Ultrasound of Uterus and Ovary

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**Introduction**

Characteristics of ovarian follicles are studied by ultrasound in several situations:

1.) In intrinsic diseases of pituitary/hypothalamic/ovarian function - disordered follicular cycling may be detected, as in polycystic ovarian syndrome and other ovarian causes of infertility.

2.) As a means of monitoring and adjusting hormonal therapy directed at the ovary (particularly ovarian stimulation). Ultrasound can also facilitate safe simple oocyte recovery.

3.) As the normal background from which non-endocrine ovarian/pelvic diseases must be distinguished, i.e. differentiation of "normal" ovarian cysts from ovarian neoplasm and pelvic infection.

We will present the following sections dealing with ovarian ultrasound.

1.) Characteristics of the normal ovary

2.) Normal ovarian cycles and stages of follicular development.

3.) Characteristics of the normal uterus and cyclic endometrial changes.

4.) Common varieties of abnormal cycles.

5.) Application of ultrasound in induced ovulation and assisted conception therapies for infertility.

**Section 1: The Normal Ovary by Ultrasound**

**Position:**

The normal ovary in the resting (menstrual) phase is moderately echogenic, well margined and located in
the lateral edge of the broad ligament.

Because it is mobile, it may be found from the pelvic cul-de-sac to the lower abdomen (often displaced superiorly by distended urinary bladder, coming to lie anterior and lateral to the iliac vessels).

Despite this variability, it is typically found lateral to the fundus of the uterus.

Resting (menstrual Baseline) Echopattern:

**Premenarchal:**

Ovaries are small, and often show a uniform moderately echogenic solid structure.

It is typical to note scattered antral follicles (small 3-6 mm cysts) during the years 9-13 preceding menarche. Follicles in younger patients however are not necessarily evidence of endocrine dysfunction.

Size of premenarchal ovaries is quite variable, making conclusions based on size alone unreliable.

**Puberty through Middle Age:**

Solid background with scattered antral follicles (3-6 mm cysts).

This pattern is punctuated by the regular cyclic development of graafian follicles.

**Post-Menopausal:**

Solid background, antral follicles may persist 4-5 years following clinical menopause. Ovarian size is smaller.

Simple cysts (Usually small) are seen in about 10% of post-menopausal women. Such cysts are worrisome, however if they are completely smooth with thin walls, they almost never become malignant. None the less, it is usual to follow any benign appearing lesion in the ovary with serial ultrasound examinations, and remove any lesion with malignant features or substantial growth.

**Normal Ovarian Size:**

In general, Post-menarchal ovaries measure 2.5-5 cm in length, and 1.5 to 3 cm. in width and depth. Volume generally is

Because of the ovary has a variable, usually oval shape, size is best expressed as an estimated volume.

Ovarian Volume is estimated as:

\[
\text{Volume (ml.)} = \text{Length (cm)} \times \text{Width (cm)} \times \text{Depth (cm)} \times 0.52
\]

Using this formula, normal ovarian size is generally

Pre-pubertal 0-8 ml.
Post-pubertal 0-18ml
Post-Menopausal 0-8 ml.

The Ratio of larger to smaller ovary should normally be less then 2:1
Volume Estimates as a function of age:

Age 0-10 yr. : Mean 1.7 ml. 0.2 - 4.9 ml (95% Confidence Interval)
Age 11-20 yr. : Mean 7.8 ml. 1.7 - 18.5 ml. (95% Confidence Interval)
Age 21-30 yr. : Mean 10.2 ml 2.6 - 23.0 ml. (95% Confidence Interval)
Age 31-40 yr. : Mean 9.5 ml. 2.6 - 20.7 ml. (95% Confidence Interval)
Age 41-50 yr. : Mean 9.0 ml 2.1 - 20.9 ml. (95% Confidence Interval)
Age 51-60 yr. : Mean 6.2 ml. 1.6 - 14.2 ml. (95% Confidence Interval)
Age 61-70 yr. : Mean 6.0 ml. 1.0 - 15.0 ml. (95% Confidence Interval)

This Normal resting Ovary is a non-descript ultrasound structure:

![Ovary on Day 6](image)

**Section 2: Ultrasound of Normal Ovarian Follicular Cycles**

**Introduction:**

Although the hormonal background of follicular development is among the more complex endocrine control sequences, the resulting sequence of gross morphologic changes visualized by ultrasound is a simple sequence of enlarging cysts.

