

Atrophy and Decreased Fertility

Regressive changes of the testis

Testicular pathology • mechanism, morphology and clinicopathologic correlation

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What this lecture explains

- Recognize the main etiologies of testicular atrophy listed by Robbins.
- Trace the microscopic progression from tubular injury to loss of spermatogenesis.
- Distinguish germ-cell depletion from preservation of interstitial Leydig cells.
- Interpret selected clinicopathologic patterns without overcalling a specific cause.

The source places atrophy among regressive changes

This topic	Related context
• Regression of seminiferous structures • Decreased sperm-producing capacity • Possible extreme loss of testicular tissue	• Cryptorchidism provides its morphology model • Genetic hypogonadism provides another pattern • Endocrine and systemic disease may converge

Two anatomical compartments have different functions

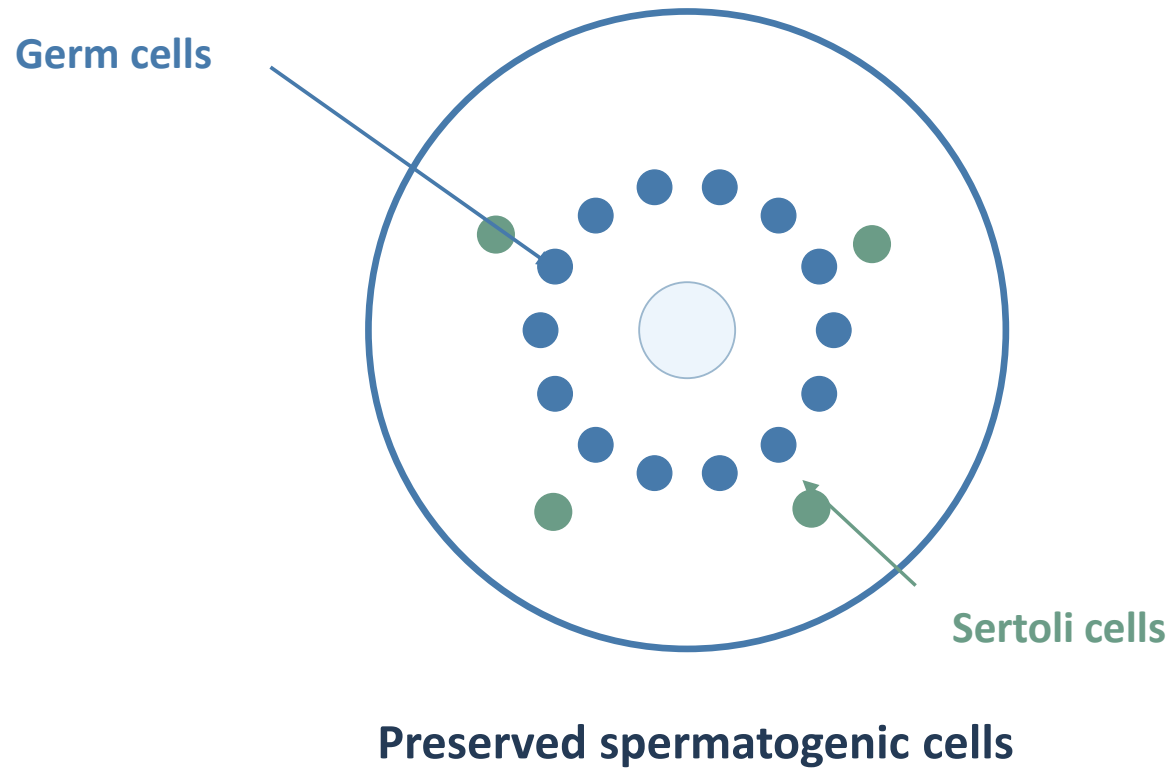
**Seminiferous
tubules**

Interstitial tissue

- Tubules contain germ cells and Sertoli cells: The spermatogenic compartment.
- Interstitial Leydig cells support the endocrine function of the testis.
- The two compartments may be affected to different degrees.

Spermatogenesis depends on an intact tubular compartment

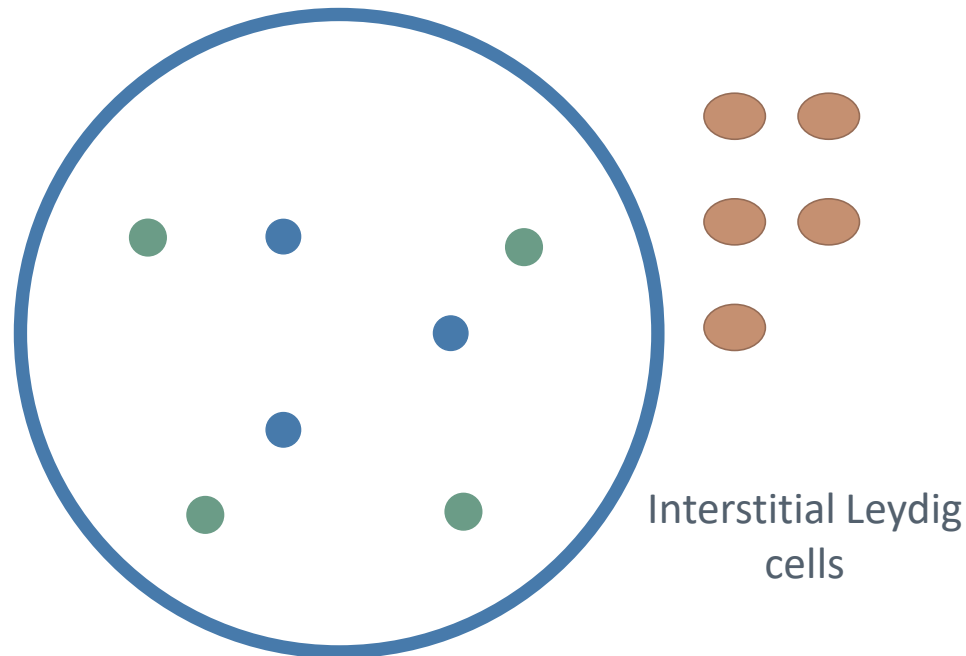
Simplified seminiferous-tubule schematic



- Active spermatogenesis requires viable germ cells within tubules.
- Sertoli cells are distinct from the germ-cell population.
- A tubule containing Sertoli cells alone cannot show normal spermatogenesis.

Leydig cells may remain visible despite tubular failure

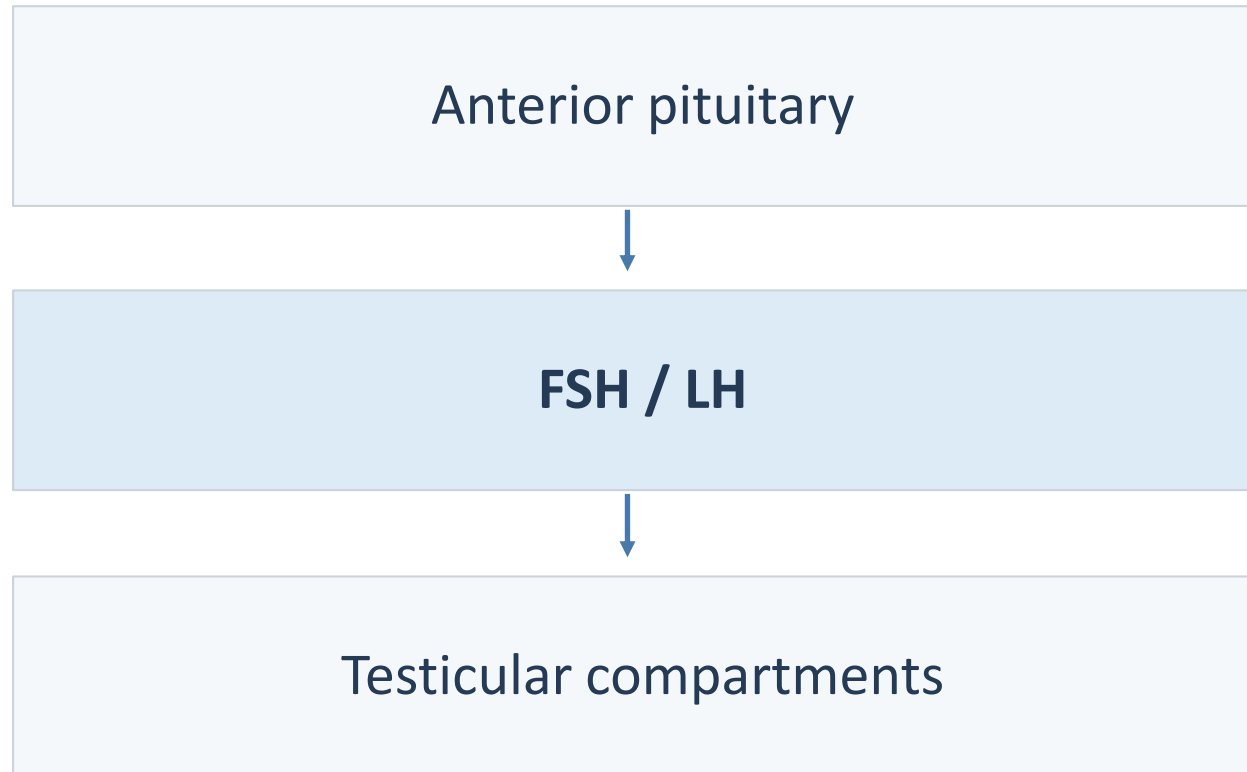
Simplified seminiferous-tubule schematic



Regressed tubule with interstitial Leydig cells

- Leydig cells lie outside the seminiferous tubules.
- With tubular regression they may appear relatively prominent.
- Apparent prominence is not synonymous with increased testosterone secretion.

