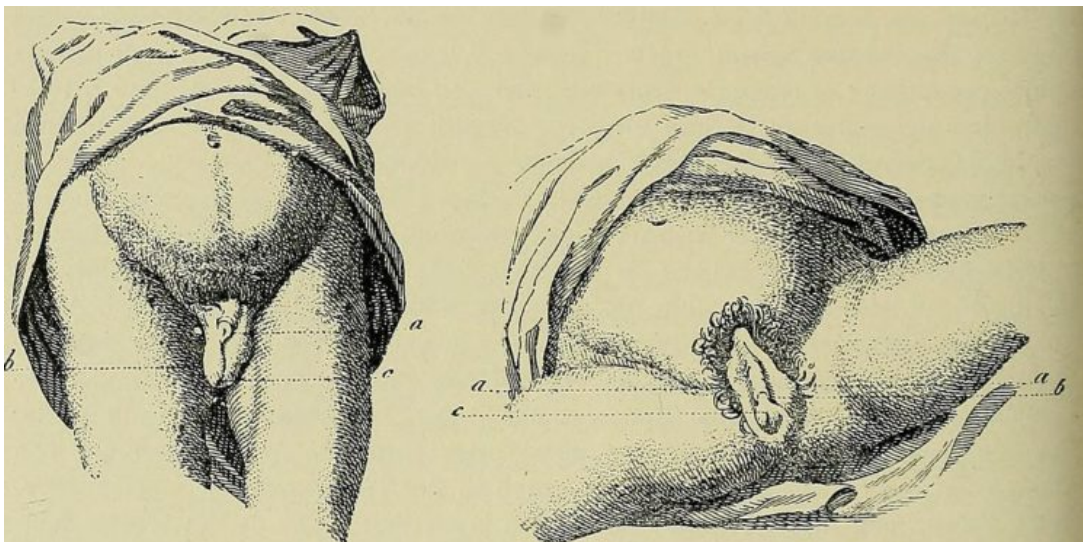


## True Hermaphroditism — Ovotesticular Disorder of Sexual Development

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**Ovotesticular disorder of sexual development is characterized by the presence of an ovotesticular gonad that contains both ovarian and testicular elements. Patients are usually born with ambiguous genitalia but the diagnosis is rarely confirmed before puberty. The most common karyotype is 46, XX but 46, XY can be identified in approximately 10% of the cases. Medical treatment of ambiguous genitalia is usually emergency based to treat life threatening conditions such as salt-wasting syndrome in congenital adrenal hyperplasia. Conservative surgery to remove part of the ovotestis gonad is the treatment of choice for this condition.**



### Definition of Ovotesticular Disorder of Sexual Development

Ovotesticular disorder of sexual development, also known as **true hermaphroditism**, is defined as the **presence of gonads that contain ovarian follicles and testicular tubules** in the same subject. The diagnosis can be confirmed only by **histologic confirmation** of the presence of ovarian and testicular elements in the same gonad and not by the ambiguity of the sexual characteristics of the subject.

### Epidemiology of Ovotesticular Disorder of Sexual

# Development

Ovotesticular disorder of sexual development (ODSD) is a **rare condition** that is responsible for only 10% of the cases of ambiguous genitalia. The cases are usually **sporadic and not familial**. Approximately, 400 cases have been reported in the literature so far.

This condition is associated with an **increased risk of mortality and morbidity** due to **malignant transformation** of the ovotesticular gonad.

ODSD is far more common in Africans from southern Africa regions. The diagnosis can be difficult as only 20% of the cases are diagnosed by the age of 5 years. Even at the age of 20 years, only 75% of the cases have been diagnosed.

## Etiology and Pathophysiology of Ovotesticular Disorder of Sexual Development

ODSD is a **genetic condition** that is characterized by: the presence of an **ovotestis gonad**, the presence of a **normal ovary in one side and an ovotestis gonad on the other**, the presence of a **normal testis on one side and an ovotestis gonad on the other** or the presence of a **normal testis on one side and a normal ovary on the other**.

Ovotestis gonads are usually subdivided into **compartments** where connective tissue separate testicular and ovarian elements. They are present in approximately 60% of the patients with ODSD who can have any **karyotype, female or male**.

The ovotestis gonad is usually in the location of the ovary **intra-abdominally**. The ovarian part of the ovotestis is usually functionally normal and responds to **estrogens**. A functional ovarian tissue would result in excess estrogen which would inhibit **spermatozoa development** and make the testicular part of the ovotestis non-functional.

Patients with ovotestis gonads can develop a **uterus**. **Mullerian ducts** do not develop near the ovotestis but can develop near the side with the normal ovary.

The presence of testicular and ovarian elements that are partially functional result in **ambiguous genitalia** in the majority of the cases at birth. Patients with a 46, XX karyotype might menstruate. The exact etiology of ODSD is unknown but is largely believed to be genetic based. Sex determining region on the Y chromosome (SRY) is responsible for testicular development in the male fetus.

