

Gestational Trophoblastic Disease

Molar pregnancy • pathogenesis • morphology • clinicopathologic interpretation

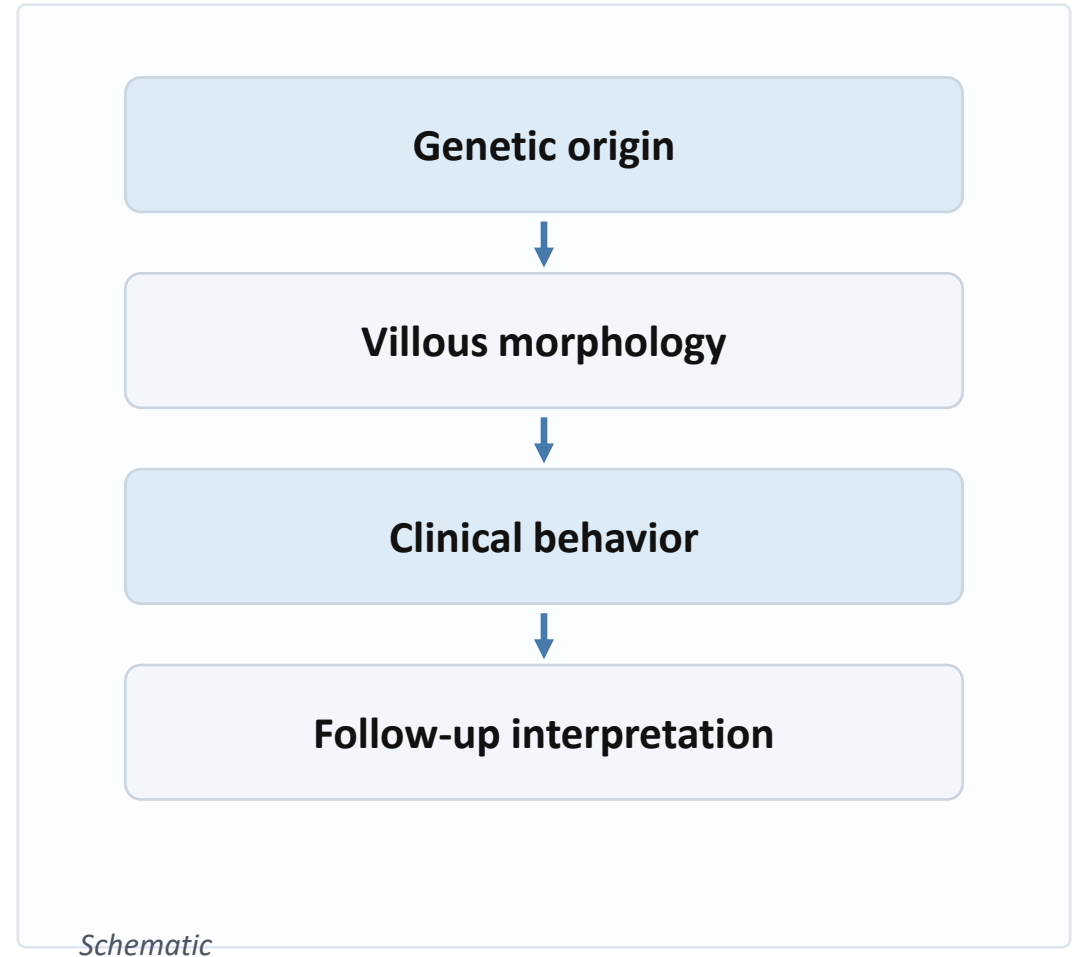
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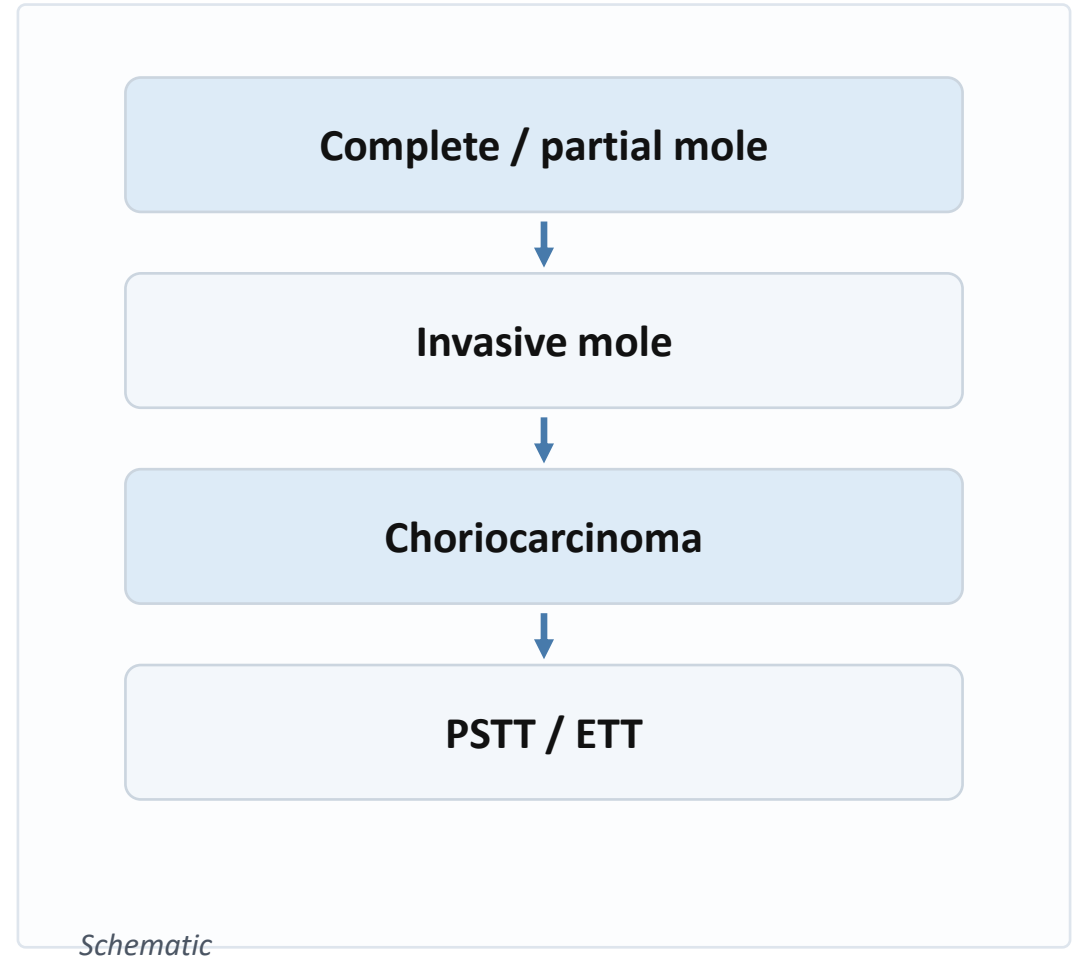
Learning objectives

- Classify the major entities in gestational trophoblastic disease.
- Derive complete and partial mole genotypes from fertilization events.
- Recognize defining gross and microscopic features of molar pregnancy.
- Connect hCG behavior and myometrial invasion with clinical follow-up.



The defining abnormality is trophoblastic proliferation

- Gestational trophoblastic disease (GTD) comprises tumors and tumorlike disorders of placental tissue.
- The proliferating tissue is trophoblastic; Chorionic villi may or may not be present.
- Morphology and behavior span noninvasive molar lesions through overt malignancy.

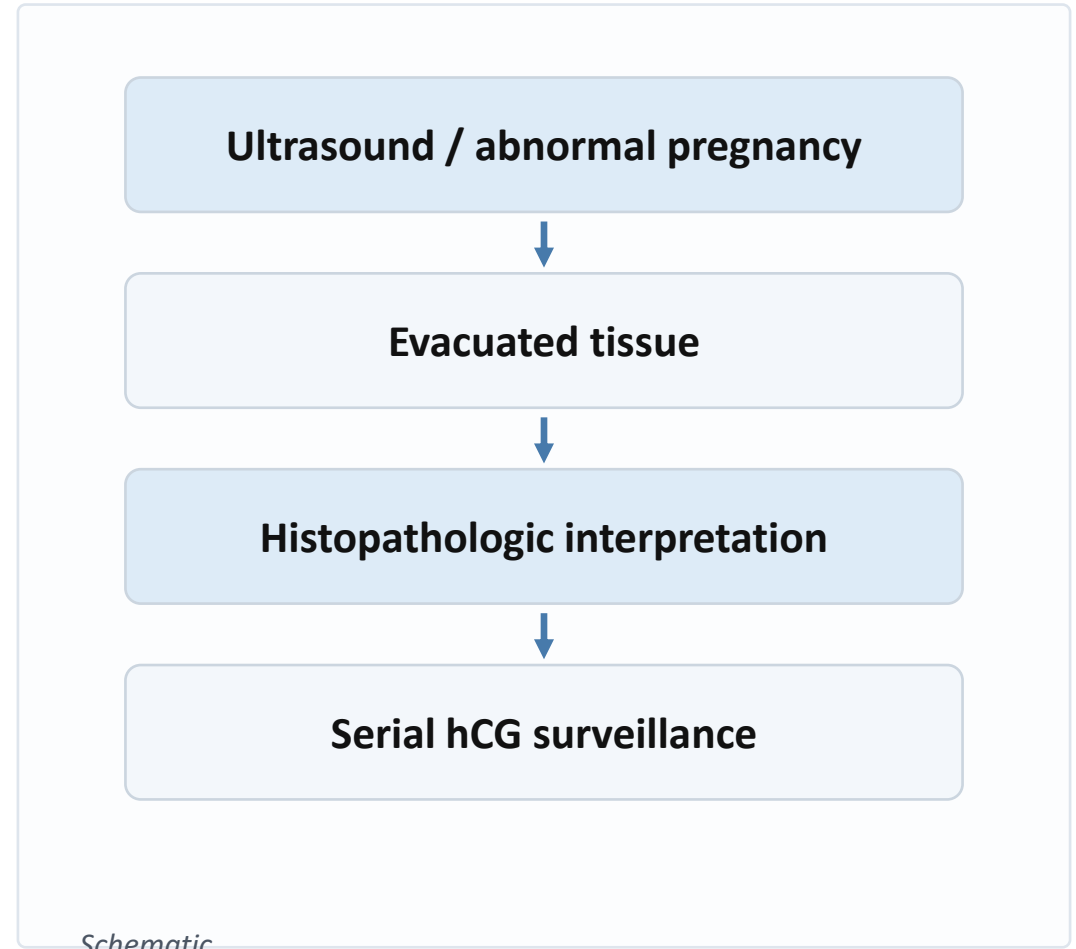


Classification: The major trophoblastic entities

Entity	Core diagnostic concept
Complete hydatidiform mole	Noninvasive molar pregnancy; exclusively paternal nuclear genome
Partial hydatidiform mole	Noninvasive molar pregnancy; usually triploid
Invasive mole	Hydropic chorionic villi invade the uterine wall
Gestational choriocarcinoma	Malignant trophoblast without chorionic villi
PSTT / ETT	Uncommon extravillous trophoblastic tumors

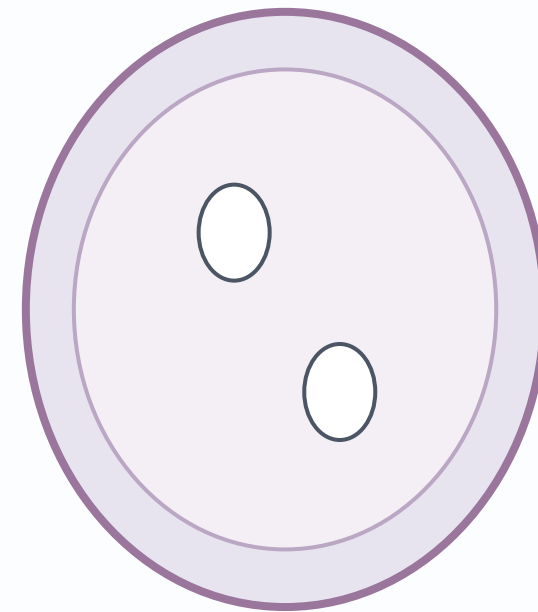
Why distinguishing these entities matters

- A molar pregnancy must be recognized because persistent trophoblastic disease can follow.
- Complete and partial moles differ in genetic origin, morphology, and risk.
- Villi within invasive tissue distinguish invasive mole from choriocarcinoma.
- Post-evacuation hCG behavior reveals clinically important persistence.



