

Endometriosis and adenomyosis

Pathology | etiopathogenesis · morphology · clinical correlations

Ectopic endometrial tissue

Endometrial tissue in myometrium

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Learning objectives

- Localize ectopic endometrial tissue and compare endometriosis with adenomyosis.
- Explain proposed origins and mechanisms sustaining lesions.
- Identify morphology, clinical consequences and neoplastic associations.

Distribution

Pathogenesis

Morphology

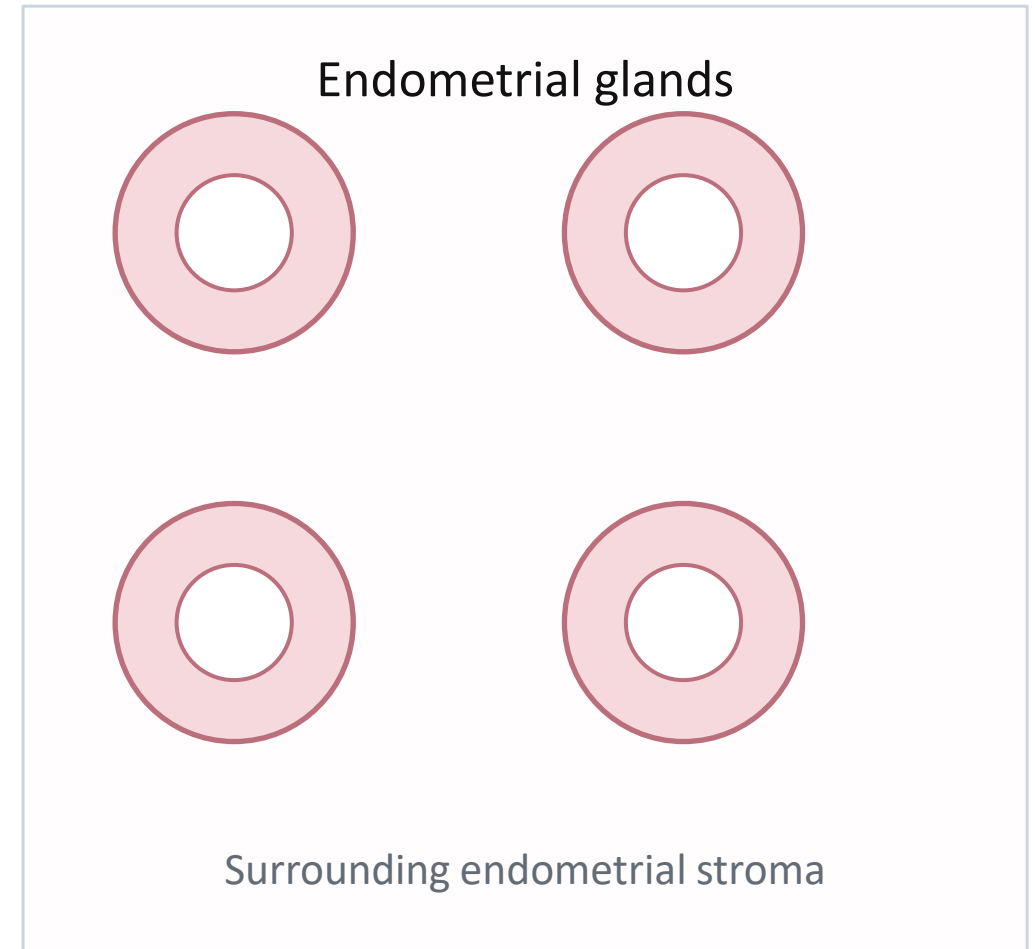
Clinical relevance

The central anatomic distinction

Feature	Endometriosis	Adenomyosis
Location	Outside the uterus	Within uterine myometrium
Relation to endometrium	Ectopic at extrauterine sites	Continues with endometrium

Endometriosis: Defining components

- Ectopic implants usually contain endometrial glands and stroma.
- In some lesions, only endometrial stroma is evident.
- An anatomic definition—not merely a symptom complex.



Illustrative geometry — not a diagnostic specimen

Endometriosis is predominantly pelvic

- Listed distribution begins with ovaries and uterine ligaments.
- Other frequent pelvic sites include rectovaginal septum, cul-de-sac and peritoneum.

Ovary

Uterine ligaments

Rectovaginal
septum

Pelvic peritoneum

Sites beyond the principal pelvic locations

- Bowel and appendiceal serosa may be involved.
- Cervical, vaginal and tubal mucosa can contain endometriotic foci.
- Laparotomy scars are an additional recognized site.

Bowel / appendix

Genital-tract mucosa

Surgical scars

Clinical context and prevalence

- Most commonly encountered during active reproductive life.
- Typical age distribution: Third and fourth decades.
- Textbook estimate: Approximately 10% of females are affected.

Reproductive-age disease

Third and fourth decades

Approx. 10%

Three morphologic forms of endometriosis

- Superficial peritoneal endometriosis.
- Ovarian endometriosis.
- Deep infiltrating endometriosis.

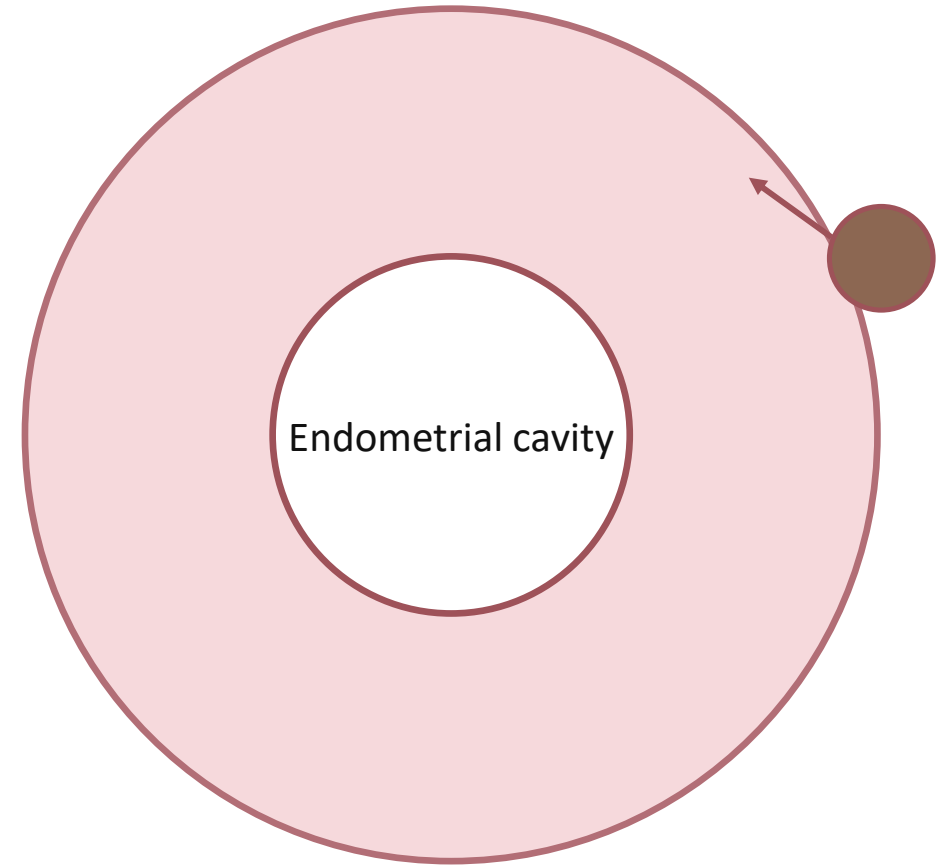
Superficial peritoneal

Ovarian

Deep infiltrating

Superficial peritoneal endometriosis

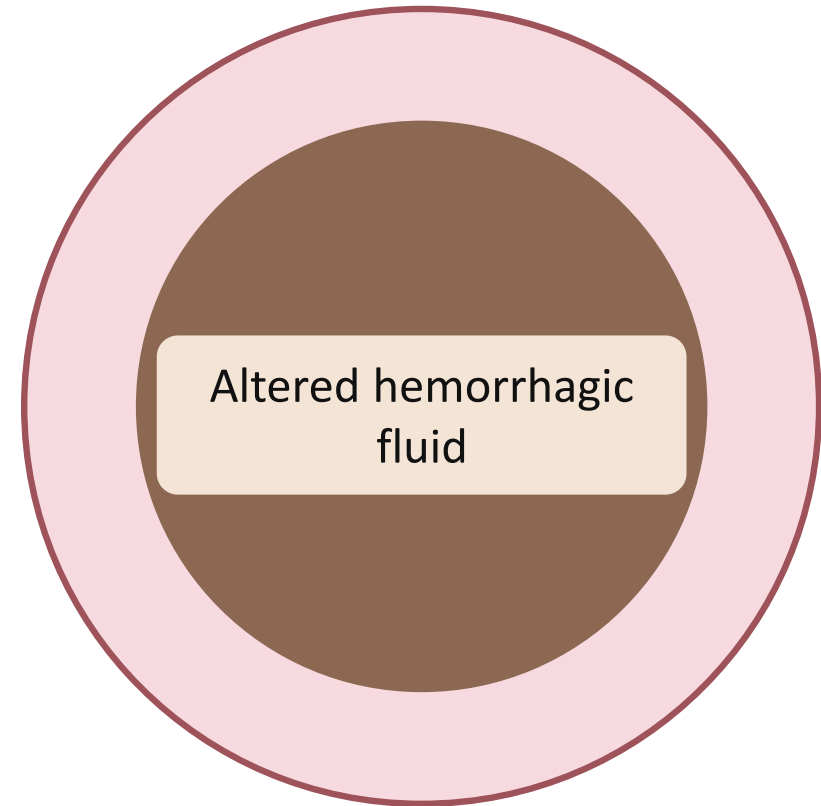
- Implants occur on or just under peritoneal surfaces.
- Periodic hemorrhage contributes to visible lesion color and local inflammation.



