

The Basics of AIS

Whether XX or XY, every fetus has the capacity to develop a male or female reproductive system. AIS interrupts reproductive system development in a child conceived with male (XY) sex chromosomes. Androgens cannot cause male genital development due to a rare insensitivity of the fetal tissues. External genital development continues along female lines and development of female internal reproductive organs is suppressed by a mullerian inhibiting substance from the fetal testes.

AIS is an X chromosome linked recessive condition, either inherited along the maternal line or, in up to a third of cases, resulting from a spontaneous chromosomal change. A mother who carries the altered gene has a one in two chance of any XY child having AIS and a one in two chance of any XX child being a carrier like herself. Carrier testing is now available. The reproductive organs or genitalia are partly at variance with the person's genetic sex. This is not the same as transsexuality or gender identity disorder.

AIS is an example of an intersex condition. The term DSD (Disorder of Sex Development) is gaining acceptance among parents and in the medical community as it incorporates a broader spectrum of conditions that involve variations in chromosomal make up, phenotype and in the development of internal/external sex and reproductive anatomy.

Estimates of AIS frequency vary from one in 13,000 to one in 65,000 XY births, with PAIS thought to be only 1/10th as common as CAIS. Based on 2005 population figures, it is estimated there are 8,000 AIS women in the U.S. and Canada.

Complete (CAIS) and Partial (PAIS)

In CAIS, the bodily tissues are wholly insensitive to androgens. In PAIS, the tissues are insensitive to varying extents. So, in AIS a spectrum of genital appearances can occur. In AIS Grades 6 & 7, the external genitalia is female and the sex of rearing is invariably female. In PAIS, the outward genital appearance can fall anywhere along a continuum from completely female (Grade 6), through mixed male/female, to completely male (as in Grade 1 where otherwise normal men may experience infertility). Some PAIS babies are raised as males. Although PAIS can vary somewhat between affected siblings, the complete and partial forms do not occur in the same extended family.

Conditions Associated with AIS

In years past, AIS has also been labeled as the following syndromes: androgen resistance, testicular feminization, male pseudo-hermaphroditism, Goldberg-Maxwell, Morris, Lubs, Reifenstein, Gilbert-Dreyfus and Rosewater. Other XY conditions associated with female genital development include Leydig cell hypoplasia, pure gonadal dysgenesis (Swyer), 17 beta hydroxysteroid dehydrogenase deficiency, 5-alpha reductase deficiency, Denys-Drash, Smith-Lemli-Opitz and embryonic testicular regression. XX conditions that cause failure of development of female internal genitalia include MRKH, vaginal atresia and mullerian dysgenesis. The terms male pseudo-hermaphroditism and testicular feminization are now considered to be scientifically inaccurate and stigmatizing. The AIS Support Group provides support to women and families affected by AIS and a wide variety of similar conditions.

CAIS Outcomes

In AIS there are no ovaries, fallopian tubes, or uterus and the vagina is blind-ending and possibly short or absent. Undescended testes can result in an inguinal (groin) hernia in infancy. In approximately 50% of cases this is when CAIS is discovered in an otherwise normal female child. CAIS may not be discovered until puberty as a result of failure to menstruate (primary amenorrhea). Female puberty occurs since the testes produce some estrogen and the testosterone produced is converted to estrogen in a process known as aromatization. However, there will be no menstruation and no possibility of bearing children. Some coarse pubic or underarm hair may develop (AIS Grade 6) but this does not occur in true CAIS (Grade 7) because androgen action is needed for its growth. The same holds true with the occurrence of acne. Nipples may remain underdeveloped and pale in color.



Timing of Gonadectomy

There is a risk of cancerous changes occurring in the gonads (testes) after age 20. After spontaneous feminizing puberty has occurred, removal of the gonads (referred to as gonadectomy or orchidectomy) is usually recommended. Deferring the removal of the testes has physical and psychological advantages over puberty induced by exogenous (in pill form) hormones. Although the risk of pre-adult cancer is too small to justify it before adulthood, gonadectomy is sometimes done in infancy or childhood, usually with the intention of avoiding a psychological crisis when the need for an operation later on must be explained. Arguably, this violates a patient's right to informed consent and to optimal treatment.