Normal villous architecture provides the reference

- Trophoblast covers the chorionic villous core.
- Maternal blood surrounds villous surfaces; The villus is a distinct structure.
- Interpret trophoblastic growth relative to villous size and shape.

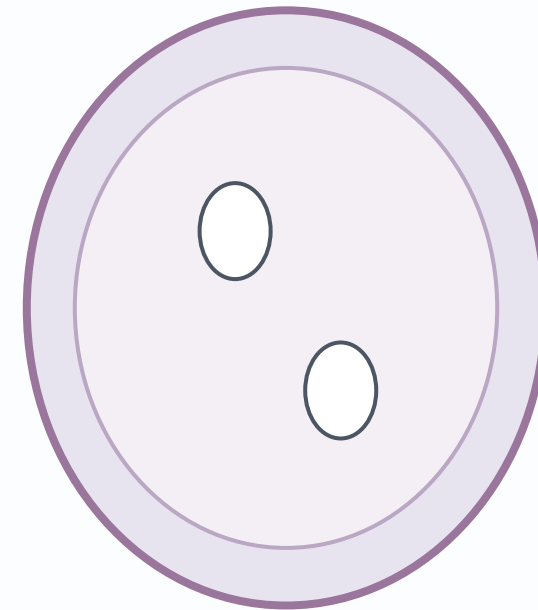


Villous stroma

Schematic

The histologic unit is the chorionic villus

- The villous stroma forms the central core.
- Cytotrophoblast and syncytiotrophoblast form trophoblastic coverings of villous coverings.
- Both stromal edema and the pattern of trophoblastic proliferation are needed to interpret molar pathology.

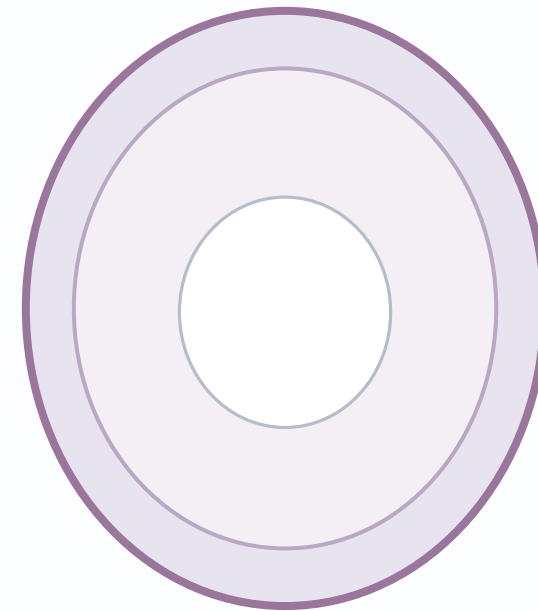


Villous stroma

Schematic

Hydropic change expands the villous stroma

- Excess stromal fluid enlarges villi.
- Advanced edema can produce central cavitation (cisterns).
- An edematous villus alone does not specify complete versus partial mole.

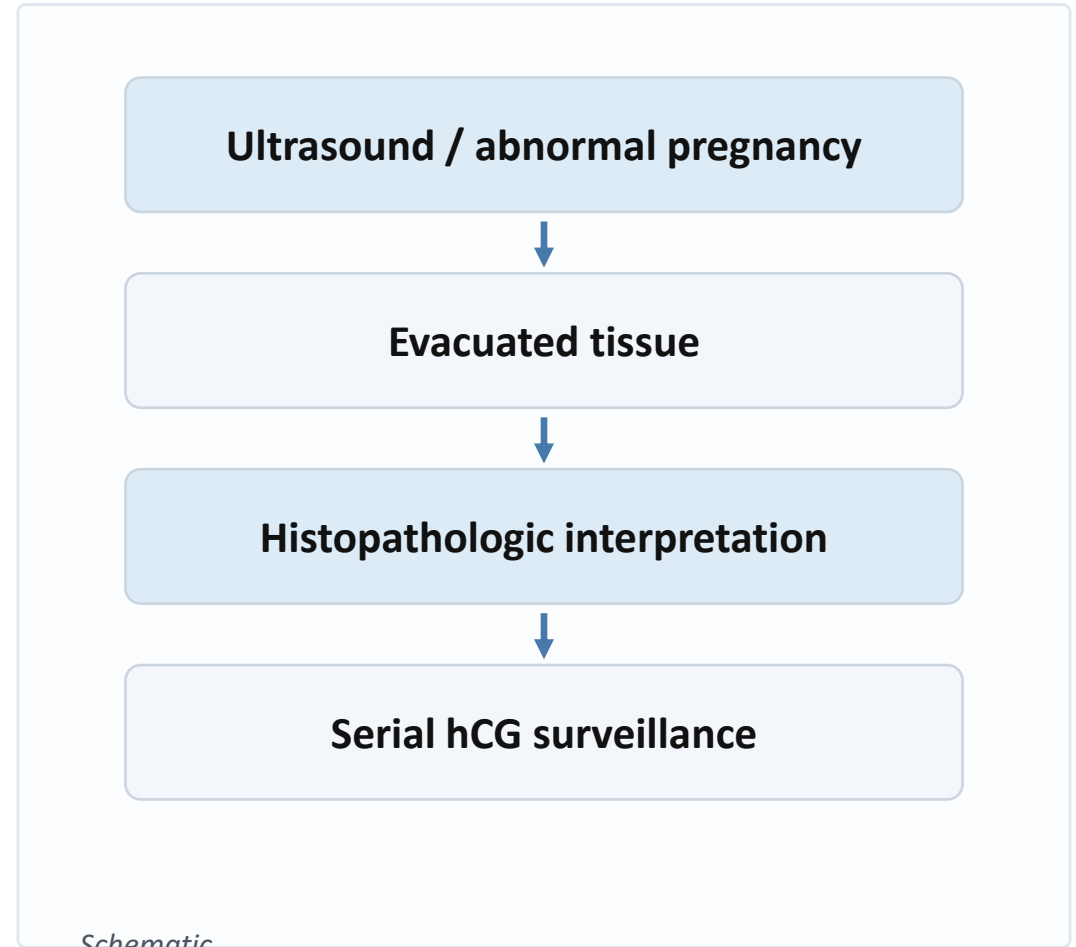


Expanded edematous stroma

Schematic

Hydatidiform moles are detected early

- Pelvic sonography usually detects molar change in early pregnancy.
- A mean gestational age near 9 weeks at diagnosis.
- Many early cases are identified following miscarriage or evacuation of abnormal pregnancy tissue.



Distribution varies with reproductive age and geography

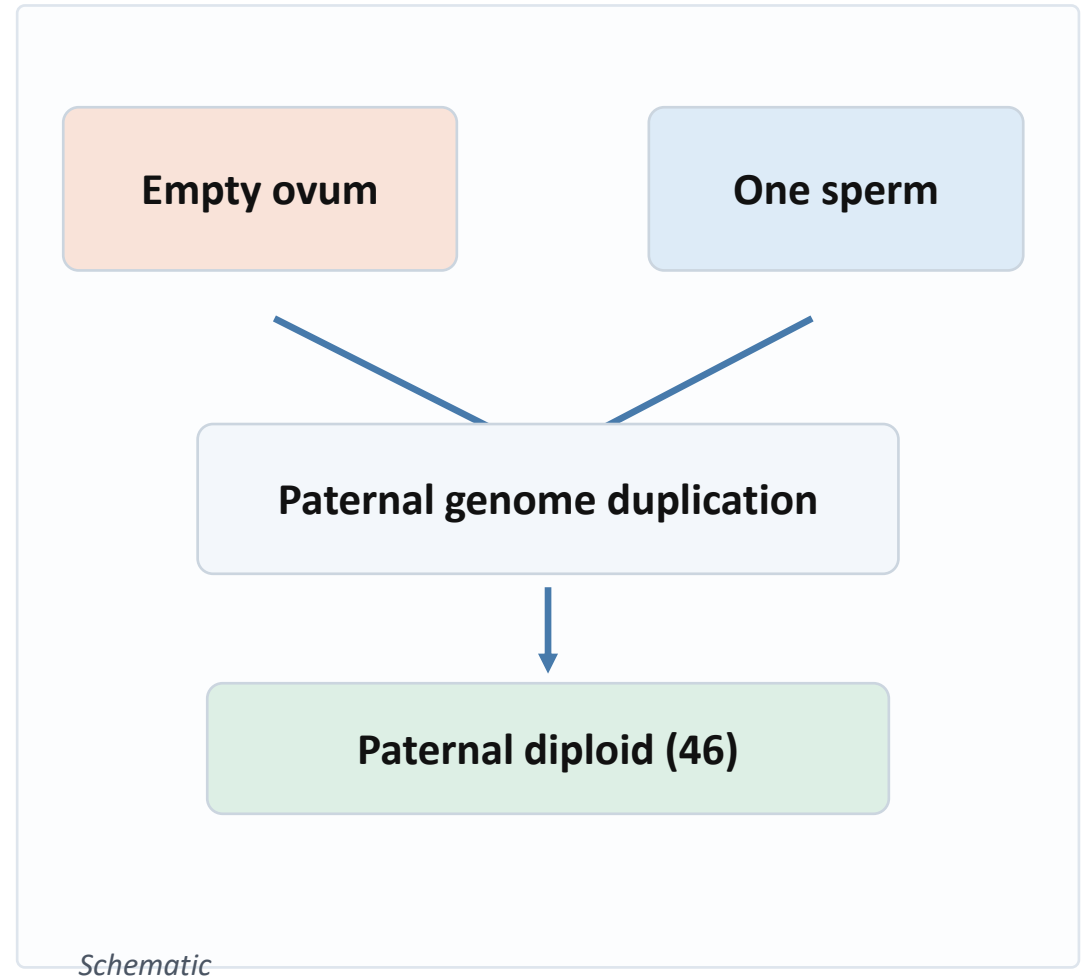
- Molar pregnancy can occur at any reproductive age.
- The risk is increased at the extremes of reproductive life.
- Approximately 1 in 1,000–2,000 pregnancies in the United States.
- Reported incidence is approximately twice as high in Southeast Asia.

