

Benign Enlargement

Benign prostatic hyperplasia

Mechanisms · Morphology · Clinicopathologic consequences

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Learning objectives

- Define BPH and distinguish histologic hyperplasia from malignancy.
- Explain DHT, androgen-receptor and growth-factor mechanisms.
- Recognize gross and microscopic patterns and consequences of obstruction.
- Connect medical and procedural treatment to pathophysiology.

What benign prostatic enlargement means

- BPH is a nodular increase in prostatic stromal and glandular tissue.
- The lesion is benign; Expansion can still impair urinary outflow.
- The central clinical relationship is transition-zone growth around the urethra.

Stromal + glandular proliferation



Transition-zone nodules



Urethral compression

Hyperplasia is the appropriate morphologic term

- Hyperplasia refers to increased cell number within glandular and stromal components.
- The textbook also mentions the traditional term “benign prostatic hypertrophy.”
- “Nodular hyperplasia” describes the characteristic growth pattern.

Hyperplasia

Hypertrophy

Cell-number increase

Cell-size increase

Glandular + stromal

**Not the preferred label for
BPH**

BPH does not represent a premalignant lesion

- The benign epithelial and stromal proliferation does not define a cancer precursor.
- Do not infer malignant progression from nodular enlargement alone.
- The prostate also develops carcinomas, but their zonal predilection differs.

BPH

Prostatic carcinoma

Benign nodules

Malignant neoplasm

**Transition-zone
predilection**

**Peripheral-zone
predilection**

BPH is a common disorder of aging

- BPH as the most common benign prostatic disease after age 50.
- Its burden should be described separately as histologic prevalence and symptomatic disease.
- Age-associated frequency does not make clinically significant obstruction harmless.

~30%

Symptomatic BPH

American males of European descent
>50 y

Moderate-to-severe symptoms

**Up to
90%**

Histologic BPH

Males by age 80 y

Histologic evidence

Different measures and populations — not directly interchangeable

Interpret epidemiologic figures carefully

- Approximately 30% applies to moderate-to-severe symptoms in a specified American ancestry group older than 50.
- Up to 90% by age 80 refers to histologic evidence, not the same symptomatic endpoint.
- These textbook observations cannot be treated as universal population estimates.

Clinical symptoms

Histologic evidence

**Patient-reported disease
burden**

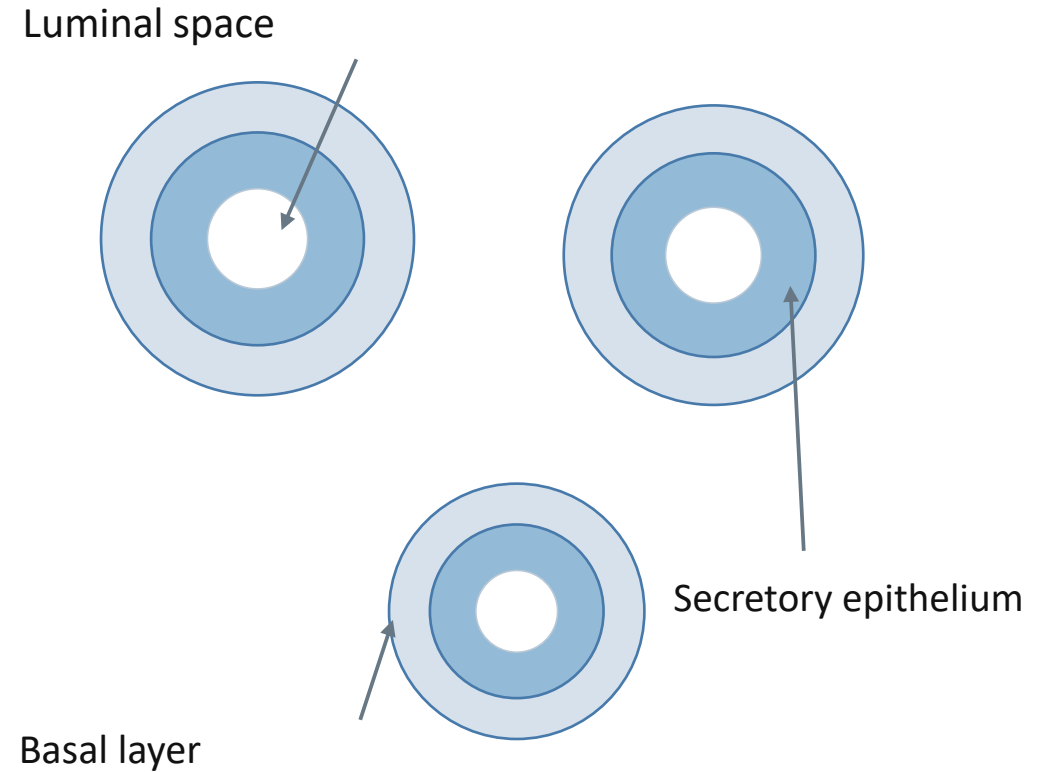
**Tissue-based microscopic
finding**

**Population qualification
matters**

**Different denominator
and endpoint**

The adult prostate: Glands in fibromuscular stroma

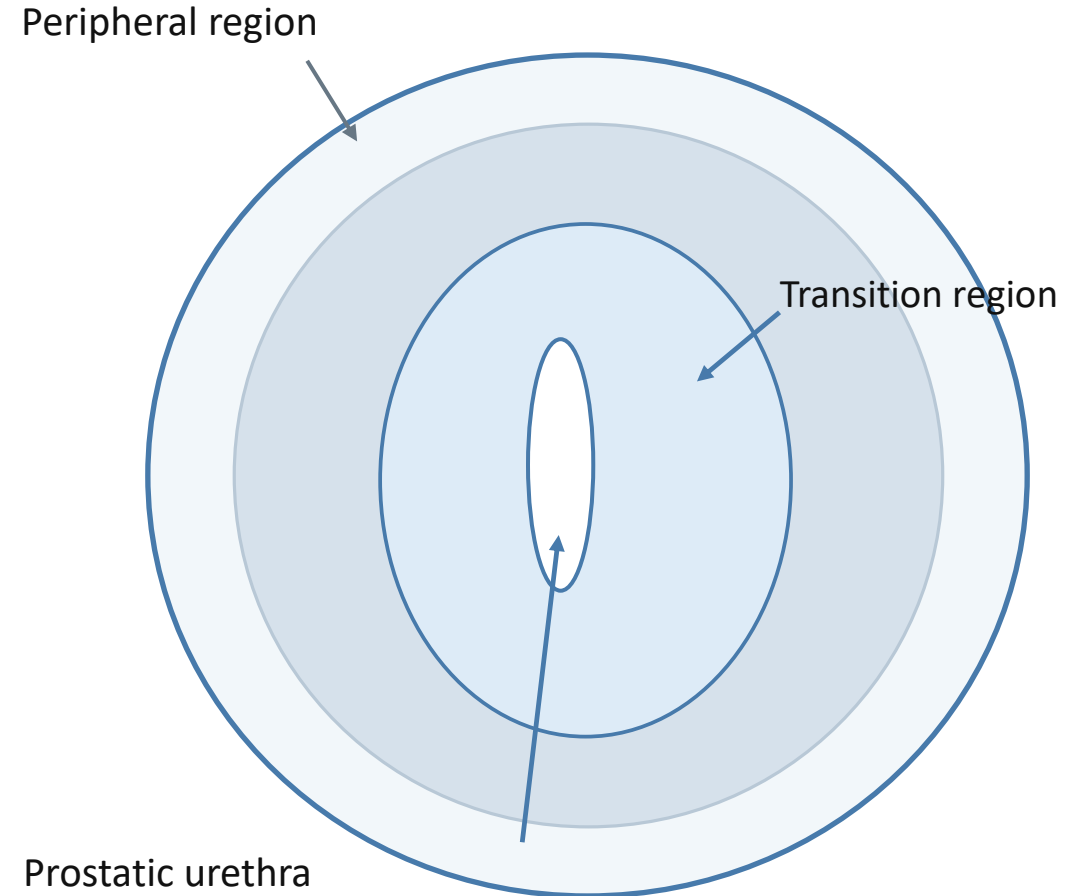
- The normal organ surrounds the proximal urethra and weighs about 20 g.
- Glands reside within abundant fibromuscular stroma.
- Both cellular compartments are implicated in BPH.



Schematic glands; Diagnostic features require genuine H&E review

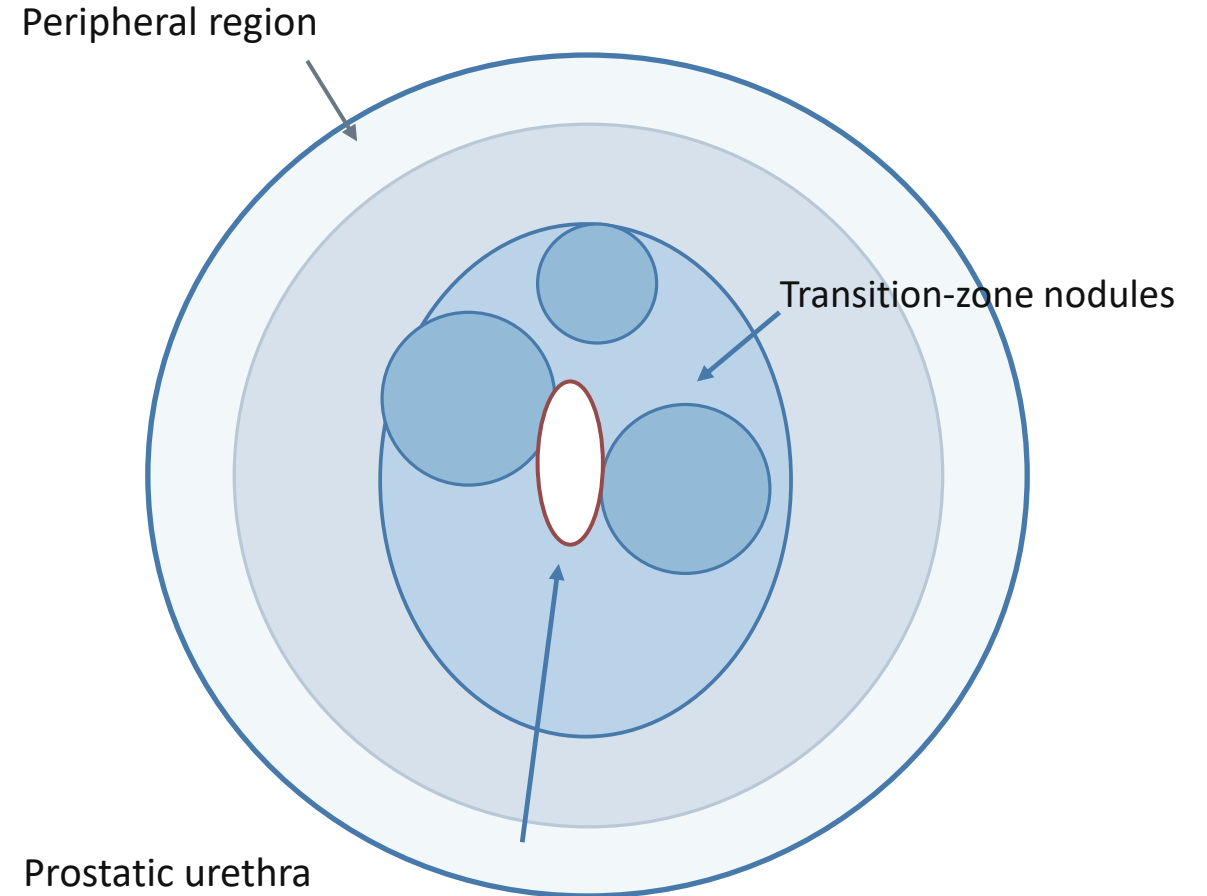
Prostatic zones are biologically distinct

- The chapter distinguishes peripheral, central, transition, and periurethral regions.
- Their differing lesion distributions provide diagnostic context.
- BPH predominantly affects the transition and inner periurethral regions.



Transition-zone position explains obstruction

- The transition zone lies close to the prostatic urethra.
- Expanding nodules can reduce the lumen even without malignant invasion.
- Clinical impact depends on both tissue bulk and associated smooth-muscle tone.



BPH and adenocarcinoma: Distinct usual origins

- The textbook places most hyperplasia in the transition zone.
- Most adenocarcinomas are instead described as arising in the peripheral zone.
- This is an anatomic distinction, not a method for excluding coexisting pathology.

