33 (49%) patients were remitted from primary care, 26 (38%) from the Department of Pediatrics, 5 (7%) from the Department of Child Psychiatry and the remaining 4 from other hospital clinics. The patients were all examined by a gynaecologist with experience in child and adolescent gynaecology. The vulva was inspected thoroughly in every case. Most of the preadolescent patients were examined on the examination table in a frog-leg position (7) or in a position where the girl kept her heels at the edge of the table with her knees maximally flexed. The very young children were examined in their parent's lap. Adolescents were examined in the normal lithotomy position. Labia majorae, mons pubes and the anal region were carefully inspected using a good light source and a colposcope if needed. Labial separation and traction methods were used to visualize the vestibulum, introitus, hymen and the outer third of the vagina (8). The vagina was inspected with the help of a speculum or by vaginoscopy, only if indicated by symptoms or clinical findings. Likewise, rectal or vaginal bimanual palpation and sonography were carried out when clinically indicated.

Microbiological samples, Gram stain and a Pap smear were obtained from the vulva and vagina from all patients irrespective of their symptoms and clinical findings when this was possible without causing too much discomfort. Q-tips were moistened in saline before sampling. The swab samples were cultured on

Table 1. Reasons for referral.

	<i>n</i>	%
Vulvitis, vulvovaginitis	20	29
Leucorrhoea	12	18
Labia synechia	9	13
Dermatological problem	4	6
Urinary symptoms	6	9
Vaginal bleeding	5	7
Suspected foreign body	2	3
Other ^a	10	15
All	68	100

^a Including: suspected sexual abuse 4, abdominal pain 2, trauma 2, vulvar pain 2 patients.

Table 2. Symptoms reported by the patient or guardian and signs observed in the examination.

	<i>n</i>	%
Leucorrhoea	22	32
Itch	14	21
Burning, pain	15	22
Genital redness	9	13
Discharge, bloody	7	10
Urinary symptoms	20	29
Rash	2	3
Soreness	2	3
Pain	5	7
No symptoms	6	9
Other	4	6

One patient could have several symptoms or signs.

blood agar, human blood bilayer Tween agar, chocolate agar and gonococci -selective media aerobically with 5% carbon dioxide and on Dixon media aerobically. Samples for *Mycoplasma* and *Ureaplasma* were cultured on special media. The detection of *Chlamydia trachomatis* was carried out by a culture in McCoy cells. A Gram stain was made from the swabs in order to look for leucocytes, clue cells and various bacteria. The patients were treated according to their clinical and bacteriological findings. The patients were asked to attend a control visit or to contact the clinic if their symptoms continued. The study was approved by the hospital ethics committee.

Results

The age distribution of the 68 patients is presented in Fig. 1. Vulvar problems were most common in girls aged 2–4 y, with 26 (38%) patients, and 5–7 y, with 15 (22%) patients.

Forty-eight girls (71%) were prepubertal (Tanner stage M1P1) and 20 (29%) were in different stages of pubertal development.

The most common reasons for referral to the examination were vaginal discharge, signs of vulvar infection (redness, itching, burning) and fusion of the labia minora (Table 1). The symptoms are presented in Table 2. In total, 62 patients had symptoms or signs: 44 (70%) of them had abnormal findings on the gynaecological examination (= abnormal clinical finding) and 18 (30%) had normal findings. Six asymptomatic patients were examined, two patients because of labial fusion and four because of suspicion of sexual abuse. Sexual abuse was also considered in nine patients with symptoms.

Many patients had had long-standing symptoms. The mean duration of symptoms was 134 d (range 3 d to 3 y), i.e. 19 wk among the 46 (68%) patients from whom this information was available. Nineteen (41%) of these patients had had symptoms for 1–6 mo before referral and 9 (20%) patients had had symptoms for over 6 mo.

Table 3. Patients examined within 1 wk of the beginning of symptoms.

Age	Symptom or sign	Diagnosis
2.8	Urinary retention	Suspected sexual abuse
3.8	Redness, rash	Kawasaki disease
4.0	Vulvar contusion	perineal contusion
6.6	Vaginal bleeding	Vulvar synechia
8.9	Vulvar contusion	Vulvar contusion
9.7	Vaginal bleeding	Vaginal bleeding
12.4	Pain, redness	Vulvitis NOS

NOS: not otherwise specified.

Only 7 (10%) patients had had symptoms for 1 wk or less (Table 3).

In gynaecological examination 48 patients (71%) had abnormal clinical findings, i.e. redness, leucorrhoea or labial synechia (Table 4). Most abnormal clinical findings were identified on vulvar inspection. The frequency of abnormal results as regards microbiology and Pap smears is presented in Table 5. No samples were obtained from five patients. Clinically significant results were obtained in bacterial cultures, yeast cultures and Pap smears. There were no cases of *Gonorrhoea*, *Chlamydia*, *Mycoplasma* or *Ureaplasma* infection.

Eleven patients had a *S. pyogenes* infection and all of them had symptoms and abnormal clinical findings (Table 6). Nine of them were prepubertal. In six of the patients with the *S. pyogenes* infection samples were taken for culture from both the vulva and vagina and in every case all cultures confirmed the infection. The duration of symptoms among these patients varied from 14 to 150 d.

Six patients, one of them pubertal, had a *Candida* infection. *Candida* was cultured from the symptomatic area, either the vulva or vagina. Two patients had a *Gardnerella vaginalis* infection, both pubertal. There were only two asymptomatic patients with findings in microbiological cultures, one *Candida* and one *Haemophilus parainfluenzae*. No microbiological aetiology was found for 26 patients with both symptoms and clinical findings.

The possibility of sexual abuse was considered in 13

Table 4. Examinations and abnormal clinical findings.

Method	No. (% of total)	Abnormal finding (% of tests)
Vulvar inspection	68 (100)	42 (62)
Vaginal inspection with speculum	9 (13)	1 (11)
Vaginoscopy	9 (13)	4 (44)
Colposcopy	2 (3)	1 (50)
Vaginal palpation	3 (4)	1 (33)
Rectal palpation	14 (21)	0 (0)
Sonography	8 (12)	0 (0)
Any finding	68 (100)	48 (71)

One patient could have more than one abnormal clinical finding.

Table 5. Samples showing abnormal results.

Test	No. (% of total)	Abnormal result (% of tests)
Pap smear	22 (32)	6 (27)
Bacterial culture	56 (82)	13 (23)
<i>Candida</i> culture	59 (87)	4 (7)
Gram stain	29 (43)	1 (2)
<i>Gonococcus</i>	23 (34)	0
<i>Chlamydia</i>	18 (26)	0
<i>Mycoplasma</i>	11 (16)	0

of the patients. Six girls were seen because they had given a history suggestive of sexual abuse. In four cases the examination was based on the mother's suspicion and three patients had somatic symptoms which raised the suspicion. Three patients had no abnormal clinical findings on examination, nine had findings in the vulvar area such as redness and/or discharge and one girl had palpable abdominal tenderness. Nine of these patients had normal flora, two had *S. pyogenes* infection, and one had *H. parainfluenzae* infection. One patient had exophytic condylomas. The patients' somatic clinical findings supported the suspicion of sexual abuse in two patients; one girl had exophytic condylomas and the other an enlarged anal opening and vulvar irritation.

Streptococcus pyogenes infections were treated with oral antibiotics in seven cases and with local treatment in one case. Three patients did not need any treatment because their symptoms had resolved spontaneously. Five patients with *Candida* infection received local antimycotic treatment and one patient with *Candida* had concomitant vulvar synechia which was opened mechanically. Both patients with *Gardnerella vaginalis* took a course of oral metronidazole treatment. One of the three *Klebsiella pneumoniae* infections was treated with an oral antibiotic, amoxicillin. *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Pseudomonas* and *H. parainfluenzae* infections can be considered as disturbances of the bacterial flora and do not require oral antibiotic treatment.

Seventeen patients with no bacteriological findings

Table 6. Association between clinical findings and microbiological results.

	Abnormal clinical findings (n)	Normal clinical findings (n)
<i>Streptococcus pyogenes</i>	11	0
<i>Candida</i>	4	2
<i>Gardnerella vaginalis</i>	1	1
<i>Streptococcus pneumoniae</i>	1	0
<i>Haemophilus parainfluenzae</i>	0	1
<i>Klebsiella pneumoniae</i>	1	2
<i>Klebsiella oxytoca</i>	1	0
<i>Pseudomonas</i>	1	0
Any pathogen	16	5
Normal flora	25	15
No cultures	7	0

Four patients had two pathogens.

were treated with topical creams containing corticosteroid and/or an antifungal drug, five with local oestrogen preparations and three with systemic antibiotics. The choice of the treatment was guided by clinical impression on examination and could be criticized afterwards. Labial synechiae were opened with a wet cottonbud without anaesthesia in three patients. One skin lesion, a birth mark, was removed and one patient with vulvar condylomas received laser treatment. All patients were advised about the importance about proper hygiene. Sixteen patients without clinically relevant bacteriological findings did not receive any specific treatment.

Discussion

Vulvar problems are considered to be the most common gynaecological conditions of children and young adolescents. Symptoms and signs are most common between the ages of 2 and 7 y, before any oestrogen effect has appeared. The lack of an oestrogen effect and anatomical protection together with poor hygiene predispose children to vulvar symptoms and infections (2). *Streptococcus pyogenes*, *H. influenzae* and *Candida* are the most important pathogens which cause childhood vulvovaginitis.

As pubertal development starts, the oestrogen effect begins to protect the mucosa of the vulva and vagina. The normal vaginal flora and pathogens of adult women are strikingly different from those among children. Among the present patients 20 (29%) had entered puberty but only one had a *S. pyogenes* and one a *Candida* infection. In contrast, 10 of the prepubertal girls had a *S. pyogenes* infection. This agrees with the results of previous studies (2, 5). *Gardnerella vaginalis* was identified in two pubertal patients. Bacterial vaginosis caused by *G. vaginalis* is quite common in adult women, but seldom diagnosed before puberty.