While the majority of the cases with ODSD do not have Y chromosome or the SRY gene, an **autosomal gene called SOX9** has been found to be over-expressed in many cases. SOX9 is known to interact with SRY and might play a role in the development of testicular elements in the ovotestis gonad.

## Clinical Presentation of Ovotesticular Disorder of Sexual Development

These patients are usually born with **ambiguous genitalia**. The development of the **uterus** and **fallopian tube** can occur in a few patients with ODSD. Patients who are

raised as males can develop **feminization characteristics** during puberty which is the most common presentation of ODSD. Patients with ambiguous genitalia should be evaluated to rule out life threatening conditions such as **congenital adrenal hyperplasia**.

Newborns with **hyperpigmented skin** due to **elevated serum adrenocorticotropic hormone levels** should be evaluated to exclude congenital adrenal hyperplasia as the etiology of the ambiguous genitalia. Examination of the **labioscrotal fold** is indicated as it can have a testis or an ovotestis, especially on the right side.

A pubertal female without pubic and axillary hair might have **androgen insensitivity** while a male with fine body hair that is feminine could have ODSD.

Females with ODSD and a 46 XX karyotype can have a uterus which is likely to be abnormally structured. The presentation of **delayed menstruation** or **lower abdominal pain** because of **menstrual flow obstruction** can also occur.

Many patients with ambiguous genitalia are eventually assigned to a **male phenotype**. Those who have ODSD will have **breast development** and **thelarche** in 90% of the cases.

## Diagnostic Work-up for Ovotesticular Disorder of Sexual Development

Patients with suspected ODSD usually undergo **karyotyping** as the first step in their workup. Up to 80% of the cases have a **peripheral 46, XX karyotype**. In these patients, other conditions such as **congenital adrenal hyperplasia**, **maternal androgen ingestion**, and **excess maternal androgen production** should be excluded as they can lead to increased **masculinization** in a female newborn.

10% of the cases have a **46, XY karyotype**. In these patients, other causes of ambiguous genitalia should be excluded such as **deficiency of testosterone**, and complete or partial **androgen insensitivity syndrome**.

The remainder of the cases usually has some form of **mosaicism**. Once the diagnosis of ODSD is suspected, it is important to determine whether the testicular part of the ovotestis is functional or not.

Administration of **human chorionic gonadotropin** for five days that is accompanied by a rise in the baseline testosterone level is suggestive of functioning testicular tissue. Most patients with ODSD, however, do not have functioning testicular elements but have functional ovarian follicles which can be stimulated by the administration of **gonadotropin** or **clomiphene** to produce **estrogen**.

Patients with ODSD should undergo **scrotal ultrasonography** to identify if the gonads are normal or not. **Abdomino-pelvic magnetic resonance imaging** or **computerized tomography scans** are indicated to evaluate intra-abdominal gonads structure and the presence of a uterus. A **genitogram** is indicated to visualize the presence of a vagina. Intravenous pyelography is done to rule out associated renal tract malformations. Prenatal diagnosis is done by amniocentesis when genital ambiguity is found in ultrasonography.

The only way to confirm the diagnosis of ODSD is to perform a histologic examination on a **biopsy** taken from the ovotesticular gonad. **Laparoscopy** can be used to have access

to the intra-abdominal gonad.

## Treatment of Ovotesticular Disorder of Sexual Development

Treatment for patients with ODS is **different based on the presenting age**. Newborns with ambiguous genitalia need **emergency medical treatment** to correct **salt wasting disorders** such as **congenital adrenal hyperplasia**.

Patients with **delayed puberty** either due to **estrogen deficiency** or **testosterone deficiency** and based on which sex they have been assigned to might need **sex hormone replacement therapy**.

Once the diagnosis of ODS is confirmed by biopsy, it is important to **remove the abnormal gonad** especially if the other gonad on the contralateral side is normal. This approach maximizes **fertility potential**. Minimally invasive surgery is recommended for patients with ODS and **laparoscopy** is an option.

Patients with an **XY karyotype** should have their **ovotestis gonad removed** because the risk of **malignant transformation** is highest in this group. Patients with an XY karyotype might benefit from **conservative surgery** in which one part of the ovotestis, usually the testicular part, is removed. Patients who undergo conservative surgery might achieve **pregnancy**.

Patients who are assigned to a **female sex phenotype** should have **plastic corrective surgery** to resect the clitoris, and for vaginoplasty.

## Complications

- Patients with genital ambiguity may have emotional insecurities and may face social stigma.
- 6% of all cases of ovotesticular disorder of sexual development have a tendency to develop malignant tumors. Benign tumors may also develop.
- Obstructed genital tract due to cervical atresia may give rise to cryptomenorrhoea, hematometra, and endometriosis.
- Inguinal hernia is common
- There is a tendency for gonadal torsion along with other associated structures due to malposition of gonads.
- Infertility is contributed by defective spermatogenesis
- Patients with true hermaphroditism have a normal intelligence level and most of the patients lead a normal life expectancy.

## References

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