BPH

Transition / periurethral

Benign stromal +
glandular nodules

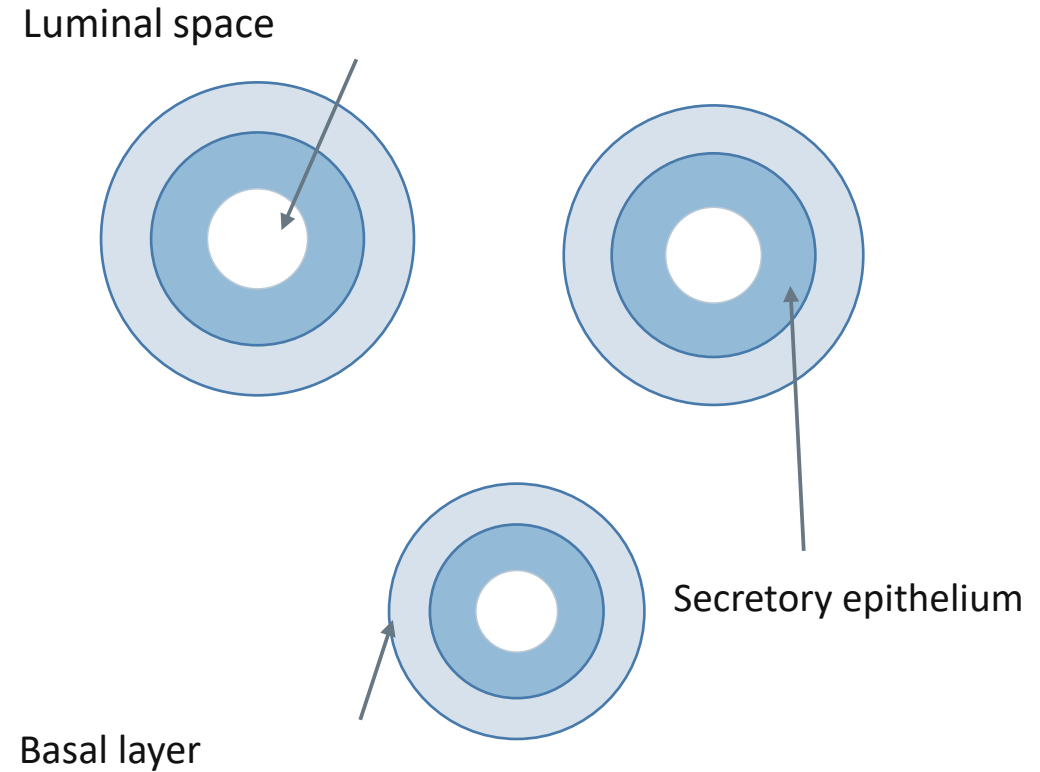
Adenocarcinoma

Predominantly peripheral

Malignant epithelial
tumor

The normal gland contains two epithelial layers

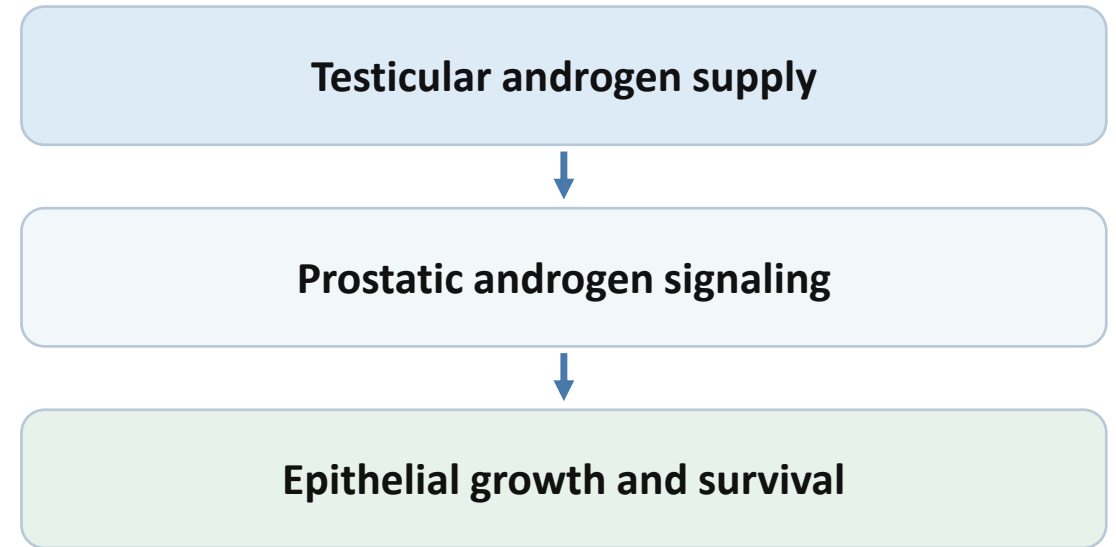
- An inner columnar secretory layer lines the glandular lumen.
- An outer layer of basal cells is cuboidal or flattened.
- Recognition of both layers is important when describing benign glandular structures.



Schematic glands; Diagnostic features require genuine H&E review

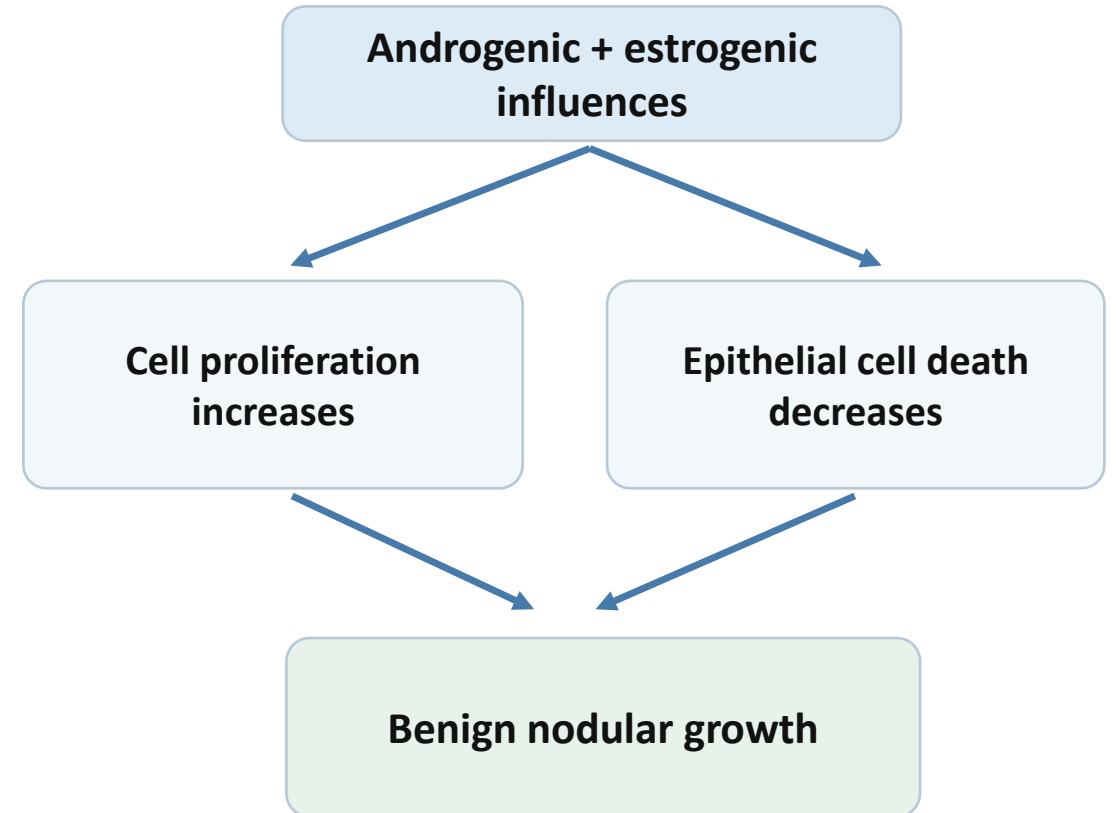
Prostatic maintenance is androgen dependent

- Testicular androgens regulate prostatic cell growth and survival.
- The parent chapter describes epithelial apoptosis and glandular atrophy after castration.
- BPH therefore arises in a hormonally responsive tissue compartment.



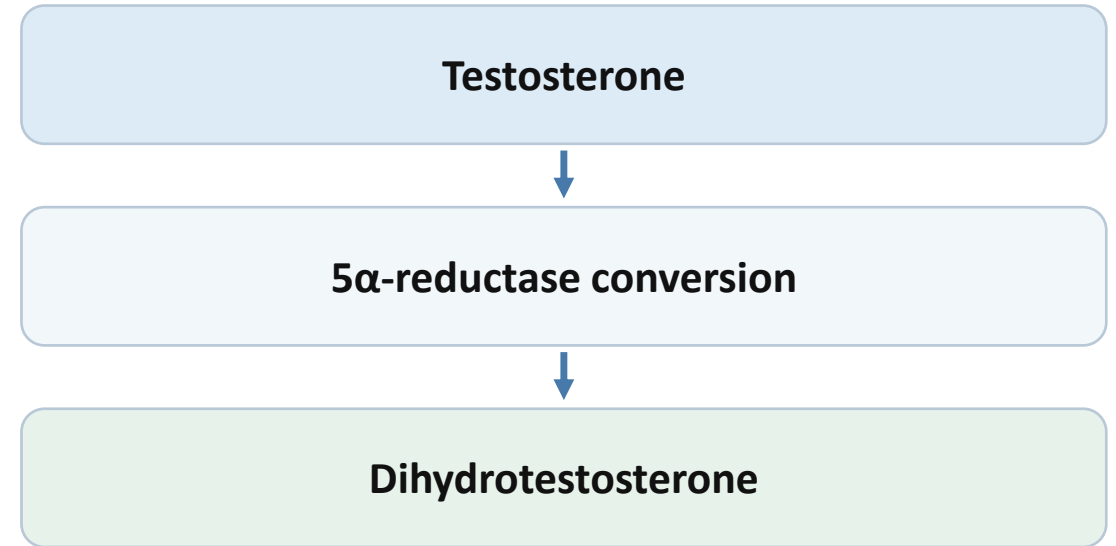
Overview: Prostatic hyperplasia is multifactorial

- DHT provides a dominant androgen signal.
- Androgen-responsive growth factors connect stromal and epithelial compartments.
- Estrogen-related pathways further favor a net increase in tissue mass.



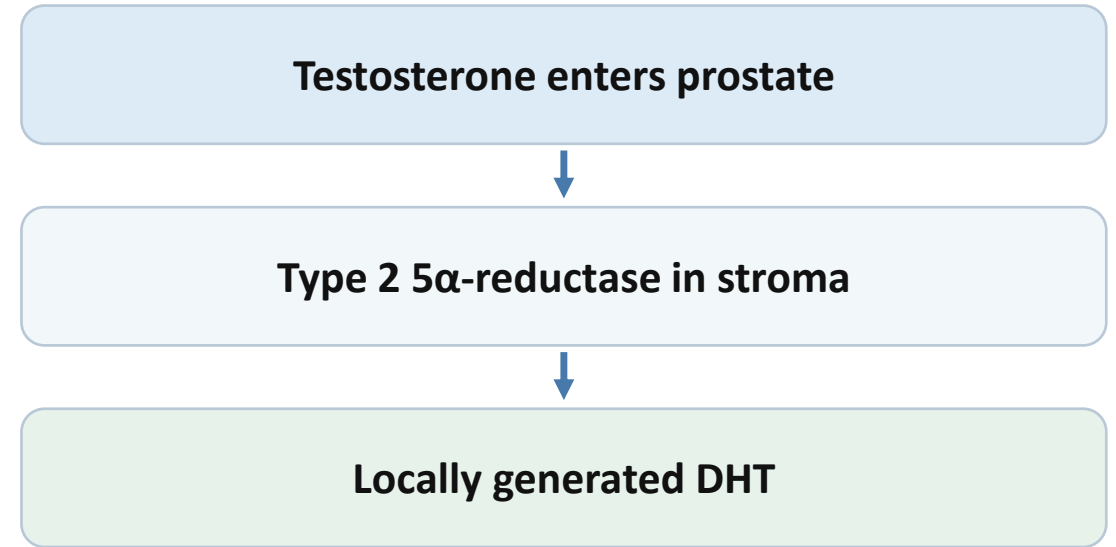
Testosterone supplies the substrate for DHT

- Testosterone reaches the prostate and undergoes local metabolic conversion.
- Dihydrotestosterone (DHT) is the principal intraprostatic androgen emphasized by Robbins.
- This conversion provides a therapeutic target rather than merely a circulating hormone measurement.



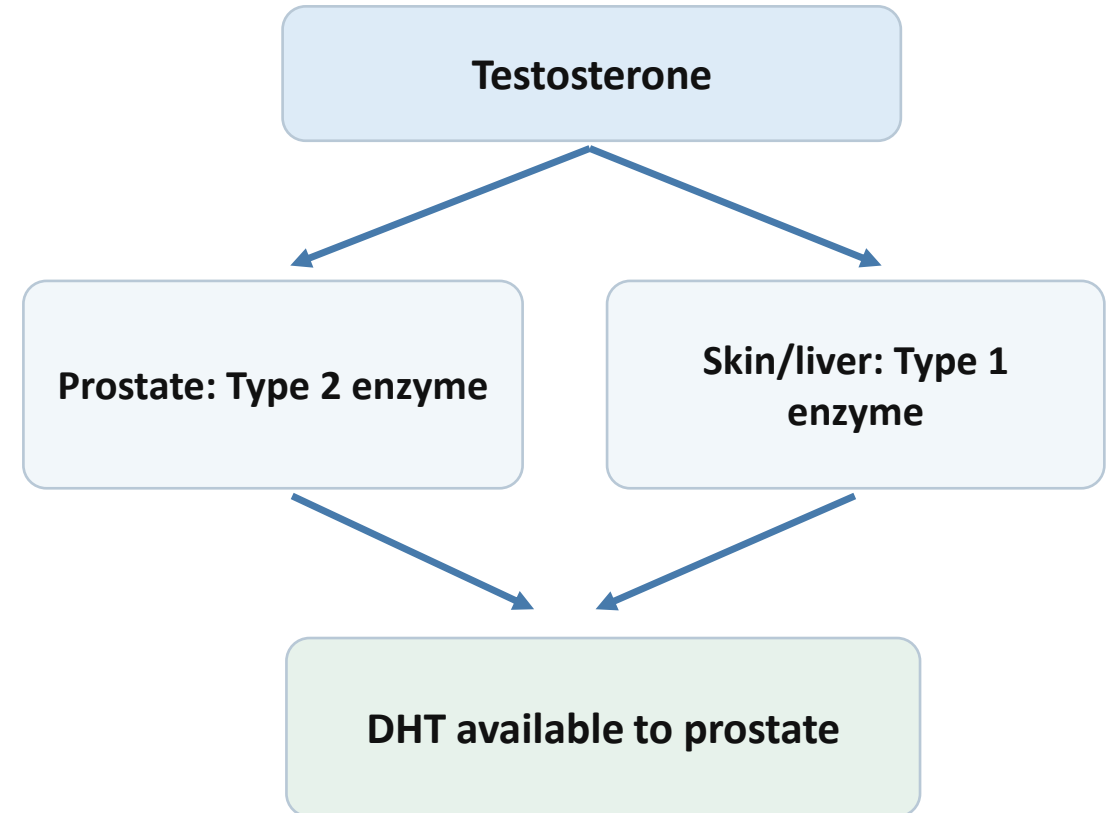
Type 2 5 α -reductase is predominantly stromal

- The chapter localizes type 2 5 α -reductase primarily to stromal cells.
- It specifies that type 2 enzyme is not expressed in prostatic epithelial cells.
- The stroma is therefore a major site of local DHT generation.