Ectopic implant outside uterus

Ovarian endometriosis

- Ovarian lesions may accumulate altered blood within cystic spaces.
- The resulting endometriotic cyst is an endometrioma (chocolate cyst).



Ovarian endometrioma — schematic

Deep infiltrating endometriosis

- Lesions invade tissues and induce fibrosis and adhesions.
- The deep form can behave locally aggressively without implying invasive carcinoma.

Deep extension into tissue

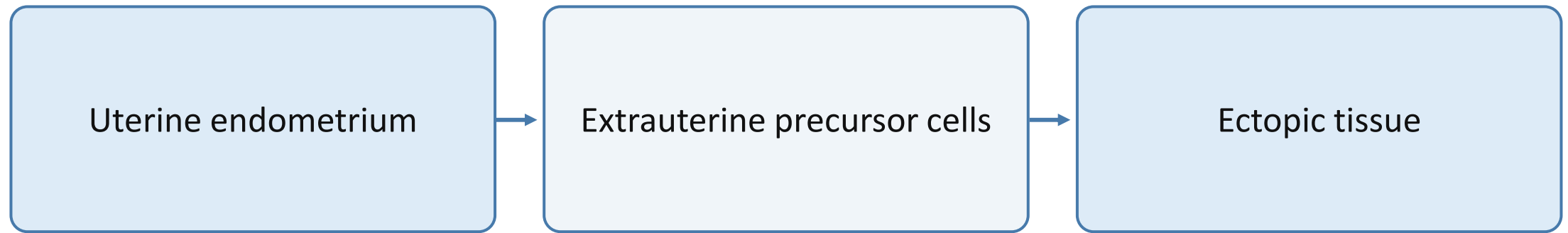
Fibrotic response

Adhesions

Phenotypes and malignant association

Form	Characteristic location	Textbook malignant association
Superficial	Peritoneal surface	Occasional
Ovarian	Ovarian tissue / cyst	Occasional
Deep infiltrating	Deep tissue involvement	Extremely rare

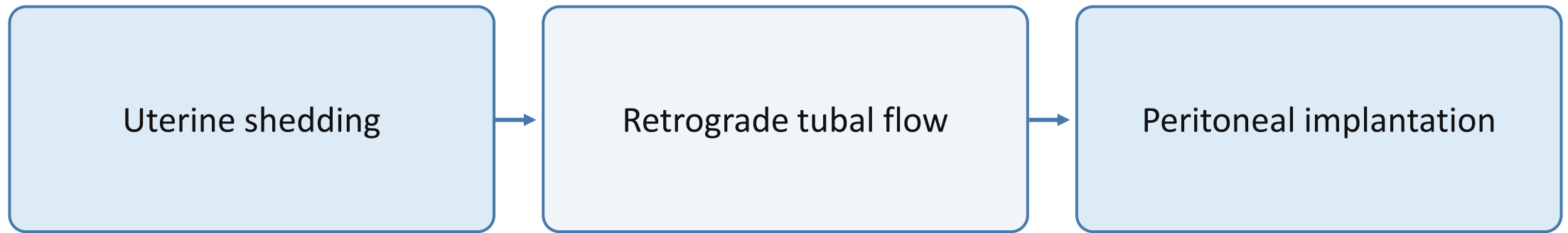
Pathogenesis: Origins remain unresolved



Proposals fall into uterine-endometrium–derived and extrauterine-cell–derived origins.

No single theory accounts for all observed presentations.

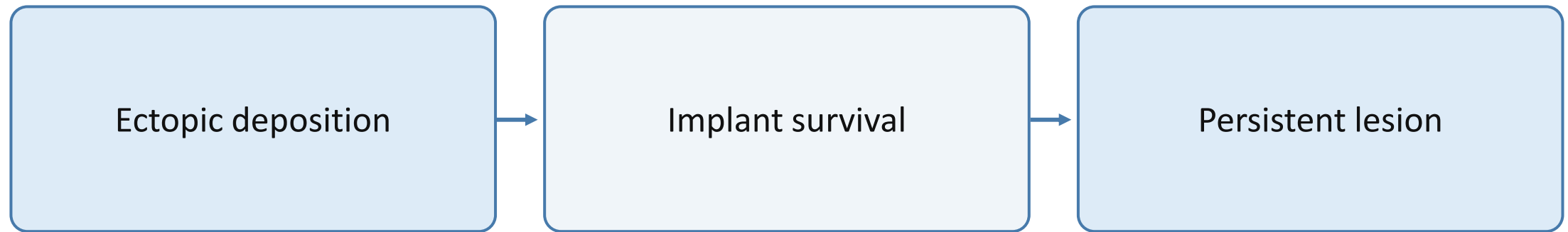
Regurgitation theory



Retrograde menstrual flow carries endometrial tissue through the fallopian tubes.

Cells are proposed to implant on peritoneal or pelvic surfaces.

Regurgitation: Mechanistic sequence



The source of the tissue is intrauterine endometrium.

Pelvic distribution is compatible with reflux through the tubes.

Sustained ectopic growth still requires permissive local factors.

Why regurgitation is plausible

- Retrograde menstruation is common.
- Most endometriosis occurs in the peritoneal cavity.
- The theory directly connects these observations, but is incomplete.

Common retrograde flow

Frequent pelvic disease

Partial explanation

Regurgitation cannot explain every patient

- Cases are described in amenorrheic patients, including gonadal dysgenesis.
- The occurrence of lesions without ordinary menstrual reflux indicates other mechanisms.

Amenorrhea

No conventional menstruation

Alternative origins needed

Unusual distribution challenges reflux

- Endometriotic tissue has been observed in distant organs, including lung, brain and bone.
- Urogenital endometriosis has also been described in males receiving high-dose estrogen.

Distant organ sites

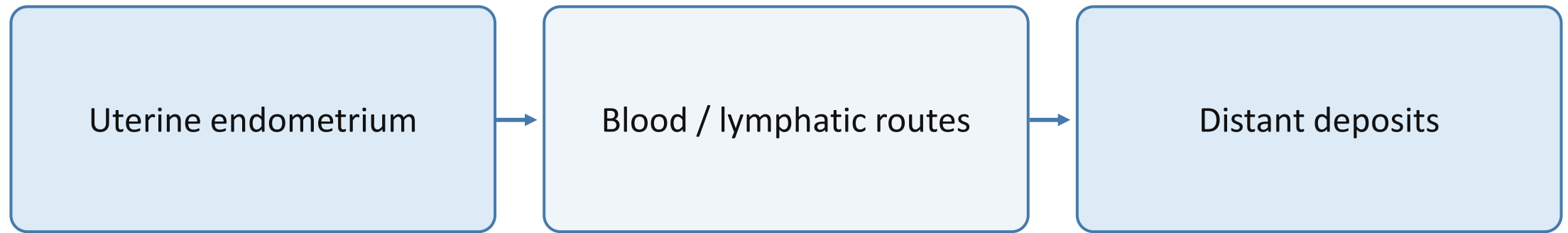
Estrogen-treated male cases

Reflux alone insufficient

Frequency paradox of retrograde flow

Observation	Approximate frequency	Interpretive implication
Retrograde flow	Up to 90%	Common phenomenon
Endometriosis	About 10%	Additional susceptibility / survival mechanisms

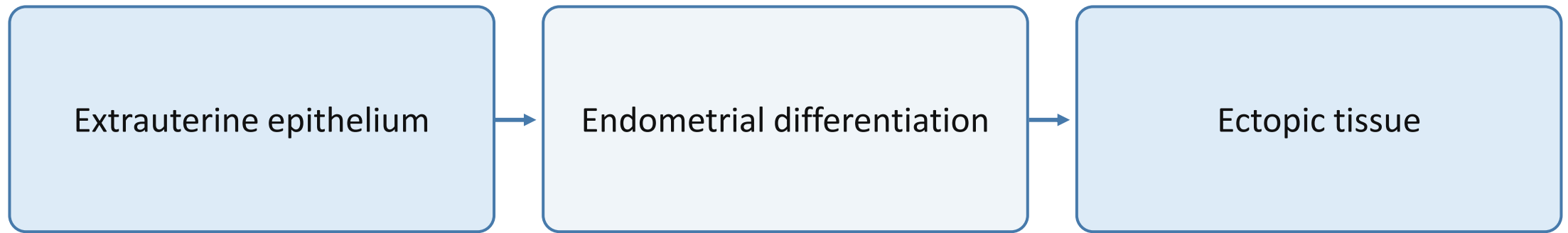
Benign metastasis hypothesis



Uterine endometrial cells may disseminate in blood vessels or lymphatic channels.

This theory addresses rare endometriosis in organs far from the pelvis.

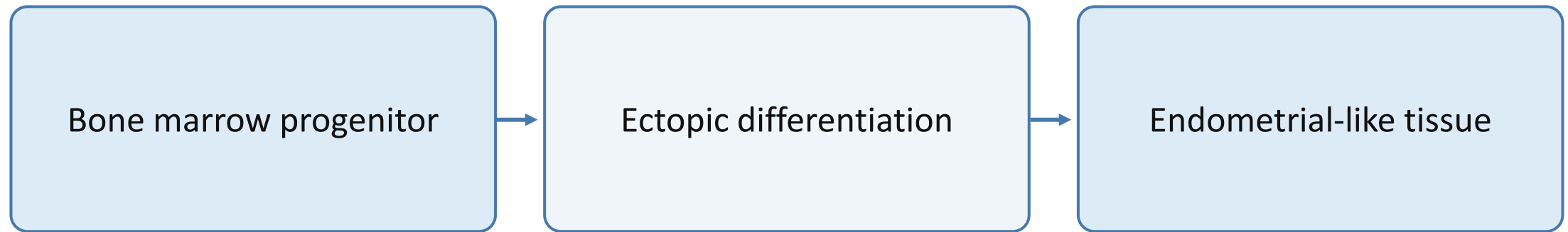
Metaplastic theory



Coelomic epithelium may differentiate toward endometrial tissue.

