

Benign prostatic hyperplasia

Nodular glandular and stromal proliferation

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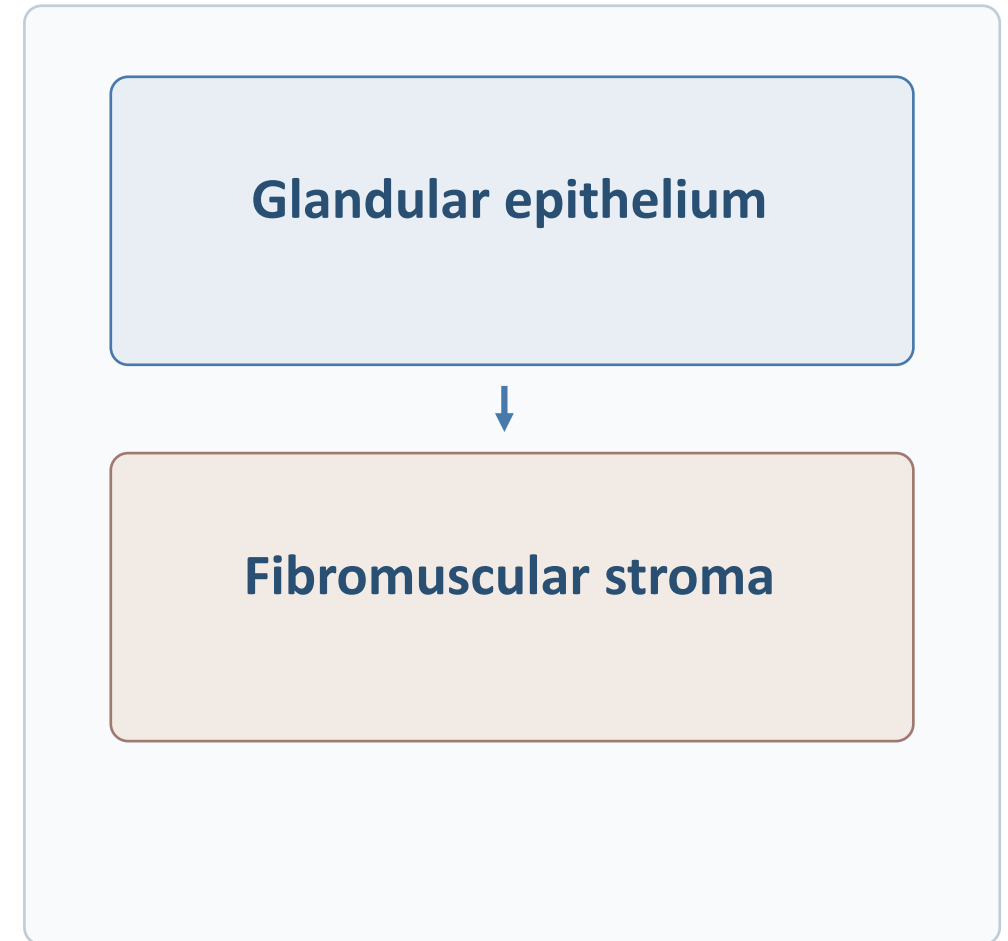
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Learning objectives

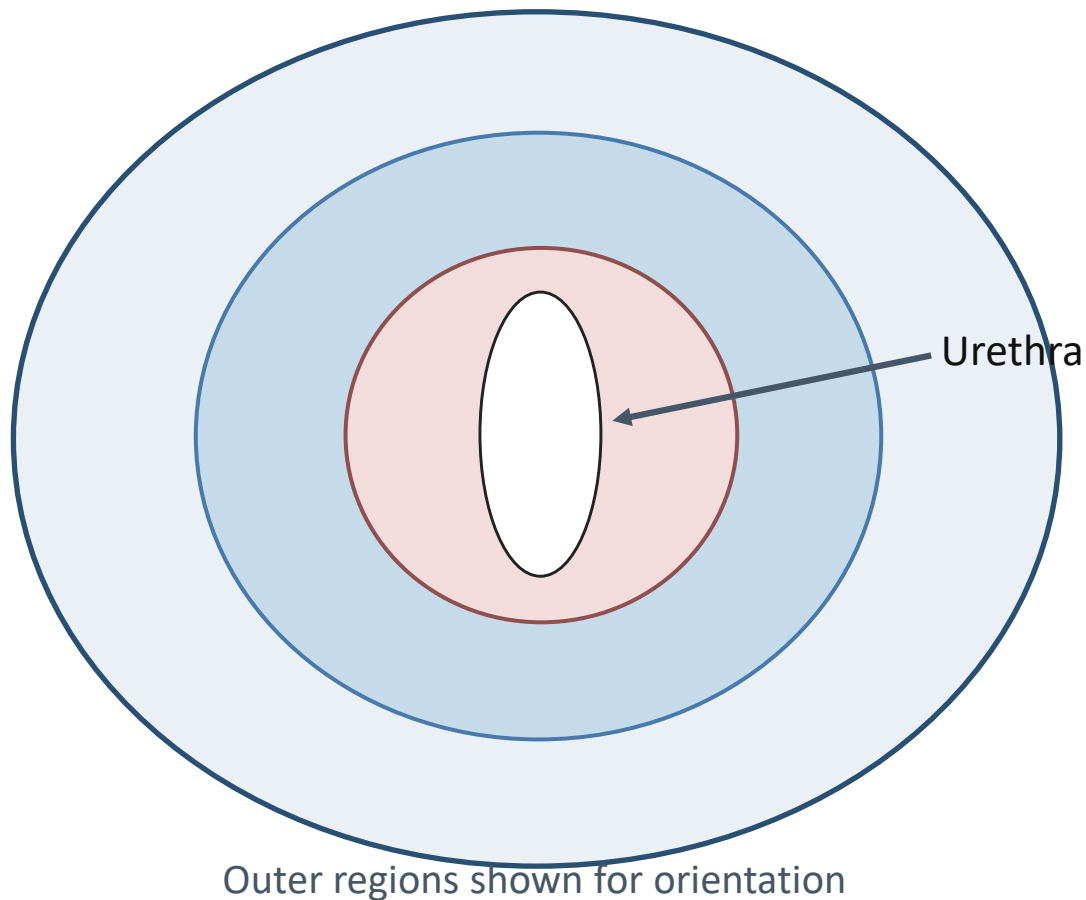
- Explain the zonal origin and benign proliferative nature of BPH.
- Trace the DHT–androgen receptor pathway and stromal–epithelial signaling.
- Recognize gross and microscopic patterns of nodular hyperplasia.
- Connect urethral obstruction with symptoms, complications and treatment targets.

BPH is a benign nodular proliferation

- BPH is also termed nodular hyperplasia.
- Both glandular and fibromuscular stromal compartments expand.
- The defining problem is location-associated urethral obstruction, not malignant growth.

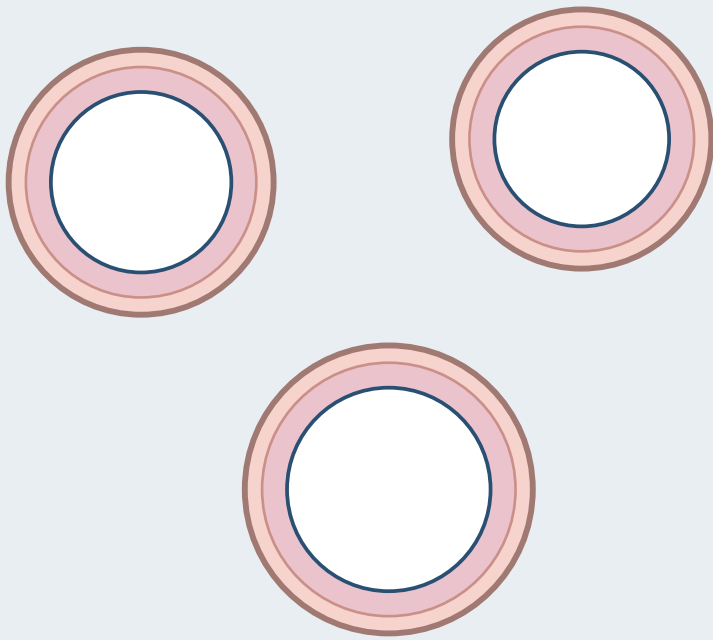


Prostate zones determine disease patterns



- The transition zone lies close to the proximal urethra.
- The peripheral zone accounts for most prostatic carcinomas.
- Zonal location explains why BPH frequently obstructs urinary outflow.