Extraprostatic tissues also generate DHT

- Type 1 5 α -reductase contributes to testosterone conversion in the liver and skin.
- The resulting DHT can reach the prostate via the circulation.
- BPH hormone exposure includes both local and extraprostatic sources.



DHT has more sustained receptor binding

- DHT binds androgen receptors with greater affinity than testosterone.
- Its androgen receptor complex is more stable.
- Greater receptor affinity explains why it is a potent intraprostatic androgen signal.

Testosterone–AR

DHT–AR

Lower relative affinity

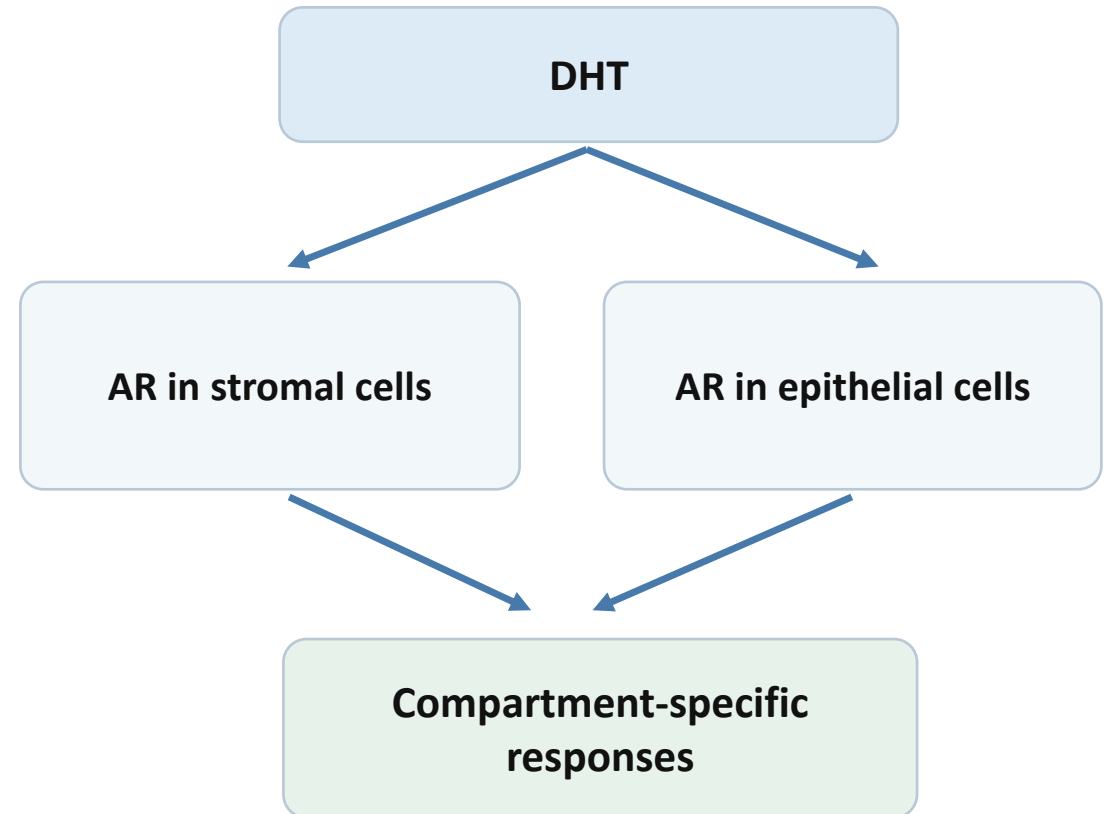
Higher relative affinity

Less stable complex

More stable complex

Androgen receptors occur in both compartments

- Stromal cells contain androgen receptors.
- Prostatic epithelial cells also contain androgen receptors.
- DHT therefore influences a coupled stromal–epithelial tissue system.



Androgen receptor activation is nuclear

- DHT binding activates cytoplasmic androgen receptors.
- The activated receptors translocate to the nucleus.
- Nuclear AR signaling regulates transcription of androgen-dependent genes.

DHT binds cytoplasmic AR



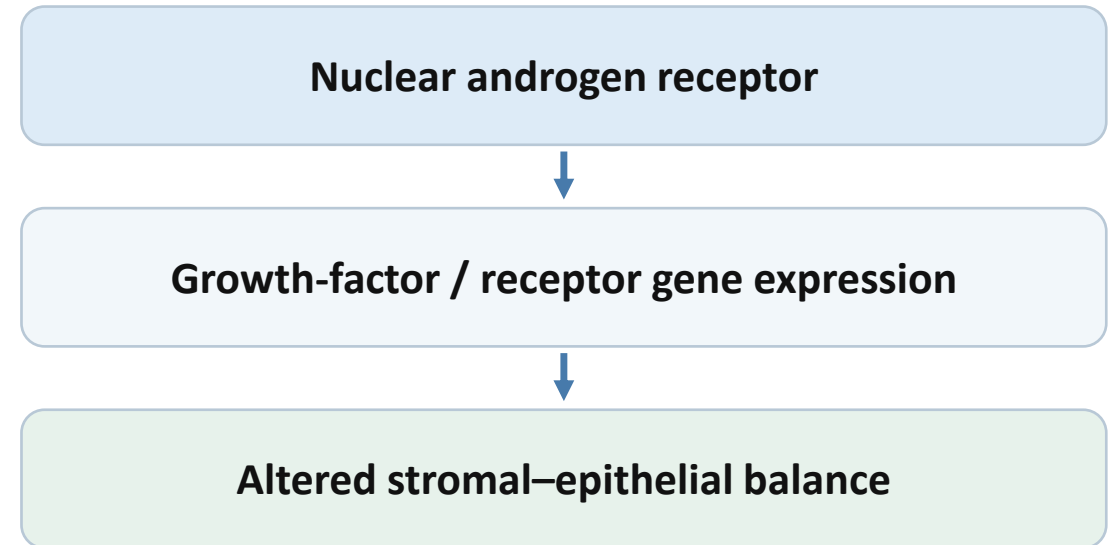
Activated AR enters nucleus



Androgen-responsive gene transcription

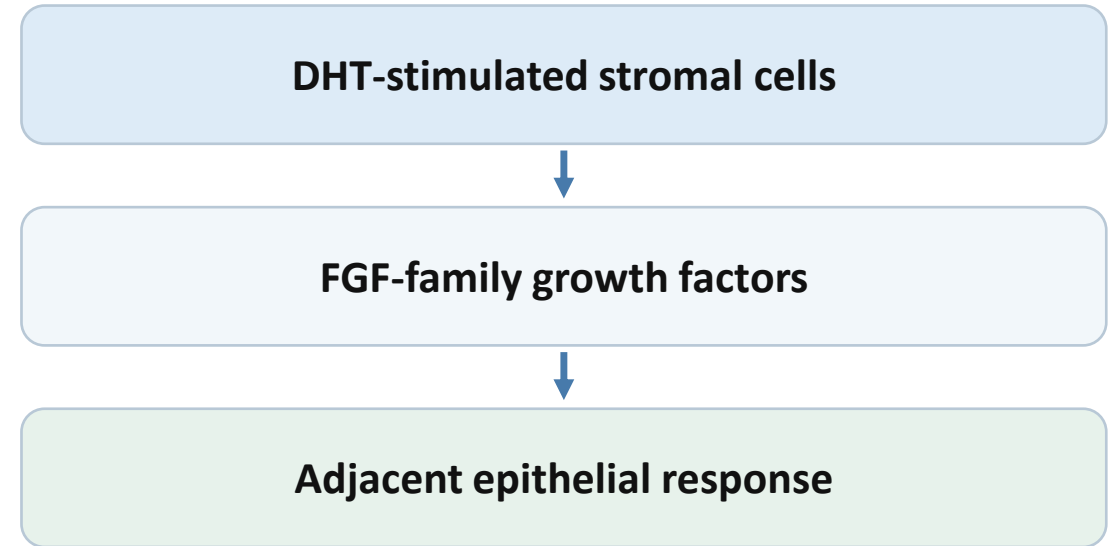
Androgen-dependent genes alter growth signaling

- AR target genes include growth factors and their receptors.
- Fibroblast growth factor (FGF) and transforming growth factor- β (TGF- β).
- The growth response is mediated indirectly as well as through receptor activation.



Stromal FGFs provide paracrine signaling

- FGF-family ligands are produced by stromal cells.
- Their paracrine effects support androgen-stimulated epithelial growth.
- Stromal–epithelial communication is central to the pathogenesis model.



BPH may reactivate developmental programs

- FGF pathways regulate epithelial growth during embryonic prostate development.
- The textbook proposes partial reawakening of these pathways during adulthood.
- This is a proposed mechanism rather than a proven complete causal explanation.

Development

FGF-regulated organ growth

Physiologic embryonic program

Adult BPH

Potential pathway reactivation

Pathologic nodular enlargement

TGF- β effects differ by target cell

- TGF- β stimulates fibroblasts and other mesenchymal cells.
- The same factor can inhibit epithelial proliferation.
- Its effects must not be summarized as uniformly pro-proliferative.

Stromal / mesenchymal

Epithelial

TGF- β : Mitogenic action

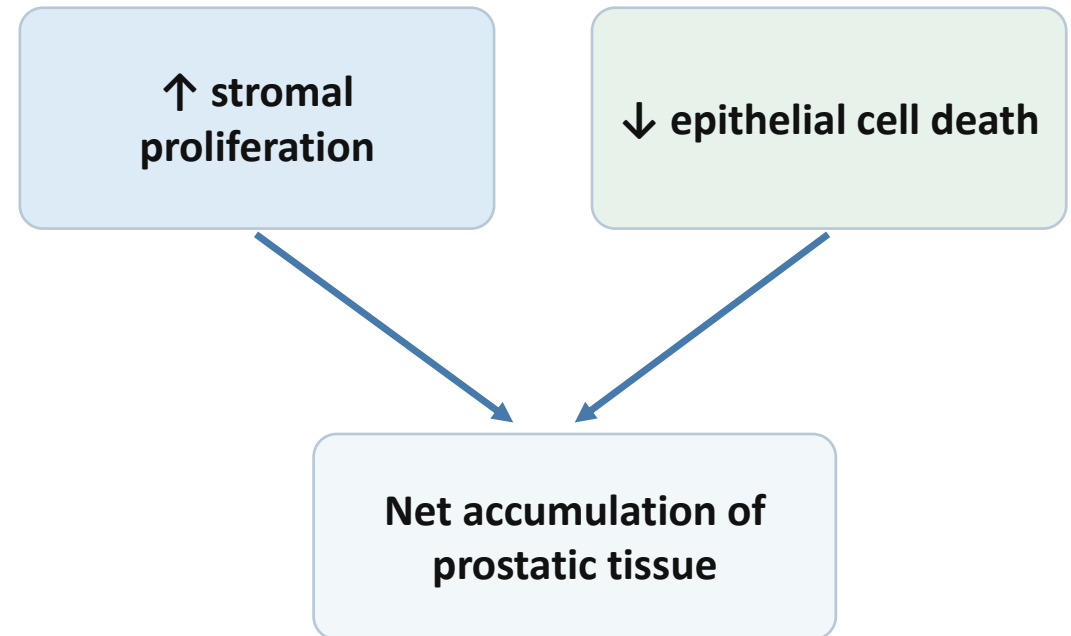
TGF- β : Proliferation inhibition

Cell-specific response

Different target-cell response

Hyperplasia reflects a proliferation–death imbalance

- Increased proliferation of stromal cells.
- Reduced epithelial cell death also contributes to tissue expansion.
- Net growth is not equivalent to unchecked epithelial mitosis alone.



Schematic — qualitative balance; No numerical effect size implied

Stromal growth is not a secondary afterthought

- BPH is histologically a mixed stromal and glandular process.
- Androgen metabolism, FGF production, and mesenchymal proliferation all involve stroma.
- The fibromuscular component contributes to gland size and obstruction.

