

Polycystic ovaries and stromal hyperthecosis

Ovarian morphology • androgen excess • clinical correlation

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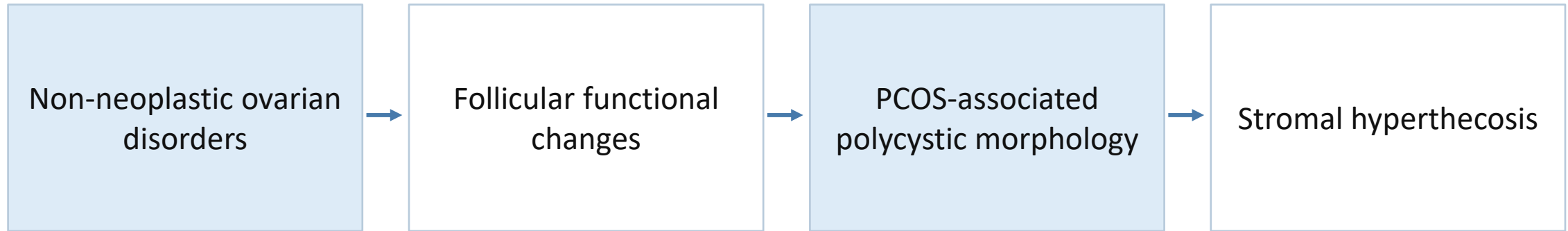
Learning objectives

- Distinguish polycystic ovarian morphology from the syndrome PCOS.
- Trace androgen excess and insulin resistance to reproductive and metabolic consequences.
- Recognize the gross and microscopic phenotype of ovarian stromal hyperthecosis.
- Compare the clinical and pathologic implications of the two conditions.

Two disorders, two diagnostic starting points

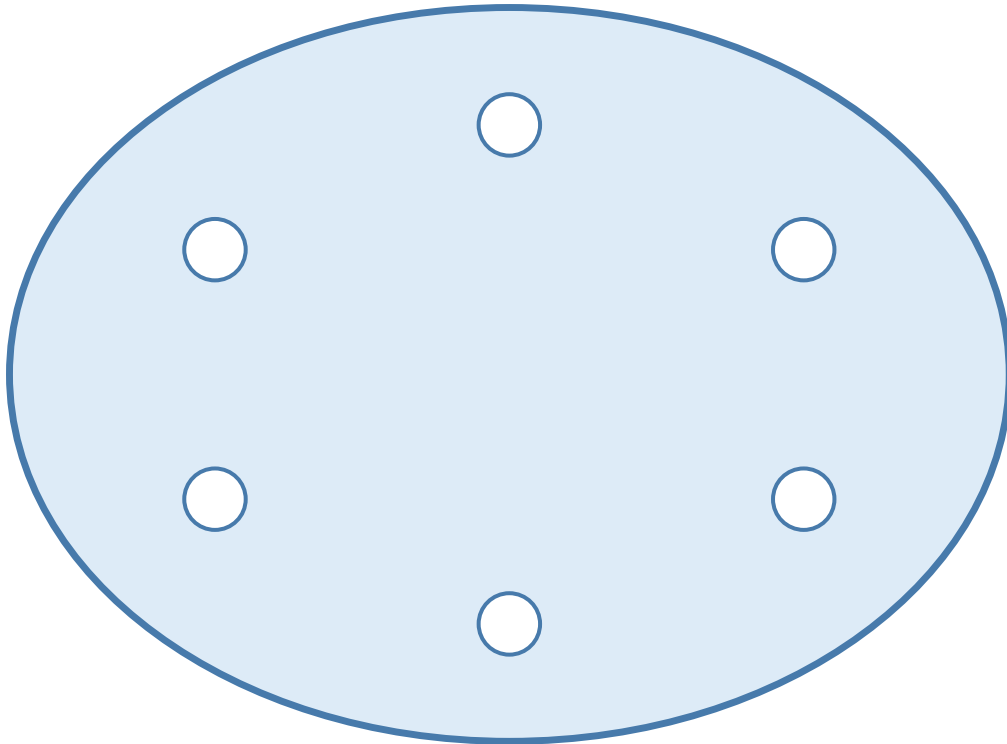
Aspect	Polycystic ovary syndrome	Stromal hyperthecosis
Primary process	Complex endocrine–metabolic syndrome	Diffuse ovarian stromal disorder
Typical setting	Reproductive age	Usually postmenopausal
Characteristic ovarian clue	Numerous cystic follicles	Luteinized stromal-cell nests
Clinical concern	Anovulation; Metabolic disease	Marked androgen excess; Virilization

Place in ovarian pathology



The core entities here are not primary epithelial ovarian neoplasms.

Follicles, stroma, and steroidogenesis



Schematic—not a histologic specimen

- Developing follicles provide the structural setting for ovulatory function.
- Theca-associated steroidogenesis contributes to ovarian androgen production.
- The surrounding stromal compartment may undergo hyperplasia and luteinization.

PCOS is a syndrome, not an ultrasound finding

- Hyperandrogenism and ovulatory dysfunction are central clinical features.
- Polycystic ovarian morphology can accompany the syndrome.
- An isolated morphologic appearance cannot establish PCOS.
- Diagnostic assessment must integrate history and endocrine findings.

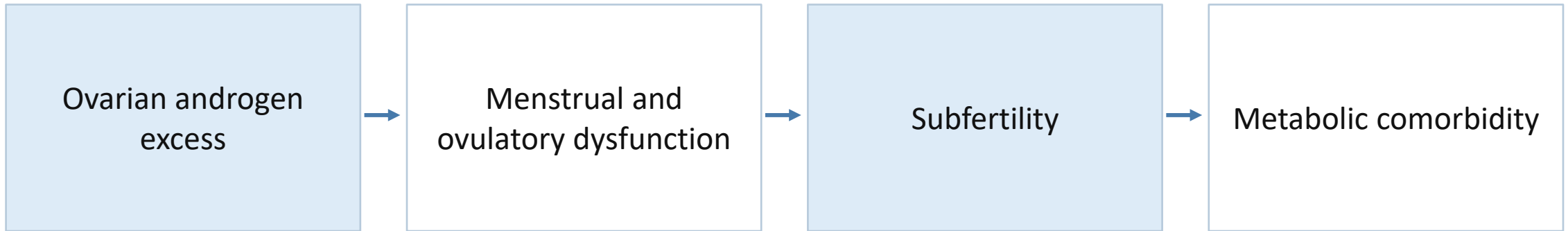
PCOS: Population burden

6–10%

**Reproductive-age females affected
(textbook estimate)**

- Prevalence depends on diagnostic definition and population.
- The disorder has reproductive and metabolic manifestations.
- Do not equate population prevalence with the frequency of polycystic ovarian morphology.