The normal gland has two epithelial layers



Schematic tissue architecture — not a photomicrograph

- Secretory columnar cells form the inner luminal lining.
- Basal cuboidal or flattened cells form an outer layer.
- Fibromuscular stroma surrounds and separates glandular structures.

BPH becomes increasingly common with age

>50 years

Most common benign prostatic
disease in this age group

Up to 90%

Histologic evidence by age 80 years

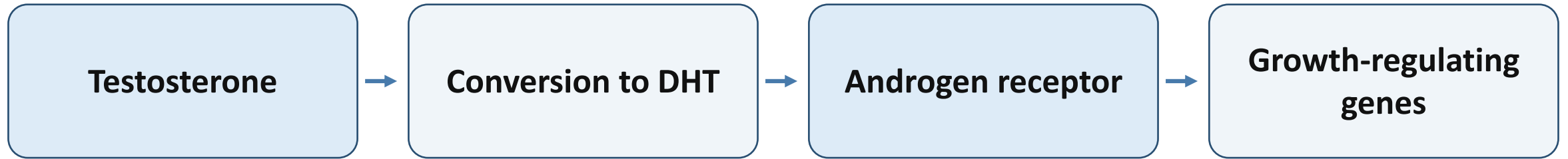
Clinical symptoms do not equal histologic prevalence

Histologic BPH	Symptomatic BPH
Benign nodules recognized in the prostate	Lower urinary tract symptoms attributed to obstruction
May be present without prominent symptoms	Depends on degree and effects of obstruction
Up to 90% by age 80 years (Robbins)	~30% have moderate–severe symptoms among US males of European descent >50 years (Robbins)

BPH is not a premalignant lesion

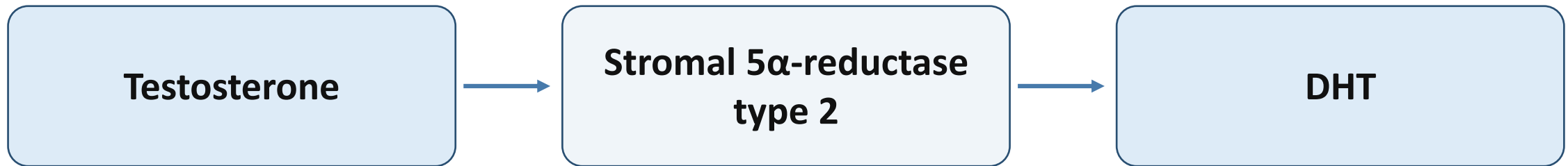
Benign prostatic hyperplasia	Prostatic carcinoma
Benign glandular and stromal nodules	Malignant epithelial neoplasm
Mainly transition/periurethral zones	Most arise in peripheral zone
Urinary outlet compression is central	A distinct disease process, not progression from BPH

Prostate growth depends on androgen signaling



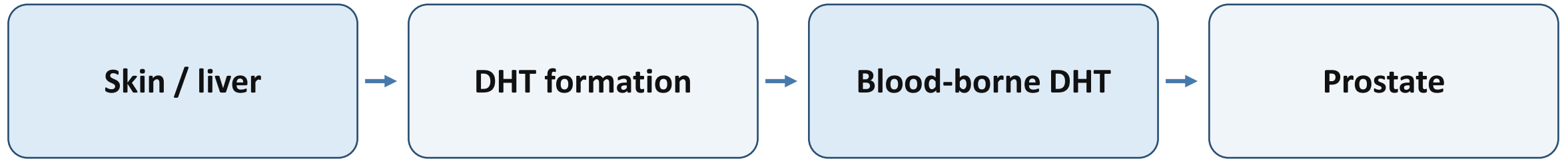
- Testicular androgens support normal prostatic growth and survival.
- BPH retains an androgen-dependent growth program.

Type 2 5 α -reductase makes DHT locally



- Type 2 5 α -reductase is expressed mainly in stromal cells.
- Prostatic epithelial cells do not express this isoenzyme in the Robbins account.

Type 1 5 α -reductase provides another DHT source



- Type 1 activity in extraprostatic sites contributes DHT to circulation.
- Skin and liver are examples of sites.

DHT is more potent than testosterone at AR

Testosterone	Dihydrotestosterone (DHT)
Precursor of intraprostatic DHT	Principal androgen acting in the prostate
Binds androgen receptor	Higher AR affinity
Less stable ligand–receptor complex	Forms a more stable ligand–receptor complex

Both stromal and epithelial cells express AR

Stromal compartment



AR activation → growth-factor production

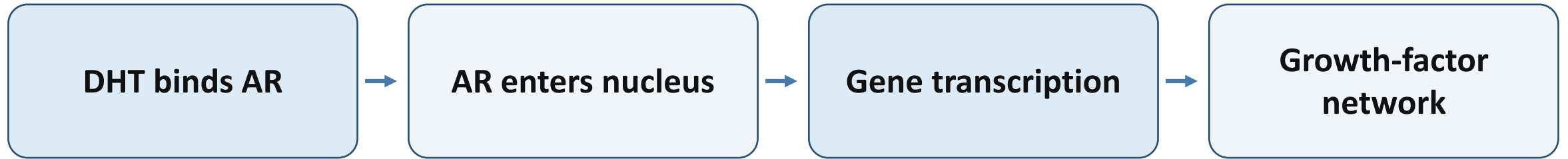
Epithelial compartment



AR activation → growth/survival responses

- The stromal and epithelial compartments both respond to DHT.
- Their downstream responses interact through local growth-factor signaling.

Activated AR translocates to the nucleus



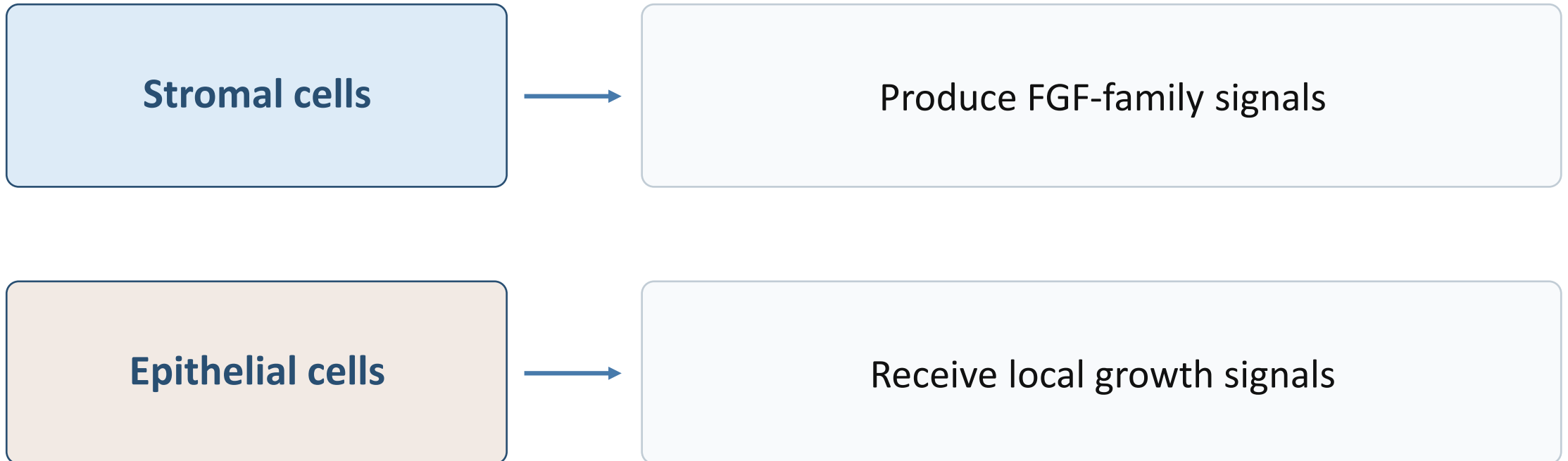
- DHT–AR binding triggers receptor movement from cytoplasm to nucleus.
- Nuclear AR regulates transcription of androgen-dependent genes.