Stromal androgen response



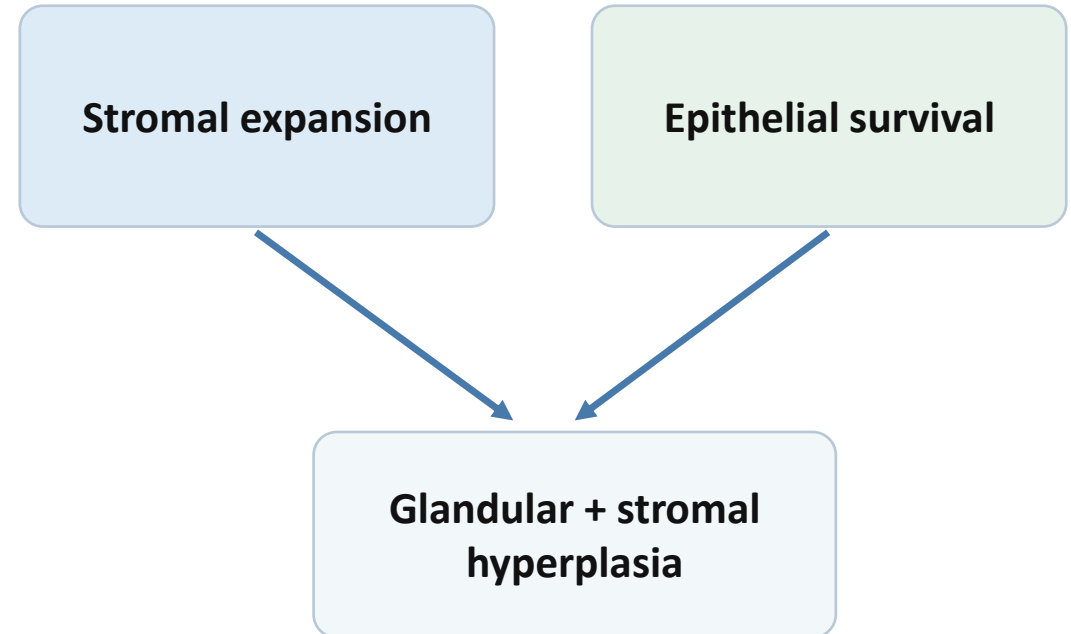
Growth-factor and mesenchymal effects



Fibromuscular expansion

Epithelial accumulation includes enhanced survival

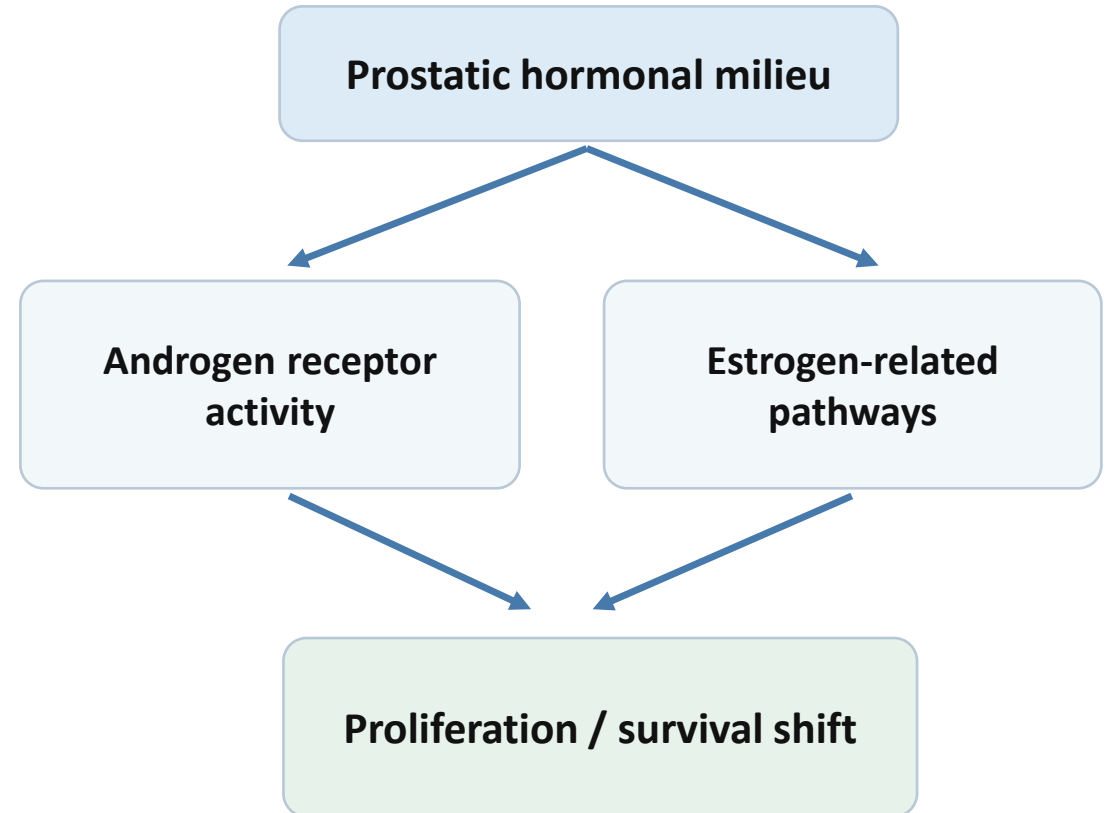
- A decrease in epithelial cell death increases epithelial mass over time.
- This can occur alongside stromal proliferative activity.
- Altered cell turnover as part of the integrated BPH mechanism.



Schematic — qualitative balance; No numerical effect size implied

Androgens are permissive, not the whole cause

- Androgen availability is required for the characteristic prostatic growth response.
- The ultimate initiating cause of BPH remains unknown.
- Additional estrogen-dependent and tissue-regulatory mechanisms are implicated.



Estrogens participate in the growth balance

- The chapter cites multiple lines of evidence for estrogen involvement.
- Estrogen effects may favor proliferation over cell death.
- Their role is best viewed as contributory and mechanistically complex.

Estrogen-linked signaling



Cell-type-specific responses



Shift toward prostatic growth

Estrogen receptors have opposing effects

- ER α is associated with pro-proliferative effects in the source model.
- ER β is associated with antiproliferative effects.
- A single undifferentiated “estrogen effect” obscures receptor subtype biology.

ER α

ER β

Proliferative effect

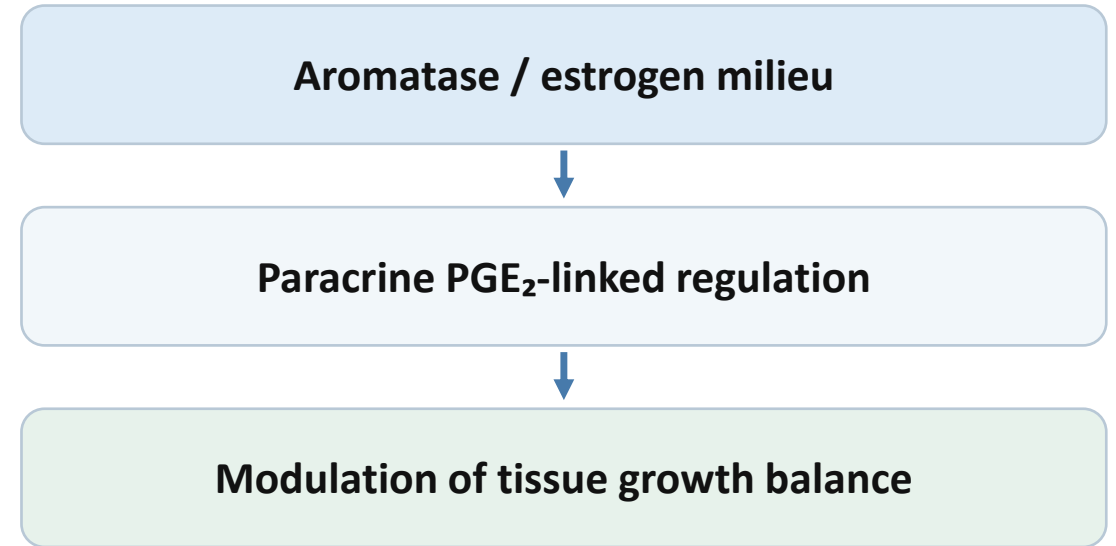
Antiproliferative effect

Receptor-specific pathway

Opposing receptor activity

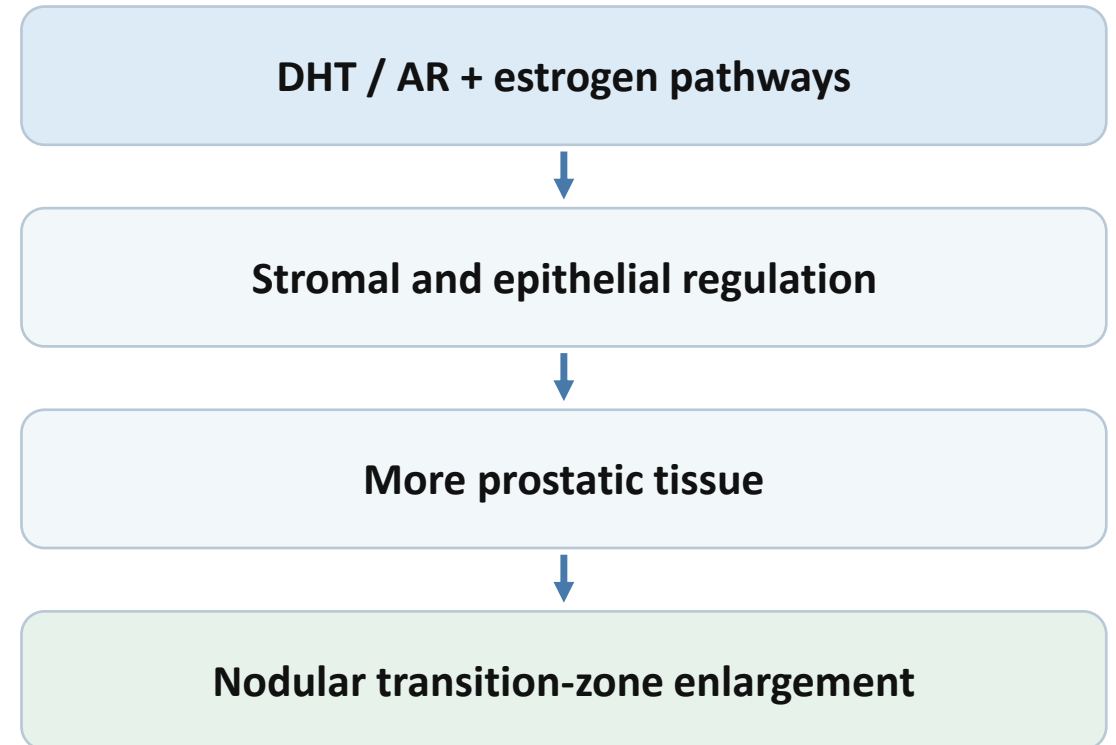
Aromatase and PGE₂ are implicated pathways

- Estrogen actions with aromatase expression.
- Paracrine regulation involving prostaglandin E₂ also appears in the model.
- These associations do not establish a quantitative contribution for either pathway.



Integrated model: Hormones to nodules

- DHT–AR signaling modifies growth-factor expression.
- FGF and TGF- β actions vary between stromal and epithelial targets.
- Estrogen pathways contribute to cell turnover favoring enlargement.



Grossly, BPH can markedly increase gland weight

- The normal prostate is described as weighing roughly 20 g.
- BPH commonly produces a three- to fivefold increase, approximately 60–100 g.
- Even greater enlargement can occur; Gland weight is not itself a cancer criterion.