Mesonephric remnants also may undergo endometrial differentiation.

Extrauterine stem/progenitor-cell theory



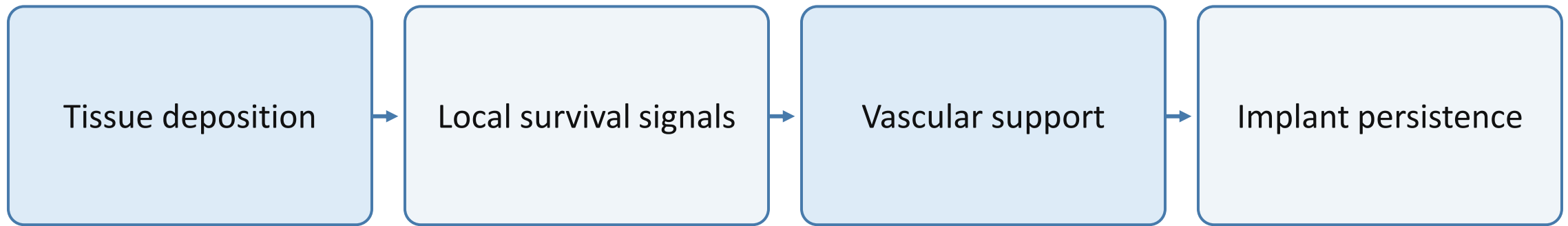
Bone-marrow-derived stem/progenitor cells have been proposed as a source.

Endometrial differentiation at extrauterine sites is hypothesized.

Origin theories: Complementary explanations

Hypothesis	Cell source / movement	Principal explanatory strength
Regurgitation	Retrograde uterine tissue	Common pelvic implants
Benign metastasis	Vascular / lymphatic spread	Distant sites
Metaplasia	Coelomic / embryonic remnants	Nonuterine origins
Stem/progenitor	Extrauterine progenitors	Alternative cell origin

Establishing an ectopic implant



Arrival of cells alone is insufficient for persistence.

Survival involves inflammatory signaling, angiogenesis, and matrix remodeling.

Inflammatory mediator network

- Implants and associated macrophages release proinflammatory factors.
- The source includes PGE₂, IL-1, TNF, IL-6 and IL-8.

Endometriotic
implant

Activated
macrophages

Cytokines / PGE₂

Inflammatory milieu

Macrophages amplify the lesion environment



Inflammatory mediators recruit macrophages to implants.

Activated macrophages can release additional inflammatory and growth-promoting factors.

Local chemokines and cytokines

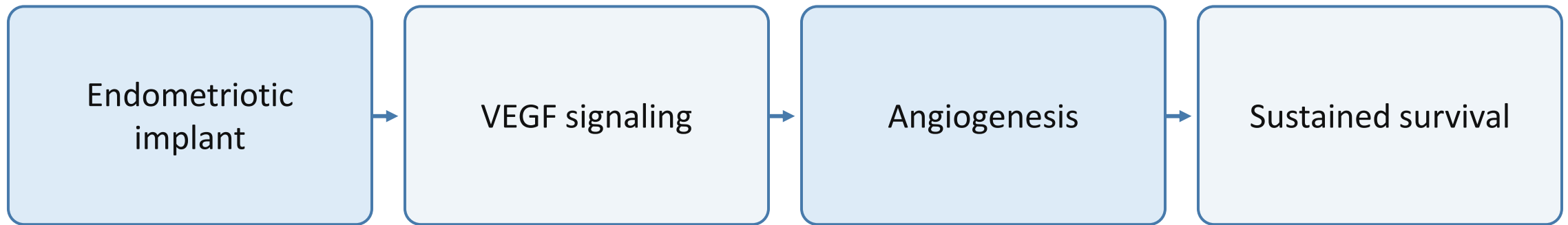
- Monocyte chemoattractant protein-1 (MCP-1/CCL2) participates in the network.
- IL-6 and IL-8 are among the inflammatory factors detected.

MCP-1 / CCL2

IL-6

IL-8

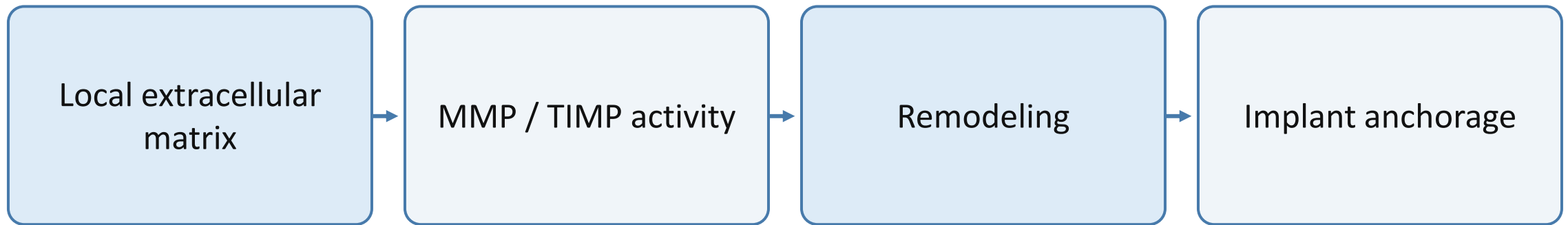
Angiogenesis supports ectopic survival



Establishment and continued growth require a blood supply.

VEGF is a representative proangiogenic mediator.

Matrix remodeling permits implantation



Matrix metalloproteinases (MMPs) remodel extracellular matrix.

Tissue inhibitors of metalloproteinases (TIMPs) also participate in this regulated system.

Immune persistence is multifactorial

- Inflammatory and tissue-remodeling factors may help lesions avoid immune clearance.
- This as a proposed contribution, not a fully established universal mechanism.

Inflammation

Tissue remodeling

Possible immune evasion

Nerve growth factor in endometriosis

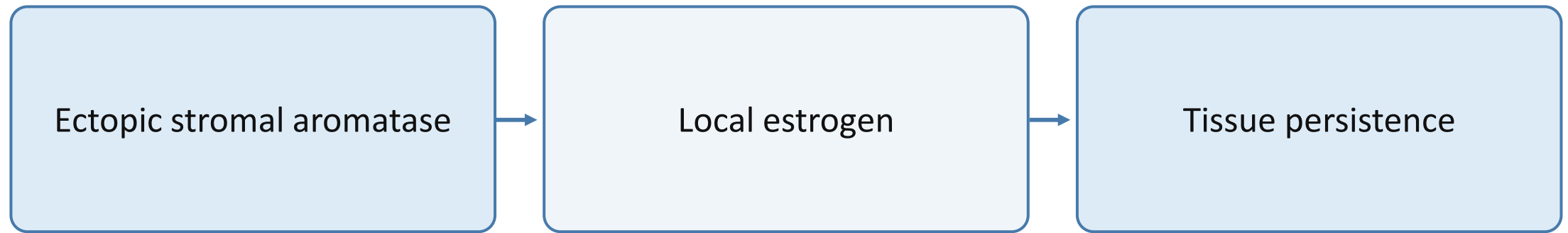
- NGF is among the factors found in the implant inflammatory environment.
- It is a biologic link to neural signaling; The textbook does not specify an exact clinical dose-response.

NGF

Local microenvironment

Neural signaling

Local aromatase production

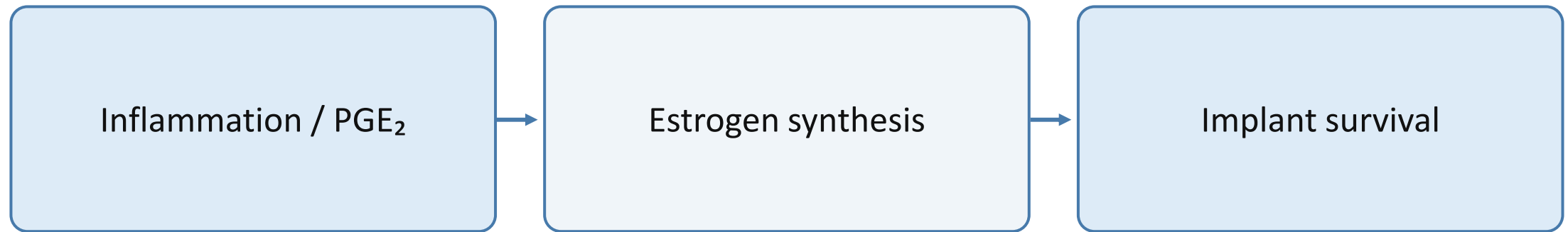


Ectopic endometriotic stromal cells produce aromatase.

Normal endometrial stroma lacks this activity.

Local estrogen synthesis favors implant survival and persistence.

Inflammation–estrogen coupling



Prostaglandin E₂ can stimulate local estrogen synthesis.

Estrogen in turn promotes maintenance of ectopic endometrial tissue.

Increased estrogen responsiveness

- Epigenetic changes are associated with enhanced estrogen responses.
- In a hormonally responsive tissue, this supports proliferation and survival.

