The Ovary
from Birth to Adolescence

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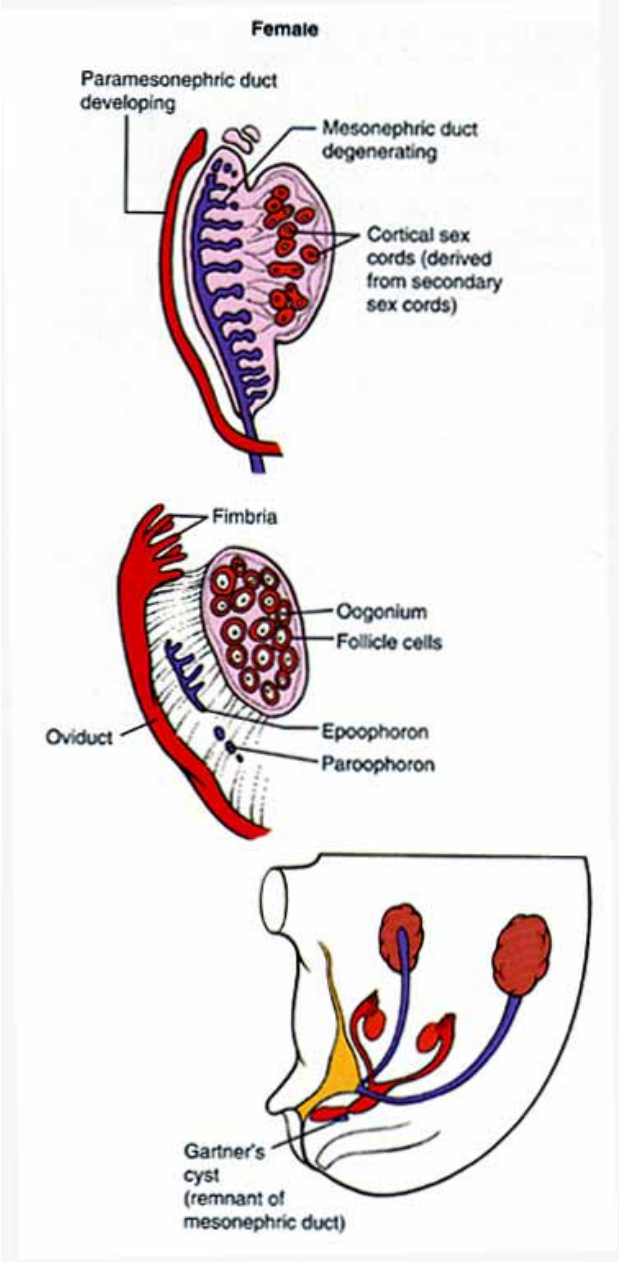
Ovarian Development

During fetal life, the development of the human ovary can be traced through four stages:

- • The indifferent gonad stage
- • The stage of differentiation
- • The period of oogonial multiplication and oocyte formation, and
- • Stage of follicle formation



Ovarian Development *cont.*

- • At 6-8 weeks the first signs of ovarian differentiation are reflected in the rapid mitotic multiplication of germ cells reaching 6-7 million oogonia by 16-20 weeks.
- • From this point in time germ cell content will continue to decrease until some 50 years later, the store of oocytes will be finally exhausted.

Ovarian Development *cont.*

- At 18-20 weeks the highly cellular cortex is gradually perforated by blood vessels originating in the deeper medula areas, and this marks the beginning of follicle formation.

Ovarian Development *cont.*

- Pre-ovulatory follicles can be found in the 6th month of gestation at variable ripening even undergoing atresia; however, full maturity as expressed in ovulation does not occur during fetal life.

Ovarian Development *cont.*

- The ovary at birth and in the first year of life can contain cystic follicles of varying size stimulated by the reactive gonadotropin surge accompanying the withdrawal of the neonatal hypothalamus and pituitary from the negative feedback of fetoplacental steroids.
- Ovarian cysts can also be occasionally detected in fetuses by ultrasonography.

Ovarian Development *cont.*

- The hypothalamic-pituitary portal circulation is functional by the 12th week. FSH peak at 20-23 weeks circulating levels peak at 28 weeks. These levels are higher in female fetuses than in males until the last 6 weeks of gestation.
- In fact, the FSH levels in the neonatal period are greater than the levels reached during a normal adult menstrual cycle decreasing to low levels usually by one year of age.