Pituitary gonadotrophs link the axis to testicular function



- Anterior-pituitary gonadotrophs secrete FSH and LH.
- These hormones regulate spermatogenesis and testosterone production in males.
- Pituitary disease can therefore affect testicular function upstream of the gonad.

Atrophy is a structural endpoint—not one diagnosis

Morphologic observation	Etiologic interpretation
• Reduction of functional tubular elements • Small, firm testis in the cryptorchid model • Late scarring and tubular hyalinization	• Vascular, inflammatory, developmental, endocrine • Nutritional, iatrogenic, hepatic, genetic • Cause needs clinical and anatomic context

Ten conditions are explicitly listed by Robbins

1. Age-related vascular narrowing

2. End-stage inflammatory orchitis

3. Cryptorchidism

4. Hypopituitarism

5. Malnutrition / cachexia

6. Irradiation

7. Prolonged antiandrogens

8. Cirrhosis

9. Genetic primary failure

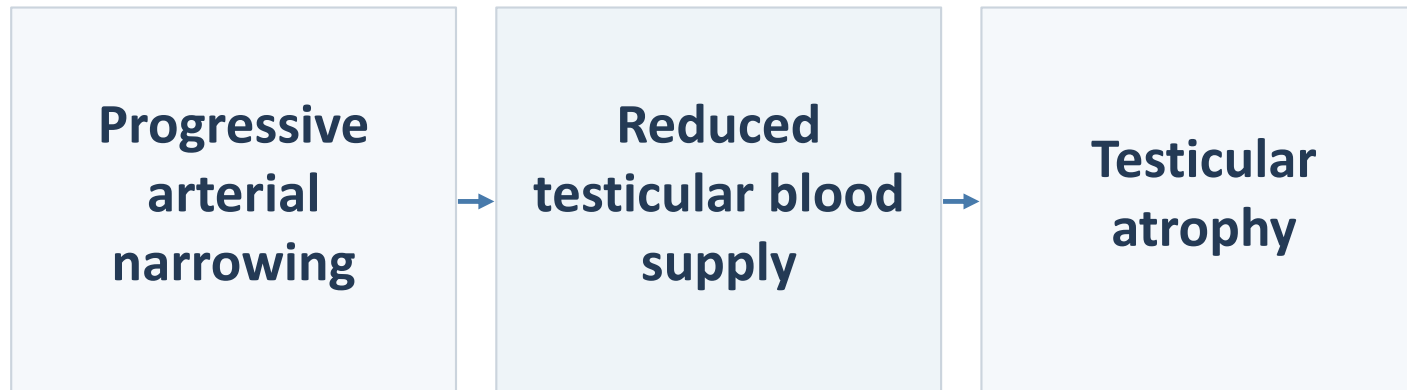
10. Sustained high FSH

A useful etiologic grouping is mechanism-based

Grouping is an educational synthesis; The causes individually.

Dominant context	Examples
Vascular / inflammatory	Age-related atherosclerotic narrowing; End-stage orchitis
Developmental / genetic	Cryptorchidism; Klinefelter syndrome
Endocrine / systemic	Hypopituitarism; Malnutrition or cachexia; Cirrhosis
Treatment-related / hormonal	Irradiation; Prolonged antiandrogens; Sustained high FSH

Atherosclerotic narrowing is an age-associated cause



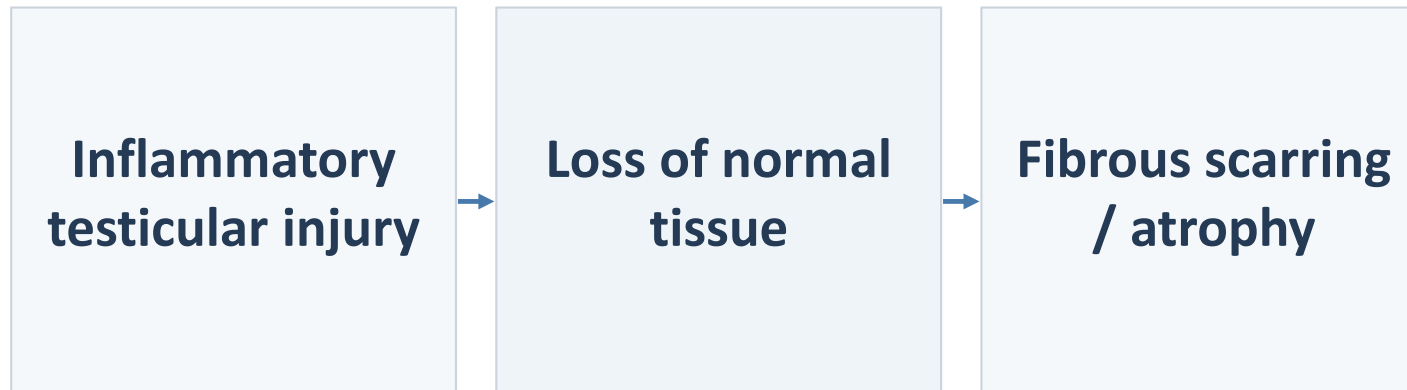
Interpretive causal schematic

- Progressive atherosclerotic narrowing in old age.
- A vascular history strengthens this etiologic possibility.
- A small testis by itself does not prove vascular causation.

Vascular insufficiency differs from acute infarction

Atrophy in this section	Different process
• Progressive reduction of supply • Chronic regressive endpoint • Included among causes of testicular atrophy	• Acute torsion may produce infarction • An acute vascular event is not the same process • Do not equate all vascular damage with chronic atrophy

End-stage orchitis can produce testicular atrophy



Interpretive causal schematic

- Inflammatory orchitis is an explicitly listed etiologic pathway.
- End-stage damage should be separated from active inflammation.
- Severity of scarring matters for residual sperm production.

Inflammatory scarring may impair fertility

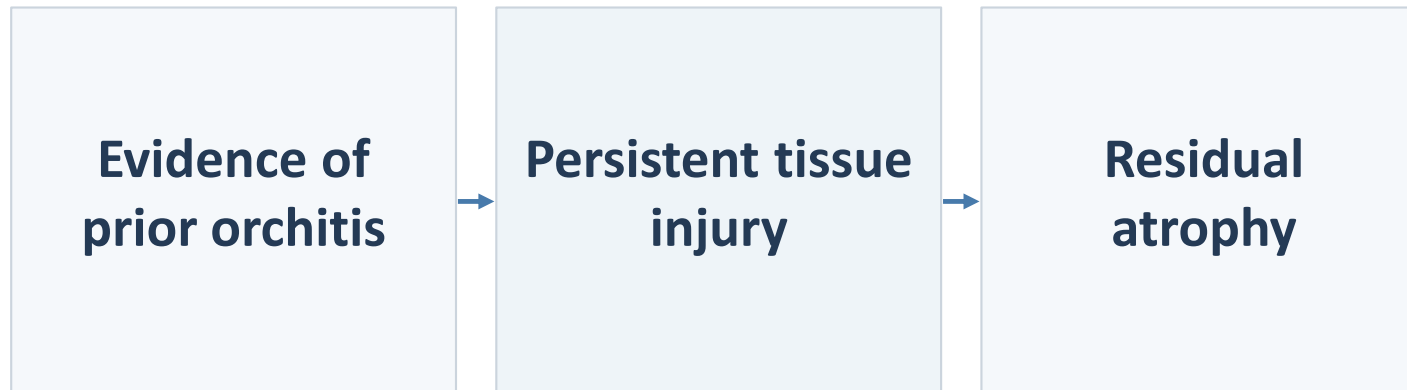
Epididymis

- Infection may begin in the epididymis
- Destruction and subsequent fibrosis can follow
- Scarring can interfere with reproductive function