Vulvar symptoms and findings in young patients are often not associated with any microbiological or other specific aetiology (9). In the present study, 18 patients with symptoms had no abnormal clinical findings, while 26 girls had symptoms and abnormal clinical findings but no specific microbes could be cultured. Poor hygiene and chemical irritants together with the lack of an oestrogen effect are the most likely reasons for vulvar irritation in such cases. Vulvar irritation may predispose girls to bacterial infections and labial synechiae.

The long duration of symptoms before examination, even in patients with *S. pyogenes* vulvitis, shows that paediatric vulvar problems are not very well recognized among parents and physicians. There were no cases of acute bacterial vulvitis among the patients examined within 1 wk of the beginning of the symptoms. Half of the patients in the study came from hospital clinics, where physicians are aware of the special gynaecological services for children. Children from primary care

are underrepresented in the material, since the patients were probably remitted to the hospital clinic after the expectation period and prior treatment attempts.

With appropriate examination techniques the whole vulva, anal region and one-third of the vagina can be easily visualized. Examination under anaesthesia is very seldom needed. A problem in investigating vulvar symptoms and vaginal discharge among children is the collection of microbiological samples. The use of a cotton bud, even a wet one, is uncomfortable and may be painful for the child. This limits the number of samples that can be taken. In the present study, in all cases of *S. pyogenes* the cultures were positive in samples from both the vagina and vulva. *Candida* was cultured in samples from the symptomatic areas. Only one patient without symptoms or clinical findings had a positive but clinically not significant microbiological finding (*H. parainfluenzae*). According to this study in children, microbiological sampling can be limited to symptomatic patients and areas. It is often sufficient to take samples from the vulva. If vaginal samples are needed, a plastic suction catheter can replace a cotton bud.

Nowadays physicians often have to consider the possibility of sexual abuse when examining children. Most children (84%) referred for sexual abuse evaluation because of anogenital symptoms have not been found to have somatic findings suggestive or indicative of abuse (10). In the present material 2 patients out of 13 (15%) where sexual abuse was considered had somatic findings suggestive of abuse. In the evaluation of child sexual abuse it is important to know the normal anatomic findings and variations in the vulvar area and hymen, and changes in these areas caused by sexual abuse. Physicians should recognize the diseases causing vulvar symptoms and findings in children: infections, vulvar synechiae, skin diseases, trauma and anatomic variations. It is important to bear in mind the diagnostics of infections, sexually transmitted diseases and pregnancy testing.

Vulvar symptoms of children cause distress to the patient and her family. Patients whose symptoms can be related to a microbiological aetiology can be treated with specific systemic or local antibiotics. Patients with symptoms and findings but with an unresolved aetiology should be advised about proper hygiene, told to avoid chemical irritants and be advised to use ointments to protect the mucosae. Symptoms can be relieved by the intermittent use of mild corticosteroids locally. The possibility of control visits to the physician also gives assurance to the parents. With advancing puberty, vulvar problems of childhood usually disappear.

Conclusions

Knowledge and experience of evaluation of normal anatomy and different conditions causing vulvar symptoms in children are extremely important when physi-

cians evaluate childhood vulvar problems. Such experience is even more important when the possibility of child sexual abuse is considered. Sampling in the vulvar area requires special knowledge and techniques. Often the number of microbiological samples taken has to be limited because of the discomfort caused to the child. The present results imply that sampling can be limited to symptomatic patients and symptomatic areas. In 20% of cases a clear microbiological aetiology can be found and treatment assigned accordingly. In other patients with symptoms but unresolved aetiology, advice about proper hygiene, intermittent mild local treatment and control visits should be offered.

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Surgery for Ovarian Masses During Childhood and Adolescence: A Report of 79 Cases

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Abstract. *Study Objective:* Abdominal pain is a common symptom in female children and adolescents that may be caused by appendicitis, other gastrointestinal or urological conditions, or gynecological problems. This study evaluates retrospectively the preoperative work-up and the operative treatment of ovarian masses in young girls at our institution.

Settings: The medical records of all female patients aged 17 years or less operated on for an ovarian mass in 1971–1995 at the Tampere University Hospital were reviewed.

Results: Seventy-nine patients were identified. In the 1970's preoperative sonography was done on only 15% of the patients. In the 1990's the figure was 65%. Thirty-seven (47%) of all operations were emergency procedures; of these, 41% were performed by a gynecologist. Seven of the tumors were malignant. Thirty-four patients had a benign neoplasm and 26 had functional ovarian cysts. Eight patients were operated on for an adnexal torsion and four patients had other adnexal conditions. Unilateral salpingo-oophorectomy was performed on 20 patients, unilateral oophorectomy on 12 patients, and ovarian resection on 27 patients. An occasional appendectomy was performed on 37 patients.

Conclusions: Surgery for benign neoplasms and functional lesions seems to be too extensive. This is likely to be due to inadequate preoperative work-up and to the fact that many of the operations were performed on an emergency basis and by non-gynecologists. A gynecological examination with sonography should be included in the diagnostic work-up of a young girl's abdominal complaints. With a proper preoperative work-up adequate treatment, which often consists of expectation, can be chosen for the patient and subsequent problems related to fertility and abdominal complaints can be avoided.

Key Words. Ovarian masses—Ovarian neoplasms—Sonography—Surgery, ovarian—Tumors, pediatric—Adolescent females

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Introduction

Ovarian neoplasms constitute 1% of all childhood malignancies, and 8% of all malignant abdominal tumors of children are of ovarian origin.^{1,2} Of the ovarian neoplasms operated on during childhood or adolescence, 10%–30% are malignant.^{1,3,4} Benign neoplasms or functional cysts are, however, the most common ovarian masses during childhood and adolescence. Surgery on benign ovarian neoplasms and functional ovarian lesions may reduce the follicular capacity of the ovaries and cause adhesions. Laparotomy may also cause lower abdominal symptoms later in life. The preoperative diagnostic work-up of pediatric patients with ovarian masses should include gynecological sonography and an evaluation of the hormonal status and of serum tumor markers. If sonography suggests that there is a neoplastic or inflammatory process, computerized tomography (CT) or magnetic resonance imaging (MRI) may provide further information about the site of origin and the nature of the pelvic mass. After a thorough diagnostic work-up it is easier to choose proper therapy for the patient. Often observation and expectation are enough and even tumors can be operated on conservatively. Laparoscopic surgery might provide more satisfactory results.⁵ This study evaluates the clinical practice and outcome of the operative treatment of ovarian masses in childhood and adolescence at our institution over the past 25 years.

Patients, Materials, and Methods

All girls up to 17 years of age who had been operated on because of an ovarian mass at The Tampere University Hospital, Tampere, Finland from 1971 through 1995 were included. Information was collected retrospectively from the hospital medical records. The following data were recorded: presenting symptoms, preoperative diagnostic work-up, preoperative sonography, details of op-

erations, histological diagnosis, and later gynecological and obstetrical outcome. The histology of the malignant neoplasms was reviewed (A.R.).

Results

Age and Symptoms

Seventy-nine patients were identified. Symptoms in relation to the age groups are presented in Table 1.

Six of the patients were premenarchal and 73 were postmenarchal. The most common presenting symptoms were abdominal pain (78%), palpable abdominal tenderness (25%), vomiting (18%), and abdominal swelling (14%).

Diagnostic Work-up

Thirty patients were primarily examined by a surgeon, 5 by a pediatrician, and 44 patients by a gynecologist. Surgeons and pediatricians consulted a gynecologist 17 times preoperatively and 19 times during the operation. In three cases a gynecologist was not consulted at all. Thirty-eight patients underwent sonography. In the 1970's sonography was done only on 15% (3/20) of the patients, and during the last five years of the study on 65% (17/26) of the patients. Sonography agreed with the surgical findings in 100% during the 1970's, in 83% during the 1980's, and in 71% during the 1990's (Table 2).

The interval from the symptoms' debut to the time of treatment varied from emergency treatment to an expectation period of more than six months. Eighteen (23%) of the patients were operated on within 24 hours from the beginning of the symptoms, 10 (13%) within 2 to 3 days, 15 (19%) within 4 to 7 days, 15 (19%) within 1 to 4 weeks, 16 (20%) within 1 to 6 months, and the remaining 5 (6%) after an observation period of at least six months.

Surgery and Histology

Of all operations, 52 (66%) were performed by a gynecologist and 27 (36%) by a surgeon. Thirty-seven (47%)

Table 2. Accuracy of Sonography

	Sonography		(Patients)	(Patients)
	+	-	Not done	Total
1971-1980				
Malignant neoplasia	1	0	2	3
Benign neoplasia	2	0	10	12
Functional tumor	0	0	3	3
Ovarian torsion, necrosis	0	0	2	2
Total	3	0	17	20
1981-1990				
Malignant neoplasia	1	0	0	1
Benign neoplasia	9	0	7	16
Functional tumor	3	2	8	13
Ovarian torsion, necrosis	2	1	0	3
Total	15	3	15	33
1991-1995				
Malignant neoplasia	3	0	0	3
Benign neoplasia	4	0	4	8
Functional tumor	4	3	5	12
Necrosis	0	2	0	2
Adhesions	0	1	0	1
Total	11	6	9	26

of the operations were emergency procedures. Of all ovarian neoplasms, 7 (9%) were malignant, 34 (43%) were benign, and 26 (33%) were functional cysts, half of which were histologically verified. Eight patients (10%) had ovarian torsion, and four patients were operated on because of a suspected ovarian mass, while they actually had other gynecological conditions. Two of the patients also had appendicitis (Tables 3, 4, and 5). Among the 7 malignant tumors there were 3 mucinous cystadenocarcinomas (one with a low malignant potential), 1 sarcoma, 1 small cell carcinoma, 1 arrhenoblastoma, and 1 juvenile granulosa cell tumor.

All malignant neoplasms were operated on by a gynecologist; the primary operation was either a unilateral oophorectomy or salpingo-oophorectomy. In the cases of benign neoplasms, oophorectomy or salpingo-oophorectomy was performed on 19 and an ovarian resection on 15 of the patients. Twenty-nine of the 34

Table 1. Symptoms in Different Age Groups*

	0-6 y	7-13 y	14-17 y	Total	
	n = 1	n = 13	n = 65	n = 79	(%)
Abdominal pain		9	53	62	78
Abdominal swelling		2	9	11	14
Palpable abdominal tenderness		2	18	20	25
Vomiting		5	9	14	18
Menstrual disorder		0	4	4	5
Endocrinological symptoms		2	1	3	4
Fatigue		1	1	2	3
Vaginal discharge		0	1	1	1
Urinary symptoms		1	0	1	1
Fever		0	2	2	3
Incidental finding	1	0	4	5	6

*One patient could have had several symptoms.