PCOS phenotype spans multiple organ systems

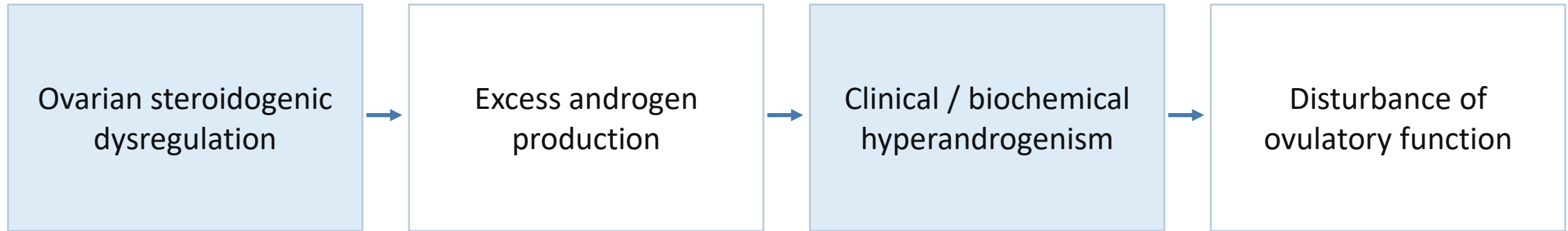


One patient need not express every feature with the same severity.

Why etiology remains incomplete

- PCOS as an incompletely understood complex disorder.
- Disordered ovarian androgen biosynthesis is a central finding.
- Insulin resistance and adipose metabolism contribute to the phenotype.
- Avoid attributing all cases to a single initiating lesion.

Dysregulated androgen biosynthesis

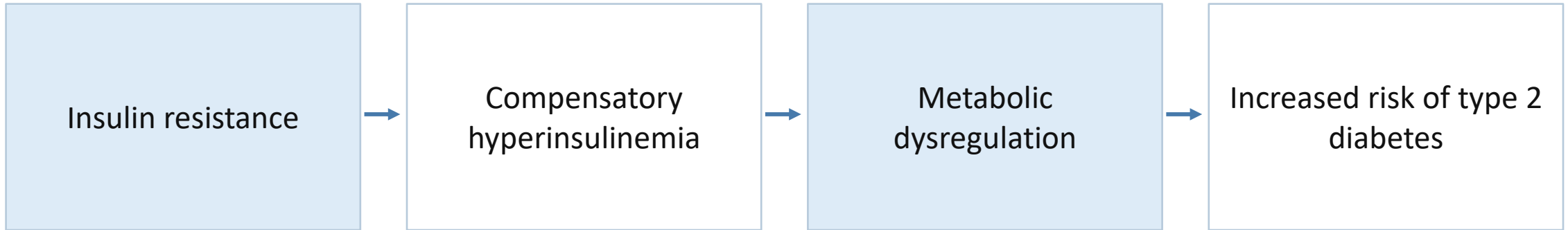


Conceptual causal model; Mechanistic heterogeneity is acknowledged.

Androgen excess: The clinical signal

- Hirsutism and acne are important manifestations of hyperandrogenism.
- Female-pattern hair loss may be present, but alone is less specific.
- Severity and rate of progression inform the differential diagnosis.
- Marked or rapidly progressive virilization warrants investigation beyond typical PCOS.

Insulin resistance is a distinct PCOS axis

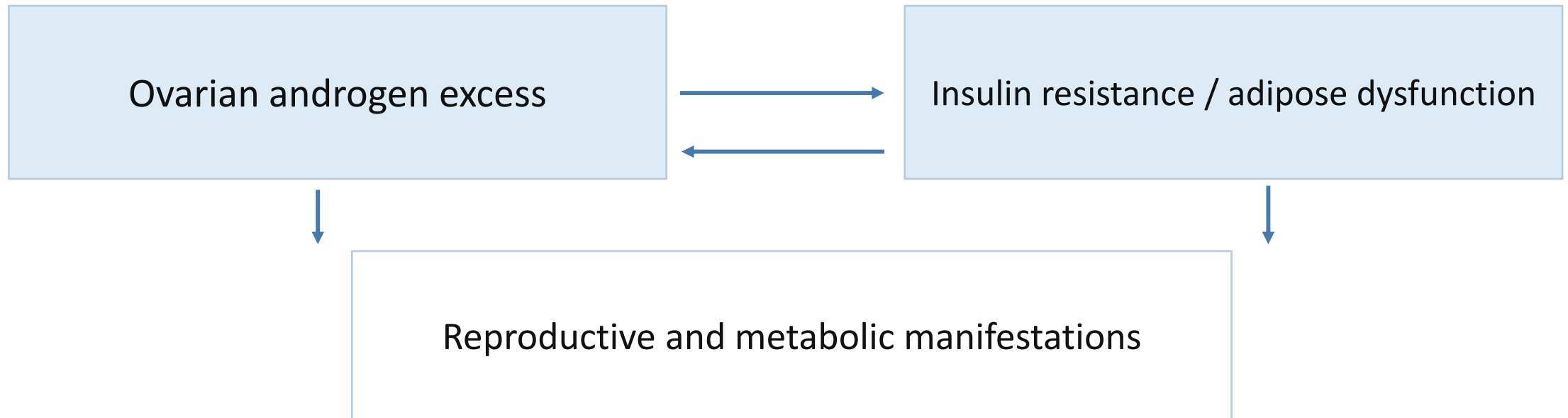


Insulin resistance is common but not an obligatory feature in every patient.