Testis

- Infection may spread into testicular tissue
- Tubules may be injured during orchitis
- Late fibrosis is a cause of regressive change

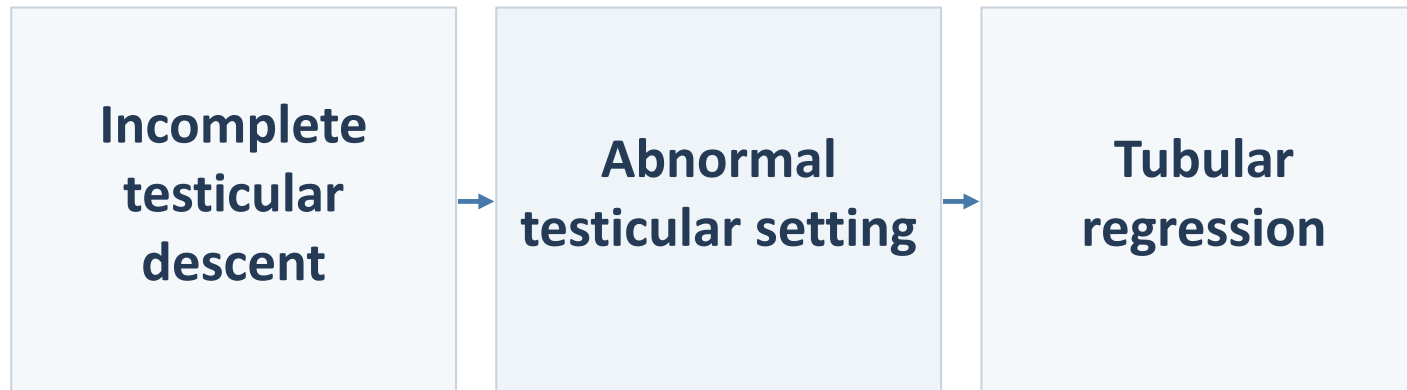
The clinical question is active or postinflammatory disease



Interpretive causal schematic

- Current inflammation and healed atrophy are different morphologic phases.
- Past orchitis can explain atrophy but is not identifiable from size alone.
- Aetiologic assessment requires chronology and distribution.

Cryptorchidism is a developmental cause of atrophy



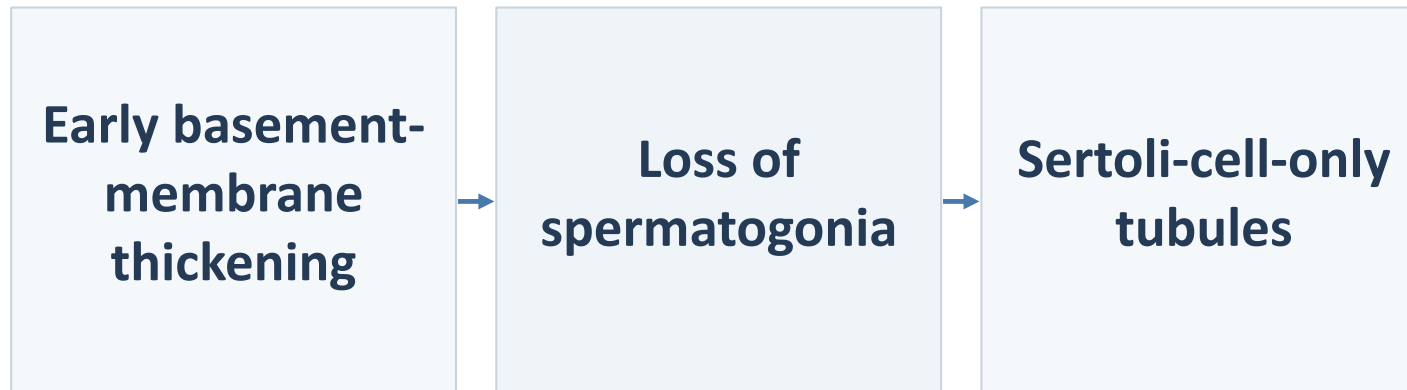
Interpretive causal schematic

- Cryptorchidism is explicitly included among causes of atrophy.
- Its characteristic morphology is the comparator for other atrophic testes.
- Even a contralateral descended testis may show related alterations.

Undescended testes are typically small and firm

Clinical anatomy	Gross pathology
• One or both testes fail to descend • The inguinal canal is a common arrest site • An empty hemiscrotum may be noticed	• Affected testis often small • Increased firmness in regressive disease • Histology determines tubular integrity

Tubular injury in cryptorchidism begins early

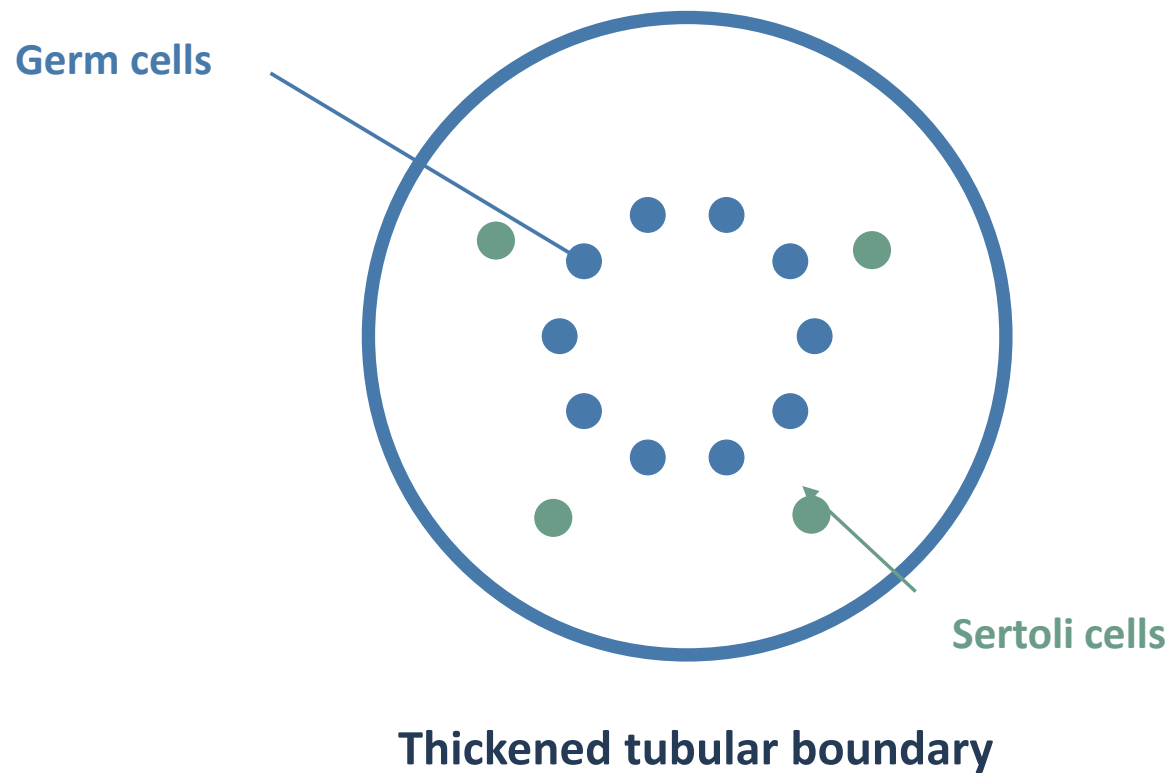


Interpretive causal schematic

- The source describes histologic changes beginning as early as two years.
- Loss of germ cells follows initial architectural change.
- The end result is loss of active spermatogenesis.