Table 3. Histology of Ovarian Tumors

	Patients
Malignant	
Mucinous cystadenoma, borderline	1
Arrhenoblastoma	1
Small cell carcinoma	1
Carcinosarcoma	1
Mucinous cystadenocarcinoma	2
Juvenile granulosa cell tumor	1
Benign	
Serous cystadenoma	5
Mucinous cystadenoma	8
Benign teratoma	20
Fibroma	1
Functional	
Luteal or follicular cyst	13
Ovarian necrosis, due to torsion	8
Clinical diagnosis	
Cyst rupture	10
Ovarian cyst	3
Others	4

Others histologies include adhesions, parovarian cyst, serous tubal cyst, and normal findings.

patients with benign neoplasms were operated on by a gynecologist (Tables 4 and 5). In the eight cases of ovarian torsion, removal of the ovary or tuba was necessary. Twenty-six patients had a functional ovarian cyst and 13 of them were histologically verified. More conservative techniques were used to treat functional cysts (i.e., ovarian resection, suturation, or puncture). Surgical procedures on the contralateral ovary were performed in 13 patients with benign tumors, in 11 cases by a gynecologist. Incidental appendectomy was performed on 33 patients; of the 27 patients operated by a surgeon 23 underwent appendectomy.

Thirty-seven laparotomies were made as emergency procedures, 10 because of a neoplasm. Two of the patients operated on in an emergency for a neoplasm had a malignant tumor. Emergency procedures were performed on 18 patients for functional cysts, on 4 for torsion, and on 5 for other adnexal conditions. Twenty-three (62%) of the emergency operations were performed by a surgeon. Gynecologists performed 14 (41%) of the emergency operations. Of these, 6 were for neoplastic tumors, 4 for a functional cyst, and 4 for some other adnexal condition. Fourteen of the patients operated on in an emergency by a surgeon had functional cysts.

Follow-up

Of the patients with malignant tumors, 3 are alive and 4 patients have died, with a mean postoperative survival time of 22 months (range 6 to 50 months). Further gynecological and obstetrical data were available on about 33 patients (46%) with benign neoplasms or functional ovarian cysts; 26 of these patients were older than 25 at the time of last visit. Twenty-six of these 33 patients had

been pregnant. Twenty-one of these women have delivered 34 babies. Ten patients have had an induced abortion and 7 patients spontaneous abortion. Ten patients have received in-patient treatment for gynecological infections. Twelve patients have had abdominal pain requiring hospitalization, and 6 women have had recurrent ovarian cysts. Four women now aged 31 to 44 years have received infertility treatment at hospital level.

Discussion

According to previous studies, 64% of ovarian masses encountered in children and adolescents are neoplastic while 36% of masses are nonneoplastic or physiologic.⁶ Thirty-five percent of these neoplasms are malignant. In the present study benign neoplasms constituted 43%, malignant neoplasms 9%, and functional cysts 33% of the cases. The malignancy rate of the neoplasms was 16%. Malignant neoplasms require proper preoperative work-up and staging followed by operative treatment. If malignancy can be ruled out, cysts and other functional ovarian lesions can often be successfully treated by expectation and observation.⁷

The symptoms experienced by our patients, like abdominal pain (78%), palpable tenderness (25%), and vomiting (18%) are also typical for appendicitis. This accounts for the primary examination by a non-gynecologist in 44 (56%) cases, and to the great proportion of operations performed on an emergency basis. Malignant tumors and symptomatic ovarian torsions should, of course, be operated without delay. Still, since 72 (91%) of the ovarian masses in our material were benign and 26 of these actually functional cysts, many patients were obviously over-treated.

If persistent lower abdominal pain or an ovarian mass is present in a young female patient it is essential that a thorough clinical work-up be performed and a correct diagnosis reached. A gynecological examination with sonography is compulsory, and an evaluation of the hormonal status of the patient together with a search for any elevated tumor markers should be considered. Sonography is an excellent noninvasive method to examine the female pelvis in the diagnostic work-up of gynecological disorders regardless of the patient's age. Sonography is a reliable method for determining the site of origin of a mass and can even suggest the specific diagnosis in pediatric patients with ovarian neoplasms.⁸ The use of sonography helps to avoid unnecessary surgery.⁹ If sonography identifies a neoplasm a CT and/or MRI may give additional information.

The rate of gynecological sonographies performed increased from 15% of the patients in the 1970's to 65% in the 1990's. The diagnostic value of sonography in our study seemed to be better in the 1970's than in the 1980's or 1990's. This can be explained by the fact that initially

Table 4. Surgical Procedures and Histology in Benign Tumors, Gynecologists

Diagnosis	Total	S-o-ect. O-ect.	Salpingectomy	Ovarian Resection	Puncture Suturation	Diagnostic Laparoscopy	Appendectomy	Procedure on Other Ovary
Neoplasms	29	16		13			9	6
Functional tumors	11			7	1	2	1	2
Ovarian torsion, necrosis	4	3	1					3
Appendicitis, or others	2		1			2		
Total	46	19	2	20	1	4	10	11

Abbreviations: O-ect., oophorectomy; S-o-ect., salpingo-oophorectomy.

Table 5. Surgical Procedures and Histology in Benign Tumors, Pediatric and General Surgeons

Diagnosis	Total	S-o-ect. O-ect.	Salpingectomy	Ovarian Resection	Puncture Suturation	Appendectomy	Procedure on Other Ovary
Neoplasms	5	3		2		4	
Functional tumors	10			5	5	13	
Ovarian torsion, necrosis	8	4			4	2	1
Appendicitis, or others	4		1		3	3	1
All	27	7	1	7	12	23	2

Abbreviations: O-ect., oophorectomy; S-o-ect., salpingo-oophorectomy.

sonographies of children were usually done by experts in the field. In the 1990's the volume of examinations has increased markedly with a concomitant reduction in true positive findings. Sonography is currently performed by every gynecologist, and not everybody is familiar with the gynecological problems of children and adolescents or with the examination techniques needed for sonography of children and adolescents. All this considered, preoperative sonography was still accurate in 64% of the patients in the 1990's. Importantly, nevertheless, laparotomy was performed on 35% of the patients without prior sonographic examination of the pelvis in the 1990s.

The surgical procedures for benign neoplasms and functional cysts were quite extensive in this study. In the treatment of benign neoplasms, the ovary was completely removed from 19 patients and the contralateral ovary manipulated in 6. The operative treatment of functional cysts including ovarian resection was done in 12 patients and the "healthy ovary" was manipulated in 2 patients. The true neoplasms were mainly operated on by gynecologists. The functional cysts were often first diagnosed during laparotomy, which in 19 patients operated on would not have been at all indicated according to the surgical and histological findings; the tumors were small or already ruptured, there was no intra-abdominal bleeding, and the appendix was normal.

After menarche abdominal symptoms related to the different phases of the menstrual cycle are common. One should bear this in mind, especially if a young female patient has lower abdominal complaints, and take the time for appropriate preoperative diagnostics, which often includes expectancy and observation. The differential diagnosis of appendicitis is notoriously difficult but sonography is informative also in this respect.¹⁰

Many of the patients in the present study subsequently

became pregnant. However, at least four women have needed infertility treatment at hospital level thus far. There was no specific etiology for the infertility that could be related to the previous operation, and the number of cases is too small to allow any definite conclusions. Many of the patients have later had abdominal pain or recurrent cysts. Further studies will be needed to determine the role of a laparotomy in causing gynecological and endocrinological problems later on in the life of patients who have undergone a gynecological operation in childhood or adolescence.

Conclusions

The preoperative work-up of female children and adolescents with abdominal complaints was insufficient in this group of patients. The surgical procedures appear to have been often quite extensive or even unnecessary, and the healthy ovary was often manipulated. A trend favoring more thorough examinations, including sonography, emerged during the study period. Only very few patients need emergency operative treatment. Still, every young girl with lower abdominal pain or a suspected ovarian mass needs a thorough evaluation including sonography by an experienced gynecologist before laparotomy is performed. Improvements in the diagnostic work-up of appendicitis could prevent many unnecessary laparotomies and adnexal interventions. If a true neoplasm is found, it should be treated as conservatively as possible with modern operative techniques. The very common functional tumors can often be successfully treated by observation only.

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Use of percutaneous estrogen gel for induction of puberty in girls with Turner syndrome

Abbreviated title: Estradiol gel for induction of puberty

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Abstract

The aim of pubertal induction by estrogen in hypogonadic girls is to achieve physical and psychological development similar to that in natural puberty. We investigated the use of percutaneous estradiol gel for induction of puberty in girls with Turner syndrome (TS). Twenty-three girls with TS and hypogonadism were included in the study. The initial percutaneous dose of 0.1 mg ended as 1.5 mg in the fifth year. The efficacy of the treatment was monitored by measuring height, weight, skeletal age, pubertal status and serum hormone levels and gynecological ultrasonographic examinations throughout the study. Mean serum estradiol concentrations increased from 22.2 pmol/l at baseline to 162.2 pmol/l as mean FSH levels decreased from 77.4 IU/l to 19.2 IU/l after five years. There were no significant differences between GH users and non-users as regards height-SDS, weight-SDS, bone age acceleration or adult height. The development of secondary sexual characteristics, and uterine growth, progressed gradually during the study. All girls reached at least stage B4P4. With percutaneous estradiol gel the development of secondary sexual characteristics, and uterine growth, proceeded gradually, mimicking natural puberty. Estradiol gel was safe, easy to use and well accepted by the subjects and provides an excellent way to individualize pubertal induction.