AR regulates growth factors and receptors



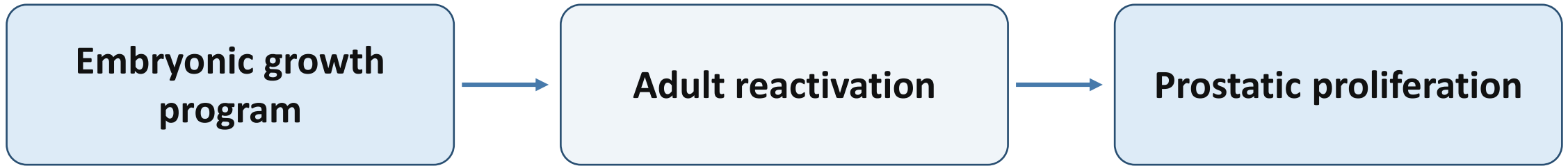
- Growth-promoting programs are mediated indirectly as well as directly.
- FGF-family factors and TGF- β are emphasized in the Robbins discussion.

FGFs link stroma to epithelial growth



- Stromal fibroblast growth factors act through paracrine signaling.
- This stromal–epithelial dialogue is established in prostatic development.

BPH may reactivate developmental pathways



- FGF-dependent signaling is important in embryonic prostate development.
- The same pathways may be reawakened in adult BPH.

TGF- β has compartment-dependent effects

Mesenchymal/stromal cells	Epithelial cells
TGF- β can stimulate fibroblast and mesenchymal proliferation	TGF- β inhibits epithelial proliferation
Supports stromal expansion	Its direct effect is not uniformly growth promoting
Net BPH response requires multicellular context	Avoid equating every signal with mitogenesis

The imbalance involves proliferation and death

Net accumulation of tissue

Increased stromal proliferation

Decreased epithelial cell death

Combined effect: Benign tissue accumulation

- Increased stromal proliferation and reduced epithelial cell death.
- The net result is accumulation of benign glandular and stromal tissue.

Androgens are permissive, not the whole explanation

- Androgen signaling is essential to the pathobiologic model.
- The ultimate cause of BPH remains incompletely understood.
- Additional influences, including estrogen pathways, shift local growth–death balance.

Estrogens also influence prostatic growth

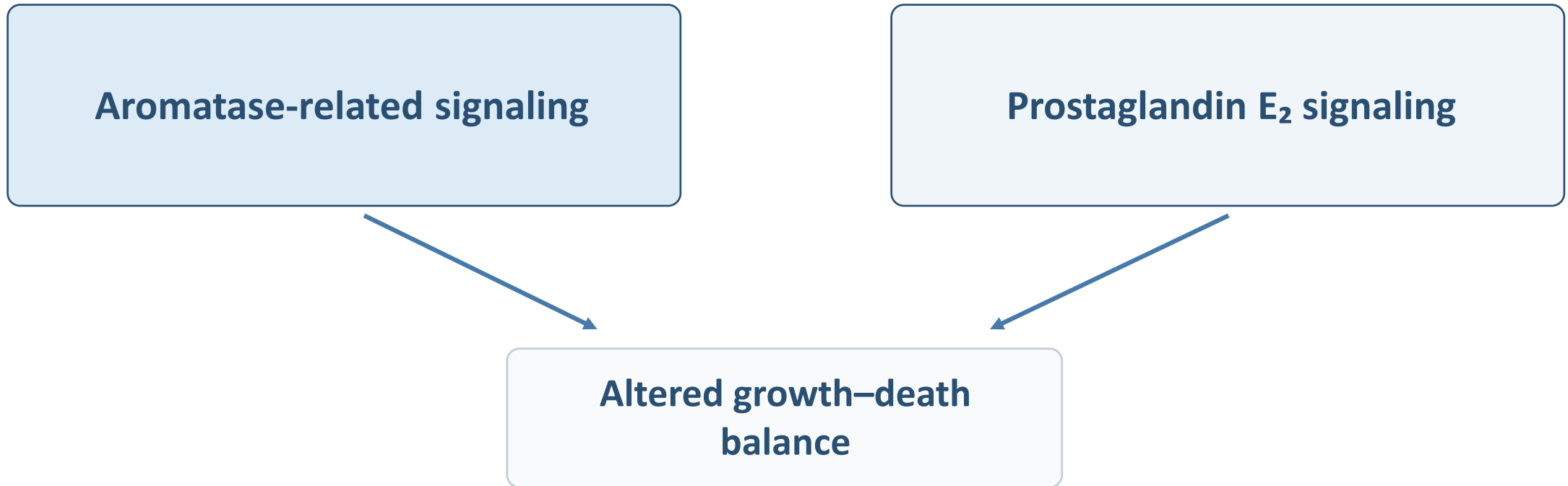


- Evidence supports an estrogen contribution to BPH.
- The relevant outcome is a shift toward net cellular accumulation.

ER α and ER β exert opposing influences

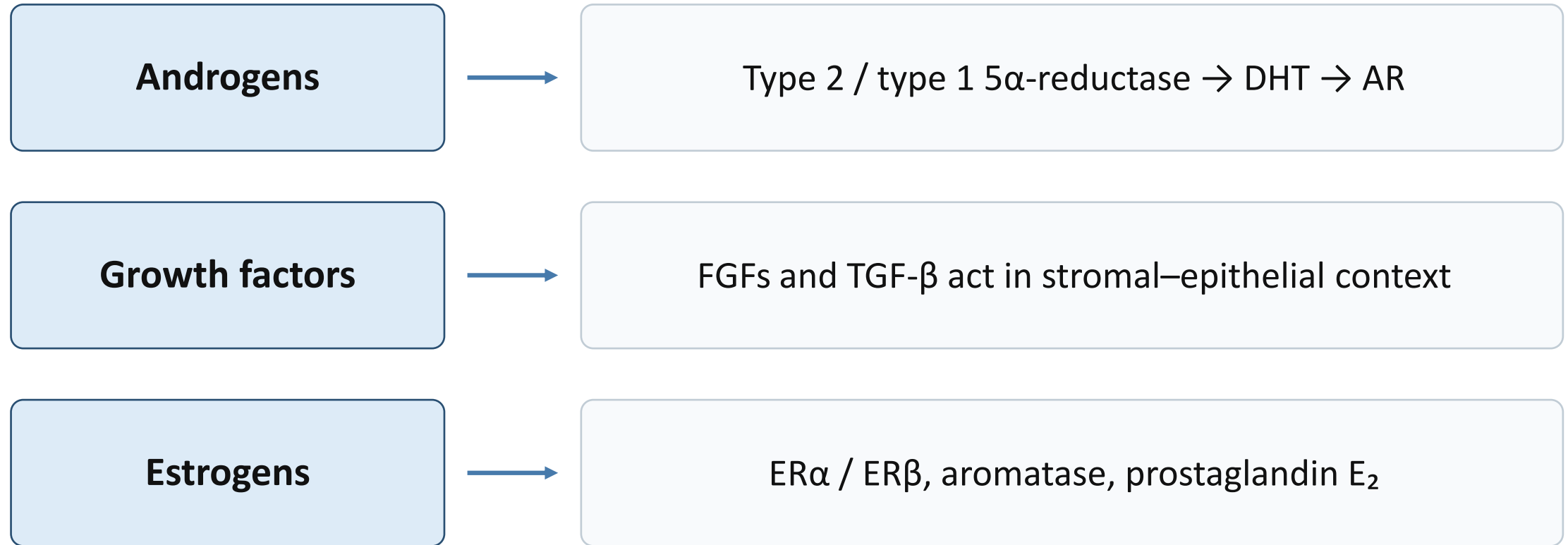
Estrogen receptor α (ER α)	Estrogen receptor β (ER β)
Proliferative influence in the Robbins model	Antiproliferative influence in the Robbins model
May favor cellular accumulation	May restrain cellular accumulation
Net balance depends on receptor context	Neither receptor acts in isolation