Basement-membrane thickening marks early regression

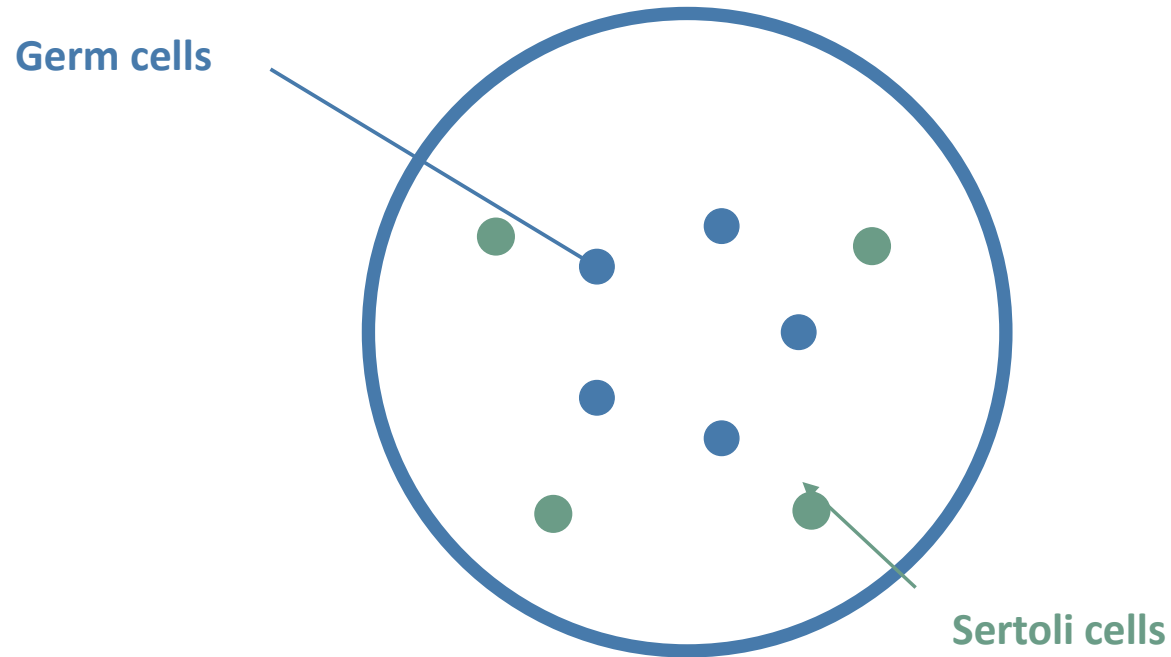
Simplified seminiferous-tubule schematic



- Compare the outer tubular boundary with a normal tubule.
- Basement-membrane thickening is described as an early finding.
- This precedes the most advanced hyaline scarring.

Germ-cell depletion is the pivotal fertility lesion

Simplified seminiferous-tubule schematic

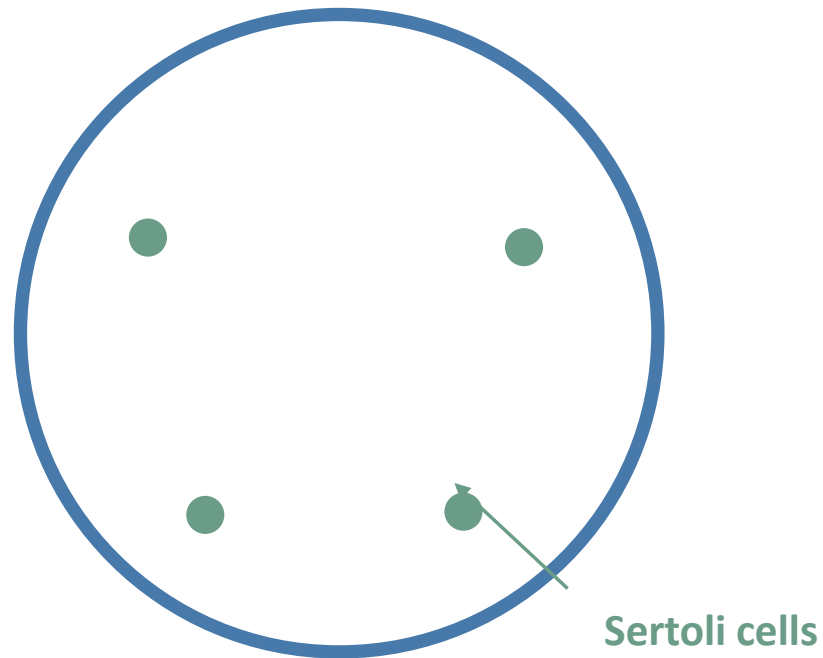


Decreased germ-cell population

- Progressive loss of spermatogonia depletes the germ-cell compartment.
- Tubules may retain Sertoli cells after the germ cells disappear.
- Reduced sperm production follows from loss of the cells that generate sperm.

Sertoli-cell-only tubules lack spermatogenesis

Simplified seminiferous-tubule schematic

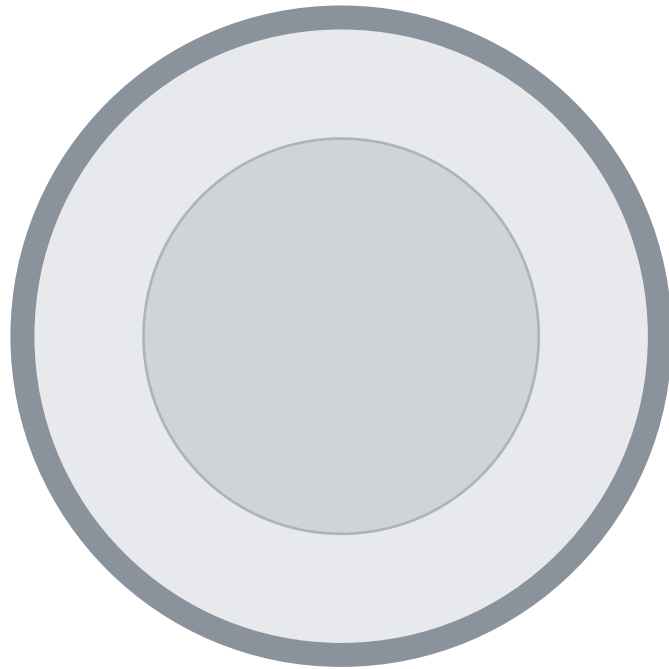


Sertoli cells without germ cells

- Remaining Sertoli cells do not imply preserved sperm production.
- A tubule may have an intact outline but no germ-cell maturation.
- Identify the cellular compartment rather than judging only tubule diameter.

Late atrophy may replace tubules with hyaline cords

Simplified seminiferous-tubule schematic



Hyaline collagenous tubular scar

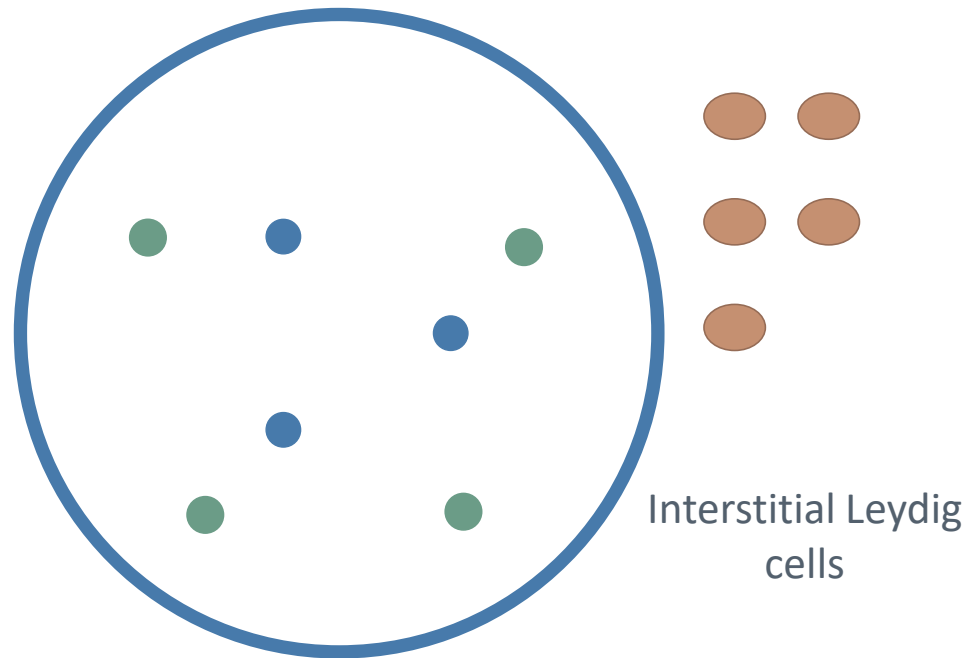
- Severely scarred tubules become dense hyaline connective-tissue cords.
- The normal seminiferous epithelial organization is lost.
- The appearance represents an advanced regressive endpoint.

Interstitial stroma becomes more conspicuous

Tubular change	Interstitial change
• Loss of tubular epithelial elements • Progressive thickening and hyalinization • Reduced relative functional tubule area	• Concomitant stromal increase • Leydig cells remain easier to recognize • Relative prominence need not mean proliferation

Leydig cells are relatively spared in cryptorchid atrophy

Simplified seminiferous-tubule schematic



Regressed tubule with interstitial Leydig cells

- The adjacent Robbins morphology description says Leydig cells are spared.
- The tubules lose germ cells while interstitial endocrine cells persist.
- This explains why fertility and androgen status may diverge.