Epigenetic alterations

Estrogen responsiveness

Enhanced survival

Decreased progesterone responsiveness

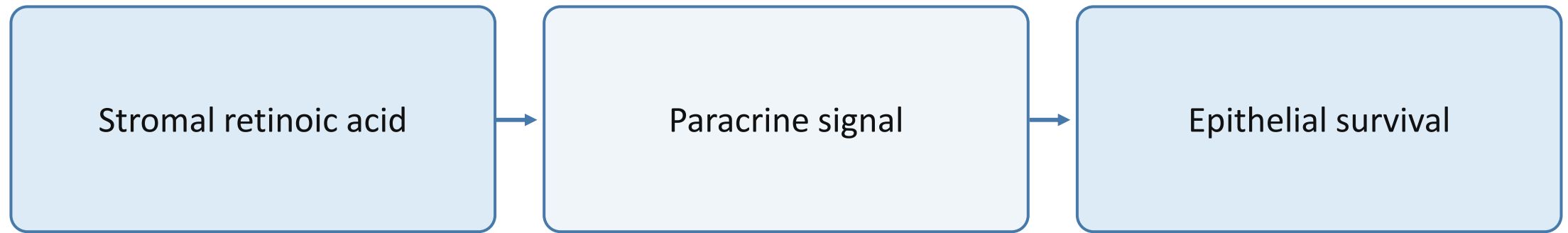
- Endometriotic tissue has reduced responsiveness to progesterone.
- This alteration is described alongside heightened estrogen responsiveness.

Reduced progesterone response

Altered hormonal balance

Ectopic persistence

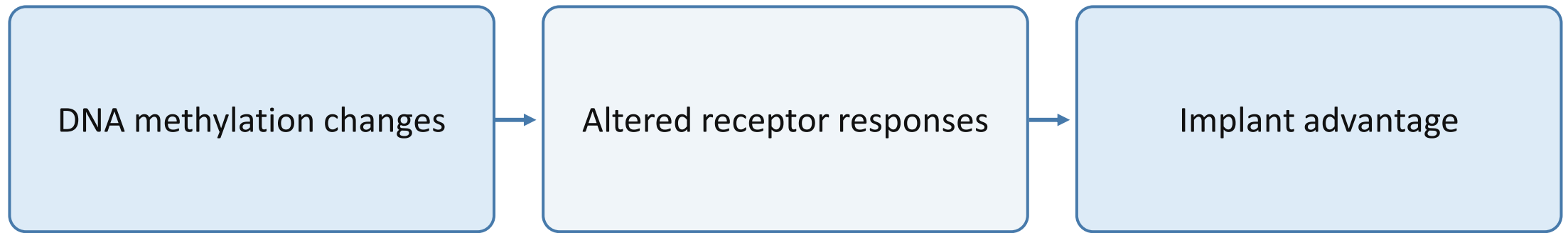
Retinoic acid and paracrine support



Retinoic acid produced by stromal cells promotes epithelial-cell survival.

The effect is described as paracrine signaling from stroma to epithelium.

Epigenetic changes in endometriosis



DNA methylation changes are described in affected tissue.

They contribute to increased estrogen and reduced progesterone responses.

The uterine endometrium may also differ

- Related abnormalities are found at lower levels in eutopic endometrium of affected patients.
- These observations suggest endometrial susceptibility beyond the ectopic site alone.

Ectopic lesion changes

Milder eutopic changes

Potential field susceptibility

Integrated model of implant persistence

- Proinflammatory recruitment, neovascularization and tissue remodeling cooperate.
- Local estrogen synthesis and altered hormonal responsiveness reinforce survival.

Inflammation

Angiogenesis

Matrix remodeling

Estrogenic
persistence

Somatic genetic alterations are documented

- Deep infiltrating lesions may harbor KRAS, PIK3CA, PPP2R1A or ARID1A mutations.
- These alterations are described in the epithelial component.

KRAS / PIK3CA

PPP2R1A / ARID1A

Epithelial somatic changes

Genetic findings require careful interpretation

- The significance of driver-like mutations in deep lesions is uncertain.
- They may contribute to local aggressive behavior, but malignancy is not inferred from mutation alone.

Somatic mutation

Possible local growth advantage

Not automatically cancer

Association with specific ovarian cancers

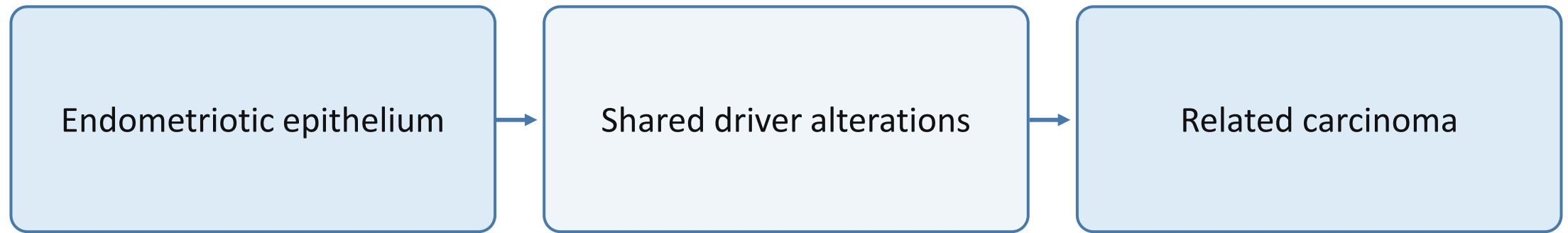
- Epidemiologic studies link endometriosis to ovarian endometrioid and clear cell carcinomas.
- The histotype association is more informative than a nonspecific statement about ovarian cancer.

Endometriosis

Ovarian endometrioid carcinoma

Ovarian clear cell carcinoma

Shared mutations suggest clonal relationships



In some patients, a carcinoma and adjacent endometriosis share somatic mutations.

These observations support a pathogenic relationship in a subset of cases.

Malignant progression is not inevitable

- Ovarian carcinoma may develop in association with an endometriotic cyst.
- Atypical endometriosis is considered a likely precursor in this setting.
- Most lesions are not presented as malignant in the source.

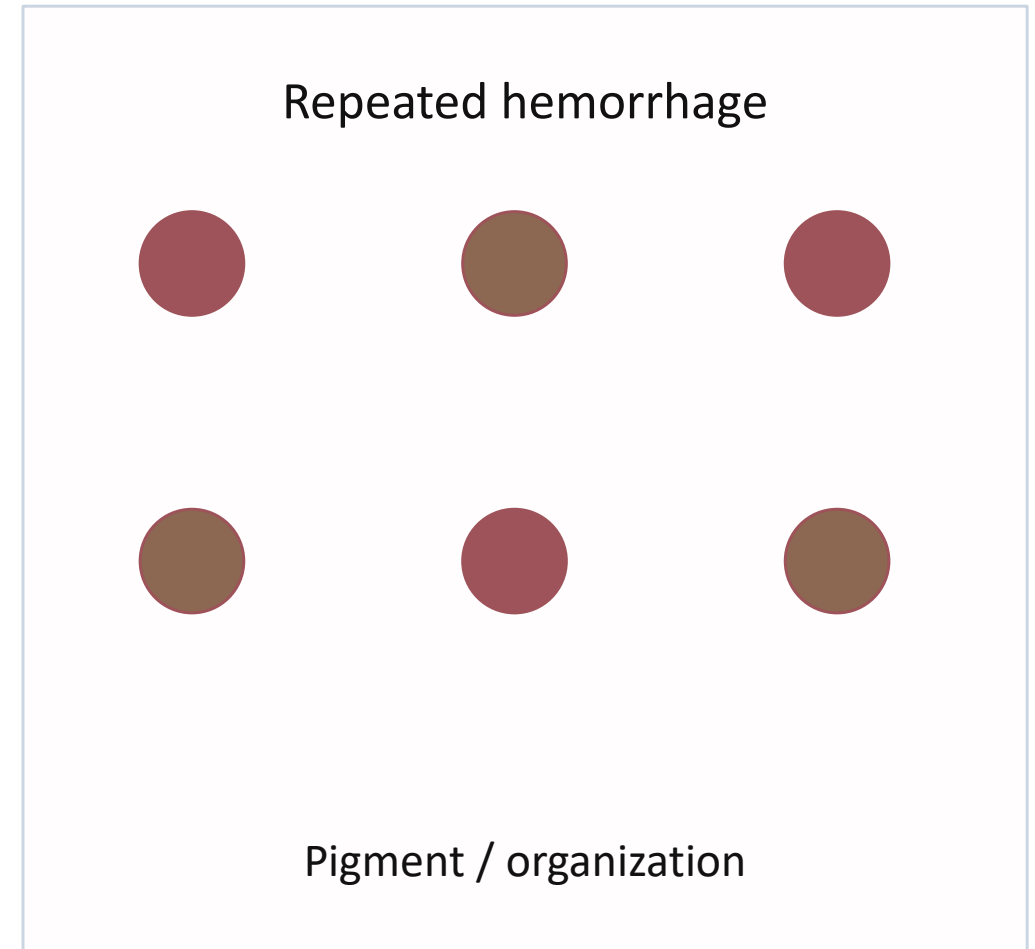
Typical endometriosis

Atypical endometriosis

Associated carcinoma

Why endometriotic lesions change color

- Ectopic tissue can bleed in response to hormonal stimulation.
- Repeated hemorrhage produces red-blue to yellow-brown lesions.



Illustrative geometry — not a diagnostic specimen

Gross lesions: Nodules and superficial foci

- Nodules may lie on or immediately below mucosal and serosal surfaces.
- Hue reflects hemorrhage and its evolution over time.