Two noninvasive molar types

Dimension	Complete mole	Partial mole
Genetic origin	Paternal nuclear genome only	Maternal plus additional paternal genome
Typical ploidy	Diploid	Triploid
Embryonic development	Absent	May occur, abnormal
Villous edema	Most or all villi	Subset of villi
Trophoblast proliferation	Marked, circumferential	Focal, less marked

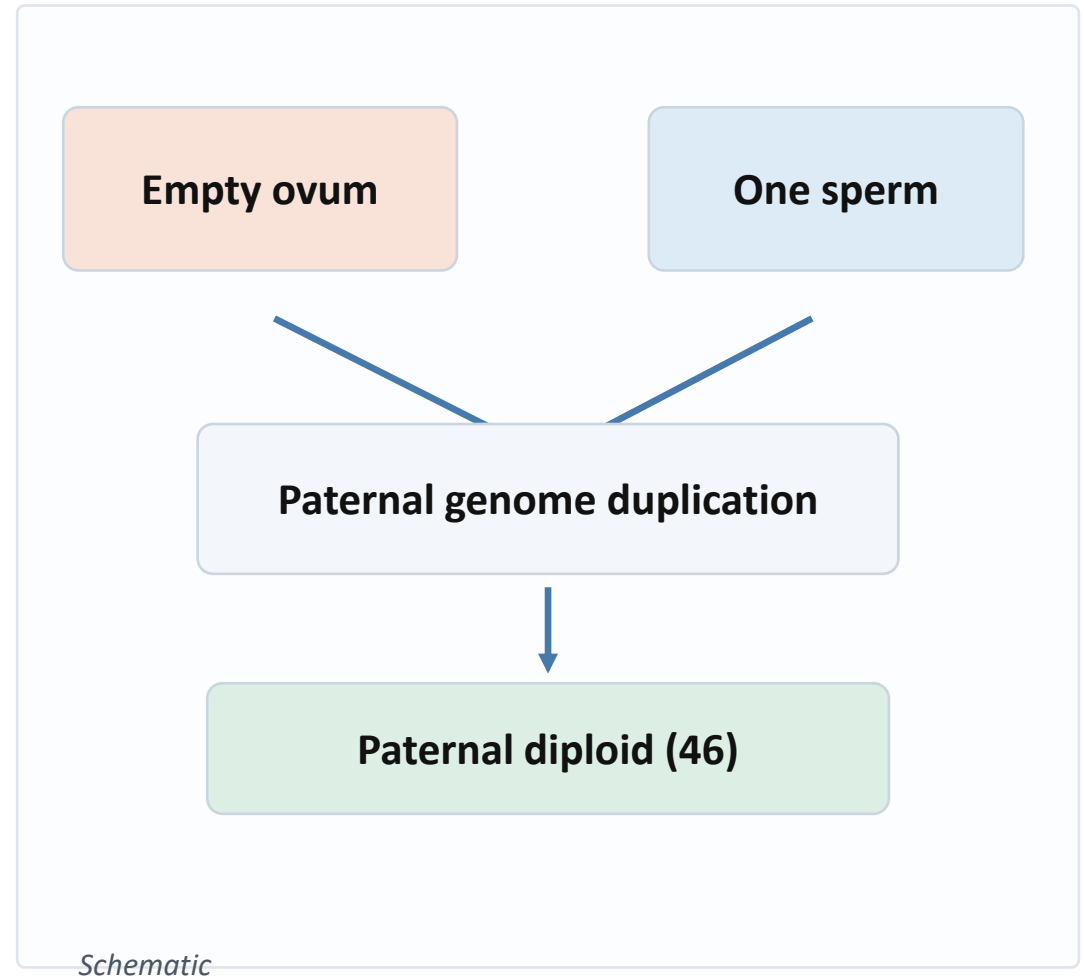
Complete mole begins with an “empty” ovum

- The ovum lacks a retained maternal nuclear chromosome complement.
- The resulting conceptus derives its nuclear genome from paternal chromosomes.
- The common event is monospermic fertilization followed by chromosome duplication.



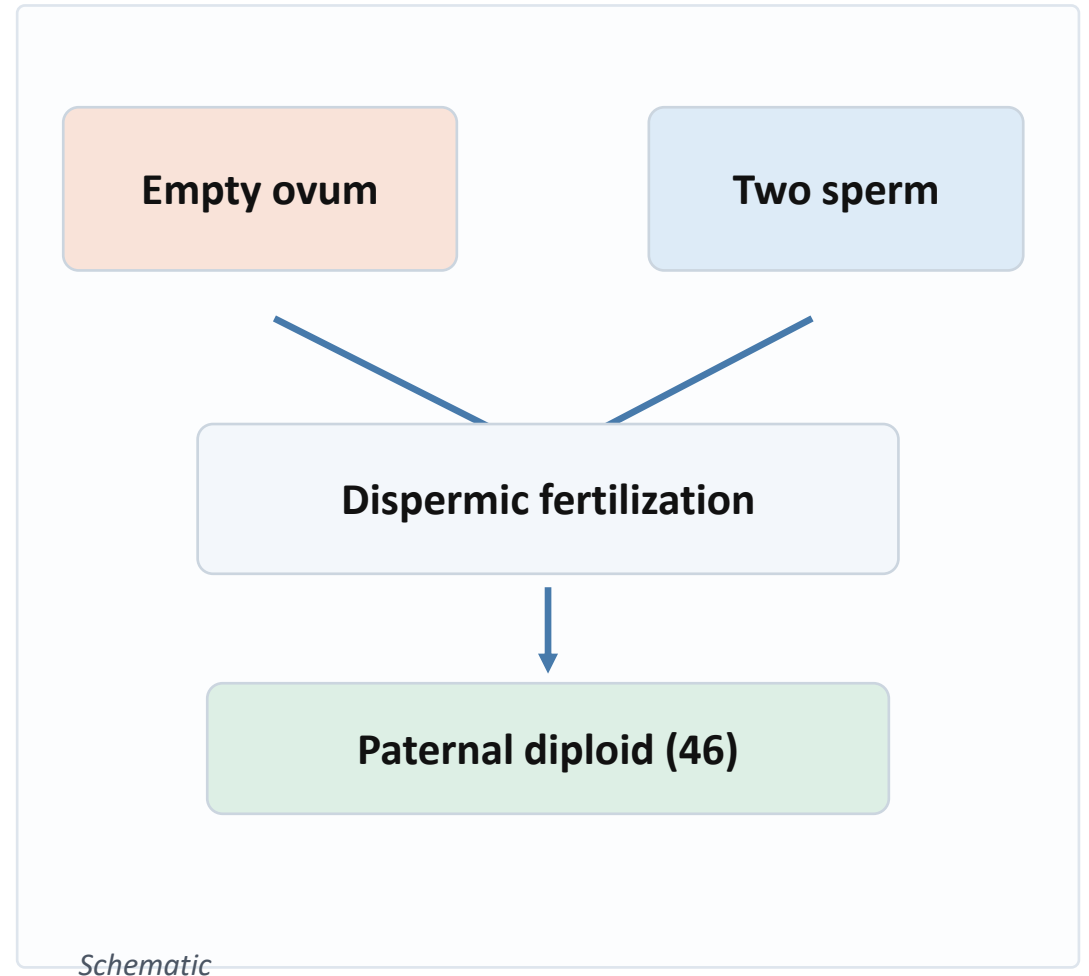
Monospermic complete mole: Androgenesis

- Single sperm contributes its haploid genome.
- Duplication restores a diploid complement.
- The common result is 46,XX with paternal-only nuclear genetic material.



Dispermic complete mole: Two paternal contributions

- Two sperm fertilize an ovum lacking maternal nuclear chromosomes.
- The resulting complete mole may have 46,XX or 46,XY karyotype.
- The nuclear genome remains entirely paternal in origin.



Most complete moles are 46,XX

Robbins: Approximately 90% are monospermic, androgenetic complete moles.

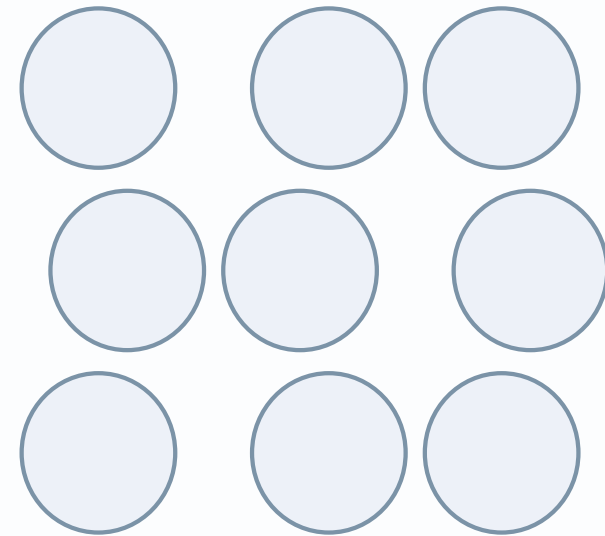
- The remaining approximately 10% are dispermic complete moles.
- A diploid chromosome count alone is insufficient to prove a normal biparental conceptus.

Complete mole: Consequence for embryogenesis

- A complete mole does not support embryonic development.
- Its growth reflects abnormal placental villi and trophoblast rather than viable embryogenesis.
- Absence of embryonic development is one useful discriminator from partial mole.

Complete mole: Gross appearance

- Classic lesions consist of delicate, friable, translucent cystic structures.
- Grape-like vesicles correspond to fluid-distended hydropic villi.
- The gross pattern is most conspicuous in well-developed lesions.

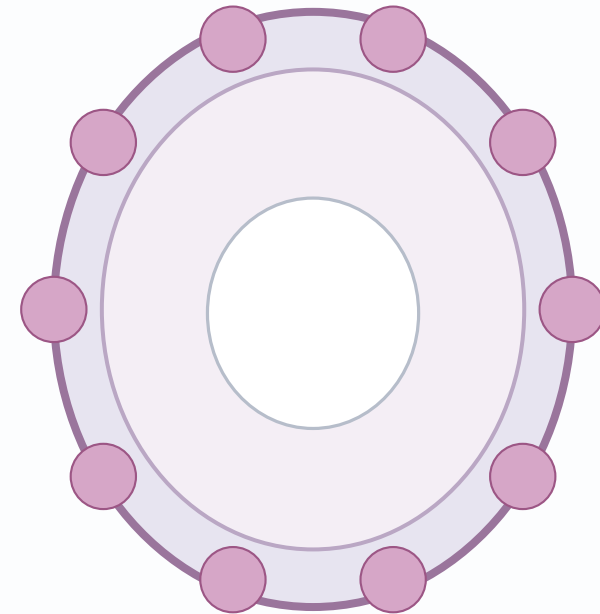


Grape-like, fluid-distended villi

Schematic

Complete mole: Diffuse villous enlargement

- Most or all villi display edema and enlargement.
- Villous profiles tend to be smooth, rounded or oval.
- The diffuse distribution matters as much as the abnormality in any single villus.