Unilateral cryptorchidism does not ensure a normal partner

Undescended testis	Contralateral descended testis
• Typically shows the characteristic tubular changes • Degree of atrophy varies with the lesion • Risk of diminished spermatogenesis	• Can share histologic changes • Suggests underlying gonadal-development abnormality • Anatomical descent alone is not the entire story

Cryptorchidism links infertility and cancer risk

Fertility concern	Separate oncologic concern
• Tubular atrophy and impaired spermatogenesis • Can occur in unilateral or bilateral disease • May persist after repositioning	• Increased risk of germ-cell neoplasia • Orchiopexy does not abolish this risk • Do not conflate risk of neoplasia with atrophy

Hypopituitarism reduces upstream gonadal drive

Anterior pituitary



FSH / LH



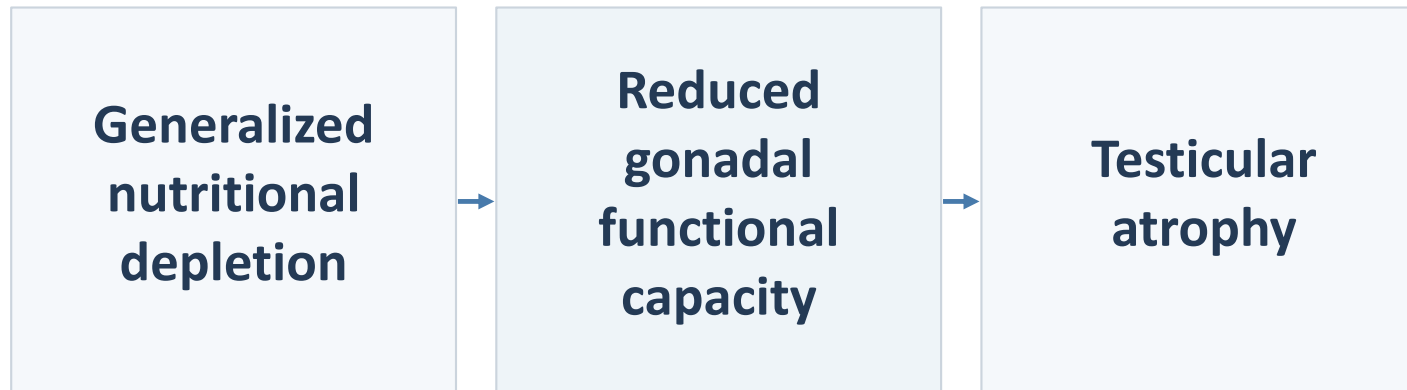
Testicular compartments

- Hypopituitarism is included' cause list.
- Pituitary gonadotrophs supply FSH and LH.
- Testicular under-stimulation differs conceptually from primary gonadal failure.

Central versus primary failure is a key distinction

Upstream failure	Primary gonadal failure
• Example: Hypopituitarism • Abnormality originates in hormonal drive • Testis is affected secondarily	• Example: Klinefelter syndrome • Primary disease affects the testis • Gonadotropins may be elevated

Malnutrition and cachexia are systemic causes



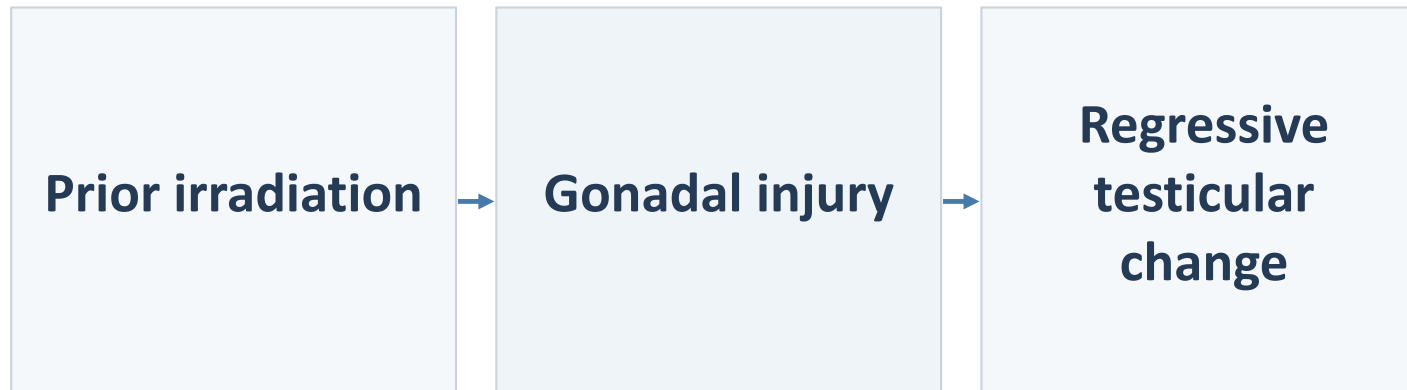
Interpretive causal schematic

- Generalized malnutrition and cachexia.
- Neither is restricted to a primary testicular disorder.
- Interpret gonadal findings in the context of systemic disease.

The nutritional context may coexist with other causes

Systemic state	Pathologic interpretation
• Generalized malnutrition • Cachexia due to major disease • Nonspecific physiologic burden	• Regression may be multifactorial • Other listed causes can coexist • Morphology may not specify the dominant factor

Irradiation is a treatment-associated cause



Interpretive causal schematic

- Irradiation appears explicitly etiologic list.
- Document exposure before assigning a treatment-associated explanation.
- The short source paragraph does not specify a dose-response threshold.

Antiandrogen exposure can cause testicular regression



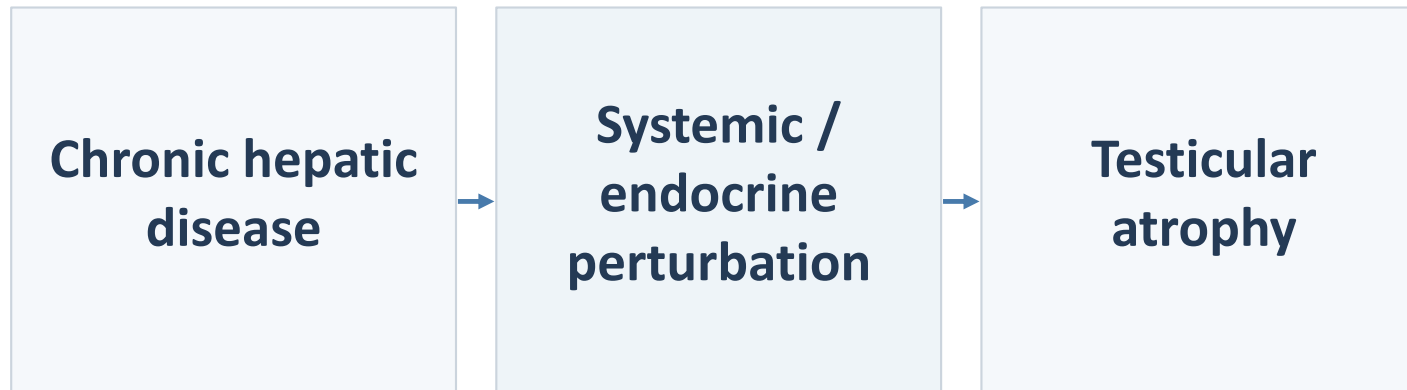
Interpretive causal schematic

- Robbins specifies prolonged administration rather than brief exposure.
- Treatment of prostate carcinoma is the example provided.
- Treatment history is essential when explaining the lesion.

Therapeutic and pathological mechanisms must be separated

Intended treatment context	Atrophic endpoint
• Antiandrogens may be used for prostate carcinoma • Gonadal consequences can accompany prolonged treatment • The drug exposure precedes the pathologic interpretation	• Seminiferous tissue may regress • Small size is not a specific drug signature • Do not infer medication solely from testicular morphology

Cirrhosis belongs in the systemic differential



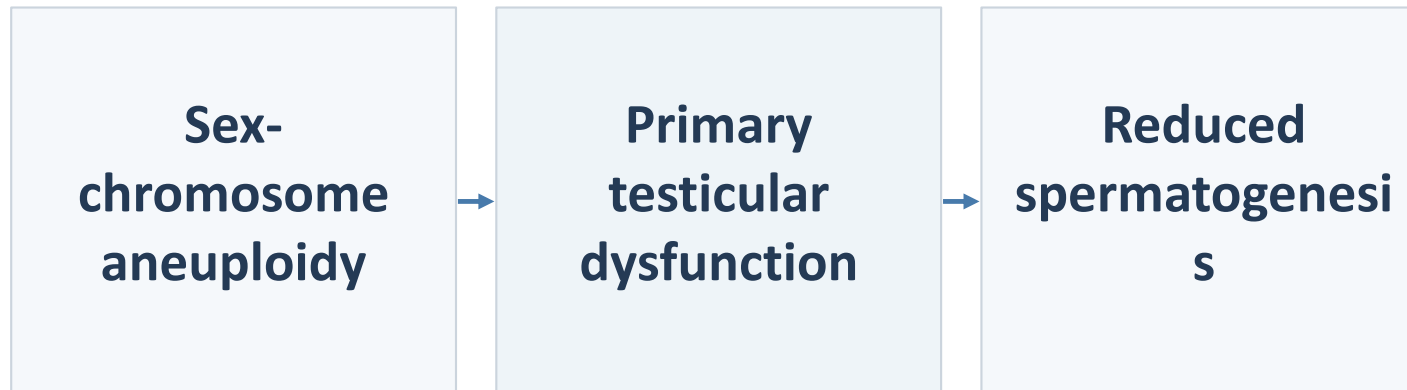
Interpretive causal schematic

- Cirrhosis is explicitly listed as a cause.
- The source also shows testicular atrophy among clinical sequelae of cirrhosis.
- Coexisting nutritional or hormonal abnormalities may complicate interpretation.