Using measures of size, number, and temporal progression, ultrasound can verify normal sequences, or in many cases, diagnose ovulation failure by recording at what point follicular development is arrested.

**Normal Development:**

The resting ovary contain a women's full complement of potential follicles. The resting primordial follicles
are too small to be seen grossly, or by ultrasound examination.

**Follicular Phase:**
Initial follicular development occurs during the proliferative (follicular) phase of the menstrual cycle, approximately days 1-14 counting from the first day of menstrual flow, and ends with ovulation.

During the follicular phase, a small subset of the primordial follicles are stimulated to develop, and accumulate follicular fluid, with enlargement ultimately visible by ultrasound. The granulosa layer of the developing follicles secrete estrogen.

It is the pulsatile release of Gonadotrophin Releasing Hormone (GnRH) in the pituitary that stimulates Follicle Stimulating Hormone (FSH) secretion which acts to stimulate follicular development.

Developing Follicles are first seen by ultrasound as a group of 4-8 antral follicles 3-5mm size by day 6-7. This image shows the small antral follicles.

Within a given ovary, only one of the developing follicles is "selected" to become a dominant mature graafian follicle, and to ovulate.

By day 7, the selected follicle begins to outstrip the growth of the subordinate follicles. The process of selection is not well understood. In part local factors may operate. In part, the dominate follicles secrete large amounts of estrogen, which feeds back on the pituitary, reducing FSH stimulation to further follicular development.

By Ultrasound, early antral follicles are 2-4mm in size. Developing follicles range between 5-10 mm. The dominate "selected ", follicle will continue to grow, reaching 10mm on day 8-9 and reaching final mature size of 18-24 mm. on day 14 prior to ovulation. Typically subordinate (non-dominate follicles reach 10 mm and then become atresic. Follicles 11 mm or larger are usually dominate follicles. This following image shows a dominate follicle. Ovulation of this follicle occurred shortly after this image, a follow-up image is shown in the next section in which ovulation results in disappearance of the follicle.
The drawing below shows the development cycle from upper left primordial follicle, through antral follicles which progress to a Mature follicle and several atresic follicles. On the right margin is the mature follicle, ready for ovulation and the end of the follicular phase.

**Secretory Phase (Luteal Phase):**
On about day 14, the mature follicle expels the oocyte. In most cases, loss of fluid associated with expulsion of the oocyte results in disappearance or substantial decrease in size of the mature follicle. This abrupt change in size represents the Ultrasound sign of ovulation. The image below shows disappearance of the mature follicle shown in the previous section as a result of ovulation.
The defect in the follicle heals in 2-5 days. The wall thickens as cells are "luteinized" (lining cells enlarge and fill with lipid), and in most cases, the antrum fills with blood to form a "corpus hemorrhagieum. The follicle becomes a "corpus luteum", contributing hormone secretion, particularly progesterone to support the Secretory Phase.

On ultrasound, the corpus luteum reappears in several forms. About 1/3 are a typical cyst of similar size to the mature follicle or larger. About 1/3 are more echogenic, forming a nearly "solid" ultrasound appearance. About 1/3 are not apparent at ultrasound examination.

If pregnancy occurs, HCG secreted by the trophoblast maintains the corpus luteum through the 10 week of gestation. If pregnancy does not occur, the Corpus Luteum usually disappears within a day or two of the onset of menses.

Clinical Importance:
Because almost all functional ovarian cysts disappear by the 5th day of the subsequent cycle, concerns regarding neoplastic origin of unusually large functional of cysts can usually be dispelled by demonstrating their disappearance by 3-5 days into the next cycle.

For the same reason, screening for early ovarian tumors must be done during the first 5 days of the cycle to avoid needless confusion with physiologic cysts.

The following figure demonstrates the relationship of the key hormones involved in the normal ovarian cycle. Estrogen dominates the follicular phase, produced by the developing follicle, progesterone dominates the luteal phase, produced by the corpus luteum.
FSH and LH function together to facilitate follicular development. A mid-cycle LH surge serves to complete follicular maturation and trigger ovulation.

**Section 3: Ultrasound of the Uterus and Cyclic Endometrial Changes**

**Normal Uterine Size:**

By ultrasound, the normal postmenarchal nulliparous uterus is 5-8 cm in length, 1.5-3 cm thick, 2.5-5 cm. wide.

**Myometrium:**

The normal myometrium is hypoechoic, homogeneous, and reasonably well demarcated from the endometrial echos.