Normal prostate

BPH enlargement

Approximately 20 g

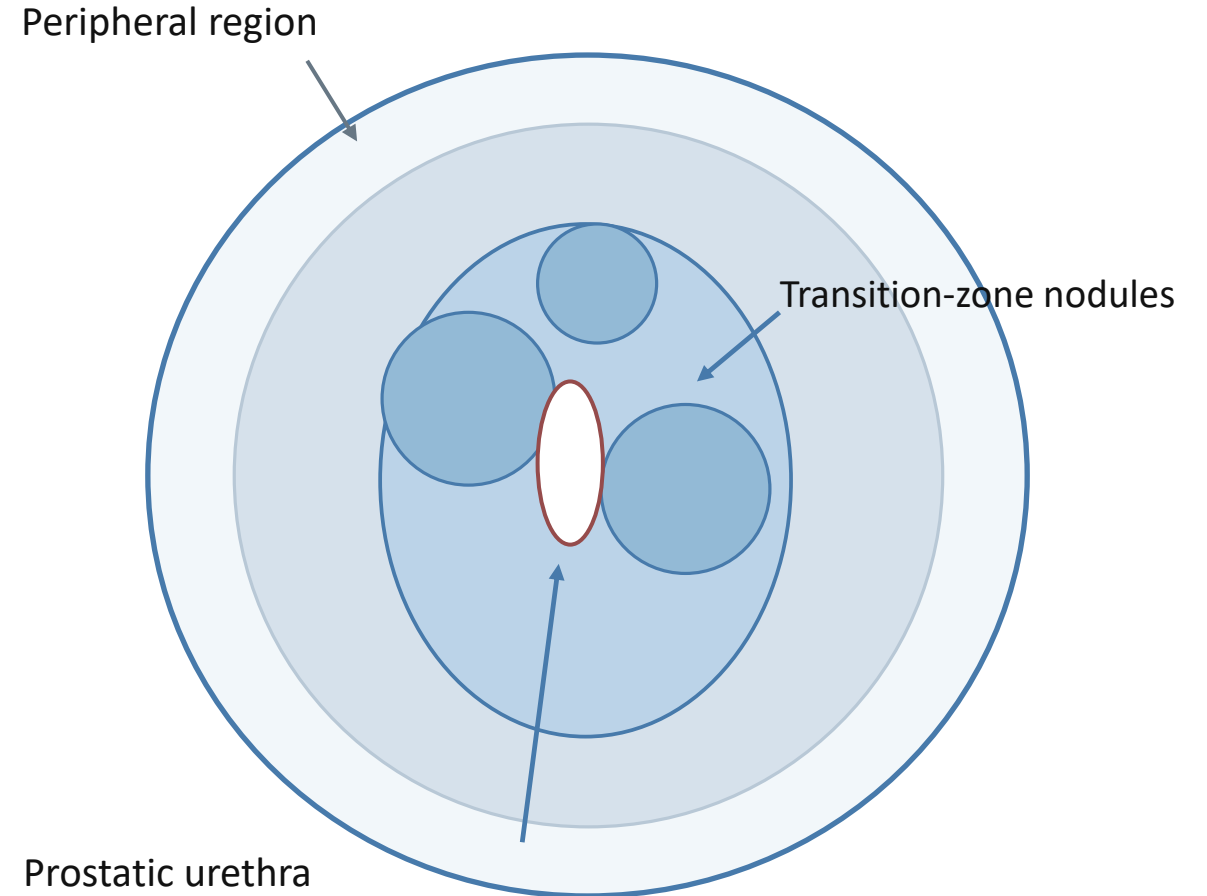
Often 60–100 g

Parent chapter baseline

Sometimes larger

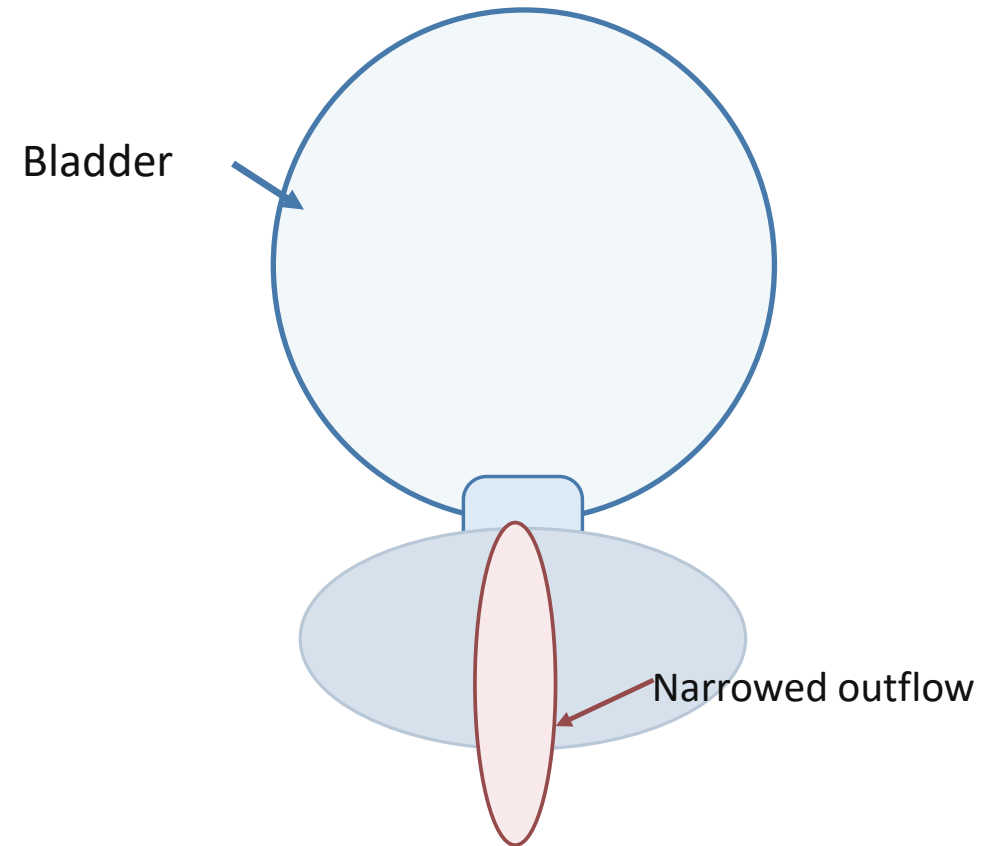
Hyperplastic nodules cluster near the urethra

- BPH affects transition-zone and inner periurethral tissue.
- Well-defined nodules can project inward as they expand.
- The urethral channel may become visibly constricted.



Prostatic urethral narrowing can be slit-like

- Large transition-zone nodules can compress the prostatic urethra.
- A slit-like urethral orifice in affected glands.
- Lumen narrowing is the structural counterpart of the obstructive component.



Schematic — bladder and prostatic outlet; Not anatomical scale

Nodular heterogeneity has a tissue basis

- The gross character of a BPH nodule varies with its cellular composition.
- Gland-predominant nodules appear and feel different from stromal-predominant ones.
- Sampling can therefore show a mixture of distinct tissue patterns.

Gland-predominant

Stroma-predominant

Yellow-pink; Soft

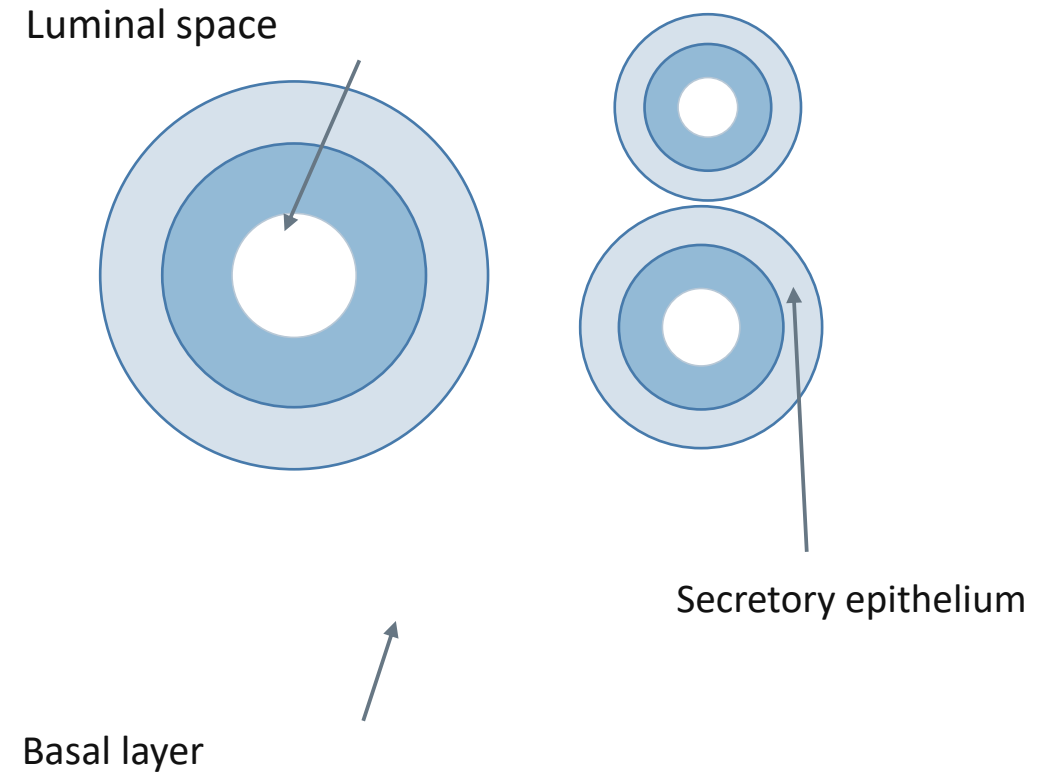
Pale-gray; Firm

Milky secretions possible

Fibromuscular-rich

Gland-rich nodules are soft and secretory

- Gland-predominant nodules are described as yellow-pink and relatively soft.
- They may release a milky-white prostatic fluid when cut.
- These are gross morphology correlations, not standalone diagnostic criteria.



Schematic glands; Diagnostic features require genuine H&E review

Stroma-rich nodules are firm

- Fibromuscular nodules are pale-gray and firm.
- Greater stromal abundance explains their different gross consistency.
- BPH remains a mixed epithelial–stromal proliferative process overall.

Glandular tissue

Fibromuscular stroma

Secretory spaces

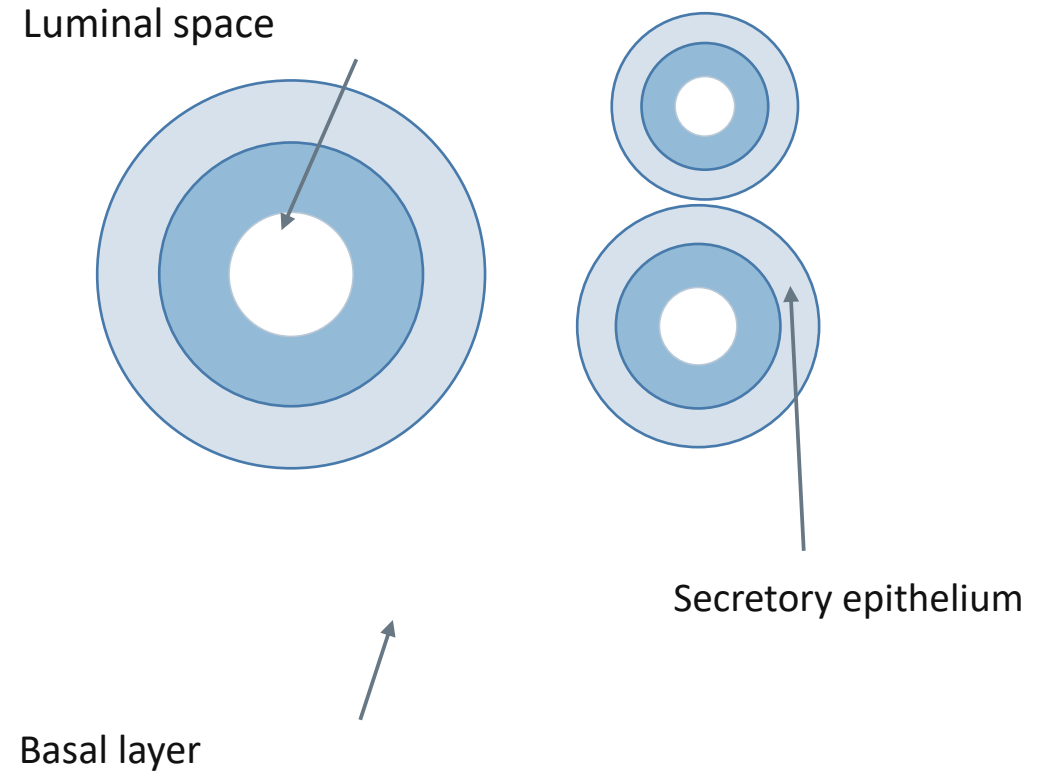
Spindle-cell tissue

**Softer yellow-pink
nodules**

Firmer pale-gray nodules

Microscopic nodules mix glands and stroma

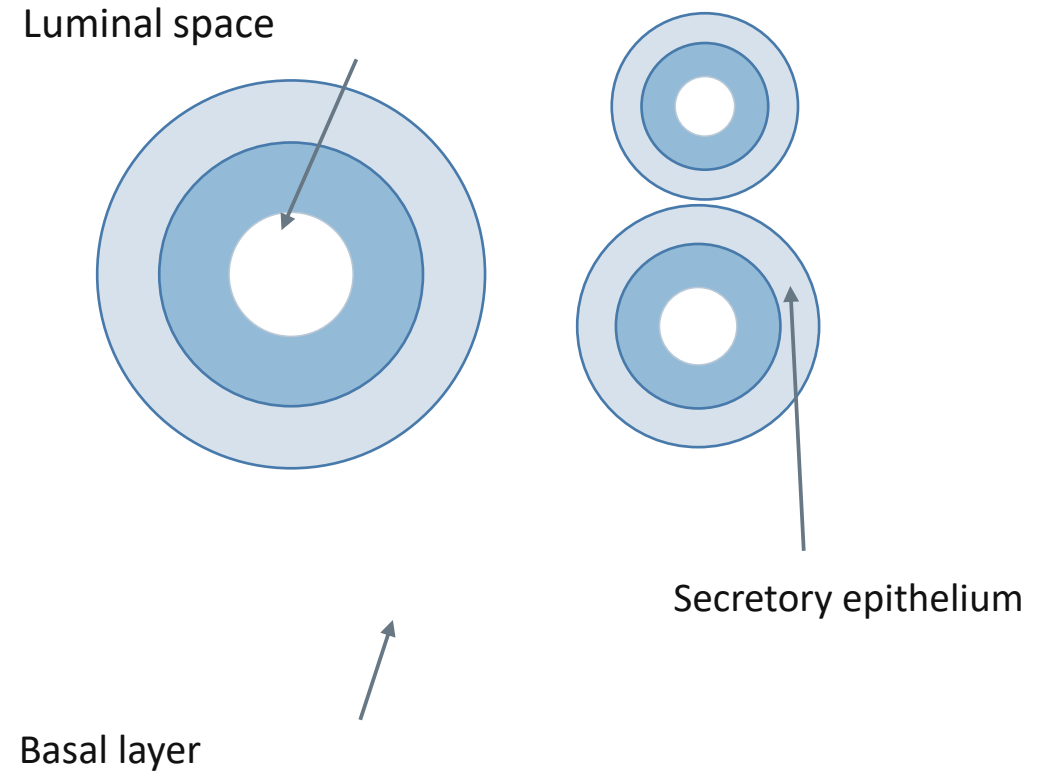
- Small, medium, and enlarged glands appear within nodules.
- They are separated by bland spindle-shaped stromal cells.
- Architectural variability is compatible with benign nodular hyperplasia.