Ovarian Development *cont.*

- Follicular response to the antral stage is relatively common in the first 6 months of life in response to the elevated gonadotropin levels.
- Functional ovarian cysts then exist in the fetal and neo-natal period due to the gonadotropin activity from maternal origin.

Ovarian Development *cont.*

- Therefore, the most common cause of abdominal masses in fetuses and newborns is ovarian cysts, a consequence of gonadotropin stimulation.
- After the post-natal rise, gonadotropin levels reach a nadir during early childhood by about 6 months of age in males and 1-2 years in females and then rise slightly between 4 and 10 years.

Ovarian Development *cont.*

- The childhood period is characterized by low levels of gonadotropins in the pituitary and in the blood, little response of the pituitary to GNRH, and maximal hypothalamic suppression.
- The ovary, however, is not quiescent during childhood. Follicles begin to grow at all times and frequently reach the antral stage.

Ovarian Development *cont.*

- Ultrasound detects ovarian follicular cysts during childhood, raging from 2-15 mm.
  These small unilocular ovarian cysts are not clinically significant.

Ovarian Development *cont.*

- The lack of gonadotropin support prevents full development and functions up to puberty.
- The average size of pre-ovulatory follicle is 2 cm.

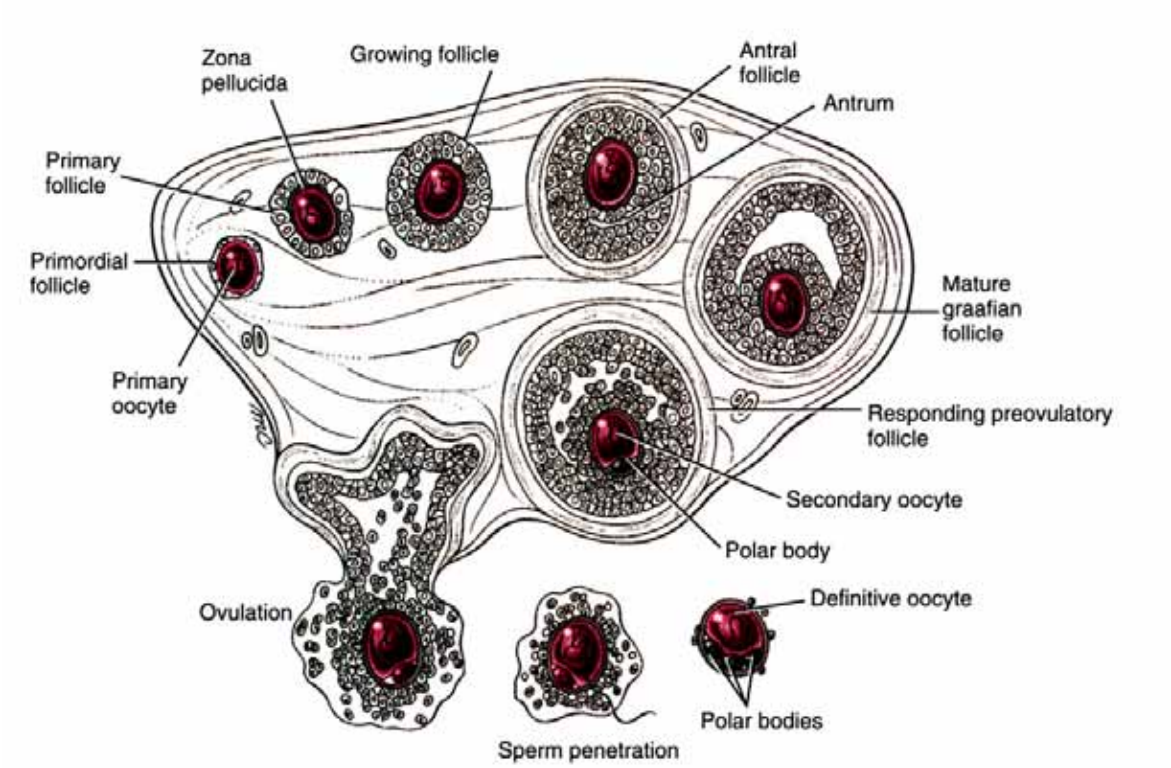
Ovarian Development *cont.*

- After ovulation, a corpus luteum is produced from the residual cellular components of the ovulatory follicle.
- Functional ovarian cysts are 3cm or larger fluid-filled ovarian structures that are not neoplastic but the result of gonadotropin stimulation of the ovary.
- Physiologic and functional cysts occur both in ovulatory and anovulatory cycles