Aromatase and prostaglandin E₂ participate



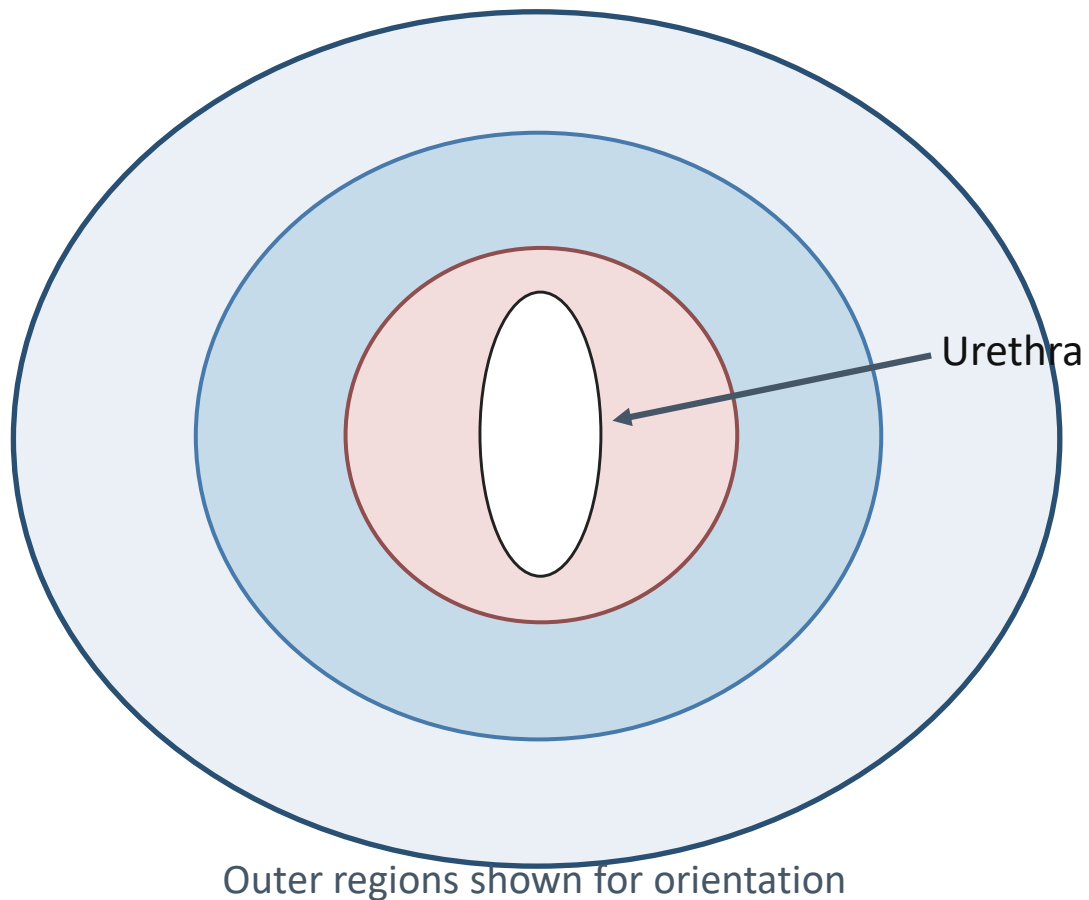
- The source identifies aromatase expression among estrogen-related mechanisms.
- Paracrine signaling through prostaglandin E₂ is also implicated.

Integrated hormonal model of BPH



- This is a mechanistic model, not a single proven initiating event.
- DHT/AR, growth factors and estrogen-related signaling converge on tissue accumulation.

Hyperplasia arises in the transition zone



Periurethral / transition

- Transition and inner periurethral zones are characteristically affected.
- A centrally located nodule has direct access to the prostatic urethra.

Prostate weight may rise several-fold

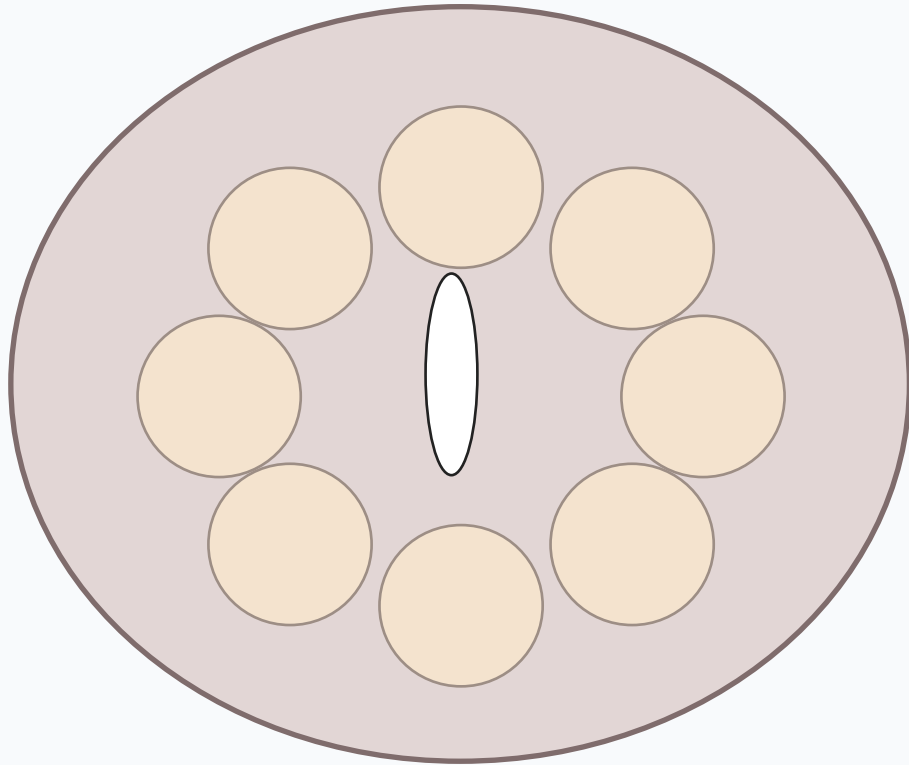
~20 g

Approximate normal adult prostate
weight

60–100 g

Common BPH enlargement:
Approximately three- to five-fold

Enlargement is often nodular rather than uniform

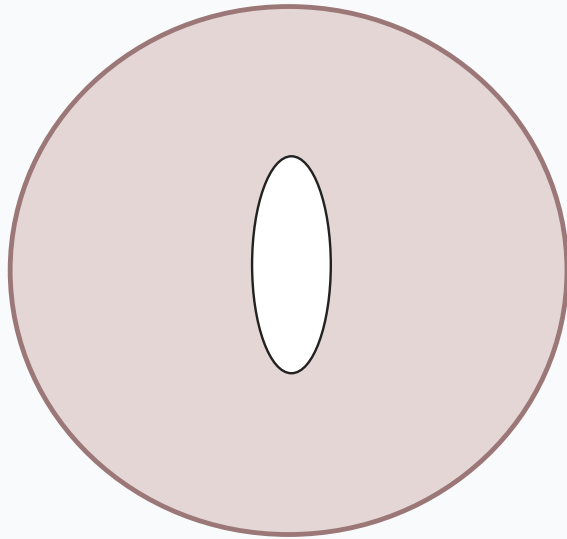


Schematic — not a gross specimen

- Discrete hyperplastic nodules expand within the gland.
- Gross and microscopic appearance varies with relative glandular and stromal content.