Introduction

For girls with verified hypogonadism, induction of puberty followed by continuous estrogen replacement therapy is needed for several reasons. The development of secondary sexual characteristics, and the maturation of female identity during the induction of puberty are essential for such girls. Sufficient uterine growth and development of the endometrium, with menstrual periods, can be achieved, which later is needed if embryo transfer is considered during adult life (1). Growth hormone (GH) is a well-documented promoter of growth in girls with Turner syndrome (TS) and early started estrogen substitution therapy may also have a positive effect on the final height (2). Addition of low dose estrogen to a GH regimen has been shown to improve bone deposition and calcium metabolism in girls with TS (3). Estrogen at low doses has also been found to be beneficial as regards verbal and nonverbal memory in young girls with Turner syndrome (4).

The dosage and timing of GH and estrogen treatment during the induction of puberty is important. Chernausek *et al.* (5) used equine estrogen at a dose of 0.3 mg/d for six months, followed by 0.6 mg/d, with medroxyprogesterone acetate at 10 mg/d for 1 week each month for girls with TS, beginning at ages 12 and 15. Using these estrogen doses they concluded that delaying the initiation of estrogen therapy was advantageous to growth. The number of years of GH therapy prior to the initiation of estrogen treatment was the most important factor determining final height. Rosenfield *et al.* (6), on the other hand, found that using very low doses of systemic estradiol, starting with 0.2 mg of depot estradiol before the age of 15 to induce puberty in girls with TS who are also treated with GH, instead of using routine estrogen therapy, can result in increased final height. With transdermal nocturnal application of 17 β -estradiol patches it has been possible to mimic the appropriate levels and the diurnal pattern of serum 17 β -estradiol in early puberty (7).

The purpose of this study was to investigate the use of percutaneous estradiol gel for the induction of puberty in hypogonadal girls. We wanted to introduce a therapeutic programme for induction of puberty starting with low initial percutaneous estrogen doses and a gradual increase of doses, to mimic natural puberty, with satisfactory feminization and good compliance. The development of secondary sexual characteristics and uterine growth and the effects on bone maturation, growth and final height were studied.

Material and methods

Subjects

Twenty-three girls with TS (17 XO karyotypes and 6 mosaics) and hypogonadism were enrolled in an uncontrolled open multi-center study, which was carried out between 1992 and 1999. Hypogonadism was verified by elevated gonadotropin and low estrogen levels in the serum. The girls were over 12 years of age and had a skeletal age over 9 years at the onset of the study. One girl aged 10.7, who did not fulfil the age criterion, was accepted for treatment. Patients with previous or ongoing estrogen therapy were excluded. All five major pediatric endocrinology centers in Finland participated in the study and in recruitment and all eligible patients were included in the study. The study was approved by the ethics review boards of each of the hospitals. Written informed consent was obtained from each girl and her legal representative.

Treatment protocol

The study medication, developed by Orion Pharma, Finland, for percutaneous estrogen therapy, consisted of estradiol in hydroalcoholic gel. Single-dose sachets containing 0.1 mg estradiol were prepared specifically for the study. Sachets containing 0.5 mg estradiol in 0.5 g of gel and 1.0 mg in 1 g of gel are commercially available (Divigel[®], Orion Pharma, Finland). Increasing doses of estradiol gel were applied once daily on the skin of the lower trunk or

thighs, preferably in the evenings by the girl herself. The girls were instructed to wash their hands after the application. The estradiol doses were: 0.1 mg for the first year, 0.2 mg for the second, 0.5 mg for the third, 1.0 mg for the fourth and 1.5 mg for the fifth year. The doses used were chosen based on the experiences on estrogen replacement therapy on adults and the bioequivalence of oral estrogens, transdermal patches or estradiol gel. The starting dose of 0.1 mg of estradiol equalled to 0.13 mg of estradiol valerate or 0.04 mg of conjugated equine estrogen. The studies performed with Divigel have shown that transdermal estradiol in a hydro-alcoholic gel is absorbed at a comparable rate and in almost equal amount as oral estradiol valerate tablets. The total duration of the study treatment was five years. Starting from the third year a progestin test with 10 mg of medroxyprogesterone acetate daily for 10 days to induce menstrual bleeding was performed every six months. After a positive test result cyclic monthly progestin administration using the above dosage was started. If breakthrough bleeding occurred earlier, cyclic progestin was started. Compliance was assessed by asking the girls to return the unused medication.

Clinical follow-up and safety

Serum concentrations of estradiol, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were measured at every yearly visit. Annual assessment also included a GnRH test, and assay of DHEAS and testosterone. To evaluate absorption of the medication a serum estrogen profile was also obtained yearly: estradiol was not administered during the previous evening and estradiol concentrations were measured next morning before administration and 2 and 4 hours after administration of the medication. Serum estradiol concentrations were measured using a radioimmunoassay, with an analytical sensitivity of 0.02 nmol/l. Serum FSH and LH concentrations were measured using a time-resolved fluoroimmunoassay, both assays had the analytical sensitivity of 0.10 IU/l.

The efficacy of the treatment was assessed by following pubertal development and growth. Height, weight, skeletal age and pubertal status (according to Tanner) were evaluated every six months. Breast development was also evaluated, by measuring areolar and mamillar diameters. Heights were measured by standard methods, using a Harpenden stadiometer. Heights were analyzed as standard deviation scores. Ranke growth standards for girls with TS (8) were used for evaluating height and weight. Bone age X-rays were assessed according to Greulich and Pyle (9). Ten subjects had received GH for at least two years, mainly as part of a GH study protocol, always starting after 9 years of age. Use of GH was not a controlled variable in this study. Abdominal ultrasonography was carried out at baseline and every 6 months after one year of therapy to follow uterine growth and endometrial development. Timing of ultrasonography was not adjusted to any specific time of the menstrual period. Bone age radiographs were centrally read by one of the authors (IS) and ultrasonographies by another author (SP). The interpreters were blinded.

Blood pressure, hematological data, liver enzymes, fasting cholesterol, HDL cholesterol and triglycerides were investigated to evaluate the safety of the medication. Side-effects such as skin irritation and any other adverse events were recorded at every visit.

Data processing and statistical methods.

Descriptive statistics are presented for all continuous variables as means and standard deviations. The numbers and proportions of subjects were calculated for categorial variables. All girls who received study medication were included in the efficacy and safety analyses. No imputation of missing data was performed and all data available were used in the analyses. The statistical analyses were performed with SAS[®] for Windows.

Results

The age of the 23 girls at enrollment ranged from 10.7 to 17.7 years, the median being 13.6 years. One girl aged 10.7, who did not fulfill the age criterion, was accepted for treatment and taken into account in the analysis. All girls were of Caucasian origin. Compliance was good. The median use of medication was 100% in all but the 6-month (94.4%) and 4.5-year (93.1%) visits. Administration of the gel was easy. None of the girls had difficulties in using the therapy.

Hormone levels

The mean serum estradiol concentration at baseline was 22.2 pmol/l and it increased steadily to 162.2 pmol/l at five years of treatment. At the same time the mean FSH concentration decreased from 77.4 IU/l at baseline to 19.2 IU/l after five years and the mean LH concentration decreased from 20.6 IU/l to 6.6 IU/l. The concentrations of FSH and LH after stimulation with GnRH decreased as the study progressed and estrogen doses were increased. The decline of FSH and LH values at 60 minutes was statistically significant between every yearly test ($p < 0.01$). With estrogen doses of 1 mg and 1.5 mg there were however only slight elevations in FSH and LH concentrations in the GnRH tests (Figure 1). Absorption of estradiol from the gel was observed in the estrogen profile as a rise in concentrations after application of the gel (Figure 2). Individually, the estrogen profile was very variable. An elevation of mean serum DHEAS values from 4.67 $\mu\text{mol/l}$ to 6.53 $\mu\text{mol/l}$ over the five-year period was observed. Serum mean testosterone levels remained constantly low, ranging between 0.59 and 0.86 nmol/l during the study.

Growth

Ten girls had received GH during or before this study. The mean GH dose was 0.1 IU/kg/d and the mean duration of therapy 4.4 y (range 2.1–6.1 y). There were no significant differences between the GH users and non-users as regards height-SDS, weight-SDS, bone age acceleration or adult height. The adult height was 153.1 ± 4.8 cm in the whole group

(+1.08 SDS in the GH group and +1.05 SDS in the non-GH group). The mean age, height and weight, height- and weight-SDS and bone age at yearly visits is shown in Table 1.

Sexual characteristics

The pubertal stage advanced gradually along with the increasing estrogen doses (Figure 3). According to our data information on the pubertal status after five years of treatment was available on 83 % of the patients. Of these girls 79% reached B5 and 58% P5 stages. All girls had reached at least stage B4P4. Mean areolar diameter increased from 20 mm at baseline to 47 mm after five years of treatment. Breast development progressed gradually and symmetrically during the whole study. Treatment with GH did not have an effect on the development of secondary sexual characteristics.

Uterine development

Abdominal ultrasonographic data were obtained from 18 girls. Mean uterine length increased from 33 (15–66) mm (mean + range) at baseline to 67 (48–91) mm at five years of therapy. Mean uterine volume increased from 5.5 (1.7–12.6) ml at one year of treatment to 31.5 ml (8.2–82.8) ml at five years. Mean endometrial thickness increased gradually to 3.9–2.8 mm at 4–5 years of therapy (Figure 4). The maximum endometrial thickness measured during the study was 11 mm. Regular menstrual periods were induced with progestins, according to the protocol, between 2.5 and 3.5 years of treatment in 19 cases. In three cases regular progestins were started at 6 months because of spontaneous bleeding and in one case it was at 1.25 years.

Safety

Blood pressure remained normal. Mean fasting total cholesterol levels fell from 4.60 mmol/l (range 3.30–6.20) to 4.27 mmol/l (range 2.50–6.10) at five years, and a similar decline in triglyceride concentrations, from 1.11 mmol/l at baseline to 0.91 mmol/l after five years was observed. Mean levels of HDL cholesterol rose at the same time, from 1.29 mmol/l at baseline to 1.45 mmol/l after five years. Mean serum alanine transaminase levels remained

between 17 and 32 U/l throughout the study. A single ALAT level of 231 U/l was found in one case. Routine hematology results remained unaltered.