Cirrhosis-related atrophy requires systemic correlation

Testicular finding	Contextual clues
• Small, regressed testis may be seen • Atrophy is not histologically unique to cirrhosis • Fertility may be affected	• Established chronic liver disease • Concurrent malnutrition may be relevant • Avoid a single-cause claim without supporting history

Klinefelter syndrome is a primary genetic cause



Interpretive causal schematic

- Klinefelter syndrome among causes of atrophy.
- Classic Klinefelter syndrome usually has a 47,XXY karyotype.
- Its hallmarks include small testes, hypogonadism and infertility.

47,XXY connects chromosomal dosage with gonadal disease

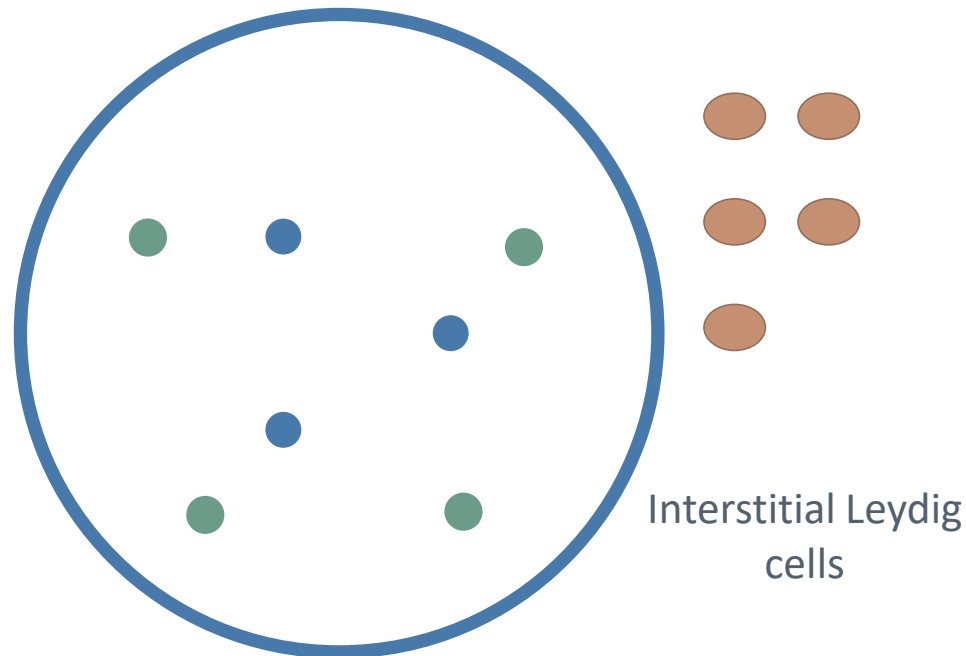
Genetic context	Clinical context
• Two or more X chromosomes with a Y chromosome • Classic form: 47,XXY • Sex-chromosome nondisjunction	• Testicular atrophy and hypogonadism • Reduced spermatogenesis • Variable external manifestations

Klinefelter tubules may show multiple atrophic patterns

Tubular pattern	Pathologic meaning
Completely hyalinized tubules	Collagenous tubular ghosts
Normal and atrophic tubules intermixed	Heterogeneous regressive injury
Primitive non-lumen-forming cords	Failure of full tubular maturation

Leydig prominence in Klinefelter is not paradoxical

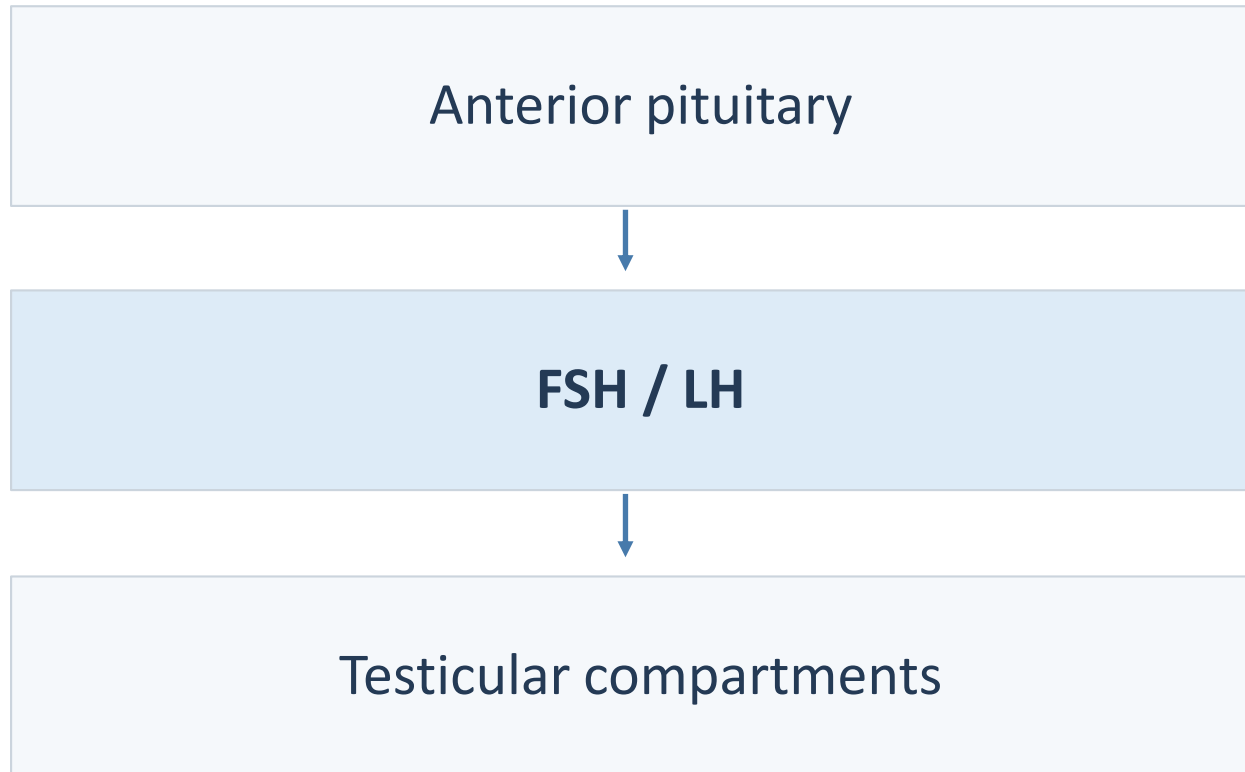
Simplified seminiferous-tubule schematic



Regressed tubule with interstitial Leydig cells

- Severe germ-cell compartment atrophy makes interstitial cells stand out.
- Gonadotropin elevation can contribute to apparent Leydig-cell prominence.
- This pattern may coexist with variably reduced testosterone.