Adipose metabolism modifies the phenotype

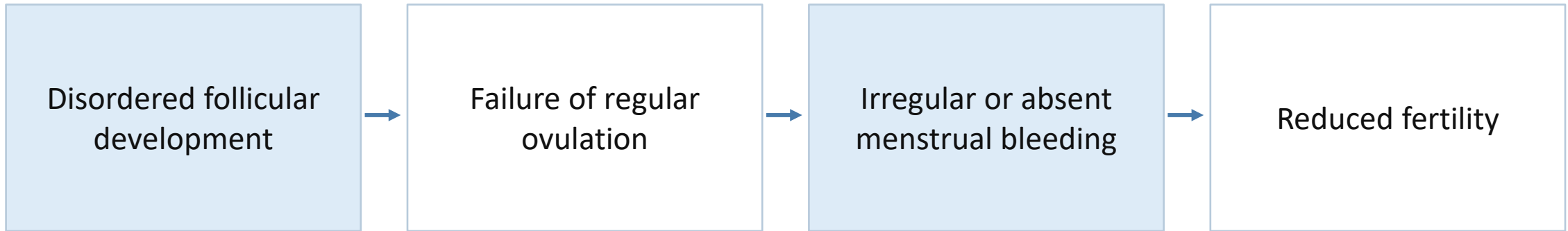
- Altered adipose metabolism with obesity and diabetes.
- Adiposity and insulin resistance can amplify metabolic burden.
- Normal body mass does not exclude a diagnosis of PCOS.
- The reproductive and metabolic phenotypes need separate assessment.

Endocrine and metabolic pathways interact



Bidirectional associations; Simplified conceptual representation.

Chronic anovulation produces cycle disruption



Not every irregular cycle is PCOS; Evaluate alternative causes.

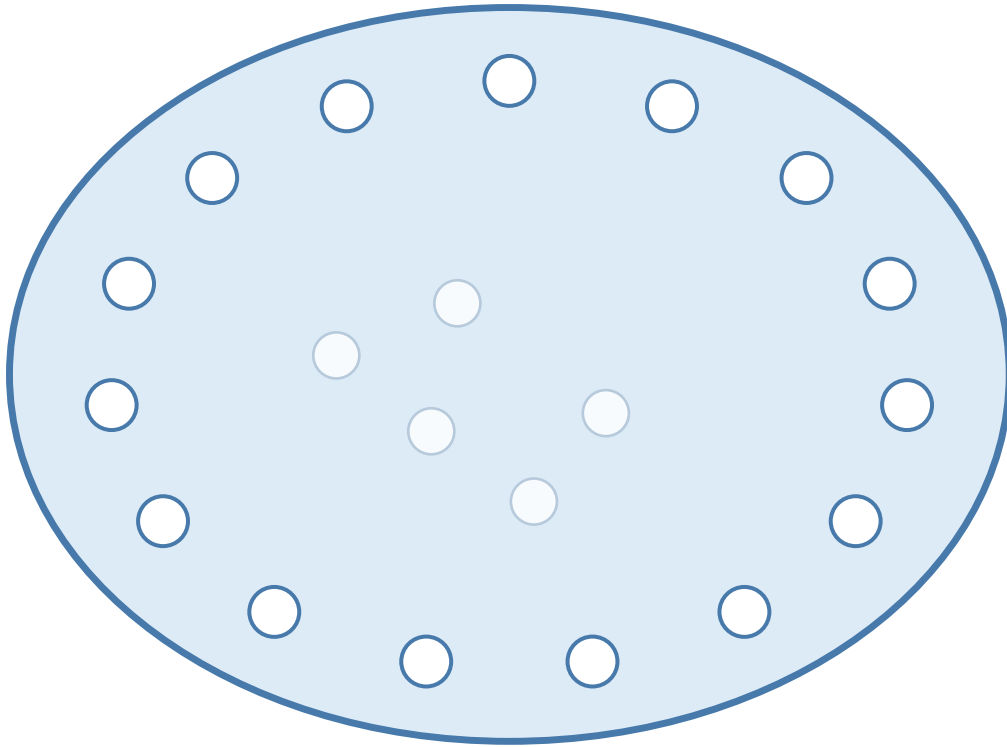
Menstrual abnormalities: What to establish

- Characterize cycle intervals, pattern, and duration of irregularity.
- Relate ovulatory dysfunction to the endocrine phenotype.
- Assess pregnancy and alternative endocrine causes where relevant.
- In adolescents, normal pubertal transition must not be overcalled as PCOS.

Subfertility is linked to anovulation

- Inconsistent ovulation reduces predictable opportunities for conception.
- Anovulation is a functional consequence, not direct proof of ovarian neoplasia.
- Fertility assessment also considers non-PCOS contributors.
- Clinical management is individualized; Pathology identifies the underlying pattern.