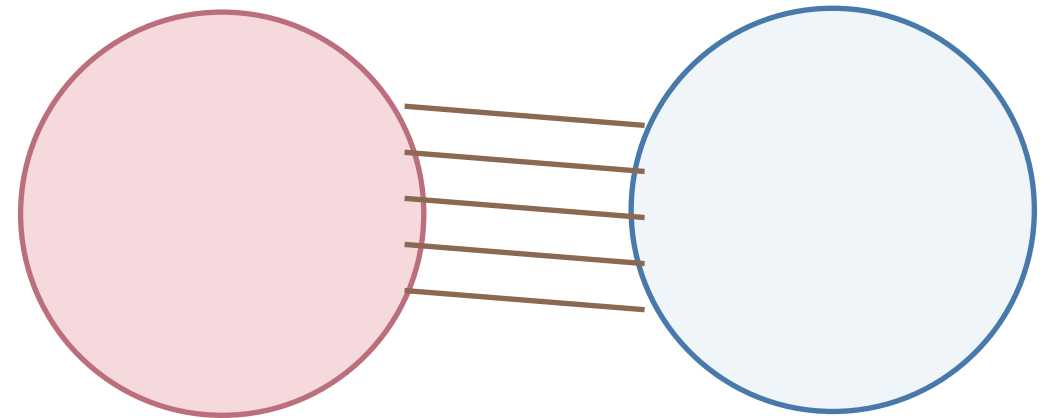
Serosal / mucosal implant

Periodic hemorrhage

Red-blue / yellow-brown focus

Organized hemorrhage causes adhesions

- Repeated bleeding and organizing tissue repair promote fibrous adhesions.
- Adhesions may join the tubes, ovaries and adjacent pelvic structures.



Adhesions after organized hemorrhage

Obliteration of the pouch of Douglas

- Widespread lesions can produce dense pelvic adhesions.
- Organization and fibrosis can obliterate the cul-de-sac (pouch of Douglas).

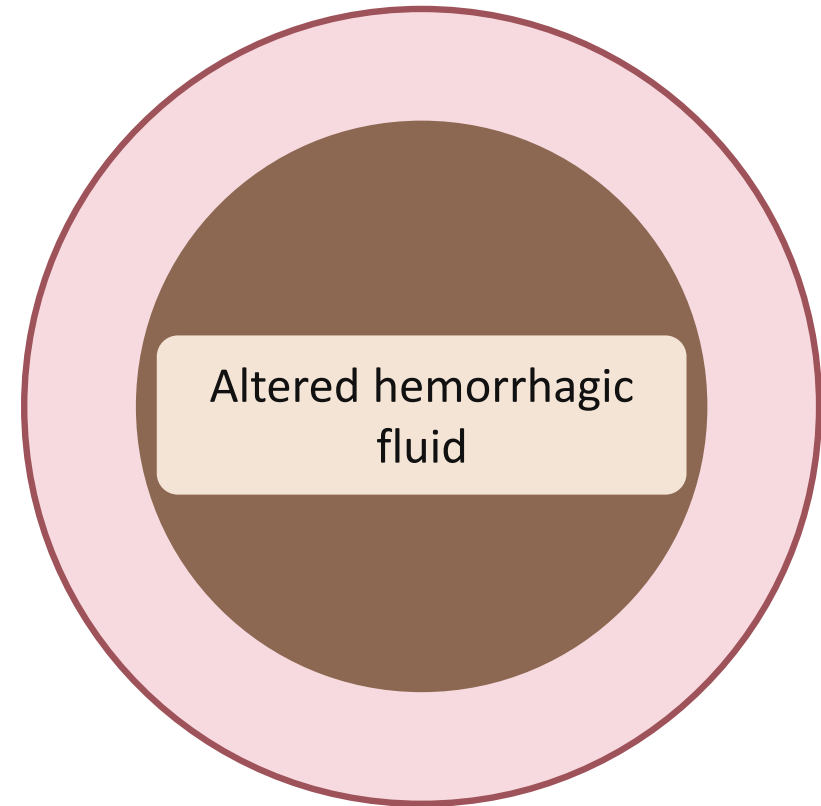
Numerous ectopic foci

Hemorrhage + fibrosis

Cul-de-sac obliteration

Endometrioma: The chocolate cyst

- Ovarian cysts may be distorted by repeated bleeding.
- Cystic masses roughly 3–5 cm filled with brown fluid.



Ovarian endometrioma — schematic

Deep lesions produce tissue distortion

- Deep infiltration may involve adjacent tissue planes.
- Fibrosis and adhesions are major morphologic consequences.

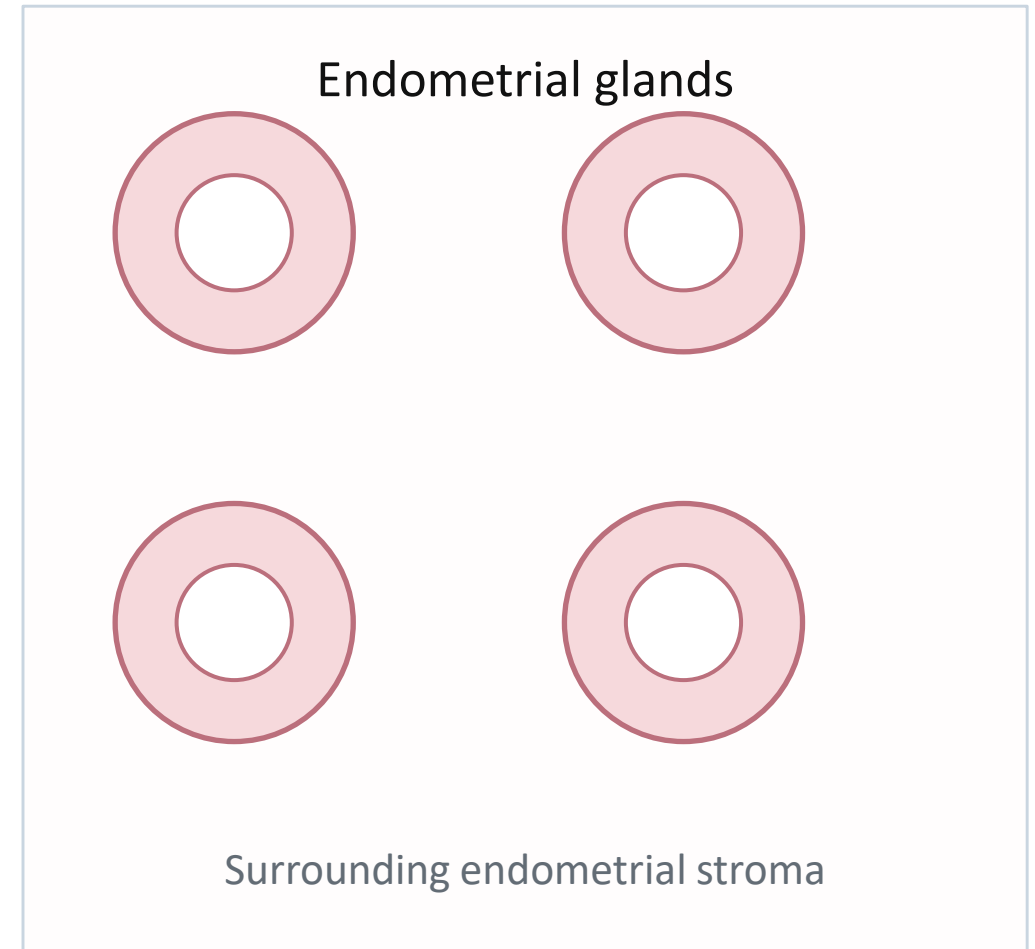
Deep lesion extension

Fibrotic response

Anatomic distortion

Histology: Endometrial glands and stroma

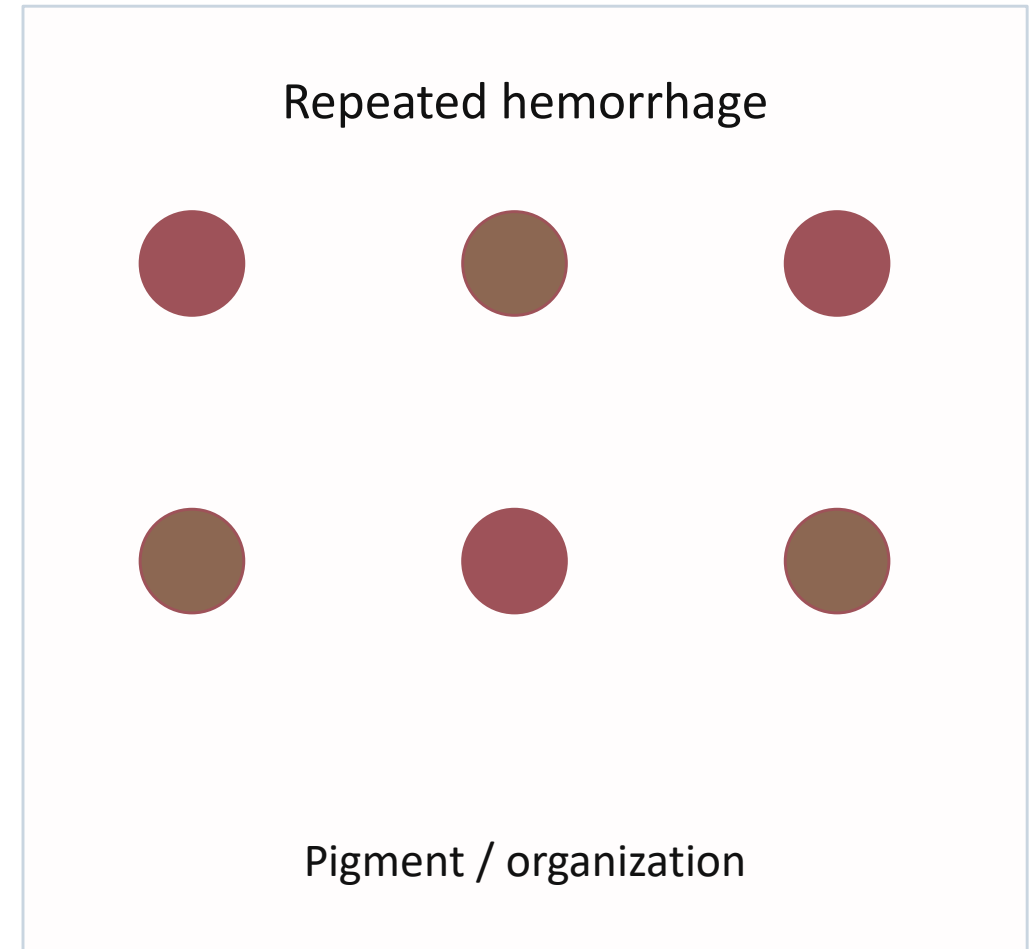
- Coexistence of endometrial glands and endometrial stroma is the characteristic pattern.
- Hemosiderin may or may not be identified.