**Endometrial Structure:**

The endometrium consists of a constant basal layer (basalis), and a cycling functional layer (functionalis). The Functional layer includes a thin compactum layer and a thick spongiosum layer.

**Endometrial Measurement:**

The myometrial/endometrial interface is usually a hypoechoic halo created by the Basal (Basalis) and Inner Compactum (Functionalis) layers, which represent the deepest endometrial layers. The Basalis is constant through the menstrual cycle.

The thickest portion of the active endometrium is the spongiosum which presents varying degrees of hyperechogenicity during the cycle. It is this hyperechoic portion that is typically included in ultrasound measures of endometrial thickness.

By convention, measurement of endometrial is the thickest portion in a mid-sagittal (longitudinal) view, from anterior hyperechoic border, to posterior hyperechoic border. Thus it represents a double layer thickness, and predominately includes the outer compactum and spongiosum portion of the functionalis layer.

**Cyclic Endometrial Thickness:**

The endometrium is thinnest during menses. At that time is is seen as a thin hyperechoic line, usually 1-4 mm. thick.

Progressive thickening of the functionalis occurs during the follicular (proliferative) phase. Thickness reaches 8-12 mm by the end of the follicular phase, and remains at this thickness during the luteal (secretory) phase. At the onset of menses, there is a rapid decrease, sometimes associated with visible fluid blood.
Ultrasound appearance of cyclic endometrium.

Menstrual Endometrium: The menstrual endometrium is composed of only three ultrasound layers. The basalis is a constant hypoechoic line on either side of a thin hyperechoic band constituting residual functionalis and the endometrial cavity. The double layer sagittal echo consists of:

- Anterior hypoechoic line (Basalis)
- Thin hyperechoic band (Cavity and both layers of residual functionalis)
- Posterior hypoechoic line (Basalis)

Follicular (Proliferative) Phase Endometrium:

The follicular phase is characterized by progressive thickening of the functionalis which is mildly hypoechoic. By day 7-8, appreciable thickening of 4-5 mm (standard double layer measure) can be seen. From this point progressive thickening occurs through the end of the follicular phase (Ovulation on about day 14), usually reaching 8-12 mm. This represents a plateau, since little additional thickening is seen during the luteal (secretory) phase.

On ultrasound, the outer hypoechoic line remains, and a slightly hypoechoic band develops, sandwiched between thin hyperechoic lines (one at the basalis junction, one at the canal).

The resulting double layer echo pattern actually consists of:

- Thin hypoechoic line (anterior Basalis echo)
- Thin hyperechoic line (anterior interface with functionalis)
- Thick hypoechoic band (anterior proliferating functionalis)
- Thin hyperechoic line (endometrial canal echo)
- Thick hypoechoic band (posterior proliferating functionalis)
- Thin hyperechoic line (posterior interface with functionalis)
- Thin hypoechoic line (posterior basalis echo)

However, this is simply described as the "Triple Layer", identifying only the two proliferating bands, and the central canal echo.
**Luteal (secretory) Phase Endometrium:**

During the luteal phase, endometrial thickness does not appreciably increase. Instead, echogenicity increases often to a point where hyperechoic interface and canal echos blend with the thickened functionalis is a uniform "single band" surrounded by the thin hypoechoic basalis.

The increase in echogenicity is thought to result from increasing tortousity of endometrial glands, and the progressive secretion of mucin and glycogen. The secretory accumulation is reflected in increased through transmission of ultrasound, evident as acoustic enhancement of the myometrium deep to endometrium.

The resulting double layer echo pattern actually consists of:

- Thin hypoechoic line (anterior Basalis echo)
- Thick hyperechoic band (anterior secretory functionalis)
- Thin hyperechoic line (endometrial canal echo) may blend with adjacent bands
- Thick hyperechoic band (posterior secretory functionalis)
- Thin hypoechoic line (posterior basalis echo)
Secretory endometrium is normally 8-14 mm, but occasionally it may reach 15-20 mm. In such instances, it is indistinguishable from hyperplasia or even carcinoma. However, a follow-up study done during the next menses can readily demonstrate return to normal thickness.
Most changes in appearance with hormone therapy are similar to natural hormones. Tamoxifen is an exception, it may produce not only general thickening, but also an unusual pattern of many small cysts in a thickened endometrium and small amounts of endometrial fluid. These changes are common and should not be assumed to be malignant.

In general, if the maximum thickness of the endometrium is less than 5 mm. (double layer), endometrial pathology is effectively excluded.

Measurements of 6-14 mm are often seen in normal premenopausal women, but may occasionally harbor significant pathology.