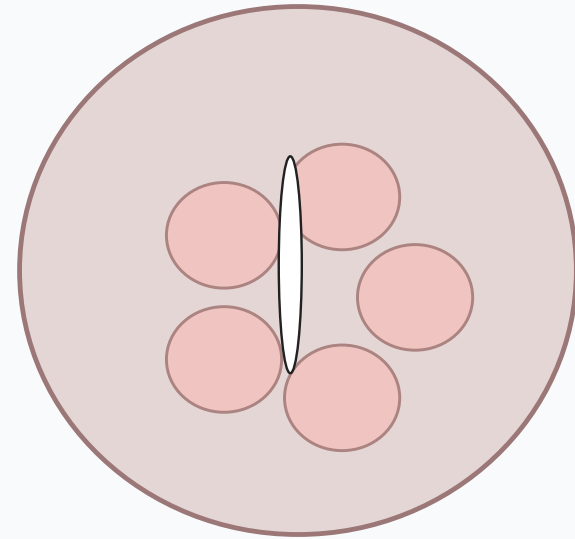
Nodules narrow the urethral lumen

Open outlet



Patent urethral channel

BPH compression



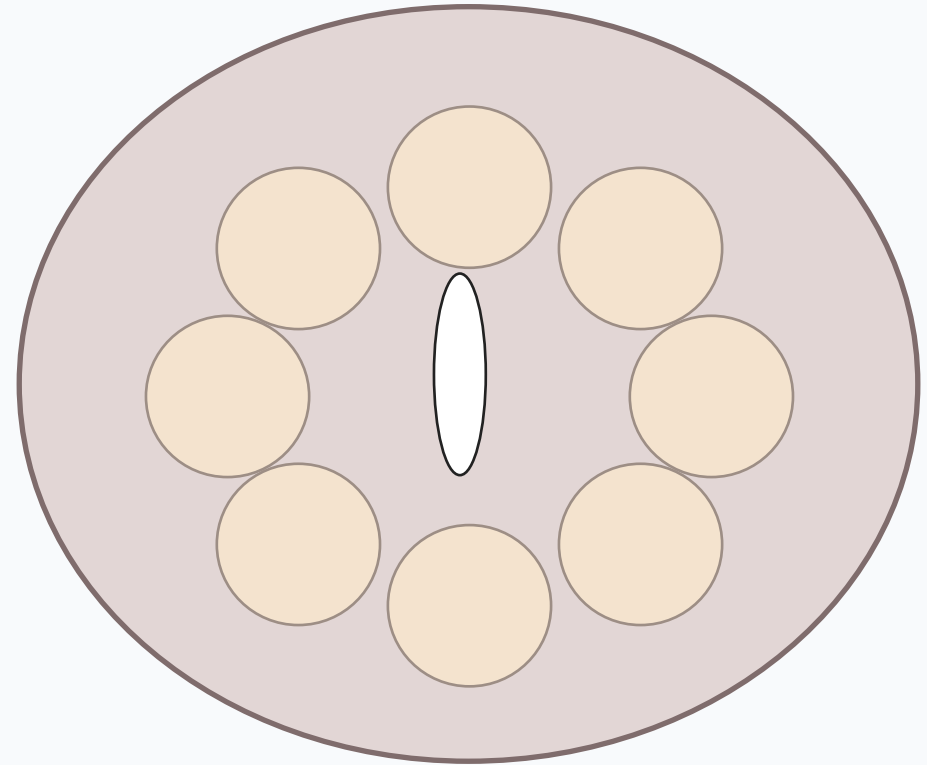
Narrow slit-like lumen

Gland-rich and stroma-rich nodules differ

Predominantly glandular	Predominantly fibromuscular
Yellow-pink and soft	Pale gray and firm
May exude milky prostatic fluid	Firm due to stromal predominance
Numerous glandular lumina	Greater smooth muscle / fibrous tissue contribution

The gross glandular nodule is soft

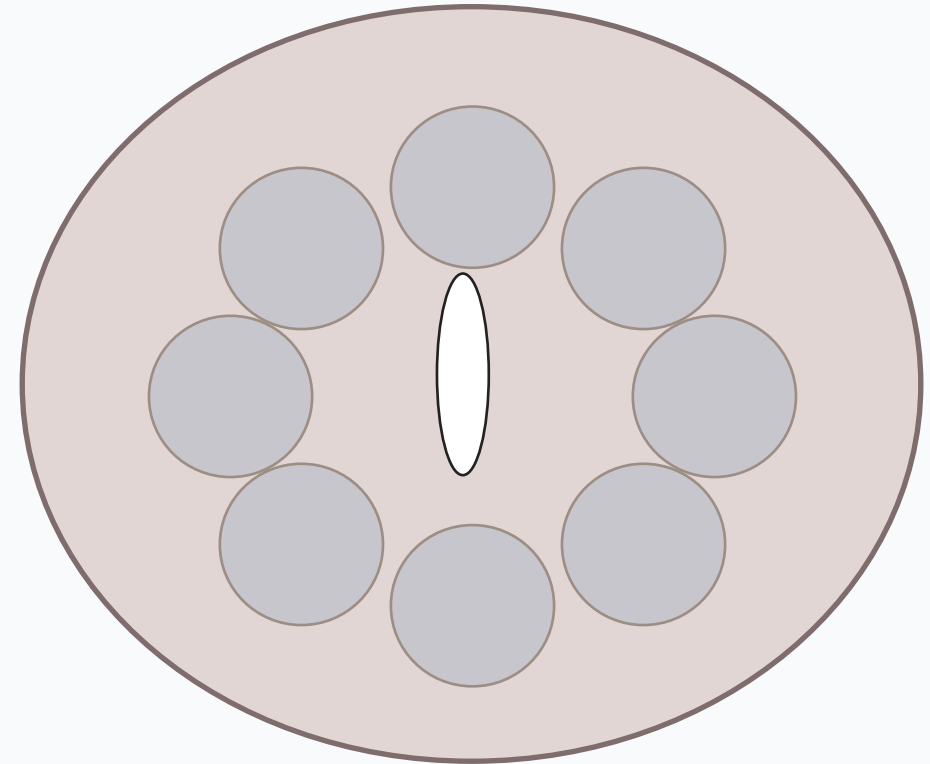
- Gland-dominant nodules are described as yellow-pink.
- Their soft cut surface may express milky white prostatic fluid.
- Gross characteristics reflect the tissue composition of a nodule.



Schematic — not a gross specimen

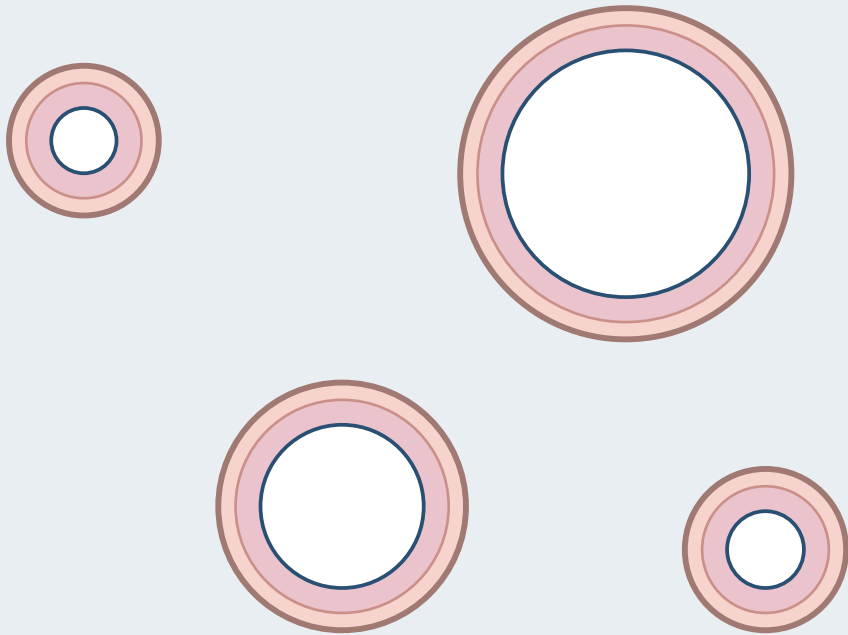
The stromal nodule is comparatively firm

- Fibromuscular-rich nodules are pale gray and firm.
- Cellular composition, not malignancy, accounts for this texture.
- Grossly different nodules can coexist in the same enlarged gland.