The Adult Ovary

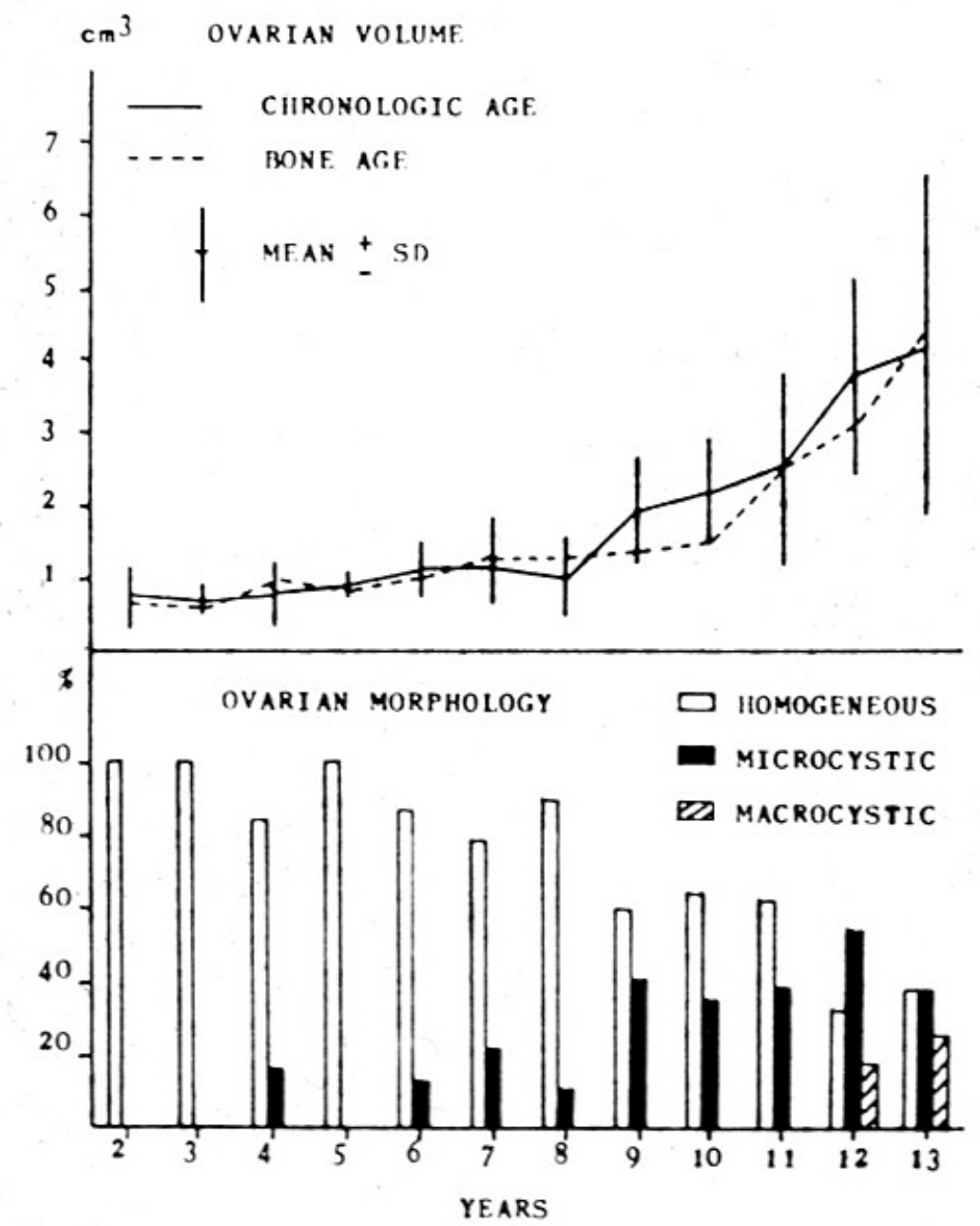
- At the onset of puberty the germ cell mass has decreased to 300,000 to 500,000 units.
- During the next 30-40 years of reproductive life, 400-500 will be selected to ovulate.
- For every follicle that ovulates, close to 1,000 will pursue abortive growth periods of variable length.