Measurements 15 mm. or greater are suspicious, and should usually be rechecked to exclude progressive pathology.

**Section 4: Ultrasound of Abnormal Ovarian Cycles**

Ovarian cycles which do not result in ovulation are relatively common.

Sporadic failure is noted in about 7% of cycles.

In addition, some women demonstrate chronic ovulation failure in defined patterns or syndromes.

Sporadic Anovulatory Mechanisms: Three basic mechanisms appear to result in a occasional ovulation failure.

1.) Follicular Atresia:

In these cycles, the proliferative maturing effects of E2 (estrogen) are not properly synchronized with the the LH (luteinizing hormone). The resulting follicle does not reach full size or ovulate.

Ultrasound shows a dominate follicle which does not reach full mature size (16-24mm.) and become rapidly atresic. This is the morphologic pattern most frequently observed in patients taking oral contraceptives.

2.) Empty Follicle Syndrome:

Follicular development is grossly normal, but aspiration or natural ovulation does not produce an oocyte. Failure to demonstrate a cumulus oophorus with a mature follicle on very high resolution ultrasound may be seen. However visualization of the cumulus is difficult under optimal conditions, the accuracy of ultrasound in demonstrating the syndrome in probably low. Under routine study, these cycles are likely to appear normal.

3.) Luteinized Unruptured Follicle Syndrome:

In this syndrome, an apparently normal mature luteinized follicle fails to rupture and ovulate. It goes on to behave as a luteinized follicle. The syndrome can be recognized as a follicle which fails to collapse in association with the expected LH peak.
The luteinized unruptured follicle secretes estrogen and progesterone normally, and measured hormone levels are normal. At least in some cases, ultrasound produces a false positive diagnosis.

Chronic Ovulation Failure: Three groups of syndromes are associated with chronic anovulatory cycles:

1.) **Hypergonadotropism:**

Here primary ovarian failure leads to small ovaries and low secretion of estrogen. The anestrogenic state leads to lack of feedback on gonadotrophin secretion and Hypergonadotropism.

Causes include primary failure, autoimmune damage, and chromosomal mosaicism.

Ultrasound shows small or absent ovaries without follicles. Except in autoimmune causes, this group of patients do not respond to treatment.

2.) **Hypogonadotropism:**

In this group, FSH and LH levels are found to be low, and evaluation for pituitary tumor is indicated. Ovarian function is often normal and may be recovered through correction of pituitary problems, or exogenous FSH and HCG (LH replacement). Due to inadequate stimulation, these patients also have low estrogen levels.

3.) **Polycystic Ovary Syndrome (PCO):**

These patients are oligomenorrheic or amenorrheic but are estrogenized. Pituitary secretion is acyclic, ovaries produce androstenedione, peripheral tissues (adipose) produce estrogen. They respond to progesterone with menses and spontaneous menses are usually estrogen breakthrough bleeding. Low FSH levels fail to stimulate complete follicle development, LH levels are high.

On ultrasound, these patients ovaries may be "normal", but are more often enlarged ( > 6ml.), and tend to have an increased number of small incompletely developed follicles (>11) and no dominant size follicles. The stroma in the central part of the ovary is usually abundant and hyperechoic.

Doppler blood flow has been reported to be faster in PCO.

Diagnosis is complicated however, because some PCO patients are within normal limits, and some normal patients have large ovaries, or numerous follicles.

In women with the typical ultrasound appearance of PCO (Large echogenic ovaries and many small follicles), half will have clinical PCO, one-quarter will have a PCO variant, and one-quarter are normal.
Section 5: Ovarian Ultrasound in Infertility

Ovulatory disorders present in 15-25% of infertile women
Except for premature ovarian failure and hyperprolactinemia, ovulatory disorders frequently respond to drug therapy. Drug mechanisms include primary CNS receptor alteration, with clomiphene, direct gonadotropin replacement with HMG (Human Menopausal Gonadotropin) and HCG (Human Chorionic Gonadotropin), and secondary receptor stimulation with synthetic Gonadotropin Releasing Factor (GnRH).

Although multiple ovulation is uncommon with natural cycles, with stimulated cycles, multiple mature follicles and multiple ovulation as much more common. (Natural cycles - 5-11% multiple, Clomiphene 60%, HMG - 80%).

If natural conception is to occur, large numbers of ovulating follicles may lead to unnecessary morbidity due to high multiple gestation, and hyperstimulation, thus if many follicles are developing, the cycle may be stopped without maturation doses (HCG).