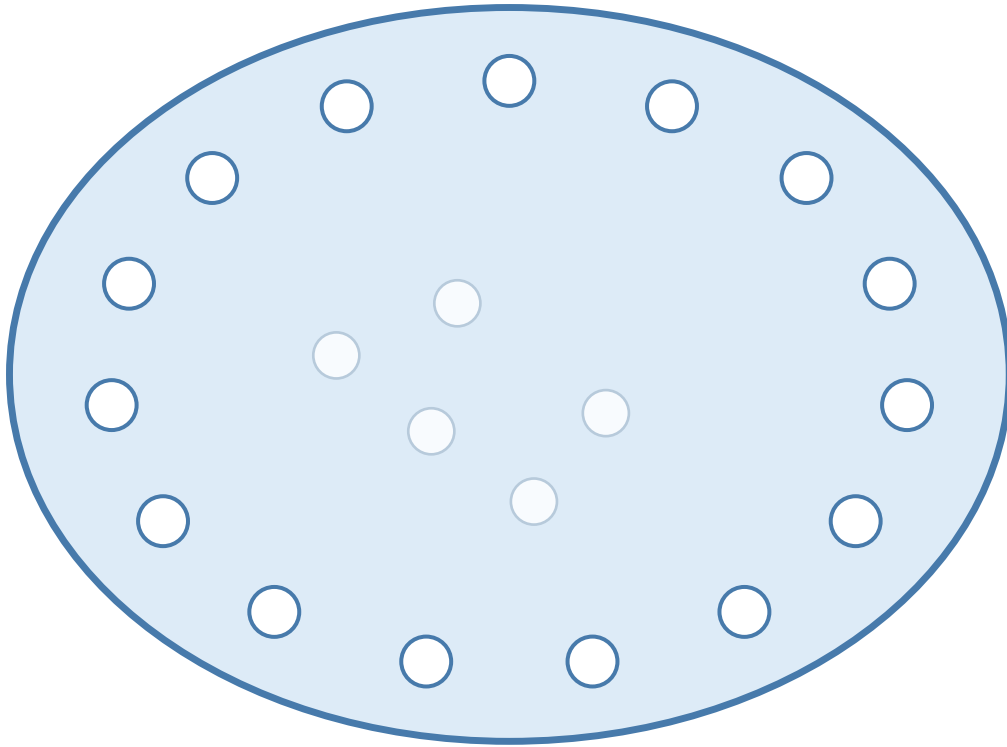
How multiple cystic follicles arise



Schematic—not a histologic specimen

- Persistent or arrested follicular structures create a multifollicular appearance.
- Numerous follicle cysts may enlarge the ovarian outline.
- This structural finding must be interpreted alongside the clinical syndrome.

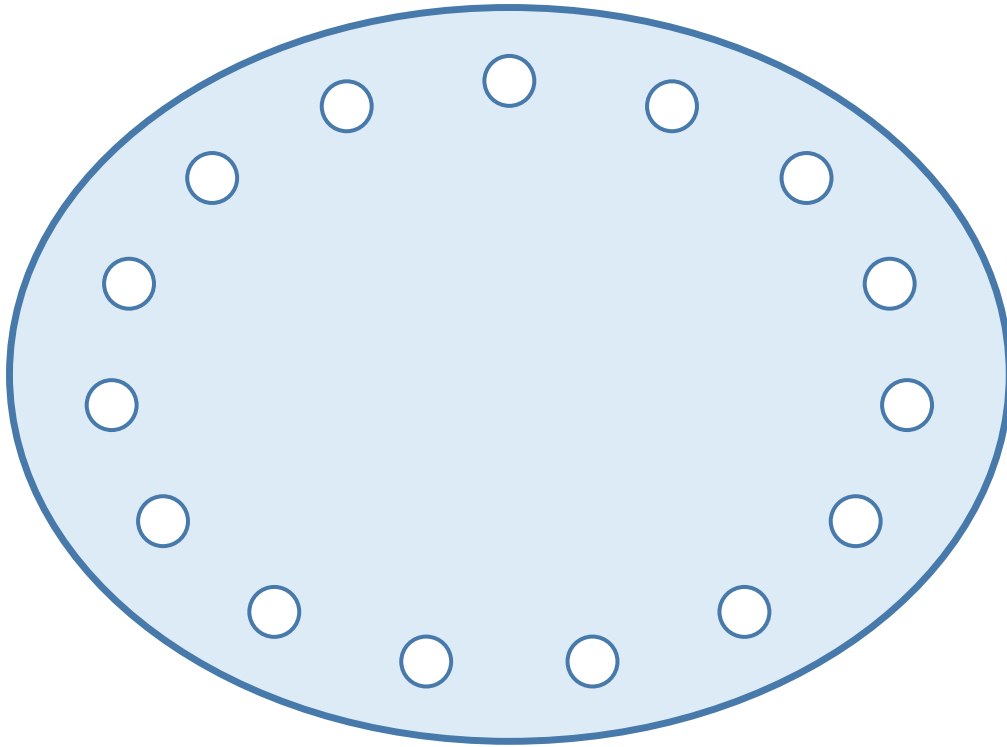
Gross PCOS morphology



Schematic—not a histologic specimen

- Ovarian enlargement may be associated with multiple cystic follicles.
- The ovarian cut surface emphasizes the abundance of follicular structures.
- Gross morphology alone does not prove a syndromic diagnosis.

Microscopic interpretation of polycystic ovaries



Schematic—not a histologic specimen

- A follicular-cyst pattern explains the many rounded cystic profiles.
- Microscopy describes ovarian architecture; It does not substitute for endocrine history.
- Avoid diagnosing PCOS from a single cystic follicle.

Polycystic morphology is not specific

20–30%

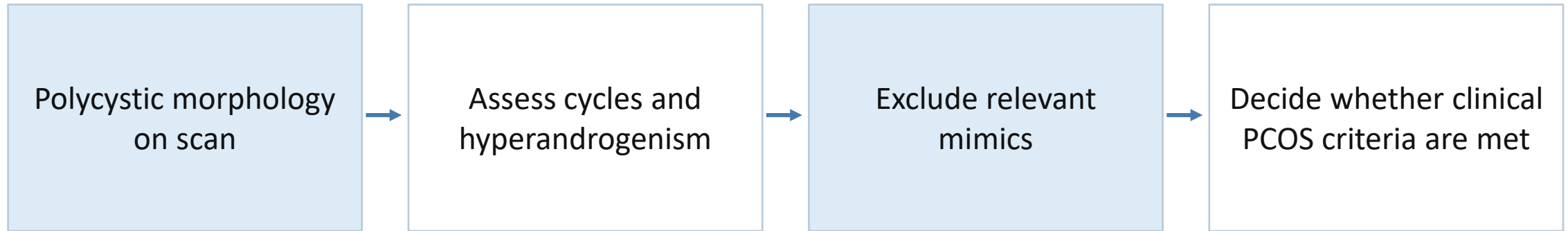
**Females with polycystic ovaries in the
Robbins estimate**

- An ovarian morphology finding may occur without clinical PCOS.
- This is why ovarian imaging is not a stand-alone endocrine diagnosis.
- The denominator differs from the quoted PCOS prevalence.

Functional follicular cysts are a different category

Feature	Functional follicular cyst	Polycystic ovarian pattern
Pathologic unit	Individual unruptured or resealed follicle	Numerous follicular structures
Interpretive basis	Non-neoplastic functional change	Pattern requiring clinicopathologic context
Diagnostic implication	Does not establish PCOS	Does not alone establish PCOS

Avoid the ovary-to-syndrome fallacy



Structural observation is the beginning of an evaluation, not its conclusion.