The Adult Ovary



With the establishment of the hypothalamic-pituitary-gonadal interactions during the repro-ductive period the typical cycle of follicle maturation, including ovulation and corpus luteum formation, will be realized.

Ovarian volume (upper part of the figure) and changes in ovarian morphology (lower part) as determined by ultrasonography from ages 2 to 13.

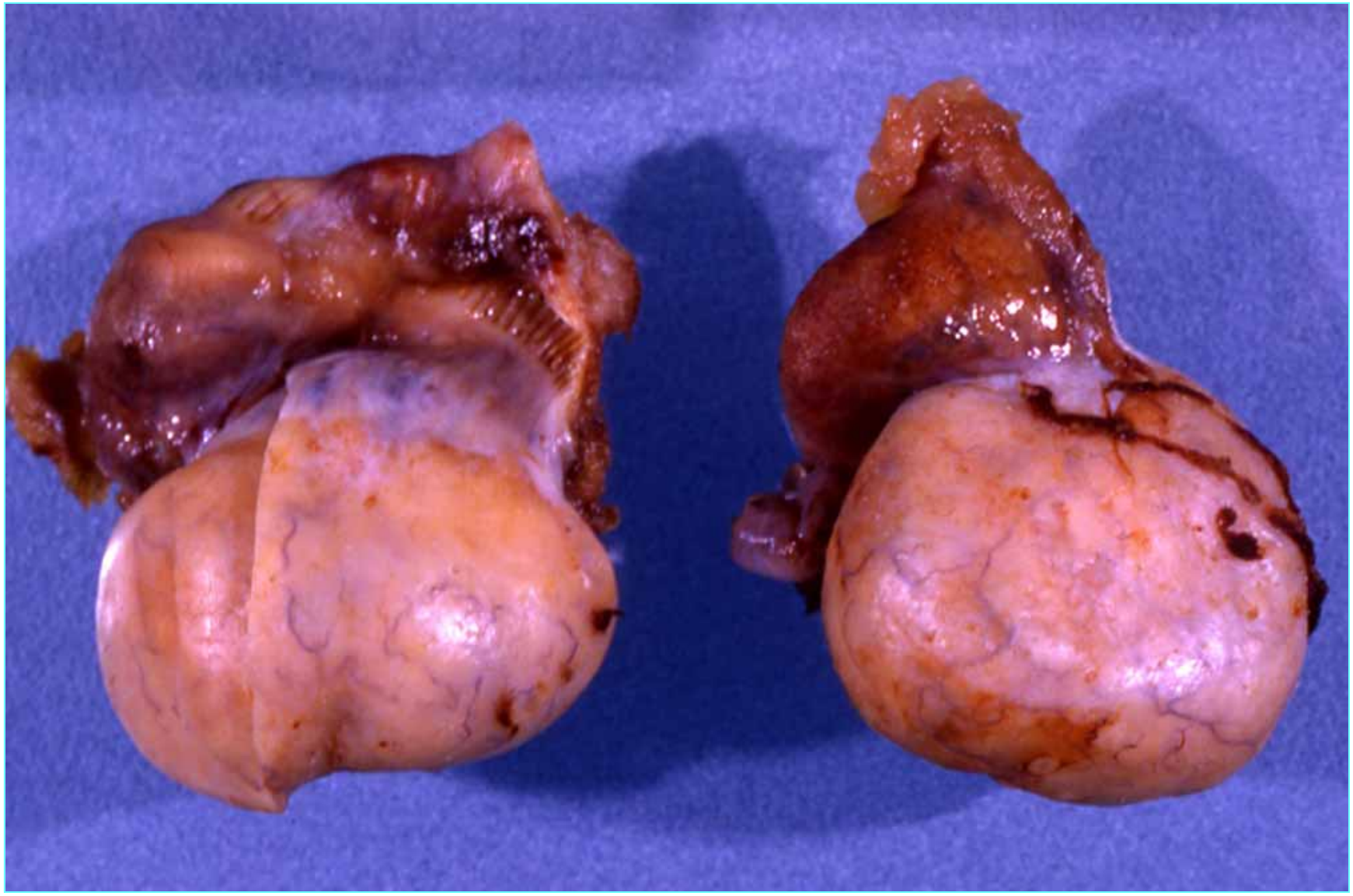


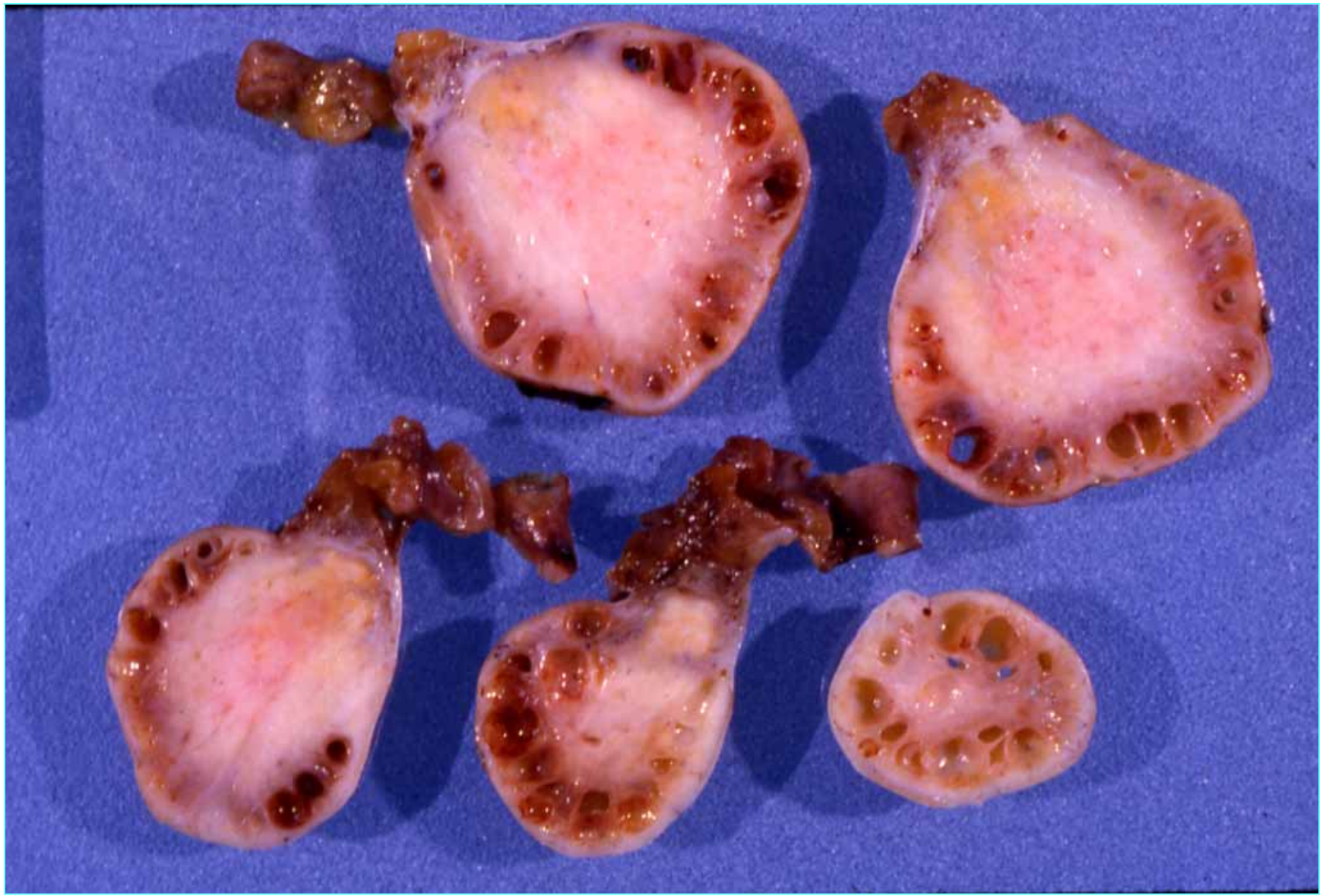
Ovarian Morphology - Normal adolescent ovaries

- Ovaries have multiple follicles (at least 6) usually 4-10mm in size.
- The follicles are randomly distributed.
- Normal ovarian stroma volume.