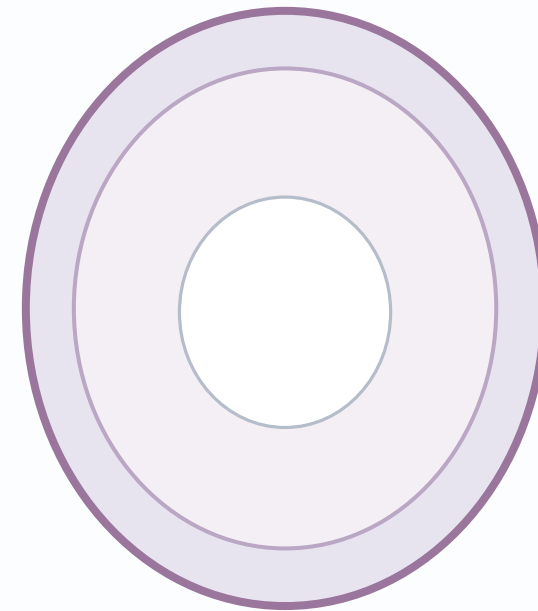


Diffuse hydropic enlargement

Schematic

Complete mole: Central cistern formation

- Prominent stromal edema may create internal cavitations.
- These central cavities are termed cisterns.
- Central cavitation complements, but does not replace, evaluation of the trophoblast.

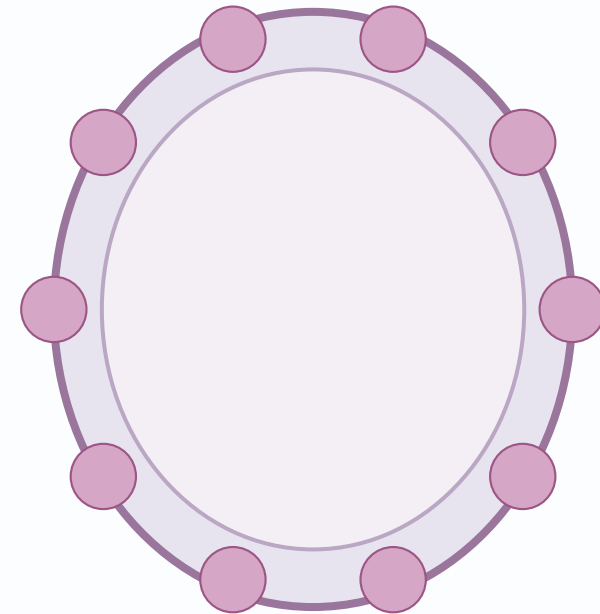


Central cistern

Schematic

Complete mole: Circumferential trophoblast growth

- Trophoblastic proliferation surrounds enlarged villi.
- Both cytotrophoblast and syncytiotrophoblast are involved.
- The distribution of hyperplasia is characteristically circumferential.

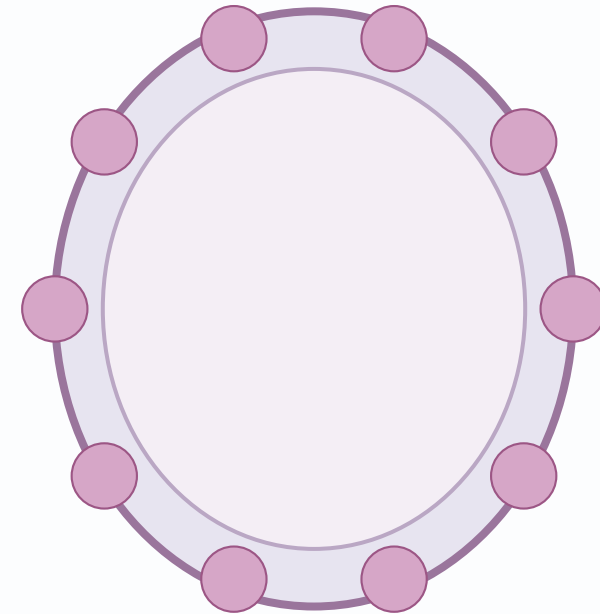


Circumferential growth

Schematic

Recognizing biphasic proliferation

- Cytotrophoblast and syncytiotrophoblast are both increased.
- Assess the trophoblastic rim rather than attributing thickening to a single cell type.
- This contrasts with the more focal, predominantly syncytiotrophoblastic pattern described in partial mole.



Circumferential growth

Schematic

Complete mole: Morphology checklist

Component	Expected finding
Villi	Diffuse enlargement; smooth, oval contours
Stroma	Marked edema; central cisterns often evident
Trophoblast	Circumferential, biphasic proliferation
Embryonic structures	No embryonic development
Genetics	Diploid, entirely paternal nuclear genome

Complete mole: Why hCG is conspicuous

- Proliferating trophoblastic tissue produces human chorionic gonadotropin (hCG).
- The source describes serum levels greatly exceeding a normal pregnancy at similar gestational age.
- The rate of increase can exceed normal singleton or multiple pregnancies.

High hCG relative to gestational age



Serial assessment after evacuation

Persistent elevation → investigate

Schematic

Complete mole: Complications and persistence

- A 15% risk of persistent or invasive mole after a complete mole.
- The textbook gives a 2.5% risk of subsequent choriocarcinoma.
- These are source-reported estimates, not patient-specific forecasts.

15% persistent / invasive mole

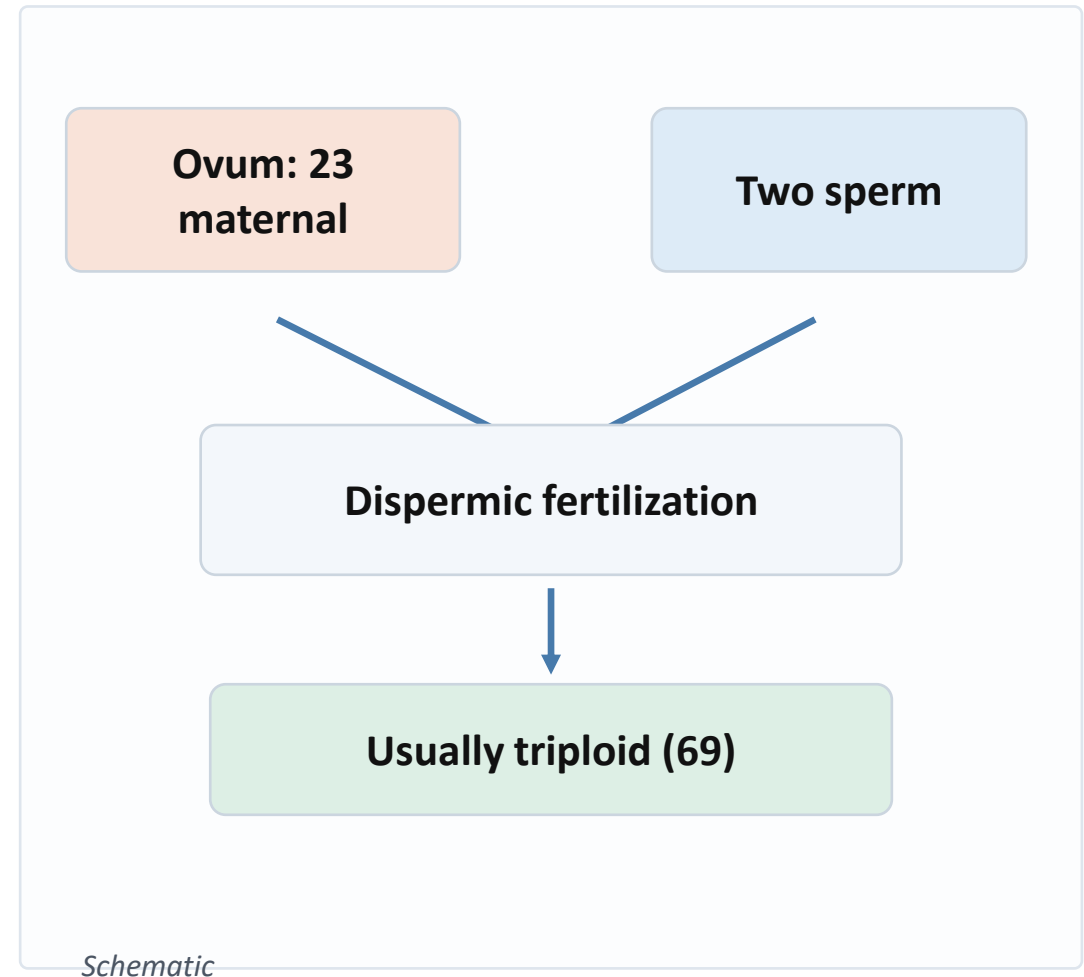
2.5% subsequent choriocarcinoma

Textbook estimates for complete mole

Schematic

Partial mole: An ovum is fertilized by two sperm

- The ovum retains a maternal haploid chromosome set.
- Dispermy supplies two additional paternal haploid contributions.
- The resulting conceptus is typically triploid.



Triploidy is typical of partial hydatidiform mole

Example: 69,XXY

- The source also recognizes occasional tetraploid partial moles (e.g., 92,XXXY).
- Genetic composition contrasts fundamentally with androgenetic complete mole.

Partial mole retains a maternal genetic contribution

- Complete mole: No maternal nuclear genome retained.
- Partial mole: Maternal nuclear chromosomes remain.
- This distinction explains why chromosomal counts and parental origin are complementary concepts.

Complete: Paternal only

Partial: Maternal + paternal

Distinct parental origin

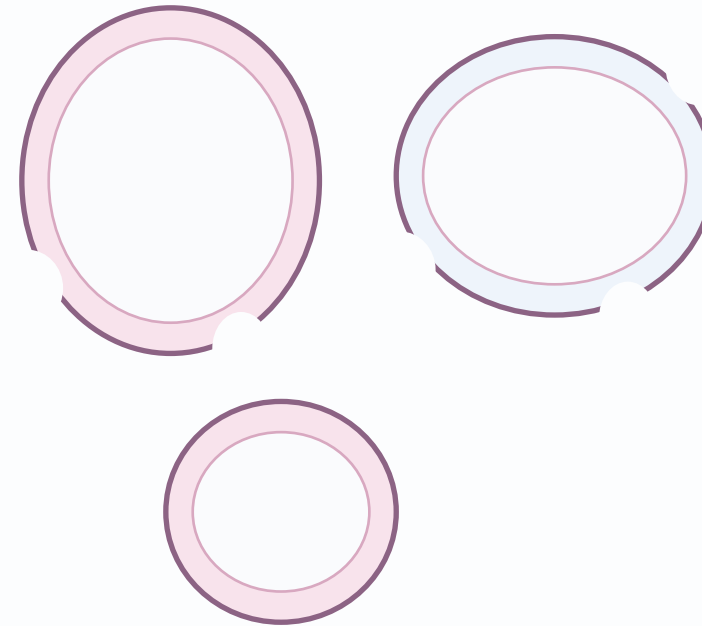
Schematic

Partial mole can show fetal development

- Embryonic or fetal development may be present.
- The fetus is generally growth restricted.
- Severe, lethal central nervous system and skeletal anomalies.
- Syndactyly is an example of a skeletal abnormality.