Illustrative geometry — not a diagnostic specimen

Hemosiderin indicates previous bleeding

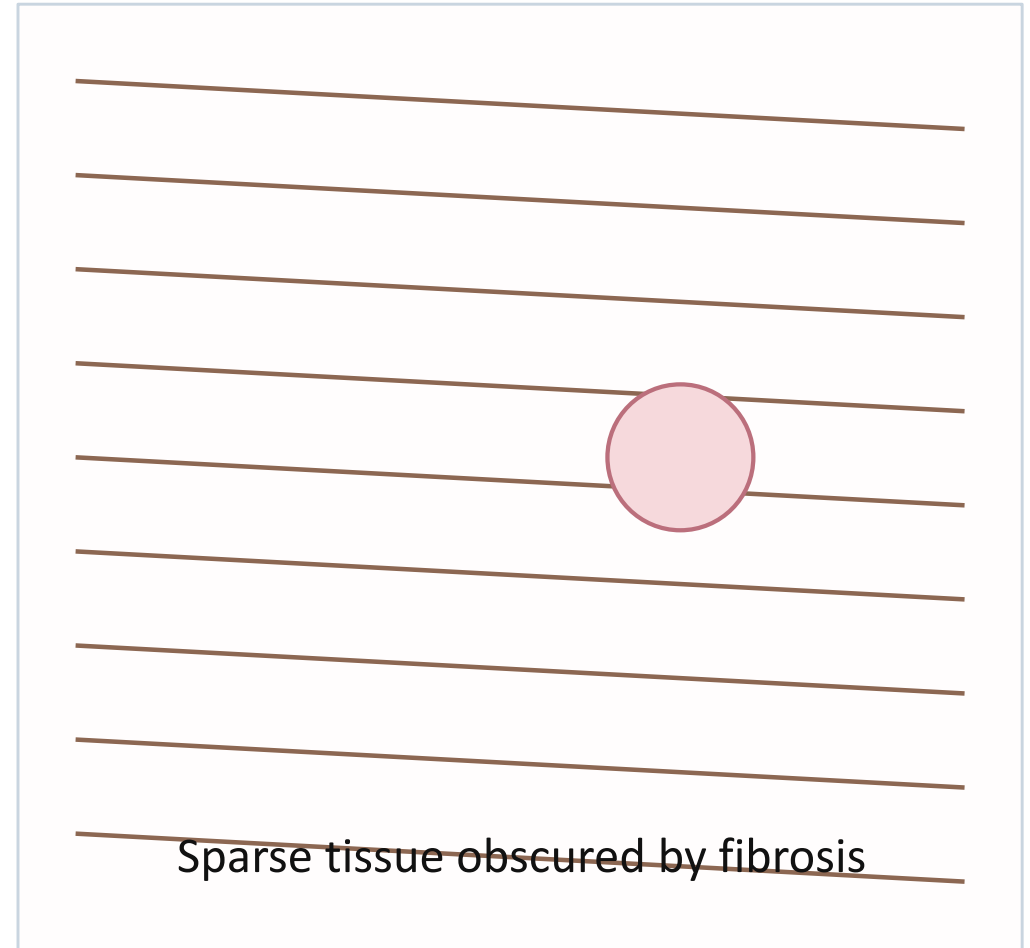
- Blood products can persist as hemosiderin after cyclic hemorrhage.
- Its presence is supportive, but the source does not require it in every diagnostic case.



Illustrative geometry — not a diagnostic specimen

Long-standing lesions can be difficult

- Secondary fibrosis may obscure the endometrial glands and stroma.
- Histologic recognition becomes harder in heavily scarred foci.



Illustrative geometry — not a diagnostic specimen

Endometriosis may be stromal-only

- Occasionally only the endometrial stromal component is identifiable.
- Absence of identifiable glands does not necessarily exclude an endometriotic focus.

Recognizable stroma

Glands not seen

Possible stromal-only lesion

Glands alone prompt a differential diagnosis

Histologic pattern	Implication	Important caveat
Glands + stroma	Characteristic endometriosis	Hemosiderin not obligatory
Stroma only	Possible endometriosis	May be difficult in fibrosis
Glands only	Do not assume endometriosis	Consider endosalpingiosis

Atypical endometriosis: Cytologic pattern

- The cyst-lining epithelium shows cytologic atypia.
- Major architectural changes are absent in this described pattern.

Endometriotic cyst lining

Cytologic atypia

Architecture largely preserved

Atypical endometriosis: Proliferative pattern

- Excessive epithelial proliferation produces glandular crowding.
- Cytologic atypia may accompany the crowded glands.

Epithelial proliferation

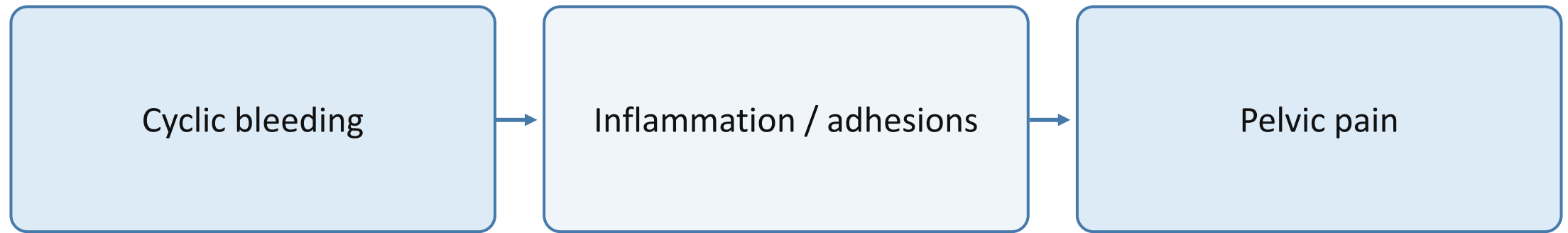
Glandular crowding

Possible cytologic atypia

The two atypical patterns are not identical

Atypical pattern	Cytology	Architecture
Cytologic	Atypical lining cells	No major changes
Proliferative	Often atypical	Crowded glands

Endometriosis causes cyclic pelvic pain



Dysmenorrhea is commonly severe.

Intrapelvic bleeding and periuterine adhesions are recognized contributors to pain.

Dyspareunia has a structural correlate

- Pain with intercourse is a typical presentation.
- Pelvic adhesions and deep lesions can be considered in the clinicopathologic explanation.

Pelvic lesion

Fibrosis / adhesions

Dyspareunia

Infertility may be the presenting problem

- Infertility as the presenting complaint in 30–40% of patients.
- This statistic concerns presenting complaint—not population infertility prevalence.

Tubal / ovarian adhesions

Distorted pelvic anatomy

Infertility presentation

Diagnosis requires anatomic and histologic context

- Clinical symptoms support suspicion but are not histologic proof.
- Characteristic ectopic endometrial glands and stroma establish the tissue pattern.
- Fibrosis, stroma-only foci and gland-only mimics complicate interpretation.

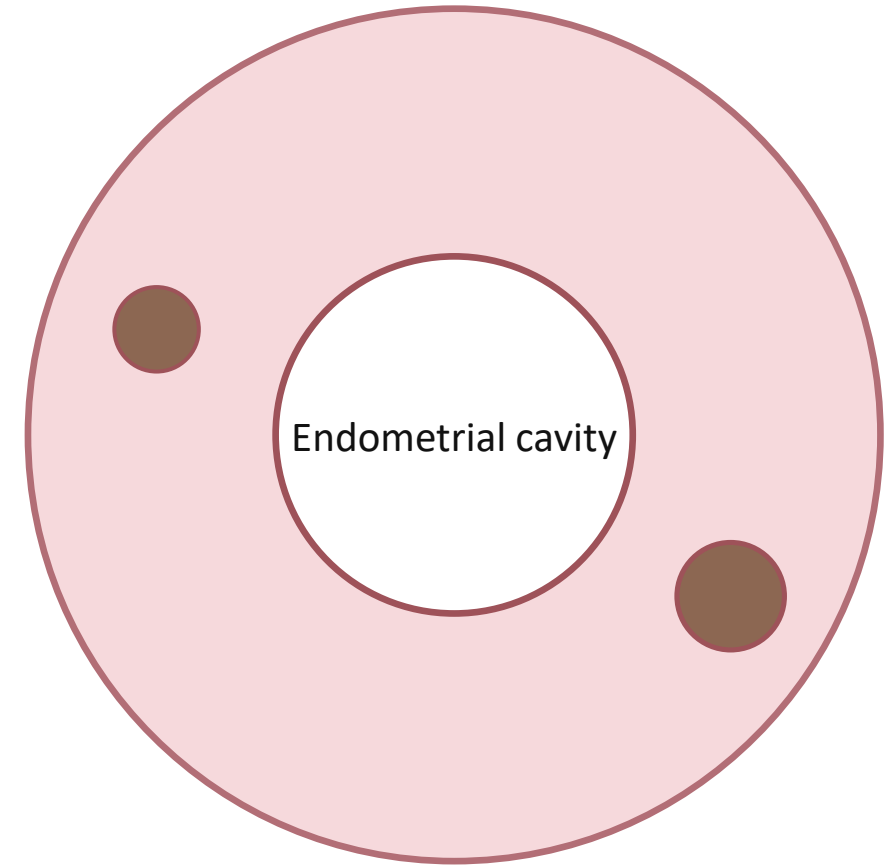
Location

Glands + stroma

Mimics / fibrosis

Adenomyosis: Endometrial tissue in myometrium

- Adenomyosis is defined by endometrial tissue within the uterine wall.
- Unlike extrauterine endometriosis, it remains continuous with uterine endometrium.