Ovarian Morphology - PCO

- Polycystic ovaries
- Ovaries are increased in size.
- Ovaries are symmetrical.
- Ovaries have increased stroma.
- Peripheral array of multiple (<8) small cysts 2.8mm diameter





Ovarian Cysts

- Ovarian cysts frequently cited as the cause of pelvic pain do not cause pain.
- The vast majority of ovarian cysts are functional cysts, namely, follicular, corpus luteum and theca luteum cysts.
- They result from gonadotropin stimulation of the ovarian cortex during the follicular phase when a cohort of follicles are recruited. These follicles mature from primordial follicles to pre-antral follicles; ultimately, one follicle becomes pre-ovulatory follicle.

Ovarian cysts cause pain by:

- Rupture of a cyst with spillage of the contents into the peritoneal cavity may cause irritation and thus pain. When this occurs from the ovulatory follicle, it is called Mittleschmerz. The pain is acute in nature and generally does not persist beyond 24-28 hrs. If pelvic pain is chronic in nature, it is most likely not secondary to cyst rupture.
- Pulling on the adnexal structure by the ovarian cysts may also cause pain, however, in patients with large polycystic ovaries or with ovarian tumours, pelvic pain is a rare complaint.

Ovarian cysts cause pain by:

- Stretching of the cortex can cause pain when cysts grow rapidly as it occurs in patients undergoing ovulation induction.
- Torsion and detorsion of the adnexae occur mainly in association with ovarian cysts or paraovarian cysts. The twisting of the blood supply results in intermittent pain.

Spanos WJ: 1973

- Cystic masses between 4 & 10 cm in 286 women aged 16-48 were treated with a 6-week course of combined estrogen-progesterones. At the end of 6 weeks 28% of the masses remained. At the time of surgical exploration, none of these masses were functional ovarian cysts.
- This treatment produces the following cyst resolution rates: 4 – 6 cms – 84%
  6 – 8 cms – 56%
  8 – 9 cms – 39%

- The conclusion was that the estrogen-progesterone therapy suppresses gonadotropin stimulation such that all functional cysts resolved.
- Further randomized studies have shown that estrogen-progesterone therapy does not hasten the resolution of functional cysts when compared with control groups receiving no therapy.

- In the female with a cystic mass of 7 cms or less, observation for a 6-week period followed by re-examination will confirm resolution of most cystic masses.
- In patients without resolution, surgical exploration should then be performed.

Role of oral contraceptives to induce cyst resolution

- The 50 mg EE containing pill (high dose formulation) substantially decrease the risk of functional ovarian cysts.
- Low dose formulations do not support this decrease as FSH suppression is much less with low-dose pills than with high dose pills.
- Patients on progesterone-only pills have a higher incidence of functional cyst formation than women on no exogenous hormones, these <u>are not</u> recommended for suppression of ovarian cysts.

Adnexal torsion

- Acute onset of unilateral abdominal pain.
- More frequent on the right side due to the anatomic suspension of the tube and ovary.
- The nature of the pain is colicky and there may be a history of similar pain in the past.
- Nausea and vomiting are associated with the onset of pain in about one-fourth of patients.
- The clinical presentation often is similar to that of appendicitis especially since the right adnexa is more commonly involved.

DD: Adnexal torsion (AT) *vs* appendicitis (A)

- With AT the onset of pain is acute, whereas with A pain tends to be more gradual and peri umbilical in onset, then migrating and becoming more acute in the RLQ.
- If nausea is present, it occurs at the onset of pain with AT but after the onset of pain with A.
- Pelvic mass is more commonly felt with AT than A. Normal ovaries, fallopian tubes and para ovarian cysts can be involved in torsion.
- On ultrasound, the appendix is usually visible with A whereas it is not visible with AT. If AT is associated with a mass, the mass is frequently seen on ultrasound.

Treatment of adnexal torsion

- Surgical excision when the torsed structure is clearly necrosed.
- Detorsion of the torsed structure with observation of reestablishment of adequate blood supply with or without oophoropexy depending on the degree of adnexal mobility.