Partial mole: The edema is heterogeneous

- Only a subset of chorionic villi are markedly enlarged.
- Other villi can be relatively less affected.
- Mixed villous populations are more useful than a single enlarged profile.

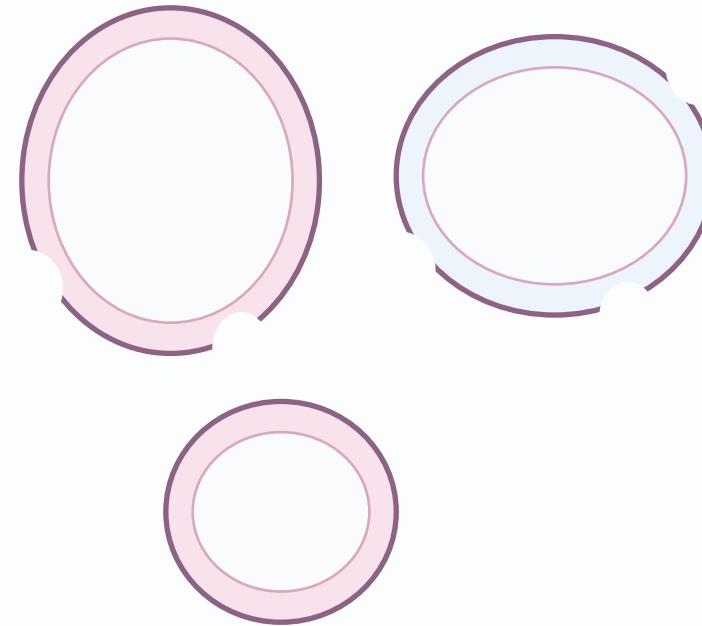


Villi of unequal size

Schematic

Partial mole: Irregular villous contours

- Affected villi often have irregular, scalloped outlines.
- This differs from the smoother, rounded villi in complete mole.
- Evaluate the contour across multiple villi at low power.

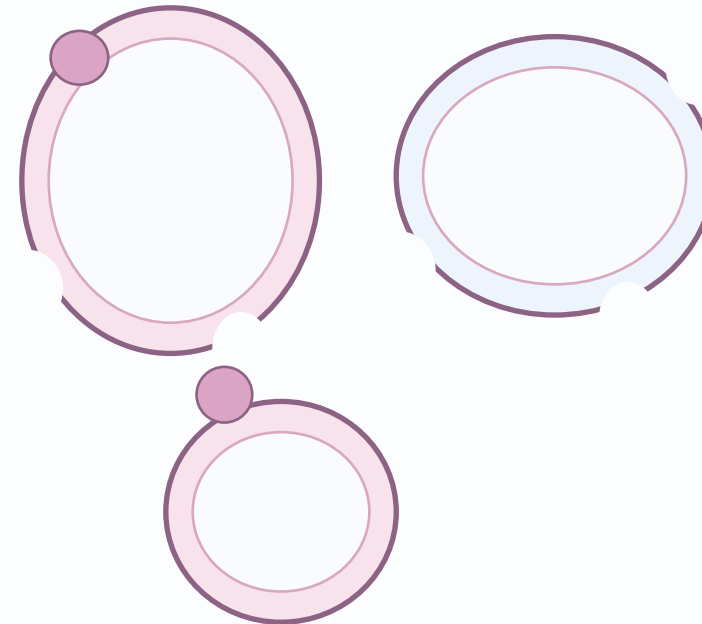


Irregular villous contours

Schematic

Partial mole: Focal trophoblast proliferation

- Trophoblastic hyperplasia is relatively mild and patchy.
- Syncytiotrophoblastic hyperplasia rather than marked biphasic growth.
- Patchiness should not be mistaken for the diffuse complete-mole pattern.

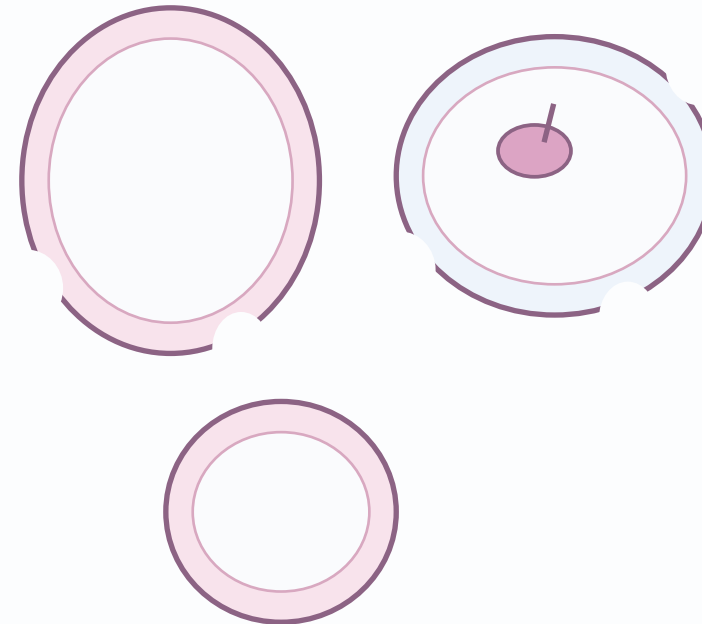


Focal trophoblast growth

Schematic

Partial mole: Trophoblastic inclusions

- Inward folds of trophoblast can be seen within irregular villi.
- These are described as prominent trophoblastic inclusions.
- Interpret inclusions in combination with scalloping, edema, and growth pattern.



Trophoblastic inclusion

Schematic

Partial mole: Morphology checklist

Component	Expected finding
Villi	Mixed sizes; only a subset hydropic
Outlines	Irregular, scalloped
Trophoblast	Focal, less pronounced proliferation
Inclusions	Often prominent within villi
Fetal development	May be present but severely abnormal
Genetics	Usually triploid

Complete vs partial: Genetic differential

Question	Complete mole	Partial mole
Maternal nuclear genome?	Absent	Retained
Paternal contribution	Only paternal chromosomes	Two paternal haploid sets typical
Chromosome complement	46,XX or 46,XY	Usually 69, e.g. XXY
Fetal development	None	Possible but anomalous

Complete vs partial: Architectural differential

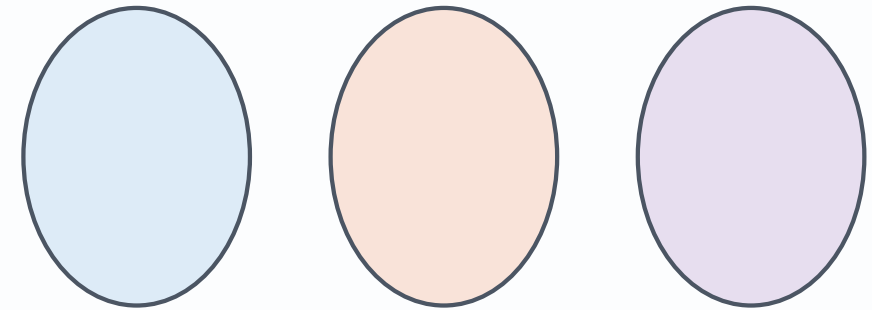
Feature	Complete mole	Partial mole
Extent	Diffuse villous changes	Heterogeneous villous changes
Villus shape	Rounded, oval	Irregular / scalloped
Edema	Marked; cisterns typical	Limited to subset
Hyperplasia	Circumferential; biphasic	Focal; less marked
Inclusions	Not defining feature	Often prominent

Complete vs partial: Clinical implications

Aspect	Complete mole	Partial mole
Typical hCG behavior	Can be markedly elevated	No quantitative pattern stated here
Pregnancy outcome	No embryo	May show malformed fetus
Postmolar persistence	15% reported for invasive / persistent mole	Risk increased; not quantified here
Choriocarcinoma	Reported subsequent risk	Not typically associated

Morphology should be read at three scales

- Low power: Determine whether edema affects most villi or only a subset.
- Intermediate power: Assess rounded versus irregular villous outlines and cisterns.
- Higher power: Assess cytotrophoblast/syncytiotrophoblast proliferation and inclusions.



Extent

Contour

Trophoblast

Schematic

Genetics resolves a distinct diagnostic question

- Histology asks how the villi and trophoblast are organized.
- Cytogenetic studies ask whether the conceptus is diploid, triploid, or rarely otherwise.
- Interpret chromosome complement together with parental nuclear contribution and morphology.