Endometrial tissue within myometrium

Adenomyosis: Proposed down-growth

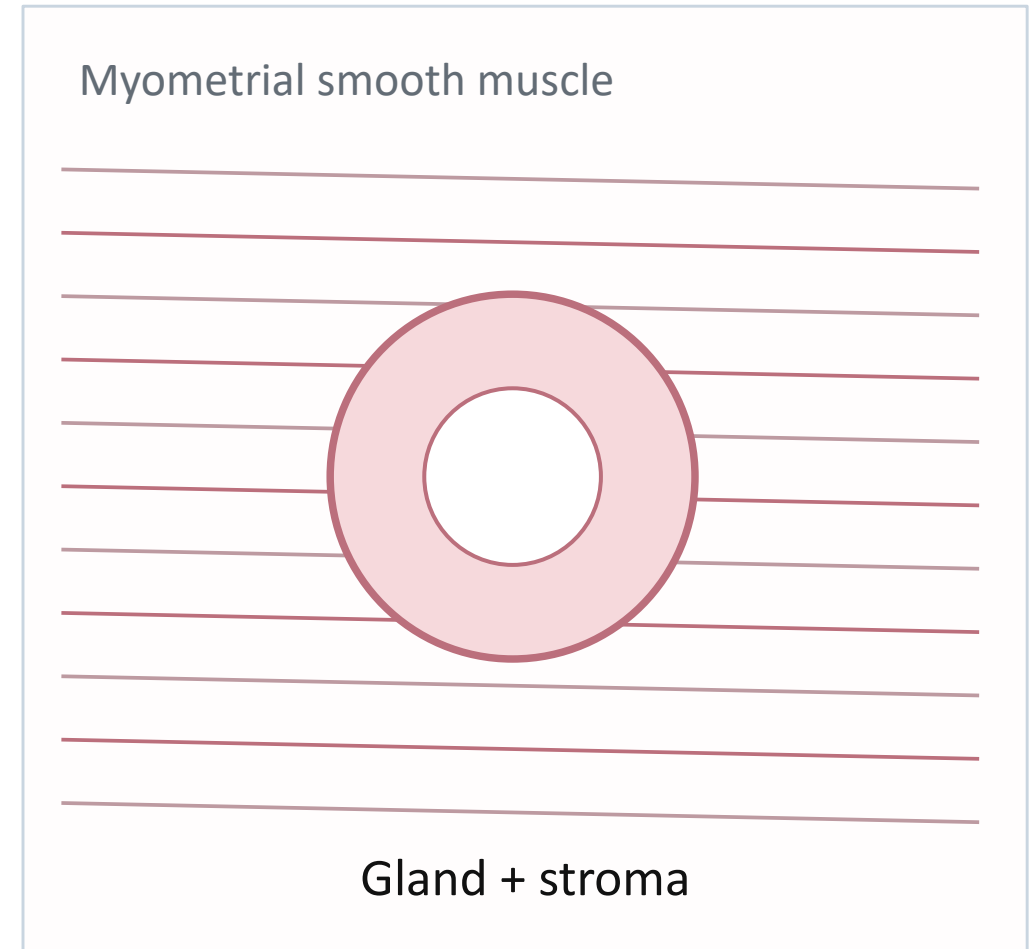


Endometrial tissue is thought to grow downward into the myometrium.

It extends between smooth-muscle fascicles rather than forming an extrauterine implant.

Adenomyosis: Microscopic pattern

- Irregular nests of endometrial stroma occur in the myometrium.
- Glands may be present or absent within those stromal foci.



Illustrative geometry — not a diagnostic specimen

Adenomyosis: Frequency in the source

- Adenomyosis occurs in up to 20% of uteri.
- This description should not be conflated with a population-based prevalence estimate.

Intrauterine wall involvement

Up to 20% of uteri

Context matters

Adenomyosis: Abnormal bleeding

- Menometrorrhagia denotes heavy, irregular menstrual bleeding.
- Bleeding symptoms are part of the clinical adenomyosis spectrum.

Myometrial involvement

Abnormal bleeding

Menometrorrhagia

Adenomyosis: Characteristic pain

- Colicky dysmenorrhea and pelvic pain are described.
- Symptoms may be especially prominent premenstrually.
- Dyspareunia can occur.

Colicky dysmenorrhea

Premenstrual pelvic pain

Dyspareunia

The two disorders can coexist

- Adenomyosis and endometriosis are not mutually exclusive diagnoses.
- Shared symptoms do not establish the anatomic location of ectopic tissue.

Endometriosis

Adenomyosis

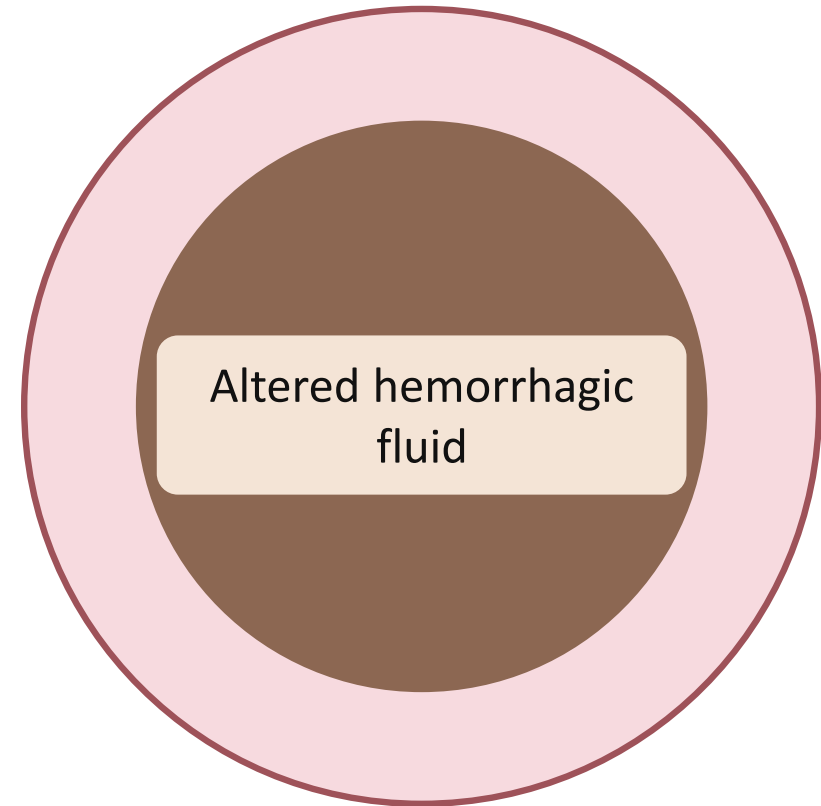
Possible coexistence

Endometriosis versus adenomyosis

Feature	Endometriosis	Adenomyosis
Tissue location	Outside uterus	Within myometrium
Relation to uterine lining	Ectopic, separated	Continuity / down-growth
Structural hallmark	Implants, cysts, adhesions	Endometrial nests in muscle
Common symptoms	Dysmenorrhea, pelvic pain, infertility	Abnormal bleeding, dysmenorrhea, pelvic pain

Clinicopathologic case: Ovarian cyst

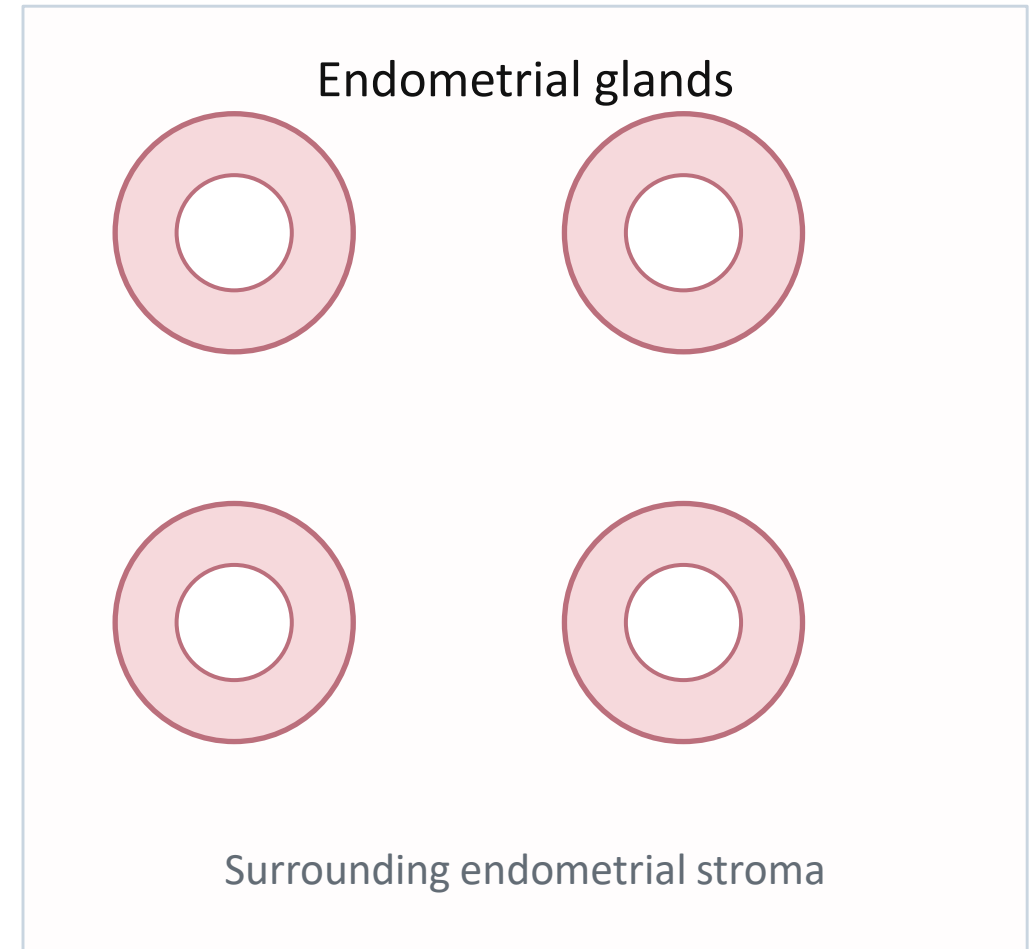
- A reproductive-age patient has severe dysmenorrhea and an ovarian cyst containing brown fluid.
- What lesion best explains the finding—and what process produced the cyst content?