If oocyte retrieval and assisted conception is planned, harvest of many oocytes is an advantage, and larger numbers of follicles will be allowed to reach maturity.

In general, anestrogenic syndromes (such as deficient gonadotrophin) produce uniform populations of follicles because the starting primordial follicles are completely unstimulated, and develop uniformly.

Women with estrogenic anovulatory syndromes show more unpredictability in the rate of follicle development, since follicles can be found which have varying levels of development prior to treatment. Regardless of the mechanism, the role of ultrasound is to document follicular development:

1.) Detect the development of mature sized follicles.

2.) Time the administration of Maturation/Ovulatory Trigger doses (HCG).

3.) Withhold trigger dose if larger number of mature follicles suggests a risk of multiple gestation (Natural Conception) or luteal hyperstimulation (Natural and Assisted conception).

4.) Guide Oocyte retrieval (Assisted conception).

5.) Document ovulation (Natural Conception).

6.) Monitor luteal function, predict hyperstimulation syndrome.

Ultrasound monitoring of cycles is a simple matter of finding, mapping, measuring, and counting follicles on serial studies. This allows characterization of mature follicles, documentation of ovulation, and monitoring of luteal size and number.

The typical Ultrasound follicular monitoring series proceeds as follows:

1.) Baseline ovarian ultrasound to identify any unresolved cysts from the previous cycle as well as other problems such as endometrioma or hydrosalpinx.
2.) Serial monitor of follicular development beginning on day 8-10. On this study developing follicles of 8-10mm size allow early assessment of likely response.

3.) Follicle monitoring goes on daily or every other day from day 8-10 until follicular size reaches mature size of 16-18 mm. At this point, an HCG pulse is often given to complete maturation and trigger ovulation.

As an alternative, serum estradiol measurements can be performed, each mature follicle produces about 400 pg/ml serum level, in this case ultrasound between 10-12 days may be used simply to count follicles.

If harvest of oocytes is the goal, a 15 mm. size may be selected, with harvest after maturation, but before spontaneous ovulation.

4.) Ovulation is detected as a sudden disappearance or substantial decrease in size (usually >50% decrease).

Baseline: Uniform solid appearance.

Serial monitoring Day 9: Small Follicles Just Apparent.

By day 13, multiple follicles are nearing mature size. In stimulated cycles, physiologic feedback is overcome, allowing numerous follicles to complete development.
By day 17 multiple mature sized follicles are evident. Although maturation by day 13-14 is typical, stimulated cycles not infrequently show slightly slower development as in this patient. In this setting, ultrasound is particularly helpful.

This patient went on to develop a mild hyperstimulation syndrome, the images showing hyperstimulation follow our description of the syndrome.

**Hyperstimulation Syndrome:**

Ovarian hyperstimulation results from numerous follicles developing during the luteal phase of a stimulated cycle, particularly if pregnancy occurs allowing luteal stimulation by trophoblastic HCG.

Hyperstimulation is characterized by pain in relation to enlarged ovaries.

In mild cases, pain with ovarian enlargement to 5-7cm will be seen.

In more severe cases, ovarian size > 10 cm occurs in association with ascites, pleural effusion, hemoconcentration, hypotension and oliguria. In severe cases ovarian torsion and rupture may occur. Symptoms develop 5-7 days following ovulation.

Ultrasound typically shows enlarged ovaries (>5 cm) with multiple large thin walled cysts, often in association with ascites.

Risk can be estimated by number of mature follicles prior to HCG maturation/trigger dose, and by high estrogen level at this time. E2 values 1000-4000 indicate a moderate risk, levels above 4000 indicate high risk.

In non-pregnant patients, the syndrome resolves over 3-7 days. If pregnancy occurs, slow improvement occurs over 6 to 8 weeks.
The ovary demonstrated in the follicular series above, is shown here with findings of mild hyperstimulation, not associated with pregnancy. Large thin walled cysts result in moderate ovarian enlargement.

**Oocyte Retrieval:**

Transvaginal ultrasound probes can be equipped with needle guides that allow very accurate targeting of follicles for oocyte aspiration.

Ultrasound guided oocyte retrieval can be preformed as an outpatient procedure with Conscious sedation and paracervical block.

The procedure is a simple cyst puncture with aspiration and irrigation with a buffered medium. Yield rates for oocytes are similar to older laparoscopic procedures but a more acceptable to most patients.

Basic Radiology Imaging Lectures