Adult PCOS diagnostic framework (2023)

Hyperandrogenism

Ovulatory dysfunction

Polycystic morphology

Any two of three after exclusion of other causes

- Adults: Two of three features after excluding other causes.
- Features: Hyperandrogenism; Ovulatory dysfunction; Polycystic morphology (ultrasound or AMH alternative).
- If hyperandrogenism and ovulatory dysfunction coexist, ultrasound or AMH is unnecessary.

Ultrasound criteria are technology-dependent

≥ 20

**Follicles per ovary in at least one
ovary: 2023 adult guideline**

- Preferred follicle-number measure with adequate imaging technology.
- Where image quality/older technology limits counts, ovarian volume ≥ 10 mL or follicles/section ≥ 10 can be used.
- Do not transfer adult sonographic thresholds to adolescents.

AMH has a circumscribed diagnostic role

- In adults, anti-Müllerian hormone can define the polycystic-morphology component.
- AMH alone is not a test for the entire PCOS syndrome.
- Ultrasound and AMH should not both be used merely to increase case detection.
- AMH is not recommended for PCOS diagnosis in adolescents.

Adolescent PCOS requires greater specificity

Criterion	Adults	Adolescents
Hyperandrogenism	Clinical or biochemical	Required
Ovulatory dysfunction	One of three components	Required
Ultrasound / AMH	May assess morphology	Not recommended to diagnose
Caution	Exclude other causes	Avoid normal pubertal misclassification

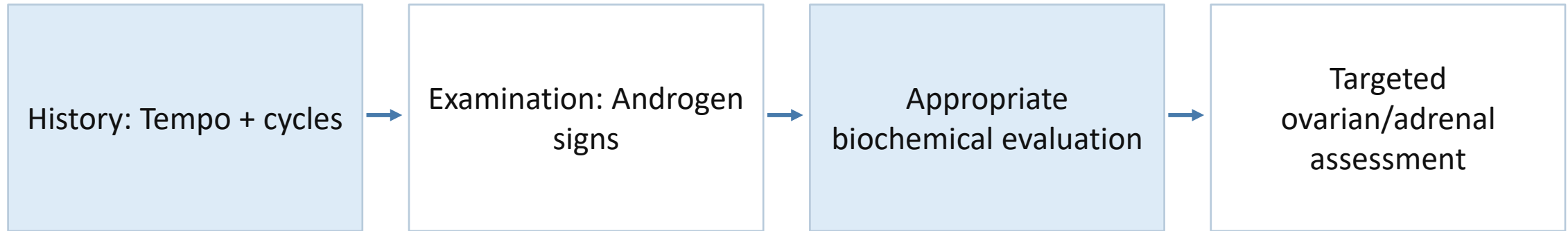
Biochemical androgen measurement matters

- Total and free testosterone are recommended for assessment of biochemical hyperandrogenism.
- Validated LC–MS/MS is preferred for total testosterone over low-precision direct immunoassays.
- Laboratory-specific reference intervals and method matter.
- Markedly increased levels or rapid progression prompt search for an alternative cause.

Hyperandrogenism is not pathognomonic

Possibility	Typical diagnostic clue	Key caution
PCOS	Reproductive-age chronic course	Exclude other disorders
Androgen-secreting neoplasm	Rapid progression / virilization	May have variable hormone levels
Ovarian hyperthecosis	Often postmenopausal, stromal	Imaging can be subtle
Adrenal / other endocrine source	Biochemistry + clinical context	Requires targeted workup

A practical initial assessment



Clinical framework based on contemporary guideline recommendations.

Cardiometabolic significance

- PCOS to obesity and type 2 diabetes.
- Insulin resistance and altered adipose metabolism are pathophysiologic contributors.
- Cardiometabolic risk requires evaluation beyond reproductive symptoms.
- Risk is not adequately characterized by ovarian morphology alone.

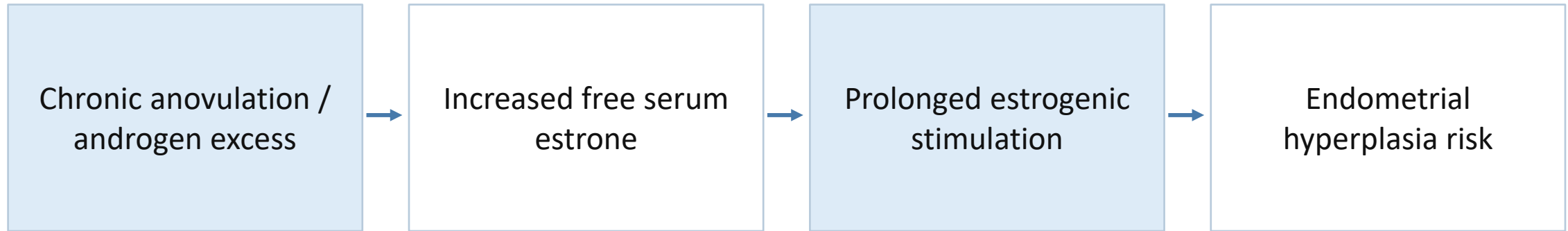
Glycaemic assessment in PCOS (2023)

- A 75-g oral glucose tolerance test is recommended as the most accurate glycaemic test in PCOS.
- Fasting glucose or HbA1c can be used if OGTT is unavailable, with lower accuracy.
- Routine insulin assays are not recommended as clinical measures of insulin resistance.
- The recommendation applies regardless of BMI.

Why cardiovascular risk assessment matters

- Premature atherosclerosis is an association noted by Robbins.
- Blood pressure, adiposity, glucose status, and other risk factors add clinical context.
- Metabolic risk is not equivalent to diagnosing atherosclerosis histologically.
- Clinical monitoring should address the whole cardiometabolic phenotype.