Ovarian endometrioma — schematic

Case interpretation: Endometrioma

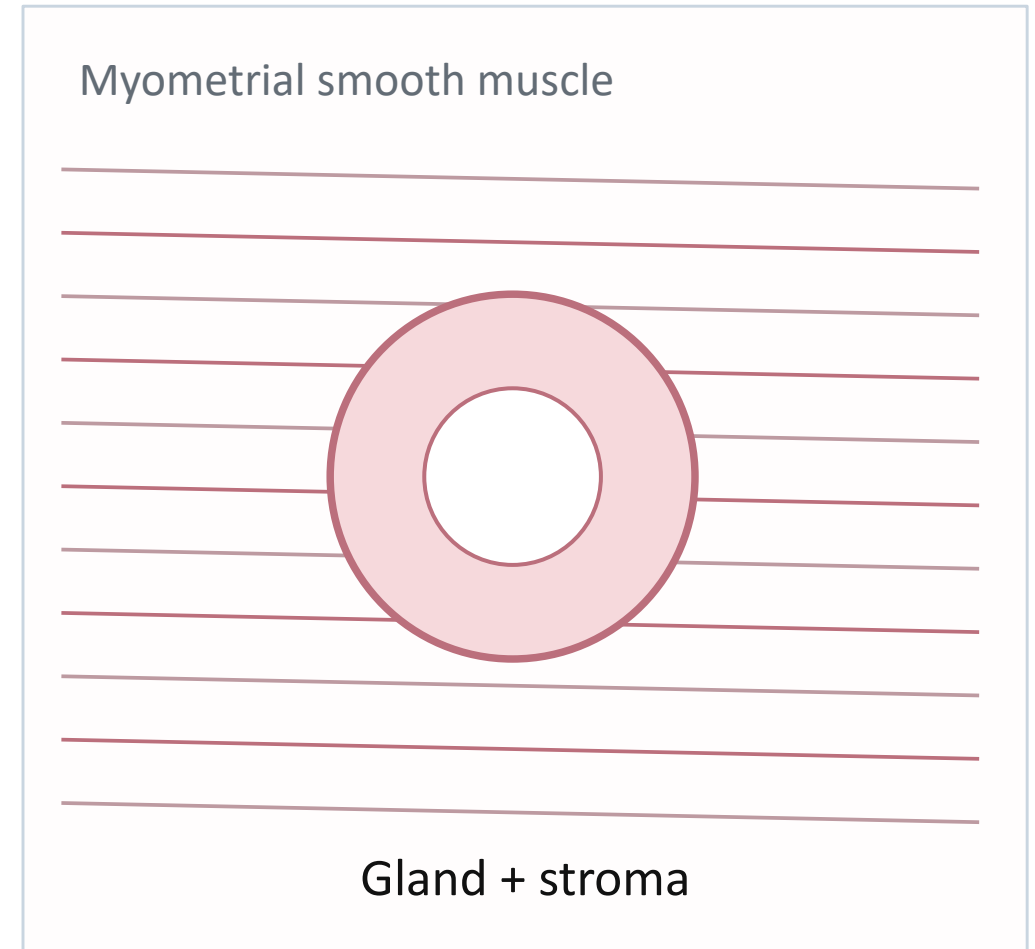
- Ovarian endometriosis can create a chocolate cyst.
- Repeated hemorrhage produces the characteristic brown contents.
- Histology may demonstrate endometrial glands, stroma and hemosiderin.



Illustrative geometry — not a diagnostic specimen

Clinicopathologic case: Uterine wall

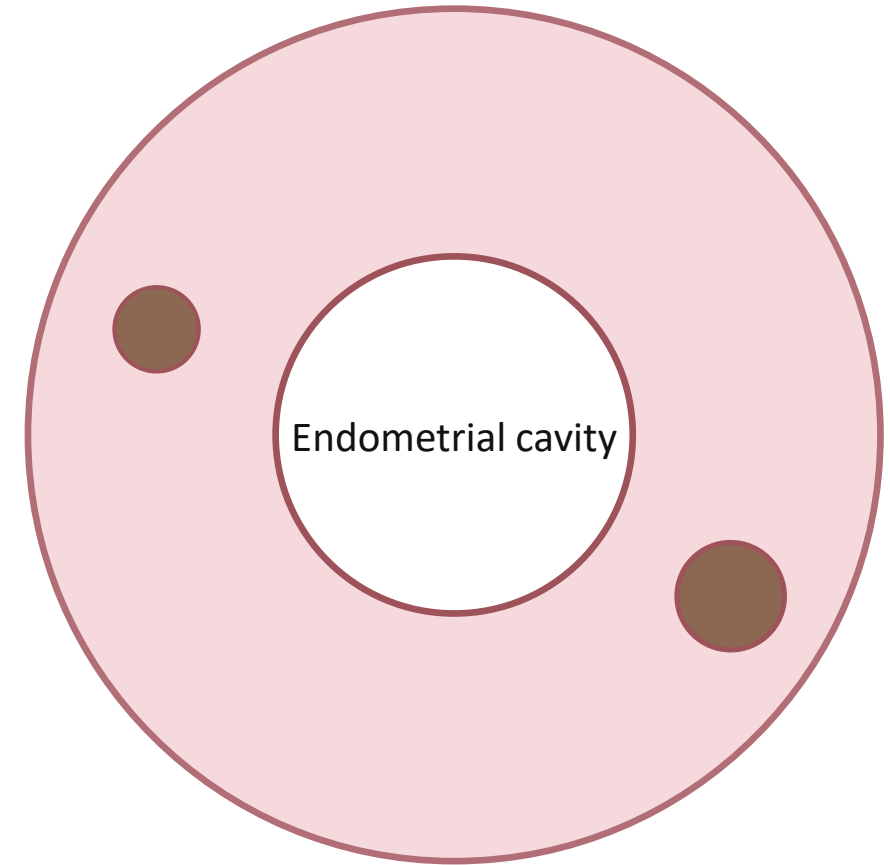
- A hysterectomy shows endometrial stroma with glands embedded among myometrial smooth-muscle fascicles.
- What is the diagnosis, and how does this differ from endometriosis?



Illustrative geometry — not a diagnostic specimen

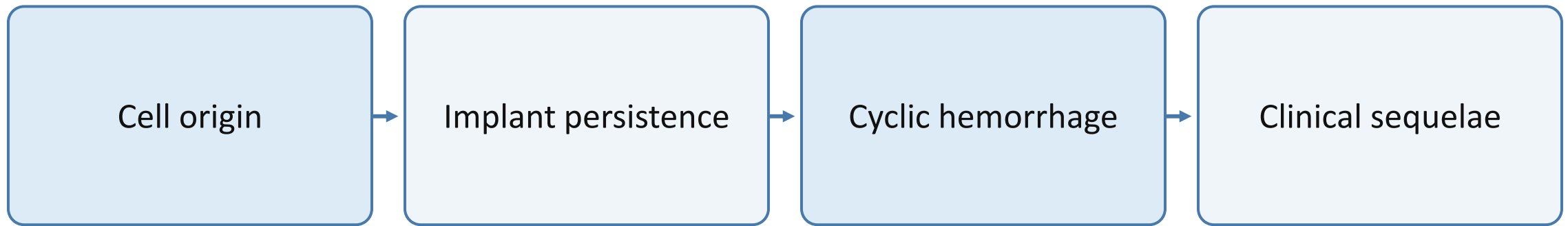
Case interpretation: Adenomyosis

- Endometrial tissue within the myometrium identifies adenomyosis.
- Continuity with the endometrium differentiates it from extrauterine endometriosis.



Endometrial tissue within myometrium

Synthesis: Disease mechanism to morphology



Ectopic survival requires more than retrograde tissue movement alone.

Inflammatory and hormonal conditions contribute to persistence.

Hemorrhage, adhesions and fibrosis translate biology into symptoms.

Four findings to remember

- Endometriosis is extrauterine; Adenomyosis is intramyometrial.
- Endometriosis characteristically contains ectopic glands and stroma.
- Repeated hemorrhage explains pigment, endometriomas and adhesions.
- Atypical endometriosis and some ovarian carcinoma share a pathogenic relationship.

Location

Morphology

Consequences

Neoplastic link

Primary reference and image provenance

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026).
- Chapter 22, The Female Genital Tract: Endometriosis and Adenomyosis, pp. 912–914.
- All visible illustrations in this deck are original editable schematics, not photomicrographs.

Textbook source

Native PowerPoint diagrams

Figure traceability in notes