Side-effects and adverse events

Mild skin irritation after application of the medication was reported four times during the study. Spontaneous menstrual bleeding or spotting before the use of cyclic progestins was reported by 11 girls. During the cyclic estrogen/progesterone therapy 9 episodes of irregular bleeding were reported by five subjects. Two girls had transient amenorrhea and two had menorrhagia. Two girls left the study prematurely at 3.5 years. One did not like the gel and changed to another form of estrogen treatment, and the other girl moved abroad.

Some girls had preexisting conditions associated with TS: there were two cases of hypothyreosis, one of aortic coarctation, and two cases of ear infection. Adverse events reported during the study included three cases of abdominal pain and four cases of upper respiratory tract infection. As regards serious adverse events one subject developed anorexia nervosa and recovered from it, one girl with menorrhagia was diagnosed as having von Willebrand disease and one girl was diagnosed as having aortic aneurysm associated with TS.

Discussion

In this study our goal was to modify the induction of puberty in girls with Turner syndrome towards spontaneous pubertal development by using percutaneous estradiol. The main target of estrogen replacement therapy in such girls has been to induce puberty and feminization sufficiently early without reducing adult height (10). The natural form of estrogen in humans is estradiol. It is relatively ineffective after oral administration because of extensive degradation in first pass metabolism in the liver (6). Transdermal estradiol patches have successfully been used in the induction of puberty (7,11). Percutaneous estradiol gel is commonly used for postmenopausal estrogen therapy. Administration of estrogen

replacement by the percutaneous route in girls with TS may have less deleterious effects on hepatic metabolism than oral estrogen (12).

According to our results the use of percutaneous estradiol gel in individualized treatment provides an excellent, safe and physiological, means to induce puberty in girls with hypogonadism. The gel provides a good option to administer the very low estrogen doses. Costs of such treatment can be considered reasonable, since adult preparations are easy to modify for pediatric use, in contrast to commercial oral preparations containing the adult doses. By reducing the estradiol concentration in the gel the starting doses can be adjusted to low levels and increased gradually. The use of known dose sachets may be preferable to free dosing from a tube, in order to keep the used dose at the recommended level. Acceptance of the treatment was excellent, since the medication was easy to use and not visible.

Transmission of estradiol between individuals in skin contacts is unlikely, but can be prevented when medication is applied on an area covered by clothing. According to safety parameters and adverse events the use of percutaneous estradiol was safe for the subjects. However 11 girls reported menstrual bleeding before the initiation of the cyclic progestin, which means that the initiation of progestin according to protocol was too late. With ultrasonography the development of endometrium can be followed individually and cyclic progesterone should be started at 3 mm endometrial thickness.

The steady increase of mean estradiol concentrations proves the efficacy of percutaneous estradiol therapy for the induction of puberty. The estradiol concentrations within and between individual subjects showed great variation and cannot alone be used in treatment follow-up. Declines in the basal and stimulated FSH and LH concentrations with increasing estradiol doses are more useful in measuring the efficacy of estradiol therapy. The very small increases in FSH and LH concentrations in GnRH tests with the 1.0 mg and 1.5 mg doses of estradiol indicate that for some of the subjects smaller doses would have been sufficient. By following gonadotropin concentrations and by means of ultrasonographic measurement of

uterine growth and endometrial thickness we can tailor individual pubertal induction with percutaneous estradiol gel in hypogonadic subjects.

Percutaneous estradiol therapy resulted in excellent gradual development of secondary sexual characteristics. At five years all girls had reached Tanner stage B4P4, of the 83 % of girls with information available 79% reached B5 and 58% P5 stages. According to ultrasonographic examinations of uterine length, normal uterine development was reached at age 16 (13). The mean uterine volume reached was 7 ml more than in normal puberty at Tanner stage B4–5 (14). Achieving normal adult uterine size is important if infertility treatments (embryo transfer) are considered during later life. Endometrial thickness was in the normal range during the menstrual cycle, which indicates endometrial safety of the treatment. Even though liver enzymes may rise during treatment, estrogen should not be considered to be the main cause of elevated liver enzymes in Turner syndrome (15).

In our study no significant difference in growth was found between subjects receiving GH and those not receiving it. The study was not designed to evaluate the effect of estradiol on GH treatment and the indications to start GH varied in different centers. Hence we can only conclude that estradiol treatment did not have a negative effect on the growth of the subjects.

Fluctuation of estradiol concentrations over twenty-four hours might have a positive effect as regards the natural development of puberty (7). Such an effect could be achieved in our study by means of percutaneous application of the gel in the evenings. In this regard use of gel might be preferable to use of estradiol patches. Percutaneous estrogen has become standard practice for pubertal induction in our clinic. After this study even more attention has been paid to the very low starting dose and the gradual increase of doses during the therapy. During the use of growth hormone estradiol concentrations are kept very low, with only a slight decline in FSH concentrations. With estradiol gel the doses used can be individually adjusted to pubertal Tanner stages, gynecological ultrasonographic data and circulating FSH concentrations.

Conclusions

The use of percutaneous estradiol gel provided a safe, individual and well-accepted treatment for the induction of puberty in hypogonadic girls. Secondary sexual characteristics and uterine growth proceeded gradually during the treatment, mimicking natural pubertal development.

The regimen with very low initial doses and gradual increase of the dose did not have a negative effect on adult height. With the gel the estrogen dose can be individually tailored for natural pubertal development. Efficacy of therapy can be followed by means of pubertal signs, ultrasonographic measurement of uterine growth and endometrial thickness, and circulating gonadotropin concentrations.

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Table 1. Growth during the study

Visit years	Age mean,years	Height mean, cm	SDS*		Weight mean,kg	SDS*		Bone age	
			mean	+/- SD		mean	+/- SD	y	+/- SD
Baseline	13.7	142.0	1.53	1.03	42.6	0.80	1.26	11.3	0.9
1	14.7	147.0	1.85	1.02	46.6	0.78	1.28	12.9	1.1
2	15.8	150.3	1.91	0.98	51.1	0.99	1.28	13.9	1.1
3	16.7	151.4	1.70	1.01	53.3	0.89	1.17	15.2	1.1
4	17.6	152.8	1.61	0.83	56.4	0.92	0.90	16.6	0.9
5	18.5	153.1	1.51	0.86	55.4	0.58	0.78	17.3	0.6

*According to Ranke growth standards for Turner girls

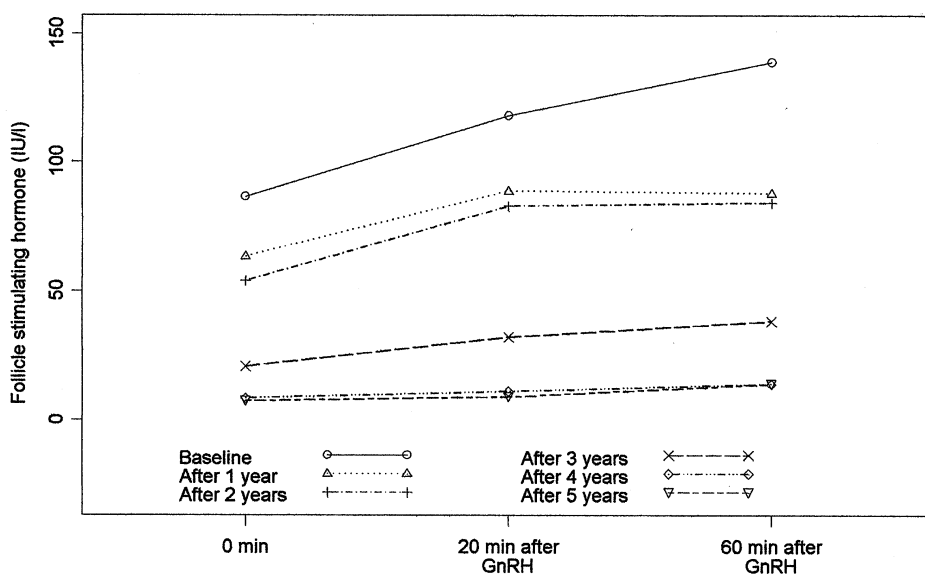
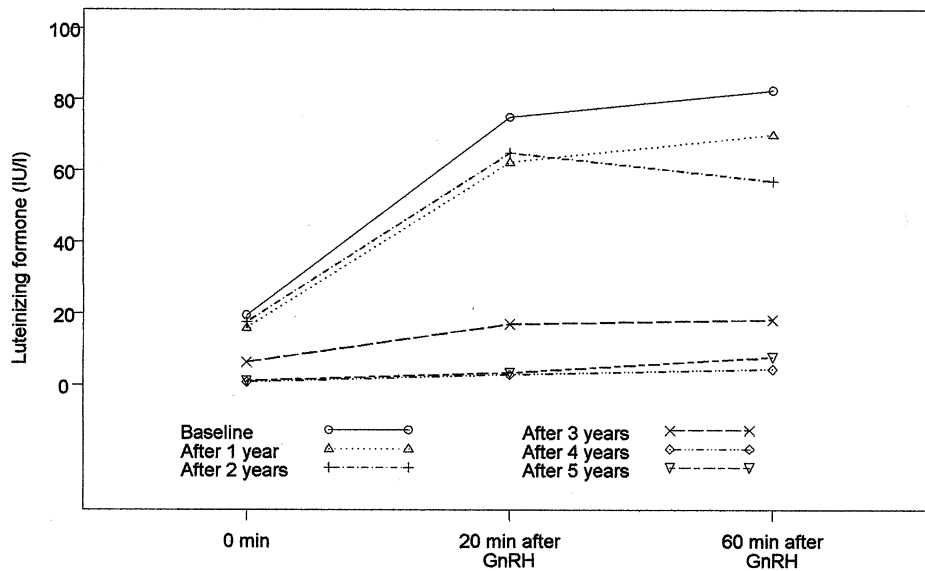