Estrone links ovarian dysfunction to the endometrium

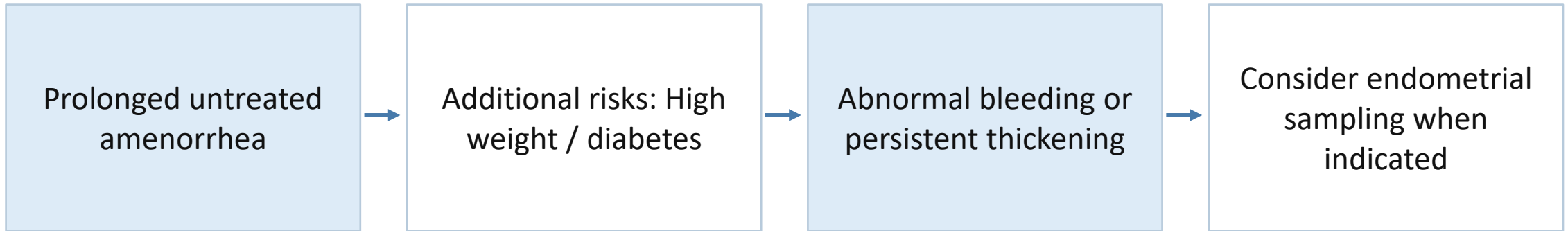


Endometrial carcinoma risk is increased in PCOS.

Endometrial risk is important—but not absolute

- Increased risk of endometrial hyperplasia and carcinoma.
- The 2023 guideline recognizes increased relative risk while overall endometrial cancer probability remains low.
- Routine endometrial cancer screening is not recommended for every person with PCOS.
- Persistent abnormal bleeding or suspicious endometrial findings require clinical assessment.

Endometrial vigilance is clinically selective



Guideline context: Risk-adapted evaluation is distinct from universal screening.

Case 1: Incidental polycystic morphology

Case vignette

An adult with regular cycles and no clinical hyperandrogenism has an ultrasound reporting numerous small ovarian follicles.

Reasoning prompt

Is PCOS established by this finding?

No. Morphology by itself does not establish the endocrine syndrome.

Case 1: An evidence-based interpretation

- Document the ovarian morphology as observed.
- Evaluate symptoms and cycle history before invoking PCOS.
- Do not use ovarian cyst number as a substitute for syndrome criteria.
- Avoid automatic endocrine labels in a pathology or imaging report.

Stromal hyperthecosis: Defining lesion

- A non-neoplastic disorder characterized by hypercellular ovarian stroma.
- Stromal luteinization produces identifiable nests of steroidogenic-appearing cells.
- Robbins also uses the term cortical stromal hyperplasia.
- Often associated with clinically important androgen excess.

Age distribution changes the differential

Reproductive age

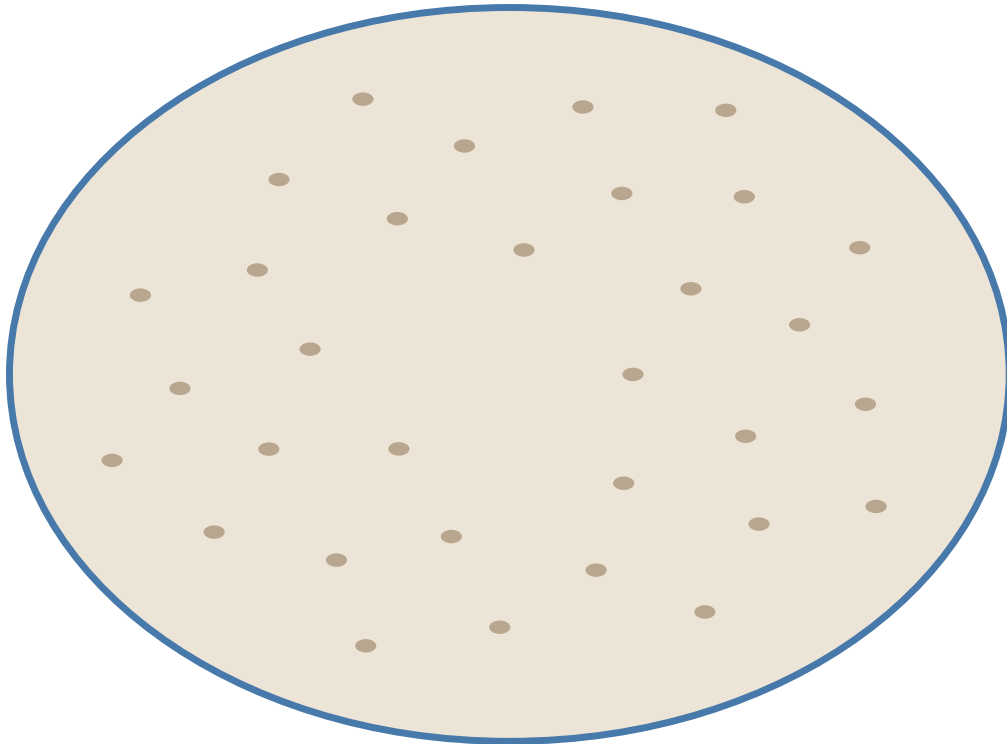
PCOS most typical

Postmenopause

Hyperthecosis most typical

Overlap exists; Neither age group is absolute.

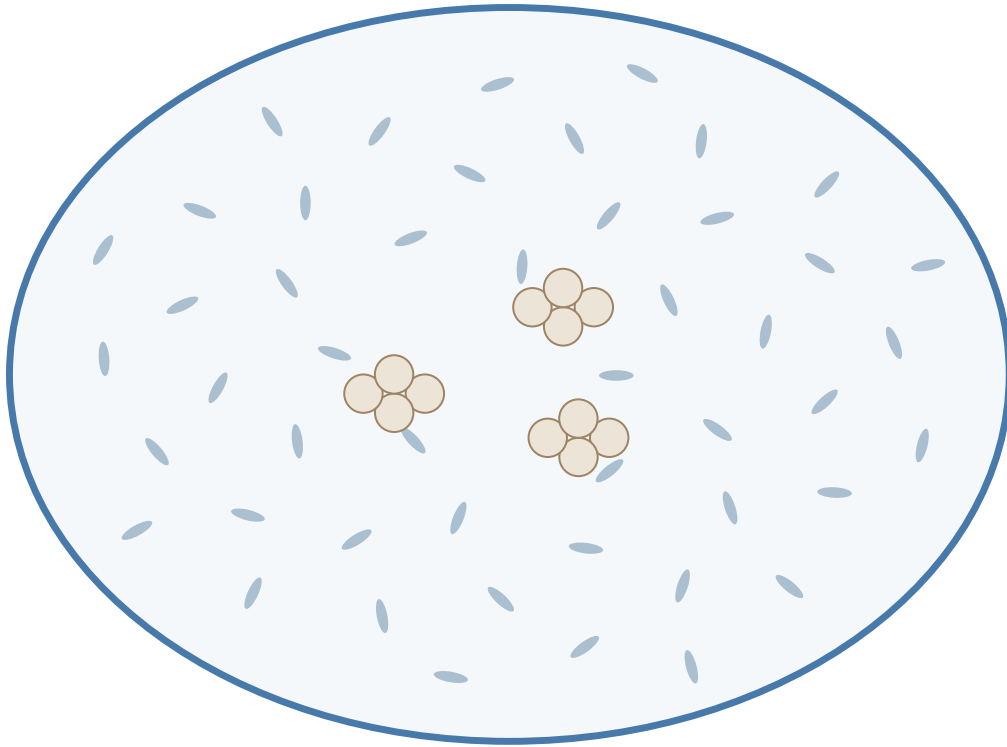
Gross appearance in stromal hyperthecosis