Complete: Paternal only

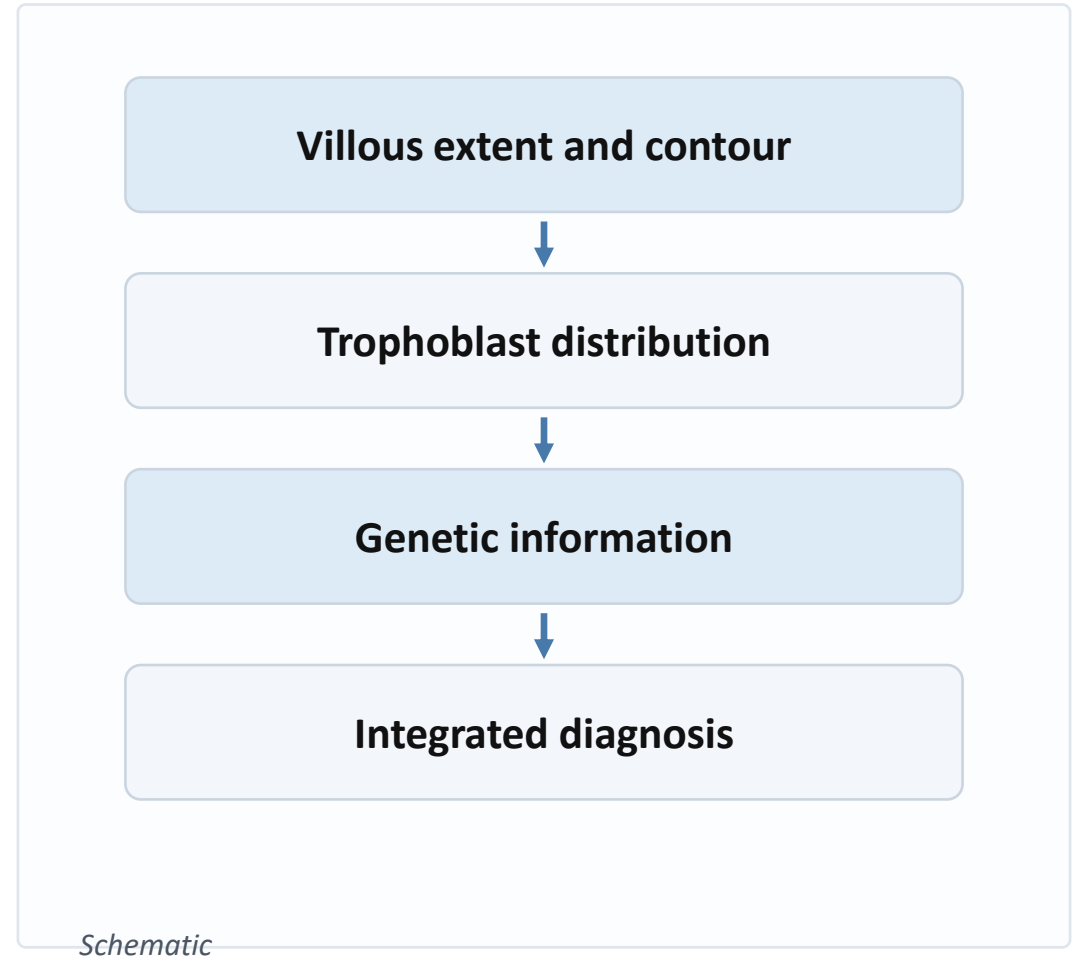
Partial: Maternal + paternal

Distinct parental origin

Schematic

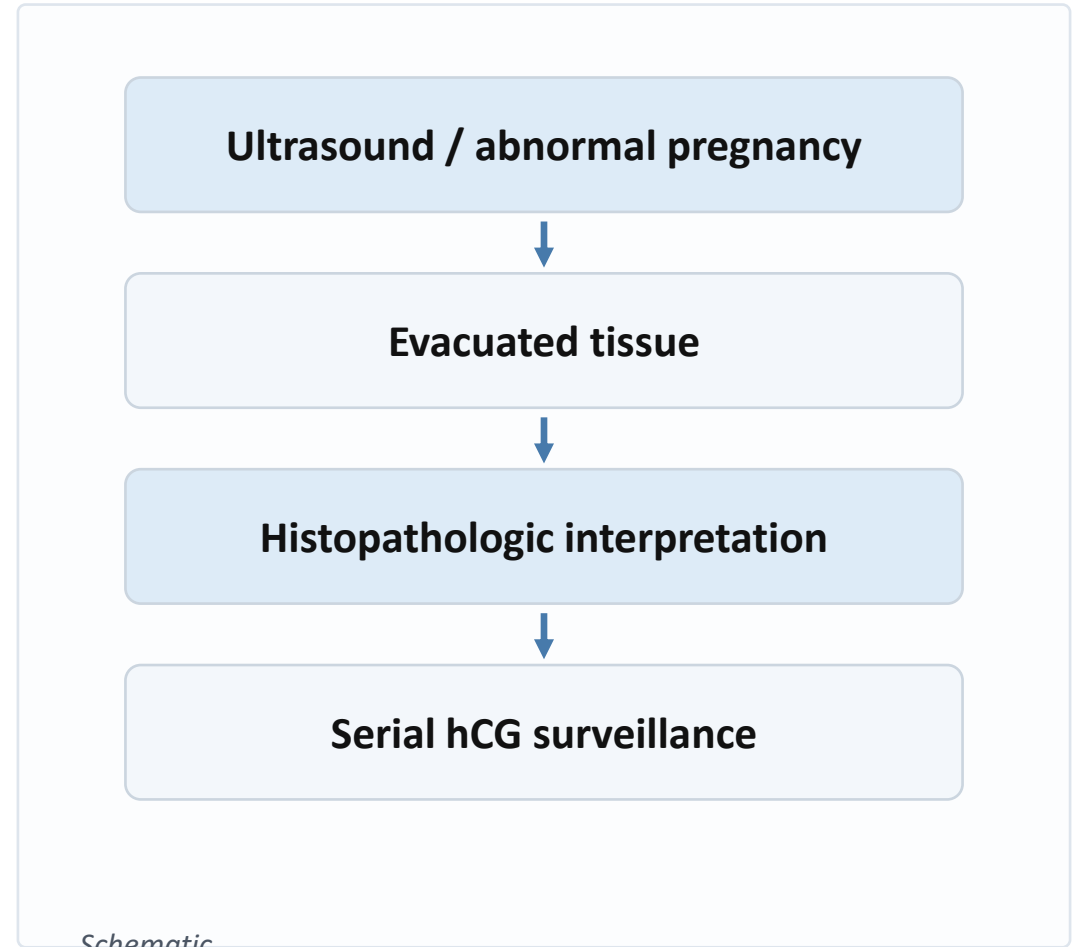
A practical interpretation sequence

- Establish whether chorionic villi are present.
- Characterize the extent and contour of villous hydropic change.
- Characterize distribution and cell types of trophoblast proliferation.
- Integrate with available clinical and cytogenetic information.



The clinical presentation may resemble miscarriage

- Early partial and early complete moles commonly present as pregnancy loss.
- Alternatively, ultrasound reveals abnormal villous enlargement prompting curettage.
- A classic macroscopic grape-like mass is not necessary for early diagnosis.



Sonography identifies abnormal early gestation

- Pelvic sonography can disclose abnormal villous enlargement.
- Imaging provides a clinical trigger for tissue evacuation and pathologic assessment.
- The source does not give sensitivity, specificity, or ultrasound thresholds.

HCG must be interpreted in temporal context

- Complete molar pregnancies can have strikingly high hCG for gestational age.
- Persistently elevated hCG after evacuation raises concern for continuing trophoblastic tissue.
- Serial measurements assess resolution, not merely the initial concentration.

High hCG relative to gestational age



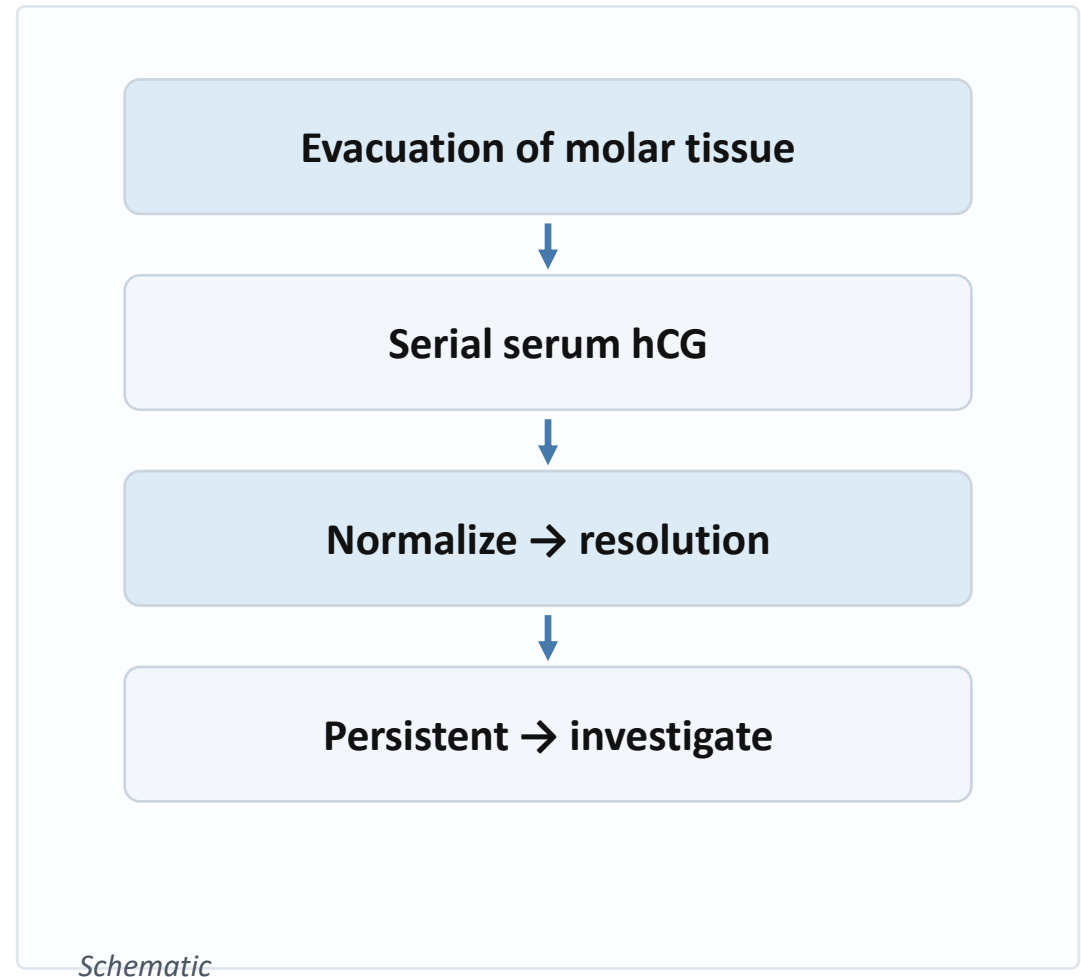
Serial assessment after evacuation

Persistent elevation → investigate

Schematic

The post-evacuation pathway

- Molar tissue is commonly removed by curettage.
- Serial hCG surveillance aims to document return to nonpregnant levels.
- Failure to decline appropriately prompts evaluation for persistent disease.



Follow-up duration in the source

- Monitoring for 6 months to 1 year after evacuation.
- This is a textbook description, not a universal contemporary clinical protocol.
- For individual patient management, applicable current regional protocols and risk assessment take priority.