Figure 1. Mean LH and FSH concentrations in GnRH-tests

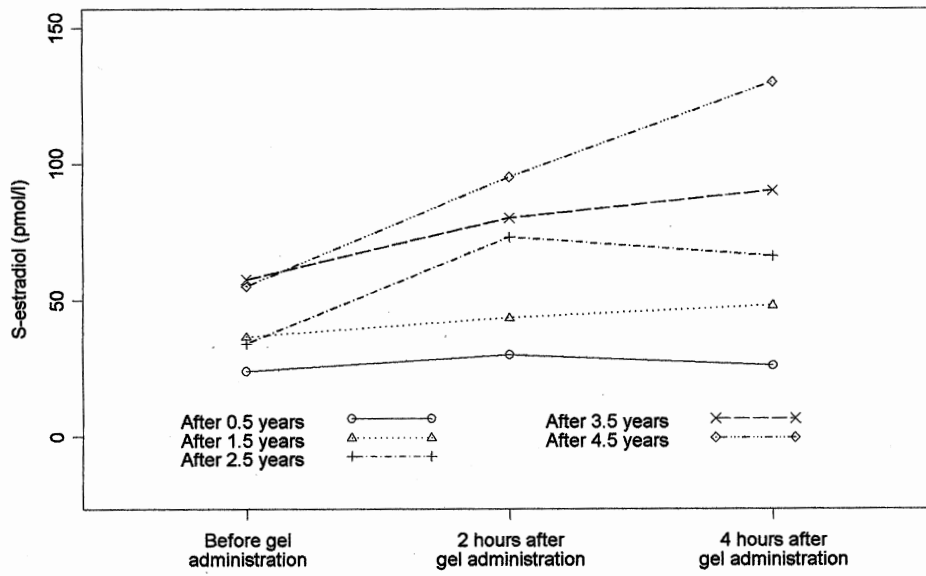
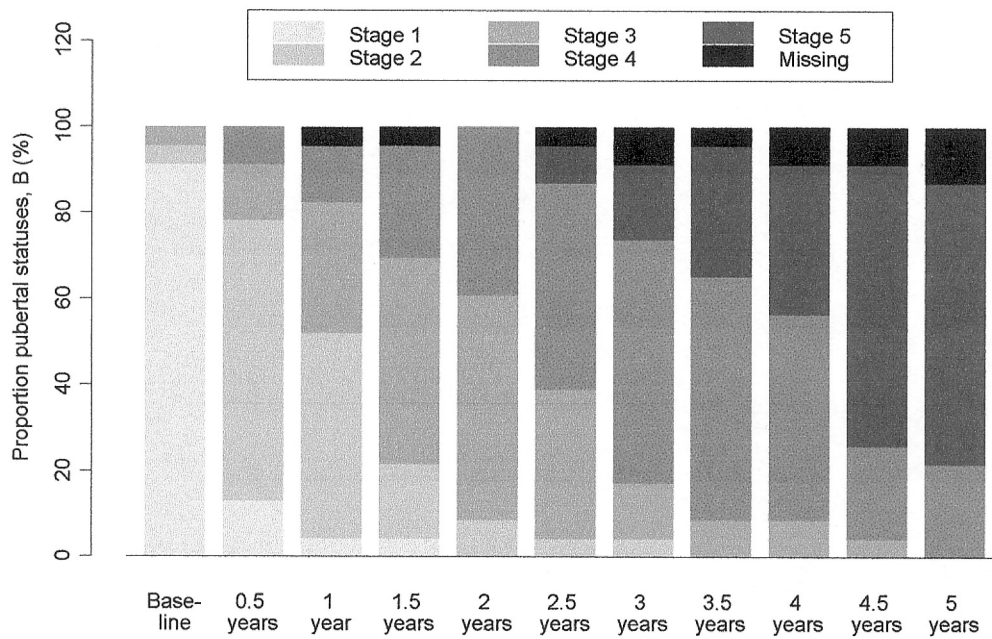


Figure 2. Serum estradiol concentrations after gel administration



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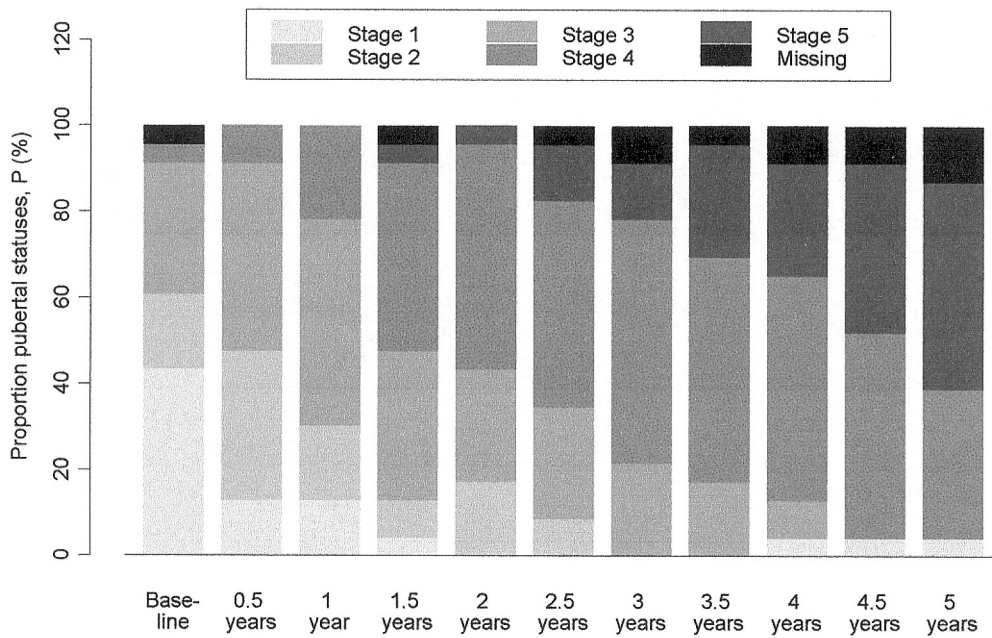


Figure 3. Pubertal development

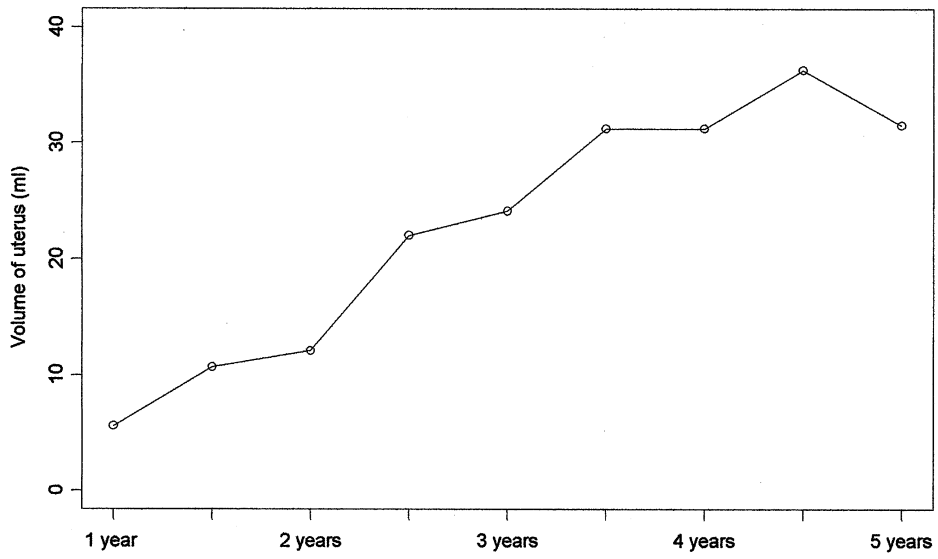
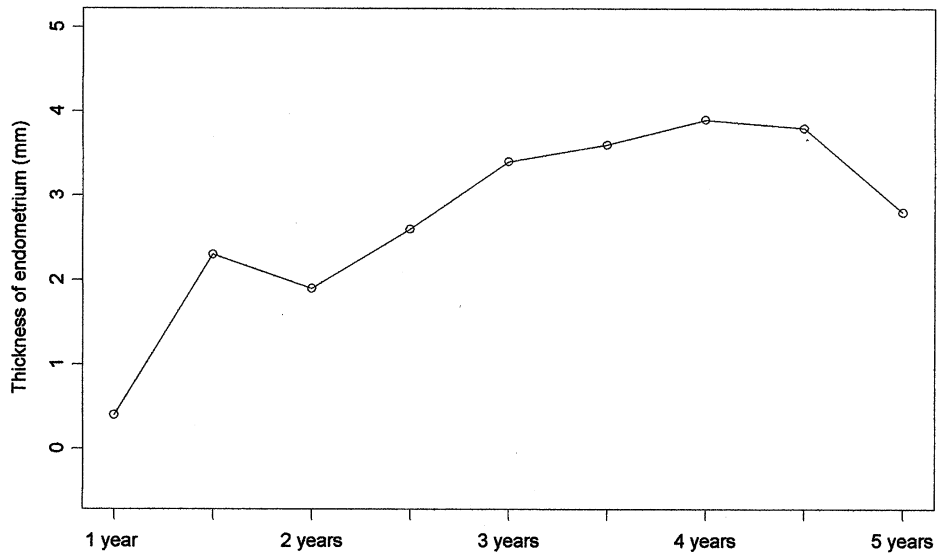


Figure 4. Development of the uterus and endometrium

Sexual Abuse of Girls: a study of 55 cases from the early and late 1990s

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Synopsis

The medical, psychosocial and legal consequences for 55 girls with suspected sexual abuse are described. The gynecological and child psychiatric assessments agreed in 72% cases.

Sexual Abuse of Girls: a study of 55 cases from the early and late 1990s

Abstract

Study Objective: This study describes and compares the characteristics of child sexual abuse cases among girls examined at Tampere University Hospital in late 1980's and in mid 1990's. We evaluate to what extent a gynecologist and a child psychiatric team agreed in their assessments and describe the medical, psychosocial and legal consequences for the patients.

Design and participants: All girls under 17 years of age examined for a suspected sexual abuse from 1989 through 1991 (24 girls) and from 1995 through 1997 (31 girls) at the unit of paediatric and adolescent gynecology, were included in the study. A general physical, and a gynecological examination with a thorough inspection of the vulvar and anal areas was performed to all but one patient. A child psychiatric evaluation was done on 43 patients.