Schematic — not a gross specimen

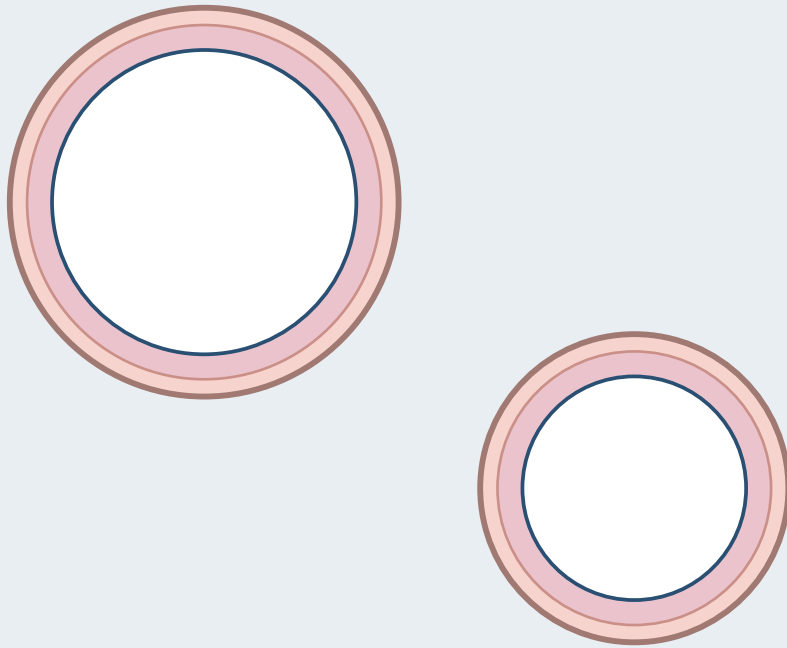
Microscopic glands span a range of sizes



Schematic tissue architecture — not a photomicrograph

- A single nodule may contain small, large and cystically dilated glands.
- Glandular size variation occurs amid proliferating stromal tissue.

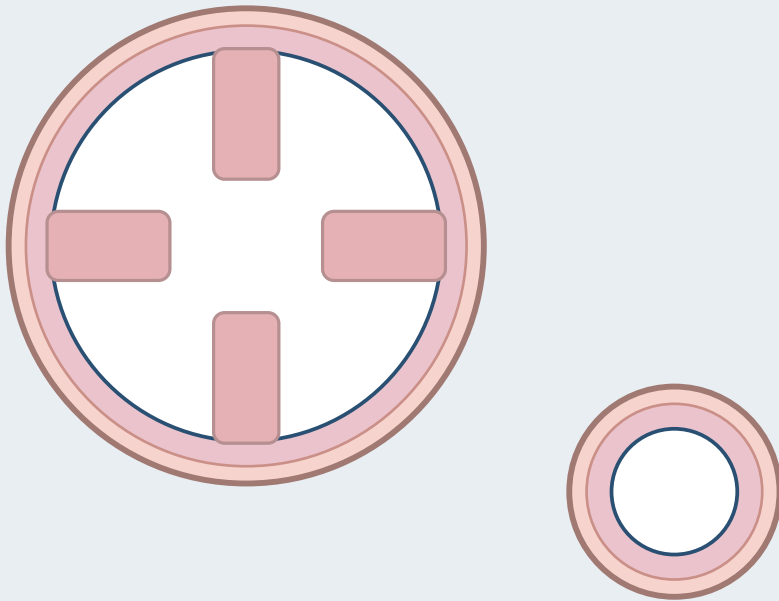
Some glands become cystically dilated



Schematic tissue architecture — not a photomicrograph

- Marked glandular dilatation is an accepted BPH morphology.
- Interpret dilatation in the setting of nodular, two-layered benign glands.

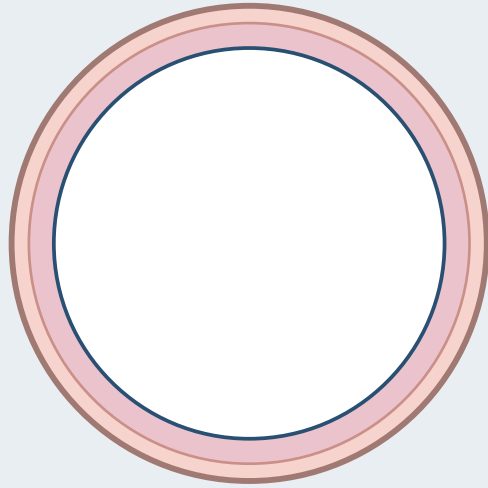
Papillary epithelial infoldings are common



Schematic tissue architecture — not a photomicrograph

- Luminal secretory epithelium may fold into the glandular space.
- Such infoldings yield a papillary contour without implying cancer.

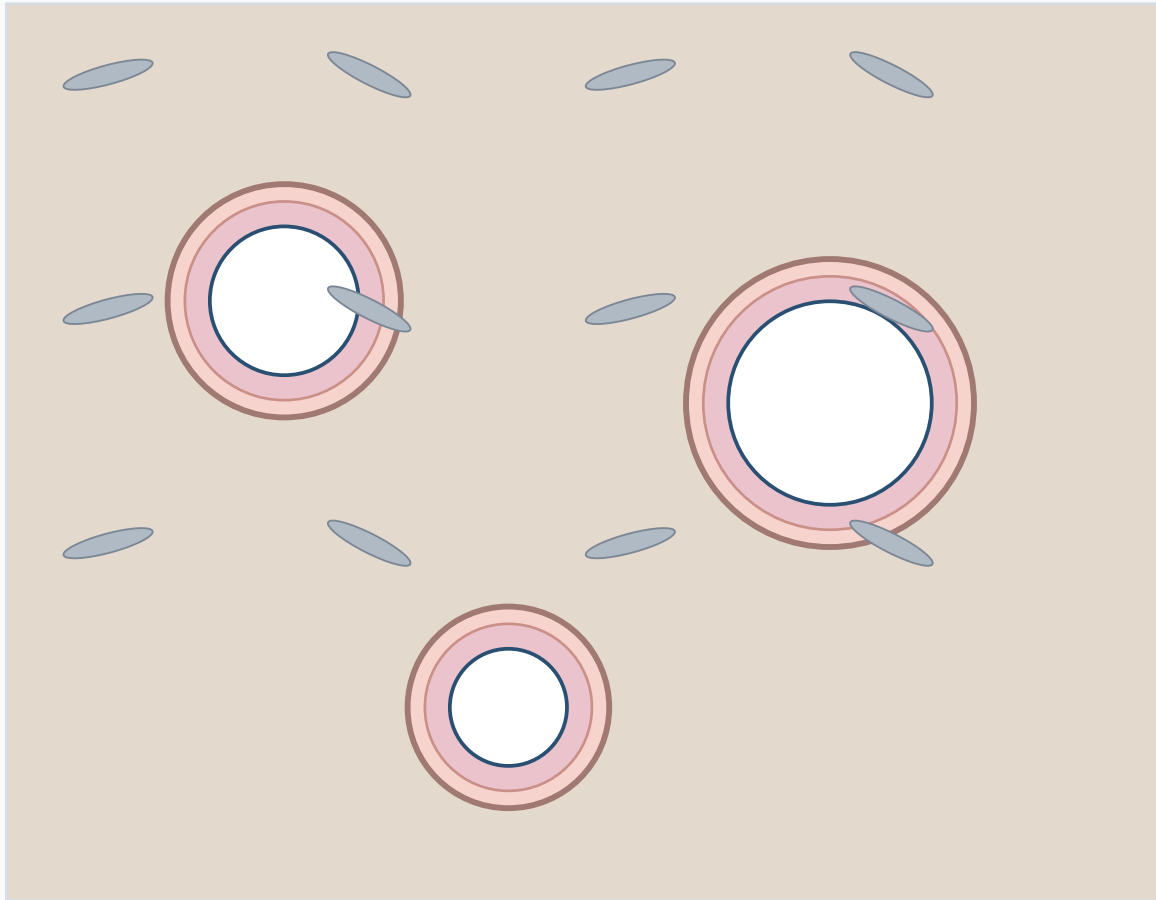
BPH glands retain a basal cell layer



Schematic tissue architecture — not a photomicrograph

- Luminal columnar secretory cells form an inner lining.
- A cuboidal or flattened basal layer remains external to them.
- Preserved bilayered architecture supports benign gland morphology.