Schematic glands; Diagnostic features require genuine H&E review

Glands often show variable luminal dilation

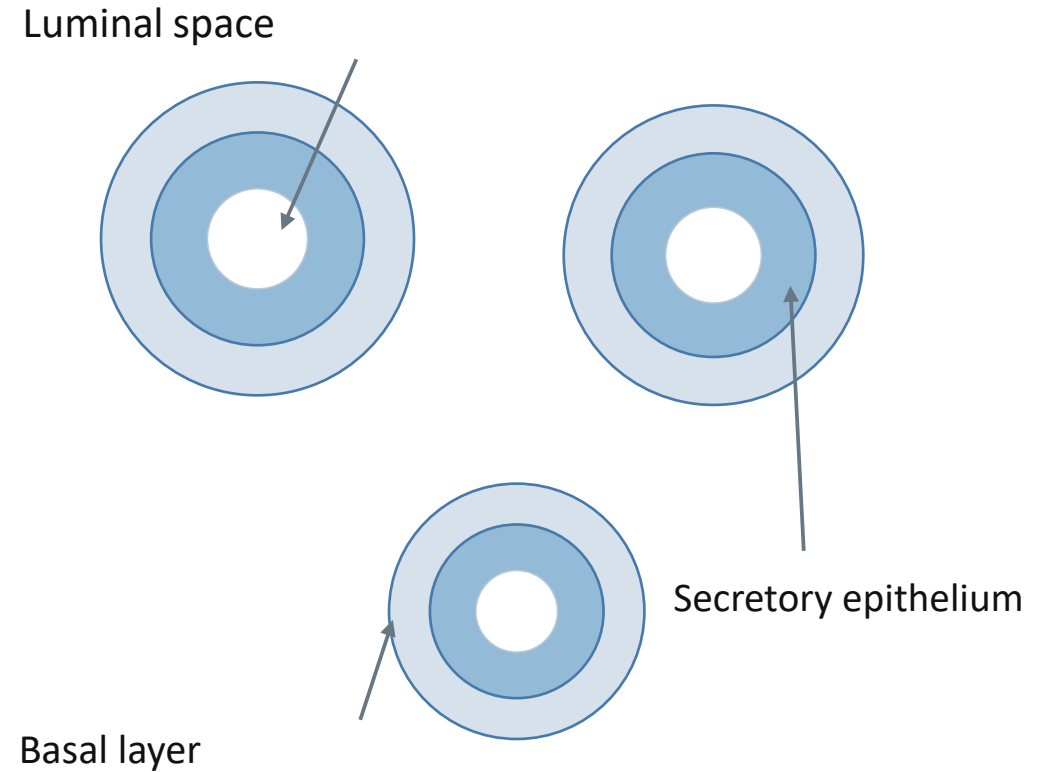
- Hyperplastic glands can range from small to cystically dilated.
- The lumen is enclosed by preserved epithelial layers in typical BPH glands.
- Variable gland caliber contributes to the heterogeneous microscopic pattern.



Schematic glands; Diagnostic features require genuine H&E review

Two-layered benign epithelium persists

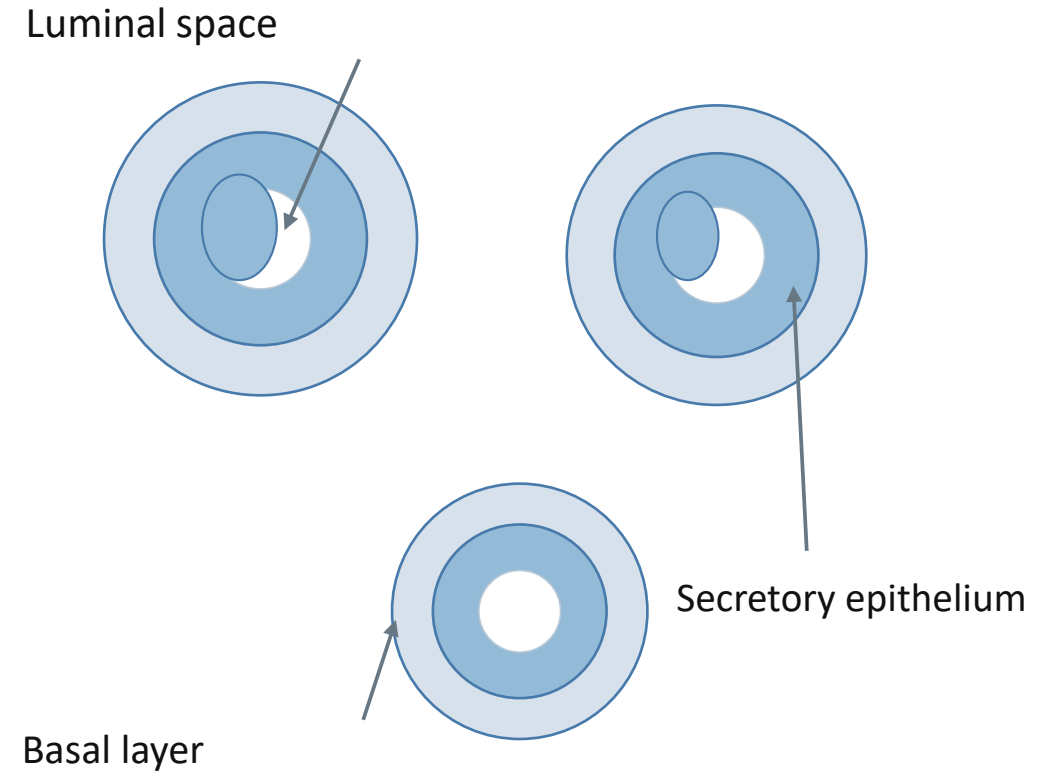
- An inner columnar secretory layer remains identifiable.
- An outer cuboidal or flattened basal epithelial layer is present.
- Preserved layered architecture is an important benign histologic feature.



Schematic glands; Diagnostic features require genuine H&E review

Secretory infoldings may simulate papillae

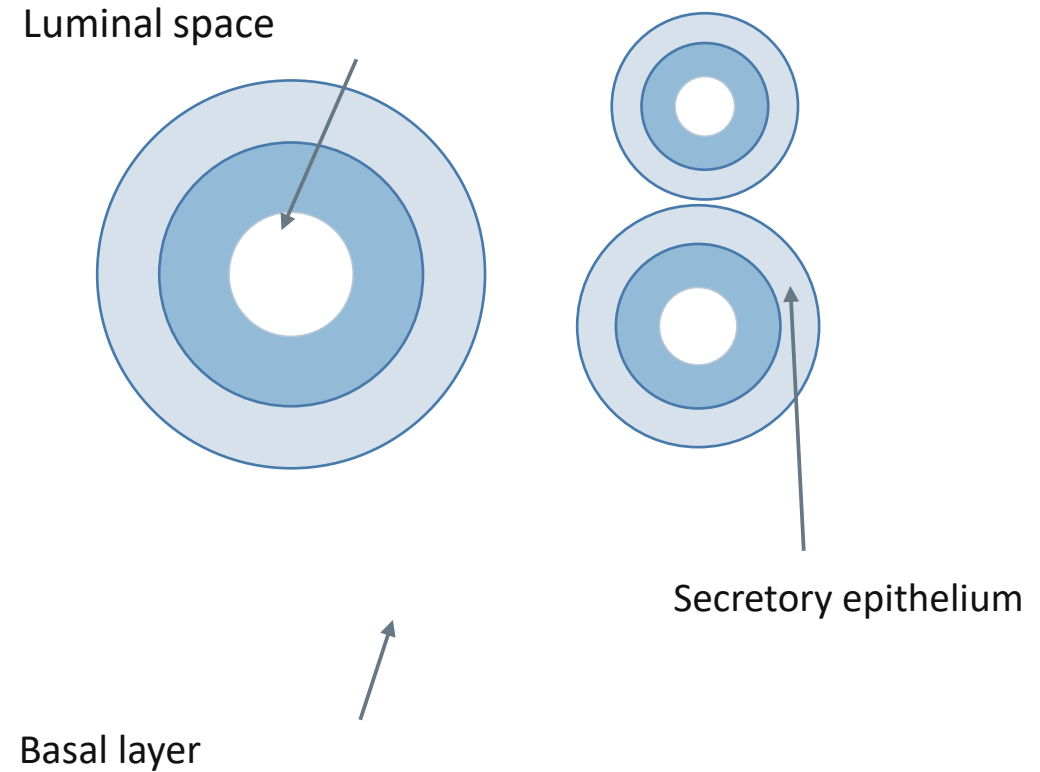
- Luminal secretory epithelium can form inward folds.
- The resulting papillary architecture is described as a feature of BPH nodules.
- Interpret papillary folds in the context of the glandular and stromal background.



Schematic glands; Diagnostic features require genuine H&E review

Bland stromal spindle cells separate glands

- Stromal elements are fibromuscular and spindle shaped.
- Nodules can be stromal dominant or gland dominant.
- The stromal component should be described rather than ignored during morphology review.



Schematic glands; Diagnostic features require genuine H&E review

Severe enlargement may compromise perfusion

- In very enlarged glands, vascular supply can be insufficient.
- Prostatic infarcts may develop in this setting.
- Infarction is a secondary effect of marked enlargement, not a necessary BPH finding.

Marked prostatic enlargement



Compromised local blood supply



Possible prostatic infarction

Squamous metaplasia can occur near infarction

- Squamous metaplasia adjacent to areas of prostatic infarction.
- This is a reactive epithelial change occurring in a specific setting.
- Its presence should be contextualized by the associated tissue injury.

Enlargement with infarction



Adjacent tissue injury



Possible squamous metaplasia

Morphology synthesis: What to recognize

- Nodular enlargement centered on transition/periurethral regions.
- Variable glands with two epithelial layers and secretory folds.
- Bland spindle-cell stroma, with occasional infarction-related changes.

Gross morphology

Microscopy

Central nodules

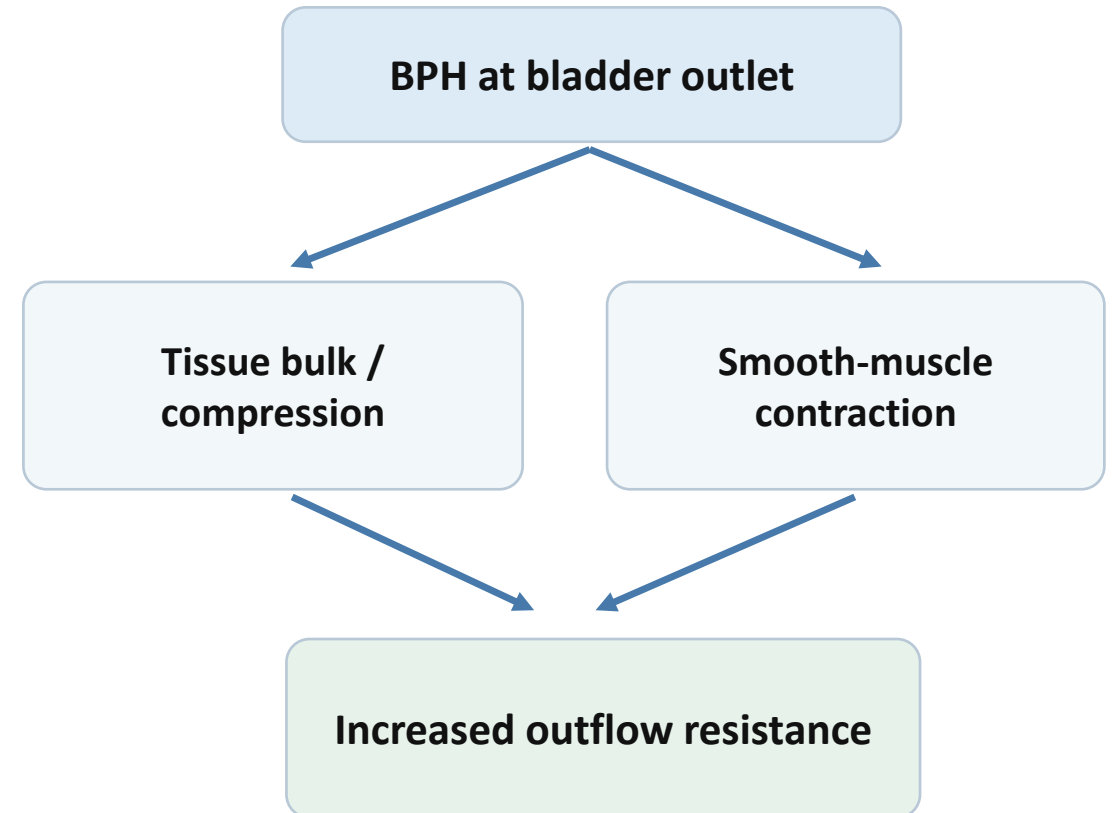
**Two-layered variable
glands**

Urethral compression

Fibromuscular stroma

Two mechanisms increase urinary outflow resistance

- Anatomic enlargement reduces the available urethral lumen.
- Stromal smooth muscle contraction adds a dynamic resistance component.
- Both mechanisms explain why tissue size is not the only treatment target.