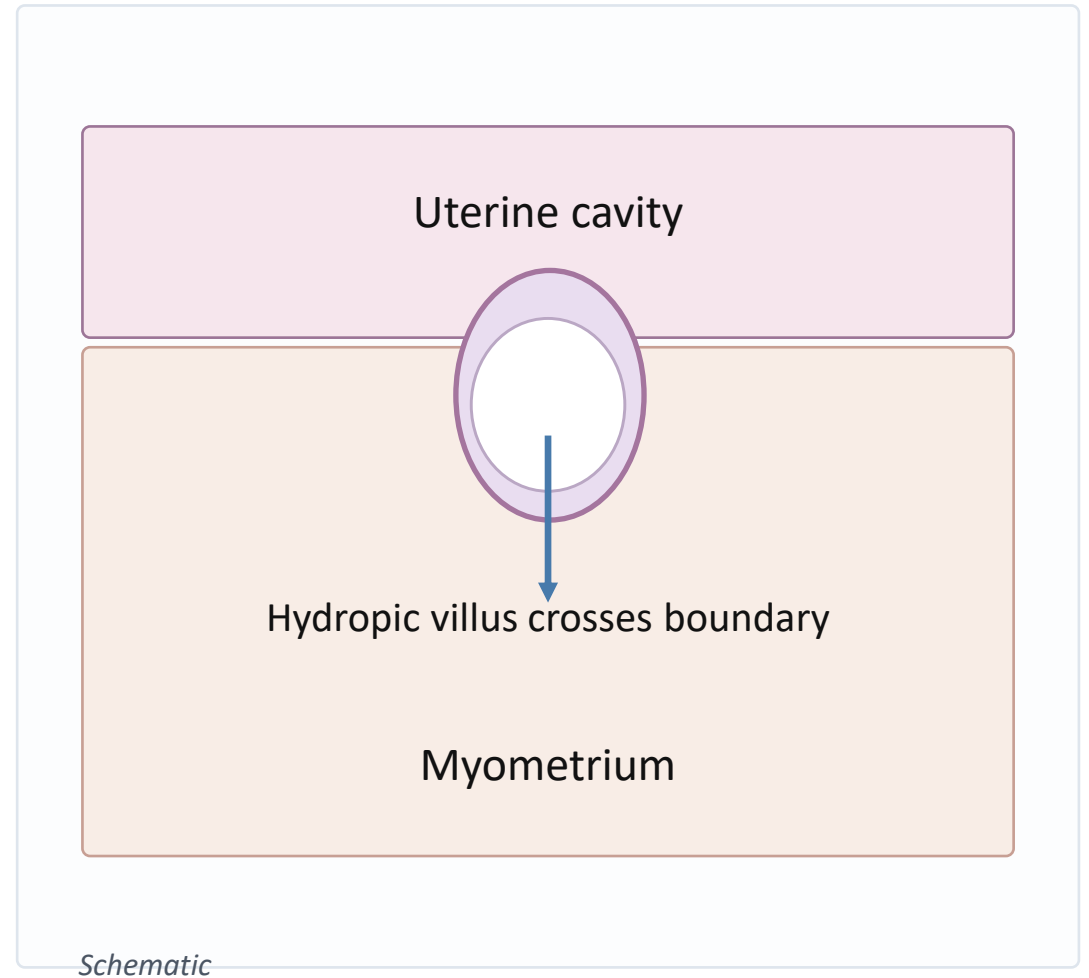
Persistently elevated hCG requires investigation

The key postmolar warning is biochemical persistence.

- Potential explanations in the source include persistent or invasive mole and choriocarcinoma.
- Further evaluation and, in some cases, chemotherapy may be required.

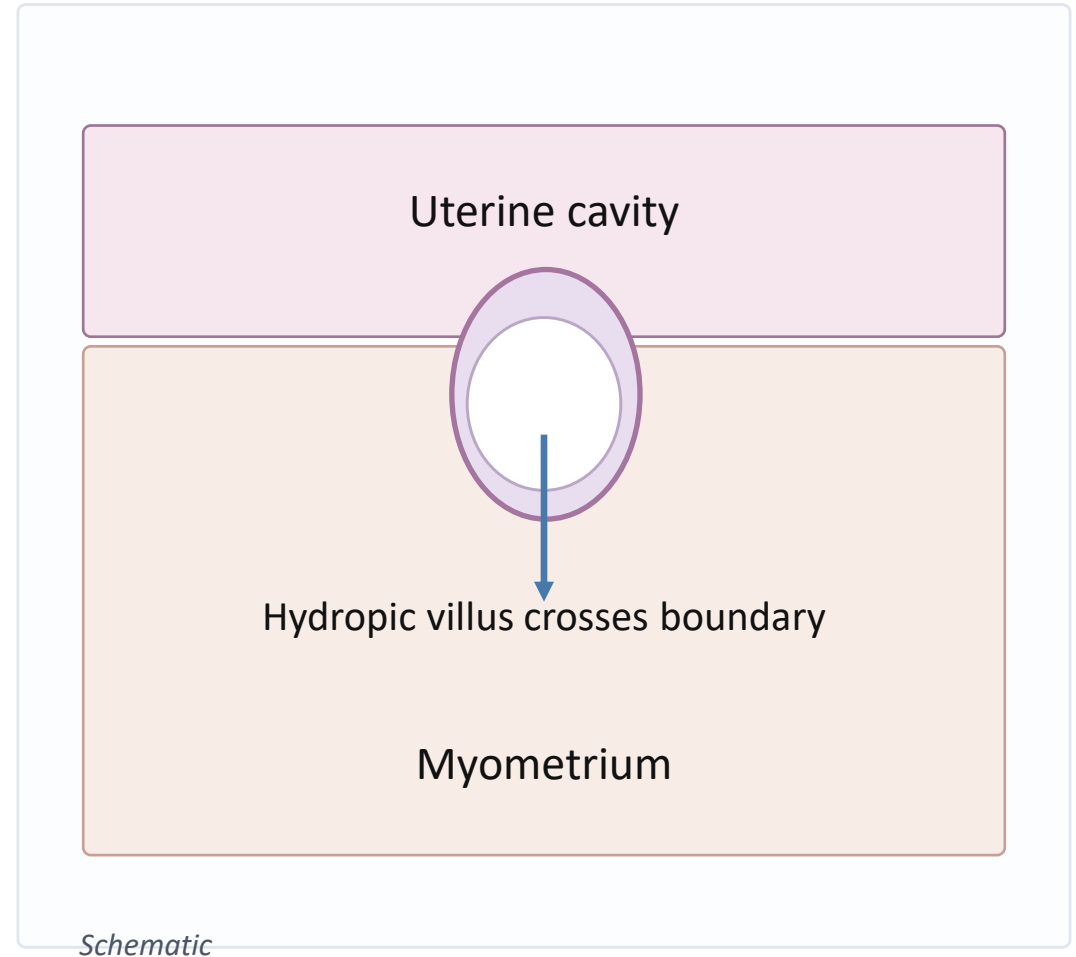
Invasive mole is defined by myometrial penetration

- Hydropic chorionic villi breach the normal uterine compartment.
- Villi and proliferating trophoblast extend into the myometrium.
- Deep extension can occasionally perforate the uterine wall.



Invasive mole: Three diagnostic anchors

- Infiltration of the uterine wall.
- Hydropic villi present within invasive tissue.
- Proliferating cytotrophoblast and syncytiotrophoblast line the invasive villi.

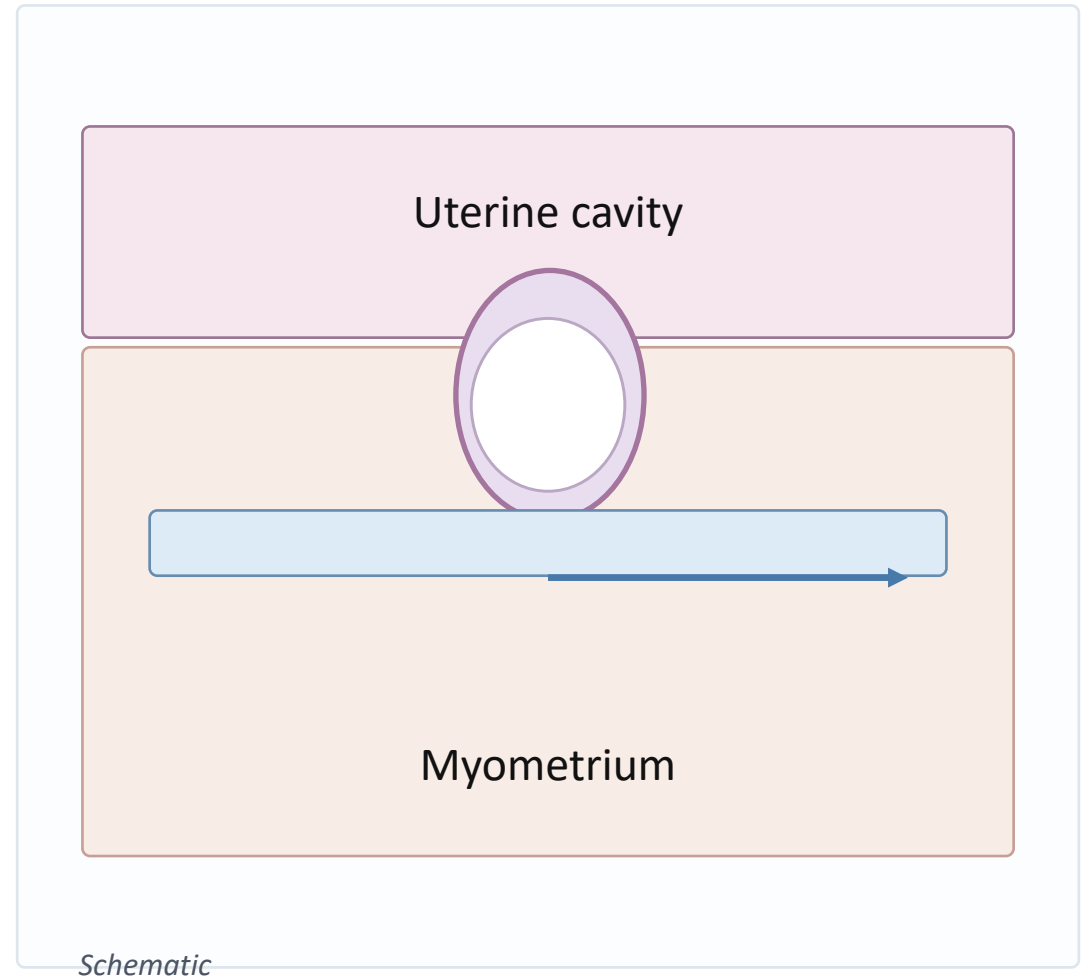


Bleeding is linked to destructive local extension

- The lesion penetrates myometrial tissue and can involve blood vessels.
- Abnormal vaginal bleeding and irregular uterine enlargement can follow.
- Serum hCG remains elevated because trophoblastic tissue persists.

Vascular entry can lead to distant villous emboli

- Invasive villi may reach parametrial tissue and maternal blood vessels.
- Embolization to distant organs is described in the source.
- The lungs and brain are named potential sites.



Pulmonary involvement: Interpret the textbook cautiously

- Lung lesions in about 5% of complete hydatidiform moles.
- Its description of spontaneous regression of small pulmonary lesions is historical textbook context.
- Do not use lesion size alone to make current treatment decisions; Specialist staging and protocols are required.