Bland spindle stromal cells separate glands



Schematic tissue architecture — not a photomicrograph

- Stromal cells have bland spindle-shaped morphology in typical BPH.
- Fibromuscular stroma is an active constituent of the hyperplastic nodule.

A BPH nodule combines multiple components

Glandular

Small to cystically dilated lumina

Epithelial

Secretory and basal layers

Architectural

Papillary epithelial infoldings

Stromal

Bland spindle-shaped cells

Large glands may develop ischemic injury



- Marked enlargement may compromise local vascular supply.
- Infarction can occur in markedly enlarged prostates.

Squamous metaplasia can border infarction



- Squamous metaplasia adjacent to prostatic infarcts.
- The finding should be interpreted in the context of local injury.

Benign morphology and symptoms are different dimensions

Pathology finding	Functional consequence
Nodules of glands and fibromuscular stroma	Urethral narrowing may impede urine flow
Preserved epithelial cell layers	No implication that BPH is premalignant
Variable glandular/stromal proportions	Both bulk and smooth muscle tone influence obstruction

Obstruction has a static and dynamic component

Static



Tissue expansion → lumen compression

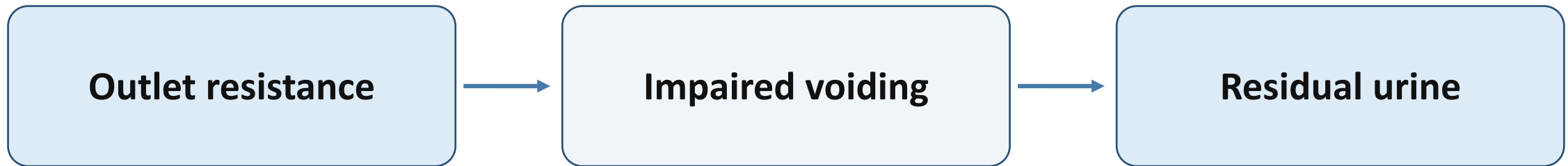
Dynamic



Stromal smooth muscle contraction → extra resistance

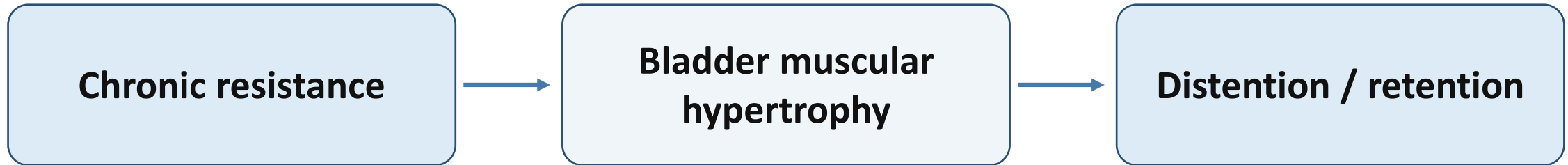
- Mechanical narrowing reflects anatomic enlargement.
- Smooth muscle contraction adds a dynamic component to outlet resistance.

Outflow resistance makes bladder emptying harder



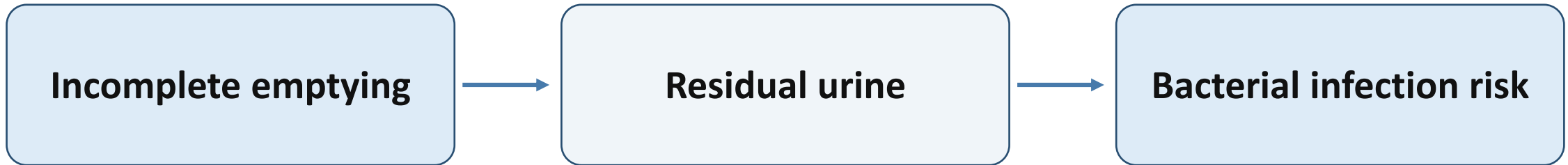
- Urine must pass through a narrowed prostatic outlet.
- Obstruction promotes incomplete emptying and retention.

The bladder responds with muscle hypertrophy



- Sustained resistance drives increased work by the detrusor.
- Muscular wall hypertrophy with bladder distention.

Residual urine creates a path for infection



- Incomplete emptying leaves residual urine after voiding.
- Retained urine can serve as a reservoir for bacterial infection.

Obstructive symptoms reflect impaired flow

Difficulty initiating



Hesitancy at the start of voiding

Difficulty stopping



Interrupted / difficult-to-control stream

Overflow dribbling



Leakage associated with retention

Storage symptoms accompany BPH

Frequency



Repeated need to void

Nocturia



Need to void during the night

Clinical meaning



Symptoms coexist with outlet obstruction

Dysuria can coexist with obstruction

- Painful micturition (dysuria) appears among reported features.
- Concurrent bacterial urinary infection is an important potential contributor.
- Symptoms require clinicopathologic assessment, not morphology alone.

Obstruction + urinary infection

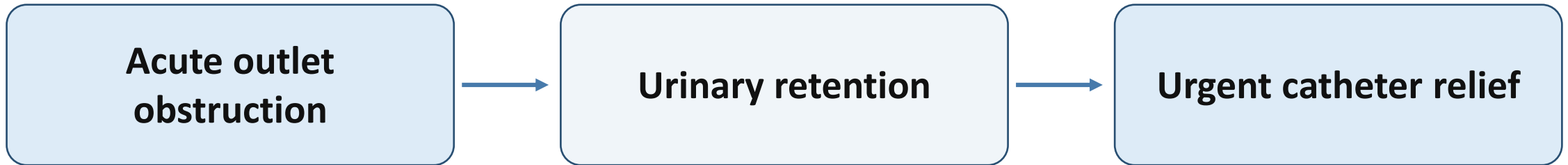
Symptoms may overlap

Infections may involve bladder or kidney



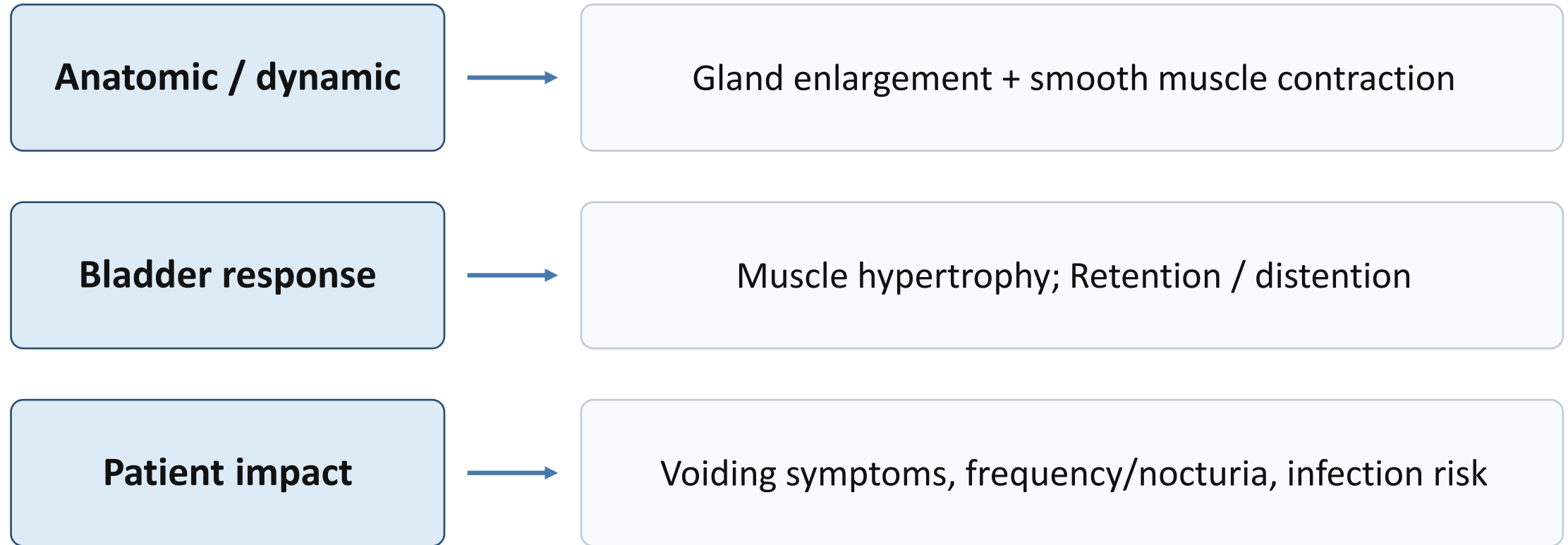
- BPH predisposes to recurrent bacterial urinary tract infections.
- Bladder and renal infections are both noted in the Robbins description.