Schematic—not a histologic specimen

- Uniform, often bilateral enlargement of ovaries.
- White-to-tan cut surface reflects increased stromal tissue.
- Enlargement up to approximately 7 cm.

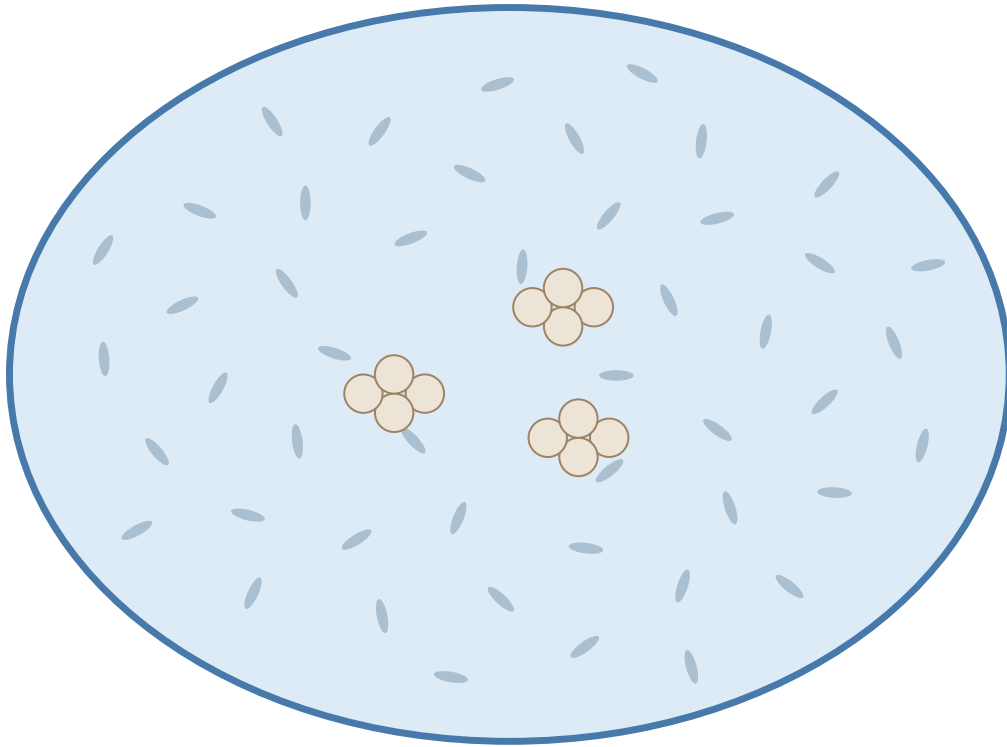
The key microscopic lesion is stromal



Schematic—not a histologic specimen

- Hypercellular, expanded ovarian stroma.
- Discrete nests of luteinized cells with vacuolated cytoplasm.
- The process may involve both ovaries, even without a mass-forming tumor.

Recognizing luteinized stromal cells



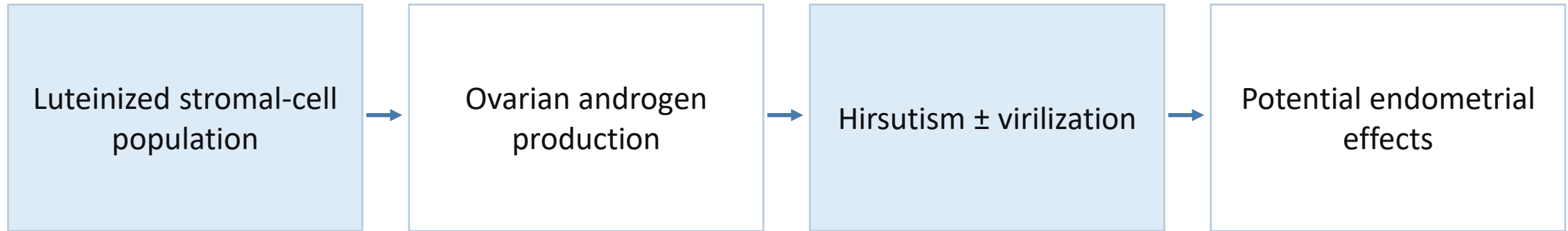
Schematic—not a histologic specimen

- Look for nests or clusters within a hypercellular stromal background.
- Vacuolated or pale cytoplasm reflects the luteinized cell phenotype.
- Interpret these cells within overall ovarian architecture—not as an isolated neoplasm.

Stromal hyperplasia versus luteinization

Morphologic feature	What to look for	Interpretation
Increased stromal cellularity	More prominent spindle-cell compartment	Stromal hyperplasia
Luteinized cell nests	Rounded cells with clear/vacuolated cytoplasm	Hyperthecosis phenotype
Bilateral ovarian expansion	Diffuse rather than a dominant focal mass	Supports diffuse process

Why hyperthecosis causes androgen excess



The morphologic finding supplies a tissue correlate for endocrine activity.