The bladder works against greater resistance

- Obstruction increases pressure required to empty the bladder.
- Bladder muscular-wall hypertrophy and distention.
- Functional changes downstream reflect chronic difficulty with urinary outflow.

Prostatic outflow resistance



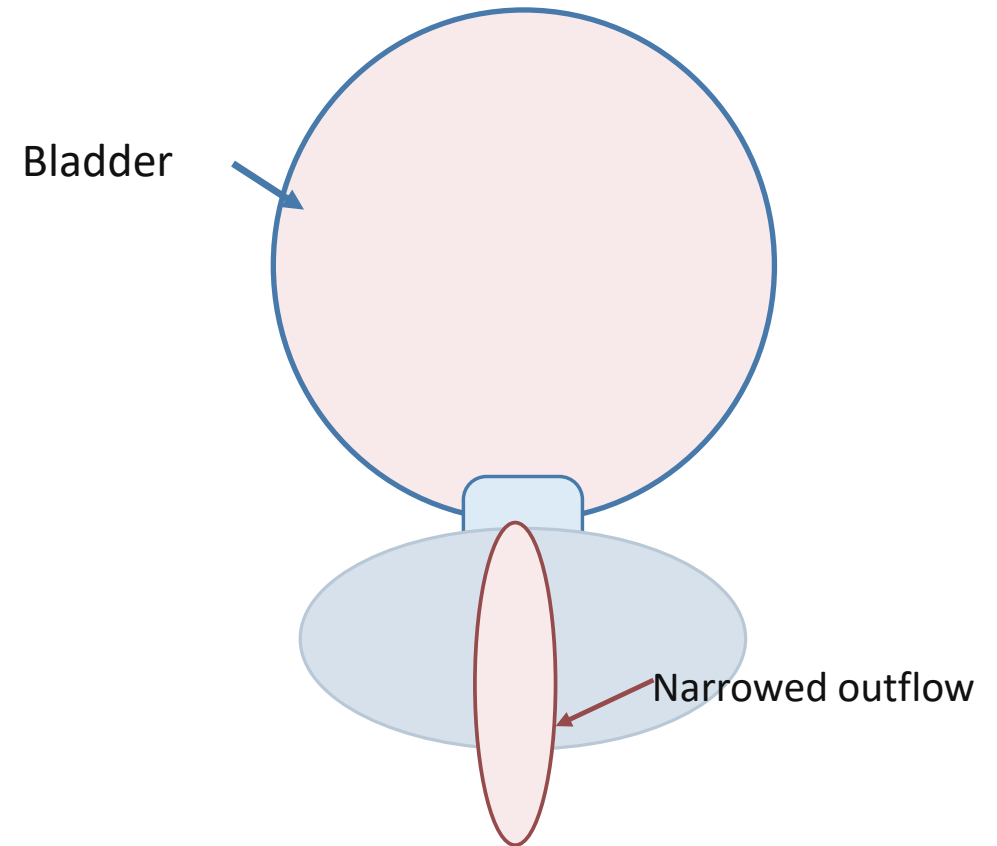
Bladder muscular-wall response



Hypertrophy and distention

Incomplete emptying leaves residual urine

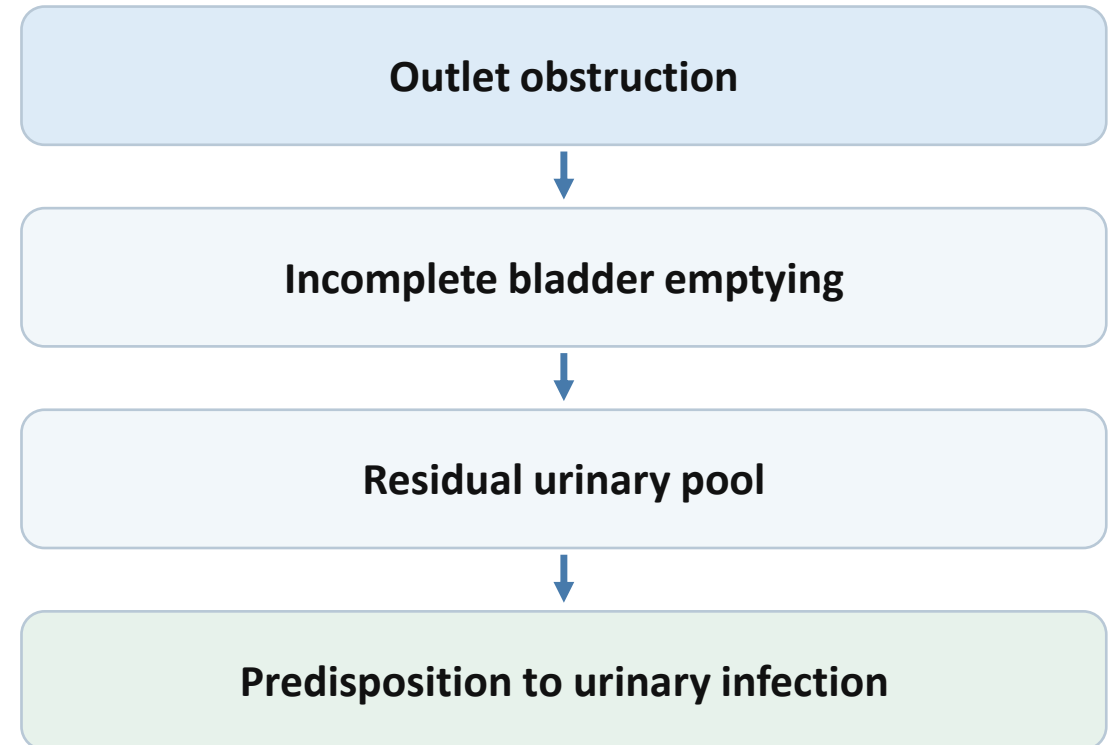
- Obstructed voiding may prevent complete bladder emptying.
- Retained urine remains after micturition.
- A persistently residual pool increases the opportunity for infection.



Schematic — bladder and prostatic outlet; Not anatomical scale

Stasis links obstruction to infection

- Residual urine is a common reservoir for bacterial growth.
- Bacterial infection of the bladder and kidney.
- Recurrent urinary infection can therefore be a downstream consequence of BPH.



Voiding symptoms reflect outlet narrowing

- Difficulty initiating the stream reflects increased resistance.
- Difficulty stopping and restarting flow is part of the textbook symptom list.
- Flow disturbance is a functional manifestation of outlet obstruction.

Reduced urethral lumen + tone



Impaired urine passage



Hesitancy / interrupted voiding

Frequency and nocturia are common presentations

- Increased urinary frequency is included among major symptoms.
- Nocturia denotes nighttime need to urinate.
- The presence of storage complaints does not exclude the obstructive mechanism.

Daytime

Nighttime

Frequent micturition

Nocturia

Storage symptom

Nighttime symptom

Dribbling and dysuria add clinical burden

- Overflow dribbling may appear with incomplete voiding.
- Dysuria means painful micturition.
- Painful urination also prompts attention to possible associated infection.

Obstruction / residual urine



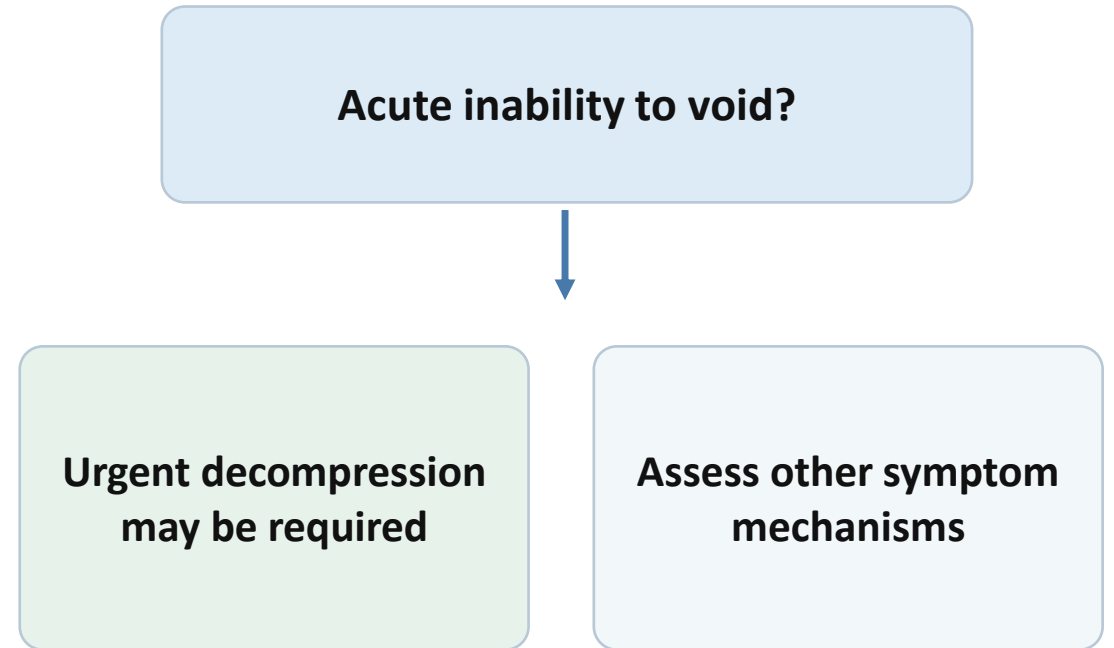
Overflow dribbling



Dysuria and possible infection

Acute urinary retention is an emergency

- Sudden inability to void can complicate BPH.
- Urgent catheterization may be required for relief.
- This acute event differs clinically from gradually progressive lower urinary symptoms.



Clinical pathway from nodule to complication

- Transition-zone enlargement compresses the outlet.
- Bladder compensatory changes and residual urine follow impaired emptying.
- Urinary infection or abrupt retention may be clinically important outcomes.

Nodular growth + smooth-muscle tone



Increased urinary outflow resistance



Residual urine / bladder changes



Infection risk or acute retention

Medical therapy targets two distinct mechanisms

- α_1 -adrenergic blockade reduces smooth-muscle tone.
- 5α -reductase inhibition lowers DHT synthesis and can reduce gland size.
- The treatments correspond to dynamic versus tissue-growth components.

α_1 -blockade

5α -reductase inhibition

Reduces muscle tone

Reduces DHT generation

**Dynamic resistance
component**

**Enlarged tissue
component**

α_1 -adrenergic blockers relax prostatic smooth muscle

- Inhibition of α_1 -adrenergic receptors as the mechanism.
- Less contraction reduces the dynamic contribution to outlet resistance.
- This treatment does not depend on directly removing a nodule.