Results: Fifty-five percent of the patients were under 7 years of age, and no girls aged 15-16 years had been referred. In 58% of cases the suspected offender was the biological father. The gynecological and/or psychiatric examinations showed evidence of sexual abuse in twelve patients (50%) in 1989-91 and in 19 patients (61%) in 1995-97. The gynecological and child psychiatric assessments agreed in 72% cases. Follow-up data was available on 33 patients and 14 instances of adverse psychosocial outcome was reported.

Conclusions: The factors affecting a case of child sexual abuse to be referred to the hospital included a young age, psychiatric symptoms and deleterious consequences. The good agreement between the gynecological and psychiatric examinations justified the custodial and legal measures taken. However the sexual abuse of adolescent girls documented in earlier epidemiological studies was not well recognized.



Key words: child sexual abuse; gynecological examination; child psychiatric examination, pediatric gynecology.

Introduction

The sexual abuse of children has received a growing attention in the U.S.A. since the late 1970's, and in Scandinavian and other European countries since the late 1980's. The prevalence of child sexual abuse in various countries ranges from 7% to 36% for girls and from 3% to 29% for boys (1). The wide variation is caused by methodological differences and the variable definitions used. Moreover, epidemiological studies have demonstrated that the low prevalence of child sexual abuse reported before the 1970's was due to a lack of professional attention (2). In a Finnish questionnaire study of 15-16-year-old school children, from the early 1990's, 18% of the girls and 7% of the boys reported a sexual experience with a person at least 5 years older than themselves (3). After the voluntary experiences had been excluded, six to eight percent of the girls and one to three percent of the boys reported experiences that could be classified as sexual abuse, such as an exposure or fondling of the genitalia, or an intercourse. Sexual experience with an adult was more common among girls aged 12 and above, so that 70% of the experiences occurred among the girls aged 14-16 years.

Any child who is suspected to have experienced an inappropriate sexual contact should have a medical examination that includes a noninvasive inspection of the external anogenital area (4). Since the gynecological examination of victims of child sexual abuse requires excellent cooperation with the patient, the physician examining these patients has to have special skills in the gynecological examination of children. There is a wide individual variation of normal genital anatomy in children and adolescents. The physician must be familiar with the normal genital findings, normal anatomical variations, and with findings related to a sexual abuse during childhood and puberty (5, 6, 7,8). Physical findings of sexual abuse are of great importance if a case ends up

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in court (9). However, even in girls in whom sexual abuse had been determined by Child protective services, the medical examination failed to reveal specific findings in 56% of victims (10).

Sexual abuse during childhood and adolescence is associated with numerous adverse psychological and social outcomes. Sexual abuse during early childhood is significantly associated with a hypersexual, exposing and victimizing sexual behavior during adolescence and adulthood (11). Moreover sexually abused children have a high risk of mental impairment later in life, with significantly increased incidences of major depression, conduct disorders, alcohol or substance abuse and suicidal behavior (12,13,14).

The purpose of the study was to describe and compare the characteristics of and the gynecological findings in consecutive cases of suspected sexual abuse of girls examined between 1989-91 and 1995-97. All the girls were examined by the same gynecologist (SP) so that the two time periods represent different levels of professional learning. Another purpose was to evaluate to what degree a gynecologist and a child psychiatric team agree in their assessments. The subsequent social, mental and legal consequences of sexual abuse for the patients and their families are also described.

Patients and methods

A Unit of Pediatric and Adolescent Gynecology at Tampere University Hospital was opened in 1988. It serves a population of 448 000 inhabitants, 89 000 of whom are less than 17 years old. The study population consists of all girls under 17 years of age referred for gynecological examination because of suspected sexual abuse in 1989-91 (24 girls) and 1995-97 (31 girls). The earlier period represents the beginning of a serious awareness of child sexual abuse among professionals in our country and the start of a systematic approach to the problem. The later period

represents an era of accumulated experience and learning. The National Center of Child Abuse and Neglect (15) definition of child sexual abuse was used. It included all forms of child sexual abuse: Any contact or interaction between a child and an adult, when a child is being used for the sexual stimulation of that adult or other person.

A general physical examination was carried out by an experienced pediatrician simultaneously with the gynecological examination. Special attention was paid for signs of maltreatment, and any findings in the oropharyngeal, mammary and abdominal areas. The gynecological examinations were carried out by a single gynecologist (S.P.), who is experienced in the physical and gynecological examination of children and sexual abuse victims. The examination included a thorough inspection of the vulva, vaginal introitus, hymen and anal region. The physical examinations of all our patients were conducted and the findings recorded using a systematic approach.

Small children were examined in a semi-sitting position in their mother's lap, and from the age of 3-4 years upward on the examination table with knees maximally flexed and heels at the edge of the table (frog-leg position). Pubertal patients were examined in the lithotomy position and an examination using a vaginal speculum was carried out if an intercourse had been reported. The examination was performed under anesthesia if the visualization of the whole vagina was necessary, either because of symptoms or for forensic purposes, and/or the child was too fearful to cooperate. Anesthesia was also used if significant degree of trauma with a need for a repair was present.

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A Pap-smear and swabs for culturing *Candida albicans*, *Trichomonas vaginalis*, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* were taken from the vaginal introitus and/or from the vagina provided it could be done without causing much discomfort. These samples were always obtained if the interval between suspected abuse and examination was less than three days, or if sampling was indicated because of local symptoms. Samples for detecting sperm, DNA and acid phosphatase were also obtained if indicated, by the history or gynecological findings.

The assessment of the probability of sexual abuse in relation to the gynecological findings in 1989-91 was based on the knowledge from the literature. At that time, e.g. the diameter of the hymenal openings was considered as a diagnostic criterium for child sexual abuse (16). During the later period, assessments from the somatic genital findings were made using the guidelines presented by Adams et al. (17). Normal findings (such as estrogen effects, hymeneal bumps, anterior hymeneal clefts) and nonspecific findings (such as increased pigmentation or erythema in the vulvar area, labial adhesions, vaginal discharge) were assessed not to represent gynecological evidence of abuse. Only findings suspicious or suggestive (hymenal cleft between 3~9 o'clock, condyloma accuminata in a child > 2yr-old) or clearly evident (acute hymenal or perineal laceration, total absence of the posterior hymen) of sexual abuse were assessed represent gynecological evidence of sexual abuse.

Child psychiatric evaluations were carried out at the University Clinic of Child Psychiatry on 18 patients in 1989-91 and on 21 patients in 1995-97. Additional 4 patients during the later period were evaluated at the Child and Family Guidance Clinic of the city of Tampere. No child psychiatric evaluation was carried out on 12 patients. The child psychiatric conclusions about the probability of child sexual abuse were drawn on the basis of a clinical judgment by the multiprofessional child psychiatric team (child psychiatrist, psychologist, social worker and/or child psychiatric nurse). The child was interviewed by the child psychiatrist, and the parents by the social worker and/or a

psychologist, who both were trained family therapists. Usually the evaluation included at least one family session. There was some variation in the structure and methods of the assessment depending on the child's age, and the developmental level of the child, the severity of psychiatric symptoms, and the degree of the co-operation by the child and the family. However, the interviews of the child and parent, including the history taking and the clinical observation of the child, were in every case an essential part of the evaluation. The child psychiatrists were informed about the physical findings before or during the child psychiatric examinations.

Data on gynecological, physical and psychiatric evaluations and follow-up were gathered from the hospital medical records, as well as information about the abusive event and the suspected perpetrator. Follow-up data until the end of 1999 on any subsequent mental health problems of the patient or her family were collected as recorded in the hospital medical records. The legal consequences for the perpetrators were obtained by reviewing all the cases that had reached court.

Cross-tabulations and the Fisher's exact test were used to examine the differences between the two different periods of interest and between the patient groups with or without evidence of sexual abuse. Statistical analysis was accomplished using the SPSS statistical software (version 9.0). The significance level of $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

The study included 55 girls, 24 examined in 1989-91, and 31 in 1995-97. The age distribution is presented in Table 1. The mean age of the patients was 7 years and the median age 6.5 years. No



girls of 15-16 years of age were examined in the gynecological clinic because of a suspected sexual abuse during the study periods.

The examinations for child sexual abuse were initiated in 21 (38%) patients when the girl herself reported the abuse to a carer (Table 2). In 19 (35%) cases the girl's mother was the first adult who noticed or who was confided to about the suspected sexual abuse. Other adults who primarily became aware of the possible child sexual abuse were social workers or day care personnel in 10 (18%) cases, friends or relatives in 6 (11%) and the primary care physician in 8 (15%) cases. In this respect the study periods did not differ from each other.

Most often the suspected offender was the child's biological father (Table 3). In 16% of cases the perpetrator was someone outside of the child's family. The type of sexual abuse suspected was genital fondling in 36% of all cases (Table 4). Intercourse or attempted intercourse was reported in 18% of patients, all among those assessed to have evidence of sexual abuse. Among girls with no gynecological or psychiatric evidence of sexual abuse the precise nature of the sexual involvement could not be given in 59% of cases.

Gynecological examination

According to the findings in the gynecological examination, 8 (33%) patients in 1989-91 and 13 (42%), patients in 1995-97 were assessed to have evidence of sexual abuse (Table 5.) The difference is not statistically significant. During the earlier study period, there was more diversity in the physical findings of patients with evidence of sexual abuse. During the later period, all children with physical evidence of sexual abuse had a hymeneal cleft or changes in the anal region.

In 49 patients the examination of the vulvar area and the hymen was performed in a good cooperation with the patient without anesthesia. Most often also the outer third of the vagina of the pre-pubertal children was successfully visualized without instrumentation. One gynecological examination in 1989-91 was performed in anesthesia for a 12-year-old girl because of a suspected urinary tract anomaly. Between 1995-97, four examinations were performed under anesthesia for girls aged 5-7 years, with a reported sexual abuse within past two days, because of acute vulvar irritation (2 patients) or fresh vulvar tears (2 patients). No vulvar examination could successfully be done during the primary examination on one patient because of a psychotic behavior.