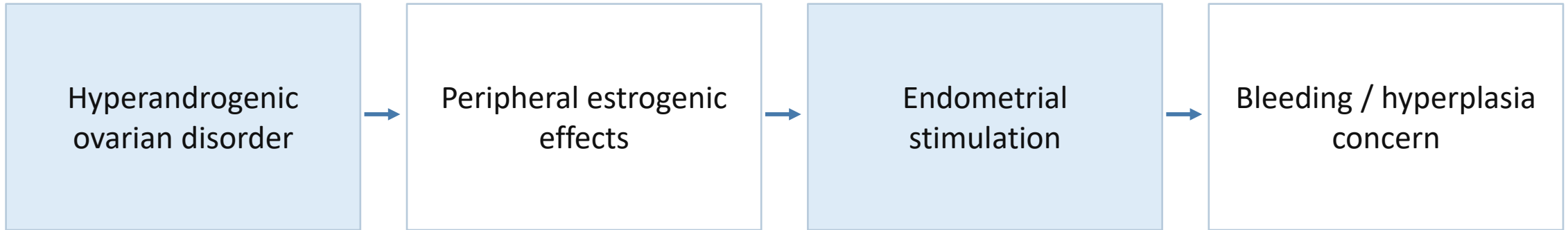
Postmenopausal virilization is a red flag

- Hyperthecosis may cause more pronounced virilization than typical PCOS.
- New or progressive deepening of voice, clitoromegaly, and androgenic alopecia merit assessment.
- An androgen-producing tumor remains an essential competing diagnosis.
- Clinical tempo and hormone assessment are more informative than morphology alone.

An apparently normal scan does not exclude it

- Ovarian hyperthecosis is often diffuse rather than a discrete mass.
- Published case reports document histologic hyperthecosis despite subtle imaging.
- Interpret ovarian dimensions in relation to age and menopausal state.
- Do not assert that normal-appearing imaging excludes stromal disease.

Endometrial consequences can parallel PCOS



Similar endometrial effects in PCOS and stromal hyperthecosis.

Hyperthecosis versus androgenic neoplasm

Clinical / pathologic clue	Stromal hyperthecosis	Androgenic ovarian tumor
Distribution	Often diffuse / bilateral	May be a localized mass
Microscopy	Hypercellular stroma with luteinized nests	Tumor-specific architecture
Hormonal phenotype	Androgen excess; Sometimes marked	May also cause marked excess
Diagnostic limitation	Imaging may be inconspicuous	Mass may be small or occult

Morphology alone is not a serum diagnosis

- Histopathology can establish stromal-cell changes in resected ovarian tissue.
- An endocrine phenotype requires clinical and biochemical correlation.
- Immunostains can support steroidogenic differentiation but are not substitutes for architecture.
- One cannot infer an exact testosterone concentration from a slide.

PCOS and hyperthecosis side by side

Dimension	PCOS	Stromal hyperthecosis
Ovarian lesion	Multiple cystic follicles	Stromal expansion / luteinization
Typical life stage	Reproductive age	Most often after menopause
Endocrine theme	Hyperandrogenism + anovulation	Often prominent androgen excess
Metabolic link	Insulin resistance and obesity	Metabolic comorbidity may coexist
Endometrium	Hyperplasia / carcinoma risk	Similar endometrial effects

Case 2: Postmenopausal androgen excess

Case vignette

A postmenopausal patient develops progressive hirsutism and virilization. Imaging does not show a convincing unilateral ovarian mass.

Reasoning prompt

Which ovarian stromal disorder must remain in the differential?

Stromal hyperthecosis—while excluding an androgen-producing ovarian or adrenal tumor.

Case 2: Morphology-directed reasoning

- Evaluate the tempo and severity of androgenic changes.
- Seek biochemical localization and exclude relevant adrenal/ovarian neoplasia.
- If tissue is available, inspect for diffuse stromal hypercellularity and luteinized nests.
- Correlate endometrial findings with bleeding history.

Case 3: Longstanding anovulation

Case vignette

An adult with clinical hyperandrogenism has chronic oligomenorrhea and prolonged intervals without bleeding.

Reasoning prompt

Which downstream tissue is at risk, and why?

Endometrium: Sustained estrogenic stimulation in anovulatory states increases hyperplasia risk.

Case 3: Clinical inference from pathology

- Establish the reproductive and endocrine phenotype first.
- Recognize estrogenic endometrial exposure as a distinct organ-level consequence.
- Investigate abnormal uterine bleeding based on clinical indications.
- Do not confuse increased relative risk with inevitable carcinoma.

Pathology reporting: What belongs in the report

- Describe actual ovarian architecture and stromal features seen on tissue.
- Specify whether follicular cysts, stromal hypercellularity, or luteinized nests are identified.
- Avoid diagnosing an endocrine syndrome from morphology alone.
- Suggest clinicopathologic correlation when an androgenic condition is suspected.

Common diagnostic pitfalls

Pitfall	Correction
Polycystic appearance automatically labeled PCOS	Apply clinical diagnostic criteria
Single cyst treated as polycystic syndrome	Describe follicular lesion accurately
Severe virilization attributed to routine PCOS	Evaluate tumors / hyperthecosis
Normal imaging taken to rule out hyperthecosis	Review endocrine context; Disease may be diffuse
Endometrial cancer presented as inevitable	Risk is increased, not deterministic

Mechanistic synthesis

PCOS

Stromal hyperthecosis

Follicular cysts + anovulation



Stromal nests + androgen excess

Both: Endocrine effects on the endometrium

Five clinicopathologic statements to retain

- PCOS is an endocrine–metabolic syndrome, not a histologic synonym.
- Polycystic follicles are common and nonspecific in isolation.
- Insulin resistance and disordered androgen production are central PCOS themes.
- Hyperthecosis shows luteinized stromal nests in expanded ovarian stroma.
- Severe postmenopausal androgen excess demands exclusion of neoplasia.

Evidence limits and proper attribution

- Robbins provides the core ovarian morphology and endocrine associations.
- The 2023 international guideline supplies updated diagnostic testing recommendations.
- Published hyperthecosis cases illustrate variability but do not determine population-level accuracy.
- Schematic illustrations in this deck are not clinical specimens or histology images.

Selected references

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Elsevier; 2026. Chapter 22, p. 923.

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