Summary

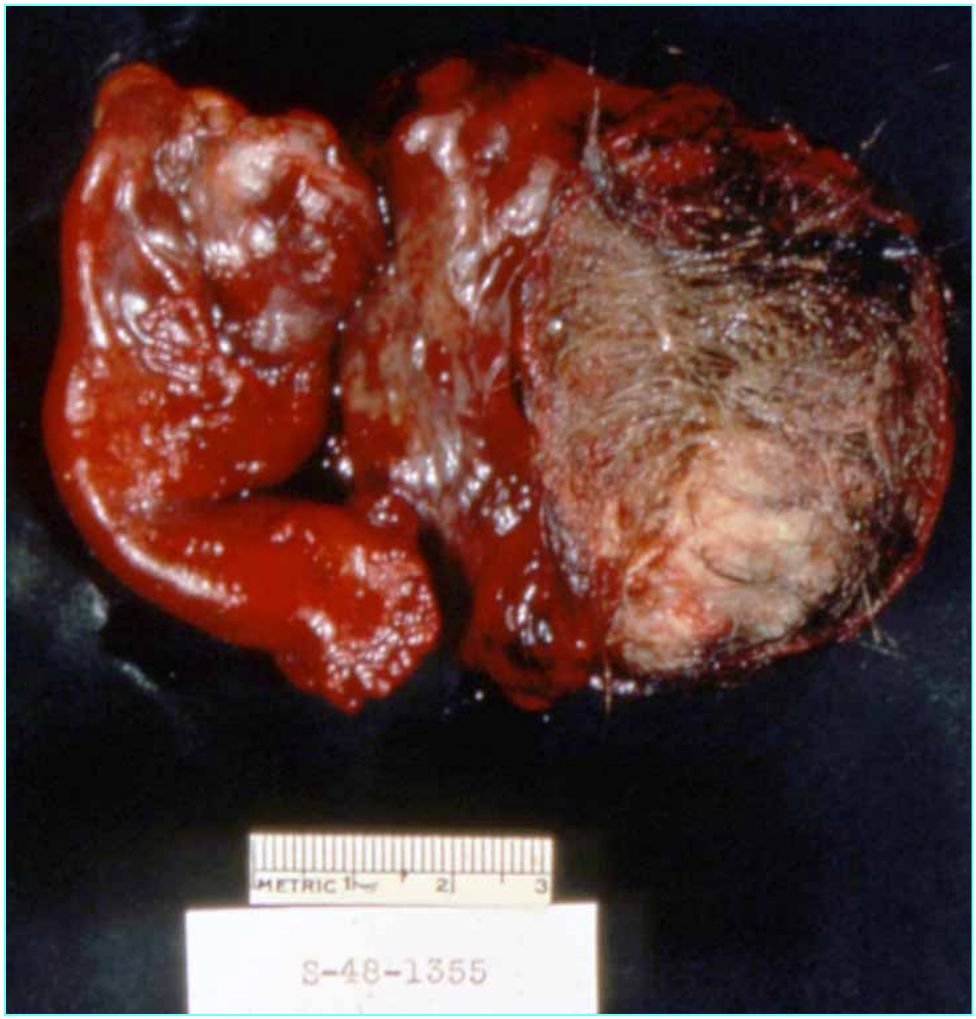
- The ovary is an active organ from fetal life to menopause.
- The vast majority of ovarian cysts (98%) are functional.
- The adolescent ovary is multifollicular with pre-ovulatory follicles measuring 2 cm.

Summary

- A cystic mass of 5-7 cm in size is usually mobile and can be managed conservatively with observation and return to the ER if the patient has acute pain. Torsion of the ovary is the greatest hazard because delay of therapy can lead to necrosis.
- Use ultrasound wisely. Unfortunately ultra-sonography has resulted in patient's contributing the pain to a cyst creating fears of cancer and undue anxiety in the patient and family.

Summary

- Mature teratomas are most common ovarian tumours in young women and 40% of these tumours have teeth, an abdominal flat plate would show a calcification.



Summary

- If a mass is palpated and feels fixed or solid, appears complex on ultrasound, larger than 5-7cm obtain tumour markers and refer the patient for definitive therapy.

Ovarian tumors in adolescents:

- Every known ovarian tumor of adults has been described in adolescents.

- While fewer than 1% of neoplasms in adolescents are ovarian tumors.

- Ovarian tumours in adolescents are by far the most common of the genital tumors.

- Most of these arise from the germ cell.

- Only 10% of adolescent neoplasms act in a malignant manner