FSH elevation can accompany primary testicular failure

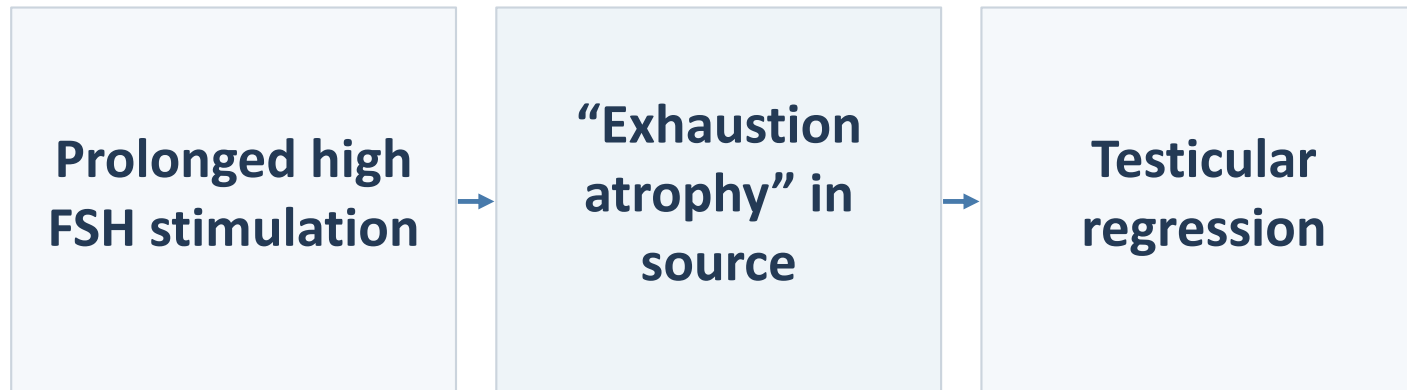


- In Klinefelter syndrome, gonadotropins—especially FSH—are elevated.
- Testosterone is variably reduced, not uniformly absent.
- An endocrine profile can refine interpretation of an atrophic testis.

Klinefelter phenotype is variable despite a common lesion

Relatively characteristic	Variable associated findings
• Small atrophic testes • Reduced spermatogenesis • Clinical hypogonadism	• Degree of masculinization • Gynecomastia may occur • Clinical features may become evident after puberty

Persistent high FSH is listed with exhaustion atrophy



Interpretive causal schematic

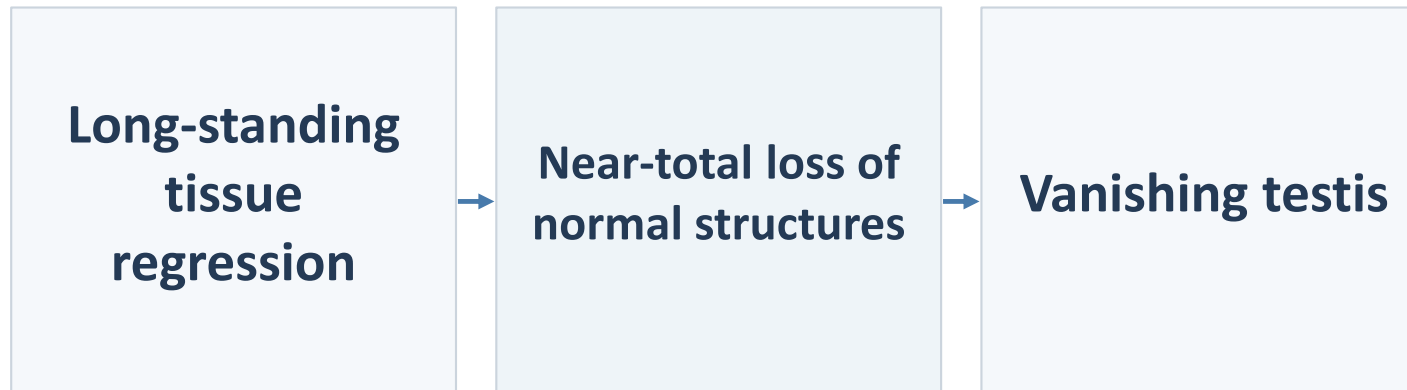
- This as a possible mechanism of testicular atrophy.
- The formulation is cautious: Atrophy “may follow” sustained high FSH.
- Do not turn this description into a universal mechanistic law.

The same atrophic pattern may have different causes

Etiologies often converge on loss of seminiferous function.

Clinical setting	Illustrative etiologic category
Undescended testis	Developmental malposition
Hypopituitarism	Reduced pituitary drive
Klinefelter syndrome	Primary genetic failure
Prostate carcinoma on antiandrogens	Treatment associated
Cachexia with chronic illness	Systemic nutritional

Extreme regression may produce a “vanishing testis”



Interpretive causal schematic

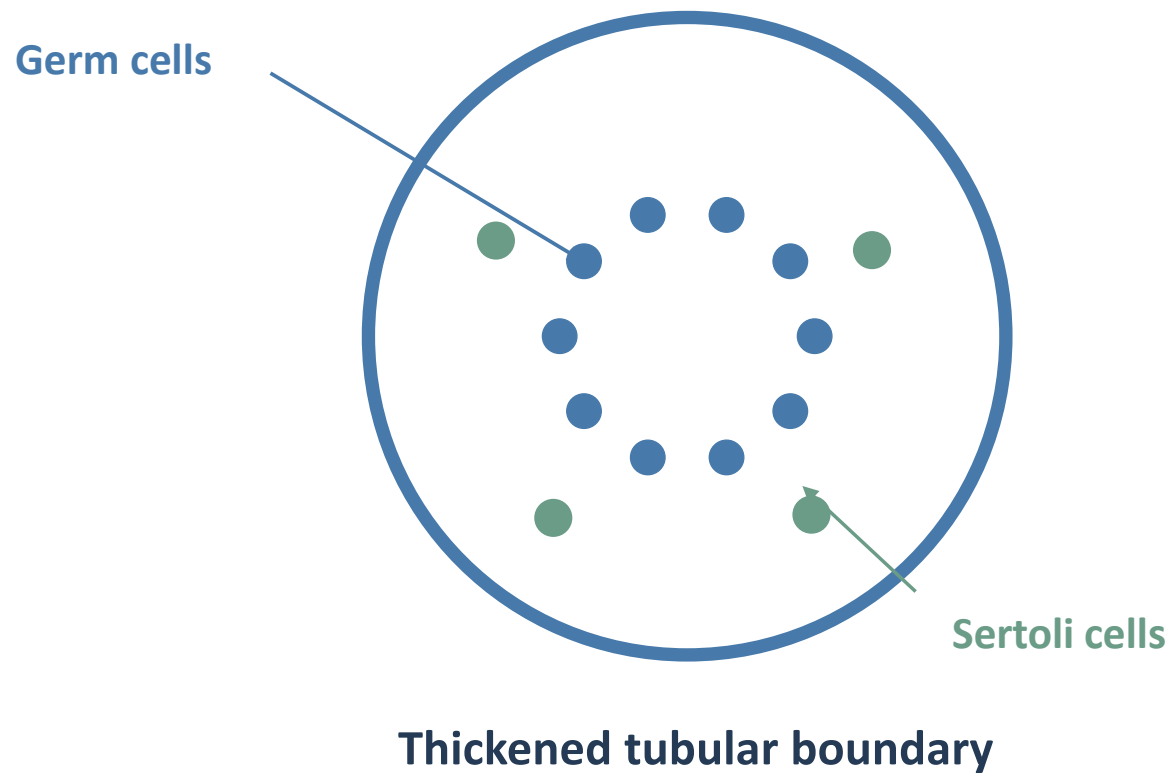
- The term denotes the extreme of the atrophic spectrum in this section.
- Not every small testis has undergone complete regression.
- The section does not assign one exclusive cause to this endpoint.

Gross interpretation begins with size and consistency

Normal architecture	Atrophic endpoint
• Organ is composed of extensive seminiferous tubules • Tubular tissue dominates the parenchyma • Spermatogenesis supported by germ-cell layers	• Often small and firm in the cryptorchid model • Functional tubules become less prominent • Microscopy establishes the nature of regression

Early tubular injury precedes complete hyalinization

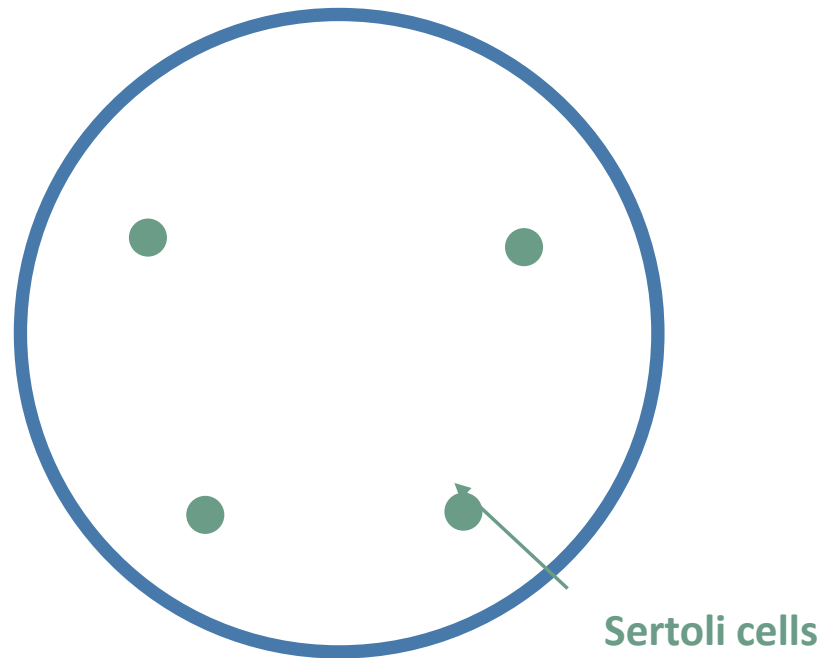
Simplified seminiferous-tubule schematic



- Thickened basement membrane may be an initial clue.
- Tubular cellularity can decline over time.
- Do not require fully sclerosed tubules before recognizing regression.