α_1 -receptor inhibition



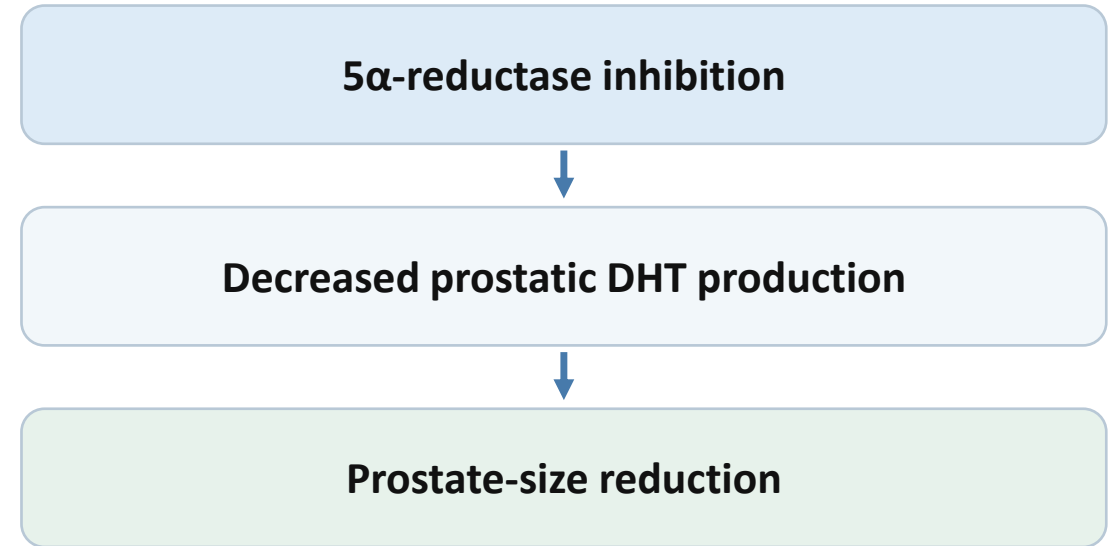
Reduced prostatic smooth-muscle tone



Lower dynamic outlet resistance

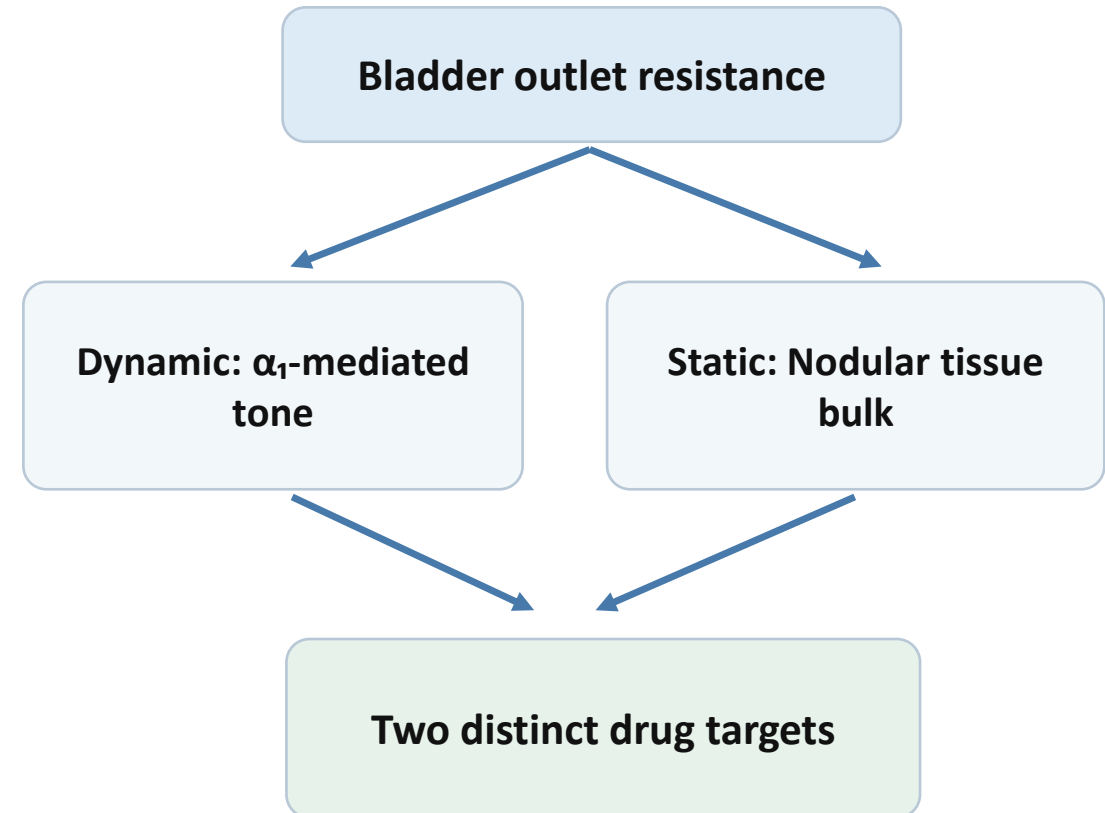
5 α -reductase inhibitors target androgen supply

- Inhibiting 5 α -reductase reduces testosterone-to-DHT conversion.
- Reduced DHT signaling is associated with physical prostate shrinkage.
- The effect addresses the hormonal growth component rather than smooth-muscle tone alone.



Why combination mechanisms are conceptually complementary

- Mechanical tissue bulk and contractile tone both impair urine flow.
- α_1 -blockers address tone; 5 α -reductase inhibitors address DHT-related mass.
- This diagram explains therapeutic targets; It is not a comparative efficacy trial.



Persistent moderate-to-severe disease may need procedures

- Procedural options for cases resistant to medical therapy.
- Transurethral resection of the prostate (TURP) was long regarded as the gold standard.
- The source also lists several alternative tissue-reducing modalities.

Persistent symptoms despite medication



Consider tissue-directed procedure



Restore functional outflow

Procedural modalities listed

- TURP removes obstructing tissue transurethally.
- Other listed approaches use focused ultrasound, laser, heat, vaporization, or radiofrequency.
- Choice and comparative outcomes require sources beyond this textbook excerpt.

TURP

HIFU

Laser treatment

Hyperthermia

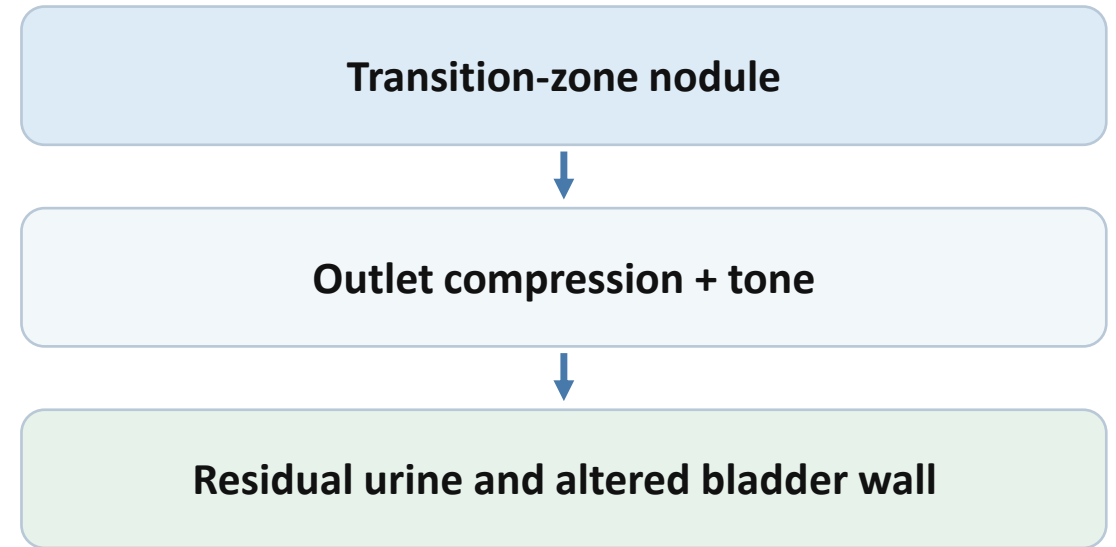
Electrovaporization

Radiofrequency ablation

Procedures listed; No comparative outcome claims

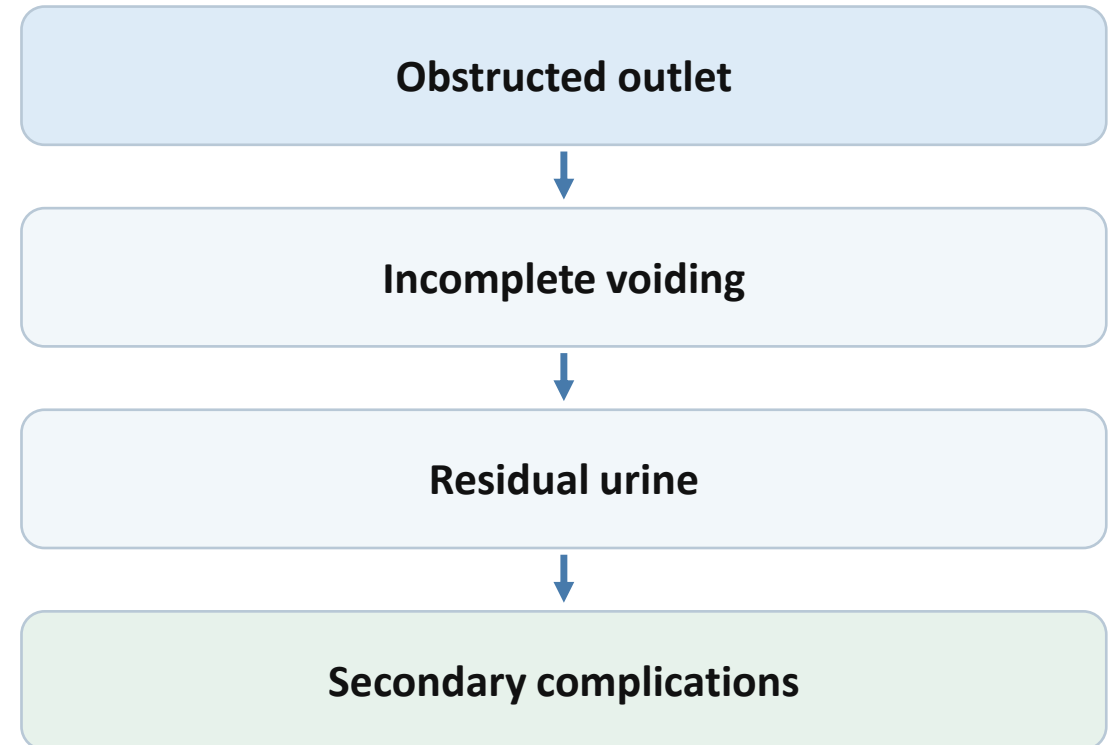
Case: Progressive lower urinary symptoms

- Hypothetical: An older man develops hesitancy, nocturia, and overflow dribbling.
- Explain how nodular enlargement and smooth-muscle tone contribute separately.
- Predict what bladder change and infection risk follow incomplete emptying.



Case interpretation: Structure to function

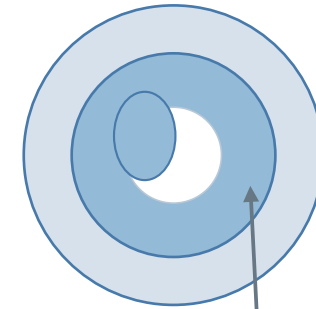
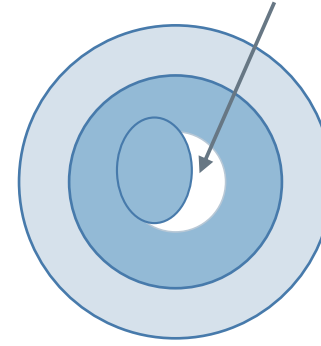
- Hesitancy reflects resistance at the prostatic outlet.
- Nocturia and dribbling fit the symptom cluster in the BPH passage.
- Retention creates residual urine, which predisposes to bacterial infection.



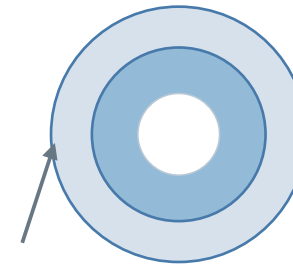
Morphology exercise: Name the components

- Hypothetical TURP chips show variably sized glands amid bland spindle-cell stroma.
- What two layers should be sought lining benign glands?
- What luminal architectural feature may be present in secretory cells?

Luminal space



Secretory epithelium

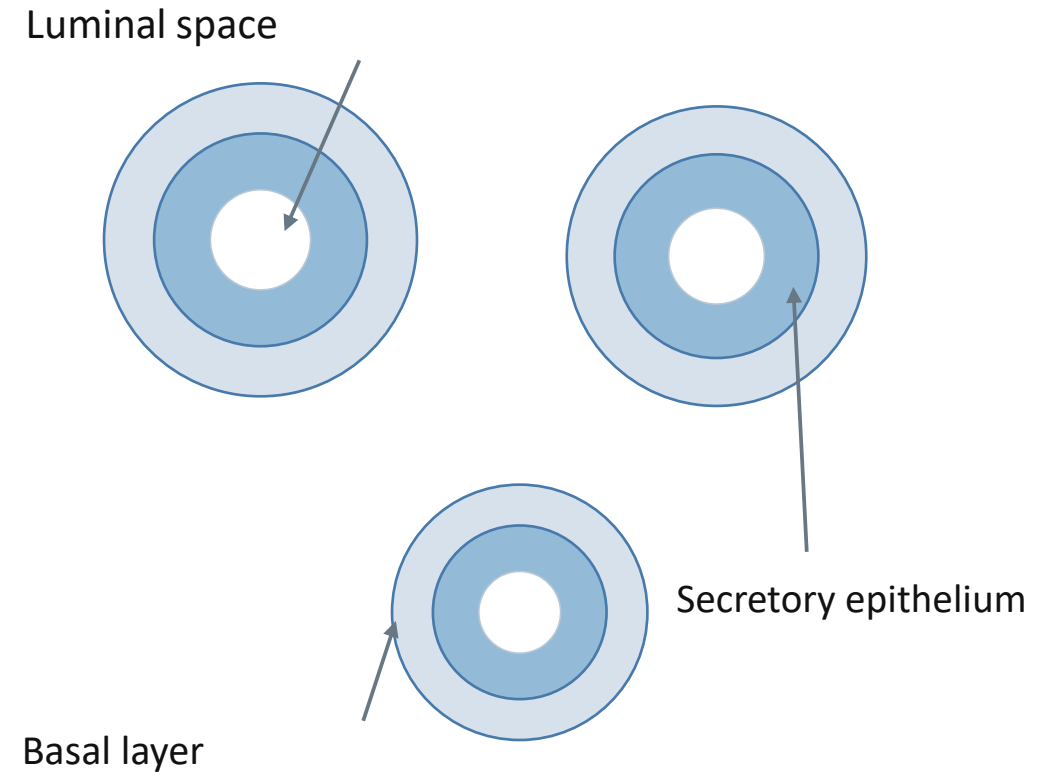


Basal layer

Schematic glands; Diagnostic features require genuine H&E review

Morphology answer: Layered glands with folds

- Benign gland lining comprises secretory columnar and basal cuboidal/flattened layers.
- Papillary infoldings of secretory epithelium may be present.
- The stromal background is an integral part of the hyperplastic process.



Schematic glands; Diagnostic features require genuine H&E review

Five concepts that organize BPH

- The pathology is benign nodular glandular and stromal hyperplasia.
- DHT/AR signaling and estrogen-related influences alter tissue turnover.
- Transition-zone growth and muscle contraction obstruct the outlet.
- Morphologic and clinical consequences determine the principal treatment targets.

Reference and image-source note

- Primary source: Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed. (2026), Chapter 21, pages 887–889.
- Source figures 21.27–21.30 were described in the text extraction but not reproduced.
- All diagrams in this lecture are original, editable conceptual schematics; no synthetic microscopy is presented as observed evidence.