A Pap smear was taken from 15 patients; one case of *Gardnerella vaginalis* and one case of *Human papillomavirus infection* were found. No sperm was detected in Pap smears. Bacterial cultures from the vulva or vagina were taken from 22 patients, with no clinically relevant findings. Samples for culture of *Candida albicans* and *Trichomonas vaginalis* were obtained from 27 patients, and one candida infection was found. Samples for culture of *Chlamydia trachomatis* were obtained from 28 patients, and one culture was positive. Samples for culture of *Neisseria gonorrhoeae* were obtained from 30 patients, with negative results in all. All abnormal results were confined to two patients, who reported intercourses and had a gynecological evidence of sexual abuse. Samples for detection of sperm, DNA and acid phosphatase were taken from four patients, with no positive findings.

Child psychiatric evaluations and the agreement between somatic and child psychiatric assessments

The results of the child psychiatric evaluations showed evidence of sexual abuse in 11 (61%) patients in 1989-91 and 18 (72%) patients in 1995-97. The difference is not statistically significant. A gynecological and a child psychiatric evaluation were both carried out on 42 patients. Twelve patients in 1989-91 and 19 in 1995-97 were concluded to have evidence of sexual abuse according



to the results of the gynecological and/or psychiatric examinations. The assessments in gynecological and child psychiatric examinations agreed in 72% of those cases where both examinations were carried out (Table 6). No child psychiatric evaluation was carried out on 6 cases in both periods (25% and 19% respectively). In 4 of these cases the gynecological examination led to a somatic diagnosis not related to sexual abuse, one bacterial vulvitis, one atopia 1, one fetal alcoholic syndrome, and one neglected child. In five cases, the gynecological examination failed to reveal any abnormal findings.

Psychosocial and legal consequences

Follow-up information from the medical records was available on 33 patients. There were 13 instances of an adverse psychiatric or psychosocial outcome among the 23 patients with the gynecological or psychiatric evidence of a sexual abuse, and one instance among the 10 patients with no evidence of an abuse. Two abused girls became teenage mothers. One girl was later raped. One abused patient and one perpetrating father have committed suicide. The deaths of four other parents have been recorded. A serious mental illness, requiring in-patient hospital treatment, developed in three of the patients with the gynecological and psychiatric evidence of a sexual abuse. Also one of the girls with no evidence of a sexual abuse was later hospitalized due to psychiatric problems. Additionally, five girls with evidence of abuse have had serious behavioral difficulties during adolescence.

All criminal proceedings took place during the later study period. There were no criminal proceedings connected to the patients with no gynecological or child psychiatric evidence of a sexual abuse. In six cases of child sexual abuse, five suspected perpetrators (I~V) have been tried and sentenced. A biological father (I) of a victim, and her uncle (II), were found guilty of child

sexual abuse. The uncle, 15-years-old at the time of the abuse, confessed and was fined. The father was sentenced for 20 months of imprisonment after supreme court rulings. In two other cases the biological fathers (III & IV) were found guilty. One was sentenced to imprisonment and the other put on probation for three months. A perpetrator (V) was tried for the abuse of three of our patients, and sentenced to 14 months of imprisonment. Additionally one father already imprisoned for the sexual abuse of his stepdaughter, was also in expectation of being charged with the sexual abuse of two of his biological daughters, committed suicide before the trial.

Discussion

Our study provides a different perspective on the problem of child sexual abuse than the epidemiological study among teenagers in Finland from the early 1990's (3). More than half of our patients were under seven years of age, and no girls between ages 15-16 were examined. The major characteristics of our cases remained the same between the study periods. Studies including hospital patients have limitations: the whole population is not represented, since all cases are not recognized by health or social services and all cases of a suspected child sexual abuse are not referred to hospital examinations. However, all gynecological examinations of child sexual abuse cases from the hospital referral area of 89 000 children aged 16 or less should have been examined in our clinic. The incidence of child sexual abuse in our study was very small (0.01% per year for girls), taking into account that the prevalence of female child sexual abuse is approximated to be 10% by the age of 16 years (12,13). According to these figures, only the younger children with severe symptoms reached the hospital level. What we really wonder is, how the need for gynecological and psychiatric services of the adolescent girls with experiences of sexual abuse, missing from our material, has been met.

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Medical evaluation is important in the examination of the child sexual abuse cases, even though the findings are often minimal or totally missing (18). A physical examination can most often be performed without anesthesia in good co-operation with the patient and her family. Many forms of child sexual abuse do not cause physical injuries, and in these circumstances an examination can not be expected to detect any physical evidence of abuse. Our results agree with previous observations that bacterial culture and Pap smear results are generally normal (19). However, sampling is important for forensic purposes and to rule out infections. Nevertheless, in this study findings in the genital or anal area indicative of sexual abuse were found in 33% of patients during the earlier period and in 42% during the later period. This large proportion of patients with gynecological evidence of sexual abuse supports the conclusion that only the very severe cases were referred to examinations made by a specialist. It would however be important that all children and young adolescents with a suspected sexual abuse will be examined, and also informed about the normal findings.

According to our clinical experience, a simultaneous physical examination by a pediatrician and a gynecologist is beneficial to all parties. Repeated physical examinations should be avoided since they might confuse or harm the patient and also change the value of evidence. A good cooperation with professionals working in different specialties was found to be important. The somatic and psychiatric assessments in our study were in relatively good agreement, which justified the medical, social and legal measures taken on behalf of the child, family and society.

The follow-up information about the adverse consequences of child sexual abuse for the victims and their families described in this study are noteworthy and in accordance with results from larger studies (12,13,14). Severe consequences occurred in 56% of the patients with evidence of sexual abuse, and with information available. Only one psychosis was recorded among the patients without

evidence of sexual abuse. The patients and their families had often had multiple long term psychosocial problems. With an earlier intervention and support , we perhaps were able to reduce the risks of serious mental difficulties and their consequences later in life.

Expert medical assessments have much impact in court. Custody and visitation rights are determined solely according to what is judged best for the child and mainly based on social information. Finding a perpetrator guilty of child sexual abuse in a trial is based on evidence, and here also the medical findings are important. Criminal proceedings against suspected perpetrators appeared during the later study period. The juridical system has become aware of this problem considerably later than the medical community. In all cases which reached court the, perpetrators were found guilty, but the penalties of fines, probation and imprisonment were mild compared to rulings in U.S. courts (9).

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Conclusions

A sexual abuse during childhood leads to long term consequences for the victims and their families. The cases analyzed here represent only the tip of an iceberg. The very severe cases, with younger victims, psychiatric symptoms and deleterious consequences reached hospital level services. According to our results sexual abuse of adolescent girls represented in epidemiological studies was not recognized by the health services. Assessments from somatic and child psychiatric examinations agreed in 72% of cases, which justified the medical, custodial and legal measures taken.

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Table 1. The age distribution of the patients

Age (y)	1989-91 n=24 n (%)	1995-97 n=31 n (%)	All n=55 n (%)
0-1 years	4 (17)	1 (3)	5 (9)
2-6 years	8 (33)	17 (55)	25 (46)
7-10 years	6 (25)	8 (26)	14 (25)
11-14 years	6 (25)	5 (16)	11 (20)
15-16 years	0	0	0

V**Table 2. The reasons leading to a suspicion of sexual abuse.**

	1989-91 n=24 n (%)	1995-97 n=31 n (%)	All n=55 n (%)
Girl's story	8 (34)	13 (42)	21 (38)
Event seen	1 (4)	3 (10)	4 (7)
Somatic symptoms	9 (38)	9 (29)	18 (33)
Psychiatric symptoms	2 (8)	5 (16)	7 (13)
Sexual abuse of a sibling	2 (8)	1 (3)	3 (5)
Information to authorities	2 (8)	0	2 (4)

Table 3. Identity of the suspected perpetrator *

	1989-91 n=24 n (%)	1995-97 n=31 n (%)	All n=55 n (%)
Father, biological	11 (46)	21 (68)	32 (58)
Stepfather	2 (8)	0 (0)	2 (4)
Mother	3 (13)	0 (0)	3 (5)
Other relative	3 (13)	2 (6)	5 (9)
Pedophile	0	4 (13)	4 (7)
Other	3 (13)	2 (6)	5 (9)
No direct suspect	7 (29)	3 (10)	10 (18)
Several abusers	5 (21)	1 (3)	6 (11)

* a case may have several suspected perpetrators

Table 4. The type of a suspected abuse among patients with no evidence and evidence of sexual abuse in the gynecological and/or psychiatric examinations

	No evidence		Evidence		All n=55 (%)
	1989-91 n=12	1995-97 n=12	1989-91 n=12	1995-97 n=19	
Genital fondling	3	4	4	9	20 (36)
Intercourse or attempt	0	0	4	6	10 (18)
Anal sex	0	0	0	2	2 (4)
Oral sex	0	0	0	2	2 (4)
Violence	1	0	0	0	1 (2)
Other	1	1	3	0	5 (9)
Not known	7	7	1	0	15 (27)

Table 5. The findings in the gynecological examination for all patients, and for patients with the gynecological evidence of sexual abuse *

	1989 -91		1995 -97	
	all n=24 n (%)	assessed abused n=8 n (%)	all n=31 n (%)	assessed abused n=13 n (%)
Bruises, maltreatment	6 (25)	0	4 (13)	1(8)
Vulvar erythema	4 (16)	0	3 (10)	1(8)
Vulvar irritation	4 (16)	1(13)	7 (23)	4(31)
Vulvar condylomas	2 (8)	2(25)	0	0
Vaginal discharge	2 (8)	2(25)	0	0
Vulvar trauma	1 (4)	0	0	0
Enlarged hymenal opening	2 (8)	2(25)	0	0
Hymenal cleft between 3-9 o'clock	3 (13)	3(38)	9 (29)	9(69)
Any abnormal gyn. finding	16 (67)	8(100)	19 (61)	9(69)
Normal gyn. findings	8 (33)	0	12 (38)	0
Anal scarring and lacerations	0	0	4 (13)	4(31)

* the patients may have more than one abnormal gynecological finding



Table 6. The association between the conclusions in the gynecological and psychiatric examinations

		Child psychiatric conclusion			All
		Abused	Non-abused	Not examined	
Gynecological conclusion	Abused	19	2	0	21
	Non-abused	9	12	12	33
	Not examined	1	0	0	1
All		29	14	12	