Advanced loss of germ cells explains sperm-production failure

Simplified seminiferous-tubule schematic

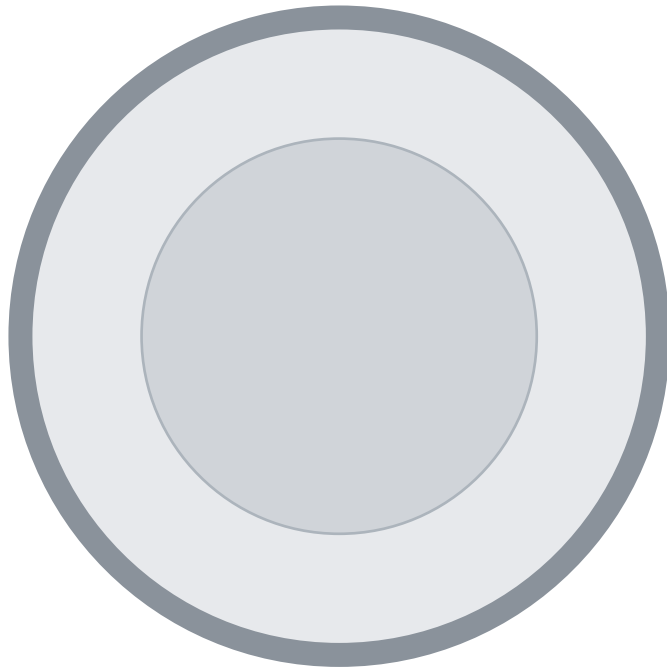


Sertoli cells without germ cells

- The source specifies loss of spermatogonia and retained Sertoli cells.
- This is a direct histologic explanation of poor sperm generation.
- Functional capacity cannot be inferred from testicular size alone.

Hyalinization is an architectural, not etiologic, diagnosis

Simplified seminiferous-tubule schematic



Hyaline collagenous tubular scar

- End-stage scarred tubules may appear as dense hyaline cords.
- The same general pattern can occur in multiple atrophy settings.
- Clinical data remain necessary to identify causation.

Tubular atrophy and Leydig preservation can coexist

Seminiferous damage	Interstitial preservation
• Germ-cell depletion • Tubular wall thickening • Loss of sperm production	• Relative Leydig cell visibility • Endocrine function may be less impaired • Do not equate tubule count with androgen level

Morphologic staging: Four recognizable patterns

Pattern	Dominant microscopic observation
Preserved activity	Spermatogenic cells in tubules
Early regression	Basement-membrane thickening
Established atrophy	Germ-cell loss; Sertoli-only tubules
Advanced scar	Hyaline tubular cords; Increased stroma

Inference from a biopsy has distinct limits

Reasonable inference	Not established by morphology alone
• Spermatogenesis is absent in affected tubules • Basement membrane and stroma show chronicity • Interstitial cells may be relatively preserved	• Exact duration of injury • One exclusive etiologic exposure • Precise current hormonal state

Fertility impairment and androgen deficiency are not identical

**Germ-cell
compartment**

**Leydig-cell
compartment**

- Tubular failure can markedly reduce sperm production.
- Leydig cells may survive despite severe tubular regression.
- Clinical assessment should not merge fertility and endocrine endpoints.

Case: Older patient with chronic vascular disease

Clinical–pathologic vignette

A patient with age-related vascular disease has progressively smaller testes without a history of cryptorchidism or orchitis.

Which listed etiology deserves consideration?

Interpretation

- Progressive atherosclerotic narrowing of testicular blood supply.
- Vascular context supports—but does not prove—causation.

Case: Regression following inflammatory orchitis

Clinical–pathologic vignette

A history of orchitis is followed by testicular firmness and reduced fertility rather than signs of current acute infection.

What pathologic endpoint explains the course?

Interpretation

- Healed parenchymal damage with fibrosis and atrophy.
- A scarred end-stage testis differs from acute orchitis.

Case: A previously undescended testis

Clinical–pathologic vignette

An undescended testis is small. Microscopy shows thick tubular walls, absent germ-cell maturation and conspicuous Leydig cells.

How are fertility and histology connected?

Interpretation

- Germ-cell loss produces deficient spermatogenesis.
- Leydig cells may be relatively spared and conspicuous.

Case: Infertility with small testes and elevated FSH

Clinical–pathologic vignette

An adult has small testes, infertility and high gonadotropin levels. Testicular tubules show hyaline collagenous ghosts.

Which primary failure is illustrated?

Interpretation

- Klinefelter syndrome is an important genetic possibility.
- Karyotype and clinical context are needed for attribution.

Case: Small testes during prostate cancer therapy

Clinical–pathologic vignette

A patient treated over a prolonged period with antiandrogens for prostate carcinoma develops reduced testicular size.

What specific etiologic category should be recorded?

Interpretation

- Prolonged antiandrogen administration is a listed cause.
- Medication context should precede histologic attribution.

Case: Cachexia with chronic liver disease

Clinical–pathologic vignette

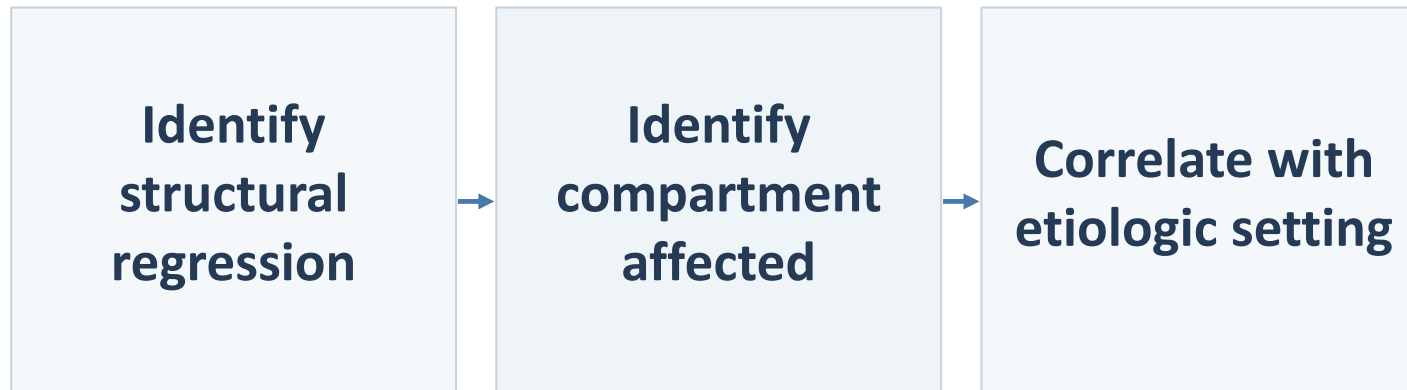
A chronically ill patient with cirrhosis and generalized wasting is found to have bilateral testicular regression.

Why is single-cause attribution difficult?

Interpretation

- Both cirrhosis and malnutrition/cachexia appear in the list.
- Coexisting systemic mechanisms may converge.

A source-grounded interpretive sequence



Interpretive causal schematic

- Start with the morphology:
Germ cells, Sertoli cells, tubular walls and stroma.
- Separate loss of spermatogenesis from Leydig-cell preservation.
- Integrate development, infection, vascular disease, systemic illness and treatments.

Common errors in interpreting an atrophic testis

Misinterpretation	Better reading
Small testis = one specific cause	Atrophy is a shared endpoint
Visible Leydig cells = normal fertility	Leydig and germ-cell compartments differ
Unilateral undescended testis = normal other side	Contralateral abnormalities are possible
Hyalinization = inherited disorder	Hyaline scars occur in more than one context

The pathologic core in four statements

- Ten etiologic settings converge on testicular atrophy.
- The morphologic sequence includes thickened tubular walls, germ-cell depletion and hyaline scarring.
- Loss of germ cells explains decreased fertility more directly than Leydig-cell appearance.
- The etiology is established by combining morphologic pattern with clinical context.