Invasive mole vs choriocarcinoma

Discriminator	Invasive mole	Choriocarcinoma
Chorionic villi	Present; hydropic	Absent
Trophoblastic pattern	Villi lined by both types	Malignant trophoblastic sheets
Typical tissue effect	Myometrial invasion; villous emboli	Destructive, hemorrhagic invasion
Clinical marker	Persistent hCG elevation	Usually high hCG; exceptions exist

Choriocarcinoma: Where it fits in the spectrum

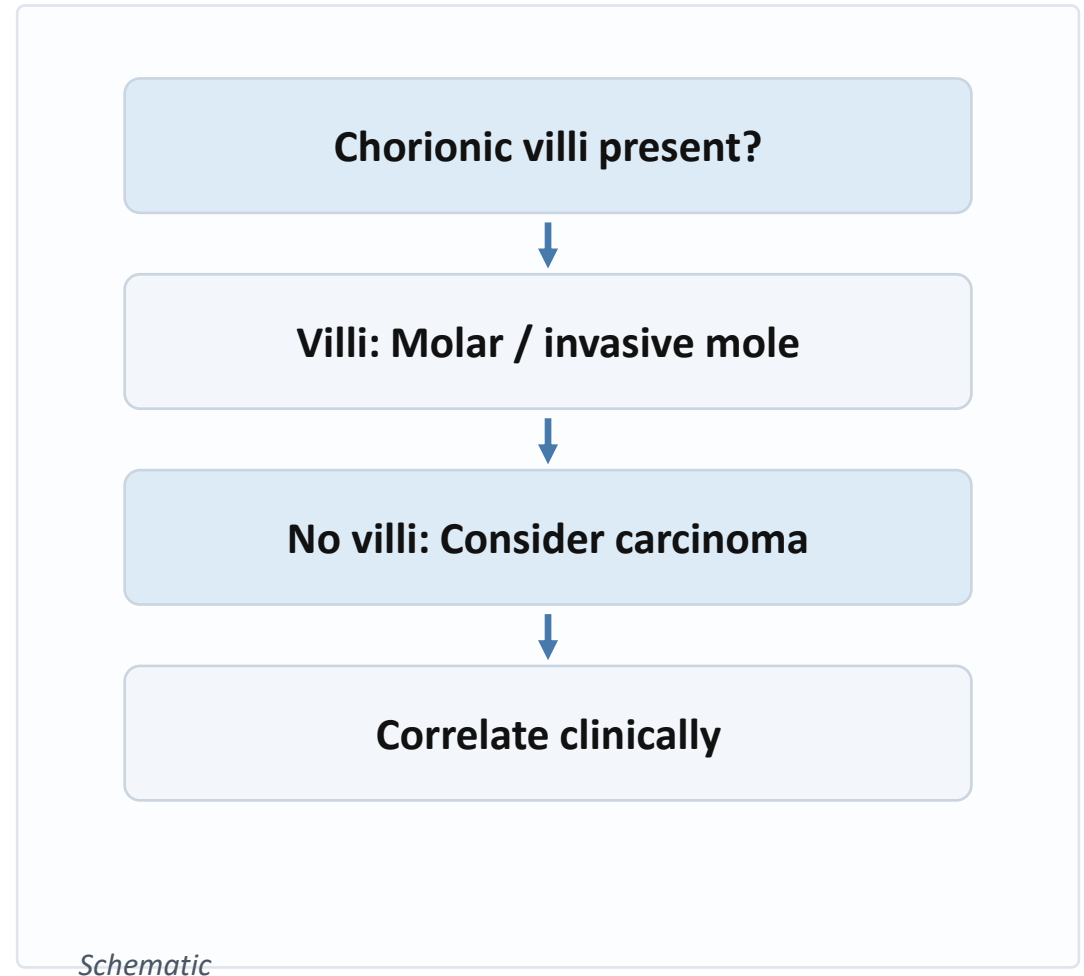
- A malignant trophoblastic tumor may follow an abnormal or normal pregnancy.
- The pathologic lesion consists of malignant trophoblast without villi.
- Hemorrhage, necrosis, vascular invasion and distant spread are characteristic.
- Its full pathology is addressed in the adjacent dedicated topic.

Other tumors: Important architectural distinctions

Tumor	Source-described distinguishing feature
Placental site trophoblastic tumor	Mononuclear or binucleated extravillous trophoblast; infiltrates between muscle fibers
Epithelioid trophoblastic tumor	Sheets of mononuclear trophoblast; often clear cytoplasm; hyaline material
Choriocarcinoma	Biphasic malignant trophoblast, no villous structures

A tissue-centered classification decision

- Identify chorionic villi first.
- If villi are present, characterize noninvasive versus invasive location.
- If villi are absent, evaluate malignant trophoblastic growth and differential diagnosis.



Case 1: Complete mole

Early pregnancy evacuation shows predominantly enlarged oval hydropic villi, central cisterns and circumferential biphasic trophoblast proliferation.

Which molar category best fits, and what nuclear genetic origin is expected?

Complete hydatidiform mole; Entirely paternal nuclear genome, generally diploid.

Case 2: Partial mole

Evacuated placental tissue contains villi of mixed sizes, scalloped enlarged profiles, trophoblastic inclusions and patchy syncytiotrophoblastic proliferation.

What diagnosis and common ploidy are suggested?

Partial hydatidiform mole; Commonly triploid after dispermy.

Case 3: Invasive mole

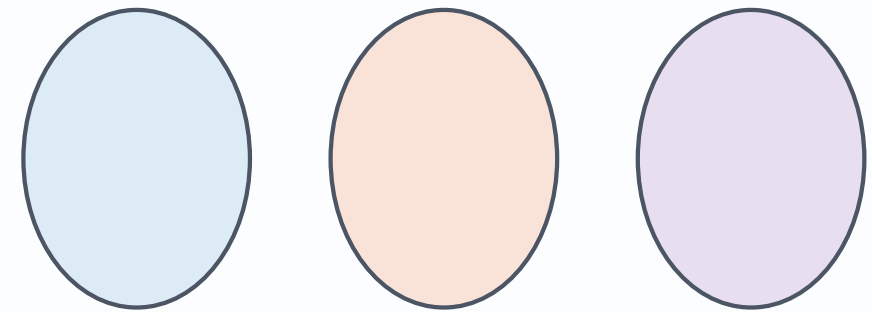
After molar evacuation, serum hCG remains elevated. An infiltrative uterine lesion shows hydropic villi extending into myometrium.

What single morphologic feature favors invasive mole over choriocarcinoma?

Presence of hydropic chorionic villi within the invasive lesion.

Diagnostic pitfalls: Focus on discriminators

- Hydropic enlargement by itself does not establish the genetic subtype.
- A partial mole can contain only a minority of conspicuously enlarged villi.
- Diffuse versus focal trophoblast proliferation should be assessed across tissue.
- Presence or absence of villi is essential in the invasive mole–choriocarcinoma differential.



Schematic

Clinical red flags after evacuation

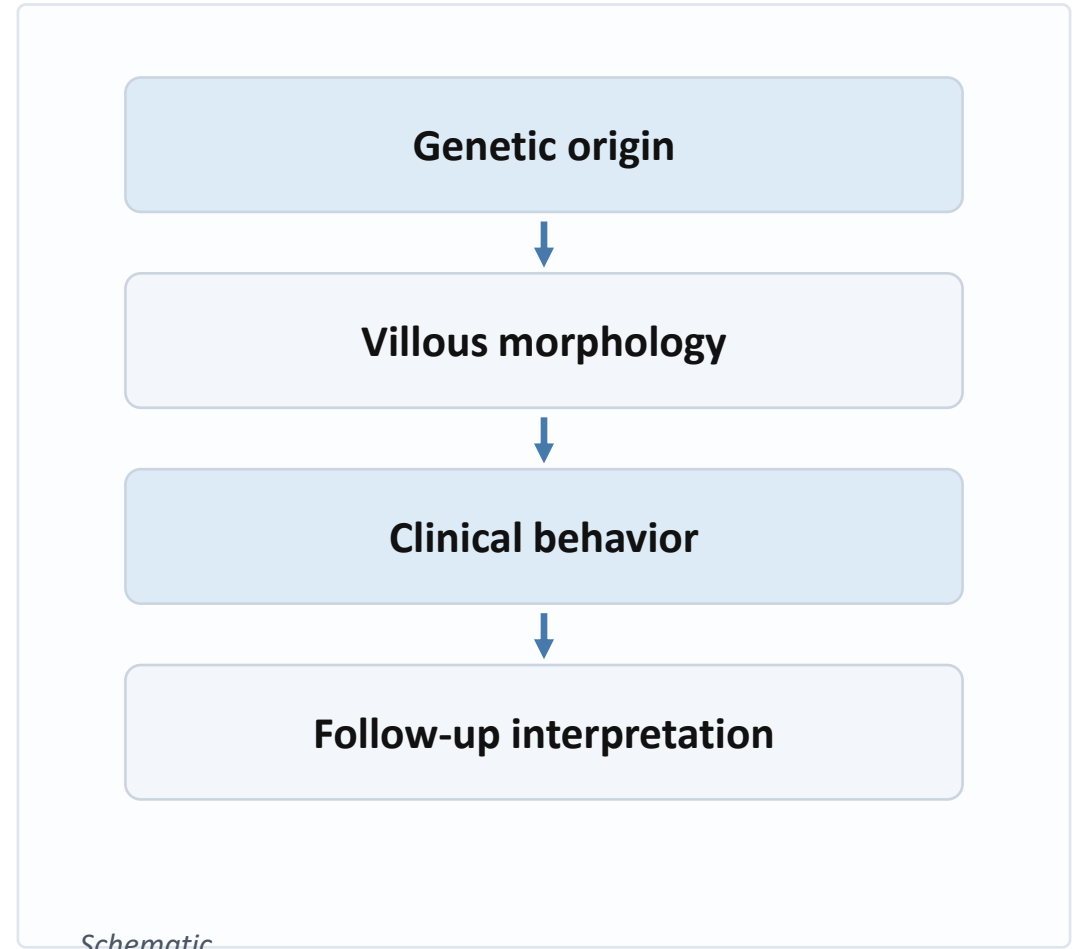
- Persistent elevation of hCG rather than decline to a nonpregnant level.
- New or sustained vaginal bleeding and uterine enlargement.
- Findings suspicious for extrauterine trophoblastic disease.
- These warrant specialist investigation rather than interpretation from one marker alone.

Integrating genotype, morphology and behavior

Entity	Genetic clue	Morphology	Behavior
Complete mole	Paternal diploid	Diffuse hydropic villi; circumferential hyperplasia	Risk of persistence
Partial mole	Usually triploid	Scalloped mixed villi; focal growth	Persistent disease possible
Invasive mole	Follows molar disease	Hydropic villi in myometrium	Locally invasive / embolic
Choriocarcinoma	Gestational origin possible	Malignant trophoblast; no villi	Invasive and metastatic

Four conclusions to retain

- Complete mole: Paternal-only diploidy, diffuse hydropic villi, circumferential biphasic trophoblast.
- Partial mole: Usual triploidy, variable scalloped villi, focal syncytiotrophoblastic proliferation.
- Invasive mole: Hydropic villi penetrate the uterine wall.
- Persistent postmolar hCG is a signal for evaluation of ongoing trophoblastic disease.



References and limits of this lecture

- Primary text: Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed., chapter 22, pp. 939–941.
- Classification and numeric estimates are taken from the supplied 2026 textbook extraction.
- Source histology figures were not available as reusable image assets; all tissue architecture drawings are original schematics.
- The textbook surveillance interval and management descriptions are not substitutes for current local GTD protocols.