Acute retention is a clinical emergency



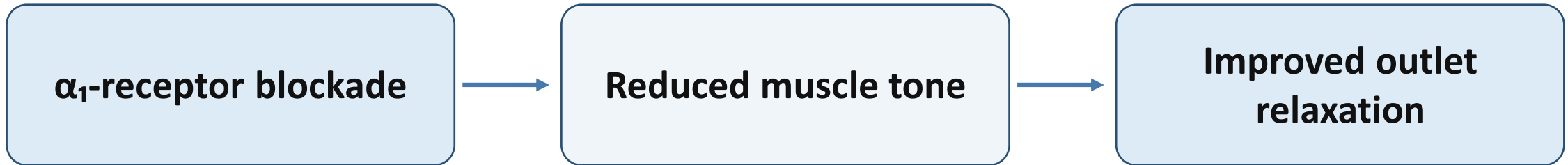
- Sudden inability to void can complicate BPH.
- Urgent catheterization to relieve acute retention.

Clinical manifestations follow a causal chain



- Relate each symptom to outlet resistance or its sequelae.
- Nodularity alone does not determine the complete symptom burden.

α_1 -adrenergic blockers target smooth muscle tone



- Blocking α_1 -adrenergic signaling relaxes prostatic smooth muscle.
- This targets the dynamic component of urinary outlet resistance.

5α -reductase inhibitors target DHT synthesis

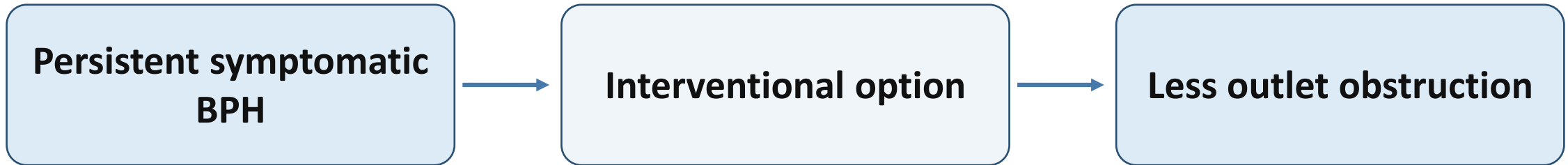


- Reduction of DHT production decreases the androgen stimulus.
- Resulting physical reduction in prostate size.

The two drug classes treat distinct mechanisms

α_1 -adrenergic blocker	5 α -reductase inhibitor
Primary target: Muscle tone	Primary target: Androgen conversion
Reduces dynamic component	Reduces DHT-dependent tissue growth
Physiologic outlet relaxation	Anatomic reduction of prostate size

Procedures address persistent obstruction



- Moderate or severe disease resistant to medical therapy may require a procedure.
- The aim is to reduce obstructing prostatic tissue.

TURP is a foundational procedural approach

- Transurethral resection removes obstructing prostate tissue.
- TURP as the longstanding procedural standard.
- The textbook also lists alternative tissue-reduction strategies.

Tissue reduction



Less urethral compression

Alternative procedural methods vary

Energy / approach	Examples
Ultrasound-based	High-intensity focused ultrasound (HIFU)
Laser and thermal	Laser therapy; Hyperthermia
Endoscopic / thermal	Transurethral electrovaporization
Other energy-based	Radiofrequency ablation

A case of progressive voiding symptoms

Teaching vignette

An older adult reports hesitancy, nocturia, an interrupted stream and persistent post-void sensation of incomplete emptying.

Which tissue-level process best explains the combined findings?

- Transition-zone nodules plus prostatic smooth muscle tone
- Direct evolution of BPH into carcinoma
- Isolated peripheral-zone growth without outlet effect

Case interpretation: Outflow resistance

Correct: Transition-zone nodules + dynamic muscle tone

- Transition-zone nodules compress the urethra.
- Stromal smooth muscle contraction adds functional resistance.
- Retention accounts for incomplete emptying; Symptom pattern fits BPH.

A case of abrupt inability to void

Teaching vignette

A person with longstanding obstructive voiding complaints develops sudden, painful inability to pass urine.

What BPH-related complication requires immediate relief?

- Acute urinary retention
- Prostatic intraepithelial neoplasia
- Uncomplicated microscopic nodularity

Case interpretation: Acute urinary retention

Correct: Acute urinary retention

- Sudden complete inability to void indicates acute retention.
- The immediate consequence is obstructive bladder distention.
- Emergency catheterization for relief.

Morphology recognition exercise

Teaching vignette

A transition-zone nodule contains variably enlarged glands, papillary luminal infoldings and intervening bland spindle cells. Two epithelial layers are appreciable.

Which diagnosis is most consistent with this described morphology?

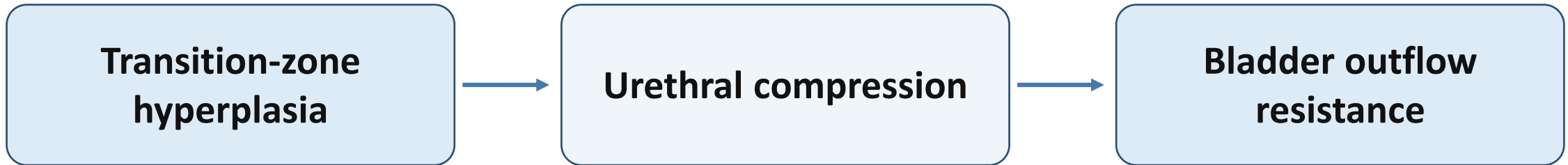
- Benign prostatic hyperplasia
- A malignant glandular neoplasm on morphology alone
- A purely inflammatory prostate lesion

Morphology recognition: BPH

Correct: Benign prostatic hyperplasia

- Nodular admixture of glands and stroma is characteristic.
- Variable gland size and papillary infoldings fit BPH.
- Two epithelial layers and bland stroma support benign architecture.

Synthesis: One anatomic location drives obstruction



- The clinically decisive site is the transition/periurethral region.
- Benign tissue accumulation may compromise the urethral lumen.

Synthesis: Hormones, histology and function

Hormones

DHT-AR + estrogen-related influences

Growth

Stromal proliferation; Epithelial survival

Morphology

Benign glandular / stromal nodules

Consequence

Urinary obstruction and retention

Five core principles

- BPH is common with aging and is not premalignant.
- DHT–AR signaling and stromal–epithelial factors are central.
- Transition-zone nodules comprise benign glands and stroma.
- Enlargement plus smooth muscle tone obstructs urinary outflow.
- Treatment targets muscle tone, DHT synthesis or obstructing tissue.