Hormones & Osteoporosis

When the testes are removed, immediate long-term hormone replacement therapy (HRT) is needed to manage menopausal symptoms and osteoporosis. In the case of gonadectomy in infancy or childhood, HRT is often started at age 10 or 11 to initiate puberty.

Women with AIS are at increased risk of osteoporosis, especially if HRT has not been used continuously after gonadectomy. Absence of HRT is a risk factor, although some AIS adults have low bone density in spite of regular HRT - possibly due to the fact that XY girls with testes have lower estrogen levels than XX girls with ovaries during the years when healthy bone should be laid down. XX girls start producing estrogen at around age eight, so supplementary low dose estrogen from this age, with or without gonads in place, may be advisable in girls with AIS.

Consult your physician on how best to combat osteoporosis, including supplemental calcium and vitamin D, and with weight-bearing exercise.

Vaginal Health

In AIS and similar conditions, a condition known as vaginal hypoplasia can mean that the top one-third of the vagina is missing. In some cases the vagina may be very shallow or even just a dimple. Parents and clinicians are advised to address this issue with pubertal AIS patients because some youngsters discover this by self-examination. Later, failed attempts at intercourse without proper preparation, including dilation (sometimes written

as dilatation), can lead to psychological and physical trauma.

Vaginal hypoplasia can be treated by non-surgical pressure dilation. This is best deferred until puberty and then, when the girl is sufficiently motivated. Dilation generally yields good results and involves minimal risk and expense. In some cases, the Vecchietti procedure (a semi-surgical way of accelerating dilation) has advantages.

There are a number of surgical methods of lengthening the vagina (vaginoplasty) using skin grafts, sections of intestine, etc. All have disadvantages and should be used only when less invasive treatments have been ruled out. Vaginoplasty in childhood often has poor results and should not be done. Surgeons sometimes fail to stress the importance of ongoing dilation in order to maintain a neovagina. If the vaginoplasty is not maintained with the use of a dilator or by means of frequent intercourse, stenosis (narrowing caused by scar tissue) will inevitably occur.

The Reality of AIS

In a misguided attempt to spare a girl with AIS inner conflict, genetic and gonadal information is often withheld. Most professional caregivers now recommend truth disclosure with psychological support and counseling. Without support, AIS patients will seek information via medical libraries or the Internet, bearing the burden alone and in silence. Many will wrestle with perplexing half-truths or reach worrisome false conclusions.

If the emotional needs and anxieties of the parents are addressed first (via psychological support and counseling from professionally trained staff) it will be easier for them to provide effective support to their child. It is important that parents encourage discussion with their child and actively seek out information on their behalf.

Keeping a secret can become more important to some parents than acknowledging their child's need for emotional support and appropriate clinical intervention. This wastes mental and emotional energy that is better spent in helping the child come to terms with the truth.

The patient's right to assign meaning to her condition via a diagnosis and to seek out a support group must be considered. Meeting others who are affected is vital and is probably the single most useful therapeutic measure. Overemphasis on a CAIS patient's femaleness with an unwillingness to allow exploration of her very real deficiencies (infertility,

lack of internal female organs, pubic hair, menstruation and diminished vaginal length) will suggest to her a very considerable anxiety and discomfort on the part of doctors/parents. Preparing the youngster for intimate personal relationships as an adult should be a priority, tempting as it maybe to divert their attention toward substitute goals.

In CAIS, the person looks like a girl and problems of psychosexual identity as a biologically determined feature of the condition are unlikely. Leanings towards lesbianism or bisexuality seem no different from females in the general population.

Our Goals

- ◆ Reduce secrecy, stigma, and taboo surrounding AIS and other intersex states, by encouraging doctors, parents and society to be more open
- ◆ Promote psychological support for young people with AIS and their parents
- ◆ Bring parents and women with AIS together
- ◆ Increase access to information on AIS and similar conditions

We Can Help!

- ◆ *Orchid Press* quarterly newsletters
- ◆ Annual US meetings since 1996
- ◆ Ask us about area regional meetings
- ◆ For more details, write or e-mail the appropriate group listed below

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AIS Support on the web

United States group: www.aissgusa.org

United Kingdom group: www.aissg.org

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Facing the facts of AIS

Androgen Insensitivity Syndrome



A self-help group providing information, contact, and support to AIS women and to parents of AIS girls